Abbreviations

TOXICOLOGY/ EMERGENCY PREPAREDNESS

Steven E. Pass, Pharm.D., BCPS, FCCM

Reviewed by R. Chris Rathbun, Pharm.D., BCPS With Added Qualifications in Infectious Diseases; Ted L. Rice, Pharm.D., BCPS, FASHP; and Elizabeth J. Scharman, Pharm.D., DABAT, BCPS, FAACT

Learning Objectives

1. Analyze general management strategies for acute poisonings.
2. Evaluate options for managing selected toxin ingestions, including their specific antidotes.
3. Assess a clinical toxicologic patient care problem and develop a patient care plan based on the best information.
4. Distinguish characteristics of chemical and radiological disaster threats.
5. Develop a treatment plan for a patient exposed to chemical or radiological weapons.
6. Design an institution-specific emergency preparedness plan.

Toxicology

Introduction

Poison exposures account for a significant amount of resource use for hospital and community pharmacies. Pharmacists should have a basic understanding of poison management. For hospital pharmacies, the need to differentiate among the more common toxic agents and their antidotes allows for a better allocation of resources. Community pharmacies need to stay informed on the most recent guidelines to answer drug information questions.

In 2003, more than 2.3 million poison exposures were reported to the American Association of Poison Control Centers (AAPCC) Toxic Exposure Surveillance System. Children under age 19 accounted for 66% of the total reported exposures, but about 52% occurred in children under age 6. Although childhood exposures accounted for the majority of total poisonings reported, they only composed 3.1% of the 1106 fatalities. Exposures were mostly unintentional (84.7% of the total), which included occupational or environmental exposures, food poisonings, and misuse (defined as improper or incorrect use of an agent) among others. Intentional exposures, such as suspected suicide or misuse/abuse of drugs or other substances, accounted for 11.9% of the total exposures.

Most reported exposures occurred in a residence (92.6%), with about 23% of those patients exposed requiring treatment in a health care facility. The most common exposure route was ingestion (76.9%), followed by dermal (7.5%), inhalational (5.8%), ocular (5.2%), and bites and stings (3.5%). The most common substances for pediatric and adult exposures are listed in Table 1-1.

General Management

General decontamination strategies for the patient vary depending on the exposure route. First and foremost, the aim is to stabilize the patient, focusing on airway, breathing, and circulation; monitoring vital signs and mental status; and administering intravenous fluids, if needed. A physical examination should be performed and a medication history obtained. A history of the ingestion or exposure should also be documented, including the exposure route, intent, any history from prehospital care providers and family members, and onset and progression of symptoms.

Some health care providers advocate immediately administering a “coma cocktail” to provide rapid treatment for common causes of decreased mental status after an exposure. Formulations for these cocktails vary, but most contain 50 mL dextrose 50% in water, thiamine 100 mg, and naloxone 0.4–2 mg. Although some clinical benefit may be associated with these agents, there are also some risks. Dextrose is given to treat hypoglycemia, which is a rare

American College of Emergency Physicians. Clinical policy for the initial approach to patients presenting with acute toxic ingestion or dermal or inhalational exposure. Ann Emerg Med 1999;33:735–61.

Abbreviations in this Chapter

2-PAM	Pralidoxime chloride
AAPCC	American Association of Poison Control Centers
Ca-DTPA	Calcium diethylenetriaminepentaacetate (pentetate calcium trisodium injection)
CNS	Central nervous system
FDA	Food and Drug Administration
GI	Gastrointestinal
SNS	Strategic National Stockpile
WBI	Whole bowel irrigation
WMD	Weapons of mass destruction
Zn-DTPA	Zinc diethylenetriaminepentaacetate (pentetate zinc trisodium injection)

complication except in patients with diabetes mellitus. Studies in both animals and humans demonstrated increased neurological damage in patients with brain ischemia who received dextrose compared with those given saline solutions. Because blood glucose concentrations can be determined quickly, it is better to confirm hypoglycemia before initiating treatment. Thiamine is administered to prevent Wernicke's encephalopathy, a rare but easily recognized disease process. Administering intravenous thiamine to prevent this condition typically requires 3 or more days of therapy and can lead to severe anaphylactic reactions. Acute Wernicke's encephalopathy may be precipitated by administration of glucose solutions; therefore, it would be reasonable to administer thiamine before glucose. Naloxone is given to reverse respiratory depression caused by an opiate overdose, but is ineffective for other causes. In addition, rapid administration of higher doses (2 mg) can precipitate an acute narcotic withdrawal, and doses up to 10 mg may need to be given before excluding an opiate ingestion. These products should be used only in patients who are unconscious with respiratory depression.

For dermal exposures to an unknown substance, general decontamination includes complete removal of clothing, irrigation of the skin with water, and cleansing with a mild soap. For inhalational exposures, the patient should be immediately removed from the suspected source. If significant respiratory depression occurs, adequate ventilation should be provided with supplemental oxygen if necessary, and pulmonary status should be assessed by measuring arterial blood gas and pulse oximetry, and obtaining a chest radiograph if necessary. For ocular exposures, contact lenses should be removed, and the eyes should be irrigated with water or saline for at least 15 minutes. An ophthalmology consult may be needed if pain or redness persists after irrigation, for foreign body exposure, or exposure to strong alkalis and bases.

Drug Screens

The most common drug screen used is a qualitative urine screen, which tests for the presence of specific drugs, which but cannot quantify the amount of the drug that is present. The drugs most commonly screened by this method include amphetamines, barbiturates, benzodiazepines, cocaine, opiates, phencyclidine, and tricyclic antidepressant drugs. To guide the management and treatment of selected drugs and poison, quantitative testing can be performed. A negative screen does not exclude a diagnosis of poisoning, especially if the suspected drug is not tested for routinely. Similarly, a positive test does not necessarily confirm the diagnosis of a poisoning, as a drug may be present but not at a toxic quantity.

Gastric Decontamination

For poison ingestions, there are many general decontamination strategies; however, several have recently been called into question. Emesis with syrup of ipecac has traditionally been considered relatively safe and effective for general decontamination of poisonings. It is easily obtainable as a nonprescription product and can easily be administered in the home. Disadvantages of syrup of ipecac are that it removes only 30%–40% of gastric contents, requires 20–30 minutes for effect, and increases the risk of aspiration pneumonia. A recent study showed that home administration of syrup of ipecac does not improve patient outcome, nor does it reduce health care resource use. Based on this and other recent initiatives, several organizations have published updated policies and statements on the use of syrup of ipecac in the home. The most comprehensive guideline, from AAPCC, recommends that syrup of ipecac should be administered only in response to a specific recommendation from a poison center, emergency department physician, or other qualified medical personnel, and only when all of the following conditions are met:

1. There is no specific contraindication to the use of syrup of ipecac;
2. There is substantial risk of serious toxicity to the victim from the poisoning;
3. There is no alternative therapy available (or effective) to decrease gastrointestinal (GI) absorption (e.g., activated charcoal);
4. There will be a delay of longer than 1 hour before the patient will arrive at an emergency medical facility and syrup of ipecac can be administered within 30–90 minutes of the ingestion; and

Rainey PM. Laboratory principles and techniques for evaluation of the poisoned or overdosed patient. In: Goldfrank LR, ed. Goldfrank's Toxicologic Emergencies. New York: McGraw-Hill, 2002:69–93.

Bond GR. Home syrup of ipecac use does not reduce emergency department use or improve outcome. Pediatrics 2003;112:1061–4.

American Association of Poison Control Centers. Guideline on the use of Ipecac Syrup in the Out-of-Hospital Management of Ingested Poisons. Available at *http://www.aapcc.org/FinalizedPMGdlns/Ipecac%20Guideline%20-%20final%20for%20JTCT.pdf*. Accessed May 23, 2006.

Table 1-1. Top 10 Substances Most Commonly Associated with Toxic Exposures

Children (under 6 years of age)	(% of total exposures)
Cosmetics and personal care products	13.4
Cleaning substances	9.7
Analgesics	7.8
Foreign bodies	7.4
Topicals	7.4
Cough and cold preparations	5.5
Plants	4.6
Pesticides	4.1
Vitamins	3.6
Antimicrobials	2.8
Adults (19 years of age or older)	
Analgesics	14.4
Sedatives/hypnotics/antipsychotics	11.1
Cleaning substances	8.9
Antidepressants	8.2
Bites/envenomations	7.5
Alcohols	5.3
Cardiovascular drugs	5.1
Food products	4.8
Cosmetics and personal care products	4.8
Pesticides	4.6

5. Syrup of ipecac administration will not adversely affect more definitive treatment that might be provided at a hospital.

For infants younger than 6 months, syrup of ipecac should be administered only by a physician. For other pediatric and adult populations, the following age-adjusted dose ranges apply: infants 6–12 months: 5–10 mL syrup of ipecac followed by 120–240 mL of water; children 1–12 years: 15 mL syrup of ipecac followed by 120–240 mL of water; children older than age 12 and adults: 15–30 mL syrup of ipecac followed by 240 mL of water. Doses may be repeated for all age groups, and syrup of ipecac can be administered effectively after the date of expiration.

Gastric lavage is another means by which toxins can be removed from the stomach. The efficacy of gastric lavage is highly variable and diminishes over time; therefore, the optimal time to perform lavage is within 60 minutes of the exposure. A large bore (36–40 French for adults, 24–28 French for children) orogastric tube is inserted into the stomach during gastric lavage. Patients who are unconscious will require oral or nasal intubation before insertion of the orogastric tube. The lavage is then performed by placing 200–300 mL aliquots of water or 0.9% sodium chloride into the orogastric tube (10 mL/kg of body weight for children), and returning the same amount. This procedure is repeated until the return fluid is clear of particulate matter. Complications associated with gastric lavage include aspiration pneumonia, laryngospasm, perforation of the esophagus or stomach, and hyponatremia due to water intoxication. Because these complications are common and can be severe, gastric lavage is not routinely recommended.

Based on current evidence, there are no indications for the use of cathartics as the sole agent in managing patients who are poisoned. Cathartics can be used as a single dose in combination with other decontamination strategies to decrease gastric absorption of toxins by increasing GI tract excretion of the poison. However, cathartic use in combination with activated charcoal has not improved outcomes and should not be used routinely. The most common cathartic agents and doses are magnesium citrate 10% 240 mL for adults and 4 mL/kg for children; and sorbitol 1–2 mL/kg of a 70% solution for adults and 4.3 mL/kg of a 35% solution for children.

Similarly, whole bowel irrigation (WBI) can be used to increase GI tract excretion of the poison, especially for ingestions of drugs with long half-lives, or for controlled-release or enteric-coated preparations. Whole bowel irrigation is also considered the preferential decontamination strategy for iron overdose, and may be useful for packers or stuffers. These terms refer to persons who insert packets of illegal substances into the GI tract for purposes of transportation (packers) or in an attempt to conceal evidence from law enforcement (stuffers). Polyethylene glycol electrolyte lavage solutions (e.g., GoLYTELY and Colyte) are given at least until the rectal effluent is clear, but may require prolonged administration to remove foreign bodies if evidence shows a continued presence of toxins in the GI tract. The doses are children 9 months to 6 years: 500 mL/hour; children 6–12 years: 1000 mL/hour; adolescents and adults: 1500–2000 mL/hour. Whole bowel irrigation is contraindicated for patients having undergone recent bowel surgery, or in patients suspected of having bowel obstruction, bowel perforation, or ileus.

One of the most common decontamination strategies is the use of an adsorbent (activated charcoal) to bind the ingested toxin in the GI tract to prevent systemic absorption. Advantages of an adsorbent are that it binds immediately, and it binds to toxins throughout the intestinal tract (compared with gastric lavage, which is limited to the stomach). Disadvantages include the potential for aspiration if patients are unconscious or cannot protect their airway, as well as the development of an intestinal obstruction (i.e.,

American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position paper: gastric lavage. Clin Toxicol 2004;42:933–43.

American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position paper: cathartics. Clin Toxicol 2004;42:243–53.

American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position paper: whole bowel irrigation. Clin Toxicol 2004;42:843–54.

American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position statement: single-dose activated charcoal. Clin Toxicol 2005;43:61–87.

American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Position Statement and Practice Guidelines on the Use of Multi-Dose Activated Charcoal in the Treatment of Acute Poisoning. Clin Toxicol 1999;37:731–51.

Table 1-2. List of Agents that Activated Charcoal does not Bind

Acids
Mineral acids
Boric acid
Alcohols
Ethanol
Methanol
Alkalis
Carbamates
Cyanide
Hydrocarbons
Metals
Lithium
Mercury
Iron
Lead
Arsenic
Organic solvents
Organophosphates

bezoar). In addition, there are several agents for which activated charcoal does not bind (see Table 1-2).

The two administration strategies for activated charcoal are single dose and multiple dose. Single-dose activated charcoal is most effective when given in the first hour after exposure. The doses are as follows: infants up to 1 year of age: 10–25 g or 0.5–1.0 g/kg; children ages 1–12: 25–50 g or 0.5–1.0 g/kg; adolescents and adults: 25–100 g. To reduce nausea and make the mixture more palatable, the activated charcoal is mixed with juice or carbonated beverages. Some patients may experience significant nausea from activated charcoal. If the nausea is persistent or severe, patients may need an antiemetic, such as promethazine or a serotonin-3 receptor antagonist (e.g., ondansetron or granisetron). Multiple-dose activated charcoal can increase the elimination of toxins, but has not reduced morbidity or mortality in patients with poisoning, and is therefore not routinely recommended. Multiple-dose activated charcoal should be reserved for patients who have ingested a life-threatening overdose of one of the following drugs: carbamazepine, dapsone, phenobarbital, quinine, or theophylline. Although there is no consensus for dosing, the typical regimen is 12.5 g of activated charcoal every hour after the initial dose listed above until clinical symptoms improve.

Antidotes

All institutions that accept emergency admissions must have a plan to stock appropriate antidotes for toxicologic emergencies. Decisions on which antidotes to stock and in what quantities should be based on efficacy of the drug, time period in which it is needed, the availability of alternative treatments, and the needs of the specific institution. A consensus panel was developed and published a guideline recommending that 16 specific antidotes be stocked and available for immediate use: *N*-acetylcysteine, antivenin (Crotalidae) polyvalent, atropine, calcium gluconate and calcium chloride, cyanide kit, deferoxamine mesylate, digoxin immune fab, dimercaprol, ethanol solution for injection (100%), fomepizole, glucagon, methylene blue, naloxone, pralidoxime chloride, pyridoxine, and sodium bicarbonate. A consensus was not achieved for routinely stocking flumazenil and physostigmine. Stocks of black widow antivenin and ethylenediamine tetraacetic acid were not recommended.

Specific Poisoning Agents

Acetaminophen

Acetaminophen, as a single drug or in combination with other drugs, was the most common of all toxic drug exposures in 2003, accounting for almost 10% of all the ingested drugs. Acute doses of 10 g in adults and 200 mg/kg in children are considered toxic, and ingestion of doses exceeding these thresholds (or in cases of unknown quantities) should be referred to an emergency department. The mechanism of toxicity is not due to acetaminophen itself, but to a toxic metabolite. The majority of an acetaminophen dose (greater than 90%) is metabolized to glucuronide and sulfate conjugates before it is excreted by the liver. About 5% is converted by the cytochrome P450 system to a toxic metabolite, *N*-acetyl-p-benzoquinoneimine (NAPQI), which under normal circumstances is then conjugated with glutathione and converted to cysteine conjugates, which are excreted in the urine. The remaining amount is excreted unchanged in the urine. In an overdose, the body's glutathione stores become depleted, leading to a buildup of *N*-acetyl-p-benzoquinoneimine, which can lead to oxidant cell injury, hepatic failure, and ultimately death.

Clinical Presentation

Clinical presentation following an acetaminophen overdose occurs in four phases. Phase I occurs within the first 24 hours of ingestion. A patient typically presents with minimal or no signs of distress, but may exhibit anorexia, nausea and vomiting, and diaphoresis. Phase II occurs 24–48 hours after the initial exposure and is marked by initial damage to the hepatocytes. It can be manifested clinically as right upper quadrant pain, an increase in liver transaminase concentrations, elevated total bilirubin concentrations, and prolonged prothrombin time: Phase III occurs 72–96 hours after initial exposure, and manifests as the peak of hepatotoxicity. Patients in this phase typically have jaundice and coagulopathies, and may develop signs of hepatic encephalopathy. The fourth phase of toxicity occurs at about 7–8 days post-exposure and marks either the recovery phase or death.

Dart RC, Goldfrank LR, Chyka PA, et al. Combined evidence-based literature analysis and consensus guidelines for stocking of emergency antidotes in the United States. Ann Emerg Med 2000;36:126–32.

Dart RC, Erdman AR, Olson KR, et al. Acetaminophen poisoning: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol 2006;44:1–18.

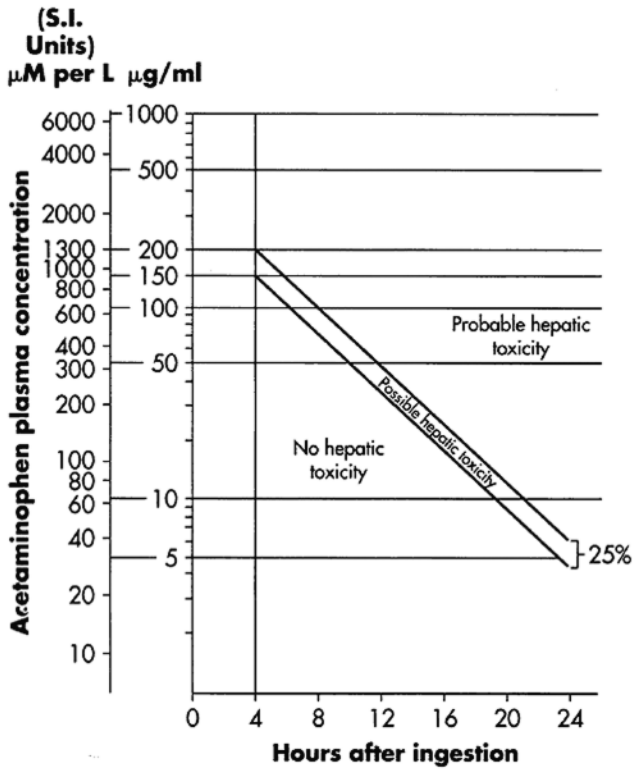

Figure 1-1. The Rumack nomogram.
Adapted with permission from the American Medical Association. Rumack BH, Peterson RC, Koch GG, et al. Arch Intern Med 1981;141:380–5. Copyright© American Medical Association.

Treatment

The goal of treatment is to reduce or prevent hepatotoxicity by administering *N*-acetylcysteine. Proposed mechanisms by which *N*-acetylcysteine reduces acetaminophen-related hepatic injury include the following: 1) increasing the synthesis and bioavailability of glutathione; 2) substituting for glutathione by binding to *N*-acetyl-p-benzoquinoneimine via its reduced sulfur group; and 3) increasing the percentage of nontoxic metabolism by supplying a substrate for sulfation. The need for therapy with *N*-acetylcysteine for acetaminophen overdose is determined by the Rumack-Matthew nomogram (Figure 1-1). If therapy is needed, it is most effective if given within 8 hours of exposure. Patients who present between 4 and 24 hours after acute acetaminophen ingestion with a plasma acetaminophen concentration above the lowest line in the nomogram are at risk for transaminase elevation and should be treated. Patients presenting following a delayed or chronic exposure to acetaminophen may not be treated in the same manner as an acute exposure, and their care should be referred to a regional poison control center for assistance. *N*-acetylcysteine is available in a liquid formulation (intended for inhalational use) that can be administered orally. Pediatric and adult dosing is as follows: loading dose of 140 mg/kg, followed by 70 mg/kg given every 4 hours for 17 doses. Some poison control centers recommend that dosing may be discontinued after acetaminophen concentrations become undetectable based on studies showing no additional benefit for continued dosing after this point. However, this practice is controversial, in part because of the multiple mechanisms of *N*-acetylcysteine that may reduce hepatocellular damage in each of the four phases of acetaminophen toxicity. In addition, several studies demonstrated a beneficial effect of *N*-acetylcysteine in patients with hepatic insufficiency even after acetaminophen concentrations were no longer detectable. Therefore, doses should be continued for the full duration of therapy unless under the specific recommendation of a supervising toxicologist or poison control center.

Administration of *N*-acetylcysteine can be one of the most challenging aspects of treating an acetaminophen overdose. Because of the sulfur component of *N*-acetylcysteine, it has an unpleasant odor and is difficult to tolerate with oral administration. Doses can be mixed with juice or carbonated beverages to mask the taste. For patients who experience severe nausea and vomiting due to oral administration of *N*-acetylcysteine, it can also be administered intravenously. An intravenous formulation of *N*-acetylcysteine recently received Food and Drug Administration (FDA) labeling and was introduced to the market (Acetadote; Cumberland Pharmaceuticals Inc., Nashville, TN). With the new guidelines addressing pharmaceutical compounding of sterile preparations provided by the United States Pharmacopeia (Chapter 797), there has been significant debate as to whether institutions should be compounding intravenous *N*-acetylcysteine when there is a marketed product available. However, the commercially available product is considerably more expensive, but it is being used with a greater frequency due to these new guidelines.

Label recommendations are for the initial dose to be administered within the first 8 hours after exposure for maximum efficacy, but the product may still be beneficial if given within the first 24 hours of the time of the reported exposure. Dosing of intravenous *N*-acetylcysteine is as follows (doses are calculated using actual body weight): loading dose: 150 mg/kg in 200 mL dextrose 5% in water infused over 60 minutes; maintenance dose: 50 mg/kg in 500 mL dextrose 5% in water infused over 4 hours, followed by 100 mg/kg in 1000 mL dextrose 5% in water infused over 16 hours. For patients weighing less than 40 kg, the dosing is the same, but requires less volume for dilution (Table 1-3). Anaphylactoid reactions (rash, urticaria, or pruritus) can occur with intravenous *N*-acetylcysteine, and are more pronounced with the initial loading dose. Some clinicians recommend keeping epinephrine, diphenhydramine, and cimetidine (or an alternative histamine-2 antagonist) readily available should these reactions occur. If Acetadote is not readily available, a local poison control center can provide compounding instructions to make an intravenous formulation using the inhalational acetylcysteine product.

Woo OF, Mueller PD, Olson KR, Anderson IB, Kim SY. Shorter duration of oral *N*-acetylcysteine therapy for acute acetaminophen overdose. Ann Emerg Med 2000;35:363–8.

Abbreviations

Methanol and Ethylene Glycol

Methanol and ethylene glycol poisonings are less common, accounting for about 3% of the total human exposures in 2003. Although rare, these poisonings remain serious and potentially fatal. Methanol is found in automotive products (e.g., brake and carburetor fluid, antifreeze, and windshield washer solution), and household products (e.g., paint remover and cleaning solvents). Ethylene glycol is a common component of antifreeze, brake fluid, and de-icing products. It has a sweet taste that makes it especially dangerous for children and pets. The toxicity of methanol and ethylene glycol is due to their toxic metabolite. Both are metabolized in the liver by the enzyme alcohol dehydrogenase. Methanol is converted to formaldehyde, which is then converted to formic acid; ethylene glycol is converted to glycoaldehyde, and then to glycolic acid. Both formic and glycolic acid are toxic. They can cause abdominal pain, nausea, vomiting, dizziness, seizures, and rarely, death.

Clinical Presentation

Patients with methanol or ethylene glycol poisonings present with symptoms such as inebriation, altered mental status, nausea, vomiting, hematemesis, nystagmus, depressed reflexes, and tetany secondary to hypocalcemia. Laboratory evaluation is typically positive for an osmolar gap early in the presentation, but the osmolar gap will narrow as the parent compound is metabolized. When this occurs, the anion gap will rise; however, significant acidosis may precede any actual increase in the anion gap itself. Osmolarity should be measured by the freezing point depression method. Examination of urine for fluorescence under a Wood's lamp can be performed for ethylene glycol, as many of the products contain a high amount of fluorescein. However, this method is not recommended due to a high incidence of false-negative results, in addition to a potential of false-positive results secondary to the plastic in urine collection cups. Ethylene glycol and methanol concentrations should be monitored to guide the duration of

Table 1-3. The Chemical Agents

Type	Agents (military designation)	Effects	Treatment
Blood agents	Arsine Cyanogen chloride (CK) Hydrogen cyanide (AC) Methyl isocyanate	Onset: minutes Effects: Loss of consciousness Seizures Apnea Respiratory failure Cardiac arrest	Decontamination Antidotes: Amyl Nitrite: Crush and inhale the vapor from a 0.3 mL ampule every 15–30 seconds until sodium nitrite started Sodium Nitrite 10 mL (3% solution): Adults: 300 mg IV over 5 minutes Children: 0.33 mL/kg over 5 minutes (maximum = 10 mL) Sodium Thiosulfate (25% solution) Adults: 12.5 g IV over 5 minutes Children: 1.65 mL/kg IV over 5 minutes
Choking agents	Ammonia Chlorine Chloropicrin (PS) Diphosgene (DP) Phosgene (CG)	Onset: minutes to hours Effects: Dyspnea Coughing Pulmonary edema	Supportive care No known antidote Decontamination Oxygen Bronchodilators
Nerve agents	Tabun (NATO designation GA) Sarin (NATO designation GB) Soman (NATO designation GD) GF VX GE VE VG VM	Onset: seconds to minutes Effects: Miosis Rhinorrhea Dyspnea Convulsions	Supportive care: Decontamination Ventilation Antidotes: Atropine 2 mg IV, then 2 mg IV every 3–5 minutes Pralidoxime chloride 1 g over 30 minutes Diazepam 10 mg IM/IV as needed
Blister/vesicant agents	Lewisite (L) Mustard-Lewisite (HL) Nitrogen Mustards (HN-1, HN-2, HN-3) Phosgene Oxime (CX) Sulfur Mustards (H, HD, HT)	Onset: minutes to hours Effects: Erythema Blisters Eye irritation Dyspnea	Supportive care Oxygen Bronchodilators Topical antibiotics British anti-lewisite

IM = intramuscularly; IV = intravenously.

American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Practice Guidelines on the Treatment of Ethylene Glycol Poisoning. Clin Toxicol 1999;37:537–60.

American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists. Practice Guidelines on the Treatment of Methanol Poisoning. Clin Toxicol 2002;40:415–46.

treatment. Ethanol concentrations may be drawn as part of a routine toxicology panel, and will also be used in the evaluation of the osmolar gap. Concentrations will not elevate except in the event of an ethanol co-ingestion.

Treatment

Therapy for methanol or ethylene glycol poisoning consists of attempting to block the production of the toxic metabolites. Alcohol dehydrogenase has a preferential affinity for ethanol; therefore, administration of ethanol will completely block the breakdown of both methanol and ethylene glycol, allowing them to be excreted unchanged in the urine. Ethanol is administered by continuous intravenous infusion diluted in dextrose 5% in water. The goal is to maintain ethanol levels of 100 mg/dL (0.1%) until symptoms have diminished and the methanol or ethylene glycol concentrations are undetectable. Although this strategy is effective, it not without its difficulties. Ethanol dosing is unpredictable and can lead to hypoglycemia, inebriation, and a change in mental status. Therefore, ethanol administration requires frequent monitoring, and, in some institutions, it requires patients to be monitored in an intensive care unit. Because of these potential issues surrounding the use of ethanol, use of fomepizole is preferred.

Fomepizole, 4-methylpyrazole, is another competitive inhibitor of alcohol dehydrogenase. It has a rapid onset of action and a volume of distribution of 0.6–1.02 L/kg. Fomepizole is metabolized by the liver via cytochrome P450, and a small amount (1%–3%) is excreted unchanged in the urine. Fomepizole induces its own metabolism; therefore, dose increases are required during therapy. The dosing of fomepizole is as follows: loading dose of 15 mg/kg; followed by a maintenance dose of 10 mg/kg every 12 hours for four dosages, then 15 mg/kg every 12 hours. Dosing can be discontinued when serum ethylene glycol or methanol concentrations are less than 20 mg/dL, and the patient is asymptomatic with a normal pH. Hemodialysis increases the clearance of fomepizole; therefore, the dosing interval should be shortened to every 4 hours if used in patients undergoing hemodialysis. Adverse effects associated with fomepizole include headache, nausea, dizziness, and a metallic taste. Hemodialysis should be considered if the patient's vital signs continue to deteriorate, a significant metabolic acidosis develops, or kidney failure or electrolyte disturbances develop that are unresponsive to conventional therapy. Some experts advocate the use of hemodialysis if the serum ethylene glycol or methanol concentrations exceed 50 mg/dL; however, in the absence of both kidney dysfunction and a significant metabolic acidosis, fomepizole may negate the need for hemodialysis.

Thiamine and pyridoxine serve as cofactors for the metabolism of ethylene glycol, but administration of these agents has not been proven to improve outcome in acute poisonings. Pyridoxine promotes the metabolism of glyoxylate to glycine, and thiamine promotes the metabolism of glycolic acid to a nontoxic metabolite. For ethylene glycol exposure, daily intravenous doses are thiamine 100 mg and pyridoxine 50 mg. Similarly, folinic acid enhances the metabolism of formic acid, but also has not been proven to improve outcome in acute methanol poisonings. For methanol exposure, the doses are leucovorin 1 mg/kg (maximum 50 mg) intravenously as a one-time dose, then folic acid 1 mg/kg (maximum 50 mg) intravenously every 4 hours for six doses.

Cardiovascular Drugs

Annually, cardiovascular drugs account for more than 40,000 adult toxic exposures, and are the fifth leading cause of death among overdoses. Two of the most common and potentially fatal cardiovascular drugs in toxic exposures are the β-blockers and calcium channel blockers.

The toxic effects of β-blockers are hypotension, bradycardia, and prolonged atrioventricular conduction secondary to a decrease in intracellular cyclic adenosine monophosphate, which causes a decrease in intracellular calcium levels. The lipophilic drugs in this class (e.g., propranolol, metoprolol, and timolol) can also cause loss of consciousness and generalized seizures. Initial treatment for β-blocker toxic exposure involves maintaining hemodynamic stability by preventing further decreases in blood pressure and heart rate. Isotonic fluids (e.g., sodium chloride 0.9%, lactated Ringer's solution) should be started, and atropine 0.5–1 mg can be given initially for symptomatic bradycardia. In some cases, the bradycardia may be resistant to atropine. If this occurs, alternative drugs such as dopamine and epinephrine can be used. Although the data regarding the use of glucagon are limited, it is the antidote most commonly used in clinical practice. Glucagon stimulates adenylate cyclase to increase cyclic adenosine monophosphate. The initial glucagon dose is 2–5 mg intravenously over 1 minute; a repeat dose of up to 10 mg can be given if needed. A continuous infusion of glucagon at a rate of 2–5 mg/hour may be started for patients who respond to the initial bolus. Adverse effects associated with glucagon include nausea, vomiting, and hyperglycemia. For patients who do not respond to glucagon, isoproterenol (2 mcg/minute), dopamine (5 mcg/kg/minute), or epinephrine (1 mcg/minute) may be used, but these drugs have produced inconsistent effects. For those patients in which drug therapy fails, transthoracic or transvenous cardiac pacing may be necessary.

Patients suffering a calcium channel blocker overdose present with hypotension, prolonged atrioventricular conduction, bradycardia, lethargy, hyperglycemia, and depressed consciousness. The mechanism of toxicity is due to the blockade of the L-type calcium channels, inhibiting calcium influx into the cell. The treatment of choice is 1–2 g of intravenous calcium chloride 10%. Intravenous calcium has a short duration of effect; therefore, a calcium chloride infusion is often required at doses ranging from 0.3–0.7 mEq/kg/hour (20–50 mg/kg/hour). There are several potential alternative options (glucagon, catecholamines, etc.) if calcium therapy fails. Although no clinical trials have been conducted with glucagon, multiple case reports demonstrated clinical improvement with glucagon bolus dosing with or without continuous infusion, and the use of glucagon has become widely accepted in clinical practice. Dosing of glucagon in calcium channel blocker overdoses is the same as for β-blocker overdoses. Catecholamines, such as epinephrine (1 mcg/minute),

dopamine (5 mcg/kg/minute), or phosphodiesterase inhibitors (milrinone 0.375 mcg/kg/minute) have produced inconsistent effects in that they do not consistently (in every patient) provide a clinical effect to help reverse the effects of the dose. Use of these drugs in combination with transthoracic or transvenous cardiac pacing may be required to maintain an adequate heart rate.

If these therapies fail, high-dose insulin, dextrose, and potassium therapy may be effective. Insulin administration leads to cellular uptake of dextrose, which improves inotropy and is also potentially cardioprotective. Limited clinical experience has demonstrated an improvement in hypotension that was considered refractory to other treatments. Administration of this mode of therapy begins with 50 mL of dextrose 50% (0.25 g/kg dextrose 25% in pediatric patients) if the glucose level is less than 200 mg/dL, and potassium chloride 40 mEq if the potassium level is less than 2.5 mEq/L. A bolus of insulin 1 unit/kg is then given, followed by an insulin infusion of 0.5–1 unit/kg/hour titrated to response.

Poison Control Centers

All pharmacists should become familiar with, and know how to contact, their regional poison control center. Each center is staffed with trained nurses, pharmacists, and physicians who provide assistance with poisoning management issues, antidote doses, antidote preparation, and other information as needed by pharmacists. The 1-800-222-1222 number can be dialed anywhere in the United States to reach a certified regional poison center serving the location of the caller. Additional information can be found on the AAPCC Web site (*www.aapcc.org*).

Emergency Preparedness

Introduction

Emergency preparedness for the threat of a terrorist attack on American soil is ever-changing. Most of the attention has centered on the use of biological agents such as anthrax, smallpox, and plague. However, chemical and radiological agents are a highly toxic and a potentially lethal option for terrorist attacks because of the potential for the significant amount of injuries to a substantial number of people. Chemical agents were first used in warfare during World War I and have been used periodically since that time; the most recent purportedly to be by Iraqi forces during the Iran War and against the Kurds in northern Iraq. Although nuclear weapons have not been used since the bombings of Hiroshima and Nagasaki at the end of the World War II, the stockpiling of these agents during the Cold War, coupled with the availability of other forms of radiation materials from medical and industrial sources, makes the threat of these agents very real.

Chemical Agents

Chemical agents are divided into four categories: vesicant or blister agents, blood agents, choking agents, and nerve agents.

Vesicant or Blister Agents

Vesicant agents, also known as the blister agents, were a common chemical weapon used in World War I. As an aerosol form with other chemical agents, vesicants were used more as incapacitating agents than for their lethal effects. Examples include the mustards (distilled mustard, mustard gas, mustard-lewisite, nitrogen mustards, and sulfur mustard), lewisite, and phosgene oxime.

Mustards are oily liquids with a light yellow to brown color, and garlic, onion, or mustard odor. Portals of entry for the mustard agents include the lungs, skin, eyes, and mucous membranes. Absorption is rapid, and is further enhanced by moisture and heat, and occurs through body areas with thin dermal layers, especially wounds. Once absorbed, the mustards rapidly distribute to all areas of the body; however, systemic effects are typically seen only at high doses. The toxic effect of the mustards is cellular death. The exact mechanism of cellular death is unknown, but it is thought to be due to DNA alkylation and crosslinking in rapidly dividing cells, as well as a direct cholinergic effect.

Lewisite is an oily, colorless liquid that smells like geraniums. It is absorbed through the skin, eyes, and lungs, and it can also be ingested. The toxic effect of Lewisite is due to its arsenic content. Phosgene oxime is a solid compound at temperatures under 95°F, but it has a high vapor pressure that allows absorption through exposed surfaces and rapid systemic distribution. The exact mechanism of toxicity of phosgene oxime is unknown.

Clinical Presentation

After exposure to mustards, the onset of symptoms can be delayed for as long as 2–24 hours after exposure. Dermal effects include erythema and formation of small vesicles (which may form bulla); at high doses, a central zone of coagulation necrosis may form. Respiratory signs and symptoms include nasal irritation or pain, laryngitis, cough, dyspnea, pseudomembrane formation, and respiratory failure. Ocular effects include redness, conjunctivitis, photophobia, pain, miosis, and corneal swelling or damage. Gastrointestinal tract effects include nausea with or without vomiting and either diarrhea or constipation. Bone marrow suppression with leukopenia, thrombocytopenia, and anemia may occur within 3–5 days, and in high doses, central nervous system (CNS) effects such as tremors, convulsions, ataxia, and coma may be seen. Lewisite effects are seen immediately, and include erythema, blister formation, and tissue necrosis; ocular pain and blepharospasm; cough; dyspnea; pulmonary edema; and in high doses, cardiovascular effects such as hypotension and atrioventricular block. The effects of phosgene oxime are also seen immediately and include skin blanching,

Shepherd G, Klein-Schwartz W. High-dose insulin therapy for calcium-channel blocker overdose. Ann Pharmacother 2005;39:923–30.

United States Army Medical Research Institute of Chemical Defense-Chemical Casualty Care Division. Medical Management of Chemical Casualties Handbook, 3rd ed, 2000. Available at *https://ccc.apgea.army.mil/*. Accessed May 23, 2006.

Centers for Disease Control and Prevention. Toxic Syndrome Description. Vesicant/Blister Agent Poisoning. CDC Chemical Emergencies: United States. Available at *http://www.bt.cdc.gov/agent/vesicants/tsd.asp*. Accessed May 23, 2006.

erythema, and necrosis; ocular pain and lacrimation; burning sensation in the throat; nausea and vomiting; and coughing and pulmonary edema.

Treatment

Patients should be removed from the source of vesicant or blister agent exposure and then decontaminated by removing clothing and washing the skin with soap and water. Maintaining an airway is vital in patients, as many will experience bronchospasm and pulmonary edema. Early intubation should be considered, as patients can develop severe laryngeal spasm and edema, which may make future intubation difficult or even impossible. Supplemental oxygen should be provided, and bronchodilators such as albuterol 2.5 mg may be given via nebulizer or by metered-dose inhaler as needed. Pain control will be necessary, and may require opioid analgesics. Fentanyl 25–50 mcg intravenously every 2 hours as needed for pain can be given. Fentanyl is a preferred analgesic for vesicant or blister agent exposure because of its short duration of effect and because of its absence of hypertensive or hypotensive effects. Burns and blistering will require irrigation and debridement, and the use of topical antibiotic agents such as silver sulfadiazine 1%. Fluid requirements for these patients exposed to vesicant or blister are significant, but less than burn patients with similar loss of skin. Eye care should include flushing and applying topical lubrication ointments and/or antibiotic agents as needed.

The only known antidote for the vesicant or blister agents is British anti-lewisite in oil (dimercaprol); therefore, treatment should focus on good supportive care. British anti-lewisite in oil may reduce systemic effects of lewisite poisoning, but it has no effect on the skin lesions. In the presence of shock or significant pulmonary injury, the dose is 3–5 mg/kg intramuscularly every 4 hours for a total of four dosages. Adverse effects include pain at the injection site, hypertension and tachycardia, nausea and vomiting, and nephrotoxicity. It should not be given to patients with kidney dysfunction or pregnant women (except in life-threatening emergencies).

Blood Agents

Unlike the vesicant or blister agents, blood agents were not designed for incapacitation, but for their rapid, lethal effect. Examples include arsine, carbon monoxide, cyanide (cyanogen chloride, hydrogen cyanide, potassium cyanide, and sodium cyanide), and sodium monofluoroacetate. This section focuses on the most common and most lethal agent in this group, cyanide.

As a weapon, liquid cyanide is contained in munitions (e.g., bombs and large shells) and rapidly vaporizes when the munitions are detonated. It can also be a colorless gas (hydrogen cyanide or cyanogen chloride) or in a crystal form (sodium cyanide or potassium cyanide). Cyanide is known for its distinct odor of bitter almonds; however, only about one-half of the general population possesses the gene necessary for recognizing this odor, and even then, the odor is not always recognizable. The exposure route as a chemical agent is through inhalation. The effects of cyanide are almost immediate (within 15 seconds), and the lethal effect occurs in 6–8 minutes. Cyanide is normally metabolized to thiocyanate in the liver by the enzyme rhodanese and excreted in the urine. The liver is unable to metabolize large quantities of cyanide, which leads to the toxic effect. The lethal effect is ultimately due to loss of intracellular oxygen utilization leading to severe metabolic (lactic) acidosis. Cyanide binds with iron in cytochrome a_3 in the mitochondria, blocking adenosine triphosphate production. Cyanide also binds to the ferric iron of methemoglobin, forming cyanomethemoglobin.

Clinical Presentation

In low to moderate exposure, the onset and severity of symptoms are less pronounced. Initial symptoms are generally nonspecific, and can include dizziness, weakness, headache, nausea and vomiting, chest tightness, and shortness of breath. Hypoxia occurs secondary to the decrease in cellular respiration, leading to an increase in anaerobic glycolysis that results in lactic acidosis. Lactic acidosis is diagnosed in the presence of an anion gap metabolic acidosis along with elevated serum lactate concentrations. Pulse oximetry should not be used as a means to measure oxygenation in suspected cyanide exposure, as the oximeter cannot distinguish oxyhemoglobin and methemoglobin, leading to falsely elevated readings. The testing of cyanide concentrations can take several days to perform, and are therefore not practical in the acute setting. If untreated, or if exposure continues, symptoms will progress to those of a high concentration cyanide exposure. As previously discussed, the effects of cyanide are almost immediate. Within 15 seconds, there is an increase in the rate and depth of breathing. At 30 seconds, the patient will experience convulsions. A complete cessation of breathing occurs within 2–4 minutes and at 4–8 minutes, asystole occurs.

Treatment

Treatment for a toxic cyanide exposure begins with supportive care. The patient should be moved from the source of the exposure to a well-ventilated area. All clothing should be removed, and the skin should be washed with soap and water. Supplemental oxygen should be supplied; administration of 100% oxygen is recommended as it has been shown to provide an additional benefit. Circulatory support with the administration of crystalloids or vasopressors should be given, if needed. Administration of sodium bicarbonate can help improve the symptoms of lactic acidosis, but its use is controversial.

An antidote kit for cyanide poisoning that contains the two key antidotes for cyanide poisoning, nitrite and a sulfur donor, is available in the United States. Nitrites are methemoglobin-forming agents and are given to dissociate bound cyanide from cytochrome a_3, which produces adenosine triphosphate. Sulfur donors are used to improve the formation of sulfane, which is used by the enzyme rhodanese to convert cyanide to thiocyanate. The cyanide antidote kit contains three components: a 0.3-mL ampule of amyl nitrite, a 10-mL vial of 3% sodium nitrite, and a 50-mL

Gracia R, Shepherd G. Cyanide poisoning and its treatment. Pharmacotherapy 2004;24:1358–65.

vial of 25% sodium thiosulfate. The kit also contains disposable syringes, stomach tube, tourniquet, and instructions for use. If intravenous access is not available, amyl nitrite is given by crushing the ampul and inhaling the vapor for 15–30 seconds. Once intravenous access is established, treatment should continue by administering 300 mg (pediatric dosing is 0.33 mL/kg up to a maximum of 10 mL) of sodium nitrite intravenously over 5 minutes, followed by 12.5 g (pediatric dosing is 1.65 mL/kg) of sodium thiosulfate intravenously over 5 minutes. If necessary, second doses of sodium nitrite and sodium thiosulfate can be given at one-half the original dose. Adverse effects associated with these agents are vasodilation and hypotension secondary to the nitrites, and an infusion-related reaction to thiosulfate. The cyanide antidote kits are expensive and may be difficult to acquire; however, the components of the kit can be purchased separately. Many experts advocate sodium thiosulfate alone as an adequate antidote, due to the questionable efficacy of the amyl nitrite ampuls and the adverse effect profile of sodium nitrite.

Another potential antidote to cyanide poisoning is hydroxocobalamin (vitamin B_{12a}). Cobalt compounds detoxify cyanide by directly chelating it to form cyanocobalamin (vitamin B_{12}). In some European studies, administration of 5 g of hydroxocobalamin has effectively reduced the toxicity associated with cyanide; however, this product does not currently have a labeled indication in the United States for this use.

Choking Agents

Choking agents include gases that affect the pulmonary system leading to generalized pulmonary edema. They are denser than air and accumulate in low-lying areas. Examples include ammonia, bromine, chlorine, methyl bromide, methyl isocyanate, osmium tetroxide, diphosgene, phosgene, phosphorous, and sulfuryl fluoride. Chlorine, phosgene, and diphosgene (which is converted to phosgene) are agents most likely to be used in a chemical attack.

Chlorine is a yellow-green gas with a distinct, pungent odor. On contact with moisture, chlorine forms hydrochloric acid, which produces tissue damage, and hypochlorous acid, an unstable compound that decomposes to form oxygen-free radicals that destroy cell function. Phosgene is a colorless gas with an odor of sweet, newly mowed hay. On contact with moisture, phosgene hydrolyzes to form carbon dioxide and hydrochloric acid, producing effects similar to those of chlorine. It also undergoes acylation with amino, hydroxyl, and sulfhydryl groups, causing leakage of fluids from the alveolar-capillary membrane. Both chlorine and phosgene are readily absorbed by inhalation. Chlorine is more soluble, and dissolves in the upper and lower airways, whereas phosgene is less soluble, and can penetrate to the level of the bronchioles and alveoli. Secondary exposure to the eyes and skin can also cause severe debilitating effects, such as watery eyes or blurred vision, and burning pain, redness, or blisters on the skin.

Clinical Presentation

Chlorine exposure causes respiratory effects, including cough, rhinorrhea, hypersalivation, laryngeal edema, chest tightness, wheezing, shortness of breath, and pulmonary edema. Other clinical symptoms include nausea and vomiting, watery eyes, and a burning sensation in the eyes and nasopharynx. Phosgene exposure initially causes irritation to the mucous membranes. A burning sensation in the eyes with or without lacrimation and conjunctivitis can also occur. Mild respiratory symptoms such as cough and chest pain are also present. After a latent period that can last up to 24 hours, more severe pulmonary symptoms develop that include dyspnea, chest tightness, crackles at the lung bases, and bronchospasm. These symptoms will ultimately progress to severe pulmonary edema, acute respiratory distress, and death.

Treatment

There are no known antidotes for the choking agents. Treatment focuses on supportive care. Patients should be removed from the source of exposure, and decontamination should be implemented by removing clothing and washing the skin with soap and water. Supplemental oxygen should be provided, and patients may require mechanical ventilation with the use of positive end-expiratory pressure. Bronchodilators such as albuterol 2.5 mg may be given via nebulizer or by metered-dose inhaler as needed. For patients with overt or latent reactive airway disease, intravenous corticosteroids can be given; however, studies have not indicated a clear benefit. The usual dose is methylprednisolone 125–250 mg intravenously every 6 hours on day 1, with a slow taper over the course of illness.

Nerve Agents

Nerve agents, classified as either G series or V series, are the most lethal of all the chemical agents. The G series, thought to have been given this designation because they were produced in Germany, were designed in the 1930s as pesticides. Examples include tabun (GA), sarin (GB), soman (GD), and GF. The V series or venomous agents were developed in the United Kingdom in the 1950s. Examples include VG, VM, VE, and VX, with VX being the only agent to have been produced in large quantities.

Nerve agents are organophosphate cholinesterase inhibitors. They are liquids at temperate conditions and are highly volatile. The exception is VX, which exists as an oily liquid, and is much less volatile than the G series agents. When nerve agents are dispersed, they produce a liquid and vapor mixture that is both lipophilic and hydrophilic, which allows for rapid absorption through the skin and mucous membranes. The mechanism of toxicity is through an inhibition of three separate enzymes: butyrylcholinesterase in the plasma, acetylcholinesterase on the red blood cell surface, and acetylcholinesterase at tissue receptor sites. The binding will become irreversible over time in a process referred to as aging; the amount of time over which this occurs is agent-specific. Without these enzymes, acetylcholine cannot be hydrolyzed.

Leikin JB, Thomas RG, Walter FG, Klein R, Meislin HW. A review of nerve agent exposure for the critical care physician. Crit Care Med 2002;30:2346–54.

Clinical Presentation

Cholinergic receptors are located on skeletal and smooth muscle, exocrine glands, and in the CNS. Clinical signs and symptoms associated with nerve agents focus on these areas, and are classified as either muscarinic or nicotinic effects. The muscarinic effects (commonly referred to by the acronym "dumbells") include defecation, diaphoresis, diarrhea, urination, mental status changes, miosis, bradycardia, bronchorrhea, bronchoconstriction, emesis, lacrimation, and salivation. Additional muscarinic effects can include wheezing, pulmonary edema, blurred vision, and abdominal cramping. The nicotinic effects include muscle twitching, fatigue, paralysis, apnea, tachycardia, and hypertension.

Treatment

Treatment of patients exposed to nerve agents centers around decontamination, ventilation, administration of antidotes, and good supportive care. Decontamination of affected patients consists of removing clothing and thoroughly washing the skin with a mild soap and water. Rescuers should use chemical protective clothing when moving or caring for patients exposed to nerve agents. Patients should be removed from the area of exposure as quickly as possible. Providing adequate ventilation may be difficult due to bronchoconstriction and an increase in airway secretions; therefore, supplemental oxygen and assisted breathing may be needed, at least until antidote administration.

The antidotes for nerve agents are atropine, pralidoxime, and diazepam. Atropine is given for its anticholinergic effect, blocking the action of acetylcholine at parasympathetic sites in smooth muscle. The dose of atropine is 2 mg for adults and 0.02 mg/kg (minimum of 0.1 mg) for children given every 2–5 minutes, but if dyspnea is severe, higher doses of up to 6 mg for adults may be given. The effects should be immediate, and repeat dosing is continued every 2–5 minutes until the patient is breathing comfortably and the excess secretions are dry. The preferred administration route is intravenous, but atropine is commonly given intramuscularly during pre-hospital care. The endotracheal route may also be used; however, the dose should be doubled to account for loss of drug in the endotracheal tube and variable lung absorption. Adverse effects associated with atropine include delirium, blurred vision, tachycardia, and urinary retention, but these effects are not typically observed in a poisoned patient. Pralidoxime chloride (2-PAM) is an oxime that reactivates cholinesterase by displacing the bond between the nerve agent and the enzyme. Pralidoxime chloride has no effect at the muscarinic sites, but reverses the nicotine effects. Timing of 2-PAM administration is critical to avoid aging. The initial dose is 1–2 g for adults (15 mg/kg for children) given by intravenous infusion over 5–10 minutes. The preferred administration route is intravenous, but it can also be given intramuscularly. If the patient experiences adverse effects such as hypertension, headache, or blurred vision, the infusion can be given slower, over 30–40 minutes. After the loading dose, a continuous infusion of 2-PAM can be started at 200–500 mg/hour if symptoms persist. Diazepam is used for its anticonvulsant properties to reduce the incidence of seizures. Diazepam is typically not given unless needed for seizure activity, but is recommended by the United States military to be administered for a severe exposure regardless of the presence of seizure activity. The diazepam dose is 5–10 mg intravenously or intramuscularly for adults, and 0.2–0.5 mg for children, repeated as needed. Tropicamide 0.5% ophthalmic solution, 1–2 drops repeated in 5 minutes, can be given as a mydriatic if needed for ocular pain or miosis.

Autoinjectors of atropine, diazepam (adult-use only), and a combination of atropine and 2-PAM (Mark-1 kits) can be used to treat patients in both the pre-hospital and hospital setting. Atropine autoinjectors are available in several strengths and sizes (0.25, 0.5, 1, and 2 mg) for both adult and pediatric use. Diazepam autoinjectors are available in a 10-mg strength (5 mg/mL, 2 mL). Mark-1 kits, prefilled syringes that contain 2 mg of atropine and 600 mg of 2-PAM, are useful for rapid intramuscular administration. Mark-1 kits can be difficult for institutions to acquire because the kits were developed for the military. These kits are contained in the Strategic National Stockpile (SNS) and as a part of the Chempack system (described later in this chapter).

Both the Mark-1 kits and the regular atropine autoinjector (1 mg/10 mL) are expensive to stock. An alternative is atropine bulk powder, which is inexpensive and can quickly be prepared as an intravenous dosage form. In one study, a pharmacist was able to reconstitute 100 6-mg atropine syringes in 29 minutes using a batching system, and in 34 minutes by hand. The process involved measuring 2 g of atropine powder, diluting it with 10 mL of sterile water, and adding it to a 1000-mL bag of 0.9% sodium chloride using a 0.2-micron filter. The estimated cost-savings for preparing 5 g of atropine using this method versus purchasing the prefilled syringes was almost $5,000. Similar production can be performed for sodium thiosulfate and for sodium nitrite, which are the antidotes for cyanide poisoning.

Ricin

Ricin (compound W) is a biotoxin derived from the bean of the castor plant, *Ricinis communis*. It has potential as a chemical weapon because it is the most toxic, easiest to extract, and most readily available of all the plant toxins. The mechanism of toxicity is related to one of the two polypeptide chains (the A-chain), which modifies the 28S ribosome, blocking protein synthesis. Ricin can be dispersed by aerosol or administered by intravenous and intramuscular injection. Ricin can also be ingested, but the oral route of exposure is much less toxic due to poor absorption and partial digestion of the bean.

Kozak RJ, Siegel S, Kuzma J. Rapid atropine synthesis for the treatment of massive nerve agent exposure. Ann Emerg Med 2003;41:685–8.

Franz DR, Jaax NK. Ricin toxin. In: Zajtchuk R, ed. Textbook of Military Medicine: Medical Aspects of Chemical and Biological Warfare. Washington, D.C.: TMM Publications Borden Institute, 1997:631–42.

Clinical Symptoms

Clinical symptoms of ricin exposure vary in their early presentation. Symptoms related to oral ingestion of ricin begins with an onset of nausea (usually within 6 hours, but may be delayed), vomiting, and abdominal pain. Symptoms related to injection of ricin begins with local pain at the injection site and progresses to flu-like symptoms, fatigue, myalgias, nausea, and vomiting. Inhalational exposure symptoms begin with a sudden onset of congestion in the nose and throat, itching of the eyes, urticaria, chest tightness, and wheezing. Symptoms then progress to a necrotizing pneumonia and severe pulmonary edema. For all exposure routes, symptoms progress over several hours to include abdominal cramping, diarrhea, anal hemorrhage, anuria, pupil dilation, fever, polydypsia, transient leukocytosis, sore throat, and headache, and within 36–72 hours to multisystem organ failure, shock, and death.

Treatment

There is no specific antidote for ricin poisoning; therefore, treatment focuses on supportive care. Patients who have been exposed to inhalational ricin should undergo general decontamination by removing all clothing and washing the skin with mild soap and water. Inhalation of ricin will require respiratory support with supplemental oxygen, and mechanical ventilation if needed. Ingestion of ricin can be treated with administration of activated charcoal if discovered early; it is most effective within the first hour. All patients exposed to ricin should receive aggressive fluid resuscitation with sodium chloride 0.9% or lactated Ringer's solution to maintain normovolemia. Electrolyte homeostasis is important, and intravenous supplementation should be given as needed.

Radiological Agents

Although the traditional notion of a nuclear war has become more remote, radiological agents pose a real threat for a terrorist attack. This type of attack is typically the least understood of all the possible threats, but one that will require specific training and preparation to adequately treat injured patients. There are five general types of radiological threats. The first involves using a simple radiological device to disperse radiation in a highly populated area, such as a mass-transit station or sporting event. Agents most likely to be used in this scenario are cobalt-60, cesium-137, and iridium-192. These agents are normally used in medical diagnostic equipment, research laboratories, and industrial facilities. The second type of threat is the use of a more complicated radiological dispersal device (commonly referred to as a "dirty bomb"). In this scenario, explosives may be attached to a simple radiological device to cause both radiological and traditional traumatic injuries. The third type of threat is the use of an improvised nuclear device, most likely by attaching explosives to uranium or plutonium from a nuclear weapon or other source. The last two threats are an attack on a nuclear reactor, considered unlikely due to the high security and containment measures in place around these facilities, and the detonation of a traditional nuclear weapon.

Radiation injury can occur from external irradiation, external contamination, internal contamination, or any of these combined with thermal or traumatic injuries. Injuries are due to exposure to the energy released from the weapon, in the form of heat, blast, or radiation. There are five types of radiation: alpha particles, beta particles, gamma rays, x-rays, and neutrons. Alpha particles are made up of two protons and two neutrons. They cannot travel far from their source, and are easily shielded by thin barriers such as clothing; therefore, external contamination is unlikely. Injury from alpha particles can occur through inhalation or ingestion, or from open wounds. Beta particles are small, negatively charged, high-energy electrons emitted from a nucleus. These particles can travel several meters through the air and can penetrate several millimeters into skin. Clothing provides some protection, and glass or plastic can provide almost complete protection. Beta particles cause direct effects to skin (known as beta burns) and to eyes (cataract lesions), and can cause carcinogenic effects to the internal organs. Neutrons are neutral particles that easily penetrate skin. They cause damage by colliding with water molecules, leading to chemical damage to the tissues. Gamma rays and x-rays are high-energy particles released from the nucleus during radioactive decay. High energy electrons passing a positive nucleus result in x-rays. Both gamma rays and x-rays are highly penetrating to skin, and lead to external injury.

Clinical Symptoms

Injury from a radiological weapon is affected by the amount of exposure time, distance from the threat, and shielding, and each will affect the severity of symptoms. The longer the exposure to radiation, the closer the distance, and the lesser the shielding will all worsen the exposure. Onset of symptoms occurs within hours to days, and begins with a prodromal phase lasting 2–4 days. Initial symptoms of radiological exposure include nausea, vomiting, and anorexia, which may persist or progress to more severe effects such as conjunctivitis, fever, respiratory distress, and erythema in larger exposures. Patients progress to the latent phase when their initial symptoms decline, which lasts 2–3 weeks. During the latent phase, stem cells in the bone marrow and cells lining the GI tract begin to decrease. Patients may appear well, but are experiencing progression of illness marked by a decrease in their white blood cells and platelet counts. After the latent phase, acute illness develops, characterized by malaise, fever, severe diarrhea, anorexia, dehydration, infection, and electrolyte disturbances. Patients may recover from the acute illness phase, or death can occur within several days to weeks.

Treatment

It can be difficult to diagnose and treat patients presenting after a radiological exposure. Depending on the exposure source, contamination may not be suspected or the radiation source will not be known. Therefore, all patients must be treated with caution, and general principles of

Leikin JB, McFee RB, Walter FG, Edsall K. A primer for nuclear terrorism. Dis Mon 2003;49:479–516.

Waselenko JK, MacVittie TJ, Blakely WF, et al. Medical management of the acute radiation syndrome: Recommendations of the strategic national stockpile radiation working group. Ann Intern Med 2004;140:1037–51.

decontamination applied to patients until the suspected agent or agents are known. Initial management is to maintain airway, breathing, and circulation, and provide close monitoring of vital signs, complete blood cell count, and electrolyte concentrations. Clothing should be removed from the body, double bagged, and removed from the treatment area to a proper radiation waste disposal site. The skin should be washed and decontaminated if possible, but treatment of traumatic injuries should not be delayed. All wounds should be treated within the first 48 hours. If surgical intervention is required, it should be performed in the first 36 hours, and no later than 48 hours after the exposure. Infection control should be strict to reduce secondary infections, and prophylactic antibiotics should be considered for patients who have significant neutropenia (absolute neutrophil count [ANC] less than 500 cells/mm^3). Recommended antimicrobial coverage includes a fluoroquinolone with streptococcal coverage (or a fluoroquinolone without streptococcal coverage plus penicillin), an antiviral drug (e.g., acyclovir), and an antifungal drug (e.g., fluconazole). Therapy should be continued until the ANC is greater than or equal to 500 cells/mm^3. Fluid resuscitation with crystalloids (sodium chloride 0.9% or lactated Ringer's solution) should be initiated to maintain normovolemia, and electrolyte supplementation given as needed.

There are several antidotes for radiation exposures. If radioactive iodine is suspected, local emergency management will use potassium iodide tablets. Potassium iodide acts as a radiation exposure antidote by saturating the thyroid gland with iodine, thereby preventing it from absorbing any radioactive iodine. It is only effective if given within 3 hours of the exposure, and does not eliminate the need for evacuation of the area. Supplies are being distributed in advance to residents living within 10 miles of nuclear power plant facilities where radioactive iodine would be expected to be released in the event of an accident. The dose of potassium iodide is a single 130-mg tablet for adults, 65 mg (one-half tablet) for children ages 3–18, 32 mg (one-quarter tablet) for children ages 1 month to 3 years, and 16 mg (one-eighth tablet) for infants up to 1 month of age given daily until environmental radioactive iodine levels are sufficiently decreased. Women who are breastfeeding should take the normal adult dose, and their infant the usual infant dose. Children weighing more than 150 pounds (68 Kg) should take the adult dose regardless of age. Adverse effects associated with potassium iodide include fever, rash, nausea, stomach pain, and metallic taste. Potassium iodide will be made available from local, state, and federal resources in the event of an attack; however, because it is an over-the-counter product, it can be purchased from most pharmacies, health and nutrition stores, and from the Internet.

If a patient has a known or suspected internal contamination with cesium or thallium, it may be treated with ferric hexacyanoferrate (Prussian blue), an ion exchange resin that binds and prevents absorption of these agents. The dose for children over age 2, adults, and breastfeeding women is initially 3 g 3 times/day for a minimum of 30 days. The dose can be reduced to 1–2 g 3 times/day when internal symptoms decline (i.e., reducing GI tract symptoms and normalizing white blood cell counts). Prussian blue is available in 500-mg capsules, which can be opened and mixed with food or beverages if patients are unable to swallow the capsules whole. Adverse effects include nausea, constipation, and a blue discoloration of teeth and feces (from the opened capsules).

Two heavy metal chelators have been approved for treating patients with known or suspected internal contamination from plutonium, americium, or curium. Calcium diethylenetriaminepentaacetate (Ca-DTPA; pentetate calcium trisodium injection) is more effective in the first 24 hours, and is given as the initial dose, followed by daily dosing with zinc diethylenetriaminepentaacetate (Zn-DTPA; pentetate zinc trisodium injection) for the duration of therapy (duration is determined by the amount of radiation exposure). If Zn-DTPA is unavailable, or in the case of pregnant women, Ca-DTPA is given for the duration of therapy, but is not preferred due to a higher adverse effect profile. The dose of both drugs is 1000 mg intravenously for adults, and 14 mg/kg (not to exceed 1 g) intravenously for children under age 12. The dose is given over 3–4 minutes as a slow intravenous push or over 30 minutes by infusion diluted in 100–250 mL dextrose 5% in water, 0.9% sodium chloride, or lactated Ringer's solution. If inhalation is the only exposure route, Ca-DTPA and Zn-DTPA can be given by nebulized inhalation diluted 1:1 with sterile water or saline. Adverse effects are mostly associated with Ca-DTPA and include headache, lightheadedness, chest pain, pruritus, dermatitis, metallic taste, nausea, diarrhea, and injection-site reactions. Prolonged therapy with these two drugs can result in a depletion of electrolytes or minerals (e.g., zinc, magnesium, or manganese); therefore, electrolyte concentrations should be monitored frequently. Good clinical practice would be to monitor electrolytes or minerals daily until stable, then 2–3 times/week). Nebulized therapy may be associated with an exacerbation of asthma, and care should be taken if patients experience these symptoms.

Institutional Preparedness

Federal resources will be available in the event of a weapons of mass destruction (WMD) event, but these resources may not be of sufficient supply or arrive quickly enough to assist in treating the earliest victims and providing prophylaxis for hospital employees. Hospital pharmacies need to develop individualized emergency preparedness plans, in conjunction with the SNS and Chempack system.

The SNS is a federal resource that was developed and is maintained by the Centers for Disease Control and Prevention. The SNS serves as a national repository to assist in the emergency response to a WMD event. Activation of the SNS is made through a request from a state government (usually the governor or designated agent) directly to the Centers for Disease Control and Prevention. The SNS contains antibiotic drugs, chemical antidotes, intravenous administration supplies, airway maintenance supplies, and other medical and surgical items in containers referred to as "push packs" designed for ease of transport. Once the SNS is activated, the push packs will arrive within 12 hours, either by truck or by air transport to a receiving, storing, and staging site designated by the state. Once the push packs

arrive at their destination, they have to be broken down and then transported to their final destination for distribution to the public or to hospitals. The SNS antibiotic inventory contains adequate supplies to treat 10,000 patients for 3 days or 1000 patients for 60 days. If additional supplies are needed to supplement the SNS, if needed items are not in the initial SNS inventory, or once the specific threat has been identified, a vendor-managed inventory may be used. Examples of items available through vendor-managed inventory include portable ventilators, additional antibiotic drugs, and vaccines.

The Chempack program responds to chemical attacks, where antidotes are needed more quickly than can be supplied by the SNS. Participation in the Chempack program is voluntary, and is determined by the states in conjunction with local communities. Chempacks consist of two separate containers, one designated for use by emergency responders and the other for hospital use. Each container consists of enough atropine, 2-PAM, diazepam, and Mark-1 kits to treat 1000 patients. The difference in the two containers is that the one designated for emergency responder use has more doses in the autoinjector form, as opposed to more multi-use vials in the hospital container. Once a site is chosen to participate in the Chempack program, the site must agree to store, monitor, maintain, and dispense the containers as needed. The containers are required to be in a secure location with adequate space and ventilation, and must be kept between 59°F and 86°F at a humidity level less than 60%. Each Chempack container also requires a dedicated power source and phone line, which allows it to be continuously monitored by the Centers for Disease Control and Prevention.

Although these resources are vital to the response to a WMD event, hospitals must develop and practice an emergency preparedness response plan, which includes a plan for acquiring and stocking of antibiotic drugs and antidotes. The plan should be based on the institution's disaster plan, and should be shared with other departments within the institution. The plan should be updated on a regular basis. One key component of a plan is to complete a threat assessment for the region. The purpose of the assessment is to look at the risk level and impact of each type of disaster, which allows for the response plan to focus on areas considered higher risk and higher impact. In addition to WMD events, natural disasters such as earthquakes, tornados, and hurricanes should also be included in this assessment plan.

Educating pharmacy staff about the specifics of the plan is important, and copies of the plan should be disseminated to all staff members. A copy of the plan should be kept on a shared computer drive that can be accessed by all staff members; however, a paper copy should also be available in case of an electrical outage. It is suggested that some or all of the following items be included in the plan: definitions of biological, chemical, and radiological agents; possible event scenarios for a WMD event and natural disasters; treatment protocols or algorithms with standardized order forms; plan for distribution of prophylaxis drugs to hospital employees, patients, and visitors; a listing of the pharmacy's primary wholesaler contacts with alternates; and a listing of Web-based and telephone resources to obtain additional information. To prepare for the large-scale dispensing during an event, preprinted labels for intravenous and oral dosage forms, patient education sheets, and record keeping forms can be created in advance and stored in key locations. Pharmacists should work with their state and local SNS coordinators to make sure that institutional or departmental planning is consistent with state and local plans.

The American Society of Health-System Pharmacists has published a statement on the role of pharmacists in emergency preparedness. The position of the American Society of Health-System Pharmacists is that pharmacists must assertively exercise their responsibilities in preparing for and responding to disasters, and that leaders in emergency preparedness on all levels should call on pharmacists to participate in all aspects of planning regarding the use of pharmaceuticals in these situations. Included in the position statement is a list of advice for hospital and health-system pharmacy directors, pharmacists, administrators, planners, and state pharmaceutical societies. Specifically for pharmacists, the American Society of Health-System Pharmacists' recommends that all pharmacists become knowledgeable on the local history and potential for disasters, as well as potential agents for use during WMD events; become informed on local and institutional preparedness plans; share evidenced-based information on disaster-related pharmaceuticals with colleagues and patients; act assertively to prevent and allay panic and irrational responses to disasters; strongly discourage individuals from developing personal stockpiles of pharmaceuticals; consider volunteering to assist in disaster response; and develop and maintain first-aid skills and basic cardiac life support certification. The American Society of Health-System Pharmacists position statement serves as an excellent starting point for institutions that need to develop a plan or improve their existing plan. The American Society of Health-System Pharmacists has also created an emergency preparedness Web site, which can be accessed at *http://www.ashp.org/emergency/index.cfm?cfid=2038631&CFToken=93012317*.

Some hospitals have taken emergency preparedness a step further. They have created teams of pharmacists dedicated to emergency response or have developed citywide response plans. An example of this approach is the pharmacy emergency response team developed at Maimonides Medical Center in Brooklyn, New York. The pharmacy emergency response team, consisting of three branches, was designed to establish command and control, conduct disaster needs analysis, identify agents involved, perform emergency cart-fill, develop resources and training, and to conduct practice drills. The first branch is command, and consists of a pharmacy administrator, drug information specialist, and a hazardous material pharmacist. The second branch is administrative, and consists of administrative support, including information systems and purchasing. The third branch consists of the clinical staff, including psychiatry, critical care, infectious disease, and nuclear specialists. The command branch is responsible for

ASHP Statement on the Role of Health-System Pharmacists in Counterterrorism. Am J Health-Syst Pharm 2002;59:282–3.

Cohen V. Organization of a health-system pharmacy team to respond to episodes of terrorism. Am J Health-Syst Pharm 2003;60:1257–63.

planning, organizing, and coordinating all aspects of the pharmacy department's activities during a disaster response. The administrative branch is responsible for backing up computer systems, purchasing, and setting up auxiliary dispensing sites if needed. The clinical pharmacists who compose the clinical branch are responsible for coordinating efforts in their respective specialty areas.

City-wide cooperation is strongly encouraged during disasters, especially in maintaining local stockpiles of pharmaceuticals. Having a list of neighboring hospitals' antidote inventory is beneficial and may help avoid hoarding and overstocking of drugs and antidotes. Having an inventory list also allows for sharing of these supplies when needed. Sharing each institution's emergency preparedness plans in this manner helps to make the community response, as well as each individual hospital's response, stronger.

Conclusion

Preparing pharmacists for response to emergency events, whether for victims of acute poisonings or WMD events, is essential for all institutions. The role of the pharmacist in providing drug information, doses of antidotes, and patient counseling is crucial. Institutions should be made aware of this role and be given updated contact information for pharmacists in the event of an emergency. Although many possible WMD agents have not been implicated in recent attacks, the events in Madrid, London, and Egypt within the past year serve as a reminder of the importance of being ready to respond in the event that a chemical or radiological weapon is used.

Annotated Bibliography

1. Watson WA, Litovitz TL, Klein-Schwartz W, et al. 2003 Annual Report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 2004;22:335–404.

   This annual report of toxic exposures from the American Association of Poison Control Centers (AAPCC) is updated annually, and published in the September issue of the American Journal of Emergency Medicine. The report summarizes all toxic exposures reported to the AAPCC in the previous year. Statistics on all aspects of the incidents, including the ages of patients, location of the incident, types of agents involved, and types of antidotes used are included. It also provides a breakdown of the most common agents associated with both childhood and adult poisonings. Previous reports can also be found online at *www.aapcc.org*.

2. Zimmerman JL. Poisonings and overdoses in the intensive care unit: general and specific management issues. Crit Care Med 2003;31:2794–2801.

   Although this article summarizes recommendations for common overdoses that may be encountered in an intensive care unit, it is a concise review that can be used by all clinical practitioners. An overview of general decontamination is well summarized in a table format. A brief, but informative, overview is provided for managing overdoses from acetaminophen, alcohols, β-blockers, calcium channel blockers, carbon monoxide, tricyclic antidepressants, cocaine, lithium, salicylates, opioids, nerve agents, and some alternative drugs. The article is a good starting point for additional information on acute poisonings and their antidotes, and as a quick reference guide for most situations.

3. Farmer JC, Jimenez EJ, Talmor DS, Zimmerman JL. Fundamentals of Disaster Management. Des Plaines, IL: Society of Critical Care Medicine, 2003:1–141.

   This hand-held book was designed to complement the Fundamentals of Disaster Management course offered as part of the Fundamental Critical Care Support program developed by the Society of Critical Care Medicine. The book is spiral-bound and printed on water-resistant paper to withstand the elements during use. It is written for the general health care provider to aid in effective disaster response. The chapters include summaries on disaster communication, mass casualty medical management, and overviews of biological, chemical, radiological, and natural disaster events. Key information is summarized in an easy-to-find table format. Most of what a practitioner would need for disaster management and emergency preparation is contained in this text.

4. Krenzelok EP. ed. Biological and Chemical Terrorism: A Pharmacy Preparedness Guide. Bethesda, MD: American Society of Health-System Pharmacists, 2003:1–232.

   This text is a compendium of resources compiled by the American Society of Health-System Pharmacists. Although it was published in 2003, most of the information is still up to date. It is divided into four sections: a history of biological and chemical terrorism, a review of the biological and chemical agents, reference resources on the biological and chemical agents, and hospital preparedness. Each section contains an introduction and overview of its intended topic, and provides a compendium of several key reprinted articles that are essential for any practitioner.

5. Farmer JC, Currie B, Kvetan V, eds. Critical Care Medicine for Disasters, Terrorism, and Military Conflict. Crit Care Med 2005;33(suppl 1):S1–S112.

   This supplement to Critical Care Medicine provides a discussion of real case management for several recent disaster scenarios. It is written more for the general intensivist, but is pertinent to all health care professionals interested in disaster response. The advantage of this supplement is that unlike other disaster management resources, it allows the reader to understand the successes and failures of the responses to events including September 11, the Toronto Severe Acute Respiratory Syndrome (SARS) experience, and the 2003 power outages on the east coast of the United States. Also included are several key treatment articles and reviews on public health issues and institutional preparedness.

Abbreviations

SELF-ASSESSMENT QUESTIONS

Questions 1–3 pertain to the following case.
T.S. is a 42-year-old woman who after an argument with her husband took 100 500-mg caplets of acetaminophen. Upon returning home 4 hours later, T.S.'s husband discovers the ingestion and brings her to the emergency department. Six hours after ingestion, the acetaminophen level was 243 mcg/mL. She is experiencing nausea and vomiting. Her vital signs are blood pressure 135/90 mm Hg, heart rate 83 beats/minute, respiratory rate 18 breaths/minute, temperature 101.8°F. Her height is 5'6", and weight is 176 pounds. Her aspartate transaminase was 24 IU/L, and alanine transaminase was 32 IU/L. The emergency department physician asks you to evaluate T.S. for possible acetaminophen toxicity.

1. Which one of the following best assesses T.S.'s risk for acetaminophen toxicity?
   A. Presence of nausea, vomiting, and abdominal pain.
   B. The amount of acetaminophen ingested.
   C. Rumack-Matthew nomogram.
   D. Elevated liver transaminase concentrations.

2. The physician places an orogastric tube in T.S. Which one of the following general management strategies is most indicated for T.S.?
   A. Administer magnesium citrate 10% 240 mL per tube once.
   B. Stabilize the patient.
   C. Perform gastric lavage.
   D. Administer activated charcoal 25 g per orogastric tube once.

3. Which one of the following best describes the use of *N*-acetylcysteine for treatment of T.S.'s acetaminophen toxicity?
   A. *N*-acetylcysteine 11,200 mg oral bolus, followed by 5600 mg orally every 4 hours for 17 dosages.
   B. *N*-acetylcysteine 11,200 mg intravenous bolus, followed by 5600 mg intravenously every 4 hours for 12 dosages.
   C. *N*-acetylcysteine 12,000 mg intravenously over 1 hour followed by 4000 mg intravenously over 4 hours, then 8000 mg intravenously over 16 hours.
   D. *N*-acetylcysteine therapy is not indicated in this patient.

Questions 4–6 pertain to the following case.
K.C. is a 44-year-old woman who presents to the emergency department appearing inebriated and complaining of abdominal pain. She reports drinking an unknown amount of antifreeze that was mixed with cola a little more than an hour ago.

4. Which one of the following laboratory tests would provide the most accurate information based on K.C.'s presentation?
   A. A renal panel to determine the anion gap.
   B. A Wood's lamp test.
   C. The serum osmolar gap.
   D. A renal panel to determine the estimated creatinine clearance.

5. Laboratory analysis indicates a sodium level of 143 mEq/L, potassium 3.9 mEq/L, blood urea nitrogen 21 mg/dL, serum creatinine 1.4 mg/dL, osmolar gap 18 mOsm/kg of water, and an ethylene glycol level of 63 mg/dL. Which one of the following is the best therapy for K.C. at this time?
   A. Alcohol 5% in dextrose 5% water titrated to a serum ethanol level of 0.1 mg/dL.
   B. Activated charcoal.

C. Fomepizole 1200 mg then 800 mg every 12 hours for four dosages, then 1200 mg every 12 hours until serum ethylene glycol levels are less than 20 mg/dL.
D. Thiamine 100 mg/day intravenously and pyridoxine 50 mg/day intravenously.

6. Despite appropriate initial treatment, 4 hours after presentation K.C. is becoming confused, slurring her speech, and is having hallucinations. Laboratory evaluation indicates an anion gap of 25, blood urea nitrogen 42 mg/dL, and serum creatinine 2.8 mg/dL. Her blood gas is pH 7.2, pCO_2 21 mm Hg, HCO_3 8 mEq/L. Which one of the following is the best option at this time to add to her treatment?
   A. Sodium bicarbonate.
   B. Coma cocktail.
   C. Thiamine and pyridoxine.
   D. Hemodialysis.

Questions 7–9 pertain to the following case.
L.K. is an 82-year-old man admitted to the emergency department with complaints of dizziness and headache. His vital signs are temperature 98.9°F, blood pressure 87/50 mm Hg, and heart rate 62 beats/minute. L.K.'s wife reports that he has a history of hypertension, and was recently diagnosed as being in the early stages of Alzheimer's disease. She brought his drugs (refilled 2 days ago) with her. They include a bottle of nifedipine XL 60 mg/day (seven tablets remaining; quantity dispensed: 30), and a bottle of galantamine 4 mg 2 times/day (56 tablets remaining; quantity dispensed: 60).

7. Which one of the following decontamination strategies would provide the most benefit for L.K.?
   A. Activated charcoal 25 g every hour until his blood pressure improves.
   B. Syrup of ipecac 30 mL followed by 240 mL of water.
   C. Polyethylene glycol-electrolyte solution 1500 mL/hour until the rectal effluent is clear.
   D. Magnesium citrate 240 mL followed by 240 mL of water.

8. Which one of the following antidotes should be administered first to L.K.?
   A. Calcium chloride 1 gram intravenously.
   B. Glucagon 5 mg intravenously.
   C. Atropine 1 mg intravenously.
   D. Epinephrine 1 mg intravenously.

9. After several doses of an appropriate antidote, L.K.'s blood pressure improved slightly, but remains low. Which one of the following continuous infusions should be administered and titrated to effect at this time?
   A. Epinephrine 1 mcg/minute.
   B. Dopamine 5 mcg/kg/minute.
   C. Milrinone 0.375 mcg/kg/minute.
   D. Glucagon 2 mg/hour.

10. A 37-year-old man is admitted to the emergency department 90 minutes after taking 50 100-mg theophylline controlled release tablets. The paramedics indicate that his initial symptoms were nausea and vomiting. His vitals are temperature 99.1°F, blood pressure 97/40 mm Hg, respiratory rate 19 breaths/minute, and heart rate 160 beats/minute. A serum theophylline concentration drawn on admission is 57 mcg/mL. Which one of the following decontamination strategies is most appropriate for this patient?
   A. Activated charcoal 50 g, then 12.5 g every hour until clinical symptoms improve.
   B. Syrup of ipecac 30 mL once, given with 240 mL of water.
   C. Immediate gastric lavage, performed until the gastric effluent is clear.
   D. Activated charcoal 50 g once and routine clinical monitoring.

11. S.W. is a 52-year-old woman who is brought to the emergency department with complaints of acute respiratory distress, sore throat, and cough. She is one of several patients that have been admitted after a suspected vesicant agent exposure. S.W. reports no previous medical history, and is allergic to penicillin. Her clinical symptoms include nausea and abdominal pain, blurred vision, and itching. Which one of the following is the best approach to managing S.W.'s vesicant exposure?
   A. Observe closely for additional clinical effects that may present in the next 24 hours.
   B. Emergently intubate to prevent development of pulmonary symptoms.
   C. Administer British anti-lewisite.
   D. Immediately apply neutropenic precautions.

Questions 12–14 pertain to the following case.
K.S. is a 24-year-old man who is the first patient admitted to the emergency department after a release of VX gas in the lobby of the convention center. He was decontaminated at the scene and given two doses of atropine 2 mg by the paramedics, the most recent being given 2 minutes before he was brought into the emergency department. He is experiencing severe respiratory distress, is tachycardic, and has begun having convulsions. Intravenous access has not been established.

12. Which one of the following therapies is the most appropriate for K.S. at this time?
   A. Administer diazepam 5 mg intramuscularly and give repeat doses as needed.
   B. Intubate K.S. and administer atropine 2 mg via the endotracheal tube.
   C. Give atropine 1 mg intramuscularly in 2–5 minutes and give repeat doses as needed.
   D. Proceed with immediate decontamination of K.S. by removing his clothing and thoroughly washing the skin.

13. Which one of the following signs and symptoms are the most problematic initially for the clinician caring for a patient with nerve gas exposure who requires immediate attention?
    A. Ocular pain, miosis, and blurred vision.
    B. Bronchoconstriction, cough, and dyspnea.
    C. Profuse sweating and muscle fasciculation.
    D. Bradycardia and first-degree heart block.

14. The emergency department physician wants to give K.S. 1 g of pralidoxime (2-PAM). An infusion of 1 g in 250 mL is started at an infusion rate of 750 mL/hour. Five minutes into the infusion, K.S. begins to experience hypertension. The nurse taking care of him asks you what to do. Which one of the following is the most appropriate response?
    A. Discontinue the infusion of 2-PAM immediately and start an atropine infusion.
    B. Continue the current infusion rate of 2-PAM and monitor the blood pressure every 5 minutes.
    C. Slow the infusion rate to 375 mL/hour and monitor the blood pressure every 5 minutes.
    D. Add labetalol 10 mg intravenously as needed.

Questions 15 and 16 pertain to the following case.
G.F. is a 43-year-old man who is admitted for worsening respiratory distress after a cyanogen chloride exposure at a local manufacturing facility. His complaints include dizziness, headache, and nausea without vomiting. G.F.'s medical history includes type 2 diabetes mellitus and hypertension, for which he is taking glyburide 10 mg once daily and lisinopril 5 mg once daily. His vital signs are temperature 99.8°F, blood pressure 120/75 mm Hg, heart rate 82 beats/minute, and respiratory rate 18 breaths/minute. A recent arterial blood gas shows pH 7.15, partial pressure of carbon dioxide 37 mm Hg, partial pressure of oxygen 65 mm Hg, bicarbonate 15 mEq/L, with an oxygen saturation by pulse oximetry of 98%.

15. Which one of the following represents the most appropriate initial therapy for G.F.?
    A. Inhale the contents of an amyl nitrite ampule.
    B. Give 2 L oxygen via face mask.
    C. Infuse a 1 L bolus of 0.9% sodium chloride.
    D. Immediately intubate G.F.

16. The hospital's supply of cyanide antidote kits has been depleted in the treatment of other victims of this exposure, and the hospital has been told to expect more patients to arrive. Which one of the following represents the most appropriate option for acquiring additional antidote?
    A. Borrow two cyanide kits that are available from a nearby hospital.
    B. Produce doses of sodium nitrite from a supply of bulk powder found in the pharmacy storeroom.
    C. Contact the hospital's main wholesaler to acquire additional antidote kits.
    D. Produce doses of sodium thiosulfate from a supply of bulk powder found in the pharmacy storeroom.

17. D.C. is an 8-year-old boy admitted to the emergency department for severe respiratory distress after he was playing in the garage of his home and opened a large bucket of swimming pool chemicals. His complaints include severe nausea, burning of the eyes, shortness of breath, chest tightness, wheezing, and a severe cough. Which one of the following treatments would be the most beneficial based on D.C.'s clinical symptoms?
    A. Administer methylprednisolone 125 mg intravenously every 6 hours for 24 hours.
    B. Remove D.C.'s clothing and wash the skin with soap and water.
    C. Administer mechanical ventilation with 100% oxygen and maximal positive end-expiratory pressure.
    D. Administer albuterol 2.5 mg via nebulizer as needed for his respiratory symptoms.

18. B.A. is a 23-year-old woman admitted to the emergency department at 9 AM after reportedly consuming 12–15 castor beans the previous evening in a suicide attempt. Further questioning reveals that she chewed and swallowed the beans. Her complaints include headache, sore throat, thirst, severe abdominal cramps, and diarrhea. Her vitals signs are temperature 101.8°F, blood pressure 125/70 mm Hg, heart rate 78 beats/minute, and respiratory rate 15 breaths/minute. Which one of the following is the most appropriate treatment for B.A.?
    A. Vasopressors.
    B. Activated charcoal.
    C. Aggressive fluid resuscitation
    D. General decontamination.

Questions 19–21 pertain to the following case.
R.S. is a 42-year-old man admitted to the emergency department after an explosion at a bus terminal. His injuries include an open right ulnar fracture with second-degree burns (7% total body surface area) after being hit by a burning piece of shrapnel. He begins to complain of severe nausea and vomiting, and his vitals signs are temperature 101.7°F, heart rate 88 beats/minute, blood pressure 137/88 mm Hg, and respirations 18 breaths/minute. R.S. is suspected to have been exposed to a radiological weapon.

19. Which one of the following is the most important approach to making an initial assessment of R.S.'s severity of exposure?
    A. Complete blood cell count.
    B. Question R.S. about his location relative to the explosion and amount of time he was exposed.
    C. Survey the type of clothing R.S. was wearing.
    D. Electrolyte concentrations.

20. Which one of the following describes R.S.'s greatest risk in the next 48–72 hours?
    A. Secondary infection.
    B. Improper bone healing due to delayed surgery.
    C. Fluid overload.
    D. Worsening nausea and vomiting.

21. The source of radiation was determined to be curium, and the health department is recommending that contaminated victims should be treated. Which one of the following is the most appropriate initial treatment for R.S.?
    A. Zinc diethylenetriaminepentaacetate (Zn-DTPA).
    B. Calcium diethylenetriaminepentaacetate (Ca-DTPA).
    C. Ferric hexacyanoferrate.
    D. Potassium iodide.

22. A 34-year-old woman who resides 5 miles from a nuclear power facility requests doses of potassium iodide from the local health department. She needs doses for herself, her 5-year-old son, and her 3-month-old daughter who is breastfeeding. Which one of the following is the best to treat her infant if an exposure occurs?
    A. 32 mg/day.
    B. 65 mg/day.
    C. 16 mg/day.
    D. Dosing is not needed as long as the mother continues to breastfeed.

Questions 23–25 pertain to the following case.

K.R. is the lead pharmacist at a community hospital located outside a large metropolitan area. She has been asked by the pharmacy director to develop an emergency preparedness plan for the pharmacy department. K.R. is overwhelmed by the magnitude of preparing the emergency preparedness plan.

23. Which one of the following resources will best assist her in prioritizing her approach to preparing the plan?
    A. Review the applicable regional threat assessment.
    B. Read the American Society of Health-System Pharmacists statement on the role of pharmacists in counterterrorism.
    C. Contact her state Strategic National Stockpile Coordinator.
    D. Create a pharmacy emergency response team.

24. Which one of the following is the most important first step for K.R. to take before developing the pharmacy's plan for responding to a chemical attack?
    A. Determine the proximity of her hospital to the Strategic National Stockpile staging site.
    B. Assess her state's participation in the Chempack program.
    C. Collect emergency preparedness plans from the metropolitan hospitals.
    D. Compile a list of neighboring hospital's antidote inventory.

25. K.R. has contacted other hospitals in the area to help develop a community-wide response plan. Which one of the following would contribute the most to this plan's success?
    A. Develop a list of antidote supplies stocked by each hospital.
    B. Appoint one hospital to take the lead role in community planning.
    C. Plan for each institution to use one wholesaler to avoid confusion.
    D. Meet on an annual basis to coordinate and update the community-wide plan.