# 2 Emergency Management of Poisoning

## A A General Approach to Poisoning

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Medical toxicology is one of the most important and dynamic fields in medicine today, since the practicing physician is continually faced with the management of poisoning, drug overdose, and adverse drug effects. The abuse of both prescription and illicit drugs in the United States continues unabated. Because the process of drug approval is more rapid, it is often not until the agent has been in use for some time, during the postmarketing period, before its toxicity is fully appreciated.

Defining the incidence of human poisoning is not easy. There are multiple sources of data on drug overdose and substance abuse. The Toxic Exposure Surveillance System (TESS) of the American Association of Poison Control Centers tabulates referrals for human poisoning called into the nation's poison centers. In 2004, it recorded 2,395,582 exposures, with 1106 deaths; analgesics were the most common cause of a fatal outcome.[1] The National Institute of Drug Abuse surveys emergency department visits through its Drug Abuse Warning Network (DAWN), and in 2002 reported that a total of 4427 deaths resulted from drug abuse, with cocaine being the most commonly implicated agent.[1,2]

However, these sources vastly underestimate the number of toxic events in humans. For example, reports of intoxicated patients who die from trauma, drowning, and fires are not consistently included in any national data set, nor are those of patients with medical complications from therapy, such as chemotherapy or anesthetics. Morbidity that results from chronic abuse (e.g., heart disease from cocaine or nicotine abuse and cirrhosis from alcohol abuse) or industrial exposures, and the long-term effects of environmental hazards, is not rigorously compiled and is probably impossible to quantify.

The most common causes of poisoning-related death in the United States have been carbon monoxide poisoning, cocaine use, and tricyclic antidepressant overdose.[1] Poisoning with analgesics, aspirin, and acetaminophen also remains a leading cause of death. Calcium channel blocker overdose has surpassed digitalis overdose as the most common cause of cardiovascular drug-related death.

### DEFINITION

*To poison* means to injure or kill with a substance that is known or discovered to be harmful. Thus, the term *poisoning* connotes clinical symptomatology. It also implies that the toxic exposure is unintentional (e.g., in the case of an elderly patient who misreads a drug label). In contrast, the term *overdose* implies intentional toxic exposure, either in the form of a suicide attempt or as inadvertent harm secondary to purposeful drug abuse. The terms *poisoning* and *drug overdose* often are used interchangeably, especially when prescription drugs are the agents, even though by definition a drug overdose does not produce poisoning unless it causes clinical symptoms.

Poisoning has a bimodal incidence, occurring most commonly in children who are 1 to 5 years of age and in the elderly. Overdose, whether motivated by suicidal intent or the result of abuse, occurs through adulthood. Toxic exposure in those between the ages of 6 and 12 years is uncommon; when it occurs, the patient must be assessed carefully to ensure that psychiatric follow-up is provided when indicated.[1]

### THE GENERAL APPROACH TO POISONING

The general approach to the poisoned patient can be divided into six phases: (1) stabilization; (2) laboratory assessment; (3) decontamination of the gastrointestinal tract, skin, or eyes; (4) administration of an antidote; (5) elimination enhancement of the toxin; and (6) observation and disposition.

#### *Emergency Management*

Because overdose patients are often clinically unstable when discovered, resuscitation with establishment of the airway, adequate support of ventilation and perfusion, and maintenance of all vital signs (including temperature) must be accomplished first. Continuous cardiac and pulse oximetry monitoring is essential. Rapid-sequence intubation (RSI) may be indicated in patients with an airway in jeopardy. Naloxone, 2 mg intravenously (IV); thiamine, 100 mg intravenously (IV); and 50% dextrose, 50 mL IV (if patients are shown on Dextrostix testing to be hypoglycemic) are generally given to all adults in coma, once an IV line has been established and appropriate blood studies have been performed.[3,4] Maintenance of blood pressure and tissue perfusion may require the provision of volume, correction of acid-base disturbance, administration of pressor agents, and antidotal therapy. Table 2A-1 lists the common emergency antidotes.

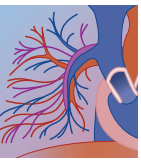




**TABLE 2A-1 Common Emergency Antidotes**

| POISON | ANTIDOTE | DOSE* | COMMENTS |
|---|---|---|---|
| Acetaminophen | *N*-acetylcysteine | 140 mg/kg initial oral dose, followed by 70 mg/kg every 4 hr × 17 doses<br>or<br>intravenously as 150 mg/kg × 15 minutes then 50 mg/kg × 4 hr then 100 mg/kg × 16 hr | Most effective within 16–24 hr; may be useful after chronic intoxication |
| Atropine, anticholinergics | Physostigmine | Initial dose 0.5–2 mg (IV); children, 0.02 mg/kg | Can produce convulsions, bradycardia |
| Benzodiazepines | Flumazenil | 0.2 mg (2 mL) (IV) over 15 sec; repeat 0.2 mg (IV) as necessary; initial dose not to exceed 1 mg | Limited indications; recommended only for reversal of pure benzodiazepine sedation |
| β blockers | Glucagon | Adult: 5–10 mg (IV) initially<br>Child: 50–150 ug/kg (IV) initially<br>Continuous infusion as needed | Stimulates cAMP synthesis, increasing myocardial contractility |
| Calcium channel blockers | Calcium chloride 10% | 1 g (10 mL) (IV) over 5 min as initial dose; repeat as necessary in critical patients; doses up to 10 g may be necessary to restore blood pressure | Avoid extravasation; tissue destructive |
| | Insulin/glucose | 0.5–1.0 U/kg initially then 0.5–1.0 U/kg/hr as needed to maintain systolic blood pressure | Monitor serum potassium and glucose |
| Carbon monoxide | Oxygen | 1–3 atmospheres | Hyperbaric oxygen may be indicated |
| Cyanide | Amyl nitrite, then sodium nitrite, then sodium thiosulfate | Administer pearls every 2 min<br>Adult: 10 mL of 3% solution over 3 min (IV)<br>Child: 0.33 mL (10 mg of 3% solution)/kg over 10 minutes<br>Adult: 25% solution, 50 mL (IV) over 10 minutes<br>Child: 25% solution, 1.65 mL/kg | |
| Digitalis | Digoxin antibody fragments | Varies by patient weight, serum digoxin concentration, and/or dose ingested | |
| Hydrofluoric acid | Calcium | Topical exposure: Apply calcium gluconate gel; if pain is not relieved, administer 10% calcium gluconate 10 mL in 40 mL $D_5W$ via IV (Bier block) infusion; if pain is not relieved, administer calcium gluconate by intra-arterial infusion over 4 hr<br>Ingestion: 10% calcium gluconate (IV) | Monitor for hypocalcemia; treat electrolyte disturbances aggressively |
| Iron | Deferoxamine mesylate | Initial dose: 40–90 mg/kg (IV or IM), not to exceed 1 g;<br>Infusion: 15 mg/kg hr (IV) | Higher infusion doses may be needed in severe overdose to achieve chelant excess; monitor and treat hypotension |
| Metals | | | |
| Mercury<br>Arsenic<br>Gold | British antilewisite (BAL), also known as dimercaprol | 4-6 mg/kg IM, every 4–8 hr | Contraindicated if patient has a peanut allergy or G6PD deficiency |
| Lead | DMSA (succimer), $CaNa_2$ EDTA | 10 mg/kg/dose, bid × 28 days<br>35–50 mg/kg/day (maximum 1.0–1.5g), bid or as a continuous infusion | Monitor liver function tests, add BAL if lead level > 70 μg/dL in children, > 100 μg/dL in adults |
| Methanol | Ethyl alcohol | 500 mg/kg of 10% ethanol, then continuous infusion of 100 mg/kg/hr | Watch for hypoglycemia, hypothermia, and lethargy in children; solution is hyperosmolar, requiring central venous catheter in children; maintain serum ethanol concentration at 100 mg/dL |
| | Fomepizole | 15 mg/kg loading dose, 10 mg/kg every 12 hr IV | Significantly safer than ethanol |
| Nitrites (and other methemoglobin formers) | Methylene blue | 1–2 mg/kg of 1% solution (IV) over 5 min | Can produce hemolysis in high dose; give no more than 7 mg/kg/day in adults, 4 mg/kg/day in children; severe or resistant cases may require exchange transfusion |

*Continued*

**TABLE 2A-1 Common Emergency Antidotes (*Cont'd*)**

| POISON | ANTIDOTE | DOSE* | COMMENTS |
|---|---|---|---|
| Opiates and opioids | Naloxone | Adults: 0.4–2.0 mg (IV or IM)<br>Child: 0.01–0.1 mg/kg (IV or IM) | Larger doses may be necessary after severe overdose or overdose of synthetic agent, e.g., propoxyphene |
| | Nalmafene | Adult: 1 mg (IV)<br>Child: 0.25 ug/kg (IV) | |
| Organophosphates, nerve agents<br>Carbamates (severe exposure) | Atropine | Adult: 0.5–2 mg IV<br>Child: 0.05 mg/kg<br>Child: 0.05 mg/kg | Enormous doses of atropine may be needed in severe cases |
| | Pralidoxime (2-PAM) | Adult: 1 g (IV) then 500–1000 mg/hr as needed<br>Child 15–40 mg/kg then 15–40 mg/kg/hr | Must be added to atropine if nicotinic or central symptoms are present |
| Tricyclic antidepressants | Sodium bicarbonate | Sodium bicarbonate 1–2 ampules (IV), bolus or infusion | Administer if QRS interval is ≥ 100 msec; maintain serum pH at 7.45–7.55; avoid severe alkalosis |

cAMP, cyclic adenosine monophosphate; DMSA, dimercaptosuccinic acid; EDTA, ethylenediaminetetraacetic acid; G6PD, glucose-6-phosphate deficiency; IM, intramuscularly; IV, intravenously.
*Dosage listed may require modification or adjunctive therapy according to specific clinical conditions; see each specific chapter for details.

**BOX 2A-1 CLINICAL CONDITIONS AND EXAMPLE AGENTS IN THE POISONED PATIENT THAT MAY NECESSITATE ENDOTRACHEAL INTUBATION**

Corrosive ingestion (sodium hydroxide, sulfuric acid)
Corrosive inhalation (ammonia, chlorine)
Envenomation (hymenoptera, crotalid)
Anaphylaxis (hymenoptera)
Pulmonary edema (opioids, chemical weapons [e.g., choking agents])
Bronchorrhea (organophosphates or nerve agents)
Severe central nervous system (CNS) depression (ethanol, opioids, barbiturates)
Cerebrovascular accident (cocaine)
Seizures (isoniazid, theophylline)
Aspiration (hydrocarbons)
Hypercarbia (CNS depressants, nerve agents, botulism)

## ADVANCED AIRWAY MANAGEMENT

In addition to basic airway management, many victims of poisoning require advanced management that includes endotracheal intubation. Clinical situations in which endotracheal intubation may be necessary in poisoned patients are numerous (Box 2A-1). Intubation offers the advantages of complete airway control, protection from aspiration of gastric contents, provision of a route for suctioning of secretions, and a means of optimizing both oxygenation and ventilation. However, the process of intubating an awake patient is difficult and is associated with potential adverse effects, including coughing, gagging, vomiting, tachycardia or bradycardia, hypertension, hypoxia, and increased intracranial pressure. Moreover, emergency intubation can be challenged by vocal cords that are obscured by secretions, unusual airway anatomy, a full stomach, or active vomiting. Therefore, this task requires a thorough understanding of advanced airway management principles and of their application in a manner that prevents worsening of the clinical situation. RSI is a method of rapidly obtaining airway control with minimal physiologic disturbance. The process of RSI involves a patterned sequence of preparation, drug administration, intubation, and postintubation management.[5-7]

In the emergency department, RSI has historically had its greatest role in the patient with severe head trauma in whom intubation could exacerbate already increased intracranial pressure. However, because it is designed to blunt or prevent all adverse responses associated with endotracheal intubation, RSI is the ideal method of intubation in the poisoned patient. With the use of drugs having a short duration of action, RSI also is advantageous because it is a measure that permits temporary airway control for the patient with mildly compromised airway reflexes who requires gastrointestinal decontamination (lavage followed by activated charcoal administration) but who does not require prolonged intubation. RSI requires several essential steps that include the use of pharmacologic agents (Table 2A-2). To be performed safely, RSI must occur in the following sequence.

### *Evaluation*

The clinician must first evaluate the patient's airway to determine the necessary equipment and the best technique for safe intubation. Particular attention should be directed to abnormalities in the cervical spine and temporomandibular joint because these will significantly impede rapid and uncomplicated intubation. If there is any question about the stability of the cervical spine, immobilization must be maintained. The oral cavity should be closely examined for the presence of foreign bodies.

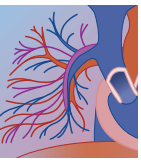




**TABLE 2A-2 Pharmacotherapy Used in Rapid Sequence Intubation**

| AGENT | DOSE* | |
|---|---|---|
| ***Pretreatment Agents*** | | |
| Atropine | 0.01–0.02 mg/kg (minimum, 0.1 mg; maximum, 1.0 mg) | |
| Lidocaine | 1–2 mg/kg | |
| ***Sedatives and Anesthetics*** | | |
| BARBITURATES | | |
| Sodium thiopental | 3–5 mg/kg | |
| Methohexital | 1 mg/kg | |
| BENZODIAZEPINES | | |
| Midazolam | 0.1 mg/kg | |
| ETOMIDATE | 0.1–0.3 mg/kg | |
| KETAMINE | 1–2 mg/kg | |
| OPIOIDS | | |
| Fentanyl | 2–5 μg/kg | |
| PROPOFOL | 2–4 mg/kg | |
| ***Skeletal Muscle Relaxants*** | | |
| DEPOLARIZING AGENTS | | |
| Succinylcholine | 1–2 mg/kg | |
| NONDEPOLARIZING AGENTS | | |
| | DEFASCICULATING DOSE | FULL DOSE |
| Pancuronium | 0.01–0.05 mg/kg | 0.1 mg/kg |
| Vecuronium | 0.01–0.05 mg/kg | 0.1–0.2 mg/kg |
| Atracurium | | 0.5 mg/kg |
| Rocuronium | | 0.5–1.0 mg/kg |

*Doses listed are for intravenous administration.

**BOX 2A-2 EQUIPMENT NEEDED FOR ENDOTRACHEAL INTUBATION**

Syringe for endotracheal cuff inflation
100% oxygen
Face mask
Bag-valve apparatus
Suction equipment
Catheter
Yankauer suction tube
Stylet
Magill forceps
Oral airway
Nasopharyngeal airway ("trumpet")
Laryngoscope handle and blades
Endotracheal tubes
Tongue depressors
Syringe for endotracheal cuff inflation
Tape
Tincture of benzoin

**TABLE 2A-3 Age-Specific Endotracheal Tube Sizes**

| AGE | INTERNAL DIAMETER (mm) |
|---|---|
| ***Infant*** | |
| Premature | 2.5 |
| Full term | 3.0 |
| 1–6 mo | 3.5 |
| 6–12 mo | 4.0 |
| ***Child*** | |
| 2 yr | 4.5 |
| 4 yr | 5.0 |
| 6 yr | 5.5 |
| 8 yr | 6.5 |
| 10 yr | 7.0 |
| ***Adolescent and Adult*** | |
| 12 yr | 7.5 |
| ≥14 yr | 8.0–9.0 |

Accompanying principles:
1. Small sizes are necessary for nasotracheal intubation.
2. Endotracheal tubes two sizes smaller than age appropriate should be immediately available.

### *Preparation*

Before intubation, all necessary equipment must be present so that serious delays or unforeseen complications can be prevented. An IV line should be established and the patient connected to a cardiac monitor and pulse oximeter. The equipment necessary for endotracheal intubation is outlined in Box 2A-2. The proper functioning of all equipment should be ensured before it is used. Appropriate endotracheal tube size also should be determined (Table 2A-3). Unanticipated difficulties with intubation are common; "difficult airway" equipment (e.g., illuminated or fiberoptic-directed endotracheal tubes) should be kept close at hand.

### *Preoxygenation*

Oxygen should be administered for 2 to 3 minutes before intubation; this produces a washout of nitrogen from the lungs, replacing this gas with an oxygen reservoir. The oxygen reservoir allows several minutes of apnea during which intubation can be performed without the risk of producing hypoxia. Assisted ventilation with bag-valve-mask apparatus should only be provided if the patient's own respiratory efforts are inadequate because it risks inflation of the stomach, which increases the likelihood of vomiting. Patients who are breathing spontaneously should be given 100% oxygen by face mask for several minutes before intubation.

### *Pretreatment*

Pretreatment involves the administration of pharmacologic agents that prevent adverse physiologic changes that may occur during intubation. Agents included in this category are lidocaine and atropine.

IV administration of the anesthetic lidocaine appears to blunt the increase in intracranial pressure that

accompanies intubation. Although scientific proof of lidocaine's efficacy is sparse, it is appropriate—particularly in the patient with suspected intracranial hypertension—to administer lidocaine, 1.0 to 2.0 mg/kg IV, 3 to 4 minutes before intubation.[8-10]

Bradycardia can accompany RSI in two circumstances. In young children, both posterior pharyngeal stimulation and administration of succinylcholine can result in severe bradycardia. Therefore, in children younger than 5 years, atropine should be administered before induction. The dose of atropine is 0.01 to 0.02 mg/kg (maximum, 1.0 mg). No less than 0.1 mg of atropine should be administered because smaller doses can produce paradoxical bradycardia.

Severe bradycardia can also occur in patients of any age who have been exposed to medications or toxins with negative chronotropic actions. For example, in patients who have ingested β antagonists (e.g., propranolol), calcium channel blockers, and digoxin, RSI can produce an abrupt decrease in heart rate or frank cardiac arrest. Therefore, in patients who are undergoing RSI after exposure to these agents, atropine should either be administered prophylactically or kept immediately available should emergency administration become necessary.

### *Induction*

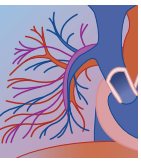
Induction consists of two components: administration of a sedative/anesthetic agent to produce unconsciousness, and the subsequent administration of an agent that produces complete skeletal muscle relaxation (paralysis); both actions facilitate intubation. Because administration of these drugs leads to apnea and paralysis, it is essential that induction proceed quickly and efficiently; this underscores the importance of having all intubation equipment immediately available and in working order.

A number of medications of different pharmacologic classes are used to produce sedation before skeletal muscle relaxation (see Table 2A-2). These drugs include benzodiazepines, opioids, barbiturates, propofol, etomidate, and ketamine. Among the benzodiazepines, midazolam, when given in a dose of 0.1 mg/kg IV (up to a range of 5 to 6 mg in an adult), is ideal because its effects are rapid in onset and short in duration. The drug also offers the advantage of producing muscle relaxation and amnesia. Opioids are another class of drugs that can be used; however, many opioids, such as morphine, may prompt histamine release, with resultant hemodynamic changes. Fentanyl in a dose of 2 to 5 μg/kg is highly effective at producing rapid sedation and relaxation with minimal cardiovascular change. Several barbiturates can produce rapid sedation and relaxation. The most popular of these is sodium thiopental (dose 3 to 5 mg/kg). Equally effective but with a shorter duration of action are methohexital, propofol, and etomidate. Finally, ketamine is a dissociative anesthetic that can produce rapid onset of a state in which the patient is insensitive to pain but maintains an awake appearance and continues to have protective airway reflexes. The typical IV induction dose of ketamine is 1 to 2 mg/kg. Unlike other sedatives/anesthetics, ketamine can produce significant elevations in pulse, blood pressure, intracranial pressure, and myocardial oxygen consumption, and such an increase in any of these could worsen the patient's clinical condition. Because ketamine has a potent bronchodilating effect, it retains its important role as an induction agent in the patient with severe bronchospasm.[11-13]

After administration of a sedative/anesthetic, skeletal muscle relaxation is performed. Skeletal muscle relaxants, all of which interrupt acetylcholine function at the myoneural junction, are typically divided into depolarizing and nondepolarizing categories. Depolarizing agents, of which succinylcholine is the model drug, produce muscle depolarization before paralysis; this results in initial generalized muscle fasciculation. Nondepolarizing relaxants produce paralysis without initial depolarization. The nondepolarizing skeletal muscle relaxants include pancuronium, vecuronium, atracurium, and rocuronium.

Succinylcholine is the most popular muscle relaxant because it has several desirable properties, including a rapid onset of action (less than 1 minute) and an extremely short duration of action. Customary paralyzing doses of succinylcholine are 1 to 2 mg/kg IV.

Despite its efficacy and popularity, succinylcholine can produce several adverse effects. These include hyperkalemia, prolonged paralysis, malignant hyperthermia, and hemodynamic changes. Hyperkalemia, which can be severe, has been most commonly associated with administration of succinylcholine to those with burns, crush injuries, select neuropathies (e.g., Guillain-Barré syndrome), and myopathies (e.g., childhood muscular dystrophies). Prolonged paralysis can occur in those who have a genetic deficiency in serum cholinesterase, the enzyme that inactivates the drug. Prolonged paralysis may also occur in patients with liver disease, the elderly, and those who have ingested anticholinesterase insecticides (carbamates or organophosphates). Malignant hyperthermia is a syndrome characterized by muscle rigidity, hyperthermia, autonomic disturbances, acidosis, rhabdomyolysis, myoglobinuria, renal failure, and coagulopathy. Occurring in genetically predisposed individuals, malignant hyperthermia may appear without warning in those who are given inhalation anesthetics or succinylcholine. The mortality rate associated with this syndrome is approximately 5% to 10%. A malignant hyperthermia-like picture can also occur in children with skeletal muscular disorders (e.g., muscular dystrophy) who are given succinylcholine. Finally, succinylcholine-induced muscle depolarization can lead to transient increases in intracranial and intra-abdominal pressure, with accompanying changes in cardiac output.[14] Because of these potential adverse effects, nondepolarizing muscle relaxants are often recommended as adjuncts to or substitutes for succinylcholine use. As adjuncts, nondepolarizing agents, when given before succinylcholine, can prevent muscle fasciculation and its attendant physiologic effects. The so-called "defasciculating dose" of a nondepolarizing agent is approximately one tenth the full dose of that agent. For example, pancuronium can be given in a dose of 0.01 mg/kg IV before the





administration of succinylcholine to prevent fasciculation. Nondepolarizing agents can also be used solely for skeletal muscle relaxation. However, they generally have a much slower onset of action (as long as 3 to 5 minutes) and produce a longer duration of paralysis. Also, many nondepolarizing agents stimulate histamine release, producing significant hemodynamic changes. Therefore, they are not ideal agents for RSI. Rocuronium appears to have the most rapid onset of all nondepolarizing agents, approaching that of succinylcholine with regard to time to complete muscle relaxation in the less than ideal conditions generally found during emergency intubation.[15] Significant warnings to succinylcholine use in the pediatric population have been recently added, based on the possibility of life-threatening cardiac arrhythmias. According to these new warnings, children with undiagnosed myopathies (e.g., a muscular dystrophy) could develop hyperkalemia sufficient to produce a cardiac disturbance.[16]

### *Intubation*

Suction must be immediately available when intubation is performed. The patient undergoing emergency intubation often has a full stomach; the risk for vomiting and aspiration is therefore significant. This risk is minimized both by the RSI technique and by the direct application of pressure on the cricoid cartilage (Sellick's maneuver), which occludes the esophagus. Adequate preoxygenation and limiting the duration of the intubation attempt to less than 20 to 30 seconds should prevent significant hypoxia.

The differences between the airway of the child and that of the adult have important implications for endotracheal intubation.

1. The child has a relatively large tongue; this makes direct visualization of the larynx difficult.
2. The child has larger tonsils, which also obscure visualization.
3. The infant's larynx is located more cephalad than that of the adult. As a result, the angle between the tongue and the glottis is more acute, and visualization of the larynx is impaired.
4. The subglottic area of the infant is the narrowest part of the larynx and may impede the passage of an endotracheal tube passed through the vocal cords.

### *Postintubation Management*

Immediately after successful endotracheal intubation, placement of the endotracheal tube must be confirmed by detection of bilateral equal breath sounds on chest auscultation, end-tidal carbon dioxide monitoring, or chest radiography; of these, chest auscultation is the least sensitive method and should never be used in isolation to confirm endotracheal tube placement. After confirmation, the tube should be secured either with a strap or with benzoin and adhesive tape. Inflation of the endotracheal tube cuff should be performed to minimize aspiration of gastric contents (although aspiration of activated charcoal around cuffed endotracheal tubes is a frequent occurrence). Until recently, because the airway of the young child has an area of narrowing ("physiologic cuffing"), cuffed endotracheal tubes were not used in the pediatric patient. Pediatric cuffed tubes are now available; their use is encouraged in most circumstances. If long-term intubation is necessary, sedatives/anesthetics and nondepolarizing muscle relaxants should continue to be administered.

In unskilled or unprepared hands, emergency endotracheal intubation can have disastrous consequences. Even when performed by the most experienced hands, this complex procedure can have complications that should be anticipated so that they can be quickly recognized and treated. These complications include:

Dental or oral cavity trauma
Gagging and vomiting
Hypoxia
Hypercarbia
Bradycardia
Tachycardia
Hypertension
Hypotension
Increased intracranial pressure
Pneumomediastinum
Pneumothorax
Cardiac arrhythmias
Myocardial ischemia or infarction
Aspiration
Laryngospasm
Esophageal intubation
Tracheal injury

## Circulatory Support

Poisoned patients often present to the emergency department with hypotension or frank shock. Provision of circulatory support through interventions that may include volume expansion, vasopressor therapy, antidote administration, and correction of electrolyte and acid-base disturbances is essential in initial management.

Many medications and toxins produce hypotension (Box 2A-3). Depending on the ingested substance, the low blood pressure may have a number of causes. For example, blood pressure depressions may occur from direct depression of myocardial contractility (e.g., quinidine), disturbances of central nervous system cardiorespiratory centers (e.g., clonidine), severe gastrointestinal fluid losses (e.g., acetaminophen, iron, arsenic, ricin, mushrooms), peripheral vasodilation (e.g., angiotensin-converting enzyme inhibitors), or a combination of these effects (e.g., theophylline, calcium channel blockers, tricyclic antidepressants). Hypotension also can result from the secondary effects of toxins (e.g., cocaine-induced myocardial infarction). Finally, blood pressure disturbances in the poisoned patient may represent accompanying trauma (e.g., severe spinal cord injury or internal hemorrhage). With the multitude of possible causes, the clinician, on the basis of the known pathophysiology of a particular drug and after having performed a thorough physical assessment, should determine, if at

**BOX 2A-3 INTOXICATIONS COMMONLY ASSOCIATED WITH HYPOTENSION**

**Pharmaceuticals**

α Antagonists
Angiotensin-converting enzyme (ACE) inhibitors
Barbiturates
β Blockers
Calcium-channel blockers
Clonidine
Digoxin
Monoamine oxidase inhibitors
Opioids
Phenothiazines
Quinidine
Theophylline
Tricyclic antidepressants

**Metals and Minerals**

Arsenic
Iron

**Envenomations**

Marine (scombroid, ciguatera, coelenterates)
Reptile (crotalid)
Hymenoptera

**Chemical Weapons**

Ricin

all possible, the probable cause of hypotension if he or she is to provide a specific intervention.

## VOLUME EXPANSION

Appropriate cardiac output relies on the adequacy of intravascular volume. After poisoning, intravascular volume may decrease abruptly. This decrease can be absolute, occurring as a result of a direct loss of intravascular volume (e.g., pulmonary edema, gastrointestinal pooling), or relative, resulting from severe peripheral vasodilation (e.g., angiotensin-converting enzyme inhibitor or α-antagonist overdose). In either case, hypotension should first be treated with the administration of volume-expanding agents.[17]

Many fluids are acceptable for emergency volume expansion. Normal saline and lactated Ringer's solution are generally the most readily available isotonic agents. Adults should receive up to 500- to 1000-mL boluses of isotonic fluid while blood pressure is monitored; children should be given 10 to 40 mL/kg. After the administration of each bolus, the patient should be reassessed for improvements in cardiac output.

Alternative fluids that can be used for volume expansion in the poisoned patient include albumin and whole blood. Each of these fluids has a role that is best determined by the pathophysiologic mechanism responsible for the hypotension. Being colloid rather than crystalloid in nature, these fluids in theory maintain intravascular volume better than saline solutions do. In clinical situations in which a "leaky capillary syndrome" is mechanistically the source of intravascular volume loss, the use of colloid solutions may be preferred. Whole blood is most valuable in situations in which there is frank blood loss. With severe hemolysis (e.g., after arsine or stibine exposure), exchange transfusion with whole blood may be necessary.

Usually, the adequacy of volume expansion is determined clinically by an increase in blood pressure. Other clinical signs of improved cardiac output include resolution of cyanosis and normalization of capillary refill time. Central venous pressure and Swan-Ganz catheter monitoring, although invasive, provide the best evidence of appropriate intravascular volume.

Fluid overload is a potential complication of volume expansion. This is most likely to occur in patients who receive excess fluids over a short period of time. Also, after an overdose of a myocardial depressant such as tricyclic antidepressants or quinidine, a fluid bolus that could be tolerated by a healthy individual can produce pulmonary edema in the overdose patient. Therefore, administration of modest boluses of fluid is generally recommended; if cardiac output remains inadequate after fluids have been given, vasopressor therapy should be initiated.

## VASOPRESSOR THERAPY

In the patient with severe hypotension, vasopressor therapy is necessary if blood pressure is not satisfactorily improved after volume expansion. Vasopressors are drugs that can be administered to maintain cardiac output. These agents have specific effects on the heart or blood vessels, augmenting myocardial function or increasing vasomotor tone, or both. With rare exception, vasopressors used in the acute management of hypotension are short-acting drugs that must be given by continuous IV infusion.[17]

Vasopressors generally act at adrenergic (α and β), D (dopamine), or glucagon receptors (Table 2A-4). The adrenergic system has been further defined with the recognition of two major α-adrenergic receptor subtypes ($\alpha_1$ and $\alpha_2$) and three β-adrenergic receptor subtypes ($\beta_1$, $\beta_2$, and $\beta_3$). Coupled with intracellular G proteins, these membrane-bound receptors effect an intracellular chain of events that includes changes in the activity of adenylate cyclase. This action goes on to modulate the level of intracellular cyclic adenosine monophosphate (cAMP), which in turn alters phospholipase activity or opens gated calcium channels. Although the cellular mechanisms of this system have become much better defined, the general principles of vasopressor action remain unchanged. For example, α-adrenergic receptor agonists produce vascular smooth muscle contraction. $\beta_1$-Adrenergic receptor agonists produce increased heart rate and contractility, whereas $\beta_2$-adrenergic receptor agonists promote generalized smooth muscle relaxation (including bronchial and vascular). Vasopressor therapy is designed to improve cardiac output through manipulation of the specific receptor most appropriate for the clinical situation. A number of vasopressors can be used to provide blood pressure support (see Table 2A-4). The

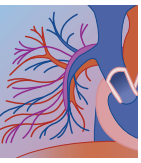




**TABLE 2A-4 Common Vasopressors by Dose Range and Mechanism of Action**

| AGENT | RECEPTOR TYPE | | | |
|---|---|---|---|---|
| | α-ADRENERGIC | $\beta_1$-ADRENERGIC | $\beta_2$-ADRENERGIC | DOPAMINERGIC |
| Epinephrine (0.1–0.5 μg/kg/min) | | | | |
| Low-dose | | +++ | +++ | |
| Moderate-dose | + | +++ | +++ | |
| High-dose | +++ | ++ | | |
| Norepinephrine (0.1–0.5 μg/kg/min) | +++ | ++ | | |
| Dopamine (2–20 μg/kg/min) | | | | |
| Low-dose | | | | +++ |
| Moderate-dose | | +++ | | |
| High-dose | +++ | | | |
| Dobutamine (2–20 μg/kg/min) | + | +++ | + | |
| Phenylephrine (0.1–0.5 μg/kg/min) | +++ | | | |
| Nonadrenergic agents | | | | |
| Amrinone (5–15 μg/kg/min) | | | | |
| Glucagon (50–150 μg/kg/hr) | | | | |
| Calcium chloride | | | | |

+, Mild effect; ++, moderate effect; +++, major effect.

indications for the use of these drugs vary slightly, depending on the clinical circumstance.

### *Epinephrine*

Epinephrine elevates blood pressure primarily through its α-adrenergic-stimulating properties. This effect also is valuable in improving myocardial and cerebral blood flow. Because it also has prominent β-adrenergic agonist effects, epinephrine is variably effective at producing marked increases in blood pressure. Epinephrine therapy is initiated at a dose of 0.1 to 0.5 μg/kg/min. Epinephrine is particularly effective in intoxications associated with hypotension and bronchospasm (e.g., Hymenoptera envenomation and anaphylactic reactions).

### *Norepinephrine*

Norepinephrine stimulates both α- and β-adrenergic receptors, with slightly greater stimulation of α-adrenergic receptors. The effect is improved vasomotor tone in conjunction with increased myocardial chronotropy and inotropy. Norepinephrine infusions are typically initiated in a dose of 0.1 to 0.5 μg/kg/min.

### *Dopamine*

Dopamine is a precursor of norepinephrine. The most popular of vasopressors, dopamine appears to have at least three mechanisms of action: (1) promotion of norepinephrine synthesis, (2) a tyramine-like effect that stimulates release of preformed norepinephrine, and (3) direct stimulation of vascular dopamine receptors.

The cardiovascular effects of dopamine are variable, depending on the infusion rate. At relatively low doses (1 to 2 μg/kg/min), the drug dilates renal and mesenteric vessels without marked increases in heart rate or blood pressure. At doses of 2 to 10 μg/kg/min, β-adrenergic receptor stimulation predominates, producing significant increases in cardiac output. Finally, at doses greater than 10 μg/kg/min, α-adrenergic receptor stimulation is the primary action, resulting in marked peripheral vasoconstriction. The general dose range for dopamine infusion is 2 to 20 μg/kg/min.

Dopamine is safe and effective for any type of drug-induced hypotension. In the past, there have been theoretic concerns that dopamine's β-adrenergic effect in the face of phenothiazine or tricyclic antidepressant intoxication would increase the peripheral vasodilatation associated with overdose, exacerbating hypotension. However, experimental data and clinical experience have failed to confirm this adverse effect from dopamine use. Also, with hypotension after monoamine oxidase inhibitor overdose, dopamine's effects are somewhat unpredictable; it may be relatively ineffective (owing to the lack of preformed norepinephrine), or it can produce an exaggerated response (because of its tyramine-like action).

### *Dobutamine*

Dobutamine is a synthetic catecholamine with almost exclusive β-adrenergic receptor-stimulating effects. Its primary mechanism of blood pressure improvement is direct myocardial inotropy; thus, reflex peripheral vasodilation may occur with its use. Unlike dopamine, dobutamine does not release preformed norepinephrine. The usual dosage range for dobutamine is 2 to 20 μg/kg/min, although doses as high as 40 μg/kg/min have been used. High-dose infusions often increase myocardial oxygen demands, which, if unmet, can result in myocardial ischemia. Nonetheless, dobutamine is extremely effective in syndromes of heart failure.

### *Phenylephrine*

Phenylephrine has both α- and β-adrenergic receptor-stimulating properties, although its α-adrenergic receptor actions predominate. Phenylephrine is a potent stimulator of vasomotor tone; it is therefore very effective in patients in hypotensive states resulting from severe peripheral vasodilation (e.g., following overdose with an α-adrenergic antagonist, such as prazocin or a phenothiazine neuroleptic, e.g., chlorpromazine). Phenylephrine

infusions are given in a typical dose range of 0.1 to 0.5 μg/kg/min.

### *Amrinone*

Amrinone is a novel, nonadrenergic cardiac stimulant that improves myocardial contractility while inducing vasodilation. Its mechanism of action appears to be direct inhibition of phosphodiesterase; the result of this is increased intracellular cAMP activity, an action that increases transmembrane calcium flux, potentiating cardiac chronotropy and inotropy. Amrinone's effects have been compared with those of dobutamine and nitroprusside combination therapy. Amrinone may be particularly valuable in the treatment of calcium channel blocker intoxication; its inhibition of cAMP breakdown results in greater phosphorylation of L-type calcium channels, potentially increasing their permeability. Experimental data support its role in this specific poisoning.[18] Amrinone can be used to treat syndromes of left ventricular failure but should not be administered in the presence of myocardial ischemia; like dobutamine, it may increase myocardial demands, resulting in infarction. Because of its potent vasodilating action, amrinone may cause a hypotensive response in those with low intravascular volume. The usual dosage range for this agent is 5 to 15 μg/kg/min; the total daily dose should not exceed 10 mg/kg per day.

### *Glucagon*

Glucagon is a single-chain pancreatic polypeptide that is an effective inotropic and chronotropic agent. Its mechanism of action is direct stimulation of myocardial glucagon receptors; these receptors, when stimulated, increase the formation of myocardial cAMP. The resultant effect is positive inotropy and, to a lesser degree, positive chronotropy. Glucagon is theoretically most effective after β blocker overdose, in which decreased β-adrenergic receptor activation leads to diminished cAMP production. The hormone may also provide therapeutic benefit in hypotension after calcium channel blocker overdose.[18] Glucagon is given in an initial dose of 1 to 10 mg (50 to 150 μg/kg in children). If effective in augmenting blood pressure, it can be given as a continuous infusion of 5 to 10 mg/hr (100 μg/kg/hr in children). Some preparations of glucagon are marketed as a lyophilized compound with a 0.2% phenol-based diluent for reconstitution. While single doses of such a product can be given after standard reconstitution, glucagon for continuous infusion should be reconstituted with saline to prevent phenol toxicity. Adverse effects from glucagon include hyperglycemia, nausea, vomiting, and ileus.

### *Calcium*

Calcium plays a key role in regulating cardiac inotropy through its binding to troponin C, an action that permits interaction between actin and myosin. Although most of the calcium that produces this change resides in an intracellular calcium pool, extracellular calcium does diffuse into cells and contributes to increased contractility. Although diffusion of calcium into the myocardium is "gated"—that is, it is tightly controlled—high concentrations of extracellular calcium, particularly in the face of channel blockade (e.g., after overdose of calcium-channel blockers), sometimes improve contractility. Administration of IV calcium chloride is indicated in the management of hypotension resulting from calcium channel blocker overdose (see Table 2A-1), hyperkalemia, and hypocalcemia.

## Clinical Evaluation

A thorough history taking and physical examination are essential to the diagnosis of the toxic patient. Poisoning should be suspected in any patient who presents with multisystem disturbance until proven otherwise. Although the initial manifestations of poisoning are myriad, a patient with acute poisoning often presents with coma, cardiac arrhythmia, seizures, metabolic acidosis, or gastrointestinal disturbance, either together as symptom complexes or as isolated events. Symptom complexes, or toxidromes (Table 2A-5), may give clues to an unknown poisoning. For example, a patient with a history of depression who presents with coma, seizures, a widened QRS complex or evidence of dysrhythmia on electrocardiography, and dilated pupils has likely taken a tricyclic antidepressant. Hepatic, renal, respiratory, and hematologic disturbances are generally delayed manifestations of poisoning.

The clinical evaluation, in addition to the history taking and physical examination, includes an assessment of major signs of toxicity presented by the patient and evaluation of the laboratory data.

### HISTORY

When one suspects poisoning or drug overdose, the primary goal of history taking is identification of the toxic agent. Sometimes diagnosis is easy, as in the case of the toddler who ingests iron tablets in the mother's presence. Sometimes it is difficult, as in the case of the patient who is hiding a history of drug abuse and passes out at work or who has an unexpected seizure. Prior medical or psychiatric history, current medications, and allergies should be obtained from family or friends if the patient is unable to relate the information. The following questions may be revealing:

- What other medicines are in the house?
- What was the patient doing that day?
- Does the patient live alone, did he or she just lose a job, or have there been recent emotionally traumatic events?
- Is the patient eating a special diet or taking a new health food, alternative medication, or performance enhancer?
- Could the patient inadvertently have taken too much of a prescribed medication?
- If it can be identified, is the substance nontoxic? (See Box 2A-4.)

### PHYSICAL EXAMINATION

The physical examination can help in determining the extent of poisoning and may reveal the presence of a

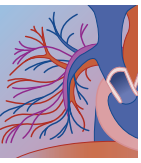




**TABLE 2A-5 Examples of Symptom Complexes, or Toxidromes**

| TOXIDROME OR COMPLEX | CONSCIOUSNESS | RESPIRATIONS | PUPILS | OTHER | POSSIBLE TOXIC AGENT/MECHANISM |
|---|---|---|---|---|---|
| Cholinergic | Coma | ↑↓ | Pinpoint | Fasciculations<br>Incontinence<br>Salivation<br>Wheezing<br>Lacrimation<br>Bradycardia | Organophosphate insecticides, carbamates, nicotine |
| Anticholinergic | Agitation, hallucinations, or coma | ↑ | Dilated | Fever, flushing<br>Dry skin and mucous membranes<br>Urinary retention | Anticholinergics (atropine, Jimson weed, antihistamines) |
| Opioid | Coma | ↓ | Pinpoint | Track marks<br>Hypothermia<br>Hypotension | Opiates, opioids |
| Extrapyramidal | Wakefulness | ↑ | — | Torsion of head/neck | Phenothiazines, haloperidol risperidol |
| Tricyclic antidepressant | Coma (initially, agitation) | ↓ | Dilated | Cardiac arrhythmia<br>Convulsions<br>Hypotension<br>Prolonged QRS interval | Tricyclic antidepressants |
| Sedative/hypnotic | Coma | ↓ | Midsize or small | Hypothermia<br>Decreased reflexes<br>Hypotension | Sedatives, barbiturates |
| Salicylates | Agitation or lethargy | ↑ | Midsize or small | Diaphoresis<br>Tinnitus<br>Alkalosis (early)<br>Acidosis (late) | Aspirin, oil of wintergreen |
| Sympathomimetic | Agitation, hallucinations | ↑ | Dilated | Seizures<br>Tachycardia<br>Hypertension<br>Diaphoresis<br>Metabolic acidosis<br>Tremor<br>Hyperreflexia | Cocaine<br>Theophylline<br>Amphetamines<br>Caffeine |

**BOX 2A-4 NONTOXIC INGESTIONS**

Abrasives
Adhesives
Antacids
Antibiotics
Baby product cosmetics
Ballpoint pen inks
Bath oil (castor oil and perfume)
Bathtub floating toys
Birth control pills
Bleach (<5% sodium hypochlorite)
Body conditioners
Bubble bath soaps (detergents)
Calamine lotion
Candles (beeswax or paraffin)
Chalk (calcium carbonate)
Colognes
Cosmetics
Crayons marked AP, CP
Dehumidifying packets (silica or charcoal)
Deodorants
Deodorizers, spray and refrigerator
Elmer's glue
Fabric softeners
Fish bowl additives
Glues and pastes
Hand lotions and creams
3% hydrogen peroxide
Incense
Indelible markers
Ink (black, blue)
Iodophil disinfectant
Laxatives
Lipstick
Lubricant
Magic Markers
Makeup (eye, liquid, facial)
Matches
Mineral oil
Modeling clay
Newspaper
Pencil (graphite lead, coloring)
Perfumes
Petroleum jelly (Vaseline)
Play-Doh
Polaroid picture coating fluid
Putty (less than 2 oz)
Rubber cement
Sachets (essential oils, powder)
Shampoos (liquid)
Shaving creams and lotions
Soap and soap products
Spackles
Suntan preparations
Sweetening agents (aspartame)
Teething rings
Thermometers (mercury)
Toothpaste with or without fluoride
Toy pistol caps (potassium chlorate)
Vitamins with or without fluoride
Watercolors
Zinc oxide
Zirconium oxide

Nontoxic is defined as producing little to no toxicity when ingested in small amounts.

**TABLE 2A-6 Important Clues on Physical Examination**

| CLINICAL FINDING | DIAGNOSTIC EXAMPLE |
|---|---|
| Needle tracks | Intravenous drug abuse |
| Characteristic odor of breath | Gasoline |
| Destruction of nasal mucosa/cartilage | Cocaine abuse |
| New significant heart murmur | Infective endocarditis |
| Pulmonary edema | Heroin abuse |
| Boardlike abdomen | Black widow spider bite |
| Salivation and lacrimation | Organophosphates |
| "Boiled lobster" skin | Boric acid poisoning |

toxic syndrome, of any underlying disease, or concomitant trauma. Repeated assessment, especially of vital signs and of cardiac, pulmonary, and neurologic status, is critical to proper management of the toxicologic patient. The physical examination also can provide valuable clues as to the particular toxin involved (Table 2A-6).

### *Vital Signs*

As part of the initial evaluation, complete determination of vital signs, including measurement of body temperature initially and throughout the emergency department assessment, is mandatory. Obtaining a core body temperature measurement may be necessary. Hyperthermia can occur with a number of ingestions and in infectious illness, but it is characteristic of poisoning with salicylates, anticholinergics, monoamine oxidase inhibitors, and dinitrophenol; it is occasionally also seen after intoxication with phencyclidine, LSD, or cocaine, especially following seizures. Life-threatening malignant hyperthermia following drug overdose may occur. Hypothermia is common and may occur because of exposure to cold, hypoglycemia, or overdose of a number of sedatives, especially barbiturates, ethanol, carbamazepine, narcotics, and phenothiazines. Bradycardia can be seen with overdose of digitalis, cholinergic agents, β blockers, and calcium channel blockers, but it also may be seen with hypothermia or spinal cord trauma. Hypertension is characteristic of intoxication with cocaine, amphetamines, phencyclidine, and sympathomimetics.

### *Skin*

The skin should be examined for needle tracks, burns, bruises, or lacerations. Needle tracks may be confined to the groin or other areas that are not readily visible. A "boiled lobster" appearance suggests ingestion of a boric acid–containing roach powder insecticide. Generalized flushing suggests an allergic reaction, niacin overdose, anticholinergic poisoning, scombroid fish poisoning, or an alcohol-disulfiram reaction.

Diaphoresis suggests hypoglycemia, salicylate or organophosphate poisoning, hyperthyroidism, drug or alcohol withdrawal, or shock from cardiac or other etiology. Jaundice may follow overdose of acetaminophen, aspirin, iron, carbon tetrachloride, mushrooms, copper, or phosphorus. Petechiae and ecchymoses suggest coumadin overdose. Bullae may be secondary to skin hypoxia or prolonged pressure and are seen after sedative-hypnotic overdoses (especially barbiturate overdose), carbon monoxide poisoning, and thermal burns. Bullae may also follow rattlesnake envenomation. Bullous lesions or soft tissue swelling should prompt evaluation for rhabdomyolysis, an occasional finding in patients following prolonged coma or severe hyperthermia, such as in cocaine abuse.

### *Breath*

It is important to smell the patient's breath. Alcohol is the most common odor detected on the breath of an intoxicated patient in the emergency department. The accurate identification of other odors varies greatly among physicians. A fruity odor may be detectable in the patient with diabetic ketoacidosis. Cyanide poisoning can be associated with the smell of almonds. The smell of cleaning fluid suggests carbon tetrachloride poisoning. Gasoline, camphor, hydrogen sulfide, ether, turpentine, methyl salicylate, paraldehyde, phenol, and organophosphate insecticides all have characteristic odors. Arsenic and tellurium intoxication is associated with the odor of garlic.

### *Ear, Nose, and Throat*

A nasal examination may reveal chronic insufflation of cocaine. An edematous, often elongated uvula may be seen with marijuana use or exposure to corrosive agents.

### *Lungs*

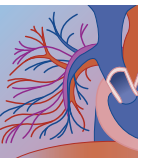
Auscultation of the lungs may provide diagnostic clues. In narcotic or tricyclic antidepressant overdose, pulmonary edema may be a complication, leading to the appearance of adventitious noises. In all overdose patients, aspiration pneumonitis, the result of a depressed gag reflex, is a possibility. Inhalation of toxic gases may produce wheezing and pulmonary compromise. Pneumothorax may be detected in patients who smoke cocaine, methamphetamine, or any other heated, impure substance. Mediastinal emphysema from marijuana or crack cocaine smoking also may be detected by auscultation.

### *Heart*

Examination of the heart may reveal a new murmur, which in an intravenous drug abuser suggests endocarditis. Bradycardia is common after the overdose of four classes of cardiac agents: calcium channel blocker, β blocking agents, digitalis preparations, and central $\alpha_2$ antagonists (e.g., clonidine or guanfacine). A ventricular arrhythmia on electrocardiography in a young patient suggests cocaine toxicity. An irregularly irregular heartbeat that is new in a patient on an alcoholic binge suggests atrial fibrillation—the so-called "holiday heart" syndrome.

### *Abdomen*

A boardlike abdomen in a patient with a history of spider bite is characteristic of black widow envenomation. Examination of the abdomen in an overdose patient often reveals an adynamic ileus. In patients with abdominal pain, a surgical abdomen must be ruled





out. Hepatomegaly suggests liver congestion (e.g., with pyrrolizidine toxicity).

### *Neurologic Assessment*

All patients should undergo a careful neurologic examination. Issues of major concern are concomitant head trauma and spinal cord trauma in comatose patients. Serial neurologic examinations are key to proper assessment (see discussion of coma in section on Level of Consciousness).

### *Extremities*

The extremities should be evaluated to detect thrombophlebitis, fracture or dislocation, or vascular insufficiency. Rhabdomyolysis and the compartment syndrome are definite concerns in overdose patients, especially in those with prolonged coma or underlying trauma.

## ASSESSMENT OF MAJOR SIGNS OF TOXICITY

The toxicologic patient presenting in the acute setting often exhibits the following, either alone or in combination: coma, cardiac arrhythmia, metabolic acidosis, gastrointestinal disturbance, and seizures.

### *Level of Consciousness*

Consciousness is defined as an awareness of self and the environment. Coma is unarousable unresponsiveness. Wakefulness implies the ability to be aroused. These three functional states are mediated by the ascending reticular activating system, a tract that courses through the diencephalon, midbrain, and pons. Diseases produce coma either by diffusely affecting the brain or by encroaching upon the brainstem. Coma may be produced by (1) a supratentorial mass lesion, such as a subdural hematoma; (2) a brainstem lesion (uncommon); or (3) metabolic disorders that widely depress or interrupt brain function.

One of the most common manifestations of acute poisoning is coma. The principles of coma management are relatively straightforward. Patients in coma must be stabilized initially by establishment of an airway, proper oxygenation with continuous pulse oximetry, insertion of an IV line with normal saline, and resuscitation, if necessary (see earlier section on Emergency Management). The clinical evaluation of the comatose patient is invaluable not only in determining the depth of coma and assessing for trauma, but also in providing a baseline for repeated clinical assessment. Coma can be assessed either using the simple AVPU (*A*lert, responsive only to *V*erbal stimuli, responsive only to *P*ainful stimuli, *U*nresponsive) or Glascow coma scales.

The major causes of coma in patients seen in the emergency department include poisoning (e.g., carbon monoxide poisoning), drug overdose, head trauma, cerebrovascular accident, anoxia, infection (e.g., meningitis), and diabetes and other systemic disorders such as renal failure, hepatic coma, and cardiac arrhythmia. The physician must rule out each condition before establishing the diagnosis of poisoning.

Supratentorial structural lesions are suggested by a rapid progression of signs, including changes in respiratory pattern, disconjugate gaze, lateralizing signs, or loss of doll's eyes movements.

A metabolic cause of coma may be indicated by the persistence of the pupillary light reflex; a depression of respiration and consciousness more pronounced than other neurologic signs; preceding altered mental states; asterixis or fasciculations, or both; the presence of a ciliospinal reflex; and extracranial signs, such as jaundice. Repeated assessment of the comatose patient is critical to proper management of poisoning.

### *Pupils*

Evaluation of the patient's pupils is most helpful. Midpoint fixed pupils or a unilateral dilated pupil suggests a structural lesion. Pinpoint pupils suggest overdose of opiates, clonidine, organophosphate insecticides, nerve agents (e.g., sarin), chloral hydrate, phenothiazines, or nicotine. Dilated pupils are nonspecific.

### *Ocular Movements*

A disturbance of ocular movements (e.g., loss of doll's eyes movements) suggests a structural lesion. *Nystagmus* suggests intoxication with phenytoin, phencyclidine, carbamazepine, and, occasionally, ethanol.

### *Respirations*

It is important to note abnormal patterns of breathing. Posthyperventilation apnea, Cheyne-Stokes respirations, and apneustic breathing strongly suggest that a structural lesion is the cause of the patient's coma. Central neurogenic hyperventilation is a classic presentation of brainstem injury. Kussmaul breathing can occur after salicylate or dinitrophenol poisoning. Compensatory hyperventilation may accompany methanol or ethylene glycol poisoning or other toxin-producing metabolic acidosis. Respiratory arrest is a common presentation in the patient who has taken a central nervous system depressant and may lead to multisystemic dysfunction resulting from severe hypoxic injury.

### *Motor Function*

Decorticate and decerebrate posturing suggests a structural lesion. It is important to realize that patients with poisoning or drug overdose (e.g., tetrodotoxin intoxication) may appear brain dead; have fixed, dilated pupils; be in an unresponsive coma; and lack the cold caloric response, yet recover fully in time.

## CARDIAC ARRHYTHMIA

A 12-lead electrocardiogram and continuous cardiac monitoring are essential for any patient with significant poisoning. Evidence of an arrhythmia or other important diagnostic clues may be present on electrocardiography, such as a widened QRS complex in cyclic antidepressant overdose or a prolonged QT interval in trazadone or arsenic poisoning overdose. Box 2A-5 lists common toxic causes of cardiac arrhythmia.

The patient with life-threatening cardiac arrhythmia or cardiac arrest should be managed on the basis of the general principles of resuscitation and the American Heart Association's advanced cardiac life support

**BOX 2A-5 COMMON TOXIC CAUSES OF CARDIAC DISTURBANCES**

**Conduction Disturbances**

***Prolonged PR Interval***
Digoxin and other digitalis compounds
Lithium

***Prolonged QRS Interval***
Chloroquine, quinine, quinidine, and related compounds
Diphenhydramine
Plant cardiac glycosides (e.g., lily of the valley)
Tricyclic antidepressants

***Prolonged QT Interval***
Arsenic
Cisapride
Disopyramide
Droperidol
Erythromycin
Haloperidol
Hypocalcemia (after hydrofluoric acid exposure)
Pentamidine
Phenothiazines
Sotalol
Thioridazine

**Rhythm Disturbances (Ventricular or Supraventricular)**

β blockers
Calcium channel blockers
Carbon monoxide
Clonidine
Cocaine
Theophylline

(ACLS) guidelines. If cyclic antidepressant overdose is suspected, administration of IV sodium bicarbonate is indicated for correction of ventricular arrhythmia or conduction disturbances. Sodium bicarbonate may also be effective in the treatment of other overdose by other agents associated with prolongation of the QRS interval, including diphenhydramine and cocaine. Administration of IV calcium chloride is the primary therapeutic measure for calcium channel blocker overdose. Use of digoxin antibody fragments is indicated for digitalis poisoning, and glucagon for β blocker overdose (see Table 2A-1). In referred patients who have already been hospitalized elsewhere, ventricular arrhythmia may be due to hyperkalemia because renal failure may have ensued; in such patients, IV sodium bicarbonate, glucose/insulin, and, if necessary, calcium chloride administration may be warranted. Magnesium has a singular role in the treatment of drug-induced prolongation of the QT interval, a conduction disturbance that is often the prelude to torsades de pointes and other life-threatening disturbances.[19] In all intoxicated patients, correction of hypoxia, metabolic acidosis, and fluid and electrolyte disturbance serves to reduce the incidence of cardiac arrhythmias.

**BOX 2A-6 CAUSES OF A HIGH–ANION GAP METABOLIC ACIDOSIS**

Alcoholic ketoacidosis
Cyanide
Diabetic ketoacidosis
Ethylene glycol
Iron
Isoniazid
Lactic acidosis
Metformin
Methanol
Salicylates
Uremia

## METABOLIC ACIDOSIS AND DISTURBANCES IN SERUM OSMOLALITY

Causes of a high-anion gap metabolic acidosis are listed in Box 2A-6. The assessment of metabolic acidosis includes not only arterial (or, less ideally, venous) blood gas analysis, but also studies of serum sodium, potassium, chloride, carbon dioxide, blood urea nitrogen (BUN), creatinine, glucose, acetone, serum osmolality, and urine pH, as well as urinalysis. Determination of the anion gap is helpful in the diagnosis and management of poisoning.

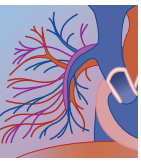
The clinician can measure serum osmolality either directly by determining the freezing point (osmometry) or by calculation. The formula for calculating osmolality is

$$\text{Serum osmolality} = 2 \times Na^{+}\ (\text{mEq/L}) + \text{BUN}\ (\text{mg/dL})/2.8 + \text{Glucose}\ (\text{mg/dL})/18$$

When laboratory data are expressed in international (SI) units, the formula for calculation of serum osmolality simply equals 2 × Na + BUN + glucose. The normal serum osmolality is 280 to 295 mOsm/L. An osmometer measurement indicating a serum osmolality that is more than 10 mOsm/L greater than the calculated osmolality is termed an osmolar gap; it suggests the presence of an osmotically active substance that is not accounted for by the calculated osmolality. Causes of an osmolar gap are listed in Box 2A-7. The most common cause of an osmolar gap is consumption of an alcohol. The osmolar gap can be used to estimate the serum concentration of an alcohol, based on that alcohol's molecular weight (Table 2A-7). A substance contributes to osmolality only if it achieves relatively high blood levels and has a low molecular weight. Most drugs or intoxicants cannot be detected with use of the osmolar gap.

## GASTROINTESTINAL DISTURBANCE

The causes of toxic gastrointestinal disturbance are many. The patient with iron, arsenic, or ricin poisoning has severe, repeated episodes of vomiting and may develop gastrointestinal hemorrhage. Theophylline overdose also causes persistent retching. Acute lithium and arsenic poisoning characteristically produce massive diarrhea. Patients with acute mercury poisoning have a mucous-type diarrhea, with the subsequent development





**BOX 2A-7 CAUSES OF AN OSMOLAR GAP**

**Diseases or Conditions**

Hyperproteinemia
Hyperlipidemia

**Alcohols**

Acetone
Ethanol
Ethylene glycol
Isopropyl alcohol
Methanol

**Pharmaceuticals**

Propylene glycol (an excipient in parenteral medications)
Intravenous contrast
Mannitol

**BOX 2A-8 COMMON TOXIC CAUSES OF SEIZURES**

Anticholinergics (e.g., diphenhydramine)
Bupropion
Camphor
Carbon monoxide
Cocaine
Insulin
Isoniazid
Lindane
Lithium
Oral hypoglycemics
Propoxyphene
Strychnine
Theophylline
Tramadol
Tricyclic antidepressants

**TABLE 2A-7 Molecular Weight of Alcohols and Their Contribution to the Osmolar Gap**

| | MOLECULAR WEIGHT (DALTONS) | OSMOLAL GAP (mOsm/kg) AT 100 mg/dL |
|---|---|---|
| Ethanol | 46 | 22 |
| Ethylene glycol | 62 | 16 |
| Isopropyl alcohol | 60 | 17 |
| Methanol | 32 | 31 |

of hemorrhagic colitis. One of the most striking presentations is caused by phosphorus poisoning, which produces luminescent vomitus and flatus. The early presentation of organophosphate or nerve agent exposure is similar to that of acute gastroenteritis and is characterized by abdominal cramps, vomiting, and diarrhea, with subsequent development of neurologic signs. Poisoning from mushrooms (see Chapter 23), toxic marine life (see Chapter 25), botulism, and food (see Chapter 26) should be included in the differential diagnosis. Chemotherapeutic agents (see Chapter 56) are well-known causes of toxic gastroenteritis.

The management of gastrointestinal disturbance in the toxic patient includes following the general principles of blood, fluid, and electrolyte resuscitation, when indicated; judicious use of parenteral antiemetics to control persistent vomiting; specific measures such as antidotal therapy (e.g., in iron or organophosphate poisoning); or interventional therapy, such as charcoal hemoperfusion (in theophylline overdose) or hemodialysis (in lithium overdose), when indicated.

## SEIZURES

Common agents that cause seizures are listed in Box 2A-8. Almost any drug or toxin is capable of producing a seizure. Delayed seizures occurring during a recovery period may be a sign of sedative-hypnotic or alcohol withdrawal.

Seizures should be managed first with establishment of an airway and oxygenation. Patients with a simple isolated seizure may require only observation and supportive care, whereas repetitive seizures or status epilepticus, which can be life threatening, must be managed aggressively. Some seizures are particularly difficult to control, such as those seen with theophylline or cocaine overdose.

The standard regimen for seizure control in overdose of an unknown agent is use of the full therapeutic dosages of benzodiazepines (e.g., diazepam or lorazepam), followed by administration of phenytoin or a barbiturate (e.g., phenobarbital or pentobarbital). In patients with status epilepticus, RSI may be necessary and the use of thiopental is indicated, with electroencephalographic monitoring to ensure control of electrical seizure activity; the use of additional paralytics, such as pancuronium bromide, may be warranted.

Specific measures to control seizures may be indicated, such as administration of pyridoxine for isoniazid-induced seizures.

## LABORATORY EVALUATION

Box 2A-9 lists specific blood studies whose results may be used for diagnosis and to direct therapy of the overdose patient. In every significant poisoning, routine studies include a complete blood count; determination of serum electrolytes, glucose, BUN, creatinine, and calcium; urinalysis; prothrombin time; pulse oximetry; end-tidal $CO_2$ monitoring, and 12-lead electrocardiography. Arterial blood gas analysis is necessary for evaluating respiratory status and acid-base abnormalities, particularly in the comatose or seizure patient. The measurement of serum salicylate and acetaminophen levels is generally added in the case of the patient with overdose of an unknown substance, because these agents are often co-ingestants or are contained in combination drugs. Measurement of hepatic enzymes is important in the evaluation of acetaminophen toxicity. The advantage of a toxicologic drug screen in initial management is equivocal. Box 2A-10 gives a partial list of drugs and toxins not commonly

**BOX 2A-9 TOXICOLOGIC BLOOD STUDIES THAT MAY DIRECT THERAPY**

Acetaminophen
Carboxyhemoglobin
Digoxin
Ethanol
Ethylene glycol
Iron
Lithium
Methanol
Salicylate
Theophylline

**BOX 2A-10 A PARTIAL LIST OF DRUGS AND TOXINS NOT COMMONLY DETECTED WITH ROUTINE DRUG SCREENING**

Antihypertensives
Organophosphates
Antiarrhythmics
Carbon monoxide
Cyanide
Digitalis
Ethylene glycol
Heavy metals
Hydrocarbons
Oral hypoglycemics
Iron
Isoniazid
Lithium
LSD
Methanol
Mushrooms
Venoms

detected with routine drug screening. Further laboratory blood studies are tailored to assess the individual diagnostic and therapeutic needs of the patient.

It is extremely important to remember to "treat the patient, not the lab." One should never withhold therapy while waiting for a confirmatory drug level in a critical patient, such as a patient with tricyclic antidepressant overdose who is exhibiting a widened QRS complex. In contrast, performing hemodialysis on a completely asymptomatic patient with lithium overdose on the basis of one test result indicating an elevated serum lithium concentration would be equally unwise.

Serial blood level determinations are often helpful in guiding therapy in patients undergoing hemodialysis; in patients in whom concretions have formed, such as those with barbiturate, iron, salicylates, or meprobamate intoxication; or in patients receiving antidotal therapy (e.g., serial measurement of lead level is useful in patients receiving IV $CaNa_2$ EDTA for management of lead poisoning).

A urinalysis is necessary. Performing a urine pregnancy test is wise in all women of childbearing age. Urine

**BOX 2A-11 RADIOPAQUE TOXINS**

**Drugs**
Chloral hydrate
Enteric-coated preparations
Phenothiazines
Sustained-release products

**Metals and Minerals**
Arsenic
Calcium
Iron
Lithium
Lead
Potassium

**Foreign Bodies**
Crack vials
Drug packets

pH monitoring is helpful in the management of salicylate overdose. Urine is the best specimen to use for "drug screening" purposes. A urinalysis is also useful in the early identification of acute renal failure or rhabdomyolysis with myoglobinuria.

The intravenous drug abuser requires special blood testing, such as evaluation for human immunodeficiency virus, a hepatitis profile, a blood culture to identify bacteremia, and evaluation for rhabdomyolysis.

Chest radiography is an aid for diagnosing aspiration pneumonia or pulmonary edema. Box 2A-11 lists agents that are radiopaque on plain film radiography of the abdomen. Computed tomography may be useful if underlying trauma is suspected. Finally, lumbar puncture may be indicated for ruling out meningitis in a patient with fever and coma.

## *Decontamination of the Eyes, Skin, and Gastrointestinal Tract*

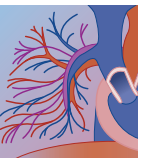
### OCULAR DECONTAMINATION

See Chapter 15.

### DERMAL DECONTAMINATION

Being the largest and most superficial organ in the body, the skin is often subject to exposure to toxins and is affected in 7.9% of reported cases. At least 50% of occupational illnesses involve the skin. The effects of these exposures can be local or systemic (Box 2A-12).

The skin provides many barriers to the absorption of toxins. The stratum corneum forms an important first barrier and is highly effective when it is completely intact. However, when skin wounds are present, when the wounds are wet, and when exposure is to certain highly lipophilic substances (e.g., organophosphate insecticides), significant absorption of toxin through the skin can occur. The skin of infants is notable for being more permeable than that of adults to substances of all classes.





**BOX 2A-12 TOXINS ASSOCIATED WITH SYSTEMIC TOXICITY AFTER DERMAL ABSORPTION**

Aniline dyes
Camphor
Dinitrophenol
Hexachlorophene
Hydrofluoric acid
Lindane (γ-benzene hydrochloride)
Organophosphate insecticide
Nerve agents
Nitrobenzene
Organic mercury
Phenol
Thallium

The range of dermal toxins is broad. Most of these substances are corrosive agents capable of producing burns that may become full thickness (i.e., third degree). Other types of agents are irritants, sensitizers (including photosensitizers), allergens, vesicants, and exfoliants.

### *Management*

As with ocular exposures, the general principles of management after exposure to dermal toxins are many. As soon as a toxic dermal exposure is recognized, decontamination efforts should begin. If the victim is immersed in a toxic fluid, the first step in management is his or her extrication without injury to the assistant. The victim should disrobe him- or herself at the scene. If the victim requires assistance, undressing should be done as safely as possible. Protective gear should be donned before assistance with decontamination is rendered. Unless the agent is highly reactive (e.g., elemental sodium), it is appropriate to wash the victim thoroughly with water, preferably in a nearby decontamination shower. Generally speaking, water should not be used to decontaminate skin in exposures to sodium, phosphorus, calcium oxide, chlorosulphonic acid, and titanium tetrachloride. When emergency medical personnel arrive to the scene, they should continue skin decontamination. Again, if the agent is known to have significant dermal absorption, emergency medical personnel should provide themselves every available level of self-protection. Certain toxins such as organophosphates can contaminate the air within the ambulance and produce ill effects among personnel if prehospital decontamination efforts are inadequate.

Upon arrival at a health care facility, the victim may require quarantine, depending on the nature of the agent. Skin decontamination in a decontamination shower should continue. Particular caution should be exercised in the decontamination of victims of organophosphate insecticide or organophosphate-based nerve gas exposure; health care personnel have been overcome secondarily by contaminants on victims when they assisted in their care without donning proper protective gear.

**TABLE 2A-8 Specific Interventions for Toxic Dermal Exposure**

| TOXIN | THERAPEUTIC INTERVENTION |
|---|---|
| Hydrofluoric acid | Calcium gluconate |
| Instant-bonding adhesive ("Super Glue") | Polyoxyethylene sorbitan (Neosporin) |
| Elemental sodium | Mineral oil |
| Organophosphate insecticide | Protected decontamination |

Water is the most commonly used skin decontaminant and is highly effective for most dermal exposures. In select cases, specific agents should be used to assist in management (Table 2A-8).

Without exception, toxin-induced skin burns should be treated according to existing burn management guidelines. These include wound débridement and dressing, monitoring for infection, fluid management, and surgical consultation when appropriate.

## ELIMINATION OF POISON FROM THE GASTROINTESTINAL TRACT

After the ingestion of a toxic substance, with the exception of agents that have a direct toxic effect on the gastrointestinal tract (e.g., iron or corrosives), that substance must be systemically absorbed and circulated before it reaches a target organ and exerts clinical toxicity. Preventing the absorption of toxin is therefore the foundation of treatment after ingestion of a toxin has occurred. The term *gastrointestinal decontamination* (GID) has been coined to describe those interventions that are useful in preventing toxin absorption. With the exception of rare interventions such as gastroscopy, GID is considered to have only three components: (1) gastric evacuation, (2) administration of adsorbent, and (3) catharsis. Gastric evacuation is accomplished through gastric lavage. Syrup of ipecac, once used as an emetic for treatment of toxic ingestions, is no longer routinely recommended for this purpose. There are several agents that can adsorb toxic substances, reducing their systemic absorption and subsequent toxicity (Table 2A-9). Of these, activated charcoal is the most important adsorbent; there are few substances that activated charcoal will not adsorb (Box 2A-13). Catharsis, once an integral part of management, also has a diminishing role in the treatment of poisoned patients.

Gastrointestinal decontamination is discussed in greater detail in Chapter 2B.

## ANTIDOTES

With the development of sophisticated new antidotes and the changing spectrum of clinical poisoning, the use of emergency antidotes is assuming an increasing role in clinical toxicology. However, antidotes are useful in only a fraction of poisonings.[1] Table 2A-1 lists the common emergency antidotes. In poisoning with a known substance, early antidote use is indicated for emergency stabilization, often within the first hour.

**TABLE 2A-9 Adsorbents Used in the Management of Toxic Ingestions**

| ADSORBENT | TOXIN |
|---|---|
| Activated charcoal | Pharmaceuticals, organic agents |
| Cholestyramine | Organochlorines (chlordecone, lindane) |
| Sodium phosphorsulfonate (Kayexalate) | Lithium, potassium |
| Fuller's earth, bentonite | Paraquat |
| Starch | Iodine |
| Potassium ferricyanate (Prussian blue) | Thallium |

**TABLE 2A-10 Additional Treatment Methods for Enhanced Elimination of Absorbed Substance**

| TREATMENT | DRUG |
|---|---|
| Hemodialysis | Lithium |
| | Ethylene glycol |
| | Methanol |
| | Salicylate |
| | Theophylline |
| | Valproate (in severe overdose) |
| Hemoperfusion | Theophylline |
| | Phenobarbital |
| Alkalinization of urine | Phenobarbital |
| | Salicylates |

**BOX 2A-13 SUBSTANCES NOT WELL ADSORBED TO ACTIVATED CHARCOAL**

**Alcohols**

Acetone
Ethanol
Isopropyl alcohol
Methanol
Glycols (ethylene glycol, propylene glycol, diethylene glycol)

**Hydrocarbons**

Petroleum distillates
Plant hydrocarbons (e.g., pine oil)

**Metals and Inorganic Minerals**

Arsenic
Boric acid
Fluoride
Iron
Lead
Sodium

**Corrosives**

Sodium hydroxide
Sulfuric or nitric acid

Hyperbaric oxygen can provide oxygen at pressures greater than normal atmospheric pressure, which is given as 1 atmosphere (atm) or 760 mm Hg. Three atmospheres is the maximal pressure humans can tolerate over a reasonable period of time; hyperbaric units generally do not exceed 2.5 to 2.8 atm. The use of hyperbaric oxygenation is becoming standard therapy for patients with significant carbon monoxide poisoning, and it is becoming more available (see Chapter 87) for carbon tetrachloride poisoning, and possibly for cyanide and hydrogen sulfide poisoning.

Admission to an intensive care unit following antidotal therapy for further management and observation is generally indicated. Further discussion of each antidote and its use is provided in the chapter on the specific poison.

## ELIMINATION ENHANCEMENT OF ABSORBED SUBSTANCES

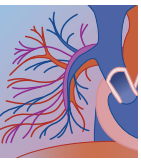
There are multiple methods by which agents in the systemic circulation, whether ingested or administered parenterally, can be removed. The four most clinically useful means of elimination enhancement are (1) multiple-dose activated charcoal, (2) hemodialysis, (3) hemoperfusion, and (4) urine alkalinization. Potential roles for these interventions are found in Table 2A-10 and Box 2A-14. Further discussion of elimination of a substance that has already been absorbed is provided in Chapter 2C.

## OBSERVATION AND SUPPORTIVE CARE

Observation and supportive care are the mainstays of therapy for the poisoned patient. Indiscriminate use of gastric lavage, antidotes, and drugs should be avoided. All too often, the toxic agent is unknown, multiple drugs have been taken, or the patient is too unstable to undergo an aggressive therapy such as hemodialysis. Monitoring of vital signs, cardiac telemetry, and oxygen saturation is mandatory.

Hospitalization in an intensive care unit is generally indicated for the patient with serious poisoning. Multisystem monitoring with blood studies and assessment of other parameters are indicated, and upon detection of any specific system disturbance, appropriate subspecialty consultation is warranted.

Some agents such as iron, mercury, acetaminophen, paraquat, carbon tetrachloride, and *Amanita phalloides* toxin have a latent phase, in which the patient appears to recover from the initial insult, only to decompensate 24 to 72 hours postingestion. Patients with overdose of sustained-release capsules, such as calcium channel blocker or theophylline preparations, also may have delayed manifestation of poisoning. Rarely, the tricyclic antidepressants have been known to cause fatal arrhythmia up to 3 days following ingestion. Some effects are not seen until later, such as hypertension following phencyclidine ingestion, hemorrhagic colitis following mercury ingestion, and disseminated intravascular coagulation following snakebite. One must also watch for the delayed pulmonary (see Chapter 9), hepatic (see Chapter 11), renal (see Chapter 12), and hematologic (see Chapter 14) manifestations of poisoning.





**BOX 2A-14 EFFICACY OF MULTIPLE-DOSE ACTIVATED CHARCOAL IN ENHANCING DRUG ELIMINATION**

**Effective**

Phenobarbital
Theophylline
Carbamazepine
Salicylates
Digitoxin
Dapsone

**Questionably Effective**

Anticholinergic/antihistaminic agents
Sustained-release pharmaceuticals
Thyroid hormone
Valproate

**Unlikely to Be Effective**

Aminoglycoside antibiotics
Anticholinergic/antihistaminic agents
Calcium channel blockers
Phenothiazines
Propoxyphene
Tricyclic antidepressants

Patients may require observation because of an underlying disease that may be exacerbated because of the overdose, such as diabetes, congestive heart failure, cardiac rhythm disturbances, or chronic lung disease. Observation may be necessary to evaluate or treat complications, such as in a patient with an overdose who fell and sustained trauma or in a patient who develops aspiration pneumonitis or interstitial pulmonary edema.

The IV use of illicit drugs is associated with multiple complications; observation is especially indicated for patients experiencing these complications, which include bacterial endocarditis, rhabdomyolysis, and neurologic sequelae.

## DISPOSITION

The disposition of the patient with intoxication may involve medical and psychiatric care as well as social follow-up. All patients admitted to the hospital with intentional overdose warrant close observation and the institution of suicide precautions. These patients may need appropriate restraint or observation if further injury or additional overdose attempts are to be prevented. Overt or subtle attempts or gestures indicate the need for psychiatric evaluation. Often, outpatient follow-up is necessary; for example, a child with kerosene ingestion may require further examination and chest radiography, and a child who has ingested anticoagulant rat poison may require serial outpatient monitoring of prothrombin times. The issue of child abuse or neglect may need consideration whenever a pediatric patient is treated. Finally, long-term follow-up may be indicated; for example, hepatitis and HIV testing may be needed in the IV drug abuser.

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# B Decontamination

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## CONTROVERSY AND CONSENSUS

The treatment of toxic exposures by application of decontamination procedures has a long history. Logic suggests that removing even a portion of a toxic dose of a substance before it can act on the organism should improve outcomes. However, clinical and experimental studies have often failed to demonstrate the anticipated benefits. As a consequence, a number of consensus conferences and position statements have been developed to address various decontamination methods. The most recent iterations of these documents are briefly reviewed here. It should be recalled in the decision-making process that the conclusions of an expert panel are limited by the quality of the available evidence base. A number of case series and randomized clinical trials examining decontamination methods have been published, with numbers of patients in the range of 300 to 1000 or more.[1-4] Unfortunately, most of the randomized clinical trials investigating decontamination methods have lacked sufficient statistical power to discern important differences for outcomes involving any specific toxicant. In fact, there are noteworthy basic obstacles to performing reproducible, informative decontamination studies. Overdose patients frequently misrepresent or are ignorant of what dose of a compound they have taken or when the exposure occurred. Clearly, decontamination procedures should have greater effect when applied early, before significant absorption has taken place. Yet many studies include patients who are already significantly poisoned (i.e., symptomatic due to absorption), in whom decontamination measures would be expected to have little impact, unless the exposure is ongoing. Enrolling a large number of patients with similar clinical presentations (single drug, similar quantity of drug ingested and time since ingestion) is very difficult in a single center or even multiple centers. Confirmation of exposure by laboratory studies is often unavailable, requiring the clinician to depend on the history (which may be inaccurate) and physical findings (which may be nonspecific) in arriving at the diagnosis of poisoning. There are likewise problems with randomization schemes,[5] and basic inclusion and exclusion criteria.

In addition, there are problems with the process of evidence-based reviews themselves. Language bias occurs in some evidence-based reviews,[6] such that non–English language publications, potentially of good quality, are often excluded from consideration. In addition, the premises on which the evidence review is based may not be universally applicable. The conclusions reached, based on studies performed in urban tertiary care centers where hospitals are capable of providing state-of-the-art intensive care, may not apply equally to a remote hospital in a rural area, or even less so to a clinic in a developing country. Thus, while careful consideration should be given to position papers and consensus conference proceedings, individual judgment will necessarily enter into the decision to employ any decontamination method for a given case of exposure. Unfortunately, an unintended consequence of the publication of position papers is that they may in fact squelch further research.[5]

## METHODS OF DECONTAMINATION

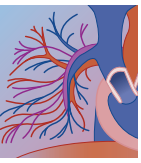
A number of methods of decontamination exist and may be employed depending on the circumstances of exposure. Decontamination of the skin and eyes, as well as the gastrointestinal tract, will be discussed. Extracorporeal methods of purification (hemodialysis, charcoal filtration, etc.) are covered in Chapter 2C.

## SKIN AND EYE DECONTAMINATION

Decontamination of the skin and eyes is employed to reduce local tissue injury (chemical burns or irritation) and/or absorption that may result in systemic consequences. The decision to perform skin and eye decontamination is often based on the presence of symptoms, such as burning or itching. This is an insensitive evaluation method; thus, decontamination of these organs should primarily depend on careful consideration of the circumstances of exposure and the physical and toxicologic properties of the compound. Protection of personnel during eye and skin decontamination is important to avoid secondary contamination of health care providers. The choice of personal protective equipment is beyond the scope of this chapter. The reader is referred to Chapter 103 and to the recent Occupational Safety and Healthy Administration (OSHA) best practices document.[7]

### *Choice of Decontamination Methods Based on Physical Properties of the Toxicant*

In almost all cases, clothing, jewelry, and shoes should be rapidly and completely removed prior to washing. It has been suggested in studies of radionuclide contamination that this process alone can remove the majority of a contaminant. This will, of course, depend on the physical properties of the toxicant but is a logical first step. Solids and dust should be gently brushed away before decontamination with a solution. In this way, the heat generated from water reactive compounds can be diminished, as is caking of solids.





In some cases, water or other decontamination solutions may be unavailable or in short supply. In such cases, dry decontamination, using an absorbent material (charcoal, flour, earth) followed by brushing or wiping may be attempted.

## Choice of Decontamination Solutions

The selection of skin decontamination solutions has historically been a choice between water for polar (water-soluble) compounds and water plus a mild soap or detergent for nonpolar compounds. Water alone is typically employed for initial eye decontamination. Physiologic saline and other saline-based eye washes are often employed for eye decontamination in health care and industrial settings. The use of these solutions has been largely empiric and practical, based on widespread availability rather than on critical evaluation of their efficacy. Yano and colleagues studied water irrigation of burns involving 1 mol/L HCl in rats, measuring subcutaneous pH as a measure of penetration of the acid and efficacy of decontamination. These investigators found that maximal subcutaneous pH depression had occurred by 7 minutes following application of the acid. Animals undergoing water irrigation at 1 or 3 minutes postexposure demonstrated some benefit; however, animals irrigated at 10 minutes had no appreciable improvement in pH, compared with control.[8] These investigators had previously demonstrated lack of efficacy of water irrigation after 10 minutes in a 2N NaOH burn model.[9] Clearly time is of the essence in irrigation of corrosive exposures. With regard to eye exposures, Kuckelkorn and colleagues[10] pointed out that water is hypotonic to corneal stroma, allowing edema and increased penetration by chemicals. They recommend use of amphoteric solutions to avoid these problems.

In recent years, a number of novel decontamination solutions have come to market. Diphoterine (Prevor Laboratories, Moulin de Verville, France), an amphoteric solution has been proposed for use in both acid and alkali exposures of eyes and skin, with emphasis on immediate irrigation (at the scene of the incident) rather than for hospital treatment. A recent article[11] that compared Diphoterine to physiological saline in alkaline eye burns demonstrated more rapid healing of grade 1 and 2 burns with Diphoterine than with saline. The study suffers from a number of deficiencies, including lack of randomization and significant delays and variability in initial irrigation (in the field) and secondary irrigation in hospital (with either Diphoterine or saline). Nonetheless, the time to corneal reepithelialization was approximately six times as long after saline for grade 1 burns and almost twice as long for grade 2 burns, compared with Diphoterine-treated eyes. There were an insufficient number of grade 3 burns to detect any significant difference between groups. Despite its shortcomings, this study suggests the potential for improved healing using Diphoterine in alkaline eye burns and warrants further investigation. The same study group had previously shown in a study of ammonia burns in New Zealand albino rabbit eyes that early application (within 10 minutes) of Diphoterine rapidly corrected pH, whereas saline irrigation did not. Furthermore, saline-treated eyes had stromal edema, whereas Diphoterine-treated eyes did not.[12] The need for early irrigation is emphasized by this experimental study; however, the cited clinical study demonstrates some benefit even with delayed treatment (mean 4.7 hours).[11] Cavallini and Casati studied Diphoterine in experimental skin burns in rats involving 52% hydrochloric acid. Skin flushing with Diphoterine reduced substance P release during the first 48 hours after burn and was associated with better wound healing and higher concentrations of β-endorphin 7 days later when compared with normal saline or 10% calcium gluconate.[13] Hall and colleagues[14] have reviewed the chemical and physical properties and proposed uses of Diphoterine. Hexafluorine, manufactured by the same company, is proposed for treatment of exposures to hydrogen fluoride. Both Diphoterine and Hexafluorine are indicated for skin and eye decontamination.*

The National Nuclear Security Administration's Sandia National Laboratories has developed decontamination foam, referred to as EasyDECON 200 or DF 200. This product is purported to be effective against a variety of chemical and biological warfare agents, including cyanide, phosgene, mustard, VX, G agents, anthrax, *Yersinia pestis*, and corona viruses. The Illinois Institute of Technology and the Southwest Research Institute have performed tests of the ability of the compound to neutralize chemical and biological agents. While there is mention on the laboratory's website of seeking U.S. Food and Drug Administration (FDA) approval of DF 200 for personal decontamination, no peer-reviewed studies of its use in humans were identified. As such, this product cannot be currently recommended for human use.

Most authors recommend against neutralization of acid and base burns due to the risk for exothermic reaction leading to thermal burns. Simple dilution with water or milk after oral ingestion of corrosives is uncommon in Europe, but the norm after ingestions in the United States. Penner demonstrated in an ingestion model that dilution of concentrated sulfuric acid with an equivalent volume of water results in a temperature elevation of approximately 80°C. Neutralization results in even greater heat production. He suggested that vigorous gastric aspiration (likewise considered controversial given the risk for esophageal or gastric perforation) prior to cold fluid lavage is the treatment of choice in patients treated immediately following acid ingestion.[15] A recent experimental study involving irrigation of rat skin exposed to 2N NaOH with 5% acetic acid suggests that neutralization may not always be contraindicated. The investigators demonstrated more rapid correction of pH, no difference in peak temperatures, and improved outcomes in animals treated with 5% acetic acid rather than water. These findings cannot

*Diphoterine and Hexafluorine are proprietary products without generic equivalents. Use of the trade name in this chapter does not constitute an endorsement.

be generalized, but indicate the need to readdress current dogma regarding neutralization.[16]

## Duration of Decontamination

The ideal duration of eye and skin decontamination is yet to be determined. Recommendations for copious irrigation are common, without further precision. Fifteen minutes is probably the most commonly recommended duration for eye irrigation. Kuckelkorn and colleagues have recommended a minimum of 30 minutes for eye irrigation after chemical exposures.[17] One retrospective study of 172 eye burn victims suggested that outcomes were better among those who had prolonged (1 to 2 hours) irrigation.[18] Irrigating to a relatively neutral pH is often attempted. If this is employed, it is helpful to remember that the pH of saline for intravenous injection (often employed for eye irrigation) is appreciably acidic (approximately 4.5) so that one should wait a few minutes after irrigation to measure the pH in order to allow the patient's own tears to replace the saline irrigation fluid in the conjunctival sac.

## Temperature

The appropriate temperature for decontamination fluids has also been poorly studied. While increasing temperature of decontamination liquids reduces the likelihood of hypothermia in inclement climes and improves water solubility, heat also dilates skin pores and blood vessels, which may lead to increased absorption. If excessive, it may aggravate chemical or thermal burns. OSHA's recently published *Best Practices Guide for First Receivers*[7] recommends a 5-minute wash with tepid water, based on recommendations from the U.S. Army for chemical decontamination.[19] Mcintyre and colleagues recommend "warm, but not excessively warm" water for decontamination.[20] Eye irrigation should be performed with room temperature solutions. Careful thought should be given to environmental conditions and risk for exposure when decontamination must be done out of doors.

### MASS CASUALTIES

The duration and type of skin and eye decontamination performed in mass casualty situations may vary from that in cases involving single patients based on triage considerations. Management of mass casualties is covered in Chapter 103.

#### *Decontamination Systems*

A great number of options have been developed in recent years for skin decontamination, due to the increased interest in hazardous materials and chemical terrorism issues. Examples of decontamination stretchers and facilities are shown in Figures 2B-1 to 2B-3. Many others exist. One of the overriding considerations in determining the kind of decontamination facilities and equipment to purchase should be their capacity for rapid deployment. The experience with the sarin terrorist attack in Tokyo revealed that hospitals may be rapidly

**FIGURE 2B-1** Portable decontamination stretcher.

**FIGURE 2B-2** Portable decontamination shower.

inundated with contaminated casualties. Decontamination protocols that are not deployable within minutes (preferably 5 to 10 minutes) after an incident may serve little purpose in protecting the facility and health care providers from contamination. Serious consideration should be given to the complexity of the setup process, one that typically will not be employed frequently. One example of a locally developed immediate deployment sheltered outdoor decontamination unit is shown in Figure 2B-4. This unit can be deployed in less than 2 minutes and provides for decontamination of both ambulatory and stretcher patients.

#### *Personnel*

It is common practice to utilize physicians, nurses, and other critical emergency department (ED) staff to do decontamination. This is probably not advisable for a number of reasons. First, decontamination does not require great technical skill, and very little stabilization


A

B

**FIGURE 2B-3** **A,** Portable decontamination trailer. **B,** Portable decontamination tent.

can be performed during the decontamination process. Furthermore, if there are problems and decontaminating personnel are unable to continue, such a practice results in incapacitation of primary emergency care providers. Neither should security personnel, in general, be tasked with this responsibility, since a mass casualty situation will require their services for security itself. A number of alternatives have been suggested. Some hospitals train housekeeping staff to perform decontamination. Others have nurses from other units (burn units have extensive experience in wound care and cleaning) don protective clothing and prepare for decontamination while the ED staff prepares the decontamination facility and the ED proper to receive casualties.

## SPECIAL SITUATIONS

### Radionuclides

Decontamination of radionuclides from the skin may be performed in a manner analogous to chemical exposures. Uranium hexafluoride exposures should be treated in a manner analogous to that for hydrofluoric acid burns. Wounds heavily contaminated with radionuclides may require surgical débridement and should be covered after initial decontamination. See Chapter 104 regarding radiation emergency management for further information.

### Fluorides

Hydrogen fluoride, ammonium biflouride, and other soluble fluorides may pose a unique case in terms of decontamination. While an initial quick flush with water is appropriate, the patient may benefit from rapid decontamination with a substance that can bind the fluoride. Hexafluorine has been reported to prevent significant skin burns in both humans and experimental animals when applied immediately after exposure.[21,22] Two randomized studies in rats found, however, that Hexafluorine was no better than water in preventing electrolyte disturbances caused by fluoride[23,24] and perhaps less effective than water or water plus calcium gluconate in reducing burn injury.[24] Thus, Hexafluorine's efficacy in fluoride injury remains controversial.[25] Researchers in hydrogen fluoride manufacturing facilities frequently recommend skin irrigation with benzalkonium chloride solution based on studies performed in pigs.[26,27] Calcium gluconate irrigation of skin[28] and eyes[29] has also been recommended to bind fluoride and prevent further injury. Other investigators have found calcium gluconate to be no more effective than water or saline and perhaps detrimental in eye irrigation.[30,31] In summary, the ideal decontamination of hydrogen fluoride burns to skin and eyes remains to be determined.

### Phenol

Phenol is unique in its capacity to cause nonpainful burns and systemic toxicity. Water irrigation may increase phenol absorption.[32] Generally accepted skin irrigation therapy consists of isopropanol[32,33] or polyethylene glycol solutions.[32,34]

### Flammable Metals and Other Water-Reactive Materials

White phosphorus is pyrophoric (i.e., it burns in the presence of air). It is thus indispensable to provide adequate copious irrigation with water. The application of copper sulfate has been recommended,[35] but an experimental study in rats demonstrated increased lethality in animals receiving topical treatment with 1% copper sulfate.[36] Eldad and colleagues have evaluated various phosphorus burn treatment recommendations and have concluded that copious water irrigation is superior to other treatments.[37]

#### HIGH-PRESSURE INJECTION INJURIES

High-pressure injection injuries should be mentioned here due to their requirement for special care and high

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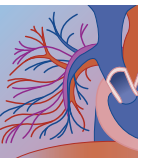
**FIGURE 2B-4** **A,** Fixed immediate deployment decontamination facility at Singapore General Hospital and Drug and Poisons Information Centre. The unit is located in the drive-through ambulance bay in front of the emergency department. This shows the unit in predeployment position. **B,** Deployment of the unit requires turning on a few switches, which control descent of the shower heads, flexible walls, and temperature control. The unit is ready for operation in approximately 2 minutes. **C,** Shower heads drop out of the ceiling for self- or assisted irrigation. **D,** Flexible walls drop from the overhead frame, providing easy ingress, egress, and protection from elements, as well as privacy. **E,** The unit is ready for use. Floor drains collect the water for appropriate disposal. (Photographs courtesy of Dr. Gaerpo Ponampalam and the Singapore Drug and Poisons Information Centre.)





risk for morbidity. Wounds inflicted by pressurized paint guns or grease guns are often deceivingly benign appearing on the surface. The temptation is to simply decontaminate the overlying skin and wash the puncture wound (if visible) from the surface. Such an approach may result in loss of function or even complete loss of a limb. Such wounds need to be explored thoroughly, perhaps best done in the operating room, for evidence of subcutaneous contamination.[38,39]

### TETANUS PROPHYLAXIS

All eye and skin exposures resulting in violation of the epithelium should prompt consideration of the need for tetanus toxoid administration.

## GASTRIC EMPTYING

### *Emetics*

The only emetic currently recommended for use in humans is syrup of ipecac. Previously employed emetics continue to be responsible for significant pathology, however. The administration of table salt has long been condemned in the literature[40]; nonetheless, recent reports illustrate that its use has not been completely abandoned and that it remains potentially lethal.[41,42] Liu reported that copper sulfate continues to be used in China for emetic purposes and has resulted in multiple fatalities in recent years.[43]

The dose of ipecac is 5 to 10 mL in children 6 to 12 months of age or 15 mL in children 1 to 12 years of age. This should be followed by 10 to 20 mL water per kg body weight. Older children and adults should receive 30 mL ipecac followed by 200 to 300 mL of water. Ipecac is contraindicated in the following situations:

Ingestion of petroleum distillates
Ingestion of strong acids or bases
Ingestion of strychnine or other proconvulsants
Unconsciousness or absence of gag reflex

Ipecac has a number of potential adverse effects, including lethargy, cramps, and diarrhea. When taken chronically, it may induce muscle cramps and both skeletal[44] and cardiac myopathy.[45] It is subject to frequent abuse by patients with eating disorders, a factor that led to a review of the product's safety by the FDA in 2003.

The American Academy of Clinical Toxicology (AACT) and the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT) reviewed the medical literature regarding the use of ipecac in 1997.[46] This combined task force more recently examined their previous findings and literature that had appeared since their earlier review. In brief, they concluded that syrup of ipecac should not be administered routinely in the management of poisoned patients. They pointed out that in experimental studies the amount of marker removed by ipecac was highly variable and diminished with time. Furthermore they concluded that there is no evidence from clinical studies that ipecac improves the outcome of poisoned patients and recommended that its routine administration in the ED be abandoned. Finally, they signaled the absence of data to support or exclude ipecac administration soon after poison ingestion, the administration of ipecac potentially reducing the effectiveness of activated charcoal, oral antidotes, and whole bowel irrigation (WBI).[47]

There are indications that the use of syrup of ipecac has dramatically declined in recent years, and it is likely that this trend will continue.[48,49] Bond examined the evolving use of ipecac in U.S. poison centers, comparing rates of referral to the ED and moderate or greater outcomes in patients younger than 6 years with unintentional ingestions. This comparison was carried out according to the frequency with which centers recommended use of ipecac. Overall, use of ipecac was extremely rare (1.8%) and significant adverse outcomes even lower (0.6%). Comparing the two groups of 32 centers each, there were no significant differences in referral rates or adverse outcomes. Bond concluded that there was no reduction in resource utilization (ED referral) or improvement in patient outcome from the use of syrup of ipecac at home and that while the data could not exclude a benefit in a very limited set of poisonings, such a benefit remained to be proven. Shannon, in an editorial in the same issue, sounded the demise of ipecac on the basis of lack of proven efficacy, changing patterns in poison center approaches to the management of pediatric ingestions (including preference for activated charcoal when decontamination is indicated), and the move by the FDA to rescind ipecac's over-the-counter status.[50] This prediction was prescient, since the American Academy of Pediatrics, based on Bond's article and the factors cited by Shannon, revised its position statement on ipecac use, calling for abandonment of the regular stocking of it in the home.[51]

More recently, a U.S. government–convened review panel of experts published their conclusions regarding ipecac use.[52] The panel concluded that the use of ipecac syrup might have an acceptable benefit-to-risk ratio when:

There is no contraindication to the use of ipecac syrup.
There is substantial risk of serious toxicity to the victim.
There is no alternative therapy available or effective to decrease gastrointestinal absorption (e.g., activated charcoal).
There will be a delay of more than 1 hour before the patient will arrive at an emergency medical facility.
Ipecac syrup can be administered within 30 to 90 minutes of the ingestion.
Ipecac syrup administration will not adversely affect more definitive treatment that might be provided at a hospital.

Given these restrictions, rural residents might consider keeping ipecac on hand for home use under poison center direction. Otherwise, these recommendations sharply limit the applicability of the drug and, thus, the induction of vomiting in general.

## Gastric Lavage

The employment of gastric lavage is controversial and varies markedly depending on geographic area and the background and training of the practitioner. Gastric lavage involves blind placement of a large-bore gastric tube into the stomach, in a patient who can either protect his or her own airway or in whom the airway has been protected by an endotracheal tube, with the goal of removing toxicant remaining in the stomach through a combination of instillation of water or physiological saline, followed by suction or gravity-induced drainage. This cycle of instillation/drainage is repeated until the effluent is clear or until several liters of water/saline have been passed through the tube. This procedure has been widely popular in the past and continues to be employed in many EDs around the world. It is, however, a largely unproven therapy.

### INDICATIONS

The indications for gastric lavage are recent ingestion (generally less than 1 hour, unless the ingestion involves agents that decrease gastric motility, such as anticholinergics) of a substance of sufficient quantity to be likely to cause serious harm in the absence of removal. The procedure should be given greater consideration in ingestions for which inadequate treatment modalities exist (paraquat) or in cases where delivery of proven effective therapy (antidotes or extracorporeal removal) is likely to be delayed.

### CONTRAINDICATIONS

Ingestion of low-viscosity petroleum products, corrosives (acids and alkalis) and inability to protect the airway (unless tracheal intubation has been performed beforehand) are contraindications to gastric lavage.

### ADVERSE EFFECTS

Serious adverse effects of gastric lavage are relatively rare but may be significant. The procedure may induce hypoxia,[53] perforation of the gastrointestinal tract or pharynx,[54,55] fluid and electrolyte abnormalities,[56] inadvertent tracheal intubation, as well as aspiration pneumonitis.[57] Tracheal intubation is not completely protective against aspiration.

### EFFICACY

The AACT/EAPCCT recently reviewed the animal and clinical literature regarding gastric lavage and published a position statement,[58] which states in part that gastric lavage should not be employed routinely, if ever, in the management of poisoned patients. The study group pointed out that in experimental studies, the amount of marker removed by gastric lavage is highly variable and diminishes with time and that few clinical studies have demonstrated a beneficial effect on outcome.

The quality of the gastric lavage literature is, for the most part, lacking. Few studies have the power to detect significant differences in outcome for a single toxicant, and it seems unscientific to compare outcomes after ingestion of widely varying products. Furthermore, there are many unknowns in any clinical trial, the most significant of these being the time between ingestion and treatment and the amount of toxicant ingested. It is fair to say that the evidence for efficacy is currently deficient, but that lack of efficacy has not been proven either.

## Endoscopy

The use of endoscopy in the diagnosis of caustic injuries is addressed in Chapter 98. Its use in the retrieval of foreign objects, such as batteries,[59] firearm cartridges,[60] and various pill fragments[61-66] has been reported in humans and studied in animals,[67] but has not been systematically addressed in humans. Faigel and colleagues report that endoscopic use of the Roth net was most effective in removal of button batteries.[67] Like other forms of decontamination, endoscopy to retrieve tablet fragments has been associated with significant complications; thus, the decision to perform endoscopy in these circumstances should be carefully weighed against the risks.[62]

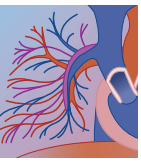
## Surgical Laparotomy for Decontamination

Surgical gastrointestinal decontamination has been employed for button battery ingestions,[68-70] cocaine and narcotic drug packets,[71-77] and bezoars of iron[78] and theophylline,[79] among others. Batteries passing the esophagus usually are expelled in the feces and are generally believed to require no intervention, although recent reports of early battery leakage have called the "wait and see" approach into question.[80,81] Button batteries, when impacted in the esophagus, should generally be removed by endoscopy unless perforation is suspected.[59,67,82] The trend toward use of smaller batteries by manufacturers has decreased the incidence of this problem. In the case of cocaine and heroin bodypackers/stuffers, many cases can be managed conservatively with WBI or other purgatives. Most researchers agree, however, that acute toxicity (drug leakage) and bowel obstruction are indications for immediate laparotomy.[71,73,75]

# ABSORBANTS

## Activated Charcoal

Charcoal binds to diverse substances, rendering them less available for systemic absorption from the gastrointestinal tract. It is obtained as a product of pyrolysis of numerous organic compounds (petroleum, wood, peat) and "activated" by heating it to 600° F to 900° F, in the presence of steam, carbon dioxide, or air. This gives the product a small particle size and large surface area. While charcoal adheres to many substances, a significant number of compounds and classes of compounds are poorly absorbed by charcoal. These include metals (lithium, sodium, iron, potassium) and alcohols. Thallium appears to be an exception, being relatively well absorbed by charcoal.[83]





Activated charcoal products containing sorbitol should be avoided where possible because (1) the efficacy of cathartics is lacking (see below); (2) sorbitol is emetogenic and can increase the risk for vomiting the charcoal; and (3) sorbitol administration in infants is associated with dehydration and other life-threatening events.

## Single-Dose Activated Charcoal

Activated charcoal is administered as a slurry, either in water or sorbitol, orally or via a nasogastric tube. Dose recommendations vary, but generally a larger dose is considered better, to assure that binding capacity exceeds the amount of toxicant present. The recommended dose is 0.5 to 1 g/kg in children or 25 to 100 g in adults.

### INDICATIONS

In general, to be maximally effective, charcoal should be administered as soon as possible after ingestion of the toxicant, preferably within 1 hour. Green and colleagues studied this issue in healthy volunteers in a randomized crossover study. After giving 4 g (the equivalent of eight extra-strength tablets) of acetaminophen to patients, then giving charcoal at 1, 2, or 3 hours after ingestion, they found no differences in the area under the curve of plasma acetaminophen. The investigators stated that "data do not support the administration of activated charcoal as a gastrointestinal decontamination strategy beyond 1 hour after drug overdose."[84] While there are obvious problems in extrapolating toxicokinetic results from a study involving a nontoxic dose to all overdoses, the results do suggest that benefit clearly decreases over time.

As for most decontamination measures, the indications for single dose activated charcoal are controversial. The recently released revision of the Single-dose Activated Charcoal Position Statement of the AACT/EAPCCT states that single-dose activated charcoal should not be administered routinely in the management of poisoned patients, but that it may be considered if a patient has ingested a potentially toxic amount of a poison (which is known to be adsorbed to charcoal) up to 1 hour previously. The researchers state that the potential for benefit after 1 hour cannot be excluded. Finally, they emphasize that there is no evidence that the administration of activated charcoal improves clinical outcome.[85]

### CONTRAINDICATIONS

Charcoal administration is generally considered contraindicated in ingestions of caustics, since it is probably ineffective in reducing their potential for harm and furthermore makes endoscopy difficult. Charcoal generally should not be administered when there is a high risk for gastrointestinal hemorrhage or perforation. Charcoal is likewise contraindicated in any patient in whom the airway protection is not assured. It should not be administered in the presence of hydrocarbons with high aspiration potential. Charcoal should not be administered in the case of ileus or mechanical bowel obstruction.

### ADVERSE REACTIONS AND COMPLICATIONS

One of the most common adverse events associated with charcoal administration is vomiting, which occurs in approximately 7% to 15% of patients. Abdominal bloating is also quite common. Both diarrhea and constipation may occur. Complications have been described, including pulmonary aspiration and direct administration into the lungs via misplaced nasogastric tube. Aspiration appears to be relatively rare, but may have serious consequences.[57,86-89]

## Multiple-Dose Activated Charcoal

Multiple-dose activated charcoal (MDAC) has been proposed for use in the case of drugs that undergo extensive enterohepatic or enteroenteric circulation. Drugs with small volumes of distribution are particularly susceptible to removal by adsorption to charcoal in the gut, which has sometimes been referred to as "gastrointestinal dialysis." Although experimental and volunteer studies have demonstrated that MDAC increased elimination of a number of compounds, there is little proof of clinical benefit.

### INDICATIONS

The AACT/EAPCCT has concluded that although many studies in animal and volunteer studies have demonstrated MDAC increases drug elimination significantly, there are no controlled studies in poisoned patients that demonstrate MDAC reduces morbidity and mortality. Pending further evidence of direct benefits, the study group recommended that MDAC be considered only if a patient has ingested a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine, or theophylline.[90]

### CONTRAINDICATIONS

The contraindications for MDAC are essentially those of single-dose activated charcoal. The admonition for use in intestinal obstruction is of even greater import in the case of MDAC. The presence of decreased peristalsis (often associated with anticholinergic drugs and opiates) should provoke extreme caution in the administration of MDAC.

## Prussian Blue

Prussian blue is an effective absorbent for the management of thallium and cesium intoxications. See Chapters 75 and 104 for further information.

## Fuller's Earth

Fuller's earth is often recommended for gastrointestinal decontamination of paraquat (see Chapter 78). Although effective for this purpose, this substance is found in few hospitals. Activated charcoal is an effective absorbent of paraquat and should be employed when Fuller's earth is not available.[91]

## ACCELERATION OF GASTROINTESTINAL TRANSIT

### *Cathartics*

Cathartics comprise another group of compounds recommended since ancient times for the purpose of eliminating toxicants from the gastrointestinal tract. The two most common categories of cathartics are the magnesium salts (e.g., magnesium citrate, magnesium sulfate) and nondigestible carbohydrates (e.g., sorbitol). Despite their long history of use, there is virtually no evidence of their efficacy. On the contrary, cathartics may induce significant harm in certain groups of patients, particularly children and those with renal disease.

#### INDICATIONS

There are no evident indications for the use of a cathartic alone in the treatment of poisoning.[92] An AACT/EAPCCT position statement concluded that experimental data are conflicting regarding the use of cathartics in combination with activated charcoal. The study group found no published clinical studies that investigated the ability of a cathartic, with or without activated charcoal, to reduce the bioavailability of drugs or to improve the outcome of poisoned patients. They went on to say that based on available data, the routine use of a cathartic in combination with activated charcoal is not endorsed and that if a cathartic is used, it should be limited to a single dose in order to minimize adverse effects of the cathartic.

#### DOSE

The dose of sorbitol is approximately 1 to 2 g/kg.[92] When given in combination with activated charcoal for single dose-activated charcoal therapy, the dose should be determined on the basis of charcoal dosing. If multiple doses of charcoal are to be administered, repeated use of sorbitol is not recommended. For magnesium citrate, the dose is 4 to 6 mL/kg in children and 300 to 480 mL in adults.

#### CONTRAINDICATIONS

Cathartics are contraindicated in the presence of bowel obstruction, in the absence of bowel sounds, or in the case of recent bowel surgery or intestinal perforation. They should likewise not be employed in the case of corrosive ingestions or when significant electrolyte disturbances, dehydration, or hemodynamic instability are present. Magnesium-containing cathartics must be avoided in patients with renal insufficiency and heart block. Caution should be employed in patients at extremes of age.

#### COMPLICATIONS

Cathartics frequently cause cramping, nausea, and vomiting. Significant dehydration may occur if catharsis is excessive, with resultant hypotension. Cathartic-related hypermagnesemia may result in cardiac dysrhythmias. Elderly patients and those with renal dysfunction are at particular risk.[93-95] Massive doses of cathartics may result in cardiopulmonary arrest.[93]

### *Whole Bowel Irrigation*

WBI involves the administration, by mouth or nasogastric tube, of large amounts of an iso-osmotic polyethylene glycol electrolyte solution (Go-Lytely [Braintree Laboratories, Braintree, MA], Co-Lyte [Schwarz Pharma, Mequon, WI], and others) with the goal of removing unabsorbed toxicant from the gastrointestinal tract as rapidly as possible by rectal expulsion. One rationale for its use includes the fact that some compounds are poorly absorbed by charcoal, particularly iron and lithium. WBI may be of particular interest in the case of sustained-release or enteric-coated compounds and in the case of drug packets (body packers). The AACT/EAPCCT's consensus panel concluded that WBI should not be used routinely and that there is no conclusive evidence that it improves the outcome of poisoned patients. Based on evidence from volunteer studies, the group recommended that WBI be considered for potentially toxic ingestions of sustained-release or enteric-coated drugs, particularly in those patients who present more than 2 hours after drug ingestion. They more strongly endorsed WBI for patients who have ingested substantial amounts of iron because the morbidity is high and there are no other effective options for gastrointestinal decontamination. Another potential indication cited for the use of WBI is expulsion of ingested packets of illicit drugs.[96]

#### DOSE

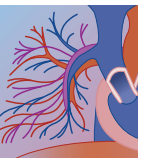
Polyethylene glycol electrolyte solution (e.g., Go-Lytely, Co-Lyte, NuLytely [Braintree Laboratories, Braintree, MA]) is administered by mouth or nasogastric tube at 25 to 40 mL/kg/hr until the rectal effluent is clear or until the desired effect is otherwise demonstrated (e.g., passage of drug packets demonstrated by imaging studies). Computed tomography (CT) with contrast has often been used to identify retained packets, but a recent case report demonstrated incomplete sensitivity of CT to detect all unexpelled drug packets.[72]

#### CONTRAINDICATIONS

WBI is contraindicated in the presence of mechanical or functional (ileus) bowel obstruction or perforation and in the presence of significant gastrointestinal hemorrhage. It should likewise be avoided if the patient is hemodynamically unstable.

#### COMPLICATIONS

Nausea and vomiting are not uncommon. Abdominal bloating and cramping may occur. Vomiting in the case of an unprotected airway may result in pulmonary aspiration.





## DECISION ANALYSIS FOR DECONTAMINATION

The decision to employ decontamination methods in an individual case must be determined based on the factors present in that individual case.

### *Dose Assessment*

First and foremost in the decision to attempt decontamination is a determination of whether a significant exposure has occurred. This is critical for numerous reasons: (1) needless decontamination procedures may delay other definitive therapy for systemic toxicity; (2) conversely, failure to adequately decontaminate the skin may increase morbidity of contaminated patients and result in secondary contamination of health care providers and facilities; and (3) decontamination, as discussed, is not without risks. It is vital to recall Hippocrates' admonition: *Primum non nocerum*. Dose/exposure assessment is extremely difficult on an acute basis due to the great number of unknowns. Young children cannot recount the quantity or quality of what they have ingested. Self-harm attempts are often accompanied by attempts to conceal or, conversely, to exaggerate the consumption of potentially toxic compounds. It is rare that contemporaneous exposure information (air concentrations or even product identification) is available after environmental exposures associated with hazardous materials releases or acts of terror. Fear associated with these events may result in psychogenic illness at times indistinguishable from that of the toxic exposure. When doubt exists, it may be safer to decontaminate, but this should be a considered decision.

### *Toxic Potential*

Once it is established that an exposure has occurred (or if exposure cannot be excluded) and some attempt has been made to determine the magnitude of the exposure, one must examine the toxic potential of the compound(s) in question, keeping in mind that the toxicity of combined substances is not always equal to the sum of their individual toxicities. Approaches to the treatment of poisoning are deeply rooted in personal experience and colored by bias in the literature. Recent studies have reexamined the need to decontaminate victims of certain exposures that were previously approached aggressively from a therapeutic standpoint.[97,98]

### *An Integrated Approach to Decontamination Procedures*

Decisions around decontamination must be individualized. A suggested approach is found in Figure 2B-5. This nonvalidated algorithm should simply be considered a pathway for considering options. There are numerous potential exceptions to the general suggestions in the figure.

#### WHEN SHOULD GASTRIC LAVAGE BE PERFORMED ALONE?

One might consider gastric lavage alone in the case of presentation of poisoning within 1 hour of ingestion by a highly toxic compound that is not readily absorbed by charcoal. Lithium is one such example.

#### WHEN IS GASTRIC LAVAGE FOLLOWED BY CHARCOAL APPROPRIATE?

Reiterating, gastric lavage is most likely to be effective in an early-presenting, potentially lethal ingestion. Cyanide is an example of a highly toxic compound that might be removed by lavage, but is also readily absorbed by charcoal.

#### IS THERE A ROLE FOR CHARCOAL FOLLOWED BY WHOLE BOWEL IRRIGATION?

Yes. Illicit drug packets containing cocaine or heroin may leak. A dose of activated charcoal given prophylactically (in the absence of symptoms) could theoretically absorb eventual leakage, while WBI accelerates passage of the packets. As a reminder, clinical evidence of toxicity (leakage) is an indication for laparotomy. Similarly, charcoal followed by WBI may be indicated for ingestions of enteric coated tablets.

#### WHEN SHOULD WHOLE BOWEL IRRIGATION BE UTILIZED?

In cases in which ingestion of a substance known to be effectively eliminated by WBI (such as lead, zinc, or iron) is not recent (and thus not likely to benefit from gastric lavage) and when the substance is not readily absorbed by charcoal, WBI alone may be indicated.

#### CONSULTATION

It should be clear from the discussion that the previously common "reflex arc" of ingestion-decontamination should not apply. The decision to apply a particular procedure or combination may not be simple. For this reason, consultation with a regional poison center and/or medical toxicologist is strongly suggested in cases of uncertainty.

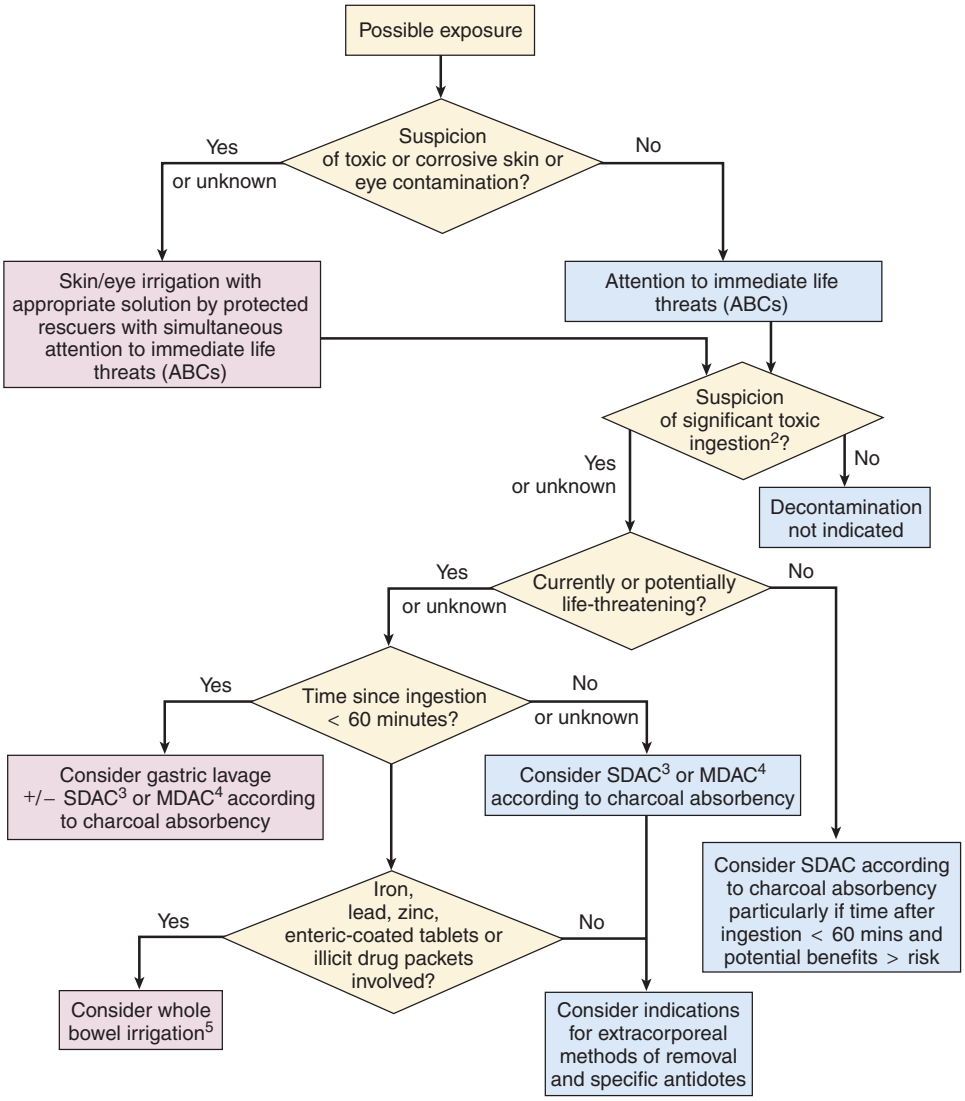
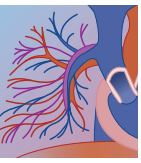



**FIGURE 2B-5** This flow diagram is essentially based on the current recommendations of the American Academy of Clinical Toxicologists and the European Association of Poisons Centres and Clinical Toxicologists. These recommendations are based on weight of evidence in the published literature, but this algorithm has not been validated. See text for details on individual decontamination procedures, indications, and contraindications.

1. Irritants, corrosives, and substances toxic by skin absorption should be removed. Liquids with high volatility and potential for secondary contamination (organic solvents) should likewise be removed. When in doubt, decontamination is appropriate; however, life-saving interventions (ABCs) take precedence over decontamination. Personnel should wear protective garments appropriate to the hazard.
2. If the history is reliable and the ingestion is clearly nontoxic, no decontamination is required. The urge to "do something" should be weighed against the maxim to "first, do no harm."
3. Single-dose activated charcoal (SDAC) is considered most effective when administered less than 1 hour after ingestion of a toxic substance. There is insufficient evidence to support or condemn its use with toxic ingestions presenting more than 1 hour later. In general, metals (lithium, iron, but not thallium) and alcohols are poorly absorbed.
4. Multiple-dose activated charcoal (MDAC) should be considered primarily if a patient has ingested a life-threatening amount of carbamazepine, dapsone, phenobarbital, quinine, or theophylline. Multiple-dose activated charcoal increases the elimination of amitriptyline, dextropropoxyphene, digitoxin, digoxin, disopyramide, nadolol, phenylbutazone, phenytoin, piroxicam, and sotalol, but evidence is insufficient to support its use in these ingestions.
5. Whole bowel irrigation should not be performed in the presence of ileus or bowel obstruction.
6. If uncertainty exists about the need for decontamination procedures, contact the regional poison control center and/or a medical toxicologist.





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