

02 - 470 Poisoning and Drug Overdose

470 Poisoning and Drug Overdose

Mark B. Mycyk

Poisoning and Drug

Overdose Poisoning refers to the development of dose-related adverse effects following exposure to chemicals, drugs, or other xenobiotics. To paraphrase Paracelsus, the dose makes the poison. Although most poisons have predictable dose-related effects, individual responses to a given dose may vary because of genetic polymorphism, enzymatic induction or inhibition in the presence of other xenobiotics, or acquired tolerance. Poisoning may be local (e.g., skin, eyes, or lungs) or systemic depending on the route of exposure, the chemical and physical properties of the poison, and its mechanism of action. The severity and reversibility of poisoning also depend on the functional reserve of the individual or target organ, which is influenced by age and preexisting disease.

EPIDEMIOLOGY More than 5 million poison exposures occur in the United States each year. Most are acute, are accidental (unintentional), involve a single agent, occur in the home (>90%), result in minor or no toxicity, and involve children <6 years of age. Pharmaceuticals are involved in 47% of poisoning exposures and in 84% of serious or fatal poisonings. Household cleaning substances and cosmetics/personal care products are the most common nonpharmaceutical exposures reported to the National Poison Data System (NPDS). Fatalities most commonly occur from intentional self-harm ingestions (suicide) of pharmaceuticals or from complications involving opioids and other psychoactive drugs of abuse. According to the Centers for Disease Control and Prevention (CDC), fatalities involving drugs have steadily increased since 1999. More than 106,600 deaths were attributed to drug overdose in the United States in 2021, with an age-adjusted overdose death rate of 32.4 per 100,000. Although prescription opioids have appropriately received attention as a major reason for the ongoing substance use disorder epidemic in the United States, the ever-expanding street availability of synthetic opioids (e.g., fentanyl) and the rapid proliferation of other psychoactive drugs of abuse (e.g., xylazine) are the main drivers of drug overdose deaths. State prescription monitoring programs, enhanced training in pain management for health care professionals, expanded harm reduction services, improved outreach education to the public, and improved partnerships with regional safety officials to monitor trends in the illicit drug supply continue to be the main prevention and response priorities for addressing this worsening epidemic. Unintentional exposures can result from the improper use of chemicals at work or play; label misreading; product mislabeling; mistaken identification of unlabeled chemicals; uninformed

self-medication; and dosing errors by nurses, pharmacists, physicians, parents, and the elderly. Excluding the recreational use of ethanol, attempted suicide (deliberate self-harm) is the most common reported reason for intentional poisoning. Recreational use of prescribed and over-the-counter drugs for psychotropic or euphoric effects (abuse) or excessive self-dosing (misuse) is increasingly common and may also result in unintentional self-poisoning. About 20–25% of exposures require bedside health-professional evaluation, and 5% of all exposures require hospitalization. Poisonings account for 5–10% of all ambulance transports, emergency department visits, and intensive care unit admissions. Hospital admissions related to poisoning are also associated with longer lengths of stay and increase the utilization of resources such as radiography and other laboratory services. Up to 35% of psychiatric admissions are prompted by attempted suicide via overdose with cases involving adolescents steadily increasing during the last decade. Overall, the mortality rate is low: <1% of all poisoning exposures. It is significantly higher (1–2%) among hospitalized patients with intentional (suicidal) overdose or complications from drugs of abuse, who account for the majority of serious poisonings. Acetaminophen is the pharmaceutical agent most

often implicated in fatal poisoning. Overall, carbon monoxide is the leading cause of death from poisoning, but this prominence is not reflected in hospital or poison center statistics because patients with such poisoning are typically dead when discovered and are referred directly to medical examiners.

DIAGNOSIS Although poisoning can mimic other illnesses, the correct diagnosis can usually be established by the history, physical examination, routine and toxicologic laboratory evaluations, and characteristic clinical course. ■ ■ **HISTORY** The history should include the time, route, duration, and circumstances (location, surrounding events, and intent) of exposure; the name and amount of each drug, chemical, or ingredient involved; the time of onset, nature, and severity of symptoms; the time and type of first-aid measures provided; the medical and psychiatric history; and occupation. In many cases, the patient is confused, comatose, unaware of an exposure, or unable or unwilling to admit to one. Suspicious circumstances include unexplained sudden illness in a previously healthy person or a group of healthy people; a history of psychiatric problems (particularly depression or bipolar disorder); recent changes in health, economic status, or social relationships; and onset of illness during work with chemicals or after ingestion of food, drink (especially ethanol), or medications. When patients become ill soon after arriving from a foreign country or being arrested for criminal activity, “body packing” or “body stuffing” (ingesting or concealing illicit drugs in a body cavity) should be suspected. Relevant information may be available from family, friends, paramedics, police, pharmacists, physicians, and employers, who should be questioned regarding the patient’s habits, hobbies, behavioral changes, available medications, and antecedent events. Patients need to be asked explicitly about their prescribed medications, use of over-the-counter or herbal medications, and recreational drug use. Drugs previously considered “illicit” such as cannabinoids are now legal in many states and prescribed for therapeutic purposes. A search of clothes, belongings, and place of discovery may reveal a suicide note or a container of drugs or chemicals. If available, a review of a patient’s recent social media posts may be helpful to the treating clinician because self-harm plans involving medications or drugs are often described there. Without a clear history in a patient clinically suspected to be poisoned, all medications available anywhere in the patient’s home or belongings should be considered as possible agents, including medications for pets. Review of the patient’s record in the

state prescription monitoring program (PMP) may disclose relevant history of Schedule II, III, IV, and V controlled substance use. The imprint code on pills and the label on chemical products may be used to identify the ingredients and potential toxicity of a suspected poison by consulting a reference text, a computerized database, the manufacturer, or a regional poison information center (800-222-1222). Occupational exposures require review of any available safety data sheet (SDS) from the worksite. Because of increasing globalization from travel and internet consumerism, unfamiliar poisonings may result in local emergency department evaluation. Pharmaceuticals, industrial chemicals, or novel psychoactive drugs of abuse from foreign countries may be identified with the assistance of a local medical toxicologist, a regional poison center, or via the Internet.

CHAPTER 470 Poisoning and Drug Overdose ■ ■ PHYSICAL EXAMINATION AND CLINICAL COURSE

The physical examination should focus initially on vital signs, the cardiopulmonary system, and neurologic status. The neurologic examination should include documentation of neuromuscular abnormalities such as dyskinesia, dystonia, fasciculations, myoclonus, rigidity, and tremors. The patient should also be examined for evidence of trauma and underlying illnesses. Focal neurologic findings are uncommon in poisoning, and their presence should prompt evaluation for a structural central nervous system (CNS) lesion. Examination of the eyes (for nystagmus and pupil size and reactivity), abdomen (for bowel activity

and bladder size), and skin (for burns, bullae, color, warmth, moisture, pressure sores, and puncture marks) may reveal findings of diagnostic value. When the history is unclear, all orifices should be examined for the presence of chemical burns and drug packets. The odor of breath or vomitus and the color of nails, skin, or urine may provide important diagnostic clues.

The diagnosis of poisoning in cases of unknown etiology primarily relies on pattern recognition. The first step is to assess the pulse, blood pressure, respiratory rate, pulse oximetry, temperature, and neurologic status and to characterize the overall physiologic state as stimulated, depressed, discordant, or normal (Table 470-1). Obtaining a complete set of vital signs and reassessing them frequently are critical. Measuring core temperature is especially important, even in difficult or combative patients, since temperature elevation is the most reliable prognosticator of poor outcome in poisoning from stimulants (e.g., cocaine) or drug withdrawal (e.g., alcohol or γ -hydroxybutyric acid [GHB]).

TABLE 470-1 Differential Diagnosis of Poisoning Based on Physiologic State

STIMULATED	DEPRESSED	DISCORDANT	NORMAL
Sympathetics			

Sympathomimetics	Ergot alkaloids	Methylxanthines	Monoamine oxidase inhibitors	Thyroid hormones
Anticholinergics	Antihistamines	Antiparkinsonian agents	Antipsychotics	Antispasmodics
Belladonna alkaloids	Cyclic antidepressants	Mushrooms and plants	Hallucinogens	Cannabinoids (marijuana)
LSD and analogues	Mescaline and analogues	Mushrooms	Phencyclidine and analogues	Withdrawal syndromes
Barbiturates	Benzodiazepines	Ethanol	GHB products	Opioids
Sedative-hypnotics	Sympatholytics	Sympatholytics	α 1-Adrenergic antagonists	α 2-Adrenergic agonists
ACE inhibitors	Angiotensin receptor blockers	Antipsychotics	β -Adrenergic blockers	Calcium channel blockers
Cardiac glycosides	Cyclic antidepressants	Cholinergics	Acetylcholinesterase inhibitors	Muscarinic agonists
Nicotinic agonists	Opioids	Analgesics	GI antispasmodics	Heroin
Sedative-hypnotics	Alcohols	Anticonvulsants	Barbiturates	Benzodiazepines
GABA precursors	Muscle relaxants	Other agents	GHB products	Xylazine

PART 14 Poisoning, Drug Overdose, and Envenomation

Abbreviations: ACE, angiotensin-converting enzyme; AGMA, anion-gap metabolic acidosis; CNS, central nervous system; GABA, γ -aminobutyric acid; GHB, γ -hydroxybutyrate; GI, gastrointestinal; LSD, lysergic acid diethylamide; MAO, monoamine oxidase.

step is to consider the underlying causes of the physiologic state and to attempt to identify a pathophysiologic pattern or toxic syndrome (toxidrome) based on the observed findings. Assessing the severity of physiologic derangements (Table 470-2) is useful in this regard and also for monitoring the clinical course and response to treatment. In cases of polydrug overdose involving different drug classes, identifying a clear toxidrome can be challenging if the different drugs counteract the physiologic effects of one another. The final step is to attempt to identify the particular agent involved by looking for unique or relatively poison-specific physical or ancillary test abnormalities. Distinguishing among toxidromes on the basis of the physiologic state is summarized next. The Stimulated Physiologic State Increased pulse, blood pressure, respiratory rate, temperature, and neuromuscular activity characterize the stimulated physiologic state, which can reflect sympathetic, Asphyxiants Cytochrome oxidase inhibitors Inert gases Irritant gases Methemoglobin inducers Oxidative phosphorylation inhibitors AGMA inducers Alcohol (ketoacidosis) Ethylene glycol Iron Methanol Other alcohols Salicylate Toluene CNS syndromes Extrapyrimal reactions Hydrocarbon inhalation Isoniazid Lithium Neuroleptic malignant syndrome Serotonin syndrome Strychnine Membrane-active agents Amantadine Antiarrhythmics Antihistamines Antipsychotics Carbamazepine Cyclic antidepressants Local anesthetics Opioids (some) Quinoline antimalarials Nontoxic exposure Psychogenic illness "Toxic time-bombs" Slow absorption Anticholinergics Carbamazepine Concretion formers Extended-release phenytoin sodium capsules (Dilantin Kapseals) Drug packets Enteric-coated pills Diphenoxylate-atropine (Lomotil) Opioids Salicylates Sustained-release pills Valproate Slow distribution Cardiac glycosides Lithium Metals Salicylate Valproate Toxic metabolite Acetaminophen Carbon tetrachloride Cyanogenic glycosides Ethylene glycol Methanol Methemoglobin inducers Mushroom toxins Organophosphate insecticides Paraquat Metabolism disruptors Antineoplastic agents Antiviral agents Colchicine Hypoglycemic agents Immunosuppressive agents MAO inhibitors Metals Other oral anticoagulants Salicylate Warfarin

TABLE 470-2 Severity of Physiologic Stimulation and Depression in Poisoning and Drug Withdrawal

Physiologic Stimulation Grade 1 Anxious, irritable, tremulous; vital signs normal; diaphoresis, flushing or pallor, mydriasis, and hyperreflexia sometimes present Grade 2 Agitated; may have confusion or hallucinations but can converse and follow commands; vital signs mildly to moderately increased Grade 3 Delirious; unintelligible speech, uncontrollable motor hyperactivity; moderately to markedly increased vital signs; tachyarrhythmias possible Grade 4 Coma, seizures, cardiovascular collapse

Physiologic Depression Grade 1 Awake, lethargic, or sleeping but arousable by voice or tactile stimulation; able to converse and follow commands; may be confused Grade 2 Responds to pain but not voice; can vocalize but not converse; spontaneous motor activity present; brainstem reflexes intact Grade 3 Unresponsive to pain; spontaneous motor activity absent; brainstem reflexes depressed; motor tone, respirations, and temperature decreased Grade 4 Unresponsive to pain; flaccid paralysis; brainstem reflexes and respirations absent; cardiovascular vital signs decreased anticholinergic, or hallucinogen poisoning or drug withdrawal (Table 470-1). Other features are noted in Table 470-2. Mydriasis, a characteristic feature of all stimulants, is most marked in anticholinergic poisoning since pupillary reactivity relies on muscarinic control. In sympathetic poisoning (e.g., due to cocaine), pupils are also enlarged, but some reactivity to light remains. The anticholinergic toxidrome is also distinguished by hot, dry, flushed skin; decreased bowel sounds; and urinary retention. Other stimulant syndromes increase sympathetic activity and cause diaphoresis, pallor, and increased bowel activity with varying degrees of nausea, vomiting, abnormal distress, and occasionally diarrhea. The absolute and relative degree of vital-sign

changes and neuromuscular hyperactivity can help distinguish among stimulant toxidromes. Since sympathetics stimulate the peripheral nervous system more directly than do hallucinogens or drug withdrawal, markedly increased vital signs and organ ischemia suggest sympathetic poisoning. Findings helpful in suggesting the particular drug or class causing physiologic stimulation include reflex bradycardia from selective α -adrenergic stimulants (e.g., decongestants), hypotension from selective β -adrenergic stimulants (e.g., asthma therapeutics), limb ischemia from ergot alkaloids, rotatory nystagmus from phencyclidine and ketamine (the only physiologic stimulants that cause this finding), and delayed cardiac conduction from high doses of cocaine and some anticholinergic agents (e.g., antihistamines, cyclic antidepressants, and antipsychotics). Seizures suggest a sympathetic etiology, an anticholinergic agent with membrane-active properties (e.g., cyclic antidepressants, phenothiazines), or a withdrawal syndrome. Close attention to core temperature is critical in patients with grade 4 physiologic stimulation (Table 470-2). The Depressed Physiologic State Decreased pulse, blood pressure, respiratory rate, temperature, and neuromuscular activity are indicative of the depressed physiologic state caused by "functional" sympatholytics (agents that decrease cardiac function and vascular tone as well as sympathetic activity), cholinergic (muscarinic and nicotinic) agents, opioids, and sedative-hypnotic γ -aminobutyric acid (GABA)-ergic agents (Tables 470-1 and 470-2). Miosis is also common and is most pronounced in opioid and cholinergic poisoning. Miosis is distinguished from other depressant syndromes by muscarinic and nicotinic signs and symptoms (Table 470-1). Pronounced cardiovascular depression in the absence of significant CNS depression suggests a direct or peripherally acting sympatholytic. In contrast, in opioid and sedative-hypnotic poisoning, vital-sign changes are secondary to depression of CNS cardiovascular and respiratory centers (or consequent hypoxemia), and significant abnormalities in these

parameters do not occur until there is a marked decrease in the level of consciousness (grade 3 or 4 physiologic depression; Table 470-2). Other clues that suggest the cause of physiologic depression include cardiac arrhythmias and conduction disturbances (due to antiarrhythmics, β -adrenergic antagonists, calcium channel blockers, digitalis glycosides, propoxyphene, and cyclic antidepressants), mydriasis (due to tricyclic antidepressants, some antiarrhythmics, meperidine, and diphenoxylate-atropine [Lomotil]), nystagmus (due to sedative-hypnotics), and seizures (due to cholinergic agents, propoxyphene, and cyclic antidepressants).

The Discordant Physiologic State The discordant physiologic state is characterized by mixed vital-sign and neuromuscular abnormalities, as observed in poisoning by asphyxiants, CNS syndromes, membrane-active agents, and anion-gap metabolic acidosis (AGMA) inducers (Table 470-1). In these conditions, manifestations of physiologic stimulation and physiologic depression occur together or at different times during the clinical course. For example, membrane-active agents can cause simultaneous coma, seizures, hypotension, and tachyarrhythmias. Alternatively, vital signs may be normal while the patient has an altered mental status or is obviously sick or clearly symptomatic. Early, pronounced vital-sign and mental-status changes suggest asphyxiant or membrane-active agent poisoning; the lack of such abnormalities suggests an AGMA inducer; and marked neuromuscular dysfunction without significant vital-sign abnormalities suggests a CNS syndrome. The discordant physiologic state may also be evident in patients poisoned with multiple agents.

CHAPTER 470 The Normal Physiologic State A normal physiologic status and physical examination may be due to a nontoxic exposure, psychogenic illness, or poisoning by "toxic time-bombs": agents that are slowly absorbed, are slowly distributed to their sites of action, require

metabolic activation, or disrupt metabolic processes (Table 470-1). Because so many medications have now been reformulated into once-a-day preparations for the patient's convenience and adherence, toxic timebombs are increasingly common. Diagnosing a nontoxic exposure requires that the identity of the exposure agent be known or that a toxic time-bomb exposure be excluded and the time since exposure exceed the longest known or predicted interval between exposure and peak toxicity. Psychogenic illness (fear of being poisoned, mass hysteria) may also follow a nontoxic exposure and should be considered when symptoms are inconsistent with exposure history. Anxiety reactions resulting from a nontoxic exposure can cause mild physiologic stimulation (Table 470-2) and be indistinguishable from toxicologic causes without ancillary testing or a suitable period of observation.

Poisoning and Drug Overdose ■ ■ LABORATORY ASSESSMENT

Laboratory assessment may be helpful in the differential diagnosis. Increased AGMA is most common in advanced methanol, ethylene glycol, and salicylate intoxication but can occur with any poisoning that results in hepatic, renal, or respiratory failure; seizures; or shock. The serum lactate concentration is more commonly low (less than the anion gap) in the former and high (nearly equal to the anion gap) in the latter. An abnormally low anion gap can be due to elevated blood levels of bromide, calcium, iodine, lithium, or magnesium. An increased osmolal gap—a difference of >10 mmol/L between serum osmolality (measured by freezing-point depression) and osmolality calculated from serum sodium, glucose, and blood urea nitrogen levels—suggests the presence of a low-molecular-weight solute such as acetone; an alcohol (benzyl, ethanol, isopropanol, methanol); a glycol (diethyl ene, ethylene, propylene); ether (ethyl, glycol); or an “unmeasured” cation (calcium, magnesium) or sugar (glycerol, mannitol, sorbitol). Ketosis suggests acetone, isopropyl alcohol, salicylate poisoning, or alcoholic ketoacidosis. Hypoglycemia may be due to poisoning with β -adrenergic blockers, ethanol, insulin, oral hypoglycemic agents, quinine, and salicylates, whereas hyperglycemia can occur in poisoning with acetone, β -adrenergic agonists, caffeine, calcium channel blockers, iron, theophylline, or N-3-pyridylmethyl-N-p-nitrophenylurea (PNU [Vacor]). Hypokalemia can be caused by barium, β -adrenergic agonists, caffeine, diuretics, theophylline, or toluene; hyperkalemia

suggests poisoning with an α -adrenergic agonist, a β -adrenergic blocker, cardiac glycosides, or fluoride. Hypocalcemia may be seen in ethylene glycol, fluoride, and oxalate poisoning. Prothrombin time and international normalized ratio are useful for risk stratification in cases of warfarin or rodenticide poisoning but are not to be relied on when evaluating overdose or complications from direct oral anticoagulant pharmaceuticals (direct thrombin inhibitors and direct factor Xa inhibitors).

The electrocardiogram (ECG) can be useful for rapid diagnostic purposes. Bradycardia and atrioventricular block may occur in patients poisoned by α -adrenergic agonists, antiarrhythmic agents, beta blockers, calcium channel blockers, cholinergic agents (carbamate and organophosphate insecticides), cardiac glycosides, lithium, or tricyclic antidepressants. QRS- and QT-interval prolongation may be caused by hyperkalemia, various antidepressants, and other membrane-active drugs (Table 470-1). Ventricular tachyarrhythmias may be seen in poisoning with cardiac glycosides, fluorides, membrane-active drugs, methylxanthines, sympathomimetics, antidepressants, and agents that cause hyperkalemia or potentiate the effects of endogenous catechol amines (e.g., chloral hydrate, aliphatic and halogenated hydrocarbons). Radiologic studies may occasionally be useful. Pulmonary edema (adult respiratory distress syndrome [ARDS]) can be caused by poisoning with carbon monoxide, cyanide, an opioid, paraquat, phen cyclidine, a

sedative-hypnotic, or salicylate; by inhalation of irritant gases, fumes, or vapors (acids and alkali, ammonia, aldehydes, chlorine, hydrogen sulfide, isocyanates, metal oxides, mercury, phosgene, polymers); or by prolonged anoxia, hyperthermia, or shock. Aspiration pneumonia is common in patients with coma, seizures, and petroleum distillate aspiration. Chest x-ray is useful for identifying complications from metal fume fever or elemental mercury. The presence of radiopaque densities on abdominal x-rays or abdominal computed tomography (CT) scan suggests the ingestion of chloral hydrate, chlorinated hydrocarbons, heavy metals, illicit drug packets, iodinated compounds, potassium salts, enteric-coated tablets, or salicylates. PART 14 Poisoning, Drug Overdose, and Envenomation Toxicologic analysis of urine and blood (and occasionally of gastric contents and chemical samples) can sometimes confirm or rule out suspected poisoning. Interpretation of laboratory data requires knowledge of the qualitative and quantitative tests used for screening and confirmation (enzyme-multiplied, fluorescence polarization, and radioimmunoassays; colorimetric and fluorometric assays; thin-layer, gas-liquid, or high-performance liquid chromatography; gas chromatography; mass spectrometry), their sensitivity (limit of detection) and specificity, the preferred biologic specimen for analysis, and the optimal time of specimen sampling. Personal communication with the hospital laboratory is essential to an understanding of institutional testing capabilities and limitations. Rapid qualitative hospital-based urine tests for drugs of abuse are only screening tests that cannot confirm the exact identity of the detected substance and should not be considered diagnostic or used for forensic purposes. False-positive and false-negative results are common. A positive screen may result from other pharmaceuticals that interfere with laboratory analysis (e.g., fluoroquinolones commonly cause false-positive opiate screens). Confirmatory testing with gas chromatography/mass spectrometry can be requested, but it often takes weeks to obtain a reported result. A negative screening result may mean that the responsible substance is not detectable by the test used or that its concentration is too low for detection at the time of sampling. For instance, recent new drugs of abuse that often result in emergency department evaluation for unexpected complications, such as synthetic cannabinoids (spice), cathinones (bath salts), and opiate substitutes (kratom), are not detectable by hospital-based tests. In cases where a drug concentration is too low to be detected early during clinical evaluation, repeating the test at a later time may yield a positive result. Patients symptomatic from drugs of abuse often require immediate management based on the history, physical examination, and observed toxidrome without laboratory confirmation (e.g., apnea from opioid intoxication). When the patient is asymptomatic or when the clinical picture is consistent with the reported history, qualitative screening is neither clinically useful nor cost-effective. Thus, qualitative drug

screens are of greatest value for the evaluation of patients with severe or unexplained toxicities, such as coma, seizures, cardiovascular instability, metabolic or respiratory acidosis, and nonsinus cardiac rhythms. In contrast to qualitative drug screens, quantitative serum tests are useful for evaluation of patients poisoned with acetaminophen (Chap. 351), alcohols (including ethylene glycol and methanol), anticonvulsants, barbiturates, digoxin, heavy metals, iron, lithium, salicylate, and theophylline, as well as for the presence of carboxyhemoglobin and methemoglobin. The serum concentration in these cases guides clinical management, and results are often available within an hour. The response to antidotes is sometimes useful for diagnostic purposes. Resolution of altered mental status and abnormal vital signs within minutes of IV administration of dextrose, naloxone, or flumazenil is virtually diagnostic of hypoglycemia, opioid poisoning, and benzodiazepine intoxication, respectively. The prompt reversal of dystonic (extrapyramidal) signs

and symptoms following an IV dose of benztropine or diphenhydramine confirms a drug etiology. Although complete reversal of both central and peripheral manifestations of anti cholinergic poisoning by physostigmine is diagnostic of this condition, physostigmine may cause some arousal in patients with CNS depression of any etiology.

TREATMENT Poisoning and Drug Overdose

GENERAL PRINCIPLES Treatment goals include support of vital signs, prevention of further poison absorption (decontamination), enhancement of poison elimination, administration of specific antidotes, and prevention of reexposure (Table 470-3). Specific treatment depends on the identity of the poison, the route and amount of exposure, the time

TABLE 470-3 Fundamentals of Poisoning Management

Supportive Care Airway protection Treatment of seizures Oxygenation/ventilation Correction of temperature abnormalities Treatment of arrhythmias Correction of metabolic derangements Hemodynamic support Prevention of secondary complications Prevention of Further Poison Absorption Gastrointestinal decontamination Decontamination of other sites Gastric lavage Eye decontamination Activated charcoal Skin decontamination Whole-bowel irrigation Body cavity evacuation Dilution Endoscopic/surgical removal Enhancement of Poison Elimination Multiple-dose activated charcoal administration Alteration of urinary pH Chelation Hyperbaric oxygenation Extracorporeal removal Hemodialysis Hemoperfusion Hemofiltration Plasmapheresis Exchange transfusion Continuous venovenous hemofiltration (CVVH) Administration of Antidotes Neutralization by antibodies Metabolic antagonism Neutralization by chemical binding Physiologic antagonism Prevention of Reexposure Adult education Notification of regulatory agencies Child-proofing Psychiatric referral Naloxone distribution Linkage to harm reduction services

of presentation relative to the time of exposure, and the severity of poisoning. Knowledge of the offending agents' pharmacokinetics and pharmacodynamics is essential. During the pretoxic phase, prior to the onset of poisoning, decontamination is the highest priority, and treatment is based solely on the history. The maximal potential toxicity based on the greatest possible exposure should be assumed. Since decontamination is more effective when accomplished soon after exposure and when the patient is asymptomatic, the initial history and physical examination should be focused and brief. It is also advisable to establish IV access and initiate cardiac monitoring, particularly in patients with potentially serious ingestions or unclear histories. When an accurate history is not obtainable and a poison causing delayed toxicity (i.e., a toxic time-bomb) or irreversible damage is suspected, blood and urine should be sent for appropriate toxicologic screening and quantitative analysis. During poison absorption and distribution, blood levels may be greater than those in tissue and may not correlate with toxicity. However, high blood levels of agents whose metabolites are more toxic than the parent compound (acetaminophen, ethylene glycol, or methanol) may indicate the need for additional interventions (antidotes, dialysis). Most patients who remain asymptomatic or who become asymptomatic 6 h after ingestion are unlikely to develop subsequent toxicity and can be discharged safely. Longer observation will be necessary for patients who have ingested toxic time-bombs. During the toxic phase—the interval between the onset of poisoning and its peak effects—management is based primarily on clinical and laboratory findings. Effects after an overdose usually begin sooner, peak later, and last longer than they do after a therapeutic dose. A drug's published pharmacokinetic profile in standard references such as the Physician's Desk Reference (PDR) is usually different from its toxicokinetic profile in overdose. Resuscitation and stabilization are the first priority. Symptomatic patients should have an IV line placed and should undergo oxygen saturation determination, cardiac monitoring, and continuous observation. Base line laboratory, ECG, and x-ray evaluation may also be appropriate. Intravenous glucose (unless the serum level is documented to be normal), naloxone, and thiamine

should be considered in patients with altered mental status, particularly those with coma or seizures. Decontamination should also be considered, but it is less likely to be effective during this phase than during the pretoxic phase. Measures that enhance poison elimination may shorten the duration and severity of the toxic phase. However, they are not without risk, which must be weighed against the potential benefit. Diagnostic certainty (usually via laboratory confirmation) is generally a prerequisite. Intestinal (gut) dialysis with repetitive doses of activated charcoal (see "Multiple-Dose Activated Charcoal," later) can enhance the elimination of selected poisons such as theophylline or carbamazepine. Urinary alkalization may enhance the elimination of salicylates and a few other poisons. Chelation therapy can enhance the elimination of selected metals. Extracorporeal elimination methods are effective for many poisons, but their expense and risk make their use reasonable only in patients who would otherwise have an unfavorable outcome. During the resolution phase of poisoning, supportive care and monitoring should continue until clinical, laboratory, and ECG abnormalities have resolved. Since chemicals are eliminated sooner from the blood than from tissues, blood levels are usually lower than tissue levels during this phase and again may not correlate with toxicity. This discrepancy applies particularly when extracorporeal elimination procedures are used. Redistribution from tissues may cause a rebound increase in the blood level after termination of these procedures (e.g., lithium). When a metabolite is responsible for toxic effects, continued treatment may be necessary in the absence of clinical toxicity or abnormal laboratory studies.

SUPPORTIVE CARE The goal of supportive therapy is to maintain physiologic homeostasis until detoxification is accomplished and to prevent and treat

secondary complications such as aspiration, bedsores, cerebral and pulmonary edema, pneumonia, rhabdomyolysis, renal failure, sepsis, thromboembolic disease, coagulopathy, and generalized organ dysfunction due to hypoxemia or shock.

Admission to an intensive care unit is indicated for the following: patients with severe poisoning (coma, respiratory depression, hypotension, cardiac conduction abnormalities, cardiac arrhythmias, hypothermia or hyperthermia, seizures); those needing close monitoring, antidotes, or enhanced elimination therapy; those showing progressive clinical deterioration; and those with significant underlying medical problems. Patients with mild to moderate toxicity can be managed on a general medical service, on an intermediate care unit, or in an emergency department observation area, depending on the anticipated duration and level of monitoring needed (intermittent clinical observation vs continuous clinical, cardiac, and respiratory monitoring). Patients who have attempted suicide require continuous observation and measures to prevent self-injury until they are no longer suicidal. Respiratory Care Endotracheal intubation for protection against the aspiration of gastrointestinal contents is of paramount importance in patients with CNS depression or seizures as this complication can increase morbidity and mortality rates. Mechanical ventilation may be necessary for patients with respiratory depression or hypoxemia and for facilitation of therapeutic sedation or paralysis of patients in order to prevent or treat hyperthermia, acidosis, and rhabdomyolysis associated with neuromuscular hyperactivity. Since clinical assessment of respiratory function can be inaccurate, the need for oxygenation and ventilation is best determined by continuous pulse oximetry or arterial blood-gas analysis. The gag reflex is not a reliable indicator of the need for intubation. A patient with CNS depression may maintain airway patency while being stimulated but not if left alone. Drug-induced pulmonary edema is usually noncardiac rather than cardiac in origin, although profound CNS depression and cardiac conduction abnormalities suggest the latter. Measurement of pulmonary artery pressure

may be necessary to establish the cause and direct appropriate therapy. Extracorporeal measures (membrane oxygenation, extracorporeal membrane oxygenation [ECMO], venoarterial perfusion, cardio pulmonary bypass) and partial liquid (perfluorocarbon) ventilation may be appropriate for severe but reversible respiratory failure. In the last decade, ECMO has been increasingly used for critically ill poisoned patients where standard resuscitative therapy or antidotes have not been helpful, but further research is still needed to determine the right toxicologic indications for this treatment strategy.

CHAPTER 470 Poisoning and Drug Overdose Cardiovascular Therapy

Maintenance of normal tissue perfusion is critical for complete recovery to occur once the offending agent has been eliminated. Focused bedside echocardiography or measurement of central venous pressure may help prioritize therapeutic strategies. If hypotension is unresponsive to volume expansion and appropriate goal-directed antidotal therapy, treatment with norepinephrine, epinephrine, or high-dose dopamine may be necessary. Intraaortic balloon pump counterpulsation and venoarterial or cardiopulmonary perfusion techniques should be considered for severe but reversible cardiac failure. For patients with a return of spontaneous circulation after resuscitative treatment for cardiopulmonary arrest secondary to poisoning, therapeutic hypothermia should be used according to protocol. Bradyarrhythmias associated with hypotension generally should be treated as described in Chaps. 251 and 252. Glucagon, calcium, and high-dose insulin with dextrose may be effective in beta blocker and calcium channel blocker poisoning. Antibody therapy may be indicated for cardiac glycoside poisoning. Supraventricular tachycardia associated with hypertension and CNS excitation is almost always due to agents that cause generalized physiologic excitation (Table 470-1). Most cases are mild or moderate in severity and require only observation or nonspecific sedation with a benzodiazepine. In severe cases or those associated with hemodynamic instability, chest pain,

or ECG evidence of ischemia, specific therapy is indicated. When the etiology is sympathetic hyperactivity, treatment with a benzodiazepine should be prioritized. Further treatment with a combined alpha and beta blocker (labetalol), a calcium channel blocker (verapamil or diltiazem), or a combination of a beta blocker and a vasodilator (esmolol and nitroprusside) may be considered for cases refractory to high doses of benzodiazepines only when adequate sedation has been achieved but cardiac conduction or blood pressure abnormalities persist. Treatment with an α -adrenergic antagonist (phentolamine) alone may sometimes be appropriate. If the cause is anticholinergic poisoning, physostigmine alone can be effective. Supraventricular tachycardia without hypertension is generally secondary to vasodilation or hypovolemia and responds to fluid administration.

For ventricular tachyarrhythmias due to tricyclic antidepressants and other membrane-active agents (Table 470-1), sodium bicarbonate is indicated, whereas class IA, IC, and III antiarrhythmic agents are contraindicated because of similar electrophysiologic effects. Although lidocaine and phenytoin are historically safe for ventricular tachyarrhythmias of any etiology, sodium bicarbonate should be considered first for any ventricular arrhythmia suspected to have a toxicologic etiology. Intravenous lipid emulsion therapy has shown benefit for treatment of arrhythmias and hemodynamic instability from various membrane-active agents. Beta blockers can be hazardous if the arrhythmia is due to sympathetic hyperactivity. Magnesium sulfate and overdrive pacing (by isoproterenol or a pacemaker) may be useful in patients with torsades des pointes and prolonged QT intervals. Magnesium and anti-digoxin antibodies should be considered in patients with severe cardiac glycoside poisoning. Invasive (esophageal or intracardiac) ECG recording may be necessary

to determine the origin (ventricular or supraventricular) of wide-complex tachycardias (Chap. 253). If the patient is hemodynamically stable, however, it is reasonable to simply observe the patient rather than to administer another potentially proarrhythmic agent. Arrhythmias may be resistant to drug therapy until underlying acid-base, electrolyte, oxygenation, and temperature derangements are corrected.

PART 14 Poisoning, Drug Overdose, and Envenomation

Central Nervous System Therapies

Neuromuscular hyperactivity and seizures can lead to hyperthermia, lactic acidosis, and rhabdomyolysis and should be treated aggressively. Seizures caused by excessive stimulation of catecholamine receptors (sympathomimetic or hallucinogen poisoning and drug withdrawal) or decreased activity of GABA (isoniazid poisoning) or glycine (strychnine poisoning) receptors are best treated with agents that enhance GABA activity, such as benzodiazepine or barbiturates. Since benzodiazepines and barbiturates act by slightly different mechanisms (the former increases the frequency via allosteric modulation at the receptor and the latter directly increases the duration of chloride channel opening in response to GABA), therapy with both may be effective when neither is effective alone. Seizures caused by isoniazid, which inhibits the synthesis of GABA at several steps by interfering with the cofactor pyridoxine (vitamin B6), may require high doses of supplemental pyridoxine. Seizures resulting from membrane destabilization (beta blocker or cyclic antidepressant poisoning) require GABA enhancers (benzodiazepines first, barbiturates second). Phenytoin is contraindicated in toxicologic seizures: Animal and human data demonstrate worse outcomes after phenytoin loading, especially in theophylline overdose. For poisons with central dopaminergic effects (methamphetamine, phencyclidine) manifested by psychotic behavior, a dopamine receptor antagonist, such as haloperidol or ziprasidone, may be useful. In anticholinergic and cyanide poisoning, specific antidotal therapy may be necessary. The treatment of seizures secondary to cerebral ischemia or edema or to metabolic abnormalities should include correction of the underlying cause. Neuromuscular paralysis is indicated in refractory cases. Electroencephalographic monitoring and continuing treatment of seizures are necessary to prevent permanent neurologic damage.

Other Measures

Temperature extremes, metabolic abnormalities, hepatic and renal dysfunction, and secondary complications should be treated by standard therapies.

PREVENTION OF POISON ABSORPTION

Gastrointestinal Decontamination

Whether or not to perform gastrointestinal decontamination and which procedure to use depends on the time since ingestion; the existing and predicted toxicity of the ingested; the availability, efficacy, and contraindications of the procedure; and the nature, severity, and risk of complications. The efficacy of all decontamination procedures decreases with time, and data are insufficient to support or exclude a beneficial effect when they are used >1 h after ingestion. The average time from ingestion to presentation for treatment is >1 h for children and >3 h for adults. Most patients will recover from poisoning uneventfully with good supportive care alone, but complications of gastrointestinal decontamination, particularly aspiration, can prolong this process. Hence, gastrointestinal decontamination should be performed selectively, not routinely, in the management of overdose patients. It is clearly unnecessary when predicted toxicity is minimal or the time of expected maximal toxicity has passed without significant effect. Activated charcoal has comparable or greater efficacy; has fewer contraindications and complications; and is less aversive and invasive than ipecac or gastric lavage. Thus, it is the preferred method of gastrointestinal decontamination in most situations. Activated charcoal suspension (in water) is given orally via a cup, straw, or small-bore nasogastric tube. The generally recommended dose is 1 g/kg body weight because of its dosing convenience, although in vitro and in vivo studies have demonstrated that charcoal adsorbs

≥90% of most substances when given in an amount equal to 10 times the weight of the substance. Palatability may be increased by adding a sweetener (sorbitol) or a flavoring agent (cherry, chocolate, or cola syrup) to the suspension. Charcoal adsorbs ingested poisons within the gut lumen, allowing the charcoal-toxin complex to be evacuated with stool. Charged (ionized) chemicals such as mineral acids, alkalis, and highly dissociated salts of cyanide, fluoride, iron, lithium, and other inorganic compounds are not well adsorbed by charcoal. In studies with animals and human volunteers, charcoal decreases the absorption of ingestants by an average of 73% when given within 5 min of ingestant administration, 51% when given at 30 min, and 36% when given at 60 min. For this reason, charcoal given before hospital arrival by prehospital emergency medical services (EMS) increases the potential clinical benefit. Side effects of charcoal include nausea, vomiting, and diarrhea or constipation. Charcoal may also prevent the absorption of orally administered therapeutic agents, so the timing and the dose administered need to be adjusted. Complications include mechanical obstruction of the airway, aspiration, vomiting, and bowel obstruction and infarction caused by inspissated charcoal. Charcoal is not recommended for patients who have ingested corrosives because it obscures endoscopy. Gastric lavage should be considered for life-threatening poisons that cannot be treated effectively with other decontamination, elimination, or antidotal therapies (e.g., colchicine). Gastric lavage is performed by sequentially administering and aspirating ~5 mL of fluid per kilogram of body weight through a no. 40 French oro gastric tube (no. 28 French tube for children). Except in infants, for whom normal saline is recommended, tap water is acceptable. The patient should be placed in Trendelenburg and left lateral decubitus positions to prevent aspiration (even if an endotracheal tube is in place). Lavage decreases ingestant absorption by an average of 52% if performed within 5 min of ingestion administration, 26% if performed at 30 min, and 16% if performed at 60 min. Significant amounts of ingested drug are recovered from <10% of patients. Aspiration is a common complication (occurring in up to 10% of patients), especially when lavage is performed improperly. Serious complications (esophageal and gastric perforation, tube misplacement in the trachea) occur in ~1% of patients. For this reason, the

physician should personally insert the lavage tube and confirm its placement, and the patient must be cooperative during the procedure. Gastric lavage is contraindicated in corrosive or petroleum distillate ingestions because of the respective risks of gastroesophageal perforation and aspiration pneumonia. It is also contraindicated in patients with a compromised unprotected airway and those at risk for hemorrhage or perforation due to esophageal or gastric pathology or recent surgery. Finally, gastric lavage is absolutely contraindicated in combative patients or those who refuse, as most published complications involve patient resistance to the procedure. Syrup of ipecac, an emetogenic agent that was once the substance most commonly used for decontamination, no longer has a role in poisoning management. Even the American Academy of Pediatrics—traditionally the strongest proponent of ipecac—issued a policy statement in 2003 recommending that ipecac should no longer be used in poisoning treatment. Chronic ipecac use (by patients with anorexia nervosa or bulimia) has been reported to cause electrolyte and fluid abnormalities, cardiac toxicity, and myopathy. Whole-bowel irrigation is performed by administering a bowelcleansing solution containing electrolytes and polyethylene glycol (Golytely, Colyte) orally or by gastric tube at a rate of 2 L/h (0.5 L/h in children) until rectal effluent is clear. The patient must be in a sitting position. Although data are limited, whole-bowel irrigation appears to be as effective as other decontamination procedures in volunteer studies. It is most appropriate for those who have ingested foreign bodies, packets of illicit drugs, and agents that are poorly

adsorbed by charcoal (e.g., heavy metals). This procedure is contra indicated in patients with bowel obstruction, ileus, hemodynamic instability, and compromised unprotected airways. Cathartics are salts (disodium phosphate, magnesium citrate and sulfate, sodium sulfate) or saccharides (mannitol, sorbitol) that historically have been given with activated charcoal to promote the rectal evacuation of gastrointestinal contents. However, no animal, volunteer, or clinical data have ever demonstrated any decontamination benefit from cathartics. Abdominal cramps, nausea, and occasional vomiting are side effects. Complications of repeated dosing include severe electrolyte disturbances and excessive diarrhea. Cathartics are contraindicated in patients who have ingested corrosives and in those with preexisting diarrhea. Magnesium-containing cathartics should not be used in patients with renal failure. Dilution (i.e., drinking water, another clear liquid, or milk at a volume of 5 mL/kg of body weight) is recommended only after the ingestion of corrosives (acids, alkali). It may increase the dissolution rate (and hence absorption) of capsules, tablets, and other solid ingestants and should not be used in these circumstances. Endoscopic or surgical removal of poisons may be useful in rare situations, such as ingestion of a potentially toxic foreign body that fails to transit the gastrointestinal tract, a potentially lethal amount of a heavy metal (arsenic, iron, mercury, thallium), or agents that have coalesced into gastric concretions or bezoars (heavy metals, lithium, salicylates, sustained-release preparations). Patients who become toxic from cocaine due to its leakage from ingested drug packets require immediate surgical intervention. Decontamination of Other Sites Immediate, copious flushing with water, saline, or another available clear, drinkable liquid is the initial treatment for topical exposures (exceptions include alkali metals, calcium oxide, phosphorus). Saline is preferred for eye irrigation. A triple wash (water, soap, water) may be best for dermal decontamination. Inhalational exposures should be treated initially with fresh air or supplemental oxygen. The removal of liquids from body cavities such as the vagina or rectum is best accomplished by irrigation. Solids (drug packets, pills) should be removed manually, preferably under direct visualization.

ENHANCEMENT OF POISON ELIMINATION Although the elimination of most poisons can be accelerated by therapeutic interventions, the pharmacokinetic efficacy (removal of drug at a rate greater than that accomplished by intrinsic elimination) and clinical benefit (shortened duration of toxicity or

improved outcome) of such interventions are often more theoretical than proven. Accordingly, the decision to use such measures should be based on the actual or predicted toxicity and the potential efficacy, cost, and risks of therapy.

Multiple-Dose Activated Charcoal Repetitive oral dosing with charcoal can enhance the elimination of previously absorbed substances by binding them within the gut as they are excreted in the bile, are secreted by gastrointestinal cells, or passively diffuse into the gut lumen (reverse absorption or enterocapillary exsorption). Doses of 0.5–1 g/kg of body weight every 2–4 h, adjusted downward to avoid regurgitation in patients with decreased gastrointestinal motility, are generally recommended. Pharmacokinetic efficacy approaches that of hemodialysis for some agents (e.g., phenobarbital, theophylline). Multiple-dose therapy should be considered only for selected agents (theophylline, phenobarbital, carbamazepine, dapsone, quinine). Complications include intestinal obstruction, pseudo-obstruction, and nonocclusive intestinal infarction in patients with decreased gut motility. Because of electrolyte and fluid shifts, sorbitol and other cathartics are absolutely contraindicated when multiple doses of activated charcoal are administered. Urinary Alkalinization Ion trapping via alteration of urine pH may prevent the renal reabsorption of poisons that undergo excretion by glomerular filtration and active tubular secretion. Since membranes are more

permeable to nonionized molecules than to their ionized counterparts, acidic (low-pKa) poisons are ionized and trapped in alkaline urine, whereas basic ones become ionized and trapped in acid urine. Urinary alkalization (producing a urine pH ≥ 7.5 and a urine output of 3–6 mL/kg of body weight per hour by the addition of sodium bicarbonate to an IV solution) enhances the excretion of chlorophenoxyacetic acid herbicides, chlorpropamide, diflunisal, fluoride, methotrexate, phenobarbital, sulfonamides, and salicylates. Contraindications include congestive heart failure, renal failure, and cerebral edema. Acid-base, fluid, and electrolyte parameters should be monitored carefully. Although acid diuresis may make theoretical sense for some overdoses (amphetamines), it is never indicated and is potentially harmful.

CHAPTER 470 Poisoning and Drug Overdose

Extracorporeal Removal Hemodialysis, charcoal or resin hemo perfusion, hemofiltration, plasmapheresis, and exchange transfusion are capable of removing any toxin from the bloodstream. Agents most amenable to enhanced elimination by dialysis have low molecular mass (<500 Da), high water solubility, low protein binding, small volumes of distribution (<1 L/kg of body weight), prolonged elimination (long half-life), and high dialysis clearance relative to total-body clearance. Molecular weight, water solubility, and protein binding do not limit the efficacy of the other forms of extracorporeal removal. Dialysis should be considered in cases of severe poisoning due to carbamazepine, ethylene glycol, isopropyl alcohol, lithium, methanol, theophylline, salicylates, and valproate. Although hemoperfusion may be more effective in removing some of these poisons, it does not correct associated acid-base and electrolyte abnormalities, and most hospitals no longer have hemoperfusion cartridges readily available. Fortunately, recent advances in hemodialysis technology make it as effective as hemoperfusion for removing poisons such as caffeine, carbamazepine, and theophylline. Both techniques require central venous access and systemic anticoagulation and may result in transient hypotension. Hemoperfusion may also cause hemolysis, hypocalcemia, and thrombocytopenia. Peritoneal dialysis and exchange transfusion are less effective but may be used when other procedures are unavailable, contraindicated, or technically difficult (e.g., in infants). Continuous venovenous hemofiltration (CVVH) has also been used successfully when conventional intermittent hemodialysis is not well tolerated because of hemodynamic lability. Exchange transfusion may be indicated in the treatment of severe arsine- or sodium chlorate-induced hemolysis, methemoglobinemia, and sulfhemoglobinemia. Although hemofiltration can enhance elimination of aminoglycosides, vancomycin, and

metal-chelate complexes, the roles of hemofiltration and plasma pheresis in the treatment of poisoning are not yet defined.

Candidates for extracorporeal removal therapies include patients with severe toxicity whose condition deteriorates despite aggressive supportive therapy; those with potentially prolonged, irreversible, or fatal toxicity; those with dangerous blood levels of toxins; those who lack the capacity for self-detoxification because of liver or renal failure; and those with a serious underlying illness or complication that will adversely affect recovery.

Other Techniques The elimination of heavy metals can be enhanced by chelation, and the removal of carbon monoxide can be accelerated by hyperbaric oxygenation.

ADMINISTRATION OF ANTIDOTES Antidotes counteract the effects of poisons by neutralizing them (e.g., antibody-antigen reactions, chelation, chemical binding) or by antagonizing their physiologic effects (e.g., activation of opposing

TABLE 470-4

Pathophysiologic Features and Treatment of Specific Toxic Syndromes and Poisonings

PHYSIOLOGIC

CONDITION, CAUSES EXAMPLES MECHANISM OF ACTION CLINICAL FEATURES SPECIFIC TREATMENTS

PART 14 Poisoning, Drug Overdose, and Envenomation

Sympathetics

Sympathomimetics

α 1-Adrenergic agonists (decongestants): phenylephrine, phenylpropanolamine

β 2-Adrenergic agonists (bronchodilators): albuterol, terbutaline

Nonspecific adrenergic agonists: amphetamines, cocaine, ephedrine

Stimulation of central and peripheral sympathetic receptors directly or indirectly (by promoting release or inhibiting reuptake of norepinephrine and sometimes dopamine)

Ergot alkaloids Ergotamine, methysergide, bromocriptine, pergolide

Stimulation and inhibition of serotonergic and α -adrenergic receptors; stimulation of dopamine receptors

Methylxanthines Caffeine, theophylline

Inhibition of adenosine synthesis and adenosine receptor antagonism; stimulation of epinephrine and norepinephrine release; inhibition of phosphodiesterase resulting in increased intracellular cyclic adenosine and guanosine monophosphate

Monoamine oxidase Phenelzine, tranylcypromine, selegiline

Inhibition of monoamine oxidase resulting in impaired metabolism of endogenous catecholamines and exogenous sympathomimetic agents

inhibitors

nervous system activity, provision of a competitive metabolic or receptor substrate). Poisons or conditions with specific antidotes include acetaminophen, anticholinergic agents, anticoagulants, benzodiazepines, beta blockers, calcium channel blockers, carbon monoxide, cardiac glycosides, cholinergic agents, cyanide, drug-induced dystonic reactions, ethylene glycol, fluoride, heavy metals, hypoglycemic agents, isoniazid, membrane-active agents, methemoglobinemia, opioids, sympathomimetics, and a variety of envenomations. Intravenous lipid emulsion has been shown to be a successful antidote for poisoning from various anesthetics and membrane-active agents (e.g., cyclic antidepressants), but the exact mechanism of benefit is still under investigation. Antidotes can significantly reduce morbidity and mortality rates but are potentially toxic if used for inappropriate reasons. Since their safe use requires correct identification of a specific poisoning or syndrome, details of antidotal therapy are discussed with the conditions for which they are indicated (Table 470-4). Physiologic stimulation

(Table 470-2). Reflex bradycardia can occur with selective α 1 agonists; β agonists can cause hypotension and hypokalemia. Phentolamine, a nonselective α 1-adrenergic receptor antagonist, for severe hypertension due to α 1-adrenergic agonists; propranolol, a nonselective β blocker, for hypotension and tachycardia due to β 2 agonists; either labetalol, a β blocker with α -blocking activity, or phentolamine with esmolol, metoprolol, or another cardioselective β blocker for hypertension with tachycardia due to nonselective agents (β blockers, if used alone, can exacerbate hypertension and vasospasm due to unopposed α stimulation); benzodiazepines; propofol

Physiologic stimulation (Table 470-2); formication; vasospasm with limb (isolated or generalized), myocardial, and cerebral ischemia progressing to gangrene or infarction. Hypotension, bradycardia, and involuntary movements can also occur. Nitroprusside or nitroglycerine for severe vasospasm; prazosin (an α 1 blocker), captopril, nifedipine, and cyproheptadine (a serotonin receptor antagonist) for mild-to-moderate limb ischemia; dopamine receptor antagonists (antipsychotics) for hallucinations and movement disorders

Physiologic stimulation

(Table 470-2); pronounced gastrointestinal symptoms and β agonist effects (see above). Toxicity occurs at lower drug levels in chronic poisoning than in acute poisoning. Propranolol, a nonselective β blocker, or esmolol for tachycardia with hypotension; any β blocker for

supraventricular or ventricular tachycardia without hypotension; elimination enhanced by multipledose charcoal, hemoperfusion, and hemodialysis. Indications for hemoperfusion or hemodialysis include unstable vital signs, seizures, and a theophylline level of 80–100 µg/mL after an acute overdose and 40–60 µg/mL with chronic exposure. Delayed or slowly progressive physiologic stimulation (Table 470-2); terminal hypotension and bradycardia in severe cases Short-acting agents (e.g., nitroprusside, esmolol) for severe hypertension and tachycardia; direct-acting sympathomimetics (e.g., norepinephrine, epinephrine) for hypotension and bradycardia (Continued)

TABLE 470-4 Pathophysiologic Features and Treatment of Specific Toxic Syndromes and Poisonings
PHYSIOLOGIC

CONDITION,	CAUSES	EXAMPLES	MECHANISM OF ACTION	CLINICAL FEATURES	SPECIFIC TREATMENTS
Anticholinergics	Antihistamines	Diphenhydramine, doxylamine, pyrilamine	Inhibition of central and postganglionic parasympathetic muscarinic cholinergic receptors. At high doses, amantadine, diphenhydramine, orphenadrine, phenothiazines, and tricyclic antidepressants have additional nonanticholinergic activity		

(see below).	Antipsychotics	Chlorpromazine, olanzapine, quetiapine, thioridazine	Inhibition of α-adrenergic, dopaminergic, histaminergic, muscarinic, and serotonergic receptors. Some agents also inhibit sodium, potassium, and calcium channels.		
Belladonna alkaloids	Atropine, hyoscyamine, scopolamine		Inhibition of central and postganglionic parasympathetic muscarinic cholinergic receptors		
Cyclic antidepressants	Amitriptyline, doxepin, imipramine		Inhibition of α-adrenergic, dopaminergic, GABA-ergic, histaminergic, muscarinic, and serotonergic receptors; inhibition of sodium channels (see membrane-active agents); inhibition of norepinephrine and serotonin reuptake		
Mushrooms and plants	Amanita muscaria and				

A. pantherina, henbane, jimson weed, nightshade			Inhibition of central and postganglionic parasympathetic muscarinic cholinergic receptors		
Depressed Sympatholytics	α2-Adrenergic agonists	Clonidine, guanabenz, tetrahydrozoline and other imidazoline decongestants, tizanidine and other imidazoline muscle relaxants	Stimulation of α2-adrenergic receptors leading to inhibition of CNS sympathetic outflow. Activity at nonadrenergic imidazoline binding sites also contributes to CNS effects.		
Antipsychotics	Chlorpromazine, clozapine, haloperidol, risperidone, thioridazine		Inhibition of α-adrenergic, dopaminergic, histaminergic, muscarinic, and serotonergic receptors. Some agents also inhibit sodium, potassium, and calcium channels.		

(Continued) Physiologic stimulation (Table 470-2); dry skin and mucous membranes, decreased bowel sounds, flushing, and urinary retention; myoclonus and picking activity. Central effects may occur without significant autonomic dysfunction. Physostigmine, an acetylcholinesterase inhibitor (see below), for delirium, hallucinations, and neuromuscular hyperactivity. Contraindications include asthma and nonanticholinergic cardiovascular toxicity (e.g., cardiac conduction abnormalities, hypotension, and ventricular arrhythmias). Physiologic depression

(Table 470-2), miosis, anticholinergic effects (see above), extrapyramidal reactions (see below), tachycardia Sodium bicarbonate for ventricular tachydysrhythmias associated with QRS prolongation; magnesium, isoproterenol, and overdrive pacing for torsades des pointes. Avoid class

IA, IC, and III antiarrhythmics. Physiologic stimulation (Table 470-2); dry skin and mucous membranes, decreased bowel sounds, flushing, and urinary retention; myoclonus and picking activity. Central effects may occur without significant autonomic dysfunction. Physostigmine, an acetylcholinesterase inhibitor (see below), for delirium, hallucinations, and neuromuscular hyperactivity. Contraindications include asthma and nonanticholinergic cardiovascular toxicity (e.g., cardiac conduction abnormalities, hypotension, and ventricular arrhythmias). CHAPTER 470 Poisoning and Drug Overdose Physiologic depression (Table 470-2), seizures, tachycardia, cardiac conduction delays (increased PR, QRS, JT, and QT intervals; terminal QRS right-axis deviation) with aberrancy and ventricular tachydysrhythmias; anticholinergic toxidrome (see above) Hypertonic sodium bicarbonate (or hypertonic saline) for ventricular tachydysrhythmias associated with QRS prolongation. Use of phenytoin is controversial. Avoid class IA, IC, and III antiarrhythmics. IV emulsion therapy may be beneficial in some cases. Physiologic stimulation

(Table 470-2); dry skin and mucous membranes, decreased bowel sounds, flushing, and urinary retention; myoclonus and picking activity. Central effects may occur without significant autonomic dysfunction. Physostigmine, an acetylcholinesterase inhibitor (see below), for delirium, hallucinations, and neuromuscular hyperactivity. Contraindications include asthma and nonanticholinergic cardiovascular toxicity (e.g., cardiac conduction abnormalities, hypotension, and ventricular arrhythmias). Physiologic depression (Table 470-2), miosis. Transient initial hypertension may be seen. Dopamine and norepinephrine for hypotension; atropine for symptomatic bradycardia; naloxone for CNS depression (inconsistently effective) Physiologic depression (Table 470-2), miosis, anticholinergic effects (see above), extrapyramidal reactions (see below), tachycardia. Cardiac conduction delays (increased PR, QRS, JT, and QT intervals) with ventricular tachydysrhythmias, including torsades des pointes, can sometimes develop. Sodium bicarbonate for ventricular tachydysrhythmias associated with QRS prolongation; magnesium, isoproterenol, and overdrive pacing for torsades des pointes. Avoid class IA, IC, and III antiarrhythmics. (Continued)

TABLE 470-4 Pathophysiologic Features and Treatment of Specific Toxic Syndromes and Poisonings
PHYSIOLOGIC

CONDITION	CAUSES	EXAMPLES	MECHANISM OF ACTION	CLINICAL FEATURES	SPECIFIC TREATMENTS
β-Adrenergic blockers	Cardioselective (β ₁) blockers:	atenolol, esmolol, metoprolol	Inhibition of β-adrenergic receptors (class II antiarrhythmic effect). Some agents have activity at additional receptors or have membrane effects (see below). Calcium channel blockers (class IV antiarrhythmic effect)	Tachycardia, hypertension, bronchospasm, heart failure, peripheral vascular disease	Discontinue β-blockers if possible. If not possible, give atropine for bradycardia. Calcium channel blockers for hypertension and heart failure. Vasodilators for peripheral vascular disease.
	Nonselective (β ₁ and β ₂) blockers:	nadolol, propranolol, timolol			
Partial β agonists	α ₁ Antagonists:	carvedilol, labetalol	Inhibition of α ₁ -adrenergic receptors	Hypotension, bradycardia, heart failure, peripheral vascular disease	Discontinue partial β agonists if possible. If not possible, give atropine for bradycardia. Vasodilators for hypertension and heart failure. Vasodilators for peripheral vascular disease.
	Membrane-active agents:	acebutolol, propranolol, sotalol			
Inhibition of β-adrenergic receptors (class II antiarrhythmic effect)	Some agents have activity at additional receptors or have membrane effects (see below).	Calcium channel blockers (class IV antiarrhythmic effect)	Inhibition of slow (type L) calcium channels	Tachycardia, hypertension, heart failure, peripheral vascular disease	Discontinue β-blockers if possible. If not possible, give atropine for bradycardia. Calcium channel blockers for hypertension and heart failure. Vasodilators for peripheral vascular disease.
	cardiovascular calcium channels (class IV antiarrhythmic effect) blockers				
PART 14 Poisoning, Drug Overdose, and Envenomation	Cardiac glycosides	Digoxin, endogenous cardioactive steroids, foxglove and other plants, toad skin secretions (Bufonidae spp.)	Inhibition of cardiac Na ⁺ , K ⁺ -ATPase membrane pump	Tachycardia, hypertension, heart failure, peripheral vascular disease	Discontinue cardiac glycosides if possible. If not possible, give digoxin-specific antibody (Digoxin Immune Fab) for digoxin poisoning.
	Cyclic antidepressants	Amitriptyline, doxepin, imipramine			
Inhibition of α-adrenergic, dopaminergic, GABA-ergic, histaminergic, muscarinic, and serotonergic receptors;	inhibition of sodium channels (see membrane-active agents);	inhibition of norepinephrine and serotonin reuptake	Inhibition of α-adrenergic, dopaminergic, GABA-ergic, histaminergic, muscarinic, and serotonergic receptors; inhibition of sodium channels (see membrane-active agents); inhibition of norepinephrine and serotonin reuptake	Tachycardia, hypertension, heart failure, peripheral vascular disease	Discontinue cyclic antidepressants if possible. If not possible, give physostigmine for delirium and hallucinations. Vasodilators for hypertension and heart failure. Vasodilators for peripheral vascular disease.
	Cholinergics	Acetylcholinesterase Carbamate insecticides (aldicarb, carbaryl,			

propoxur) and medicinals (neostigmine, physostigmine, tacrine); nerve gases (sarin, soman, tabun, VX); organophosphate insecticides (diazinon, chlorpyrifos-ethyl, malathion) Bethanechol, mushrooms (*Boletus*, *Clitocybe*, *Inocybe* spp.), pilocarpine Lobeline, nicotine (tobacco) Inhibition of acetylcholinesterase leading to increased synaptic acetylcholine at muscarinic and nicotinic cholinergic receptor sites Stimulation of CNS and postganglionic parasympathetic cholinergic (muscarinic) receptors Stimulation of preganglionic sympathetic and parasympathetic and striated muscle (neuromuscular junction) cholinergic (nicotine) receptors inhibitors Muscarinic agonists Nicotinic agonists

(Continued) Physiologic depression

(Table 470-2), atrioventricular block, hypoglycemia, hyperkalemia, seizures. Partial agonists can cause hypertension and tachycardia. Sotalol can cause increased QT interval and ventricular tachydysrhythmias. Onset may be delayed after sotalol and sustained-release formulation overdose. Glucagon for hypotension and symptomatic bradycardia. Atropine, isoproterenol, dopamine, dobutamine, epinephrine, and norepinephrine may sometimes be effective. High-dose insulin (with glucose and potassium to maintain euglycemia and normokalemia), electrical pacing, and mechanical cardiovascular support for refractory cases. Physiologic depression

(Table 470-2), atrioventricular block, organ ischemia and infarction, hyperglycemia, seizures. Hypotension is usually due to decreased vascular resistance rather than to decreased cardiac output. Onset may be delayed for ≥ 12 h after overdose of sustained-release formulations. Calcium and glucagon for hypotension and symptomatic bradycardia. Dopamine, epinephrine, norepinephrine, atropine, and isoproterenol are less often effective but can be used adjunctively. High-dose insulin (with glucose and potassium to maintain euglycemia and normokalemia), IV lipid emulsion therapy, electrical pacing, and mechanical cardiovascular support for refractory cases. Physiologic depression (Table 470-2); gastrointestinal, psychiatric, and visual symptoms; atrioventricular block with or without concomitant supraventricular tachyarrhythmia; ventricular tachyarrhythmias; hyperkalemia in acute poisoning. Toxicity occurs at lower drug levels in chronic poisoning than in acute poisoning. Digoxin-specific antibody fragments for hemodynamically compromising dysrhythmias, Mobitz II or third-degree atrioventricular block, hyperkalemia (>5.5 meq/L; in acute poisoning only). Temporizing measures include atropine, dopamine, epinephrine, and external cardiac pacing for bradydysrhythmias and magnesium, lidocaine, or phenytoin, for ventricular tachydysrhythmias. Internal cardiac pacing and cardioversion can increase ventricular irritability and should be reserved for refractory cases. Physiologic depression

(Table 470-2), seizures, tachycardia, cardiac conduction delays (increased PR, QRS, JT, and QT intervals; terminal QRS rightaxis deviation) with aberrancy and ventricular tachydysrhythmias; anticholinergic toxidrome (see above) Hypertonic sodium bicarbonate

(or hypertonic saline) for ventricular tachydysrhythmias associated with QRS prolongation. Use of phenytoin is controversial. Avoid class IA, IC, and III antiarrhythmics. IV emulsion therapy may be beneficial in some cases. Physiologic depression (Table 470-2). Muscarinic signs and symptoms: seizures, excessive secretions (lacrimation, salivation, bronchorrhea and wheezing, diaphoresis), and increased bowel and bladder activity with nausea, vomiting, diarrhea, abdominal cramps, and incontinence of feces and urine. Nicotinic signs and symptoms: hypertension, tachycardia, muscle

above and below for treatment of anticholinergic and sodium channel (membrane)- blocking effects. CHAPTER 470 Poisoning and Drug Overdose Physiologic depression

(Table 470-2) Goal-directed supportive care Physiologic depression

(Table 470-2) Goal-directed supportive care; benzodiazepines and barbiturates for seizures Signs and symptoms of hypoxemia with initial physiologic stimulation and subsequent depression (Table 470-2); lactic acidosis; normal PO₂ and calculated oxygen saturation but decreased oxygen saturation by co-oximetry. (That measured by pulse oximetry is falsely elevated but is less than normal and less than the calculated value.) Headache and nausea are common with carbon monoxide. Sudden collapse may occur with cyanide and hydrogen sulfide exposure. A bitter almond breath odor may be noted with cyanide ingestion, and hydrogen sulfide smells like rotten eggs. High-dose oxygen; IV hydroxocobalamin or IV sodium nitrite and sodium thiosulfate (Lilly cyanide antidote kit) for coma, metabolic acidosis, and cardiovascular dysfunction in cyanide poisoning or victims from a fire; ECMO (Continued)

TABLE 470-4 Pathophysiologic Features and Treatment of Specific Toxic Syndromes and Poisonings PHYSIOLOGIC

CONDITION,	CAUSES	EXAMPLES	MECHANISM OF ACTION	CLINICAL FEATURES	SPECIFIC TREATMENTS
Methemoglobin	Aniline derivatives, dapsone, local anesthetics, nitrates, nitrites, nitrogen oxides, nitro- and nitrosohydrocarbons, phenazopyridine, primaquine type antimalarials, sulfonamides	Oxidation of hemoglobin iron from ferrous (Fe ²⁺) to ferric (Fe ³⁺) state prevents oxygen binding, transport, and tissue uptake. (Methemoglobinemia shifts oxygen dissociation curve to the left.) Oxidation of hemoglobin protein causes hemoglobin precipitation and hemolytic anemia (manifesting as Heinz bodies and “bite cells” on peripheral-blood smear).	inducers AGMA		
Ethylene glycol	Ethylene glycol	Ethylene glycol causes CNS depression and increased serum osmolality. Metabolites (primarily glycolic acid) cause AGMA, CNS depression, and renal failure. Precipitation of oxalic acid metabolite as calcium salt in tissues and urine results in hypocalcemia, tissue edema, and crystalluria.			
Iron	Hydration of ferric (Fe ³⁺) ion generates H ⁺ . Non-transferrinbound iron catalyzes formation of free radicals that cause mitochondrial injury, lipid peroxidation, increased capillary permeability, vasodilation, and organ toxicity.				
Methanol	Methanol	Methanol causes ethanol-like CNS depression and increased serum osmolality. Formic acid metabolite causes AGMA and retinal toxicity.			
Salicylate	Increased sensitivity of CNS respiratory center to changes in and stimulates respiration. Uncoupling of oxidative phosphorylation, inhibition of Krebs cycle enzymes, and stimulation of carbohydrate and lipid metabolism generate unmeasured endogenous anions and cause AGMA.				

(Continued) Signs and symptoms of hypoxemia with initial physiologic stimulation and subsequent depression (Table 470-2), graybrown cyanosis unresponsive to oxygen at methemoglobin fractions >15–20%, headache, lactic acidosis (at methemoglobin fractions >45%), normal PO₂ and calculated oxygen saturation but decreased oxygen saturation and increased methemoglobin fraction by co-oximetry. (Oxygen saturation by pulse oximetry may be falsely increased or decreased but is less than normal and less than the calculated value.) High-dose oxygen; IV methylene blue for methemoglobin fraction

30%, symptomatic hypoxemia, or ischemia (contraindicated in G6PD deficiency); exchange transfusion and hyperbaric oxygen for severe or refractory cases Initial ethanol-like intoxication, nausea, vomiting, increased osmolar gap, calcium oxalate crystalluria; delayed AGMA, back pain, renal failure; coma, seizures, hypotension, ARDS in severe cases Sodium bicarbonate to correct acidemia; thiamine, folinic acid, magnesium, and high-dose pyridoxine to facilitate metabolism; ethanol or fomepizole for AGMA, crystalluria or renal dysfunction, ethylene glycol level >3 mmol/L (20 mg/dL), and ethanol-like intoxication or increased osmolal gap if level not readily obtainable; hemodialysis for persistent AGMA, lack of clinical improvement, and renal dysfunction; hemodialysis also useful for enhancing ethylene glycol elimination and shortening duration of treatment when ethylene glycol level is >8 mmol/L (50 mg/dL). Initial nausea, vomiting, abdominal pain, diarrhea; AGMA, cardiovascular and CNS depression, hepatitis, coagulopathy, and seizures in severe cases. Radiopaque iron tablets may be seen on abdominal x-ray. Whole-bowel irrigation for large ingestions; endoscopy and gastrostomy if clinical toxicity and large number of tablets are still visible on x-ray; IV hydration; sodium bicarbonate for acidemia; IV deferoxamine for systemic toxicity, iron level >90 μ mol/L

(500 μ g/dL) Initial ethanol-like intoxication, nausea, vomiting, increased osmolar gap; delayed AGMA, visual (clouding, spots, blindness) and retinal (edema, hyperemia) abnormalities; coma, seizures, cardiovascular depression in severe cases; possible pancreatitis Gastric aspiration for recent ingestion; sodium bicarbonate to correct acidemia; high-dose folinic acid or folate to facilitate metabolism; ethanol or fomepizole for AGMA, visual symptoms, methanol level >6 mmol/L (20 mg/dL), and ethanol-like intoxication or increased osmolal gap if level not readily obtainable; hemodialysis for persistent AGMA, lack of clinical improvement, and renal dysfunction; hemodialysis also useful for enhancing methanol elimination and shortening duration of treatment when methanol level is >15 mmol/L (50 mg/dL) Initial nausea, vomiting, hyperventilation, alkalemia, alkaluria; subsequent alkalemia with both respiratory alkalosis and AGMA and paradoxical aciduria; late acidemia with CNS and respiratory depression; cerebral and pulmonary edema in severe cases. Hypoglycemia, hypocalcemia, hypokalemia, and seizures can occur. IV hydration and supplemental glucose; sodium bicarbonate to correct acidemia; urinary alkalization for systemic toxicity; hemodialysis for coma, cerebral edema, seizures, pulmonary edema, renal failure, progressive acid-base disturbances or clinical toxicity, salicylate level >7 mmol/L (100 mg/dL) following acute overdose (Continued)

TABLE 470-4 Pathophysiologic Features and Treatment of Specific Toxic Syndromes and Poisonings
PHYSIOLOGIC

CONDITION	CAUSES	EXAMPLES	MECHANISM OF ACTION	CLINICAL FEATURES	SPECIFIC TREATMENTS
CNS syndromes	Extrapyr	Antipsychotics	(see above), some cyclic antidepressants and antihistamines	Decreased CNS dopaminergic activity with relative excess of cholinergic activity	reactions
Isoniazid	Interference with activation and supply of pyridoxal-5phosphate, a cofactor for glutamic acid decarboxylase, which converts glutamic acid to GABA,				

results in decreased levels of this inhibitory CNS neurotransmitter; complexation with and depletion of pyridoxine itself; inhibition of nicotine adenine dinucleotide-dependent lactate and hydroxybutyrate dehydrogenases, resulting in substrate accumulation. Lithium Interference with cell membrane ion transport, adenylate cyclase and Na⁺, K⁺-ATPase activity, and neurotransmitter release. Serotonin syndrome. Amphetamines, cocaine, dextromethorphan, meperidine, MAO inhibitors, selective serotonin (5-HT) reuptake inhibitors, tricyclic antidepressants, tramadol, triptans, tryptophan. Promotion of serotonin release, inhibition of serotonin reuptake, or direct stimulation of CNS and peripheral serotonin receptors (primarily 5-HT-1a and 5-HT-2), alone or in combination. Membrane-active. Amantadine, antiarrhythmics (class I and III agents; some β blockers), antipsychotics (see above), antihistamines (particularly diphenhydramine), carbamazepine, local anesthetics (including cocaine), opioids (meperidine, propoxyphene), orphenadrine, quinoline antimalarials (chloroquine, hydroxychloroquine, quinine), cyclic antidepressants (see above). Blockade of fast sodium membrane channels prolongs phase 0 (depolarization) of the cardiac action potential, which prolongs QRS duration and promotes reentrant (monomorphic) ventricular tachycardia. Class Ia, Ic, and III antiarrhythmics also block potassium channels during phases 2 and 3 (repolarization) of the action potential, prolonging the JT interval and promoting early afterdepolarizations and polymorphic (torsades des pointes) ventricular tachycardia. Similar effects on neuronal membrane channels cause CNS dysfunction. Some agents also block α -adrenergic and cholinergic receptors or have opioid effects (see above and Chap. 467). agent aSee above and Chap. 468. bSee above and Chap. 467. Abbreviations: AGMA, anion-gap metabolic acidosis; ARDS, adult respiratory distress syndrome; CNS, central nervous system; ECMO, extracorporeal membrane oxygenation; GABA, γ -aminobutyric acid; GBL, γ -butyrolactone; GHB, γ -hydroxybutyrate; G6PD, glucose-6-phosphate dehydrogenase; MAO, monoamine oxidase; NDMA, N-methyl-D-aspartate; 2-PAM, pralidoxime; SIADH, syndrome of inappropriate antidiuretic hormone secretion.

(Continued) Akathisia, dystonia, parkinsonism. Oral or parenteral anticholinergic agent such as benztropine or diphenhydramine. Nausea, vomiting, agitation, confusion; coma, respiratory depression, seizures, lactic and ketoacidosis in severe cases. High-dose IV pyridoxine (vitamin B6) for agitation, confusion, coma, and seizures; diazepam or barbiturates for seizures. Nausea, vomiting, diarrhea, ataxia, choreoathetosis, encephalopathy, hyperreflexia, myoclonus, nystagmus, nephrogenic diabetes insipidus, falsely elevated serum chloride with low anion gap, tachycardia; coma, seizures, arrhythmias, hyperthermia, and prolonged or permanent encephalopathy and movement disorders in severe cases; delayed onset after acute overdose, particularly with delayed-release formulations. Toxicity occurs at lower drug levels in chronic poisoning than in acute poisoning. Whole-bowel irrigation for large ingestions; IV hydration; hemodialysis for coma, seizures, encephalopathy or neuromuscular dysfunction (severe, progressive, or persistent), peak lithium level

“ 4 meq/L following acute overdose CHAPTER 470 Poisoning and Drug Overdose
Altered mental status (agitation, confusion, mutism, coma, seizures), neuromuscular hyperactivity (hyperreflexia, myoclonus, rigidity, tremors), and autonomic dysfunction (abdominal pain, diarrhea, diaphoresis, fever, flushing, labile hypertension, mydriasis, tearing, salivation, tachycardia). Complications include hyperthermia, lactic acidosis, rhabdomyolysis, and multisystem organ

failure. Discontinue the offending agent(s); benzodiazepines for agitation or signs of stimulation; the serotonin receptor antagonist cyproheptadine may be helpful in severe cases. QRS and JT prolongation (or both) with hypotension, ventricular tachyarrhythmias, CNS depression, seizures; anticholinergic effects with amantadine, antihistamines, carbamazepine, disopyramide, antipsychotics, and cyclic antidepressants (see above); opioid effects with meperidine and propoxyphene (see Chap. 467); cinchonism (hearing loss, tinnitus, nausea, vomiting, vertigo, ataxia, headache, flushing, diaphoresis), and blindness with quinoline antimalarials Hypertonic sodium bicarbonate (or hypertonic saline) for cardiac conduction delays and monomorphic ventricular tachycardia; lidocaine for monomorphic ventricular tachycardia (except when due to class Ib antiarrhythmics); magnesium, isoproterenol, and overdrive pacing for polymorphic ventricular tachycardia; physostigmine for anticholinergic effects (see above); naloxone for opioid effects (see Chap. 467); extracorporeal removal for some agents (see text).

Revision #1

Created 2026-01-06 16:36:01 UTC by Omar Ayman

Updated 2026-01-06 16:36:01 UTC by Omar Ayman