PEDIATRIC TOXICOLOGIC CONCERNS

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Suspected poisoning exposure in pediatric patients accounts for more than 130,000 presentations to emergency departments (EDs) each year. Clinicians caring for poisoned pediatric patients should develop a level of clinical competence and factual comfort in this area to optimize assessment, stabilization, and ultimately patient outcome. This article focuses on clinically relevant considerations specific to poisoned pediatric patients. Special emphasis is given to unique physical examination findings and nuances, appropriateness of the various gastrointestinal decontamination techniques, and management of toxins that commonly result in severe, life-threatening toxicity in children. Last, case examples are provided for those toxins that are dangerous to children in small doses or those that act differently in children after overdose.

EPIDEMIOLOGY

Pediatric poisonings in the United States result in a significant amount of morbidity and rarely, mortality. In 1999, greater than 2 million human poisoning exposures were reported to poison control centers across the country. Most of these exposures were in patients younger than 20 years old. Of the total number of exposures, 52% occurred in children younger than 6 years, and more than 96% were classified as causing no effect or a minor effect. Two percent of patients experienced...
moderate to major toxin-related effects and 0.002% of patients died. The top ten causes of death in children under the age of 6 years are listed in Table 1.

Children, particularly those aged 1 to 3 years, are at risk for exposure to toxins because of their innate inquisitive nature. As a child matures, caretakers tend to underestimate the child’s capabilities and can leave dangerous substances within reach.

MANAGEMENT OF POISONINGS

Initial Assessment and Stabilization of the Patient

As in all ED patients, the primary survey should include evaluation of airway (A), breathing (B), circulation (C), disability (D), and exposure (E). There are several differences in the pediatric airway that require consideration when one is completing this primary survey after pediatric poisoning.

Pediatric upper airways are of small diameter and are easily obstructed by a foreign body or edema. The laryngeal cartilage is very soft, and the tongue is large, which makes airway positioning important to avoid blocking the flow of oxygen. If the child is awake, allow him or her to remain in a comfortable position. An unconscious child should be positioned using a head tilt or jaw thrust. Infants in particular are obligate nose breathers, and any nasal obstruction can be detrimental. If the child requires intubation, a noncuffed endotracheal tube should be used because the cricoid cartilage acts as a natural cuff for the tube.

Children are at a higher risk for aspiration than adults because the larynx is more cephalad and anterior. Toxins such as hydrocarbons that are relatively nontoxic when ingested, result in significant alveolar toxicity owing to depletion of surfactant and increasing inflammatory mediators when aspirated.

A child’s chest wall is thin, soft, and pliant, which facilitates audibil-
ity of breath sounds on examination; however, children have a higher metabolic rate than adults and have less compensatory reserve, making them more susceptible to hypoxia and respiratory failure, especially after exposures to toxins that affect respiratory function. In addition, this factor is responsible for the increased dose that children receive of inhaled toxins (e.g., carbon monoxide) and can partially explain the increased risk for toxicity in pediatric patients.

The diaphragm functions as the primary muscle of respiration because the intercostal muscles and small airway muscles are poorly developed. The diaphragm tires easily during respiratory distress and becomes displaced. This can be responsible for the lack of apparent respiratory alkalosis seen in children after exposure to toxins that initiate toxicity through tachypnea and hyperpnea, such as aspirin. In aspirin-poisoned children who do not have a large respiratory reserve and capacity, metabolic acidosis is the first clinical manifestation.

Circulatory system assessment includes measurement of skin color, capillary refill, and pulses. Systolic blood pressure measurement is less reliable in children owing to higher adrenergic tone, which maintains near-normal blood pressure until 25% of the blood volume is lost. Alternatively, pediatric patients are protected against some hemodynamically acting poisonings. Patients without distal pulses or with decreased capillary refill should receive volume replacement. The pediatric population is at much higher risk for dehydration because they have a greater percentage of total water and have greater insensible losses, which is why pediatric patients should not routinely be given osmotic cathartic agents.

Once the airway, breathing, and circulation have been addressed, the child’s disability should be evaluated. The child should be inspected for any obvious injury, including evidence of any neurologic deficit. The neurologic examination can be difficult in a young child because immature reflexes persist until 2 years of age. These findings include a positive Babinski response and a posture of generalized flexion.

Infants and young children have limited glycogen stores and are at a higher risk for hypoglycemia after toxin exposure. This is especially important with toxins such as ethanol that routinely cause hypoglycemia in children but do not do so in adults. Any patient exhibiting hypoglycemia should be immediately treated with a rapid infusion of dextrose. Doses can be calculated using the Broselow tape, which uses the child’s height to estimate weight and drug doses.

Children presenting with a decrease in mental status and respiratory depression should receive 2 mg of naloxone intravenously. Higher doses can be required after exposure to synthetic opioids such as propoxyphene, fentanyl, meperidine, and methadone. If a clinical response occurs and a long-acting opioid has been ingested, a longer-lasting effect can be achieved using an continuous infusion of two-thirds of the arousal producing dose per hour.

The last step in the primary survey is exposure of the patient. The child should be completely undressed (including diaper removal).
Children have a higher body surface area–to-weight ratio and a proportionally larger head. Dermal exposures cause an increased risk for toxicity in children owing to this increased surface area, along with an increased lipid component of dermal cellular stores. There is also an increased potential for heat loss, especially in small infants, because of poor thermal regulation.

The secondary survey includes assessment of vital signs and a complete physical examination. Symptomatic patients and those with a history of ingesting a cardiac-acting toxin require cardiac evaluation and monitoring. All patients should be observed closely for signs of clinical deterioration.

**HISTORY**

A complete and accurate history is invaluable in the evaluation of the pediatric poisoned patient. Important parameters to be determined include the exact substances that the child was potentially exposed to, the release form of the substance (if applicable), the amount the child was exposed to, and the time of exposure. If suspected products are available, they should be brought with the patient to the healthcare facility. This information provides valuable insight into the toxic potential of the substance, the options for gastrointestinal decontamination, and the interpretation of drug levels when required.

If an ingestion has occurred, the dose potentially ingested should be calculated, assuming a worst case scenario. The time that has elapsed from the time of exposure helps to determine the patient’s risk for subsequent toxicity and to evaluate blood levels of specific toxins. An example is acetaminophen, for which a level at a given time after ingestion is plotted to determine risk for toxicity. When there is incomplete or inaccurate information, the clinician should rely on the physical examination and laboratory assessment to assess risk and determine treatment.

**PHYSICAL EXAMINATION**

A complete physical examination is essential to provide direction for patient treatment. Vital signs, including a rectal temperature, should be obtained, along with a neurologic examination, including assessment of mental status and reflexes. Other parameters that are useful in toxidrome development include assessment of pupillary size and response to light, bowel activity, urinary retention, and mucus membrane and skin moisture level. Once the physical examination has been completed, the patient can be classified, if appropriate, according to a toxidrome.

A toxidrome is a constellation of signs and symptoms that help to classify a patient into a category for toxin identification. Table 2 contains the signs and symptoms expected after common toxidromes, including
**Table 2. COMMON TOXIDROME FINDINGS**

<table>
<thead>
<tr>
<th>Physical Findings</th>
<th>Adrenergic Toxidrome</th>
<th>Anticholinergic Toxidrome</th>
<th>Anticholinesterase Toxidrome</th>
<th>Opioid Toxidrome</th>
<th>Sedative-Hypnotic Toxidrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vital Signs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory rate</td>
<td>Increased</td>
<td>No change</td>
<td>No change</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Heart rate</td>
<td>Increased</td>
<td>Increased</td>
<td>Decreased</td>
<td>Normal/decreased</td>
<td>Normal/decreased</td>
</tr>
<tr>
<td>Temperature (rectal)</td>
<td>Increased</td>
<td>Increased</td>
<td>No change</td>
<td>Normal/decreased</td>
<td>Normal/decreased</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Increased</td>
<td>No change/increased</td>
<td>No change</td>
<td>Normal/decreased</td>
<td>Normal/decreased</td>
</tr>
<tr>
<td><strong>Physical Examination</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental status</td>
<td>Alert/agitated</td>
<td>Depressed/confused/hallucinating</td>
<td>Depressed/confused/ hallucinating</td>
<td>Depressed</td>
<td>Depressed</td>
</tr>
<tr>
<td>Pupils</td>
<td>Dilated/Constricted</td>
<td>Dilated</td>
<td>Constricted</td>
<td>Constricted</td>
<td>Normal</td>
</tr>
<tr>
<td>Mucous membranes</td>
<td>Wet</td>
<td>Dry</td>
<td>Wet</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Skin findings</td>
<td>Diaphoretic</td>
<td>Normal</td>
<td>Diaphoretic</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Reflexes</td>
<td>Increased</td>
<td>Decreased</td>
<td>Normal/decreased</td>
<td>Normal/decreased</td>
<td>Normal/decreased</td>
</tr>
<tr>
<td>Bowel sounds</td>
<td>Increased</td>
<td>Decreased</td>
<td>Increased</td>
<td>Decreased</td>
<td>Normal</td>
</tr>
<tr>
<td>Urinary ability</td>
<td>Increased</td>
<td>Decreased</td>
<td>Increased</td>
<td>Muscle fasciculations</td>
<td>Normal</td>
</tr>
<tr>
<td>Other</td>
<td>Possible seizures</td>
<td>Possible seizures</td>
<td>Possible seizures</td>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>


cholinergic, anticholinergic, adrenergic, sedative-hypnotic, and opioid agents. Toxidromes are most useful for patients with unknown exposures, but they can also provide consistency after a known toxin exposure or when multiple toxins are suspected.

Intentionally poisoned patients often have an unreliable history. These patients should be screened routinely for exposure to the most common and most life-threatening toxins. A 12-lead ECG specifically evaluating (QRS complex duration is used to screen for exposure to tricyclic antidepressants. A QRS complex duration of >100 msec is considered significant. In adults, a rightward axis deviation of the terminal 40 msec of the QRS complex can be used as a screening tool for tricyclic antidepressant exposure. This cannot be used in children who have significant baseline rightward axes deviation. Other bedside tests that can be of value in select patients are included in Table 3.

LABORATORY EVALUATION

Laboratory studies are beneficial when a correlation can be made with a given serum level and toxicity risk, and that level can be expedited, resulting in a change in management to improve patient outcome. The laboratory tests required after a given toxin vary and depend on the patient’s history, physical examination, and time of exposure. Electrolytes should be obtained in all but the most trivial cases, with careful consideration of glucose and potassium levels and the anion gap. Other measurements of laboratory parameters related to organ function can be required, depending on the specific toxin suspected.

General qualitative toxicology screens that test for exposure to drugs of abuse are of limited—if any—value in the care of the acutely poisoned patient. When these screens studied in pediatric patients exposed to various toxins, there was no improvement in patient outcome or change in care provided. Although not useful for acute clinical care, a general qualitative toxicology screen should be obtained when child abuse is suspected. The presence of a drug of abuse in a child can provide valuable insight into psychosocial issues and consequences.

There are some toxins for which treatment can be guided using quantitative measurements of the toxin in the blood (Table 4). Some of the listed levels are important with relation to time after ingestion to form an accurate assessment of risk. Examples include iron and acetaminophen. Others require the measurement of several levels over a short period, in which a trend can be demonstrated. Examples include aspirin, theophylline, phenytoin and carbamazepine. Although all quantitative levels are not required in most patients, an acetaminophen level should be obtained in any intentionally poisoned patient. Fewer than 1 in 400 patients without a history of ingesting acetaminophen requires treatment with the antidote.
<table>
<thead>
<tr>
<th>Test</th>
<th>Logistics</th>
<th>Finding</th>
<th>Toxins Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ocular and Dermal</strong></td>
<td>Place pH paper on area</td>
<td>Acid or alkali</td>
<td>Caustics that are acid or alkali</td>
</tr>
<tr>
<td>pH Testing</td>
<td>Place pH paper on area</td>
<td>Acid or alkali</td>
<td>Caustics that are acid or alkali</td>
</tr>
<tr>
<td>Skin color</td>
<td>Place pH paper on area</td>
<td>Acid or alkali</td>
<td>Caustics that are acid or alkali</td>
</tr>
<tr>
<td><strong>Cardiac</strong></td>
<td>12 leads looking specifically at limb leads</td>
<td>Widened QRS complex duration</td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td>Electrocardiogram</td>
<td>12 leads looking specifically at limb leads</td>
<td>Widened QRS complex duration</td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td><strong>Physical Examination</strong></td>
<td>Draw sample</td>
<td>Chocolate brown appearance</td>
<td>Methemoglobinemia</td>
</tr>
<tr>
<td>Blood color</td>
<td>Draw sample</td>
<td>Chocolate brown appearance</td>
<td>Methemoglobinemia</td>
</tr>
<tr>
<td><strong>Toxidrome</strong></td>
<td>Mentation, eyes, mucous membranes, skin, bowel, bladder, and vital signs</td>
<td>Toxidrome (see Table 2)</td>
<td>Toxidrome (see Table 2)</td>
</tr>
<tr>
<td><strong>Urine</strong></td>
<td>Blowing up a blood pressure cuff, tapping the facial nerve</td>
<td>Carpal spasm, facial spasm</td>
<td>Hypocalcemia caused by ethylene glycol, hydrofluoric acid</td>
</tr>
<tr>
<td>Urine fluorescence</td>
<td>Urine placed on filter paper and placed under a Wood’s lamp</td>
<td>Positive fluorescence</td>
<td>Ethylene glycol</td>
</tr>
<tr>
<td>Urine oxalate crystals</td>
<td>Microscopic evaluation</td>
<td>Positive findings</td>
<td>Ethylene glycol</td>
</tr>
<tr>
<td>Ferric chloride</td>
<td>1–2 drops of 10% solution are placed in 2 mL of urine</td>
<td>Violet purple</td>
<td>Salicylates</td>
</tr>
<tr>
<td>Phenothiazines</td>
<td></td>
<td>Brown</td>
<td></td>
</tr>
<tr>
<td><strong>Radiograph</strong></td>
<td>Roentgenogram</td>
<td>Small opacities</td>
<td>Halogenated toxins, heavy metals, iron, lithium and densely packaged products</td>
</tr>
</tbody>
</table>
Table 4. EXAMPLES OF TOXINS FOR WHICH QUANTITATIVE LEVELS ARE OF SIGNIFICANCE

<table>
<thead>
<tr>
<th>Levels at a Set Point In Time</th>
<th>Serial Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>Aspirin and salicylates</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>Carbazepine</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Digoxin</td>
</tr>
<tr>
<td>Ethylene glycol</td>
<td>Phenobarbital</td>
</tr>
<tr>
<td>Heavy metals (24 hour urine)</td>
<td>Phenytin</td>
</tr>
<tr>
<td>Iron</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Methanol</td>
<td>Valproic acid</td>
</tr>
<tr>
<td>Methemoglobin</td>
<td></td>
</tr>
</tbody>
</table>

GASTROINTESTINAL DECONTAMINATION AND ENHANCED ELIMINATION

Gastrointestinal decontamination is desired when an attempt can be made to remove a harmful substance before it can be absorbed and cause toxic effects. Currently, there are four options used to achieve gastrointestinal decontamination, including syrup of ipecac, orogastric lavage, single- or multiple-dose activated charcoal and whole-bowel irrigation (WBI). Relative contraindications to gastrointestinal decontamination include ingestion of caustics and the ingestion of substances not harmful when ingested, but harmful when aspirated (ie, hydrocarbons). Dosing parameters are listed in Table 5.

GASTRIC EMPTYING

Gastric emptying is accomplished using syrup of ipecac or orogastric lavage. Syrup of ipecac contains the alkaloids emetine and cephaline, which are both locally and centrally active emetics. Vomiting typically occurs within 20 minutes and lasts for approximately 2 hours.\(^{45,51}\) Syrup of ipecac is considered for nonvomiting patients in whom a toxic amount of substance is thought to be in the stomach. Contraindications to syrup of ipecac include caustic ingestions, age younger than 6 months, battery or foreign body ingestion, and in cases in which there is an altered mental status or the potential for an altered mental status. Syrup of ipecac is particularly useful for ingestions of toxic substances that are large in physical size, exhibit delayed toxicity, and do not adhere to activated charcoal.

Orogastric lavage should be attempted by using the largest tube size possible for the size of the child. Although orogastric lavage removes approximately the same amount of toxin from the stomach as syrup of ipecac, there is a distinct disadvantage of using orogastric lavage in children because of small tube openings. In addition, the process of instilling and removing fluid can advance some of the toxin ingested past the pyloric opening, thereby making it inaccessible for removal.\(^{53,70}\)
### Table 5. GASTROINTESTINAL DECONTAMINATION TECHNIQUES

<table>
<thead>
<tr>
<th>Technique</th>
<th>Indication</th>
<th>Contraindication</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syrup of ipecac</td>
<td>Early, life-threatening ingestion, toxin in the stomach and no expected change in mental status, and toxin does not require oral antidote or more effective technique</td>
<td>Minimally toxic, prior vomiting, altered mental status, caustic, hydrocarbon, or foreign body</td>
<td>6 months–1 year 10 mL, 1 year–12 years 15 mL, &gt;12 years 30 mL (can be repeated once)</td>
</tr>
<tr>
<td>Orogastric lavage</td>
<td>Early, life-threatening ingestion, toxin in the stomach but airway is protected</td>
<td>Minimally toxic, prior vomiting, unprotected airway, caustic, hydrocarbon, or foreign body</td>
<td>Appropriate size largest tube</td>
</tr>
<tr>
<td>Activated charcoal</td>
<td>All potentially toxic ingestions that can adhere to activated charcoal</td>
<td>Nontoxic, unprotected airway, caustic, hydrocarbon, foreign body, ileus, or perforation</td>
<td>1 g/kg PO or by nasogastric tube</td>
</tr>
<tr>
<td>Single dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple dose</td>
<td>As single dose, but with large gram ingestions or toxins with enterohepatic or enteroenteric recirculation</td>
<td>Nontoxic, unprotected airway, caustic, hydrocarbon, foreign body, ileus, or perforation</td>
<td>Single dose every 1–6 hours</td>
</tr>
<tr>
<td>Whole bowel irrigation</td>
<td>Early, life-threatening ingestion, of sustained-release or toxin with a long absorption time and there is no more effective technique</td>
<td>Minimally toxic, when another technique is working well, unprotected airway, caustic, hydrocarbon, or foreign body, ileus or perforation</td>
<td>Up to 500 mL high-molecular-weight polyethylene glycol solution per hour (i.e., GoLYTELY, NuLYTELY)</td>
</tr>
</tbody>
</table>
Advantages of orogastric lavage over syrup of ipecac include the immediate gastric emptying and toleration of other oral antidotes such as n-acetylcysteine and activated charcoal. Contraindications to orogastric lavage include caustic exposure or cases in which the airway is inadequately protected.

There are two large studies that examined the use of gastric emptying (orogastric lavage or syrup of ipecac) prior to the use of activated charcoal administration in adults.¹⁸,⁶⁶ These studies found that for most patients without life-threatening toxicity, gastric emptying had no impact on patient outcome. Syrup of ipecac and orogastric lavage, therefore, should be considered only for patients in whom life-threatening toxic effects are exhibited or are expected based on the history of exposure or the patient’s manifestations of illness.

**ACTIVATED CHARCOAL**

Activated charcoal adheres to most ingested toxins. Exceptions include small charged toxins, such as alcohols, heavy metals, lithium, and iron.⁵⁷ Activated charcoal binds directly to toxins anywhere it comes in contact in the gastrointestinal tract, but it can also bind toxins undergoing enterohepatic recirculation and through enteroenteric recirculation (Fig. 1).

The dosing of activated charcoal is empiric and is a consequence of the largest tolerated activated charcoal dose. Most toxins that adhere to

![Figure 1. Mechanisms of multiple dose activated charcoal. Light outlined ovals = drug; heavy outlined ovals = charcoal.](image)
activated charcoal require a 10:1 activated charcoal–to-drug ratio for optimal adherence, however.\textsuperscript{63} Multiple doses of activated charcoal are used when large-dose ingestions occur that cannot be bound using a single dose of activated charcoal. For those toxins excreted through enterohepatic or enteroenic recirculation, multiple doses are also given at intervals of 1 to 6 hours, depending on the toxin and the severity of the patient’s symptoms.

Administration of activated charcoal is safe in all patients who have an adequately protected airway. Aspiration, although rare, occurs and can lead to significant morbidity and mortality because of airway occlusion and inflammation.\textsuperscript{30, 64} Also, patients require an active bowel to enable movement of activated charcoal through the gastrointestinal tract; this is especially significant when multiple doses are considered.

WHOLE-BOWEL IRRIGATION

Whole-bowel irrigation (WBI) requires a high-molecular-weight polyethylene glycol (PEG) solution that is electrolyte replete (i.e., GoLytely, NuLytely). This technique is most successful in removing sustained-release toxins or toxins with delayed release in overdoses, particularly if the toxin does not adhere to activated charcoal. The solution is administered to children at an oral dosage of up to 500 mL/h and continued until rectal effluent is clear. The dose-limiting side effect of WBI includes gastrointestinal bloating and vomiting; these effects can be minimized using slow nasogastric administration and antiemetics, including metoclopramide or ondansetron. Electrolyte abnormalities and fluid shifts are not reported even after large doses in children, and the bowel can be evacuated, when accomplished effectively, within 4 to 6 hours of initiation.\textsuperscript{74, 82}

EYE AND SKIN

Eye and skin exposure to toxins required rapid decontamination to mitigate local and systemic toxic effects. Any clothing left on the child should be removed, and the area should be immediately flushed copiously with water. Ocular exposures should be flushed for a minimum of 15 minutes prior to evaluation. If burning or irritation persists on the skin or eye, the patient should receive a thorough evaluation.

PATIENT MONITORING PARAMETERS AND ANTIDOTES

Asymptomatic patients require monitoring for varying periods depending on the toxin and its toxicokinetic and toxicodynamic properties. Symptomatic patients can be managed supportively until their symp-
Table 6. COMMON TOXINS AND RELATED ANTIDOTES

<table>
<thead>
<tr>
<th>Toxin</th>
<th>Antidote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>N-acetylcysteine</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Physostigmine*</td>
</tr>
<tr>
<td>Anticholinesterases (organophosphates and</td>
<td>Atropine, Pralidoxime</td>
</tr>
<tr>
<td>carbamates)</td>
<td></td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td></td>
</tr>
<tr>
<td>Botulism</td>
<td></td>
</tr>
<tr>
<td>Beta blockers</td>
<td></td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td></td>
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<tr>
<td>Carbon monoxide</td>
<td></td>
</tr>
<tr>
<td>Cyanide</td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td></td>
</tr>
<tr>
<td>Heparin</td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td></td>
</tr>
<tr>
<td>Isoniazid</td>
<td></td>
</tr>
<tr>
<td>Lead</td>
<td></td>
</tr>
<tr>
<td>Methemoglobinemia</td>
<td></td>
</tr>
<tr>
<td>Opioids</td>
<td></td>
</tr>
<tr>
<td>Toxic alcohols (methanol and ethylene glycol)</td>
<td>Ethanol, fomepizole, hemodialysis</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>Sodium bicarbonate</td>
</tr>
<tr>
<td>Warfarin (and superwarfarins)</td>
<td>Vitamin K1</td>
</tr>
</tbody>
</table>

*Use of flumazenil/physostigmine contraindicated in many situations.
This is useful as an educational tool but might not represent standard of care everywhere. Please consult a poison control center in case of emergency.

...tems resolve. There are some exceptions, however, in which antidotes can be warranted. The antidote can be life saving or decrease the incidence or severity of toxic effects in these instances. Table 6 lists antidotes and their uses.

**ENHANCED ELIMINATION**

Once a toxin is absorbed and free to act systemically, enhanced elimination is desired to decrease the duration of toxic effects manifest. Current enhanced elimination techniques that are used in poisoned patients include alkalization and urinary ion trapping, hemodialysis, and charcoal hemoperfusion.

Renal toxin elimination depends on the ability of the drug to be trapped in the urine and excreted. Many toxic compounds are excreted renally and are either weak acids or bases, thereby dependent on the pH of the urine for ionization. Ionized toxins are not reabsorbed in the tubular fluid and are subsequently excreted. Alkalization of the urine to enhance elimination of weak acids such as salicylates and phenobarbital has been well established.

Hemodialysis removes toxins by passing the blood through a semi-permeable membrane, where toxins diffuse across a concentration gra-
dient. Requirements for toxins include low volume of distribution, high-water solubility, low blood protein binding, and low molecular weight. Hemodialysis has been used to enhance the elimination of salicylates, methanol, lithium, ethylene glycol, phenobarbital, and procainamide.\textsuperscript{3, 6, 17, 28, 33, 35, 41, 56, 61, 65} Another benefit of hemodialysis is that it can be used to correct abnormalities such as metabolic acidosis, hyperkalemia, and fluid imbalances. Hemodialysis and charcoal hemoperfusion are of limited value in small children, in whom blood volume is inadequate to sustain the procedure without potential morbidity.

Charcoal hemoperfusion is performed by passing the blood through a cartridge containing activated charcoal or carbon. Toxins must be in the blood (low volume of distribution), but larger size is permitted, along with protein binding. The toxin must bind well to activated charcoal. Drugs that have been removed effectively by this method include theophylline, phenobarbital, carbamazepine, and procainamide.\textsuperscript{13, 15, 19, 36, 41, 65} Complications of this procedure include thrombocytopenia, hypocalcemia, leukopenia, and rigors.\textsuperscript{65}

Exchange transfusion, in which total blood volume is exchanged, is useful in neonates when extracorporeal removal is not possible or for those toxins that are located in the blood compartment. Exchange transfusion has been used successfully for theophylline overdose in neonates.\textsuperscript{5, 71}

**CASES SIGNIFICANT FOR PEDIATRICS**

In many situations, pediatric poisonings are not unique, and patients can be treated in a manner similar to that used for their adult counterparts. Pharmacokinetic and/or pharmacodynamic differences in children result in unique manifestations after exposure to select toxins, however. The cases below illustrate some toxins of particular significance to children. Other examples, with brief explanations, are listed in Table 7.

**Case No. 1**

A 2-year-old boy is brought to the ED by his mother for increased drowsiness over the past 2 hours. She denies any recent illness and states the child was acting normally until the onset of symptoms 2 hours ago. Her teenage son was just prescribed a new medication for his attention deficit hyperactivity disorder (ADHD), but she is uncertain what the medication is. On physical examination, the child is obtunded and responsive only to painful stimuli. Vital signs include blood pressure, 60/40 mm Hg; heart rate, 65 beats/min; respiratory rate, 10 breaths/min; and temperature, 37.5°C rectally. Blood glucose is 100 mg/dL. Another significant finding found on physical examination is that of constricted pupils that respond poorly to light. Breathing is deep, but his lungs are clear to auscultation. Bowel sounds are slow, and the skin is warm and dry.
Table 7. TOXINS WITH SIGNIFICANT DIFFERENCES IN CHILDREN VERSUS ADULTS

<table>
<thead>
<tr>
<th>Toxin</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEI, AG II Inhibitors</td>
<td>Lack of relying on the renin-angiotensin system for maintenance of blood pressure causes less toxicity</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Metabolize a higher percentage of acetaminophen using sulfation versus glucuronidation. It is unknown how this difference is manifest after overdose</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>Higher risk for paradoxyl CNS excitation</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>Cardiac physiology can place pediatric patients at decreased risk for manifestations of toxicity</td>
</tr>
<tr>
<td>Botulism</td>
<td>Increased risk in infants of infantile botulism due to gastric flora, allowing C. botulinum to cause infection and production of toxin</td>
</tr>
<tr>
<td>Cardiac glycosides</td>
<td>Cardiac physiology can place pediatric patients at decreased risk for manifestations of toxicity</td>
</tr>
<tr>
<td>Dermal toxins</td>
<td>Higher surface area and increased lipophilicity leads to increased tissue absorption</td>
</tr>
<tr>
<td>Dextromethorphan</td>
<td>Increased opioid like effects at low doses</td>
</tr>
<tr>
<td>Ethanol</td>
<td>Higher risk for hypoglycemia because of decreased glycogen stores</td>
</tr>
<tr>
<td>Hydrocarbons</td>
<td>Increased risk of aspiration owing to structural differences in airway anatomy</td>
</tr>
<tr>
<td>Hypoglycemic agents</td>
<td>Higher risk for hypoglycemia due to decreased glycogen stores</td>
</tr>
<tr>
<td>Inhaled toxins</td>
<td>Increased dose is caused by a higher respiratory rate</td>
</tr>
<tr>
<td>Lead</td>
<td>Increased absorption in children</td>
</tr>
<tr>
<td>Methemoglobinemia</td>
<td>Overall increased risk due to decreased detoxification mechanisms. Can also occur in infants with severe viral gastrointestinal illness.</td>
</tr>
<tr>
<td>Methylxanthines</td>
<td>Metabolic changes cause neonates to be at increased risk (decreased elimination) and children up to 12 years of age to be at decreased risk (increased metabolism)</td>
</tr>
<tr>
<td>Respiratory stimulants</td>
<td>Less respiratory reserve causes a decrease in manifested respiratory alkalosis.</td>
</tr>
<tr>
<td>Salicylates</td>
<td>Less respiratory reserve causes a decrease in manifested respiratory alkalosis.</td>
</tr>
<tr>
<td>Sedative hypnotics</td>
<td>Higher risk for paradoxyl CNS excitation</td>
</tr>
</tbody>
</table>

CLONIDINE

Clonidine is commonly used to control blood pressure in adults and ADHD in children. It is a central alpha-adrenoreceptor agonist that causes inhibition of sympathetic outflow. The clinical effects that are seen after excessive clonidine dosing occur quickly, usually within 30 to 60 minutes after exposure. Common symptoms in children include neurologic depression, hypotension, bradycardia, miosis, and respiratory depression. There is a clear dose-related response seen after clonidine exposure. Symptoms are minimal with ingestions of less than 10 μg/kg, cardiovascular compromise is seen after ingestions of 10 to 20 μg/kg, and respiratory depression is seen when doses exceed 20 μg/kg. Prescribed doses in adults range from 100 μg to 300 μg. This dose in a 10-kg child can result in significant toxicity.
Treatment after clonidine exposure is largely supportive and includes naloxone for symptomatic patients. Naloxone is used and successfully reverses the neurologic, cardiovascular, and respiratory effects of clonidine in approximately 50% of cases.\textsuperscript{23, 40, 81, 85} The reason for naloxone’s effectiveness is unclear; however, opioids and the central alpha-2 presynaptic receptor share a potassium ion channel.

Bradycardia not responding to naloxone can respond to atropine, and hypotension is generally responsive to volume expanders and vaso-pressors, if required. Gastrointestinal decontamination is effective only early after exposure, because clonidine is rapidly absorbed and distributed. Activated charcoal is the gastric decontamination technique of choice and allows for complete binding with one dose owing to the low amounts ingested to cause toxicity.

Case No. 2

A 3-year-old boy is brought in to the ED by his grandmother. While the grandmother was in the shower, the child opened up a bottle of glyburide and ingested at least two tablets. This occurred approximately 30 minutes prior to arrival, and the child has been acting appropriately since the ingestion. The child is active and playful in the examination room. The child’s vital signs are normal, and a glucometer is read as 90 mg/dL. The child’s physical examination is entirely normal.

SULFONYLUREAS

Sulfonylureas are commonly used in patients with non–insulin-dependent diabetes mellitus to control hyperglycemia. These agents exert their effect by increasing the amount of intracellular ATP, triggering the release of insulin from secretory granules, and by increasing insulin receptor sensitivity.

Symptoms that can be attributed to hypoglycemia in patients include fatigue, diaphoresis, lightheadedness, dizziness, agitation, confusion, or tachycardia. No single manifestation of altered mental status can exclude hypoglycemia, however, and any changes should be investigated. Infants and small children can be difficult to feed. More serious symptoms include status epilepticus and cardiovascular collapse. Many times, however, a child remains asymptomatic, necessitating frequent blood glucose monitoring.

After patient stabilization, gastrointestinal decontamination using activated charcoal should be considered if the exposure occurred a short time ago, within 1 to 2 hours. The child should be monitored for hypoglycemia for 24 hours, even if initially asymptomatic. Sulfonylureas have a low threshold for toxicity, with even one tablet causing hypoglycemia in a child.\textsuperscript{67} A poison control center retrospective study including 185 pediatric patients reported to have ingested sulfonylurea revealed that although 96% of the 55 hypoglycemic developed symptoms within
8 hours, 3 patients developed symptoms up to 24 hours later. There are reported cases of hypoglycemia developing 28 hours after a chlorpropamide ingestion, and up to 12.5 hours after glipizide ingestions.

The child should be allowed free access to food and drink during observation, because oral intake is the most effective means of maximizing glucose replacement (a hamburger and french fries contain up to 1000 calories, whereas an ampule of Dextrose 25 has only 50 calories). If the child develops hypoglycemia, a 10% dextrose solution can be used along with oral feeding, with a goal of maintaining blood glucose measurements greater than 80 mg/dL. Occasionally, a bolus of D-25 or D-50 also can be required during this period.

Octreotide should be considered for children who do not respond to feeding and dextrose administration. Octreotide suppresses the release of insulin by binding to a somatostatin receptor that blocks a calcium channel. Blockade of this channel reduces the secretion of insulin. One adult study demonstrated that octreotide can reduce insulin secretion back to basal rate, eliminating the need for a dextrose infusion. A dose of 1.25 mg/kg has been given to a hypotensive 5 year old after a glipizide ingestion. A normal glucose level was restored after 4 hours. Diazoxide works as a potassium channel opener, which inhibits the influx of calcium and the subsequent release of insulin. Because of the potential for hypotension, it should be considered only when octreotide is not available. In addition, when studied in healthy adults given glyburide, octreotide resulted in less rescue dextrose administration when compared with diazoxide. In children, the recommended dosage of diazoxide is 1 to 3 mg/kg up to four times per day. There are no pediatric studies to support this therapy, however.

Case No. 3

A 4-year-old boy is brought to the ED by his father for vomiting. The patient’s father states that the family is in the process of moving, and the child has not been well supervised for the last few hours. He denies any recent illness in the child or in any family members. The only medication in the home is verapamil. The child is lying quietly on the stretcher. Vital signs are as follows: blood pressure, 54/30 mm Hg; heart rate, 52 beats/min; respiratory rate, 15 breaths/min; and temperature, 36.8°C rectally. The blood glucose level is determined to be 80 mg/dL. A physical examination reveals pupils that are 3 mm and react well to light. Lungs are clear to auscultation, and his heart is regular without murmurs. Bowel sounds are active, and the skin is warm and dry.

CALCIUM CHANNEL ANTAGONISTS

Calcium channel antagonists frequently are prescribed in adults to treat hypertension and to control rapid heart rates, such as seen in patients with atrial fibrillation. Calcium channel antagonists inhibit calcium influx through slow voltage-gated (L-type) calcium channels in
myocardial and smooth muscle cells. This lessens the force of myocardial contractions, dilates vasculature, and ultimately results in a measured reduction in blood pressure. In addition, at higher doses, additive hypotension occurs owing to antagonism of peripheral alpha-adrenergic receptors. The atrioventricular (AV) node and the sinoatrial (SA) node are dependent of the activity of slow calcium channels for the formation of action potentials, and as such, overdose results in decreased automaticity and bradycardia.

There are three classes calcium channel antagonists: the phenylalkylamines (e.g., verapamil), the benzothiazines (e.g., diltiazem), and the dihydropyridines (eg, nifedipine, amlodipine, and nicardipine). All affect the slow voltage-gated calcium channel; however, each is selective, resulting in different degrees of peripheral vasodilation and SA and AV nodal depression (Table 8). Most of the life-threatening toxicity that is seen after exposure to calcium channel antagonists occurs after sustained-release preparations of verapamil or diltiazem. In fact, nifedipine and other dihydropyridines rarely require more than volume support for treatment of hypotension and can even exhibit a reflex tachycardia in response to manifest hypotension.

In overdoses, patients can present asymptomatic or with hypotension and bradycardia. Hemodynamic instability can take several hours to occur after exposure. The time from exposure to the development of symptoms varies depending on the preparation of the drug and the dose ingested. A recent review of 283 children presenting to healthcare facility after a reported ingestion of a calcium channel blocker identified 16 symptomatic children. Of these, five gave a history of ingesting just one tablet. The others reported an ingestion of three to nine tablets. Ten of the sixteen symptomatic patients reported ingesting a sustained-release preparation. Two percent of the children with a documented history of ingesting one pill or less were symptomatic, including vomiting, lethargy, low blood pressure, or low heart rate within 1 to 4 hours of ingestion of regular-release preparations and up to 14 hours after sustained-release preparations.

Treatment of patients exposed to calcium channel antagonists includes careful assessment of hemodynamic status. Early intravenous access is warranted because of the potential need for rapid intervention. A 12-lead ECG should be obtained and repeated periodically to assess for conduction delays.

Table 8. TYPES OF CALCIUM CHANNEL ANTAGONISTS

<table>
<thead>
<tr>
<th>Class</th>
<th>AV Nodal Suppression</th>
<th>Vasodilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenylalkylamine (verapamil)</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Benzothiapine (diltiazem)</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Dihydropyridine (nifedipine etc.)</td>
<td>0</td>
<td>++++</td>
</tr>
<tr>
<td>T-type (POSICOR)</td>
<td>++++</td>
<td>+++</td>
</tr>
</tbody>
</table>
Gastrointestinal decontamination plays a major role in patients who present early after exposure and who are not yet symptomatic. Calcium channel antagonists adhere well to activated charcoal, however, large gastrointestinal tract burdens can limit the usefulness of activated charcoal alone. In these cases, a high-molecular-weight polyethylene glycol electrolyte-neutral solution (e.g., GoLytely) is given at a rate of up to 500 mL/h in children and continued until the rectal effluent is clear. This process typically takes 4 to 6 hours and many times is completed before the patient would be expected to manifest symptoms of toxicity. The major limitation of effective WBI is gastric distention and nausea and vomiting, which can be mitigated with the judicious use of antiemetics that do not slow the gastrointestinal tract (e.g., metoclopramide, ondansetron) and through slowed nasogastric administration of the solution. WBI can be used successfully in children without concerns for fluid or electrolyte abnormalities.74, 82

Symptomatic patients should receive rapid corrective pharmacotherapy even in patients with normal mental status, because mentation often is preserved even when hemodynamic status is severely compromised. Fluid administration and atropine can be used as initial therapy for patients with hypotension and bradycardia, although often these interventions are inadequate. Nonresponsive patients can respond to the administration of calcium salts. Calcium salts provide more calcium available for channel activity. Available forms include calcium chloride (13.4 mEq Ca/g) and calcium gluconate (3.4 mEq Ca/g). Symptomatic pediatric patients have responded to calcium chloride at doses of 14.3 mg/kg and 19.4 mg/kg.7 An initial dose of 0.2 mg/kg of calcium chloride or 0.6 mg/kg of calcium gluconate has been recommended.60

Patients who do not respond to calcium salts could require vaso-pressors, including dopamine, epinephrine, or norepinephrine, and a trial of transcutaneous venous pacing. A more specific measurement of parameters using invasive hemodynamic monitoring is useful at this point to guide therapy.

Glucagon is successful in some patients, in whom it acts as an inotrope. Glucagon stimulates adenylate cyclase activity through a receptor independent of the beta-adrenergic receptor, to increase the production of cyclic AMP. This activates and recruits new calcium channels and finally triggers the release of calcium from the sarcoplasmic reticulum and results in actin and myosin complex.39, 89 There are several adult case reports that describe the use of glucagon at 4 to 14 mg IV, followed by a continuous infusion.20, 62, 84, 86 Children have been reported to have been given 1 to 1.5 mg safely, although both children subsequently died.50 A general pediatric dose of 50 μg/kg as a bolus is currently recommended.60 If the blood pressure improves, a maintenance dose (the successful bolus dose per hour) should be used. One should be sure to replace glucagon’s diluent, phenol, with normal saline or D5W.

Insulin and glucose should be considered in severe cases after other therapies fail. Insulin has a positive inotropic effect and can result in an increase in contractility.22 Animal studies have shown an improved sur-
vival when treating with insulin and dextrose infusion versus calcium, epinephrine, or glucagon. A case series was reviewed in severely poisoned adults treated with insulin and glucose after calcium channel blocker ingestions. All five patients were hypotensive, bradycardic, and not responsive to conventional therapies. Although the infusion rates of insulin were variable, all of the patients had a clinical improvement.

Amrinone has also been used to treat calcium channel blocker overdoses that are resistant to first-line therapy. Amrinone exerts its effect by inhibiting phosphodiesterase’s ability to break down cAMP, resulting in an increase in intracellular calcium. Amrinone should be used with caution because it also causes smooth muscle relaxation, which results in hypotension. The dosage that has been used in adults is an initial bolus of 1 mg/kg over 2 minutes, followed by a continuous infusion of 5 to 20 μg/kg/min. Dosing is not available for children.

In severe cases, an intra-aortic balloon pump can improve cardiac output. If life-threatening heart dysfunction occurs, a patient can be placed on cardiopulmonary bypass for a limited time. In one case report, a 2-year-old boy was placed on cardiopulmonary bypass for 3.75 hours after exposure to verapamil. The serum level of verapamil dropped while the patient was on bypass but subsequently rose when cardiopulmonary bypass was discontinued. Extracorporeal membrane oxygenation (ECMO) is also a viable option in severely poisoned children. The advantage of ECMO over cardiopulmonary bypass is that the patient can be maintained on ECMO for several days, which would allow time for drug clearance and recovery of cardiac function.

Asymptomatic patients should be observed after exposure to calcium channel antagonists. Children ingesting regular-release preparations can be observed for 4 to 6 hours; however, children with large ingestions or ingestions of sustained-release preparations should be observed for 24 hours because of potential delays in the onset of toxicity.

Case No. 4

A 4-year-old boy is brought to the emergency department 30 minutes after being found in his room with an open and half-empty bottle of Tylenol (acetaminophen, [APAP] 325-mg tablets). According to the mother, the bottle was just opened, and only two tablets had been removed. The child is active and playful but states that his stomach hurts. His vital signs and physical examination are not contributory.

ACETAMINOPHEN

Therapeutic doses (10–15 mg/kg) of acetaminophen (APAP) can be given every 4 hours in otherwise healthy patients. Most APAP is conjugated in the liver using glucuronidation and sulfation, resulting in the formation of inactive metabolites. A small amount (<5%) is excreted
directly in the urine, and 5% to 15% is oxidized by cytochrome P450, resulting in the formation of a highly reactive electrophile N-acetyl-p-benzoquinoneimine (NAPQI, Fig. 2). NAPQI binds to cells and induces oxidation of enzymes, resulting in cell death. To prevent toxic effects, electron donors, such as reduced glutathione, combine with NAPQI, rendering it harmless. When the body is overwhelmed by NAPQI and there are inadequate glutathione reserves, NAPQI is free to bind with hepatic cells, resulting in hepatotoxicity. Children who ingest > 150 mg/kg of acetaminophen are at the greatest risk for developing hepatotoxicity.

Early symptoms that occur during the first 24 hours after acute ingestion include decreased appetite, nausea, vomiting, or general malaise. The patient also can be asymptomatic, however. After 24 hours, chemical signs of hepatotoxicity occur, including increased levels of enzymes released from damaged hepatocytes, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and bilirubin. Signs of poor hepatic synthetic function, including an elevation in prothrombin time, also can occur. Forty-eight hours to four days after exposure, clinical signs of hepatotoxicity become apparent, including right upper quadrant

![Diagram of Acetaminophen Elimination](image-url)

**Figure 2.** Acetaminophen elimination.
pain, alterations in mental status, and jaundice, as well as marked elevation of AST and ALT levels. Renal failure also occurs during this time. Death occurs within 7 days of exposure. Patients can recover at any stage of toxicity. In those recovering patients, hepatic function returns to previous levels of function within 4 weeks of exposure.

Children seem to develop less hepatic toxicity than adults. It is unclear why fewer children exposed to acetaminophen do poorly, but some postulate that children have a greater glutathione supply to bind to the toxic metabolite NAPQI.49 Risk factors predisposing children to hepatic dysfunction include age younger than 10 years, a delay in seeking medical attention, late onset of symptoms, and multiple dosing of APAP during a febrile illness.68

Treatment includes early gastrointestinal decontamination using activated charcoal along with judicious use of the antidote, N-acetylcysteine (NAC). Activated charcoal is most useful when administered early, within 1 to 2 hours of ingestion, when it can obviate the need for antidotal treatment.

The need for treatment with the antidote NAC is determined using a serum APAP level obtained at 4 hours or greater after the time of exposure. The level is interpreted using the Rumack-Matthew nomogram.69 This nomogram predicts the risk for developing hepatotoxicity (defined as an AST or ALT > 1000 U/L) from a single APAP level at a given time. The potentially toxic line used in the United States is a full 25% lower than the line developed by Rumack and Matthew, therefore, only if the level is over the line is the patient at risk for hepatotoxicity.

N-Acetylcysteine limits the hepatocellular toxic potential of NAPQI by acting as a precursor to glutathione and by binding directly to performed NAPQI.14, 72 The dose is 140 mg/kg PO as a loading dose, followed by 70 mg/kg PO every 4 hours for a total of 18 doses. N-Acetylcysteine solution should be diluted to 5% and administered with a beverage such as cola to increase palatability. Antiemetics can be used in children who vomit, because a repeat dose is required if vomiting occurs within 1 hour of the dose. Studies demonstrate that NAC is maximally effective at preventing APAP hepatotoxicity if given within 8 hours of ingestion,73 but is useful after 8 hours and even very late after APAP exposure.29 A retrospective study of 100 patients with acute liver failure (defined as an AST > 1000 IU/L) found mortality rates to be significantly lower in patients who received NAC even late after exposure versus not treating late presenters with the antidote.29

Chronic acetaminophen toxicity is a significant problem in children owing to the multiple formulations and concentrations of acetaminophen available. Several cases of hepatotoxicity, resulting after children were given multiple high doses of acetaminophen, have been reported.32, 68 Parents should be made aware of the danger of acetaminophen formulation differences (e.g., drops versus syrup) and instructed to read product packaging carefully and consult a healthcare practitioner to avoid inappropriate dosing.

There are certain laboratory and clinical abnormalities that are pre-
dictive in adults of fulminant hepatic failure after acetaminophen overdose. Persistent acidosis is predictive of a poor outcome in many cases. Other indicators predictive for hepatic failure include increased serum creatinine, encephalopathy, and an elevated prothrombin time. These patients should also receive N-acetylcysteine therapy because this has been shown to be beneficial in reducing severe complications and mortality in patients who meet these criteria.

**SUMMARY**

Pediatric poisonings account for significant morbidity in the United States each year. Clinicians must keep current with advances in toxicology to be familiar with the latest recommended treatment regimens and antidotes. They also must be familiar in identifying toxidromes and important physical examination findings. Having these skills can enable the clinician to determine who is at risk for significant morbidity or mortality and to provide the appropriate medical care.

**References**

67. Quadrani DA, Spiller HA, Widder P: Five-year retrospective evaluation of sulfonylurea
68. Rivera-Penera JT, Guggig R, Davis J et al: Outcome of acetaminophen overdose in
pediatric patients and factors contributing to toxicity. J Pediatr 130:300–304, 1997
876, 1975
patient: Are we forcing gastric content beyond the pylorus? J Royal Soc Med 84:274–
276, 1991
71. Shannon M, Wernovsky G, Morris C: Exchange transfusion in the treatment of severe
72. Slattery JT, Wilson JM, Kalhorn TF, et al: Dose-dependent pharmacokinetics of acet-
41:413–418, 1987
75. Soylemezoglu O, Bakkaloglu A, Yigit S, et al: Haemodialysis treatment in phenobarbi-
77. Spiller HA, Krenzelok EP, Anderson BD: Sulfonylurea ingestion in children: Is an 8-
78. Spiller HA, Villalobos D, Krenzelok EP: Prospective multicenter study of sulfonylurea
79. Sporer KA, Khayam-Bashi H: Acetaminophen and salicylate serum levels in patients
80. Sugarman JM, Rodgers GC, Paul RI: Utility of toxicology screening in a pediatric
82. Tenenbein M, Cohen S, Sitar D: Whole-bowel irrigation as gastrointestinal decon-
urinary pH on the pharmacokinetics of salicylic acid, with its glycine and glucuronide
86. Wolf LR, Spadafora MP, Otten EJ: Use of amrinone and glucagon in a case of calcium
87. Wolfe TR, Cavavati EM, Rollins DE, et al: Terminal 40-ms frontal plane QRS axis as a
88. Yuan TH, Kerns WP, Tomaszewski CA, et al: Insulin and glucose as adjunctive therapy
89. Zaritsky AL, Horowitz M, Chernow B: Glucagon antagonism of calcium channel

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