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An Evidence-Based Review Of Single Pills And Swallows That Can Kill A Child

Just as you start your shift, a toddler is brought into the pediatric ED. An hour earlier he had ingested a single tablet of his grandmother's glipizide. The child is asymptomatic, shows no signs of distress, and is playful. On initial fingerstick his blood glucose is 95 mg/dL. The nursing staff reminds you that you have a full waiting room, the hospital has no beds, and the mother is eager to leave because the boy's older sibling will be getting home from school within the hour.

In the ED, clinicians routinely manage children with potential poisoning. Despite the frequency of such presentations, research pertaining to the management of children exposed to distinct toxins is limited. Numerous agents pose significant risks, even when a child ingests small amounts, such as a single pill or swallow.[1-3] (**Table 1, page 2**). Since it is beyond the scope of this article to address all of these agents individually, we will review a select number of common toxins and discuss their respective treatments.

Critical Appraisal Of The Literature

The medical literature contains a paucity of research pertaining to pediatric poisonings, and the majority of studies are retrospective, with cases series and case reports being the predominant type of review. Management of the poisoned child must be based on these reports as well as data from relevant studies in adults, isolated animal studies, and laboratory bench research. Since such scant evidence

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CME Objectives

Upon completing this article, you should be able to:

1. Identify specific drugs and chemicals that can be deadly to a child with a single swallow.
2. Discuss the proper management of children who ingest substances that are potentially deadly with a single swallow, including length of observation time.
3. Recognize the pathophysiology of specific deadly toxins commonly encountered in pediatric patients.
4. Identify the limitations of basic urine drug screens.

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makes it difficult for health care providers to make decisions regarding potentially poisoned children, the clinician must err on the side of caution when managing such cases.

Epidemiology, Etiology, And Pathophysiology

Poisonings in childhood are a common occurrence. In 2007, the American Association of Poison Control Centers reported 2,482,041 toxic exposures and 1239 resultant fatalities.[4] Mortality associated with these overdoses was less than 1%. Of these total exposures, 588,262 children were managed in a health care facility and 88,417 were admitted to a critical care unit (23.7% vs 3.6%). Poisonings are among the most preventable public health problems. The majority of exposures are accidental (83.2%) and occur in children under 6 years of age (51.2%). Children 18 to 36 months of age are at the greatest risk owing to excessive hand-to-mouth behavior and extensive exploration of the surrounding environment. Contributing to this risk are poor supervision by caretakers and their lack of awareness about what constitutes a true toxic ingestion. Childhood exposures are largely preventable if one recognizes the toxic potential of medications, household products, cosmetics, herbal products, and plants and keeps these agents out of the reach of children.

Predicting the pathophysiology of childhood poisoning is extremely difficult, since the toxicokinetics of an overdose cannot be predicted based on the pharmacokinetics of standard doses. Drug absorption is commonly delayed in toxic ingestions. In addition, the time to peak effect may be prolonged, and metabolic pathways may be saturated. Therefore, it is imperative that children be monitored for a sufficient length of time following exposure to certain agents. In addition, drugs taken inappropriately may display different pharmacologic effects from those seen when the drug is administered by the appropriate routes and in the proper doses. For example, when imidazoline decongestants are sprayed into the nose, they exhibit alpha-2-agonist activity and cause peripheral vasoconstriction; however, when ingested and absorbed systemically, these agents can cause central alpha-2-agonist activity that results in central nervous system (CNS) depression, hypotension, and bradycardia.

Table 1. Examples Of Single Pills And Swallows That Can Kill A Child

Alcohols
Ethylene glycol
Isopropanol
Methanol

Antidepressants
Cyclic antidepressants
Monoamine oxidase inhibitors

Antihypertensives
Clonidine
Diltiazem
Verapamil

Antimalarials
Chloroquine
Quinine

Benzocaine

Caustics
Ammonia fluoride/bifluoride
Boric acid
Disk batteries
Hydrofluoric acid
Selenious acid

Herbals
Camphor
Eucalyptus oil
Oil of wintergreen (methyl salicylate)
Pennyroyal oil

Hydrocarbons

Imidazolines
Naphazoline
Oxymetazoline
Tetrahydrozoline
Xylometazoline

Insecticides/Rodenticides/ Herbicides
Carbamates
Diquat
Lindane
Nicotine
Organophosphates
Paraquat

Opioids
Diphenoxylate
Methadone
Morphine
Oxycodone
Propoxyphene

Sulfonylureas
Acetohexamide
Chlorpropamide
Glimepiride
Glipizide
Glyburide
Tolazamide
Tolbutamide

Differential Diagnosis

Differentiating an unknown pediatric poisoning from another disease process may be extremely difficult. For example, a toddler who ingests a sulfonylurea hypoglycemic may present with profound hypoglycemia and changes in mental status. If the ingestion was unknown or unwitnessed, the child may need an extensive evaluation, including lumbar puncture, computerized tomography (CT) of the head, and blood work to rule-out other causes before the true diagnosis is made.[5,6] Children who are victims of medical child abuse or Münchausen syndrome by proxy is another possibility, since 34% of these cases are due to poison administration.[7] Numerous common pediatric presentations could be toxin-induced and may include gastrointestinal complaints, altered mental status, seizures, and cardiovascular compromise. The astute ED clinician will maintain a high index of suspicion for poisonings when managing children with puzzling presentations.

Prehospital Care

Research on the prehospital care of the poisoned child is limited. Prehospital care should focus on getting the child to the hospital and should not waste precious time in attempts at gastrointestinal decontamination. Syrup of ipecac, formerly a mainstay in the approach to pediatric poisoning, is no longer

recommended for routine management.[8] According to the American Academy of Pediatrics (AAP) Committee on Injury, Violence, and Poison Prevention "After reviewing the evidence, the AAP believes that ipecac should no longer be used routinely as a home treatment strategy, [and] that existing ipecac in the home should be disposed of safely."[9] On June 12, 2003, the FDA Nonprescription Drugs Advisory Committee met to discuss whether evidence for the benefits of syrup of ipecac was sufficient to outweigh the potential for misuse, abuse, and adverse effects associated with its status as an over-the-counter (OTC) drug. At the conclusion of the meeting, the committee recommended by a 6-to-4 vote that the FDA rescind ipecac's OTC status.[10] One published study found that the use of syrup of ipecac neither reduces resource utilization nor improves patient outcomes.[11]

The prehospital use of activated charcoal for pediatric poisoning is currently controversial, since its clinical efficacy has not been definitively demonstrated, and it is also premature to recommend its use in the home.[9] In a recent study, it was shown that 60% of children under age 3 drank less than one-fourth of the recommended dose of activated charcoal.[12] In another study, activated charcoal was rarely recommended in poisoning (6.4%) and was successfully administered in the home in only 65% of cases.[13] Charcoal administration is contraindicated when protective airway reflexes are inadequate unless the patient is intubated.[14] It is also contraindicated when corrosive substances (acids or alkalis) have been ingested; not only does charcoal provide no benefit in such cases, but it can also precipitate vomiting, obscure endoscopic visualization, and lead to complications if a perforation occurs and charcoal enters the mediastinum, peritoneum, or pleural space. Finally, charcoal should be avoided in cases of pure aliphatic petroleum distillate ingestion; hydrocarbons are not well adsorbed by activated charcoal, and its administration could lead to an increased aspiration risk.

ED Evaluation Of Specific Poisons

Pennyroyal Oil

Pennyroyal oil is an herbal product often used in tea, purported to treat infections of both the ear and the upper respiratory tract, the common cold, induce abortions, and to act as an insect repellent.[15-17] Although these claims are suspect, the inherent toxicity of this oil is not. The pure oil is derived from the plant species *Mentha pulegium* and *Hedeoma pulegioides*. It is readily available commercially and has a characteristic minty odor.[16] Pennyroyal's primary chemical component, pulegone, is metabolized by the liver into menthofuran, a directly hepatotoxic metabolite, using the cytochrome P450 system.[18] Furthermore, in a manner apparently independent of menthofuran, pulegone depletes glutathione stores,[19] without which the concentrations of menthofuran and other toxic metabolites increase and their hepatotoxicity is subsequently accentuated.[15,18-21] Ingestion of pennyroyal oil may result in hypoglycemia, elevated liver function tests, hyperbilirubinemia, hyperammonemia, and increased anion-gap metabolic acidosis. Other possible clinical effects include nausea, vomiting, abdominal pain, gastrointestinal bleeding, renal failure, pulmonary edema, coagulopathy, disseminated intravascular coagulation, dizziness, weakness, syncope, mental status changes, and seizures.[15,20,21]

In some reports, small doses of pennyroyal oil have led to serious toxicity, with 1 source reporting as little as 10 to 15 mL of pure pennyroyal oil causing death.[15] Coma and seizures have been reported with doses as low as 1 teaspoon (5 mL). The workup of a patient who presents to the ED after ingesting pennyroyal oil —whether it be a toddler who accidentally ingested it or an adolescent who intentionally drank it as an abortifacient— should include liver function testing, a complete blood count, a coagulation profile, and a basic chemistry panel at presentation and monitoring over the ensuing 24 hours.

Treatment of pennyroyal oil toxicity begins with good supportive care. Prompt administration of N-acetylcysteine has been advocated to reduce the degree of liver injury.[15] All children who have ingested pennyroyal oil should be admitted for observation and monitored for the development of hypoglycemia and/or hepatic dysfunction. Based on the reports from previous case reports, if after 20 hours, the patient shows no hepatic injury, no hypoglycemia, and no symptoms, N-acetylcysteine may be discontinued and the child may be discharged home.

Eucalyptus Oil

Eucalyptus oil is described as a pale yellow or colorless volatile oil distilled directly from the leaves and branches of any of the various species of eucalyptus. It has been used as a flavor additive in food, fragrance in soaps and perfumes, and as an insecticide and insect repellent. The pharmaceutical uses of this compound have included oral and inhalational administration for the treatment of cough and respiratory tract inflammation.[22] Eucalyptus oil is readily absorbed through the gastrointestinal tract, skin, and lungs, and it may act as a gastrointestinal irritant, often leading to vomiting, diarrhea, and abdominal pain.[22-26] CNS effects can include ataxia, dizziness, slurred speech, hypotonia, decreased deep tendon reflexes, and coma. Aspiration pneumonitis has also been reported.

There have been multiple case reports of dra-

matic toxicity from small doses of eucalyptus oil, with loss of respiratory effort and the gag reflex and consequently death. As little as 1 mL has caused transient coma, and death has resulted from ingestion of as little as 4 to 5 mL.[25]

The mainstay of ED treatment is supportive and symptomatic care. Intubation may be necessary. Gastrointestinal decontamination plays a limited role because eucalyptus is rapidly absorbed, and the possibility of CNS depression makes aspiration a risk. Based on the time course of previous case reports, if the child who has ingested eucalyptus oil has no signs or symptoms after a 4-hour observation period, the child may be safely discharged home.

Camphor

Camphor was originally derived from distilling the bark of the camphor tree, *Cinnamomum camphorum*, though today it is mostly made from the hydrocarbon pinene, a derivative of turpentine oil. This cyclic terpene compound has been used as a contraceptive, a muscle liniment, an aphrodisiac, an abortifacient, an analeptic, and an antiseptic. A variety of today's OTC topical preparations are used presumptively to soothe "fever blisters" and cold sores.[27] Its questionable benefit combined with its well-documented toxicity has led to criticism of its use and to a call for safer, alternative therapies.[28]

Clinical effects occur rapidly, generally within

Risk Management Pitfalls For Treating Children Who Ingest Potentially Toxic Substances

1. **"But they looked so good!"**
   Children may not demonstrate the signs and symptoms commonly seen in adults that may warn of impending cardiovascular decompensation. It is imperative that health care providers closely monitor the vital signs and mentation of potentially poisoned children.

2. **"It was an herbal product, and herbals are natural and safe."**
   A number of herbal products can be deadly to children even if small quantities are ingested. "Natural" cannot be equated with safe.

3. **"We monitor all overdoses for 4 hours."**
   Numerous toxins require monitoring for longer than 4 hours, such as the sulfonylureas and sustained-release calcium channel blockers.

4. **"The literature recommendations are too conservative regarding the length of observation time."**
   Studies pertaining to pediatric toxicology are limited. Many recommendations regarding the length of observation time are based on the available evidence. It is better to be too conservative and avoid adverse outcomes in young children as we await more comprehensive studies.

5. **"They are not moving, so they are not seizing."**
   Certain toxins can cause non-convulsive status epilepticus, such as with organophosphates toxicity. If non-convulsive status epilepticus is suspected, an electroencephalogram should be obtained.

6. **"Charcoal must be administered to every overdose patient."**
   Charcoal does not need to be administered in every case of poisoning. In fact, there are contraindications to charcoal administration such as the ingestion of caustics and hydrocarbons.

7. **"Ipecac is a mainstay of prehospital treatment."**
   Prehospital administration of syrup of ipecac is no longer recommended in the routine management of poisoning.

8. **"All caustics are the same."**
   There are numerous caustics on the market, and the astute health care provider should not only be concerned about local tissue damage, but also about systemic effects from such agents (ie, hydrofluoric acid).

9. **"The patient's oxygen saturations on a 100% non-rebreather are 98%, so he does not need to be intubated."**
   Adequate evaluation of the patient's neurologic status, ventilatory status, and gag reflex should guide the need for intubation. Too often clinicians may be complacent about the patients at risk for aspiration and carbon dioxide narcosis when a patient's oxygen saturation is adequate.

10. **"We do not need an x-ray to confirm the position of the nasogastric tube position; just push the charcoal."**
    The administration of charcoal prior to confirmation of tube position by x-ray is a dangerous practice.[75] Charcoal aspiration can lead to marked respiratory difficulty and significant long-term sequelae.[76,77] Proper placement of the nasogastric tube should be confirmed prior to administration of charcoal.

5 to 20 minutes of ingestion. Signs and symptoms of camphor ingestion are well-documented and generally reflect this agent's direct mucosal irritation and CNS effects.[29] The patient may experience oropharyngeal burning, abdominal pain, nausea, and vomiting. Most prominent and potentially devastating are camphor's CNS effects, which can result in coma and apnea. Camphor may cause pallor and lip cyanosis as well as stimulatory effects. Agitation, anxiety, hallucinations, hyperreflexia, myoclonic jerks, and seizures have been reported. Seizures may be the first manifestation of toxicity and are usually short-lived, requiring no active intervention.[30] Liver toxicity has also been reported and symptoms similar to those seen in Reye syndrome can occur, including vomiting, diarrhea, sleepiness, behavior changes, seizures, and coma.[31]

The diagnosis is clinical and based on exposure history and symptomatology. The strong smell of camphor on the child's breath or in the vomitus will be a clue to the correct diagnosis. Even in small doses, camphor has severe, even fatal, toxic effects. In 1983, the FDA recognized camphor's potential toxicity and mandated that the concentration of camphor in products not exceed 11%.[28] Prior to the FDA ruling, many toxic ingestions occurred from preparations containing camphor concentrations above 11% (eg, camphorated oil is 20% camphor). A recent, comprehensive review of the literature by Love et al looking at the toxic dose of camphor reinforced the conception that a dose of camphor of only as little as 1 teaspoonful (5 mL) can be fatal to a pediatric patient, even with today's current restrictions. For example, 4.6 mL of a 10.8% camphor solution (less than 1 teaspoonful) would deliver 500 mg of camphor. Deaths with ingested doses as small as 488 mg have been reported.[30] Fatalities generally have involved respiratory failure or status epilepticus. Generally, CNS symptoms present within 4 hours of ingestion.

Unfortunately, there is no specific antidote for camphor toxicity. In managing the child who has ingested camphor, the ED clinician should rely largely on providing supportive care and treating seizures as there is no specific antidote. Gastric decontamination is problematic given the rapid absorption of liquid camphor compounds. Camphor-induced seizures or respiratory depression would make gastric lavage and the administration of syrup of ipecac particularly dangerous. Activated charcoal has limited effectiveness and is not recommended.[32] In the case of seizures, benzodiazepines and, if necessary, barbiturates should constitute first-line therapy, with repeat dosing as necessary.[33] Asymptomatic patients should be observed for 4 hours after ingestion and may be discharged if no symptoms develop.

Methyl Salicylate/Oil Of Wintergreen

Methyl salicylate is commonly found in liniments, lotions, creams, and ointments designed to treat musculoskeletal pains. Oil of wintergreen contains 98% to 100% methyl salicylate. One teaspoon of oil of wintergreen (5 mL) is equivalent to approximately 7000 mg of salicylate, or 21.7 adult aspirin tablets.[34] One swallow of oil of wintergreen can be lethal for a young child.[35] In a number of reports, children have been found to have salicylate toxicity after ingesting oil of wintergreen.[36] A recent review of the literature documented that fewer than 5 mL of methyl salicylate has been implicated in the deaths of children under 6 years of age.[37] Because of its concentrated liquid form and quick absorption, oil of wintergreen poses a threat of severe, rapid-onset salicylate poisoning.

Children with salicylate poisoning typically present with a mixed picture of metabolic acidosis and respiratory alkalosis. Clinically, mild intoxication is associated with tachypnea, dehydration, tinnitus, lethargy, nausea, and vomiting. Severe poisoning can progress to coma, seizures, hypotension, encephalopathy, and cardiovascular collapse. Death usually results from ensuing pulmonary or cerebral edema.

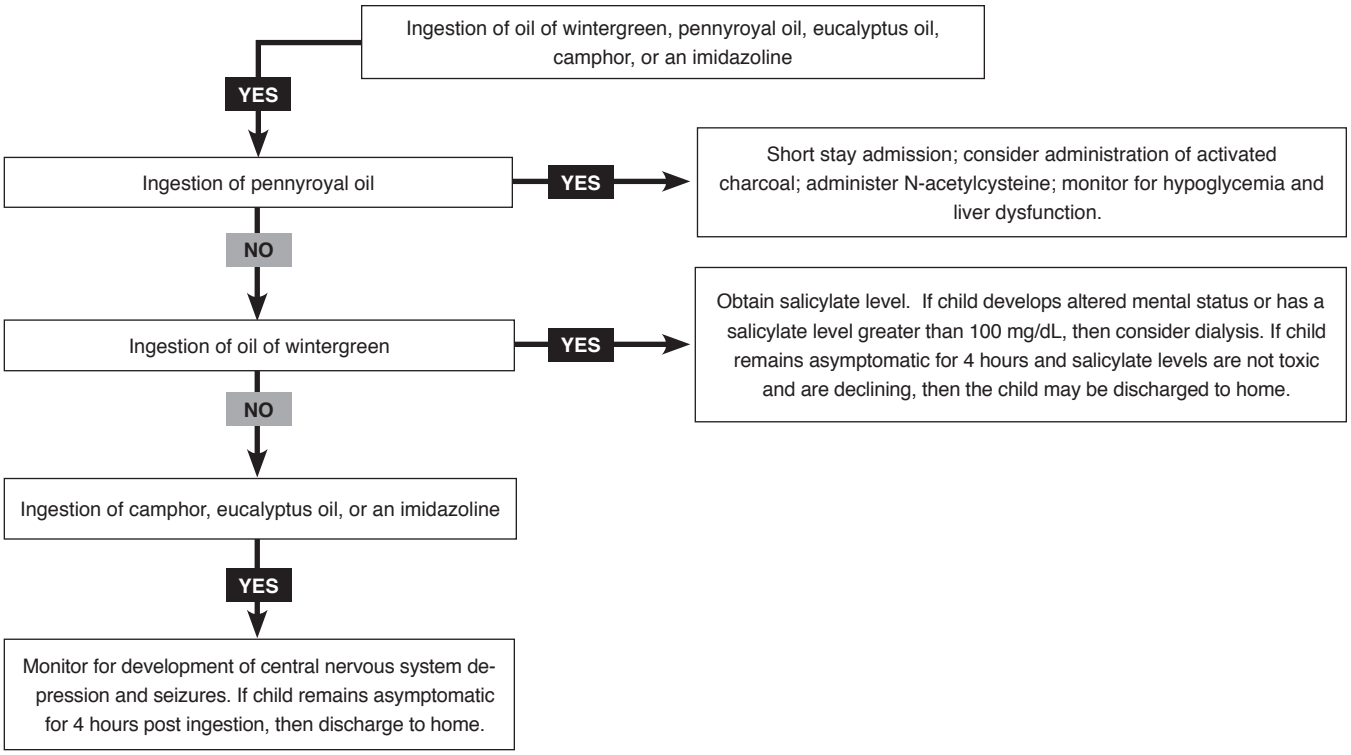
Treatment in the ED is primarily supportive. Serial salicylate and serum bicarbonate levels should be followed until improvement is documented. Fluid resuscitation should be begun to maintain adequate urine output. For symptomatic patients, a bicarbonate drip should be started to alkalinize the urine. The isotonic solution for the drip usually consists of placing 150 mEq of sodium bicarbonate along with 40 mEq of potassium in 1 liter of dextrose in water (D_5W). This solution should be delivered at a rate 1.5 times the usual maintenance infusion.

Since methyl salicylate oils are rapidly absorbed, signs and symptoms of toxicity may appear much earlier than those seen following the more typical ingestion of salicylate pills. Hemodialysis should be considered for children with serum salicylate concentrations greater than 100 mg/dL, refractory acidosis, neurologic symptoms, renal failure, or pulmonary edema.

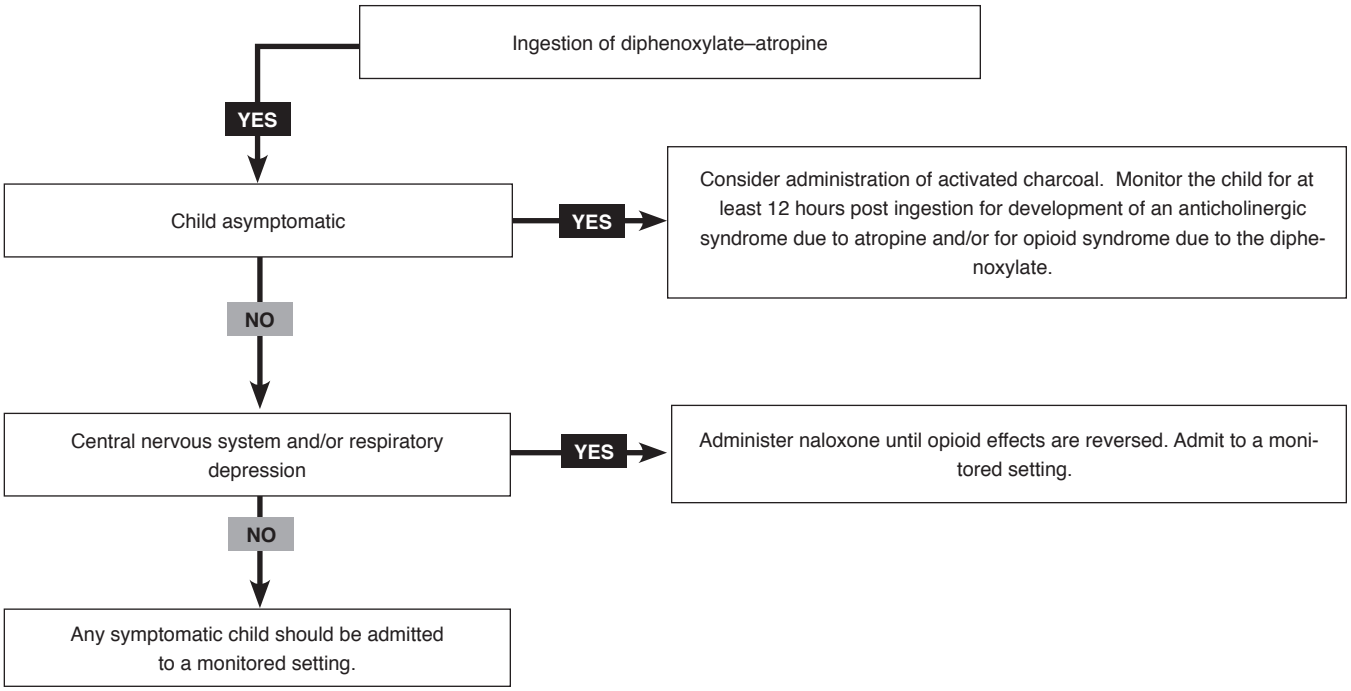
Diphenoxylate–Atropine

Diphenoxylate–atropine is a combination product used as an antidiarrheal agent that contains 2.5 mg of diphenoxylate and 0.025 mg of atropine sulfate per tablet. Diphenoxylate is structurally similar to meperidine and has the potential to cause opioid-related symptoms such as miosis, CNS depression, and respiratory depression. The combination of the opioid effects and atropine's anticholinergic effects may lead to decreased gut motility and delayed absorption. It has been recommended that children

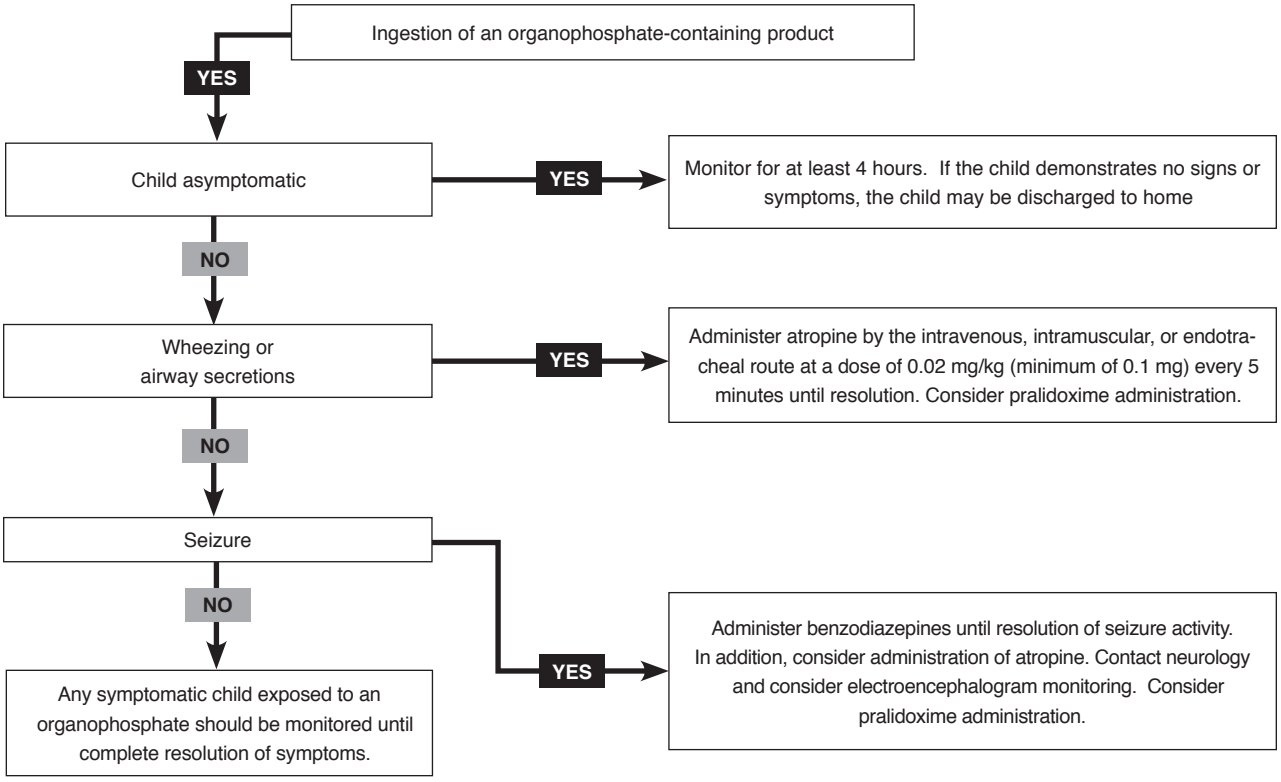
Clinical Pathway: Oil Of Wintergreen, Pennyroyal Oil, Camphor, Eucalyptus, Imidazoline Decongestant



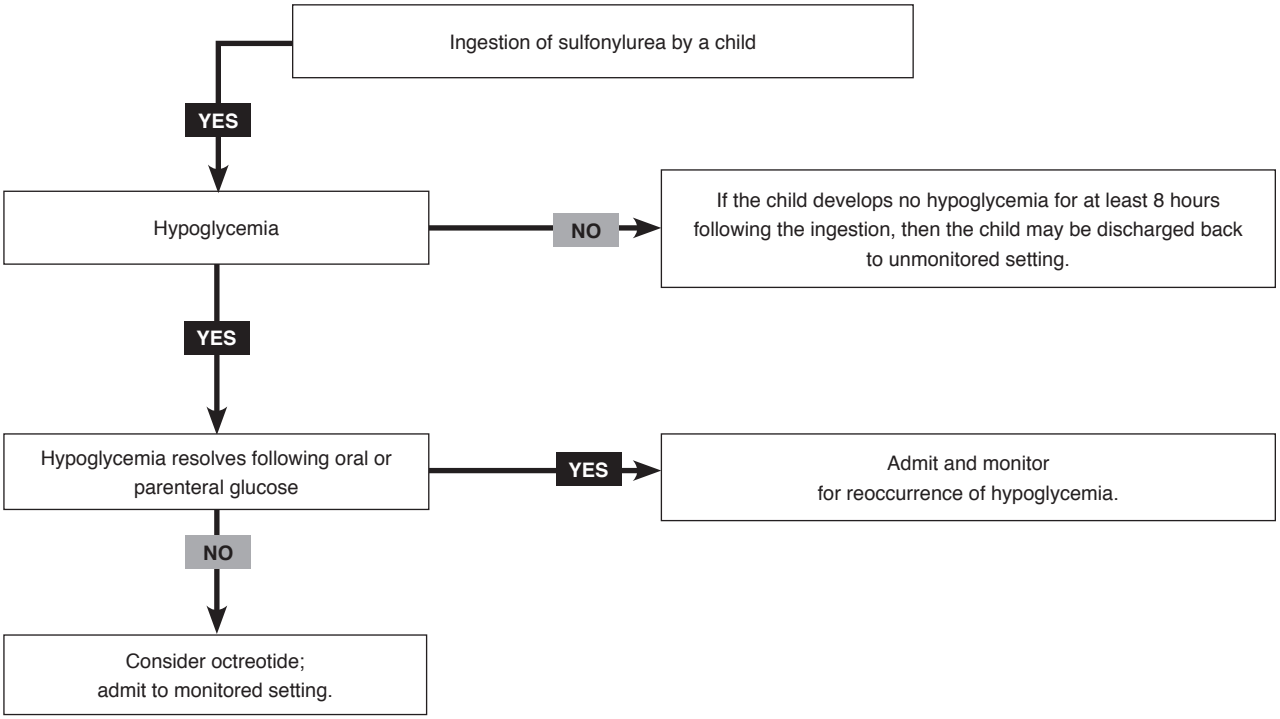
Clinical Pathway: Diphenoxylate–Atropine



Clinical Pathway: Organophosphates



Clinical Pathway: Sulfonylureas



who ingest diphenoxylate–atropine be observed for a minimum of 12 hours.[38] The reported clinical course of such ingestions in children varies between the opioid and anticholinergic effects and non-specific findings of drowsiness, irritability, and ataxia.[39] Though diphenoxylate–atropine has long been considered dangerous even in small amounts, a recent review of the available medical literature concluded that children who ingest a single tablet of diphenoxylate–atropine may be safely watched at home.[40] However, since the history may be inaccurate, all children should still be monitored in a health care setting following such ingestions. The emergency clinician may consider administering naloxone intravenously at (0.01 mg/kg) to reverse CNS and respiratory depressant effects; however, because of the possibility of delayed resedation with naloxone, any child who requires a reversal of CNS depression should be admitted for close monitoring.

Sulfonylureas

Sulfonylureas are oral hypoglycemic agents that facilitate the release of preformed insulin from the pancreatic beta-cells and are used in the treatment of diabetes mellitus. (**See Table 2** for a list of these agents.) An overdose of sulfonylureas can induce profound hypoglycemia owing to unregulated insulin release, and these agents can result in delayed hypoglycemia in children. Numerous reports in the literature describe the development of hypoglycemia in children who ingest a single sulfonylurea pill.[41] Sulfonylureas can result in delayed hypoglycemia in children. Young children who ingest sulfonylureas are at greater risk for hypoglycemia than are adults, not only because of their smaller size, but also because of their limited capacity to synthesize glucose and higher rates of glucose utilization. Signs and symptoms of hypoglycemia can vary significantly and include agitation, CNS depression, diaphoresis, dizziness, tachycardia, focal neurologic deficits, seizures, and coma.[42] In a prospective study of 185 children exposed to a sulfonylurea agent, 96% of those that developed hypoglycemia did so within 8 hours after exposure.[44] It has been recommended that a child who has ingested a sulfonylurea be observed for a minimum of 8 to 12 hours, with frequent blood glucose monitoring.[43,44] A recent review of the literature further supports the stance that ingestion of 1 or 2 tablets of a sulfonylurea can result in severe toxicity in children.[45]

If hypoglycemia develops, oral or parenteral glucose should be administered as needed to reverse it. Young children should be given doses of 2 to 4 mL/kg of D25, while adolescents can be given 1 mL/kg of D50. If the hypoglycemia becomes intractable to supplemental glucose, parenteral administration of octreotide should be considered.[46,47] Octreotide is a long-acting somatostatin analog known to suppress the secretion of insulin. In pancreatic beta-cells, octreotide inhibits a voltage-gated calcium channel via a G-protein reducing calcium influx and, in turn, insulin secretion. When given subcutaneously at 1 µg/kg, octreotide has been shown to reverse the hypoglycemic effects of sulfonylureas.[46,47]

Table 2. Pharmacokinetics Of Sulfonylureas

Drug	Time to Peak Effect (hr)	Half-Life (hr)	Duration of Action (hr)
Acetohexamide	3–4	6	12–18
Chlorpropamide	2–7	36	60
Tolazamide	4–6	8	12–24
Tolbutamide	3–4	28	6–12
Glimepiride	2–3	9	16–24
Glipizide	1–3	7	12–24
Glyburide	2–6	10	12–24

Hydrofluoric Acid And Ammonium Bifluoride

A single swallow of hydrofluoric acid or ammonium bifluoride or even a small cutaneous burn from a high concentration product can lead to rapid clinical deterioration in children.[48,49] Products containing hydrofluoric acid and ammonium bifluoride are sold as automotive cleaning products. Similar to other caustics, these 2 chemicals may rapidly corrode and penetrate the skin and mucous membranes. Ingestion may result in local mucosal caustic effects, nausea, vomiting, abdominal pain, and hemorrhagic gastritis. The absorbed fluoride ions may rapidly bind to available calcium and magnesium ions, decreasing the body's levels of these divalent cations. Hyperkalemia often follows, owing to potassium efflux into the extracellular space.[50]

All children who present with signs and symptoms consistent with hydrofluoric acid ingestion should be aggressively managed. Airway patency and adequate ventilation should be ensured. If necessary, endotracheal intubation should be performed early, before edema can lead to airway obstruction. Continuous cardiac monitoring with pulse oximetry is in order, and frequent neurologic checks should be made. The initial treatment of hypotension consists of intravenous fluids followed by vasopressors as needed. Pulmonary status should be monitored closely for clinical signs consistent with aspiration. Activated charcoal, syrup of ipecac, and gastric lavage are absolutely contraindicated in children who have ingested caustics. Initially, serum electrolyte levels including serial calcium, magnesium, and potassium levels should be measured hourly. The emergency clinician should obtain serial electrocardiograms to detect signs

of hypocalcemia (a prolonged Q–Tc interval) and hyperkalemia (peaked T waves). Large amounts of calcium and magnesium may be needed to normalize serum levels;[48] fluoride-induced hyperkalemia has been reported to be difficult to reverse. Early aggressive therapy with glucose, insulin, and/or sodium bicarbonate may be effective. In studies of fluoride toxicity in dogs, quinidine has been shown to be effective in preventing potassium efflux from cells and cardiotoxicity;[51] pending further human studies, however, this remains an interesting theoretical antidote.

Selenious Acid

Selenious acid is found in gun bluing products commonly used to clean and lubricate firearms. In addition to causing typical caustic injuries, it has the potential to cause multisystem organ failure. As little as 15 mL of selenious acid proved fatal when ingested by a toddler.[52] Initial management is primarily supportive and potential ingestions should be admitted for a short stay observation period

Organophosphate Insecticides

In young children, numerous pesticide products can potentially cause toxicity with a single swallow. Organophosphate insecticides are one such product. Studies have suggested that the clinical manifestations of organophosphate intoxication in children differ from those seen in adults, with a predominance of CNS effects in the former.[53] In a large, retrospective pediatric case review at one facility, organophosphate intoxication was associated with seizures (30%), coma (31%), and respiratory failure (35%).[54] Despite a relatively high incidence of such poisoning at this facility, one-fourth of the children referred for intensive care and delayed definitive care received this presumptive diagnosis.

Acetylcholine is a neurotransmitter found within the brain, autonomic ganglia, and postganglionic parasympathetic nervous system and at the skeletal muscle motor end-plate. Acetylcholine binds to and activates muscarinic and nicotinic receptors. The enzyme, acetylcholinesterase (AChE), regulates the activity of acetylcholine within the synaptic cleft. Organophosphates act as AChE inhibitors by binding at the enzyme's active site,[55] resulting in excessive acetylcholine stimulation. The onset, severity, and signs and symptoms of organophosphate poisoning vary widely (see **Table 3**), and both the amount and the route of exposure are factors in determining the clinical effects. Depending on these variables, the signs and symptoms can progress from gradual intoxication to cardiopulmonary collapse and death within minutes.

Atropine is the initial drug of choice in symptomatic organophosphate toxicity. It acts as a muscarinic-receptor antagonist and is useful in treating bronchoconstriction, bronchorrhea, tenesmus, abdominal cramps, nausea, vomiting, bradydysrhythmias, and seizures. Tachycardia is an effect of organophosphate poisoning and does not contraindicate atropine administration. The therapeutic end points for determining the appropriate dose of atropine are drying of respiratory secretions and resolution of bronchoconstriction. If copious secretions persist or bag-mask assisted ventilation is difficult, the dose must be increased. Since atropine does not antagonize the nicotinic receptors, it has no effect on the autonomic ganglia and neuromuscular junctions. For this reason, muscle weakness, fasciculations, tremors, and paralysis do not constitute indications for further atropine dosing. This drug does have a partial effect on the CNS and may be helpful in resolving seizures. Atropine can be administered by the intravenous, intramuscular, or endotracheal route at doses of 0.02 mg/kg (minimum dose of 0.1 mg) every 5 minutes until resolution of specific signs and symptoms resolve.

Pralidoxime chloride (2-PAM Cl,) reactivates AChE by exerting a nucleophilic attack on the phosphorus moiety. The result is an oxime–phosphate bond that splits from the AChE and leaves the regenerated enzyme. This reactivation is clinically most apparent at skeletal neuromuscular junctions, with less activity at muscarinic sites. Pralidoxime must therefore be administered concurrently with adequate atropine doses. Continuous intravenous infusion for organophosphate insecticide poisoning has been shown to be safe and effective.[56] In children, a loading dose of 25 to 50 mg/kg of pralidoxime should be followed by a continuous infusion

Table 3. Signs And Symptoms Of Acute Organophosphate Poisoning

Muscarinic Manifestations

Ophthalmic: Conjunctival injection, lacrimation, miosis, blurred vision, diminished visual acuity, ocular pain

Respiratory: Rhinorrhea, stridor, wheezing, cough, excessive sputum, chest tightness, dyspnea, apnea

Cardiovascular: Bradydysrhythmias, hypotension

Dermal: Flushing, diaphoresis, cyanosis

Gastrointestinal: Nausea, vomiting, salivation, diarrhea, abdominal cramping, tenesmus, fecal incontinence

Genitourinary: Frequency, urgency, incontinence

Nicotinic Manifestations

Cardiovascular: Tachydysrhythmias, hypertension

Striated muscle: Fasciculations, twitching, cramping, weakness, paralysis

Central Nervous System Manifestations

Anxiety, restlessness, depression, confusion, ataxia, tremors, convulsions, coma, areflexia

of 10 to 20 mg/kg/hr, depending on the severity of poisoning.[57]

Diazepam may improve survival and decrease seizure-induced morphologic damage to the cerebrum in organophosphate-poisoned patients. In the actively convulsing patient, the dose of diazepam should be adjusted to ensure seizure termination. In studies of seizures in animals, diazepam alone or in combination with atropine has been shown to protect the neuropathologic changes typically seen in the brain. Unfortunately, the cessation of convulsions might be due to organophosphate-induced muscle paralysis rather than to the therapeutic termination of seizure activity. Some authorities recommend bedside EEG's to differentiate these 2 possibilities.[58]

Benzocaine

Benzocaine is an anesthetic agent, commonly found in teething gels and is widely used both in the home and within the health care setting. However, in children who are at risk, such as those with glucose-6-phosphate dehydrogenase deficiency, even small amounts of benzocaine can cause methemoglobinemia. Such children may present with dizziness, nausea, somnolence, tachycardia, central cyanosis, low pulse-oximetry saturations, and shortness of breath. Classically, blood samples from children with methemoglobinemia are described as being the color of chocolate-agar. Treatment for methemoglobinemia includes supportive care and, for severe benzocaine poisonings, intravenous methylene blue at a dose of 1 mg/kg.

Imidazoline Decongestants

Imidazoline decongestants include drugs such as oxymetazoline, naphazoline, xylometazoline, and tetrahydrozoline and are found in numerous over-the-counter nasal sprays and eye drops. When utilized at recommended doses and routes of administration, these agents produce vasoconstriction by stimulating peripheral alpha-2 receptors on local vessels thereby decreasing nasal congestion and conjunctival injection. However, if topical imidazolines are absorbed systemically, as in childhood ingestions, they can also stimulate centrally located alpha-2 receptors.[59] This results in somnolence, hypotension, and bradycardia similar to the presentation following clonidine overdose. Ingestion of as little as 6 mL of these products has resulted in CNS depression, bradycardia, and hypotension, and these effects can be delayed for up to 4 hours.[60,61] There is no specific treatment for poisoning with these agents, and care is supportive. Both naloxone and atropine have been utilized with limited benefit.[62]

Diagnostic Studies

When evaluating a potentially poisoned child, there is no substitute for a thorough history and physical examination in solving this clinical mystery. Clues from the physical examination are generally more helpful than is an extensive laboratory workup that involves indiscriminate testing of blood or urine for multiple agents.[63] When used appropriately, diagnostic tests may be of help in the management of potential intoxication. If a specific toxin or even class of toxins is suspected, requesting qualitative or quantitative measurement of levels in the urine or blood respectively may be appropriate. Obtaining a basic metabolic panel is recommended for all symptomatic children with suspected poisoning.

When serum bicarbonate is found to be low, the emergency clinician should test for an elevated anion gap. The equation most commonly used to calculate the anion gap is: $[Na^+] - [Cl^- + HCO_3]$, which allows one to determine whether serum electroneutrality is being maintained. Although the primary cation (sodium) and anions (chloride and bicarbonate) are represented in the equation,[64] there are other contributors to this equation that are "unmeasured."[65] The normal range for the anion gap is accepted to be 8 to 16 mEq/L. Practically speaking, an increase in the anion gap beyond the normal range and accompanied by metabolic acidosis represents an increase in unmeasured endogenous anions (eg, lactate) or exogenous anions (eg, salicylates).[66] A list of the more common causes of this phenomenon are presented in the classic MUDPILES mnemonic. (**See Table 4.**) In evaluating the child who presents with an increased anion-gap metabolic acidosis, it is imperative that the clinician determine the cause of the acidosis. Many symptomatic poisoned children may have mild metabolic acidosis upon presentation due to the processes that lead to an elevated serum lactate. However, with adequate supportive care, including hydration and oxygenation, the anion-gap metabolic acidosis should improve. If the acidosis worsens despite adequate supportive care, persists, or fails to improve, the clinician should consider either toxins that form

Table 4. Potential Causes Of Increased Anion-Gap Metabolic Acidosis ("MUDPILES")

Methanol
Uremia
Diabetic ketoacidosis
Iron, **I**nhalants (ie, carbon monoxide, cyanide, toluene), **I**soniazid, **I**buprofen
Lactic acidosis
Ethylene glycol, ethanol ketoacidosis
Salicylates, starvation ketoacidosis, sympathomimetics

acidic metabolites (ie, ethylene glycol, methanol, or ibuprofen) or toxins that cause lactic acidosis by interfering with aerobic energy production (ie, cyanide or iron).[67-69]

Many clinicians regularly carry out urine drug screening in cases of suspected poisoning. However, many agents will not be detected on most such screens, including the drugs and chemicals noted previously. Urine drug screening is fraught with significant testing limitations, including false-positive and false-negative results. Urine drug immunoscreening assays use monoclonal antibodies to detect structural conformations found in drugs belonging to a specific drug classes, but unfortunately, these antibodies vary in their sensitivity and specificity.[70] Clinicians must be aware of the scope of drugs being detected and the sensitivity and specificity of the tests being ordered.[71]

Medicolegal Issues

Children who ingest potentially toxic substances must be watched for a sufficient period of time. The local poison control center can help define appropriate observation times for specific poisonings.[72, 73] During observation, the patient's neurological status and vital signs should be closely monitored. Premature discharge can lead to adverse events outside the health care system, which places the health care provider at potential risk for litigation.

The first tenet of medicine is to do no harm. This is particularly true with regards to the poisoned patient, when health care professionals are often too eager to administer antidotes without considering the potential complications of those antidotes. For example, the administration of activated charcoal to a child who has ingested a caustic substance can be damaging. Therefore, good supportive care is the mainstay of treating poisoned children.[74]

Cost- And Time-Effective Strategies For Treating Children Who Ingest Potentially Toxic Substances

1. **Avoid forceful administration of charcoal.**
   The forceful administration of charcoal in an asymptomatic child is rarely if ever indicated. For example, placing a nasogastric tube in an asymptomatic toddler to administer charcoal can potentially cause harm and takes up valuable time. Numerous techniques can be employed to encourage a child to drink charcoal voluntarily, such as mixing charcoal in a soft drink.
   Note: Charcoal administration following caustic ingestion is an absolute contraindication.

2. **Limit use of toxicology screening panels.**
   Toxicology screens provide information on a set number of chemicals. Numerous agents are not included, and false-positive and false-negative results can occur. For example, a child who ingests a fentanyl patch and presents with a pure opioid syndrome will have a negative "opioid" screen. This is because most "opioid" drugs screens test only for morphine, codeine, and heroin. If the emergency clinician relies solely on the drug screen to determine when to give naloxone, this child would not get an appropriate antidote to reverse the sedation.
   Note: Clinicians should trust in their diagnostic skills (based on the history and physical examination) rather than on toxicology screens to guide therapy.

3. **Know the indications and contraindications to antidotes.**
   Numerous antidotes are available (some tremendously expensive) and should not be administered indiscriminately. Clinicians should be aware of their specific indications and contraindications.
   Note: The vast majority of children with overdoses will recover uneventfully with supportive care alone.

4. **Call your regional poison specialists.**
   Poison centers and regional medical toxicology treatments centers are available 24/7 and can rapidly answer specific questions about possible poisonings. Health care providers should consider using these resources to obtain timely advice about management.
   Note: The entire United States now has 24/7 poison center coverage, and these centers can be contacted by calling 1-800-222-1222.

5. **Avoid unnecessary gastrointestinal decontamination techniques.**
   Gastric lavage is rarely indicated following acute poisoning. The indiscriminate practice of performing gastric lavage on all overdose patients is labor-intensive to health care providers, of no benefit to the vast majority of patients, and can result in harm (such as aspiration or esophageal perforation).
   Note: Gastric lavage following caustic ingestion is an absolute contraindication.

Summary

Numerous toxins cause significant adverse outcomes in children who ingest a single pill or swallow. Children should be observed for an appropriate length of time following ingestion of such agents, and their vital signs and mental status should be closely monitored. Good supportive care should be provided, and the administration of charcoal and specific antidotes should be weighed against the potentially adverse effects of such treatments. Münchausen syndrome by proxy should be considered in the differential diagnosis of children who have been poisoned. Despite challenges in the care of the poisoned child, most patients have a good outcome.

Case Conclusions

Despite being pressured to discharge the child who looked well 1 hour after ingestion, you correctly decided to observe him for the possible development of hypoglycemia. Four hours after he arrived, the child began to exhibit acute changes in mental status. Finger stick glucose was 35 mg/dL. While an intravenous line was being established, the child began to seize. An intraosseous line was placed, and glucose was administered, which led to the cessation of seizure activity. The child was admitted so he could be monitored, and he continued to show intermittent drops in blood glucose. After 48 hours, his condition had been child stabilized, and he had no recurrent hypoglycemia; he was discharged without sequelae.

References

Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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1. Which of the following oils are not considered toxic to a toddler following a single swallow:
a. Pennyroyal oil
b. Castor oil
c. Oil of wintergreen
d. Eucalyptus oil
e. Camphor oil

2. A child presents to the ED after having ingested an organophosphate. He was noted to be seizing by paramedics but stopped seizing en route to the hospital. He is now intubated and flaccid. The emergency clinician should contact the on-call neurologist and request which of the following:
a. Electroencephalogram
b. Lumbar puncture
c. MRI of the head
d. Nerve conduction tests
e. Brain death protocol

3. An x-ray should always be obtained prior to administering charcoal through a nasogastric tube in a child.
a. True
b. False

4. Charcoal administration to a child is absolutely contraindicated in which of the following ingestions:
a. Hydrofluoric acid
b. Sulfonylurea
c. Methyl salicylate
d. Diphenoxylate–atropine
e. Benzocaine gel

5. The minimum length of time a toddler should be monitored in the hospital setting after glyburide ingestion is:
a. 2 hours
b. 4 hours
c. 6 hours
d. 8 hours
e. 20 hours

6. **Which of the following medications is an option for the treatment of sulfonylurea-induced hypoglycemia unresponsive to intravenous glucose administration:**
   a. Atropine
   b. Pralidoxime
   c. Methylene blue
   d. Naloxone
   e. Octreotide

7. **Which of the following antidotes may be useful in reversing apnea in a child who has ingested diphenoxylate–atropine:**
   a. Atropine
   b. Pralidoxime
   c. Methylene blue
   d. Naloxone
   e. Octreotide

8. **Which of the following agents can result in methemoglobinemia:**
   a. Camphor
   b. Benzocaine
   c. Eucalyptus
   d. Oil of wintergreen
   e. Diphenoxylate–atropine

9. **Which of the following antidotes would be appropriate in a symptomatic toddler who ingested an organophosphate:**
   a. Pralidoxime
   b. Naloxone
   c. Methylene blue
   d. Octreotide
   e. Pyridoxine

10. **A typical urine drug screen can detect the majority of substances of which a single swallow can kill a child:**
    a. True
    b. False

Physician CME Information

Date of Original Release: March 1, 2010. Date of most recent review: February 10, 2009. Termination date: March 1, 2013.

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Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals & Objectives: Upon reading *Pediatric Emergency Medicine Practice,* you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical ED presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

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