Pediatric Toxicology: Emerging Trends

Maureen A. Madden¹

¹ Division of Critical Care Medicine, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, United States

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Address for correspondence Maureen A. Madden, MSN, Division of Critical Care Medicine, Department of Pediatrics, Rutgers Robert Wood Johnson Medical School, 778 Belvidere Avenue, Plainfield, NJ 07062, United States
(e-mail: maddenma@rwjms.rutgers.edu; maureen_madden@hotmail.com).

Abstract

Keywords

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Poisoning represents one of the most common medical emergencies encountered worldwide and is especially problematic for children, who constitute the population that is most vulnerable and at risk for unintentional and preventable poisonings. The scope of toxic substances involved in poisoning is very broad, requiring health care providers to have an extensive knowledge of signs and symptoms of poisoning, as well as specific therapeutic interventions and antidotes. New synthetic and herbal substances have emerged that have resulted in significant poisoning morbidity and mortality in the pediatric population.

Introduction

Poisoning represents one of the most common medical emergencies encountered worldwide and is especially problematic for children, who constitute the population that is most vulnerable and at risk for unintentional and preventable poisonings. Poisoning is a significant and persistent cause of morbidity and mortality in children and adolescents worldwide, with 3.9% or 45,000 accidental childhood deaths attributed to poisonings.¹ The scope of toxic substances involved in poisoning is very broad, requiring health care providers to have an extensive knowledge of signs and symptoms of poisoning, as well as specific therapeutic interventions and antidotes. There are multiple routes of exposure to toxic agents, with ingestions accounting for the majority of exposures.² A vast majority of children who ingest poisons suffer no harm. However, health care providers must recognize, assess, and manage those exposures that are most likely to cause serious injury, illness, or death and initiate appropriate management to minimize the physical injury that may occur. Those patients identified to be most at risk are likely to require management in an intensive care unit (ICU) setting.

Epidemiology

The 2012 National Poison Data System (NPDS), an annual report detailing poison exposure data in the United States, documented more than 2.2 million human exposures to

toxins with 93.7% having occurred in a residence. Children younger than 20 years of age accounted for 61.66% of all poisoning exposures, while children younger than 6 years comprised 48.4% of all exposures. There were 2,576 reported fatalities for 2012 in the United States. Although responsible for the majority of poisoning reports, children under 6 years of age accounted for only 21 (1.8%) fatalities, and the less than 20 year of age group comprised 6.1% (73) of the total fatalities reported. Despite having the majority of poison exposures managed safely at home, these untoward events resulted in a significant utilization of health care resources, with treatment in a health care facility necessary in 27% of all toxic exposures. Over 16.4% of all poisonings were admitted for management in the ICU.² Recent data suggest that emergency department evaluations and hospital admissions are increasing in pediatric ingestions despite significant interventions supported by the poison center movement.^{3–5}

The NPDS summary states that most poisonings can be classified as acute; accidental or unintentional; occur in the home; and involve children less than 6 years of age.² The primary goal of initial assessment is to discern which children are at clinical risk and treat them aggressively, when appropriate, while minimizing intervention in the population that has low risk of harm.

The substances involved most frequently in human exposure tend not to be the most toxic substances but rather the

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most readily accessible.^{2,4,6–8} The common agents involved in pediatric exposures are cosmetics/personal care products, analgesics, household cleaning substances, analgesics, foreign bodies/toys/miscellaneous, and topical preparations.² Toxic effects do not often occur with these agents, predominantly because children usually do not ingest amounts sufficient to produce toxicity. Substances ingested less frequently, but especially problematic due to potentially fatal effects in one dose to small children, are hypoglycemic agents, opioids, alcohols, antidepressants, theophylline, barbiturates, cocaine, iron, clonidine, and caustic substances.^{9–11} The highest number of hospitalizations, ICU admissions, and fatalities in pediatric poisonings occur with these agents. Poisoning may be acute or chronic, but the overwhelming majority of human toxic exposures were acute with unintentional ingestions outnumbering intentional ingestions.² Children may be poisoned by numerous mechanisms including ingestion, inhalation, dermal, envenomation, and ocular. Consistently, the most common of route of exposure is ingestion.

Although young children account for the majority of exposures, it is uncommon for poisoning in this age group to result in death. Most poisoning exposures in children younger than 6 years are unintentional and not associated with malicious or suicidal intent. Poisonings in this age group usually involve one substance, often nontoxic or minimally toxic. The amount ingested is usually small and children usually present for evaluation soon after ingestion.¹² Data support that the trends associated with pediatric poisoning are slowly changing, with an increase toward exposure to pharmaceutical products, both prescription and nonprescription medications.⁴ Reactions to toxic agents depend not only on the agent and the amount ingested, but also on the size of the child and the time lapse between exposure and treatment. Children have a higher metabolic rate than adults, thereby resulting in an increased risk of adverse effect.¹³

All age groups are vulnerable to iatrogenic poisonings, environmental toxins, inadvertent ingestion of substances improperly stored, and idiosyncratic reactions. The ingestion of a potentially poisonous substance typically represents a complex interaction of factors including the child, substance, and environment.¹⁴ Specifically, toddlers and adolescents demonstrate a bimodal high incidence of exposure to toxic substances.

Normal developmental characteristics of children aged 1 to 5 years increase the likelihood of ingestions in this age group. Toddlers are newly mobile, curious, and anxious to explore their environment through reaching, climbing, and tasting, yet too young to know what is dangerous.¹⁵ There are three prominent reasons that typically put children at risk for toxic exposure: improper storage of substances in the home, children spending more time in other people's homes, and caregiver distraction.¹⁶ Other factors that put children at risk are a chaotic or stressful home environment, an unemployed or single parent household, parental illness or disability, accessibility to toxic agents, lack of proper supervision, grandparent visiting or caretaking, and desire to imitate adult behavior.^{8,17,18}

Adolescents' exposure to poisons differentiates them from younger children. Most adolescent ingestions occur in the home and are intentional rather than accidental. Adolescent ingestions frequently involve multiple substances, are a result of either suicide attempts or substance abuse, and commonly a delay occurs between the ingestion and when medical attention is sought. This is why intentional exposures are more likely to be associated with worse outcomes. Adolescents also have increased access to illicit and licit drugs and alcohol than younger children.

The use of designer and over-the-counter drugs has exploded, due to internet and social media descriptions.² Over-the-counter medications, particularly those containing dextromethorphan (known as "dex") have become popular recreational drugs among adolescents in addition to the emergence of numerous synthetic compounds and herbal agents (→ **Table 1**). These emerging substances are being used for recreational purposes without any knowledge of their potential harmful effects. These new substances have resulted in significant poisoning morbidity and mortality in the pediatric population producing acute and chronic toxicity as well as numerous deaths.

It is imperative for health care providers not only to be knowledgeable about traditional causes of poisoning but also aware of emerging poisons, fads, and new evidence about pediatric poisonings.¹⁵ Despite the relative infrequency of serious clinical toxicity resulting from an exposure, some children will become seriously ill and require interventions and supportive care.

Spice, a synthetic cannabinoid, first marketed as a "herbal" product, and bath salts, synthetic cathinone stimulants that mimic cocaine-type effects, are the most well-known drug trends.^{19,20} Both types of products were marketed and sold in gas stations and over the internet without any age restrictions in the United States before the Drug Enforcement Agency banned possession and sale of the chemicals that were utilized in the production of these agents.²¹

A whole new line of synthetic and herbal products continue to emerge, marketed along the same pathways as spice and bath salts. The constantly changing names and product chemical contents create a challenging environment for health care professionals to understand the products being utilized. There are limited studies to track potency or side effects because of the nature of the constantly changing chemicals and ingredients. Many individuals are utilizing alternative or synthetic drugs under the false belief that they are legal substitutes for popular street drugs and are therefore safe. The manufacturers of these synthetic drugs change the chemical content, change the names, and mark the packaging as "not intended for human consumption" or "research chemical," which does not deter individuals from using them.^{22,23} These emerging drugs are also more readily available through legitimate sources such as convenience stores, gas station markets, gardening/plant stores, and via the internet. The rapid rise in their popularity can be attributed to widespread internet accessibility and information.

The internet is also implicated in the ingestion of everyday spices, such as cinnamon and nutmeg, under the guise of a

Table 1 Common substances, signs of toxicity, and treatment

Name	Street name	Exposure route	Clinical presentation	Management/treatment
Ethanol/ethyl alcohol	Slimming	Vodka-soaked tampon inserted vaginally or rectally	Acute ethanol intoxication can cause the following: central nervous system depression, mild vasodilatation leading to a modest decrease in blood pressure, flushed skin, urticaria hypothermia, tachycardia, myocardial depression, variable pupillary response, respiratory depression, decreased pulmonary secretion clearance, diuresis, loss of behavior inhibitions, hypoglycemia, loss of fine motor control	Supportive care; correction of dehydration and hypoglycemia
	Butt chug	Rectal use of a beer bong for alcohol enema		
	Boozy bears (drunk gummies; rummy bears)	Eating alcohol-soaked gummy candies		
	Eyeball shots (vodka eyeballing)	Pouring liquor directly into eye sockets		
	Liquid hand sanitizer	Oral ingestion		
	Smoking alcohol	Inhaling vaporized alcohol		
	Snorting alcohol	Snorting alcohol up to nostrils		
	Alcohol infused food substances	Ingesting food products, whipped cream, cupcakes, fruit popsicles		
Synthetic cannabinoid receptor agonists	Spice, K2	Smoked, ingested	Agitation, anxiety, paranoia, tachycardia, hypertension, muscle spasms, seizures, dystonia, diaphoresis, tremors, psychosis	Aggressive supportive care; benzodiazepines (lorazepam) for agitation and seizures; electroencephalography if seizures are present or unexplained altered mental status; serial cardiac enzymes if chest pain present
Synthetic cathinone stimulants				
Mephedrone, methylene, methylenedioxypyrovalerone	Bath salts, ivory wave, vanilla sky, meow meow, bliss	Sniffing, snorting, injection, rectal, oral	Agitation, insomnia, irritability, dizziness, depression, paranoia, delusions, seizures, panic attacks,	Supportive care: intravenous fluids and benzodiazepines
Dextromethorphan	DXM, Robo, Robotripping	Oral or ingesting	Nausea, vomiting, nystagmus, dilated pupils, rash, ataxia, diaphoresis, fever, hypertension, bradypnea, urinary retention, diarrhea, tachycardia, hyperthermia, toxic psychosis, coma	Administer activated charcoal if presents less than 1 h after ingestion; naloxone may be administered for sedation and coma; evaluate for toxic effects of co-ingested drugs
Salvia (<i>Salvia divinorum</i>)	Maria pastora, magic mint, diviner's sage, Sally-D, sage of the seers	Leaves; chewed, sublingual, smoked	Subtle high to vivid psychedelic experience including hallucinations, slurred speech, incoordination, psychomimetic	Supportive care, symptoms short lived up to 3 h, benzodiazepines if combative

(Continued)

Table 1 (Continued)

Name	Street name	Exposure route	Clinical presentation	Management/treatment
Energy drinks, caffeine and supplements	Red bull, monster, rock star, 5-h energy, AMP	Oral	Contains caffeine and other energy promoting substances (e.g., guarana) that result in central nervous system excitation, seizures, tachycardia, ventricular dysrhythmias; hypokalemia, hyperglycemia, vomiting, death	Benzodiazepines for agitation and seizures; dysrhythmias treated with β -adrenergic blockers or lidocaine; correction of hypokalemia; concomitant ethanol intoxication is a concern and requires supportive care and any other symptoms need to be addressed; Ondansetron for vomiting; hemodialysis if indicated
Desomorphine	Krokodil, crocodile	Injected into vein or skin	Home-manufactured synthetic heroin product that is highly impure, contaminated with various toxic and highly corrosive byproducts; highly addictive; injected for approximately a 90-min high, more intense than heroin; causes serious damage to veins and soft tissue, infections rapidly followed by gangrene and necrosis turning the skin gray, green and scaly	Krokodil gets its name from the scaly, gray-green dead skin that forms at the site of an injection. The flesh destroyed by krokodil becomes gangrenous, and, in some cases, limb amputation has been necessary to save a user's life
Nutmeg (<i>Myristica fragrans</i>)	Nutmeg	Dried powder; usually ingested	Up to a tablespoon may produce mild euphoric effect; greater amounts cause "atropine-like" symptoms: dry mouth, facial flushing, palpitations, hypotension, vertigo, nausea, extreme thirst, headache, hallucinations, seizures	Symptoms usually resolve within 24–48 h, supportive care for agitation, hypotension, and other symptoms
Cinnamon	Cinnamon challenge	Ingesting and aspirating dry cinnamon	Caustic sensation in the mouth causes coughing, choking, gagging; aspiration may result in pulmonary inflammation, bronchospasm, aspiration pneumonia, pulmonary scarring	Supportive care

“challenge” to individuals, who attempt the “challenge” for the reported intoxicating effect of the spice.^{24,25} Equally alarming are the new forms of ethanol exposure routes.^{26,27} Young adults are devising ways to use ethanol without ingesting or actually drinking it. They are still becoming intoxicated, since the delicate tissues of the vagina, anus, and eyeball absorb alcohol readily, but without the knowledge that these routes may result in injury or overdose. The prevalence of these trends is unknown but there are increasing numbers of YouTube videos on how to take the “challenge” or demonstrating new ways to “drink” alcohol. The addition of energy drinks, typically containing caffeine and other energy producing supplements, either ingested alone or in combination with alcohol, has created another circumstance where people do not comprehend the risks.^{22,28–31}

Evaluation, Decontamination, and Supportive Care

The cornerstone of treatment comprises a thorough evaluation of the poisoning exposure, careful assessment of the patient, and the application of basic supportive care as indicated. The opinion expressed by Henretig¹⁴ in 1994 holds true even today that the most important aspect of managing a child with a potential poisoning exposure is meticulous attention to detail in both routine and intensive supportive care. When a toxic ingestion is suspected, initial management is focused on stabilizing the patient's condition utilizing the priorities of resuscitation, the ABCs (airway, breathing, and circulation), and securing rapid intravenous access. The poisoned patient often represents an acute-onset emergency with a broad range of multiorgan system pathophysiology. Attention to the potentially urgent or emergent concerns related to adequacy and stability of the respiratory system

and circulatory system should supersede all other concerns. Supportive care includes monitoring to ensure airway protection especially in the obtunded child, maintaining adequate oxygenation and ventilation, correction of any hypotension or hypertension, correction of acid–base or electrolyte disturbances, monitoring for dysrhythmias, rhabdomyolysis, and awareness of current medical problems and medications.

In cases of poisoning, the letters D, E, and F can extend the initial stabilization mnemonic to include disability assessment, drugs, decontamination, electrocardiogram (ECG), and fever. These are an important focus in the assessment and management of toxic exposures. The disability assessment would include a brief neurologic examination, such as level of consciousness, pupillary size, and reactivity; drug therapy is the potential empiric use of items such as oxygen, dextrose, and naloxone. A bedside assessment of serum glucose is indicated for any patient who presents with altered mental status or lethargy and for any patient exposed to agents that might cause hypoglycemia. Hypoglycemia is one of the most easily detected and treatable effects secondary to toxic exposures. Decontamination methods are employed for urgent ocular and dermal decontamination and consideration for gastrointestinal decontamination options. ECG is a valuable tool for diagnostic and prognostic clues, especially with agents that are known to cause recognizable ECG changes such as calcium channel blockers, tricyclic antidepressants, and antidysrhythmics. The letter F represents interventions targeted at temperature regulation to facilitate normothermia and institute emergent cooling techniques for hyperthermia.

Once the ABCs have been adequately assessed and stabilized, a brief, focused physical examination should be performed, which includes reassessment of vital signs and vital

Table 2 Table of toxidromes

Toxidrome	Symptoms	Causative agents
Sympathomimetic (stimulant)	Restlessness, excessive speech and motor activity, tremor, insomnia, tachycardia, hyperthermia, mydriasis, hallucinations	Amphetamines, phencyclidine, cocaine, attention deficit and hyperactivity disorder medications, cathinones, other stimulants
Sedative/hypnotic	Sedation, confusion, delirium, hallucinations, coma, paresthesia, diplopia, blurred vision, slurred speech, ataxia, nystagmus	Barbiturates, benzodiazepines
Opioids	Altered mental status, miosis, unresponsiveness, shallow respiration, bradypnea, bradycardia, hypotension, decreased bowel sounds, hypothermia	Narcotic agents, heroin, clonidine
Anticholinergic ^a	Fever, flushing, tachycardia, urinary retention, dry skin, blurred vision, mydriasis, decreased bowel sounds, ileus, myoclonus, psychosis, hallucinations, seizures, coma	Cyclic antidepressants, antihistamines, scopolamine, certain mushrooms, over-the-counter sleep preparations
Cholinergic ^b	Salivation, lacrimation, urination, defecation, gastrointestinal distress (diarrhea), emesis, bradycardia	Organophosphates, insecticides, certain mushrooms, black widow spider bites

^aMnemonic: Hot as a hare, dry as a bone, red as a beet, mad as a hatter.

^bMnemonic: SLUDGE.

Table 3 Antidotes to common poisons

Poison	Antidote
Acetaminophen (Tylenol/paracetamol)	N-acetylcysteine
Anticholinergics	Physostigmine
Anticoagulants	Vitamin K1, protamine
Benzodiazepines	Supportive care, flumazenil ^a
Botulism	Botulinum antitoxin, botulism immune globulin
Beta blockers	Glucagon
Calcium channel blockers	Calcium, glucagon
Cholinergics	Atropine pralidoxime in organophosphate overdose
Carbon monoxide	Oxygen, hyperbaric oxygen
Cyanide	Amyl nitrate, sodium nitrate, sodium thiosulfate
Digoxin	Digoxin fab antibodies (Digibind)
Iron	Deferoxamine
Isoniazid	Pyridoxine
Lead	British anti-lewisite, ethylenediaminetetraacetic acid, dimercaptosuccinic acid
Methemoglobinemia	Methylene blue
Opioids	Naloxone (Narcan)
Sulfonylureas (oral hypoglycemics)	Dextrose, octreotide
Toxic alcohols	Ethanol infusion, dialysis
Tricyclic antidepressants	Sodium bicarbonate

^aFlumazenil may precipitate seizures when used with patients who are chronic benzodiazepine users or in situations including tricyclic antidepressant overdose.

organ functions. The clinical examination needs to be focused on the central and autonomic nervous system, eye findings, changes in skin, oral and gastrointestinal mucosa, and odors. These are the areas most likely affected in toxic syndromes.

The secondary phase of evaluation and detoxification provide identification of clinical signs and symptoms that can help with the identification of the toxin and initiation of appropriate treatment or antidote. The goal of identification is to determine which patients are at risk for toxic effects. Approximately 40% of children who present for evaluation of a suspected poisoning exposure have not been exposed to the suspected toxin.³² So it is imperative to look for clinical indicators of poisonous ingestion prior to initiating treatment. For the vast majority of patients, the clinical condition rather than the specific ingredients of the ingestion directs the management. This approach does not preclude treating specific toxins or toxidromes, but rather reinforces the concept of basic clinical management and resuscitation techniques.

The clinical syndromes, called toxidromes, comprise a constellation of signs and symptoms that suggest a specific class of poisoning. Toxidromes integrate initial vital signs, mental status changes, symptoms, clinical findings, and laboratory results to help identify the toxin and allowing initiation of appropriate treatment in a timely manner.^{33,34} The most common toxidromes are sympathomimetic, sedative/hypnotic, opioid, anticholinergic and cholinergic (►Table 2).

A thorough history is necessary whenever there is a suspicion of toxic exposure, including type and quantity of ingestion if known, the possibility of multiple agents, the time of ingestion, lapse of time to presentation, any history of vomiting, choking, coughing and/or alteration in mental status, and any interventions performed prior to presentation. In addition, past and current medical history including any chronic medications must be obtained. A complete physical examination and reassessment of the child must be performed.

In the poisoned child, after appropriate stabilization, there may be a role for laboratory testing. The most beneficial initial laboratory tests are basic assessments not uniquely indicated for the poisoned patient such as routine chemistries, blood gas analysis, and serum osmolality (to evaluate pH disturbances, anion, and osmolal gap).³⁵ There is limited value in routine toxicology screening of most poisoned patients especially for a witnessed ingestion of a single agent. Toxicology screening can be useful to help confirm toxicological diagnosis for a patient with an unknown ingestion, inform decision making regarding specific management interventions such as administration of specific antidotal therapy, and monitoring response to therapy. Regardless of the substance ingested, serum and/or urine toxicology screens may be necessary to evaluate for the possibility of additional unknown agents or as an adjunct modality in a child with an unknown diagnosis or to confirm a toxic exposure where abuse or neglect may be involved.³⁶ Although most poisonings are managed with

supportive care alone, specific antidotal therapy is indicated in specific cases. The role of antidotes is limited to a minority of drugs and the indications for and choices of antidotes are similar for children and adults with some additional considerations (–Table 3). For many poisons, the clinical effects and toxicity correlate with the serum level of the drug. Management is often dependent on the data provided by quantitative assays for these cases.

The use of specific therapies, including antidotes and enhanced elimination techniques, is limited to cases when the expectation that a defined benefit outweighs the risk of the procedure is reasonable. There are limited data and information to distinguish lethal concentrations of certain drugs and toxic substances in children and the newer or limited-use therapies have limited pediatric experience.³⁷ Therefore, indications for the use of interventions in children may be different from those in adults.

When the name or the amount of a poison ingested is unknown, the incident is not witnessed, or the history is vague, the child is treated as though a harmful substance was consumed. When there is incomplete or inaccurate information about the toxic exposure, the physical examination, laboratory tests, and potentially a toxicological screen should be used to guide management. If elements of the history provided are contradictory or questionable, it is especially important to evaluate for the possibility of trauma as a cause of the patient's clinical condition. Physical examination focuses on the potential for unreported traumatic injuries, as well as significant details related to the ingestion and clinical presentation that suggests a toxidrome. The local poison control center can provide details regarding the indications and guidelines for use of antidotes. Further management is guided by the principles of stabilization, diagnosis, and treatment simultaneously. Once the substance is correctly identified, the management can be modified to specifically implement treatment for that toxin.

Reducing the life-threatening potential of an ingested substance is an early treatment goal and depends upon the effectiveness of the several different treatment modalities described. Further management focuses on gastrointestinal decontamination through decreasing absorption of the toxin, altering metabolism to limit the production of toxic metabolites, increasing elimination of the ingested substance, or administering a specific antidote or other suitable therapy, and continued supportive care.

There is no single preferred strategy for the management of gastric decontamination in pediatric poisonings. The best gastric emptying technique is largely dependent upon clinical status. An individualized approach based on the timing of ingestion, type of substance, and amount of the ingested substance in conjunction with the clinical status will dictate treatment choices.

Summary

Children who have ingested substances, accidentally or intentionally, are a challenge in the emergency department and the ICU. The early recognition and management of pediatric poisonings will help to improve patient outcomes and help to decrease the incidence of preventable injuries.

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