Primary Care

Ingestion of Toxic Substances by Children

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INGESTION of a harmful substance is among the most common causes of injury to children less than six years of age. Fortunately, in most cases, the ingested agent has minimal or no clinically important toxic effect. Occasionally, however, such ingestion can be life-threatening or can even result in death. Although preventive measures have been remarkably successful in reducing the frequency and severity of poisoning in children, poisoning continues to occur and requires strategies for treatment and prevention that are safe and effective. In this review, I discuss the management of poisoning in children, with an emphasis on current guidelines for treatment.

EPIDEMIOLOGY

According to the Toxic Exposure Surveillance System of the American Association of Poison Control Centers, 1.08 million instances of ingestion of a toxic substance by a child less than six years of age were reported to poison centers in 1998.[1] However, the proportion of incidents reported to poison centers is estimated to be as low as 26 percent,[2] suggesting a true incidence of more than 4 million poisonings annually. According to the Consumer Product Safety Commission, approximately 85,000 young children were treated for poisoning in emergency departments in the same year (Schroeder T: personal communication), for a projected incidence of 450 per 100,000 population. The toxic substances most commonly ingested by children are listed in Table 1. Substances that are most accessible to children, such as cosmetics and personal care products, cleaning products, analgesics, and cough and cold preparations, account for 58 percent of the products listed.[1,3-5]

Table 2 lists the primary agents involved in deaths from poisoning among children from 1995 through 1998. Medications, both prescription drugs and over-the-counter drugs, were responsible for 52 percent of the deaths from poisoning. The distribution of responsible agents also reflects the common presence of such agents in the home rather than their inherent toxicity. On the basis of hazard-factor analysis (in which the number of episodes of major toxic effects or death is divided by the total number of reported cases of exposure to the substance, normalized to the rate of major toxic effects or death for all substances in the age group in question), the substances associated with the greatest risk of death to children include cocaine, anticonvulsant drugs, antidepressant drugs, and iron supplements.[6]

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TREATMENT

The ability to reduce morbidity and mortality among children who have ingested a toxic substance depends on prompt, appropriate intervention. A telephone call by the parent to a physician or poison center is often the first step in obtaining treatment. In most circumstances, after the substance and its toxicity have been identified and the amount ingested has been determined, treatment can be carried out at home without the need for referral to an emergency department.

In children brought or referred to a health care facility, assessment and stabilization of vital signs are the initial steps of treatment. Rarely, emergency management involves the administration of an antidote (e.g., naloxone after an overdose of an opioid drug) or measures to enhance the elimination of toxins that have already been absorbed (e.g., multiple doses of activated charcoal after an overdose of carbamazepine). Laboratory analysis of serum or urine should be guided by the substance ingested, its anticipated degree of toxicity, and the value of measuring these concentrations; there is rarely a need for toxicologic screening tests in children, since the ingested substance is usually known.[7]

The term "gastrointestinal decontamination" includes interventions that are used to prevent the absorption of an ingested toxin. Gastrointestinal decontamination has three distinct components: gastric emptying, administration of an adsorbent agent, and catharsis.

Gastric Emptying

In principle, if the contents of the stomach can be rapidly and completely evacuated after the ingestion of a toxin, the toxin will not have the opportunity to enter the small intestine, the main site of absorption. Consequently, the clinical effects of the poisoning can be mitigated. Gastric evacuation can be accomplished either by chemically induced emesis or by mechanical removal with a lavage tube.

Emesis is mediated in the central nervous system, either by direct stimulation of the chemoreceptor trigger zone in the area postrema or by gastric irritation mediated by vagal afferent fibers, with resulting stimulation of the vomiting center in the medulla.[8,9] Agents that have been used in children in the past for

TABLE 1. AGENTS MOST COMMONLY INGESTED BY CHILDREN LESS THAN SIX YEARS OF AGE, 1995 TO 1998.*

AGENT INGESTED	NO. OF CHILDREN
Cosmetics and personal care products	568,856
Cleaning products	500,791
Analgesics	354,722
Plants	322,991
Cough and cold preparations	278,460
Foreign bodies	256,263
Topical agents	234,997
Pesticides	164,277
Vitamins	151,871
Hydrocarbons	106,269

*Data are from Litovitz et al.[1,3-5]

TABLE 2. PRIMARY AGENTS INVOLVED IN FATAL POISONINGS AMONG CHILDREN LESS THAN SIX YEARS OF AGE, 1995 TO 1998.*

CATEGORY (NO. OF DEATHS REPORTED)	SPECIFIC AGENTS
Analgesic drugs (11)	Acetaminophen, ibuprofen, methadone, oxycodone, salicylates, morphine
Cleaning products (6)	Corrosives, fluoride-based solutions
Electrolytes and minerals (6)	Elemental iron
Hydrocarbons (6)	Gasoline, paint thinner, lamp oil
Antidepressant drugs (4)	Amitriptyline, imipramine, desipramine
Insecticides and pesticides (4)	Propoxur, organophosphates
Cosmetics and personal care products (2)	Ethanol, baby oil
Anticonvulsant drugs (2)	Carbamazepine, valproate sodium
Stimulants and illicit drugs (2)	"Crack" cocaine, heroin
Plants (2)	Cayenne pepper, pennyroyal tea
Foreign bodies (2)	Activated charcoal†
Sedatives and hypnotic drugs (2)	Promethazine, chloral hydrate
Cardiovascular agents (1)	Nifedipine
Tobacco (1)	Cigarette butts
Cough and cold preparations (1)	Phenylpropanolamine
Hormones and hormone antagonists (1)	Glipizide
Chemicals (1)	Diethylene glycol
Alcohols (1)	Ethanol
Gastrointestinal preparations (1)	Bismuth subsalicylate

*Data are from Litovitz et al.[1,3-5]

†Deaths were attributed to the administration of activated charcoal.

this purpose include parenteral apomorphine, copper sulfate, fluid extract of ipecac, hydrogen peroxide, and ipecac syrup. Among these, ipecac syrup has proved to be the safest, most reliable emetic agent; the others are contraindicated for the treatment of poisoning. Ipecac syrup contains two active alkaloids, cephaline and emetine. Both stimulate gastric sensory receptors linked to the vomiting center in the brain. In addition, cephaline acts at the chemoreceptor trigger zone. The primary advantage of ipecac syrup is its ease of administration by parents or caretakers.

Emesis usually begins about 20 minutes after ipecac syrup is given.[10] Eighty-two percent of children will vomit after a single 15-ml dose, and 99 percent will vomit after two doses.[11] The duration of vomiting is typically one to two hours. Guidelines for doses are presented in Table 3. Administration can be repeated if vomiting does not begin within 20 to 30 minutes. The administration of additional fluid after ipecac syrup does not appear to improve the efficacy of the agent.[12] The use of ipecac syrup should be considered in cases in which children have ingested a potentially toxic substance in the preceding hour. However, the efficacy of ipecac syrup, even under these circumstances, has not been proved.[10] Because uncontrolled vomiting will occur for at least one to two hours, ipecac syrup should not be administered after the ingestion of certain substances or under certain clinical conditions (Table 4).

Increasingly, both the safety and the efficacy of ipecac syrup have been questioned.[10] Although the drug has an impressive safety profile, there have been reports of adverse effects, including prolonged vomiting, sedation, Mallory–Weiss syndrome, gastric rupture, and fatal aspiration.[13,14] The efficacy of ipecac syrup, measured in terms of the elimination of ingested toxins or improvement in outcomes, also appears to be limited. In studies in animals, ipecac syrup removes 10 to 60 percent of an ingested substance; in clinical studies, within one hour after ingestion, a mean of 30 percent of a toxin can be recovered.[10] When administered 90 minutes or more after a toxic substance has been ingested, ipecac syrup has no identifiable benefit.[15] Saincher et al. have suggested that ipecac syrup is no longer beneficial between 5 and 30 minutes after the ingestion of a toxic substance.[16]

Gastric lavage is an alternative method of removing the contents of the stomach. For lavage to be performed properly, competence of the gag reflex should first be confirmed. Once properly restrained, the child should be placed in a left lateral decubitus Trendelenburg's position in order to limit the movement of the gastric contents into the duodenum and minimize the risk of aspiration.[17,18] A large-bore (24-to-32-French), single-lumen tube should be placed by an orogastric route. The proper placement of the tube is confirmed by the spontaneous or aspirated return of gastric contents or by auscultation of in-

TABLE 3. AGENTS USED FOR GASTROINTESTINAL DECONTAMINATION IN CHILDREN.*

AGENT	DOSE	POTENTIAL RISK
Emetic		
Ipecac syrup	Age 6–9 mo, 5 ml Age 10–11 mo, 10 ml Age 1–12 yr, 15 ml	Prolonged vomiting, aspiration
Adsorbent		
Activated charcoal	1 g/kg (maximum, 50–60 g)	Aspiration, tracheal instillation, constipation, vomiting
Cathartic		
Magnesium citrate in 6 percent suspension	4 ml/kg	Dehydration, hypermagnesemia
Sorbitol	1–2 g/kg	Hypernatremic dehydration
Polyethylene glycol (whole-bowel irrigation)	Age 9 mo–5 yr, 500 ml/hr Age 6–12 yr, 1000 ml/hr	Vomiting, bloating, abdominal cramping

*Doses of activated charcoal and sorbitol are expressed in grams per kilogram of body weight. The dose of magnesium citrate is expressed in milliliters per kilogram of body weight.

TABLE 4. CIRCUMSTANCES UNDER WHICH ADMINISTRATION OF IPECAC SYRUP SHOULD BE AVOIDED.

TOXIN OR CONDITION	POTENTIAL RISK
Substance that produces a rapid change in consciousness	Aspiration
Proconvulsant agent	Aspiration
Calcium-channel blocker, beta-blocker, digitalis, clonidine	Exaggerated vagal stimulation with gagging, severe bradycardia
Corrosive agent	Worsening of oral or esophageal injury
Low-viscosity hydrocarbon	Aspiration pneumonitis
Obtundation	Aspiration
Depressed gag reflex	Aspiration
Coagulopathy or bleeding diathesis	Gastroesophageal hemorrhage
Age of less than 6 mo	Toxicity of ipecac (safety not established)

sufflated air when a stethoscope is placed over the stomach. After placement of the tube, room-temperature aliquots of 10 to 15 ml of saline per kilogram of body weight are instilled through the tube and then aspirated. This process continues until the aspirated contents are clear. Volumes as large as several liters may be necessary to produce a clear aspirate.

As compared with induced emesis, gastric lavage has several advantages with respect to the treatment of poisoning. It can be performed promptly and completely, whereas emesis induced by ipecac syrup is associated with a delay in the onset of vomiting and a prolonged effect. The lavage tube also makes available a means of promptly administering an adsorbent to complete the decontamination process.

However, the safety and efficacy of lavage have also been challenged. Although there have been conflicting reports about whether lavage is superior[19,20] or inferior[21] to emesis, recent data indicate that the two methods of gastric decontamination have similar efficacy. When performed one hour after the ingestion of a toxic substance, lavage retrieves less than 30 percent of the toxin.[17] If not properly performed, gastric lavage has the potential complication of propelling toxins into the duodenum, thereby increasing the likelihood that the toxin will be absorbed.[21] The greatest risk associated with gastric lavage is the inadvertent placement of the tube into the trachea or a mainstem bronchus.[18,22] Other potential complications in children are esophageal injury, hypothermia, hyponatremia, and water intoxication.[17,18] Gastric lavage is contraindicated if protective airway reflexes are absent or depressed and if a low-viscosity hydrocarbon or a corrosive agent has been ingested.

Administration of Adsorbent

Adsorbents bind toxins, reducing the amount of free agent available for absorption into the gastrointestinal mucosa. There are several adsorptive agents that are useful in the treatment of poisoning: fuller's earth (for paraquat), potassium ferrocyanate (for thallium), milk (for fluoride), sodium polystyrene sulfonate (for lithium), and cholestyramine (for lindane). However, activated charcoal is the most broadly effective adsorbent available. The adsorptive capacity of activated charcoal is a function of its binding surface area, which ranges from 1000 to 2000 m^2 per gram.[23] The types of activated charcoal that have binding surface areas as large as 3000 m^2 per gram bind a greater proportion of the toxin than those with smaller binding surface areas.[24] Activated charcoal maintains its attachment to toxins through covalent binding and van der Waals forces.[25] It does not appear that clinically significant desorption of toxins from charcoal occurs. The most frequently encountered substances for which adsorption to activated charcoal is clinically negligible are alcohols, hydrocarbons, metals, and minerals. On the other hand, multiple doses of activated charcoal are effective in enhancing the elimination of certain toxins that have already been absorbed, such as theophylline, phenobarbital, and carbamazepine.[26]

When administered within one hour after ingestion, activated charcoal can reduce the absorption of toxins by up to 75 percent.[27] Optimal adsorption occurs when the ratio of charcoal to toxin is 10:1 or higher.[17,28] However, a fixed dose of 1 g per kilogram is recommended (Table 3). Activated charcoal is administered as a slurry. Additives, such as chocolate or fruit syrup, make charcoal more palatable without reducing its efficacy.[29] Because less than half of young

children will voluntarily drink activated charcoal quickly enough for it to work optimally, placement of a nasogastric tube may be necessary for its prompt administration.

The main hazards associated with the administration of activated charcoal are vomiting and aspiration, which can result in pneumothorax or empyema. Vomiting occurs in approximately 15 percent of patients to whom activated charcoal alone is administered.[27] Although activated charcoal is often described as inert, data from experimental studies indicate that aspirated charcoal can produce pulmonary parenchymal injury or bronchiolitis obliterans.[30,31] The instillation of charcoal into the lungs through the inadvertent placement of an orogastric or nasogastric tube into the trachea has had disastrous results, including death.[3,32]

Catharsis

Cathartic agents are administered after poisoning has occurred, to increase gastrointestinal motility and hasten the expulsion of the toxin or the toxin–adsorbent complex. There are three classes of cathartic drugs — stimulants, osmotic agents, and bulk-forming agents — but only osmotic agents (e.g., magnesium citrate and sorbitol) are used in cases of ingestion of toxic substances. Osmotic agents promote the retention of colonic fluid and activate constitutive, calcium-dependent nitric oxide synthase, which stimulates gastrointestinal motility through the release of cholecystokinins and alters gastrointestinal pH.[33-35] Magnesium citrate in a 6 percent suspension is given in a dose of 4 ml per kilogram (Table 3); larger doses do not produce more rapid results.[36] Doses of more than 0.5 g of sorbitol per kilogram will reliably produce diarrhea[37]; the recommended dose of sorbitol is 1 to 2 g per kilogram (Table 3). Sorbitol is not recommended for use in children less than one year of age.[17] Ingestion of anticholinergic drugs does not lessen the cathartic efficacy of osmotic agents.[38,39]

Although generally safe, the use of cathartic agents in children has occasionally been associated with adverse effects. Administration of sorbitol to infants has resulted in hypernatremic dehydration and cardiovascular collapse.[40,41] Cathartic agents also promote emesis. Magnesium-based cathartic agents have the potential to produce hypermagnesemia if given repeatedly or if given to children with renal disease.[42]

Whole-bowel irrigation has recently emerged as a means of gastrointestinal decontamination.[43] In this procedure, large volumes of solution are administered enterally until the rectal effluent is clear. Polyethylene glycol–electrolyte lavage solution has been formulated to prevent extensive absorption or secretion of fluid across the gastrointestinal mucosa. Whole-bowel irrigation is safe in children; volumes as large as 44 liters have been administered without ill effects.[44] Typical rates of administration are 500 to 1000 ml per hour, orally or by nasogastric tube (Table 3). The adverse effects associated with this procedure consist of vomiting, abdominal cramps, and bloating.

The place of whole-bowel irrigation in the treatment of poisoning in children has not been well established. Data suggest that the most important role of whole-bowel irrigation is as an intervention for the removal of substances that are poorly adsorbed to activated charcoal — for example, iron and lithium.[45]

Decisions about Management

There are few data from experimental studies and no rigorous clinical investigations in children to indicate that any means of decontamination produces an important clinical benefit. However, substantial indirect evidence supports the continued use of decontamination. For example, the clinical efficacy of activated charcoal was first demonstrated in 1831, when Touery drank an ordinarily lethal dose of strychnine along with charcoal and suffered no ill effects.[46]

In cases of ingestion in which the anticipated outcome is mild toxic effects or none, gastrointestinal decontamination should not be performed, since its risks may outweigh any benefit. Similarly, if the interval between ingestion and intervention is so long that it is unlikely that the toxin is still in the gastrointestinal tract, no intervention is warranted. The decision to begin decontamination should be based on clinical need, estimated according to the highest amount of toxin that may have been ingested; decontamination should not be considered a requirement for every ingestion.[10]

In cases in which it is undertaken, decontamination should begin as soon as possible. If the child is outside a health care facility, the clinician should determine whether ipecac syrup should be given in the home or whether the child should be referred directly to a health care facility. Usually, this decision is best made in consultation with a toxicologist or regional poison center. In cases in which serious toxicity is possible, decontamination can be initiated at home with ipecac syrup if there are no contraindications to its use. The decision about whether to refer a child to a treatment facility is based on the need for clinical assessment, additional decontamination, or close monitoring.

Rigorously performed studies have not found any substantial value associated with gastric emptying in the emergency department for the management of poisoning.[10,47] In large, prospective, randomized studies, the clinical outcomes of patients who underwent gastric evacuation before receiving activated charcoal were no better than the outcomes of those who received activated charcoal only.[48-50] Gastric emptying may, in fact, increase the risk of adverse outcomes after decontamination.[49,51] For children given ipecac syrup in the emergency department, as compared with children who do not undergo gastric emptying, the successful administration of activated charcoal is delayed and the stay in the emergency department is

20 percent longer.[52] Administration of ipecac syrup in the emergency department is therefore not recommended.[53,54] Gastric lavage has a similar lack of benefit and is not routinely recommended.[17]

In general, activated charcoal is the sole intervention needed to treat serious poisonings. A slurry consisting of activated charcoal and a flavoring agent should be given to the child. If it has not been swallowed within 20 minutes after ingestion of the toxin, activated charcoal should be administered through a nasogastric tube by trained personnel who are able to identify and treat any complications of the procedure.

Administration of a cathartic agent as the sole intervention for gastrointestinal decontamination is ineffective. Moreover, the combination of cathartic drugs and activated charcoal does not provide a better clinical outcome than activated charcoal alone after a poisoning.[33,38] Given their potential risks, cathartic agents should not be used routinely in the treatment of poisoning in children.[38,54] These agents remain potentially valuable in the treatment of poisonings that require multiple doses of activated charcoal, because they may prevent inspissation of the charcoal. Although whole-bowel irrigation has few proved indications, its primary role is in the treatment of poisoning with iron supplements, modified-release pharmaceutical drugs, or illicit drugs (e.g., cocaine or heroin).[55,56]

New approaches to the treatment of poisoning in children have begun to focus on identifying the smallest dose of activated charcoal needed for effective decontamination. The availability of activated charcoal with high adsorbency, which theoretically permits the administration of volumes of charcoal that are small enough to eliminate the need for a nasogastric tube, may allow this antidote to be kept in the home for administration by parents or caretakers.

PREVENTION

The reduction in the incidence of childhood poisonings in the past half-century has been dramatic. This reduction is largely the result of the combination of highly effective active and passive methods of intervention.[57] Important passive interventions have included the federal regulation of products and product safety and the introduction of child-resistant containers for drugs and other dangerous household products. Child-resistant containers have been particularly effective in reducing the incidence of death from the ingestion of prescription drugs by children.[58] Active interventions, which require a change in behavior by parents and caretakers, have included the safe storage of household products.[57] Finally, poison centers, which were established nearly 50 years ago, will continue to have a vital role in the management of poisoning in children by effectively reducing unneeded visits to the emergency department[59] and providing education about poisoning to the public.

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