Toxicology Overview

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LEARNING OBJECTIVES

- 1. Analyze the role of poison control centers in providing assistance in poisoning cases.
- 2. Evaluate commonly available xenobiotics and household chemicals that are harmful to children in a single dose.
- 3. Apply knowledge of toxidromes in designing a treatment plan for the acutely poisoned patient.
- 4. Apply knowledge of risk-benefit in evaluating the use of GI decontamination in acutely poisoned patients.
- 5. Justify the role of qualitative versus quantitative toxicology testing in the treatment of acutely poisoned patients.

ABBREVIATIONS IN THIS CHAPTER

NPDSNational Poison Data SystemPCPoison control centerWBIWhole bowel irrigation

Table of other common abbreviations.

INTRODUCTION

Poisoning is the leading cause of unintentional deaths in the United States (Rudd 2016; CDC 2012). This is not unique to the United States, and various reports note that unintentional poisoning deaths are a global health concern. Since 2000, more than 300,000 people in the United States have died of opioid overdose, many because of unintentional poisoning (Rudd 2016).

Unintentional poisoning resulting in injury in pediatric patients is not a new phenomenon (Franklin 2008). In fact, the first poison control center (PC) was created in the United States in 1953 after the Committee on Accident Prevention formed by the American Academy of Pediatrics identified that unintentional poisonings were a significant cause of pediatric poisonings. Before its existence, reliable information was lacking on active ingredients in household products, and information was minimal about managing such exposures. Since the first PC was created, several changes and advances have been made, including the addition of highly trained, certified health professionals and extensive information available to both the public and health care communities.

The reach of PCs goes far beyond an information center. Poison control centers not only interpret and provide clinical treatment recommendations for treating poisoned patients, but are also integral in collecting epidemiological data on the incidence and severity of poisonings, linking epidemiologic data as part of public health surveillance, reducing health care costs to prevent unnecessary hospitalizations through improving patient care, and providing education to members of the health care community. Poison control centers provide their services 24 hours a day, 7 days a week, free of charge to the public, partly because of federal funding through the Health Resources and Services Administration PC stabilization grant. In 2006, the National Poison Data System (NPDS) was created, which now serves as the single, central repository for all of the U.S. PCs.

The NPDS is the only system of its kind that can routinely monitor real-time surveillance. Poison control centers upload their data to NPDS in real time, which enables real-time national toxicosurveillance. A case is uploaded to the NPDS on average within 7.82 minutes (Mowry 2015). The NPDS data are evaluated twice daily using three different methodologies: call volume, clinical effect volume, and case-based definitions. This allows for rapid detection, analysis, and reporting of NPDS surveillance anomalies from a local, regional, and/or national perspective.

One of the goals of the NPDS is to identify early markers of chemical, environmental, drug, foodborne, biological, and radiological events in order to provide an effective and rapid public health response. This data system is monitored continuously by a national toxicosurveillance team and toxicologists from the CDC, which allows for rapid detection of potential public health concerns/threats. In 2014, 3.5 million exposure calls were made to PCs, with pediatric exposure calls responsible for greater than 1.3 million (Mowry 2015). Poison control center calls largely underrepresent the true incidence of poisonings because many exposures and deaths are not reported to PCs. Specific reasons for underreporting have not been identified; however, they may involve lack of awareness of PCs' free service, increased Internet use for management advice, misunderstanding of potential for legal ramifications, or simply lack of desire to use telephone conversation as a communication source. As technology advances, implementing communication with PCs by online chatting as well as text messaging is being investigated and likely will become a routine part of PC operations.

A large proportion of calls to PCs are the result of unintentional pediatric exposures. About 75% of these exposures can safely be managed on-site and not in health care

BASELINE KNOWLEDGE STATEMENTS

Readers of this chapter are presumed to be familiar with the following:

 General knowledge of the approach to the poisoned patient

Table of common laboratory reference values.

ADDITIONAL READINGS

The following resources have additional background information on this topic:

- Goldfranks' Toxicologic Emergencies 10th edition
- Erickson TB et al. <u>The Approach to the Patient with</u> <u>an Unknown Overdose</u>. Emerg Med Clin N Am 2007;25:249-81.
- Abruzzi G et al. <u>Pediatric Toxicologic Concerns.</u> Emerg Med Clin N Am. 2002;20:223-47.

facilities. In one study, almost 95% of parents who brought their child to an ED for acute poisoning had not contacted the PC before arrival, and more than 60% of those children did not require health care intervention. In a survey of 589 callers to a single PC, 79% of callers said they would have used the emergency care system had the PC not been available, and more than 80% of caregivers said they would bring their child to a health care facility if PCs were not available (Kearney 1995). The financial impact of PCs remains unclear; however, a single study estimated that the return on investment in PC exposure calls in rural areas is \$5.90 per \$1.00 spent (Zaloshnja 2006). These are just a few examples of the health and financial value of PCs.

Many efforts have been aimed at reducing pediatric poisonings. Examples include poison education outreach and poison programs focusing on teaching primary and secondary prevention techniques, creation of a single toll-free number (1-800-222-1222) for all U.S. PCs, and the 1970 Poison Prevention Packaging Act, which significantly reduced pediatric fatalities after child-resistant packaging was enforced (Franklin 2008; Rodgers 1996). Despite such efforts, however, pediatric poisonings continue to occur, and it is imperative that health care providers identify an acutely intoxicated patient as well as the common xenobiotics that result in significant morbidity and mortality, especially those that do so after one or two doses, which is the most common scenario in pediatric poisonings.

We will not discuss these specific toxins in detail; however, we will provide a general overview of the approach to

Box 1-1. Drugs and Drug Classes That Are Toxic in Small Amounts

- Antidysrhythmics
- Benzonatate
- β-Blockers
- Bupropion
- Calcium channel blockers
- Camphor
- Clonidine
- Concentrated THC edible products
- Ethanol
- Ethylene glycol
- Guanfacine
- Laundry pods
- Liquid nicotine
- Lomotil (diphenoxylate/atropine)
- Methanol
- Methyl salicylate
- Opioids
- Oxymetazoline/naphazoline
- Powdered caffeine
- Sulfonylureas
- Synthetic cannabinoids
- Tricyclic antidepressants

THC = tetrahydrocannabinol.

Box 1-2. Substances Resulting in Pediatric (\le 5 yr) Fatalities in 2014

- Fumes/gases/vapors (n = 10)
- Analgesics (n = 7)
- Household cleaning substances (n = 7)
- Alcohols (n = 3)
- Antihistamines (n = 2)
- Cardiovascular drugs (n = 2)
- Sedatives/hypnotics/antipsychotics (n = 2)
- Cough and cold preparations (n = 1)
- Stimulants and street drugs (n = 1)
- Liquid nicotine (Eggleston 2016) (n = 1)
- Total No. of Pediatric Fatalities = 50

Information from: Mowry JB, Spyker DA, Brooks DE, et al. 2014 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 32nd Annual Report. Clin Toxicol (Phila) 2015;53:962-1147; Eggleston W, Nacca N, Stork CM, et al. Pediatric death after unintentional exposure to liquid nicotine for an electronic cigarette. Clin Toxicol (Phila) 2016;54:890-1.

Box 1-3. Substance Categories Most Often Involved in Pediatric (≤ 5 yr) Exposures in 2014

- Cosmetics/personal care products (n = 150,530)
- Household cleaning substances (n = 118,207)
- Analgesics (n = 100,399)
- Foreign body/toys (n = 72,099)
- Topical preparations (n = 62,053)
- Vitamins (n = 48,214)
- Antihistamines (n = 45,915)
- Cough and cold preparations (n = 23,830)
- Cardiovascular drugs (n = 22,059)
- Alcohols (n = 11,088)
- Antidepressants (n = 10,897)
- Tobacco/nicotine/e-cigarette products (n = 10,571)
- Hydrocarbons (n = 9546)

Information from: Mowry JB, Spyker DA, Brooks DE, et al. 2014 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 32nd Annual Report. Clin Toxicol (Phila) 2015;53:962-1147.

the acutely poisoned patient and identify common pediatric exposures that can be life threatening (Abbruzzi 2002). Box 1-1 lists drugs and drug classes that are dangerous in small amounts. Box 1-2 lists fatalities in single-agent ingestion in children 5 years and younger reported by PCs. Box 1-3 includes the most commonly reported substances involved in pediatric poisonings.

GENERAL APPROACH TO THE POISONED PATIENT

The initial approach for the acutely poisoned patient is identical to that for any patient presenting for emergency care. The phenomenon of treating the patient rather than the poison has changed the overall approach and resulted in improved outcomes. Antidotes may play a critical role in managing some exposures; however, except for a few antidotes (e.g., cyanide antidotes, naloxone, acetylcysteine), high-quality supportive care is more essential. Adults and adolescents presenting for health care after an acute overdose often have an unreliable or unobtainable history, combined with several xenobiotics ingested. Pediatric exposures are quite different. Their exposure history, as well as time of ingestion, is usually well known, and usually, only one or two toxins have been ingested.

Rapid assessment and intervention to address immediately life-threatening conditions, including airway compromise, breathing difficulties, and circulation problems (ABCs), are critical. Assessing the mental status is crucial and can provide additional insight into the substance ingested. In comatose patients, airway patency and respiratory effort should be assessed immediately. Respiratory status can be assessed in several ways, including respiratory rate, depth of respirations, pulse oximetry, capnography, and blood gas measurement. In a comatose patient with respiratory depression, bag-valve mask ventilation should be initiated. Naloxone, an opioid antagonist, should be considered at this time if the patient ingested opioids or if the ingested substance is unknown. Naloxone may reverse the clinical effects of clonidine/imidazoline poisoning and should be given in symptomatic patients (Seger 2002). If naloxone is not indicated or is ineffective, endotracheal intubation may be indicated. Once the respiratory status is corrected, circulation should be assessed, including pulse (rate, strength, regularity, and presence/ absence of peripheral pulses) and blood pressure. A pointof-care glucose should be obtained immediately and hypoglycemia treated, if necessary. Pediatric patients are at particular risk of developing hypoglycemia because of their decreased glycogen stores. Even a small dose of ethanol or a single tablet of a sulfonylurea can cause hypoglycemia in children. Salicylates cause central neuroglycopenia, and in a known aspirin poisoning case, glucose should be administered for an altered mental status, regardless of the fingerstick glucose.

In patients with an altered mental status, these interventions should be considered and administered within the first 3-5 minutes: (1) high-flow oxygen (to treat hypoxia); (2) 0.5-1 g/kg of D₁₀W or D₂₅W (D₅₀W in an adult) as an intravenous bolus; and (3) naloxone 0.01 mg/kg intravenously for opioid-induced respiratory depression or suspected clonidine toxicity. Doses of up to 0.1 mg/kg intravenously can be given if the previous dose was ineffective. Dextrose administration should only be omitted if hypoglycemia is excluded rapidly with a measurement of fingerstick glucose. If the etiology is unknown, naloxone should be administered for patients with an altered mental status and respiratory depression. A 12-lead ECG should be obtained once the ABCs are assessed and stabilized. Many xenobiotics cause changes in the ECG from different mechanisms, including hypoxia, electrolyte disturbances, and direct effect on the cardiac conduction system. The ECG will alert the provider to potentially life-threatening arrhythmias that are related to the exposure either directly or indirectly secondary to hypoxia, electrolyte disturbances, or even extremes of temperature. For example, ECG provides invaluable insight in the setting of wide QRS complex duration and right axis deviation, which is suggestive of tricyclic antidepressant poisoning or other xenobiotics known to cause sodium channel blockade (Boehnert 1985). Rapidly identifying and administering specific treatments (e.g., sodium bicarbonate), as well as avoiding certain medications, may decrease morbidity.

Core temperature should be addressed early. Several xenobiotics produce hyperthermia, and severe hyperthermia (temperature higher than 41°C [105.8°F]) requires correction within 30 minutes to prevent irreversible cell damage. Hypothermia is not without significant risk, and identification is essential because the pharmacokinetics of drugs may be significantly altered in a hypothermic state.

Vital signs and physical examination findings provide valuable clues and insight into the toxicologic etiology. Toxidromes are a constellation of signs and symptoms that point to a specific group of toxins according to their pharmacologic effect (Mofenson 1985). Toxidromes provide consistency in a known overdose and invaluable insight into creating a differential diagnosis in an unknown overdose. Various references describe several toxidromes; some of the most well-established include opioids, sedative-hypnotics, sympathomimetic/ adrenergic agonists, salicylates, cholinergics, and anticholinergics. Physical examination findings that provide the most valuable information include vital signs, mental status, pupil size, bowel sounds, and skin and mucous membrane findings. Table 1-1 summarizes common toxidromes.

As mentioned earlier, pediatric patients are often easier to evaluate because they usually have single-product exposures. Countless toxins result in an altered heart rate, blood pressure, respiratory rate, and temperature. Discussion of specific toxins is beyond the scope of this chapter.

Once the initial stabilization has occurred, further workup with specific laboratory testing as well as consideration of the potential usefulness of GI decontamination or antidote administration should occur. We will discuss specific laboratory assessments later in this chapter.

Table 1-2 lists several antidotes with initial pediatric dosing considerations and the scenarios in which to consider

Group	Specific Drugs or Toxins	Mental Status	Pupils	BP	HR	RR	Temp	Bowel Sounds	Other
Adrenergic agonists	Cocaine; amphetamines	Hyperalert; agitated	Mydriatic	\uparrow	\uparrow	↑	¢	Hyperactive	Tremor; seizures; diaphoresis
Anticholinergics	TCAs; antihistamines	Agitation; delirium	Mydriatic	1	¢	↑	Ŷ	Hypoactive	Dry mucous membranes; urinary retention; flushed skin
Opioids ^a	Morphine; hydrocodone	Depressed	Miotic	\downarrow	\downarrow	\downarrow	\downarrow	Hypoactive	Hyporeflexia
Sedative- hypnotics⁵	Benzodiazepines; ethanol; barbiturates	Depressed	±	\downarrow	\downarrow	\downarrow	\downarrow	±	Hyporeflexia; ataxia; nystagmus
Cholinergics	Organic phosphorus compounds; carbamates	Normal to depressed	Miotic	\downarrow	\downarrow	±	±	Hyperactive	Bronchorrhea; salivation; urination; weakness; fasciculations
Salicylates	Aspirin; methyl salicylate	Normal to agitated	Normal	±	\uparrow	↑	Ŷ	Normal	Hyperpnea; tinnitus; diaphoresis

^aMild reduction in vital signs after oral ingestion.

^bBenzodiazepines alone after oral ingestion often result in minimal, if any, change in vital signs.

BP = blood pressure; HR = heart rate; RR = respiratory rate; TCA = tricyclic antidepressant.

Table 1-2. Common Antidotes for Treatments of Poisoning

Antidote	Indications	Common Adverse Events/Risks of Administration	Pediatric Dosing
Atropine	Cholinesterase inhibitors; bradydysrhythmias	Mydriasis; elevated heart rate	Cholinesterase inhibitors: 20 mcg/kg up to 2 mg IV dose; doubled every 5 min until resolution of bronchorrhea
Calcium gluconate	β-Blocker; calcium channel blocker; fluoride; hydrofluoric acid	Hypercalcemia; irritating to the vein	60 mg/kg of 10% solution given over 5–10 min; can repeat in 10–20 min up to three or four doses
I-Carnitine	Valproate-induced hyperammonemia	Transient nausea and vomiting	100 mg/kg IV (up to 6 g) loading dose, followed by 15 mg/kg IV every 4 hr
Deferoxamine	Iron poisoning	Anaphylactoid reactions; acute lung injury	IV continuous infusion initiated at 5 mg/kg/hr and titrated to 15 mg/kg/hr (total daily dose of 6–8 g)
Digoxin-specific FAB fragments	Cardiac glycoside poisoning; digoxin	Well tolerated; rare allergic reactions	Empiric dosing = 10 vials IV over 30 min (can push if cardiac arrest; can repeat if necessary)
Fatty acid emulsion	Local anesthetic cardiovascular collapse; refractory cardiovascular collapse from toxins	Pulmonary toxicity; pancreatitis; laboratory interferences	20% solution: 1.5 mL/kg (up to 100 mL) IV bolus
Flumazenil	Benzodiazepine (when dependence excluded); paradoxical reaction to benzodiazepine administration	Acute withdrawal if given to tolerant patients	0.01 mg/kg IV over 1 min (would not repeat unless direct consultation with toxicologist or PC)
Fomepizole	Ethylene glycol; methanol	Well tolerated; local irritation	15 mg/kg IV over 30 min, followed by 10 mg/kg IV every 12 hr x four doses; then 15 mg/kg every 12 hr until ethylene glycol or methanol concentrations < 20 mg/dL
Glucagon	β-Blocker; calcium channel blocker poisoning	Nausea and vomiting	0.05 mg/kg IV over 1–2 min; can be repeated in 10 min; if effective, continuous infusion of 0.05-0.1 mg/kg/hr can be initiated (would start infusion at the effective dose)
Hydroxocobalamin	Cyanide poisoning	Skin discoloration; hypertension; red urine; laboratory interferences	70 mg/kg IV (up to 5000 mg) over 7–15 min; can be repeated once at the same dose
Methylene blue	Methemoglobinemia	Hemolysis if underlying G6PD	1–2 mg/kg IV over 5 min; can be repeated if methemoglobin recurs
Naloxone	Opioid toxicity; clonidine; guanfacine (and other imidazolines)	Well tolerated unless opioid tolerant	0.01 mg/kg IV up to 2 mg; for clonidine/ guanfacine: start with 2 mg and titrate until response to 10 mg (continuous infusion at two-thirds the effective dose in long-acting opioids or in imidazolines)
N-Acetylcysteine	Acetaminophen poisoning	Nausea and vomiting (after oral use); anaphylactoid reactions (after IV use)	Special IV dilution is required for children ^a Oral: 140 mg/kg orally; then 70 mg/kg every 4 hr IV: 150 mg/kg over 60 min; 50 mg/kg over 4 hr; 100 mg/kg over 16 hr

Antidote	Indications	Common Adverse Events/Risks of Administration	Pediatric Dosing
Octreotide	Sulfonylurea-induced hypoglycemia	Nausea; pain at injection site	1.25 mcg/kg (up to 50 mcg) SC every 6 hr
Physostigmine	Anticholinergic delirium	Avoid in TCA poisoning; bradycardia; increased secretions	0.02 mg/kg (up to 0.5 mg) over 5–10 min; can be repeated after 10 min; max dose 2 mg
Pralidoxime	Cholinesterase inhibition	Well tolerated at therapeutic doses	30 mg/kg (up to 2 g) Ⅳ over 15 min, followed by 10−20 mg/kg/hr (max 650 mg/hr)
Prothrombin complexes (factors II, VII, IX, and X)	Urgent reversal of acquired coagulation factor deficiency induced by vitamin K antagonists	Administer with vitamin K Repeat dosing has not been well studied, thus not routinely recommended	Dosed according to INR, INR 2–4: 25 units/kg (max 2500 units); INR 4–6: 35 units/kg (max 3500 units); INR > 6 50 units/kg (max 5000 units)
Pyridoxine	Isoniazid	Well tolerated at therapeutic doses	70 mg/kg (up to 5 g) IV infused at 0.5 mg/min; can repeat the dose x 1 if seizures do not stop
Vitamin K	Restoring vitamin K; warfarin toxicity; superwarfarin toxicity	IV administration has been associated with anaphylaxis; consider oral or SC routes as first option; avoid IM	Dosing and route according to clinical presentation (degree of bleeding) and INR value

aInformation is available at www.acetadote.com.

G6PD = glucose-6-phosphate dehydrogenase; IM = intramuscular(Iy); IV = intravenous(Iy); PC = poison control center; SC = subcutaneous(ly).

Information from: Marraffa JM, Cohen V, Howland MA. Antidotes for toxicological emergencies: a practical review. Am J Health Syst Pharm 2012:69:199-212.

administration. However, use of specific antidotes depends on specific patient situations, and recommendations change. Consultation with a regional PC at 1-800-222-1222 and/or a medical/clinical toxicologist is always recommended.

GI DECONTAMINATION

The concept behind GI decontamination is to prevent the absorption of ingested toxins. Gastrointestinal decontamination is a highly controversial topic in the field of toxicology; it should be considered in patients who ingest poisons with a high toxicity profile. However, because not all toxins have similar properties, not all are amenable to the same approach to GI decontamination. In fact, some toxins are not at all amenable to GI decontamination. Because of variable responses to these interventions, consultation with a medical or clinical toxicologist is recommended before carrying them out.

The role of GI decontamination has long been debated in the field of clinical toxicology. Controversy remains over which modality, if any, plays a role in improving the care of acutely poisoned patients. Consistent with the field of toxicology, few rigorous studies show the effect of GI decontamination. We will focus on the available techniques and approach in choosing one or more of these modalities when treating acutely poisoned patients. Moreover, we will focus on gastric emptying (lavage/induced emesis) as one mode of GI decontamination and prevention of absorption (charcoal/ whole bowel irrigation [WBI]) as the second mode.

Gastric Emptying

The concept of gastric emptying is simple: remove the toxin before absorption and thereby decrease or prevent any toxicity. The two primary techniques to achieve gastric emptying are induced emesis and gastric lavage.

Induced Emesis

For years, syrup of ipecac was used both prehospital and in EDs to induce emesis, primarily by expulsion of GI contents before absorption. However, because of its lack of clinical benefit and risk of abuse, syrup of ipecac is no longer recommended and is no longer available in the United States. Chronic abuse is associated with a cardiomyopathy (Schneider 1996; Hopf 1993).

Patient Care Scenario

A 2-year-old boy is noticed to be acting strange at the babysitter's house. When his mother came to pick him up, the child was extremely lethargic and not able to stand or walk normally on his own. The mother noted that he was diaphoretic. The boy had not previously been ill and has had no sick contacts. His mother immediately brings him to the ED, where he continues to be lethargic. Vital signs include: heart rate 115 beats/minute, blood pressure 90/palp, respirations 20 breaths/minute, and 97% oxygen saturation on room air. His pupils were 3-4 mm and

ANSWER -

The differential diagnosis to a child with altered mental status can be quite long, and some clinicians find mnemonic helpful in assisting their diagnosis. The AEIOU-TIPS is a mnemonic used for altered mental status and can be used in approaching infants, children, adolescents and adults. The components of AEIOU-TIPS are defined in the table below.

Toxins represent a large majority of possibilities and given the sudden nature of toxicity in this child, the likelihood of excluding etiologies such as infection, sepsis, and uremia is high. In any patient with altered mental status, rapid assessment and correction within the first 3-5 minutes is imperative and include: high flow oxygen (to treat hypoxia); fingerstick glucose to identify hypoglycemia (and treatment with glucose if present); naloxone for respiratory depression or in a patient with suspected clonidine overdose.

Laboratory testing including basic metabolic profile (to identify any electrolyte derangements) and ethanol level

sluggishly reactive. The patient's heart was regular, lungs were clear bilaterally, and he is moving all four extremities. No tremor or rigidity is present. He is noted to have an odd smell on his clothing.

The boy's medical history is non-contributory: he was born at 37 weeks without complications. He is up to date on all immunizations and is taking no chronic medications. What is the differential diagnosis for this child's sudden onset of altered mental status? And what laboratory tests would best assist in the diagnosis?

should be obtained in all pediatric patients with altered mental status. Further laboratory testing including CBC, LFTs and blood cultures may also be required. Diagnostic imaging (e.g., head CT) should also be done if other etiologies can't be excluded.

This child had a fingerstick glucose resulted as 50 mg/dL and received an IV bolus of D10W with improvement in mental status. He still did remain lethargic with slurred speech. Additional laboratory results returned and revealed a normal basic metabolic profile and an ethanol level of 100 mg/dL. Further investigation by Child Protective Services found that there was vodka in a water bottle that he was accidentally given.

The child overall did well but this case illustrates the importance of rapid assessment of fingerstick glucose as well as obtaining a serum ethanol level in the work up of a child with altered mental status.

A	Alcohol/Abuse of substances Acidosis	Acute alcohol or drug intoxication Diabetic ketoacidosis
E	Environmental Epilepsy Electrolyte derangements Encephalopathy Endocrine disease	Hypothermia; hyperthermia Seizure Hyponatremia; hypernatremia; hypoglycemia; hypocalcemia Thyroid disease
I	Infection	Sepsis; meningitis
0	Overdose Oxygen deficiency	Нурохіа
U	Uremia	Kidney failure
т	Trauma Tumor	
I	Insulin	Hypoglycemia
Р	Poisons	Carbon monoxide; psychosis
S	Stroke Shock	Hemorrhagic or thrombotic stroke

1. Wolfson AB, Hendey GW, Ling LJ, et al. Clinical Practice of Emergency Medicine. Philadelphia, PA: Lippincott Williams & Wilkins, Inc.; 2009.

2. Abbruzzi G, Stork CM. Pediatric toxicologic concerns. Emerg Med Clin North Am 2002;20:223-47.

3. Souganidis E, Grala M, Chinsky J. Six-year-old with altered mental status: no "LACk" of clues. Pediatr Emerg Care 2016;32:180-2.

Although syrup of ipecac is no longer recommended, many caregivers find themselves instinctively using their fingers to manually induce vomiting in children. This can cause local tissue trauma and is not recommended.

Gastric Lavage

Orogastric lavage is performed using a large-bore orogastric tube, typically a 36–40 French tube in adults and a 22–28 French tube in children, as a means of gastric emptying. Orogastric lavage is generally reserved for life-threatening ingestions that have occurred within 1 hour of presenting to a health care facility (Vale 2004). In children, 10- to 15-mL/ kg (up to 250 mL) aliquots of room temperature saline lavage solution should be instilled by a lavage syringe and continued until at least 500–1000 mL is reached in a child or until the effluent lavage solution is clear.

Orogastric lavage has widely been used for removing toxins from the stomach, though evidence of its clinical benefit is sparse. Two studies looked at the efficacy of syrup of ipecac, gastric lavage, and activated charcoal in acutely poisoned patients. In these studies, in about 1400 patients, gastric emptying showed no benefit over activated charcoal alone. However, in both studies, the sickest of patients received gastric emptying (Pond 1995; Kulig 1985). These studies show that many acutely poisoned patients can be treated with activated charcoal alone, and in some scenarios, gastric lavage would be considered.

Orogastric lavage, which is not without risk, should be carried out under the close supervision of an experienced practitioner. Because of the large tube size, most practitioners agree that the patient's airway should be secured with endotracheal intubation. To avoid pushing drug past the pylorus, the patient should be placed in the left lateral decubitus position. Esophageal and stomach injury have been reported after lavage. Fluid and electrolyte abnormalities have also been reported after large volumes of lavage solution were used.

Prevention of Absorption

Activated Charcoal

Activated charcoal is the most commonly used GI decontamination technique. It reduces the systemic absorption of xenobiotics and enhances elimination by disrupting the enterohepatic or enteroenteric cycle. Activated charcoal is a fine black powder prepared by pyrolysis of carbonaceous materials, followed by treatment at high temperatures of oxidizing agents to increase the adsorptive capacity by increasing the surface area. Typical preparations have a surface area of 950 m²/g. Activated charcoal's adsorptive capacity makes it an ideal choice in several oral overdoses. Similar to the data for gastric emptying, a lack of evidence reporting clinically significant end points for activated charcoal (Isbister 2011; Chyka 2005).

Several studies of healthy volunteers describe the adsorptive capacity of activated charcoal as well as the reduced serum concentrations of orally administered drugs. In a simulated acetaminophen ingestion, serum concentrations were reduced when activated charcoal was given within 1 hour (Yeates 2000). Activated charcoal is most effective if given within the first 60 minutes; however, one-fourth of participants still have about a 30% reduction in absorption 4 hours after ingestion (Jürgens 2009).

Outcomes of studies in healthy volunteers are difficult to extrapolate to acutely overdosed patients. While there are certainly more data describing the impact of activated charcoal on pharmacokinetic effect (i.e., reduction in absorption) in healthy volunteers, there are few papers showing clinically significant improvements in outcome after. However, there is an example of when pharmacokinetic studies and studies on clinical outcome align. The bioavailability of citalopram was significantly reduced when charcoal was administered 30 minutes to 4 hours after a citalopram overdose (Friberg 2005). One study showed reduced QT prolongation after charcoal was administered in citalopram overdoses (Isbister 2007). Another example of positive clinical outcomes after activated charcoal administration is from a single study in Sri Lanka, where several doses of activated charcoal reduced mortality after oleander poisoning (Kulig 1987).

The efficacy of several doses of activated charcoal in reducing drug concentrations by interrupting enteroenteric recirculation has been described when intravenous aminophylline was administered and activated charcoal resulted in reduced serum concentrations (Goldberg 1987; Kulig 1987). Because of these older data, there are some scenarios when a toxicologist would recommend several doses of activated charcoal. The dose is 1 g/kg of actual body weight of oral activated charcoal or a 10:1 ratio of charcoal to xenobiotic, whichever is greater. Preparations of charcoal are available both with and without sorbitol. Although a single dose of sorbitol is not expected to cause significant electrolyte shifts, most would recommend that activated charcoal be given without sorbitol in pediatric patients. Heavy metals, iron, and lithium do not adsorb to activated charcoal, and other modalities for GI decontamination need to be used.

Whole Bowel Irrigation

Whole bowel irrigation is the process of evacuating the GI tract before drug absorption. It is done with osmotically balanced polyethylene glycol electrolyte lavage solution. Data to either support or refute WBI are limited (Thanacoody 2015). Several healthy volunteer studies evaluate the role of WBI; however, each has similar limitations, such as small overdoses of drugs, concomitant use of activated charcoal, and pharmacokinetic data only (Ly 2004; Tenenbein 2004).

Whole bowel irrigation has effectively been used and described in several case reports and case series. One pediatric case report describes the successful use of WBI in lead pellet ingestion (Schwarz 2008).

The ideal use of WBI is after ingestion of sustained-release formulations, xenobiotics that are not adsorbed to charcoal (e.g., iron, lead), and unique scenarios such as body packers. The pediatric dose is 250–500 mL/hour of polyethylene glycol electrolyte lavage solution until rectal effluent is clear. This process, when done correctly, takes about 4–6 hours (Thanacoody 2015). Because of the volume and rate of administration, a nasogastric tube is generally required.

Approach to GI Decontamination

For most scenarios, many pediatric exposures can be managed with no GI decontamination or with a single dose of activated charcoal. The few exceptions that are imperative to recognize usually pertain to a toxin that is modified release or that does not adsorb to charcoal. The regional PC at 1-800-222-1222 or a medical/clinical toxicologist should be consulted on each case because each is unique. Whole bowel irrigation may be considered when iron, sustained-release calcium channel blockers, body packers, modified-release bupropion, and sustained-release β -blockers are involved.

TOXICOLOGY LABORATORY

Available laboratory testing for the acutely poisoned patient varies from hospital to hospital. Assessing laboratory findings in an acutely intoxicated patient can provide valuable information, including confirming or excluding the toxic exposures suspected because of the original history or physical examination findings, providing insight into unknown exposures, and dictating a specific antidotal therapy when a toxic concentration is identified. Results of certain testing also confirm the severity of poisoning and may dictate additional treatment recommendations such as extracorporeal removal.

When approaching an acutely poisoned patient, the decision to order certain laboratory tests often depends on the ingestion, patient history, and availability of medication-specific rapid quantitative testing, as well as toxidromes that suggest a specific toxin.

In all patients with an altered mental status, a rapid fingerstick glucose should be measured quickly. Many xenobiotics can cause hypoglycemia and altered mental status. Pediatric patients can develop delayed, recurrent hypoglycemia after exposure to a single-pill ingestion of sulfonylureas (Abbruzzi 2002), ingestion of ethanol (Souganidis 2016), and β -blocker ingestion (Poterucha 2015). Rapid assessment and correction of hypoglycemia is critical. A serum ethanol concentration should be obtained in all pediatric patients with an unexplained altered mental status.

All intentional overdoses should have an acetaminophen concentration obtained, regardless of history (Ashbourne 1989). Acetaminophen does not have a unique toxidrome, and in one study, about 1 in 500 patients with no history of acetaminophen overdose had treatable acetaminophen concentrations, when measured. We will discuss acetaminophen poisoning in detail elsewhere in this text.

The rapid urine drug screens (commonly called the "u. tox" are available emergently in the ED; these immunoassay screening tests identify a structural class of drugs

(e.g., cocaine metabolites, tetrahydrocannabinol [THC] metabolites, opioids, amphetamines) and are subject to false-positive results. An amphetamine screening test may be positive simply because a patient is taking OTC pseudoephedrine – a drug structurally related to the amphetamine that triggered the positive test. Dextromethorphan use in OTC cough syrup can trigger a positive result for phencyclidine (PCP) because of their structural similarities. An opioid screening test may be positive because of poppy seed ingestion. These screening tests are also subject to false negatives, such as when a drug being abused is not structurally related to the drug screen's target analyte (e.g., a negative THC assay in someone abusing synthetic cannabinoids such as "K2" or "Spice"). Finally, a true positive result simply means prior use of the drug, which may be days or even weeks prior. Table 1-3 provides insight into some common xenobiotics resulting in false-positive urine toxicology screens. The literature discusses that the urine toxicology immunoassay screening is flawed and does not provide pertinent information to acutely treat adult patients in the ED (Tenenbein 2009). Despite the limitations of the urine toxicology screen, it does provide some insight into the pediatric population. In fact, it may provide insight into social situations (e.g., a child testing positive for cocaine or THC) as well as the potential for xenobiotic exposure.

Furthermore, more comprehensive tests can be done, but these typically need to be sent to a specialty laboratory for analysis. The methodology for such testing is generally quantitative rather than qualitative. Comprehensive toxicology testing generally tests for the top 200 drugs on the U.S. market; specific tests can be done for various different substances/xenobiotics, including newer drugs of abuse. These results are not available for 5–7 days and will not provide immediate value to the acute care of the pediatric patient. These may be considered when the etiology of symptoms cannot otherwise be explained.

Practice Points

In determining the optimal approach and pharmacotherapy for the management of the acutely intoxicated pediatric patient, practitioners should consider the following:

- A targeted physical examination including assessment of mental status; pupils; vital signs; skin findings; bowel sounds and reflexes provide useful information in determining a specific toxidrome
- Rapid attention to airway, breathing and circulation is essential in managing all acutely intoxicated patients regardless of the history of exposure
- Many xenobiotics cause hypoglycemia particularly in pediatric patients and a rapid fingerstick glucose should be obtained in all patients with altered mental status
- There are numerous antidotes that may be considered in managing a pediatric patient. Consultation with a regional poison center or medical/clinical toxicologist should be employed as often, therapies and doses may change.

Substance Tested by Immunoassay	Xenobiotics Associated with False-Positive Result	Xenobiotics Associated with False-Negative Result	
Amphetamines	Decongestants; ephedrine; bupropion; selegiline	Designer, synthetic amphetamines (e.g., MDMA, cathinones) often not detected	
Cocaine	False-positive tests unlikely	N/A	
ТНС	Marinol; proton pump inhibitors	Synthetic cannabinoids do not test positive	
Opioids	Quinolones	Semisynthetic and synthetic opioids (e.g., fentanyl; buprenorphine; oxycodone) minimally react and not detected	
Benzodiazepines	Oxaprozin	Alprazolam and lorazepam often not detected	
РСР	Dextromethorphan; diphenhydramine; ketamine and venlafaxine	N/A	
Tricyclic antidepressants	Cyclobenzaprine; carbamazepine; diphenhydramine; quetiapine	N/A	
Barbiturates	N/A	N/A	
Methadone	Quetiapine	N/A	

CONCLUSION

The best care for a potentially poisoned patient is to use the principles of basic and advanced life support first. In addition, using physical examination findings as well as a medical history to determine a toxicologic etiology and appropriate antidotal therapy is critical. Pediatric patients pose a unique situation; in many instances, the exposure is from a single dosage form with a known time of ingestion, but many xenobiotics can cause morbidity and mortality, even in small doses. Consultation with a regional PC and/or medical/clinical toxicologists is essential in evaluating and treating poisoned patients.

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Self-Assessment Questions

- A 15-year-old male adolescent is brought to the ED by police after he is found wandering the streets agitated and naked. It requires several police officers to restrain him, and he is mumbling incoherently. Physical examination shows him to be awake and agitated. Vital signs include oral temperature 101°F, heart rate 130 beats/ minute, blood pressure 150/80 mm Hg, respiratory rate 22 breaths/minute, and 98% Sao₂ on room air. Other findings include pupils 6 mm and reactive, positive bowel sounds, and diaphoresis. Which one of the following toxins and toxidrome does this patient most likely have?
 - A. Toxin: phencyclidine; toxidrome: anticholinergic
 - B. Toxin: diphenhydramine; toxidrome: adrenergic
 - C. Toxin: methamphetamine; toxidrome: adrenergic
 - D. Toxin: amitriptyline; toxidrome: anticholinergic
- 2. A 17-year-old male adolescent is found unresponsive and cyanotic at the bottom of the stairs in a known drug house. He had previously been sober for 3 months. On arrival by emergency medical services, he was unresponsive with new track marks on his arms bilaterally. Physical examination reveals that he is unresponsive to painful stimuli. Vital signs include tympanic temperature 96°F, heart rate 60 beats/minute, blood pressure 90/60 mm Hg, respiratory rate 4 breaths/minute, and 90% Sao₂ on room air. Fingerstick glucose was 90 mg/dL. Pupils: 2 mm and sluggish; hypoactive bowel sounds; diminished reflexes. Which one of the following is the optimal order of therapeutic interventions for this patient?
 - A. Give intranasally 2 mg of naloxone and bag-valve mask ventilation; initiate intravenous line.
 - B. Give bag-valve mask ventilation and 2 mg of intravenous naloxone; initiate intravenous line.
 - C. Give bag-valve mask ventilation; initiate intravenous line; give 0.4 mg of intravenous naloxone.
 - D. Give intravenously D_{50} W bolus, 2 mg of naloxone, and bag-valve mask ventilation.
- A 2-year-old boy is brought to the ED by his parents for nausea, vomiting, and irritability. His older siblings have been ill all week with upper respiratory infections and nausea and vomiting. The patient is awake, although lethargic. He takes no chronic medications but has been receiving an OTC cough and cold preparation. Physical examination reveals that he is awake, though lethargic; crying in his mother's arms. Vital signs include temperature 99°F (rectal), heart rate 110 beats/minute, systolic blood pressure 90 mm Hg, respiratory rate 20 breaths/ minute, and 98% Sao₂ on room air. Fingerstick glucose is 100 mg/dL; pupils: 3–4 mm; reactive; dry mucous

membranes; positive bowel sounds; making wet diapers. For unclear reasons, a urine toxicology screen is ordered. The EMIT (enzyme multiplied immunoassay technique) drug screen results come back presumptively positive for both amphetamines and PCP. Child protective services are called. The mother denies exposure to any illicit substances. Which one of the following common OTC cough and cold preparation ingredients most likely caused this patient's positive results on the urine drug screen?

- A. Acetaminophen and dextromethorphan
- B. Phenylephrine and dextromethorphan
- C. Chlorpheniramine and acetaminophen
- D. Guaifenesin and dextromethorphan
- 4. A 16-year-old male adolescent is found at the local homeless shelter with generalized tonic-clonic seizure activity. He has no history of seizures. An empty bottle of isoniazid is found in his belongings. Intravenous lorazepam is administered by prehospital providers without effect. On arrival at the ED, he is intubated and continues to have generalized tonic-clonic seizure activity despite three additional doses of lorazepam. Phenobarbital 15 mg/kg intravenously is given without cessation of seizure activity. Which one of the following is best to recommend for this patient?
 - A. Change to a different benzodiazepine such as midazolam
 - B. Do nothing; it is likely a pseudoseizure
 - C. Give hydroxocobalamin 5 g intravenously
 - D. Give pyridoxine 5 g intravenously
- A 16-year-old female adolescent presents to the ED after 5. intentionally ingesting 60 tablets of cyclobenzaprine 10 mg. No other medications were involved in the ingestion. On arrival at the ED, the patient is agitated, delirious, and actively hallucinating. She is mumbling and picking at things in the air. Vital signs include rectal temperature 99°F, heart rate 130 beats/minute, blood pressure 130/70 mm Hg, respiratory rate 20 breaths/minute, and 98% Sao, on room air. Fingerstick glucose is 110 mg/dL. Pupils are 6 mm and minimally reactive; mucous membranes are dry; skin is flushed; and bowel sounds are negative. Electrocardiography finds sinus tachycardia; QRS 80 milliseconds; and QTc 440 milliseconds. Which one of the following represents the most likely toxidrome and potential antidote for this patient?
 - A. Adrenergic toxidrome and physostigmine
 - B. Cholinergic toxidrome and atropine
 - C. Anticholinergic toxidrome and atropine
 - D. Anticholinergic toxidrome and physostigmine

- 6. One hour ago, a 15-year-old female adolescent intentionally overdosed on acetaminophen 500-mg tablets. She says that she took 200 pills. She is awake and alert and has not vomited. Which one of the following GI decontamination modalities is best to consider for this patient?
 - A. Orogastric lavage
 - B. Multiple doses of activated charcoal
 - C. Single-dose activated charcoal
 - D. Whole bowel irrigation (WBI)
- 7. A 16-year-old female adolescent presents to the ED about 3 hours after intentionally ingesting 100 of her grandmother's theophylline tablets. On arrival, she is awake and tearful. She appears jittery. Vital signs include temperature 98°F, heart rate 110 beats/minute, blood pressure 110/50 mm Hg, respiratory rate 22 breaths/minute, and 99% Sao₂ on room air. Which one of the following GI decontamination methods is best to recommend for this patient?
 - A. Syrup of ipecac
 - B. Orogastric lavage
 - C. Single dose of activated charcoal
 - D. Multi-dose activated charcoal
- 8. A 14-year-old girl is pulled out of a house fire. On arrival at the ED, she is hypotensive and hemodynamically unstable. Cyanide toxicity is considered. Which one of the following is the most appropriate antidote to administer to this patient?
 - A. Pyridoxine 5 g intravenously
 - B. Hyperbaric oxygen
 - C. Sodium bicarbonate
 - D. Hydroxocobalamin 5 g intravenously
- 9. A 17-year-old Amish farmer is found in his family's barn with an empty bottle of diazinon and a suicide note next to him. On arrival to the ED, he has an altered mental status. Physical examination reveals that he is unresponsive to voice; not following commands. Vital signs are as follows: afebrile, heart rate 50 beats/minute, blood pressure 110/70 mm Hg, respiratory rate 16 breaths/minute, and 92% Sao₂ on room air. Eye examination finds pinpoint pupils with lacrimation. He has copious oral secretions. Lung examination finds bilateral wheezing and rhonchi. Abdomen is soft, nontender, with hyperactive bowel sounds and diarrhea. Which one of the following toxidromes best describes this patient's clinical presentation?
 - A. Adrenergic
 - B. Opioid
 - C. Anticholinergic
 - D. Cholinergic
- 10. A 14-year-old male adolescent is found agitated and delirious. He is tachycardic; his skin is warm and dry. His pupils are dilated, and he has no bowel sounds. Which

one of the following is the most likely cause of this patient's symptoms?

- A. Pyridostigmine
- B. Belladonna
- C. Hydrocodone
- D. Cocaine

Questions 11 and 12 pertain to the following case.

K.T. is a 3-year-old girl who arrives at the ED with an altered mental status after being at her grandmother's house earlier in the day. In the ED, K.T. is very lethargic and found to have a fingerstick glucose of 40 mg/dL.

- 11. Which one of the following did K.T. most likely ingest?
 - A. Metformin
 - B. Lisinopril
 - C. Rosiglitazone
 - D. Glyburide
- 12. Which one of the following, in addition to glucose, is best to recommend for K.T.?
 - A. Atropine
 - B. Octreotide
 - C. Diazoxide
 - D. Physostigmine
- 13. A 3-year-old boy is found with his older sibling's medication for attention-deficit/hyperactivity disorder, and a few tablets are missing. About 30 minutes later, the child is unresponsive, and emergency medical services is called. On presentation, the child is unresponsive, although he withdraws to painful stimuli. Vital signs include heart rate 65 beats/minute, systolic blood pressure 80/palp, respiratory rate 10 breaths/minute, and 95% Sao₂ on room air. Fingerstick glucose is 100 mg/dL. Pupils are 2 mm and sluggish, mucous membranes are moist, bowel sounds are hypoactive, and hyporeflexia is present. Electrocardiography reveals sinus bradycardia; QRS and QTc are both normal. Which one of the following is best to recommend for this patient?
 - A. Glucagon 10 mg intravenous push; symptoms consistent with β-blocker ingestion of atropine 1 mg intravenous push; symptoms consistent with organophosphate pesticide ingestion
 - B. Physostigmine 1 mg intravenously over 5 minutes; signs/symptoms consistent with anticholinergic toxicity
 - C. Naloxone 2 mg intravenous push; symptoms most consistent with clonidine toxicity
 - D. Oral acetylcysteine 140 mg/kg; symptoms most consistent with acetaminophen toxicity
- 14. A 16-year-old female adolescent intentionally overdosed on 100 tablets of prenatal vitamins containing ferrous

sulfate 325 mg. About 4 hours later she presents at the ED. She is awake and alert, has had five episodes of vomiting, and is retching. Abdominal flat plate radiography reveals radio-opaque pills. Which one of the following is best to recommend for this patient?

- A. Activated charcoal
- B. Orogastric lavage
- C. Syrup of ipecac
- D. WBI

Questions 15–17 pertain to the following case.

K.G. is a 15-year-old female adolescent who calls 911 to report an intentional overdose of unknown medications after an argument with a friend. On arrival at the ED, about 3.5 hours after the ingestion, K.G. is sleepy with slurred speech. Her vital signs include heart rate 90 beats/minute, blood pressure 110/60 mm Hg, respiratory rate 14 breaths/minute, and 98% Sao₂ on room air.

- 15. Which one of the following laboratory tests is best to immediately order for K.G. and address within the first 3 minutes?
 - A. Thyroid function tests
 - B. Aspirin
 - C. Acetaminophen
 - D. Glucose
- 16. K.G.'s electrocardiography reveals normal sinus rhythm with a QRS complex duration of 80 milliseconds and QTc interval of 430 milliseconds. Given this initial ECG, which one of the following toxins most probably can be ruled out for K.G.?
 - A. Acetaminophen
 - B. Aspirin
 - C. Amitriptyline
 - D. Ethanol
- 17. K.G.'s urine toxicology screen is positive for PCP. She denies ever using PCP; but does admit to taking an OTC cough suppressant for the past few days. Which one of the following most likely resulted in this false-positive result on K.G.'s urine toxicology drug screen?
 - A. Phenylephrine
 - B. Dextromethorphan
 - C. Chlorpheniramine
 - D. Doxylamine
- 18. A 2-year-old boy is found with a bottle of clonidine 0.1 mg in his hands. There is a white powdery substance in his

mouth, and his mother believes 4 pills are missing. On arrival at the ED, he is sleepy but withdraws to pain. Vital signs include heart rate 50 beats/minute, blood pressure 80/palp, respiratory rate 10 breaths/minute, and 94% Sao_2 on room air. Which one of the following is best to administer as an antidote for this patient?

- A. Flumazenil
- B. Naloxone
- C. Physostigmine
- D. Hydroxycobalamin
- 19. A 14-year-old boy presents at the ED after an intentional overdose of acetaminophen 500-mg tablets. A 4-hour acetaminophen concentration is 200 mg/L, which is a toxic, treatable concentration when plotted on the Rumack-Matthew nomogram, and he requires antidotal therapy with N-acetylcysteine. About 15 minutes into the infusion of the loading dose, the patient develops a rash and itching skin. The infusion is turned off, and the physician wants to know what to do next. Which one of the following is best to recommend for this patient?
 - A. Discontinue N-acetylcysteine; he is allergic.
 - B. Reinitiate N-acetylcysteine but double the infusion rate.
 - C. Reinitiate N-acetylcysteine but at a slower infusion rate.
 - D. Give epinephrine, diphenhydramine, and ranitidine for anaphylaxis.
- 20. A 4-year-old boy who was recently initiated on valproate for refractory seizures presents to the ED with increasing lethargy. Blood is drawn and results show valproate at 55 mcg/L and ammonia at 155 mmol/L (normal range: 15–65 mmol/L). Which one of the following is best to recommend for this patient?
 - A. L-Arginine
 - B. Vitamin K
 - C. L-Carnitine
 - D. Omega 3 Fatty Acids