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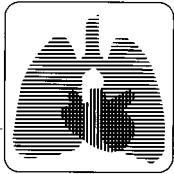
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critical care review

Adult Toxicology in Critical Care*

Part I: General Approach to the Intoxicated Patient

Babak Mokhlesi, MD; Jerrold B. Leiken, MD; Patrick Murray, MD; and Thomas C. Corbridge, MD, FCCP

Intensivists are confronted with poisoned patients on a routine basis, with clinical scenarios ranging from known drug overdose or toxic exposure, illicit drug use, suicide attempt, or accidental exposure. In addition, drug toxicity can also manifest in hospitalized patients from inappropriate dosing and drug interactions. In this review article, we describe the epidemiology of poisoning in the United States, review physical examination findings and laboratory data that may aid the intensivist in recognizing a toxidrome (symptom complex of specific poisoning) or specific poisoning, and describe a rational and systematic approach to the poisoned patient. It is important to recognize that there is a paucity of evidence-based information on the management of poisoned patient. However, the most current recommendations by the American Academy of Clinical Toxicology and European Association of Poisons Centers and Clinical Toxicologists will be reviewed. Specific poisonings will be reviewed in the second section of these review articles. (CHEST 2003; 123:577–592)

Key words: critical care; ICU; poisoning; toxicology; toxidromes

Abbreviations: GL = gastric lavage; pKa = negative logarithm of the acid ionization equilibrium constant

A high index of suspicion for intoxication is warranted in the practice of critical care medicine. The protean manifestations of intoxication challenge even the most astute clinicians, particularly when patients present with altered mental status or when there is no history of intoxication. Recognition of a specific toxic syndrome (or toxidrome) helps (Table 1), but symptoms are often nonspecific (as in early acetaminophen poisoning) or masked by other conditions (eg, myocardial ischemia in the setting of carbon monoxide poisoning).

In the first of this two-part series, we will review the epidemiology of poisonings, both intentional and

unintentional, provide an approach to the diagnosis of the poisoned patient, and discuss strategies for general supportive care. In part II, we will review the assessment and management of specific intoxications.

EPIDEMIOLOGY

Since 1983, the American Association of Poison Control Centers has compiled data from the Toxic Exposure Surveillance System. In their 2000 annual report, 63 poison centers reported a total of 2,168,248 human toxic exposure cases. Adults accounted for approximately one third of exposures. Most exposures were unintentional (71% of cases) and involved a single toxic substance (92%). Fewer than 5% of cases involved an adverse reaction to a medication or food. Oral ingestion was the commonest route of exposure (Fig 1). Most exposures occurred at the patient's own residence, and most patients (75%) were managed on-site with assistance from a poison information center and did not require an emergency department visit. Only 3% of patients required critical care.

The categories of substances/toxins with the larg-

*From the Division of Pulmonary and Critical Care Medicine (Dr. Mokhlesi), Cook County Hospital/Rush Medical College, Chicago; Evanston Northwestern Healthcare-OMEGA (Dr. Leiken), Chicago; Section of Nephrology (Dr. Murray), University of Chicago, Chicago; and Medical Intensive Care Unit (Dr. Corbridge), Northwestern University Medical School, Chicago, IL.

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Correspondence to: Babak Mokhlesi, MD, Division of Pulmonary and Critical Care Medicine, Cook County Hospital/Rush Medical College, 1900 West Polk St, Chicago, IL 60612; e-mail: Babak_Mokhlesi@rush.edu

Table 1—Common Toxidromes

Toxidrome	Features	Drugs/Toxins	Drug Treatment
Anticholinergic “Hot as a hare, dry as a bone, red as a beet, mad as a hatter”	Mydriasis Blurred vision Fever Dry skin Flushing Ileus Urinary retention Tachycardia Hypertension Psychosis Coma Seizures Myoclonus	Antihistamines Atropine Baclofen Benztropine Tricyclic antidepressants Phenothiazines Propranolol Scopolamine	Physostigmine (for life-threatening events, do not use in cyclic antidepressant overdose because of potential worsening of conduction disturbances)
Cholinergic “SLUDGE”	Salivation Lacrimation Urination Diarrhea GI cramps Emesis Wheezing Diaphoresis Bronchorrhea Bradycardia Miosis	Carbamate Organophosphates Physostigmine Pilocarpine	Atropine Pralidoxime for organophosphates
β -Adrenergic	Tachycardia Hypotension Tremor	Albuterol Caffeine Terbutaline Theophylline	β -Blockade (caution in asthmatics) Potassium replacement
α -Adrenergic	Hypertension Bradycardia Mydriasis	Phenylephrine Phenylpropanolamine	Treat hypertension with phentolamine or nitroprusside, not with β -blockers alone
β - and α -Adrenergic	Hypertension Tachycardia Mydriasis Diaphoresis Dry mucus membranes	Amphetamines Cocaine Ephedrine Phencyclidine Pseudoephedrine	Benzodiazepines
Sedative/hypnotic	Stupor and coma Confusion Slurred speech Apnea	Anticonvulsants Antipsychotics Barbiturates Benzodiazepines Ethanol Meprobamate Opiates	Naloxone Flumazenil Urinary alkalization for phenobarbital
Hallucinogenic	Hallucinations Psychosis Panic Fever Mydriasis Hyperthermia Synesthesia	Amphetamines Cannabinoids Cocaine Lysergic acid diethylamide Phencyclidine (may present with miosis)	Benzodiazepines
Extrapyramidal	Rigidity/tremor Opisthotonos Trismus Hyperreflexia Choreoathetosis	Haloperidol Phenothiazines Risperidone Olanzapine	Diphenhydramine Benzotropine
Narcotic	Altered mental status Slow shallow breaths Miosis Bradycardia Hypotension Hypothermia Decreased bowel sounds	Dextromethorphan Opiates Pentazocine Propoxyphene	Naloxone

Table 1—Continued

Toxidrome	Features	Drugs/Toxins	Drug Treatment
Serotonin	Irritability	Fluoxetine	Benzodiazepine
	Hyperreflexia	Meperidine	Withdrawal of drug
	Flushing	Paroxetine	Cyproheptadine
	Diarrhea	Sertraline	
	Diaphoresis	Trazodone	
	Fever	Clomipramine	
	Trismus		
	Tremor		
Epileptogenic	Myoclonus		
	Hyperthermia	Strychnine	Antiseizure medications
	Hyperreflexia	Nicotine	Pyridoxine for isoniazid
	Tremors	Lindane	Extracorporeal removal of drug (lindane, camphor, xanthines)
	May mimic stimulant patterns	Lidocaine	Physostigmine for anticholinergic agents
		Cocaine	Avoid phenytoin for theophylline induced seizures
		Xanthines	
		Isoniazid	
		Chlorinated hydrocarbons	
		Anticholinergics	
		Camphor	
Solvent	Depersonalization	Phencyclidine	
	Lethargy	Hydrocarbons	Avoid catecholamines
	Confusion	Acetone	Withdrawal of toxin
	Headache	Toluene	
	Restlessness	Naphthalene	
	Incoordination	Trichloroethane	
	Derealization	Chlorinated hydrocarbons	
Uncoupling of oxidative phosphorylation	Depersonalization		
	Hyperthermia	Aluminum phosphide	Sodium bicarbonate for metabolic acidosis
	Tachycardia	Salicylates	Patient cooling
	Metabolic acidosis	2,4-Dichlorophenol	Avoid atropine and salicylates
		Dinitrophenol	Hemodialysis in refractory acidosis
		Glyphosate	
		Phosphorus	
	Pentachlorophenol		
	Zinc phosphide		

est number of deaths were analgesics, antidepressants, sedative/hypnotics/antipsychotics, stimulants, “street” drugs, cardiovascular drugs, and alcohols (Table 2). Of all deaths, 920 fatalities, a 5% increase compared to 1999, 88% occurred in 20- to 99-year-old individuals. The mortality rate was higher in intentional rather than unintentional exposures (79% vs 10.5%, respectively).¹

DIAGNOSIS OF TOXIC INGESTION

History and Physical Examination

Table 3 includes clinical features mandating consideration of toxic ingestion. Although the history is important, it may be unreliable or incomplete.² Consider that family members, friends, and pharmacists may have additional information. In the absence of a classic presentation or toxidrome, separating patients with suspected poisoning into broad categories based

on vital signs, ocular findings, mental status, and muscle tone can help determine drug or toxin class.³

Vital Signs

Anticholinergic and sympathomimetic substances increase heart rate, BP, and temperature. In contrast, organophosphates, opiates, barbiturates, β -blockers, benzodiazepines, alcohol, and clonidine cause hypothermia, bradycardia, and respiratory depression. Table 4 lists various toxins altering temperature. Drugs/toxins causing tachycardia or bradycardia are listed in Table 5.

Ocular Findings

Anticholinergics and sympathomimetics cause mydriasis. In contrast to anticholinergic overdose, the pupils remain somewhat light responsive in cocaine intoxication. Table 6 lists drugs that affect pupil size. Horizontal nystagmus is common in alcohol intoxi-

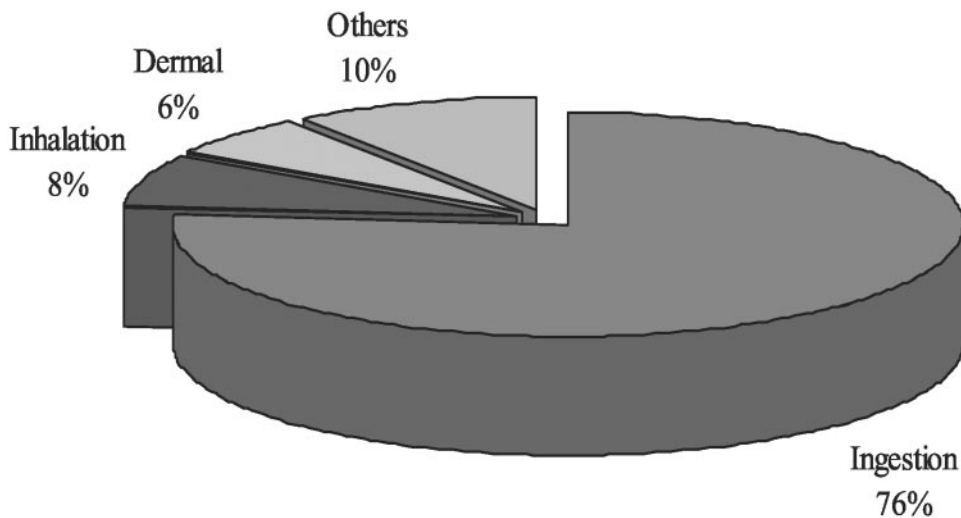


FIGURE 1. Route of exposure for human poisoning. Data from the 2000 Toxic Exposure Surveillance System of the American Association of Poison Control Centers.¹

caution. Other drugs causing nystagmus are lithium, carbamazepine, solvents, meprobamate, quinine, and primidone. Phencyclidine and phenytoin cause horizontal, vertical, and rotary nystagmus.

Mental Status, Behavior, and Muscle Tone

It is important to determine whether the patient is comatose, stuporous, lethargic, delirious, confused, or alert (Table 7). Some toxins cause seizures (Table 8); others alter muscle tone (Table 9).

Laboratory Evaluation

Three gaps are important in toxicology: the anion gap, osmolal gap, and oxygen saturation gap. Toxicology screening confirms (or not) toxin exposure but rarely alters management (see below).

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Anion Gap

The normal range of anion gap may vary from 3 to 12 mEq/L in some laboratories.⁴ An increase in anion gap (> 20 mEq/L) suggests lactic acidemia, uremia, ketoacidemia, or selected intoxications

Table 2—Most Lethal Human Toxin Exposures Reported to Poison Control Centers in 2000*

Substance/Toxin Category	Adult Exposures, No. (% of All Adult Exposures)	Total Deaths per Category Including Children and Adults, No.†
Analgesics	92,245 (13.3)	405
Alcohols (ethanol and nonethanol)	37,451 (5.4)	103
Antidepressants	55,429 (8)	242
Cardiovascular drugs	28,941 (4.2)	108
Sedatives/hypnotics/antipsychotics	67,946 (9.8)	225
Stimulants and street drugs	17,423 (2.5)	187

*Data obtained from cases reported by 63 poison control centers during 2000. Not all poisonings and intoxications are reported to poison control centers.¹

†No. of deaths are based on an unlimited number of substances coded per exposure.

Table 3—Clinical Features Mandating Consideration of Toxic Ingestion*

History of drug overdose or substance abuse
Suicidal ideation or prior suicide attempt
History of other psychiatric illness
Agitation and hallucinations
Stupor or coma
Rotary nystagmus
Delirium or confusion
Seizures
Muscle rigidity
Dystonia
Cardiopulmonary arrest
Unexplained cardiac arrhythmia
Hyper/hypotension
Ventilatory failure
Aspiration
Bronchospasm
Liver failure
Renal failure
Hyper/hypothermia
Rhabdomyolysis
Osmolal gap
Anion gap acidosis
Hyper/hypoglycemia
Hyper/hyponatremia
Hyper/hypokalemia
Polypharmacy

*Modified with permission from Corbridge and Murray.⁶⁸

Table 4—Drugs Affecting Temperature

Hypothermia	Hyperthermia
Alcohols	Amphetamines
Barbiturates	Anticholinergics
Cyclic antidepressants	Antihistamines
Hypoglycemic agents	Cocaine
Opioids	Cyclic antidepressants
Phenothiazines	Drug withdrawal
Colchicine	Lysergic acid diethylamide
Akee fruit poisoning	Monoamine oxidase inhibitors
Lithium	Malignant hyperthermia
	Neuroleptic malignant syndrome
	Phencyclidine
	Phenothiazines
	Salicylates
	Serotonin syndrome

(Tables 10, 11). A normal anion gap does not preclude intoxication because most toxins do not elevate the anion gap or there may be a coexisting condition that lowers the gap (Table 10). Common among these conditions is hypoalbuminemia: for every 1 g/L decrease in the plasma albumin, the anion gap falls by 2.5 mEq/L.⁵ Intensivists should pay special attention to this correction factor to avoid missing a clinically significant anion gap. Also, in methanol or polyethylene glycol poisoning, concurrent ethanol use delays the development of an elevated anion gap metabolic acidosis. In this case, an elevated osmolal gap may be the only early clue to the diagnosis.⁶

Table 5—Selected Drugs/Toxins Causing Tachycardia and Bradycardia*

Tachycardia	Bradycardia
Amphetamines	Antiarrhythmics (types 1a and 1c)
Anticholinergics	β-Blockers
Antihistamines	Calcium-channel blockers
Caffeine	Carbamates
Carbon monoxide	Clonidine
Clonidine	Cyclic antidepressants
Cocaine	Digoxin
Cyanide	Lithium
Cyclic antidepressants	Metoclopramide
Drug withdrawal	Opioids
Ephedrine	Organophosphates
Hydralazine	Phenylpropanolamine
Hydrogen sulfide	Physostigmine
Methemoglobinemia	Propoxyphene
Phencyclidine	Quinidine
Phenothiazines	
Pseudoephedrine	
Theophylline	
Thyroid hormone overdose	

*Modified with permission from Corbridge and Murray.⁶⁸

Table 6—Selected Drugs Affecting Pupil Size*

Miosis	Mydriasis
Barbiturates	Amphetamines
Carbamates	Anticholinergics
Clonidine	Antihistamines
Ethanol	Cocaine
Isopropyl alcohol	Cyclic antidepressants
Organophosphates	Dopamine
Opioids (meperidine may cause mydriasis)	Drug withdrawal
Phencyclidine	Glutethimide
Phenothiazines	Lysergic acid diethylamide
Physostigmine	Monoamine oxidase inhibitors
Pilocarpine	Phencyclidine

*Modified with permission from Corbridge and Murray.⁶⁸

Osmolal Gap

Low-molecular-weight drugs and toxins increase the discrepancy between measured and calculated plasma osmolality (Table 12). Normal plasma osmolality is 285 to 295 mOsm. The calculated value is determined as follows:

Table 7—Selected Drugs Altering Mental Status

Depressed Physiologic State	Agitated Physiologic State	Delirium and Confusion
Sympatholytics	Sympathomimetics	Alcohol/drug withdrawal
Adrenergic blockers	Adrenergic agonists	Anticholinergics
Antiarrhythmics	Amphetamines	Antihistamines
Antihypertensives	Caffeine	Carbon monoxide
Antipsychotics	Cocaine	Cimetidine
Cyclic antidepressants	Ergot alkaloids	Heavy metals
Cholinergics	Monoamine oxidase inhibitors	Lithium
Bethanechol	Theophylline	Salicylates
Carbamates	Anticholinergics	
Nicotine	Antihistamines	
Organophosphates	Antiparkinsonian drugs	
Physostigmine	Antipsychotics	
Pilocarpine	Antispasmodics	
Sedative/hypnotics	Cyclic antidepressants	
Alcohols	Cyclobenzaprine	
Barbiturates	Drug withdrawal	
Benzodiazepines	β-blockers	
Gamma hydroxybutyrate	Clonidine	
Ethchlorvynol	Ethanol	
Narcotics	Opioids	
Analgesics	Sedative/hypnotics	
Antidiarrheal agents	Hallucinogens	
Other	Lysergic acid diethylamide	
Cyanide	Marijuana	
Hydrogen sulfide	Mescaline	
Hypoglycemic agents	Phencyclidine	
Lithium	Other	
Salicylates	Thyroid hormones	

Table 8—Common Drugs and Toxins Causing Generalized Seizures*

Amphetamines
Antihistamines/anticholinergic agents
Antipsychotics
Caffeine/theophylline
Carbamates
Carbon monoxide
Cocaine
Cyclic antidepressants
Ethylene glycol
Isoniazid
Lead
Lidocaine
Lithium
Methanol
Organophosphates
Phencyclidine
Hypoglycemic agent (focal)
Chlorambucil (focal)
Propranolol
Salicylates
Withdrawal from alcohol or sedative/hypnotics

*Modified with permission from Corbridge and Murray.⁶⁸

$$\text{calculated osmolality} = 1.86[\text{Na}^+] + \text{BUN}/2.8 + \text{glucose}/18 + \text{ethanol}/4.6$$

in which Na⁺ (in millimoles per liter) is multiplied by nearly two to account for accompanying anions (chloride and bicarbonate), and measured BUN, glucose, and ethanol are converted from milligrams per deciliter to mmol/L by the appropriate denominator.

The osmolal gap must be interpreted with caution. Measurement of osmolality by vapor pressure osmometry does not detect volatile alcohols such as ethanol and methanol; however, it does detect ethylene glycol. Freezing point depression osmometry, the most frequently used method, measures all of these solutes.^{7,8} Therefore, it is important for clinicians to know the method used by their institution to avoid missing methanol poisoning. By using the standard formula, the normal osmolal gap may range from - 9 mOsm to + 5 mOsm; 10 mOsm is consid-

Table 9—Selected Drugs Affecting Muscle Tone*

Dystonic Reactions	Dyskinesias	Rigidity
Haloperidol	Anticholinergics	Black widow spider bite
Metoclopramide	Cocaine	Malignant hyperthermia
Olanzapine	Phencyclidine	Neuroleptic malignant syndrome
Phenothiazines	Risperidone	Phencyclidine
Risperidone		Strychnine
		Fentanyl

*Modified with permission from Corbridge and Murray.⁶⁸

Table 10—Common Causes of Abnormal Anion Gap

Elevated Anion Gap	Decreased Anion Gap
Lactic acidosis (type A)	Increased unmeasured cation
Uremia	Hyperkalemia
Sepsis	Hypercalcemia
Rhabdomyolysis	Hypermagnesemia
Ketoacidosis	Acute lithium intoxication
Diabetic	Elevated IgG (myeloma; cationic paraprotein)
Alcoholic	Decreased unmeasured anion
Starvation	Hypoalbuminemia
Toxic ingestions*	Drugs
Ethylene glycol	Bromide
Methanol	Iodide
Paraldehyde	Lithium
Salicylate	Polymyxin B
Metabolic alkalosis with volume depletion	Tromethamine
	Analytical artifact
	Hypermagnesemia (> 170 mEq/L)
	Hyperlipidemia

*See Table 11.

ered the upper limit of normal.⁹ However, an osmolal gap of 10 mOsm in a patient who started at - 9 mOsm may be significantly elevated.¹⁰⁻¹²

Oxygen Saturation Gap

An oxygen saturation gap is present when there is more than a 5% difference between the saturation calculated from an arterial blood gas and the saturation measured by co-oximetry. Co-oximetry determines oxygen saturation by detecting the absorption of four different wavelengths, enabling it to directly measure levels of four types of hemoglobin species: oxyhemoglobin, reduced hemoglobin, carboxyhemoglobin, and methemoglobin. However, arterial blood gas analysis calculates oxygen saturation from the measured oxygen tension using an assumed standard

Table 11—Selected Drugs Associated With an Elevated Anion Gap Metabolic Acidosis

Acetaminophen (> 75 g)	Ketamine
Amiloride	Metformin
Ascorbic acid	Methanol
Carbon monoxide	Niacin
Chloramphenicol	Nitroprusside
Colchicine	Nonsteroidal anti-inflammatory drugs
Nitroprusside	Papaverine
Dapsone	Paraldehyde (hippuric acid)
Epinephrine	Phenformin
Ethanol	Propofol
Ethylene glycol	Salicylates
Formaldehyde	Terbutaline
Hydrogen sulfide	Tetracycline (outdated)
Iron	Toluene (hippuric acid)
Isoniazid	Verapamil

Table 12—Drugs/Toxins Associated With an Elevated Osmolal Gap*

Ethanol (if not included in the formula)
Ethylene glycol/glycolaldehyde
Glycerol
Glycine
IV immunoglobulin (maltose)
Isopropanol/acetone
Mannitol
Methanol/formaldehyde
Propylene glycol
Radiocontrast media
Hypermagnesemia (> 9.5 mEq/L)
Sorbitol

*Modified with permission from Corbridge and Murray.⁶⁸

oxygen-hemoglobin dissociation curve. Toxins that are associated with an elevated oxygen saturation gap include carbon monoxide, methemoglobinemia, cyanide, and hydrogen sulfide (sulfhemoglobin is not routinely measured by co-oximetry). Pulse oximetry estimates oxygen saturation by emitting a red light (wavelength of 660 nm) absorbed mainly by reduced hemoglobin and a near-infrared light (wavelength of 940 nm) absorbed by oxyhemoglobin.¹³ Methemoglobin absorbs almost equally at both these wavelengths. At high methemoglobin levels (35%), the oxygen saturation by pulse oximetry tends to regress toward 85% and plateaus at that level despite further increments in methemoglobin levels. Thus, if the actual oxygen saturation by co-oximetry is > 85%, the pulse oximetry would be underestimating it; if it is < 85% by co-oximetry, it would be overestimating oxygen saturation.¹⁴ Therefore, pulse oximetry may become unreliable in the setting of methemoglobinemia registering falsely high in patients with severe methemoglobinemia and falsely low with mild methemoglobinemia. Since many laboratories do not routinely use co-oximetry, a more commonly seen gap may be the disparity between measured oxygen saturation by blood gas and that measured by pulse oximetry.¹⁵ Oxygen saturation measured by pulse oximetry may be falsely elevated in methemoglobinemia and should be utilized with caution in determining the oxygen saturation gap.^{16,17} Carbon monoxide has a wavelength absorption coefficient similar to that of oxyhemoglobin; therefore, it is registered as oxyhemoglobin by pulse oximetry leading to overestimation of oxygen saturation when compared to co-oximetry. An abnormally high venous oxygen content (arteriolization of venous blood) is characteristic of cyanide and hydrogen sulfide poisoning.

Toxicology Screening

In spite of providing direct evidence of intoxication, screening tests alter management in < 5% of

Table 13—Drugs Commonly Included in Urine Substances-of-Abuse Screens (Available in 30 min)*

Amphetamines
Barbiturates
Benzodiazepines
Cannabinoids
Cocaine
Opioids
Phencyclidine

*Immunoassay technique; modified with permission from Corbridge and Murray.⁶⁸

cases.^{18,19} Toxicology screening can identify a specific toxin for which an antidote is available and in some instances quantify a toxin allowing for titrated therapy.

Most institutions offer urine testing for six or seven of the most commonly abused drugs (Table 13). Results are generally available in 30 min. More comprehensive urine screening (usually performed off-site) may take up to 2 to 3 h. Testing of blood or gastric contents is rarely indicated.²⁰ However, blood quantification of certain toxins is useful, particularly in cases of alcohol (ethanol and nonethanol), acetaminophen, salicylate, phenobarbital, theophylline, digoxin, iron, and lithium intoxication. A strong argument can be made for checking acetaminophen levels in all cases of suspected intoxication given the subtle manifestations of early acetaminophen poisoning and importance of targeted therapy.

Poison Control Center Consultation

Regional poison control center consultation is highly recommended in cases of suspected poisoning and to help guide management in confirmed cases.²¹ These centers provide 24-h emergency and up-to-date technical information. They are staffed by nurses, pharmacists, pharmacologists, and physicians trained and certified in toxicology. The national toll-free number for poison control centers is 800-222-1222.

INITIAL SUPPORTIVE MEASURES

Airway, Breathing, Circulation

Supportive measures including the “ABCs” (airway, breathing, circulation) are often required before confirmation of intoxication. With cervical spine precautions in place (unless trauma has been excluded), airway patency must be ensured in all cases. Endotracheal intubation is not always necessary when cough and gag reflexes are present and there is adequate spontaneous ventilation, but when there is concern regarding airway protection and clinical

Table 14—Selected Causes of Hypoxemia in Drug Overdose and Toxic Ingestion*

Cause	Drugs/Toxins
Hypoventilation	Alcohols
	Barbiturates
	Benzodiazepines
	Botulinum toxin
	Cyclic antidepressants
	Neuromuscular blockade
	Opioids
	Sedative/hypnotics
	Snake bite
	Strychnine
	Tetanus
	Aspiration
Pneumonia	Drugs resulting in aspiration; IV drug abuse with pulmonary seeding of infectious agents; inhalation injury interfering with lung protective mechanisms
Cardiogenic pulmonary edema	Antiarrhythmics
	β -Blockers
	Cyclic antidepressants
Inert gases	Verapamil
	Carbon dioxide
	Methane
Noncardiogenic pulmonary edema	Nitrogen
	Propane
	Cocaine
	Ethylene glycol
	Hydrocarbons
	Inhalation injury
	Opioids
	Phosgene
	Paraquat
	Salicylates
Bronchospasm	β -Blockers
	Cocaine
	Heroin
	Organophosphates
	Drugs resulting in aspiration
	Drugs associated with myocardial depression (cardiac asthma)
Alveolar hemorrhage	Cocaine
	Anticoagulants
	Thrombolytics
	Amiodarone
	Paraldehyde
	Nitrofurantoin
	Penicillamine
	Toluene
Pneumothorax	Cocaine
	IV drug abuse with aberrant venipuncture or bullous lung disease
	Kerosene
Cellular hypoxia	Carbon monoxide
	Cyanide
	Hydrogen sulfide
	Methemoglobinemia
	Sulfhemoglobinemia

*Modified with permission from Corbridge and Murray.⁶⁸

deterioration it is better to secure the airway. Intubation is indicated in acute respiratory failure (Table 14 for causes of hypoxemia in intoxicated patients). Other specific indications include the need for high levels of supplemental oxygen in carbon monoxide poisoning and the need to protect the airway for gastric emptying. Endotracheal intubation decreases (but does not eliminate) the risk of aspiration (which is approximately 11% in the comatose patient with drug overdose).^{22–24}

Depending on the intoxication, patients may present with hypotension or hypertension, bradyarrhythmias or tachyarrhythmias. The pathogenesis of hypotension varies and may include hypovolemia, myocardial depression, cardiac arrhythmias, and systemic vasodilation. Treatment should be individualized, but an initial strategy of rapid IV normal saline solution infusion is indicated in most instances. Vasopressors may be required for refractory hypotension. The vasopressor of choice depends on the type of intoxication (see below). Hypertension occurs in the setting of sympathomimetic drugs, anticholinergics, ergot derivatives, phenylpropanolamine overdose, and withdrawal from nicotine, alcohol, and sedatives. Treatment of the hypertension depends on its chronicity and severity and the inciting agent (see below). Hypertension-induced (reflex) bradycardia generally should not be treated.

Coma Cocktail

Immediately after establishing IV access, a “cocktail” of thiamine, dextrose, and naloxone should be administered to patients with depressed mental status. This cocktail can be both therapeutic and diagnostic.²⁵ Thiamine (100 mg by vein) is administered to treat and/or avoid Wernicke-Korsakoff syndrome in comatose patients. This strategy is not well supported by the literature, and few patients regain consciousness following thiamine infusion. Still, routine use of thiamine is safe, inexpensive, and prevents the possibility of delayed deterioration secondary to nutritional deficiency.²⁵ Thiamine is particularly important in the nutritionally deplete alcoholic. There is no evidence that dextrose should be withheld until thiamine is administered.²⁶ Comatose patients should receive dextrose, 50 g IV. A normal value by blood dipstick does not necessarily exclude low serum glucose. A high value on dipstick testing should lead to rapid confirmation by blood draw, thus avoiding unnecessary dextrose (although administration of dextrose to hyperglycemic patients is unlikely to cause harm).²⁵ Naloxone rapidly reverses coma, respiratory depression, and hypotension induced by opioids. An initial dose of 0.2 to 0.4 mg is administered IV (or endotracheally). If there is no

response after 2 to 3 min, an additional 1 to 2 mg can be administered and repeated up to 10 mg as required. Using a higher dose up front may precipitate large cardiovascular changes in opioid dependent patients. Several opioids such as meperidine, propoxyphene, diphenoxylate, methadone, and pentazocine require large doses of naloxone,²⁷ but lack of response to 10 mg of naloxone generally excludes opioid toxicity. Opioid antagonism with naloxone lasts 1 to 4 h requiring repeat doses or continuous infusion in significant intoxication.²⁸ Acute pulmonary edema,^{29,30} opioid withdrawal,³¹ and seizures³² have been reported with naloxone administration.

Flumazenil should be considered in cases where benzodiazepine overdose is suspected or reversal of therapeutic conscious sedation is desired.^{25,33} Case reports have cautioned clinicians of the risk of precipitating seizures with flumazenil when there is a suspicion of benzodiazepine plus cyclic antidepressant overdose.^{34,35} Nonetheless, data suggest that flumazenil is safe as part of the coma cocktail even with coma induced by the combination of benzodiazepines and cyclic antidepressants.³⁶ In a large prospective trial of unconscious patients suspected of benzodiazepine overdose, Weinbroum et al³⁶ randomized patients to receive either placebo or flumazenil in addition to usual care. Seventy-one percent of the patients had concomitant cyclic antidepressant ingestion. These investigators did not observe any significant side effects with flumazenil, even in patients with coma caused by a mixed overdose of benzodiazepine and cyclic antidepressants. We typically administer an initial 0.2 mg of IV flumazenil over 30 s followed by another 0.3-mg dose if necessary. Doses beyond 3 mg generally do not provide additional benefit. Repeat sedation may occur in the setting of high-dose or long-term use of benzodiazepines. Although flumazenil is successful in improving the Glasgow coma scale score, it does not appear to alter cost or major diagnostic/therapeutic interventions in patients presenting with decreased level of consciousness due to an intentional unknown drug overdose.³⁷ Therefore, the cost-effectiveness of routine use of flumazenil as part of the coma cocktail remains controversial,³⁸ except in cases of acute benzodiazepine overdose.³⁶

PREVENTION OF ABSORPTION

The route of entry for toxic substances can be dermal, ocular, GI, inhalational, or parenteral (Fig 1). Skin decontamination requires removal of the toxin with nonabrasive soap and water. Contaminated clothing may serve as a reservoir for continued

exposure and must be removed with caution and placed in plastic bags or other containers that are impervious to the toxin. This will limit exposure to medical personnel and patient. Ocular decontamination may require prolonged periods of irrigation with normal saline solution using a Morgan lens (MorTan; Missoula, MT). Inhalational exposure presents a greater challenge since the toxin cannot be accessed and removed. Inhalational lung injury is beyond the scope of this review. The majority of toxin exposures and poisonings managed by intensivists occur through the GI tract. There are four methods of GI decontamination including three mechanical approaches (emesis, gastric emptying or gastric lavage [GL], and whole-bowel irrigation) and the use of activated charcoal combined with a cathartic.

Emesis

Ipecac-induced emesis should be considered only in fully alert patients, and is virtually never indicated after hospital admission. Ipecac is generally less traumatic than GL, and is therefore the preferred method of gastric emptying in pediatric patients. Ipecac may be helpful at home if administered immediately after ingestion. In the best of circumstances, a 30 to 40% removal rate can be achieved within 1 h after ingestion.³⁹ Because of questionable efficacy hours after ingestion, in-hospital use is decreasing.^{40,41} Contraindications to its use include poisoning with corrosives, petroleum products, or antiemetics. The potential for aspiration precludes its use in situations where there is a high risk of seizures (ingestion of a rapidly acting convulsant such as strychnine) or altered consciousness.⁴² The usual dose of ipecac syrup in adults is 30 mL followed by 16 oz of water. This dose usually induces vomiting within 20 to 30 min. The dose can be repeated once after 30 min if vomiting does not occur. There is little evidence that ipecac prevents drug absorption or systemic toxicity,⁴³ and there are no convincing data that it significantly alters the clinical outcome of patients who are awake and alert on presentation to the emergency department. Ipecac is rarely used (approximately 1% of all overdoses reported to the poison centers),¹ and its use may soon be confined to the medical history books.

Gastric Emptying

GL through a 28F to 40F Ewald tube is similarly aimed at physically removing a toxin. Prior to inserting the Ewald tube, the mouth should be inspected for foreign material and equipment should be ready for suctioning. Large gastric tubes (37F to 40F) are less likely to enter the trachea than smaller nasogas-

tric tubes, and are necessary to facilitate removal of gastric debris. After insertion, proper position needs to be confirmed by aspirating acidic stomach contents and auscultating the left upper abdominal quadrant during insufflation of air. Experienced personnel should perform GL in a facility where resources are available to manage complications. Nonintubated patients must be alert (and be expected to remain alert) and have adequate pharyngeal and laryngeal protective reflexes. In semicomatose patients, GL should be performed only after a cuffed endotracheal tube has been inserted. Intubation for the sole purpose of gastric emptying is reasonable only if there is a high likelihood that a highly lethal agent remains in the stomach.

GL is performed by instilling 200-mL aliquots of warmed tap water until there is clearing of aspirated fluid. Stomach contents should be retained for analysis. Tap water may avoid unnecessary salt loading compared to normal saline solution. Neither irrigant has been shown to significantly alter blood cell or electrolyte concentrations.⁴⁴ After clearing, the Ewald tube may be replaced by a nasogastric tube for subsequent intermittent suctioning and/or administration of activated charcoal.

GL has been advocated in the initial management of many orally ingested agents. The risks associated with this procedure include aspiration, arrhythmias, and stomach perforation.⁴⁵ Because of these risks, GL should not be performed in patients who have ingested a nontoxic substance, a nontoxic amount of a toxic substance, or when the toxin is no longer expected to be present in the stomach. Examples include patients who have vomited extensively prior to hospital admission, patients who present several hours after ingesting an agent that does not decrease gut motility, and patients who have received agents that are readily absorbed from the GI tract. Although GL has been common in the management of patients with toxic ingestion, its use remains controversial.⁴⁶ In obtunded patients, GL results in a more satisfactory clinical outcome only if performed within 1 h⁴⁷ or 2 h of ingestion.⁴⁸ Kulig et al⁴⁷ compared the utility of GL plus activated charcoal in 72 obtunded patients with 44 obtunded patients who received only activated charcoal by nasogastric tube and supportive care. They reported an improved clinical course if lavage was performed within 1 h of ingestion. In contrast, Pond et al⁴⁹ performed a prospective, randomized, controlled trial of 347 obtunded patients receiving GL plus activated charcoal or activated charcoal alone. There was no significant difference in outcome even when patients presented within 60 min of ingestion. Because of limited data, the American Academy of Clinical Toxicology does not recommend routine use of GL in the manage-

ment of poisoning unless a patient has ingested a potentially life-threatening amount of a poison and the procedure can be undertaken within 60 min of ingestion.⁵⁰ Although controversial, some experts suggest that the time limit may be extended to 12 h in cases of poisoning with agents that delay gastric emptying such as tricyclic antidepressants, opioids, or salicylates. In addition, gastric emptying may be beneficial if the ingested drug is not adsorbed by activated charcoal (eg, ferrous sulfate, lithium). In cases of ingestion of a caustic liquid such as kerosene or its derivatives, GL should be avoided because of the risk of aspiration-induced lung injury. Clinical studies evaluating the efficacy of GL are limited by small study size, heterogeneity of toxins studied, and different methodologies. There is also a concern that GL may propel material into the duodenum increasing the chance of drug absorption.⁵¹

Activated Charcoal

Charcoal is a by-product of the combustion of various organic compounds such as wood, coconut parts, bone, sucrose, rice, and starch. Its adsorptive capacity is increased or activated by removing materials previously adsorbed by a process that involves steam heating and chemical treatment, thereby increasing the surface area available for adsorption to between 1,000 m²/g and 3,000 m²/g. This results in a powerful, inert, nontoxic, and nonspecific adsorbent that irreversibly binds intraluminal drugs and interferes with their absorption. It is particularly effective in binding high-molecular-weight compounds. Activated charcoal decreases serum drug levels in some cases by creating a favorable diffusion gradient between blood and gut, referred to as *GI dialysis* (see below).⁵² The efficacy of activated charcoal has led to a resurgence of its use over the past few years.

Charcoal can be administered after both GL or ipecac-induced emesis, but it is usually administered as the sole GI decontaminating agent. Airway protection is imperative in stuporous, comatose, or convulsing patients. Prior gastric stapling is an additional risk factor for emesis and aspiration with single or repeated doses.⁵³ Charcoal aspiration has been associated with pneumonia⁵⁴ (including fungal pneumonia⁵⁵), bronchiolitis obliterans,⁵⁶ ARDS,⁵⁷ and death.⁵⁸

Despite the mentioned complications, activated charcoal is generally effective and well tolerated. Complications are infrequent. The ideal dose should give a charcoal-to-drug ratio of 10:1. However, since the quantity of poison ingested is usually unknown to the clinician, the dose is based on actual patient weight (1 g/kg). It is commonly co-administered with a cathartic (see below) to facilitate evacuation of the

Table 15—Toxins and Drugs Not Adsorbed by Activated Charcoal

Alcohols
Hydrocarbons
Organophosphates
Carbamates
Acids
Potassium
Dichloro diphenyl trichloroethane (DDT)
Alkali
Iron
Lithium

toxic substance and avoid constipation. Commonly used agents include magnesium sulfate, magnesium citrate, or sorbitol. Mixing the solution with juice may increase acceptance of this black and gritty adsorbent in children and adults. Single-dose activated charcoal is effective against most toxins and drugs. Table 15 lists selected toxins for which charcoal is not particularly effective. Based on volunteer studies, the effectiveness of activated charcoal decreases with time; the greatest benefit is within 1 h of ingestion.⁵⁹

Catharsis

The use of cathartics with activated charcoal may reduce the transit time of drugs and toxins in the GI tract and decrease the constipating effects of charcoal. Sorbitol is the cathartic of choice. It is generally administered only with the first dose of activated charcoal. The usual dosage is 1 to 2 mL/kg of a 70% solution of sorbitol titrated to several loose stools over the first day of treatment (total dose, 1 g/kg). Magnesium-based cathartics (2 to 3 mL/kg po of a 10% solution of magnesium sulfate) may lead to magnesium accumulation in the setting of renal failure, and sodium-based products carry the risk of exacerbating hypertension or congestive heart failure. Oil-based cathartics, if aspirated, may produce lipid pneumonia.

Cathartics have never been shown to decrease morbidity and mortality or to decrease hospital stay.⁶⁰ In a cross-over study, Keller et al⁶¹ demonstrated that activated charcoal with sorbitol led to a 28% decrease in the absorption of salicylates when compared to activated charcoal alone. However, McNamara and colleagues⁶² were unable to demonstrate enhanced efficacy of activated charcoal with sorbitol catharsis in a simulated acetaminophen overdose. Based on available data, the routine use of a cathartic in combination with activated charcoal is not endorsed by the American Academy of Clinical Toxicology and the European Association of Poisons Centers and Clinical Toxicologists. If a cathartic is

administered, it should be limited to a single dose in order to minimize adverse effects.⁶³

Whole-Bowel Irrigation

Whole-bowel irrigation with a polyethylene glycol, electrolyte solution (Colyte; Schwarz Pharma; Milwaukee, WI) or potassium chloride (Golytely; Braintree Laboratories; Braintree, MA), 1 to 2 L/h, in adults is used to push tablets or packages through the GI track. The optimal regimen in regards to volume infused per hour, duration of use, and dosage of activated charcoal prior to whole-bowel irrigation has not been well established.⁴⁶ It may take 3 to 5 h for complete bowel irrigation to clear the rectal effluent. These isotonic solutions are not absorbed and do not cause major electrolyte shift or imbalance.⁶⁴ The technique is time consuming and requires a cooperative patient. Most studies supporting this approach are limited to case reports, and there are no established indications for its use. However, whole-bowel irrigation may have a role in intoxications where activated charcoal is not effective, such as ingestion of iron and sustained-release tablets, lithium, or in cases of “body packing” with packages of illicit drugs.⁶⁵ Contraindications to whole-bowel irrigation include ileus, GI hemorrhage, and bowel perforation.

ENHANCEMENT OF ELIMINATION

Forced Diuresis and Urinary pH Manipulation

Routine use of volume-loading to promote diuresis has not been well studied or supported in the literature and cannot be recommended. Its goal is to augment elimination of renally excreted toxins through inhibition of tubular reabsorption. Thus, in order to be effective, the toxin needs to undergo extensive tubular reabsorption that can be inhibited by forced diuresis. However, forced diuresis has the potential to cause electrolyte imbalance, pulmonary edema, and raised intracranial pressure.⁶⁶ The technique consists of achieving a urine flow rate from 3 to 6 mL/kg/h with a combination of isotonic fluids and/or diuretics.⁶⁷ When tubular reabsorption of a toxin is pH sensitive, then increased urine flow does not significantly increase urinary drug elimination when added to alkaline or acid diuresis.

Manipulation of urinary pH can be used therapeutically to enhance elimination of some intoxicants (Table 16). The limits of urinary pH are 4.5 to 7.5 under conditions of enhanced acidification and alkalization. Thus, elimination of very strong (negative logarithm of the acid ionization equilibrium constant [pKa] < 3) or very weak (pKa > 8) acids is unaltered by urinary pH manipulation. Other acidic or basic

Table 16—Toxins Eliminated by Urinary Alkalinization

2,4 Dichlorophenoxy-acetic acid
Fluoride
Isoniazid
Mephobarbital
Methotrexate
Phenobarbital
Primidone
Quinolone antibiotics
Salicylic acid
Uranium

drugs do not undergo renal tubular absorption, irrespective of urinary pH, since they are polar in their nonionized form.

Urinary alkalinization (pH > 7) is most often used to eliminate salicylates and phenobarbital. It can be achieved by administration of IV sodium bicarbonate (1 to 2 mEq/kg every 3 to 4 h); this may be administered as two 50-mL ampules of 8.4% sodium bicarbonate (each containing 50 mEq of NaHCO₃) per liter of 5% dextrose in water infused at 250 mL/h. Complications of this therapy include alkalemia (particularly in the presence of concurrent respiratory alkalosis), volume overload, hypernatremia, and hypokalemia. It is particularly important to avoid hypokalemia, which prevents excretion of alkaline urine by promoting distal tubular potassium reabsorption in exchange for hydrogen ion. Accordingly, bicarbonate administration in the presence of significant hypokalemia will not alkalinize the urine, yet will increase the risk of alkalemia. Since urinary alkalinization therapy can cause hypokalemia (due to alkalemia-induced intracellular potassium shift and increased urinary potassium loss with alkaline diuresis), addition of potassium chloride to the bicarbonate infusion is commonly required. Acetazolamide should not be used to alkalinize urine. Resultant metabolic acidosis can increase toxicity of certain poisonings (particularly in the case of salicylate poisoning).⁶⁸

Urinary acidification (pH < 5.5) increases renal clearance of some nonpolar weak bases with pKa values between 6 and 12. Arginine or lysine hydrochloride or ammonium chloride have been used for urinary acidification. However, due to the potential of urinary acidification to exacerbate myoglobinuric renal tubular injury, this therapy is virtually never used. Also, systemic acidosis must be avoided in order to avoid potential additive effects with toxin-induced metabolic or respiratory acidosis.⁶⁸

Multiple-Dose Activated Charcoal

Multiple-dose activated charcoal can be an effective way to enhance the elimination of toxins that

have been absorbed.⁶⁹ The mechanism by which this modality accomplishes enhancement of elimination is either by interrupting the enterohepatic/enterogastric circulation of drugs or through the binding of any drug that diffuses from the circulation into the gut lumen (called *GI dialysis*). However, it has limited application because the toxin must have a low volume of distribution, low protein binding, prolonged elimination half-life, and low pKa, which maximizes transport across mucosal membranes into the GI tract.⁶⁷ Although optimal dosage and frequency of administration following the initial dose of activated charcoal is not well established, most experts recommend a dose not < 12.5 g/h.⁷⁰ After the initial dose of 1 g/kg, activated charcoal may be administered at 0.5 g/kg every 2 to 4 h for at least three doses. Cathartics are generally not administered to avoid hypernatremia, hypokalemia, and hypermagnesemia. Multiple dosing should be used with caution in patients with decreased bowel sounds, abdominal distension, and persistent emesis. Unless a patient has an intact or protected airway, the administration of multidose charcoal is contraindicated. In a review of all the relevant scientific literature, the American Academy of Clinical Toxicologists reported that although multidose charcoal enhances drug elimination significantly, it has not yet been evaluated in a controlled trial of poisoned patients with the objective of demonstrating a reduction in morbidity and mortality.⁷¹ Table 17 provides a list of drugs and toxins where there may be a role for multiple dosing of activated charcoal.⁶⁷ However, based on experimental and clinical studies, it should be considered only in patients with a life-threatening ingestion of carbamazepine, dapsone, phenobarbital, quinine, or theophylline.⁷¹

Table 17—Toxins and Drugs Eliminated by Multiple Dosing of Activated Charcoal*

Amitriptyline	Meprobamate
Amoxapine	Methyprylon
Baclofen (?)	Nadolol
Benzodiazepines (?)	Nortriptyline
Bupropion (?)	Phencyclidine
Carbamazepine	Phenobarbital
Chlordecone	Phenylbutazone
Dapsone	Phenytoin (?)
Diazepam	Piroxicam
Digitoxin	Propoxyphene
Digoxin	Quinine
Disopyramide	Salicylates (?)
Glutethimide	Sotalol
Maprotiline	Theophylline

*? Represents equivocal data.

Table 18—Antidotes*

Drug/poison	Antidotes
Acetaminophen	N-acetylcysteine
Anticholinergics	Physostigmine
Anticholinesterases	Atropine
Benzodiazepines	Flumazenil
Black widow spider bite	Equine-derived antivenin
Carbon monoxide	Oxygen
Coral snake (Eastern and Texas) bite	Equine-derived antivenin
Cyanide	Amyl nitrite, sodium nitrite, sodium thiosulfate, hydroxycobalamin
Digoxin	Digoxin-specific antibodies
Ethylene glycol	Ethanol/fomepizole, thiamine, and pyridoxine
Heavy metals (arsenic, copper, gold, lead, mercury)	Dimercaprol (BAL), EDTA, penicillamine
Hypoglycemic agents	Dextrose, glucagon, octreotide
Iron	Deferoxamine mesylate
Isoniazid	Pyridoxine
Methanol	Ethanol or fomepizole, folic acid
Methemoglobinemia	Methylene blue
Opioids	Naloxone
Organophosphate	Atropine, pralidoxamine
Rattlesnake bite	Equine-derived antivenin

*EDTA = ethylenediamine tetra-acetic acid.

EXTRACORPOREAL REMOVAL OF TOXINS

In situations where previously mentioned supportive measures fail to improve a patient's condition, extracorporeal removal of toxins can be lifesaving.^{72,73} Although clear proof that extracorporeal toxin removal favorably alters the course of any intoxication is generally lacking,⁷⁴ it should be considered when the intoxication is projected to undergo delayed or insufficient clearance because of other organ dysfunction, the intoxicating agent produces toxic metabolites, or delayed toxicity is characteristic of the intoxication. In addition to physicochemical properties of the intoxicant, serum toxin levels or certain clinical features may mandate extracorporeal removal techniques. Three methods for extracorporeal removal of toxins are generally available: (1) dialysis (usually hemodialysis rather than peritoneal dialysis), (2) hemoperfusion; and (3) hemofiltration. Plasmapheresis and exchange transfusion are rarely used and will not be further discussed in this review. A complete list of drugs and toxins that may be removed by different extracorporeal removal techniques is beyond the scope of this review.^{67,68}

Hemodialysis

Hemodialysis is the primary extracorporeal method to remove toxins or drugs. Toxins for which

Table 19—Criteria for Admission of the Poisoned Patient to the ICU*

Respiratory depression (PaCO ₂ > 45 mm Hg)
Emergency intubation
Seizures
Cardiac arrhythmia (second- or third-degree atrioventricular block)
Systolic BP < 80 mm Hg
Unresponsiveness to verbal stimuli
Glasgow coma scale score < 12
Need for emergency dialysis, hemoperfusion, or ECMO
Increasing metabolic acidosis
Pulmonary edema induced by toxins (including inhalation) or drugs
Hypothermia or hyperthermia including neuroleptic malignant syndrome
Tricyclic or phenothiazine overdose manifesting anticholinergic signs, neurologic abnormalities, QRS duration > 0.12 s, or QT > 0.5 s
Body packers and stuffers
Concretions caused by drugs
Emergency surgical intervention
Administration of pralidoxime in organophosphate toxicity
Antivenom administration in Crotalidae, coral snake, or arthropod envenomation
Need for continuous infusion of naloxone
Hypokalemia secondary to digitalis overdose (or need for digoxin-immune antibody Fab fragments)

*ECMO = extracorporeal membrane oxygenation.

hemodialysis may be useful should have a low molecular weight (< 500 d), be water soluble, have low protein binding (< 70 to 80%), and have a small volume of distribution (< 1 L/kg). It can especially be effective in correcting concomitant electrolyte abnormality and metabolic acidosis. Toxins in which hemodialysis may be required in an early stage of intoxication include methanol, ethylene glycol, boric acid, salicylates, and lithium. Hemodialysis can also be used for heavy metal chelation in patients with renal failure.

Hemoperfusion

Hemoperfusion is defined as direct contact of blood with an adsorbent system.⁷⁵ Charcoal hemoperfusion involves pumping blood through a charcoal canister. Unlike hemodialysis, drug clearance is not limited by low water solubility, high molecular weight, or increased protein binding, but on the ability of the adsorbent to bind to the drug/toxin. However, the toxin needs to be present in the central compartment for hemoperfusion to be effective. Hemoperfusion is essentially the parenteral analog of oral activated charcoal. Complications of hemoperfusion include the following: (1) cartridge saturation; (2) thrombocytopenia that commonly occurs due to platelet adsorption, inducing up to 30% decrement in platelet count; (3) hypoglycemia and hypocalcemia; (4) access complications; (5) hypo-

thermia, since hemoperfusion pumps do not warm blood as hemodialysis does; and (6) charcoal embolization (prevented by a filter in the line returning effluent blood to the patient).

Most drugs are extractable by hemoperfusion, which is particularly suitable for extracorporeal removal of toxins that are of high molecular weight, highly protein bound, or lipid soluble. It has been effectively used to enhance elimination of theophylline, phenobarbital, phenytoin, carbamazepine, paraquat, and glutethimide. Drugs poorly extracted by hemoperfusion include the following: heavy metals (lithium, bromide), some alcohols (ethanol, methanol), carbon monoxide, and some illicit drugs (cocaine, phencyclidine, and others). Efficacy of intoxicant removal is diminished for substances with a large volume of distribution that are highly lipid soluble and/or extensively tissue bound. These intoxicants may be more effectively removed by hemofiltration.

Hemofiltration

Hemofiltration achieves drug and toxin removal by convection. It transports solutes through a highly porous membrane that is permeable to substances with weights of up to 6,000 d, including virtually all drugs. In some cases, hemofiltration membranes are permeable to substances weighing up to 20,000 d.^{76,77} Although the application of this technique has not been vigorously studied in poisoned patients, there are increasing numbers of case reports of extracorporeal intoxicant removal by either the continuous arteriovenous or venovenous hemofiltration methods.^{78–80} Hemofiltration is potentially useful for removal of substances with a large volume of distribution, slow intercompartmental transfer, or extensive tissue binding. Specific highly porous hemofiltration cartridges are also particularly useful for removal of large-molecular-weight solutes or complexes, such as combined digoxin-Fab fragment complexes, or desferoxamine complexes with iron or with aluminum.

ANTIDOTES

An antidote is a substance that increases the mean lethal dose of a toxin, or that can favorably affect the toxic effects of a poison. Some are toxic themselves and therefore should be used only when indicated. Table 18 lists antidotes for specific drugs/poisons. These will be discussed further next month in part II of this article.

INDICATIONS FOR ICU ADMISSION

In the current health-care climate, the practice of routinely admitting the poisoned patient to the ICU is being questioned. Brett et al⁸¹ identified eight clinical risk factors that can predict ICU interventions: (1) PaCO₂ > 45 mm Hg, (2) need for endotracheal intubation, (3) toxin-induced seizures, (4) cardiac arrhythmias, (5) QRS duration ≥ 0.12 s, (6) systolic BP < 80 mm Hg, (7) second- or third-degree atrioventricular block, and (8) unresponsiveness to verbal stimuli. In this retrospective study, if a poisoned patient did not exhibit any of the eight characteristics, no ICU interventions (intubation, vasopressors or antiarrhythmics, and dialysis or hemoperfusion) were required. Other indications for ICU admission include a Glasgow coma scale score < 12,⁸² need for emergency dialysis or hemoperfusion, progressive metabolic acidosis, and a cyclic antidepressant or phenothiazine overdose with signs of anticholinergic cardiac toxicity.^{83,84} Severe hyperkalemia, wide alterations in body temperature, and need for continuous infusion of naloxone are also reasons to admit a patient to an ICU. In addition, staffing issues such as the availability of a “sitter” in cases of attempted suicide may impact patient disposition. Table 19 provides a list of criteria for ICU admission.⁶⁷

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Babak Mokhlesi, Jerrold B. Leiken, Patrick Murray and Thomas C. Corbridge

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