Childhood Poisoning Safeguarding Young Children from Addictive Substances

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Introduction

The opioid crisis has brought renewed attention to the varied groups of people tragically affected by substance use and addiction, and the complex and multifaceted set of strategies needed to control this health emergency. This crisis is occurring against a backdrop of increasing availability of prescription and illicit opioids, which has been well documented,¹ but also other addictive substances, especially marijuana, nicotine, and caffeine products. Aside from higher odds of addiction and the adverse health and social effects associated with greater population-wide accessibility to addictive substances, a significant but less recognized consequence is the risk to young children who inadvertently handle or ingest these highly toxic substances.

In 2016,* an estimated 30,520 exposures to a range of addictive substances[†] among children aged 5 and younger were reported to poison control centers in the United States. Symptoms from such exposures range from mild to severe, and because young children's brains and bodies are undergoing rapid development, they are especially sensitive to the toxins contained in these substances. Despite this, the myriad ways in which young children are vulnerable to unintentional exposure to potentially toxic addictive substances are underappreciated and often overlooked in discussions of the perils of substance use and addiction.

The danger to young children of rising availability of addictive substances is highlighted by the current opioid crisis, since one of its many tragic consequences has been the proliferation of dangerous drugs in many homes -- homes in which caregivers' abilities to monitor and supervise their young children might be compromised by drug use.² Even in homes where adults or teens do not use illicit drugs, the presence of unsecured addictive products like liquid nicotine, alcoholic drinks, caffeinated energy drinks, or prescription pain medications, combined with the natural curiosity and explorative tendencies of babies and toddlers, presents a potentially fatal scenario.

Available data on pediatric exposures to addictive substances likely underestimate the prevalence of this public health issue. Incidents of exposure often go unreported due to a variety of factors, including a fear by caregivers of being held responsible or legally liable, and a lack of recognition that the incident is potentially dangerous to the child and may require professional intervention. The ways in which exposure incidents are tracked also contribute to their underestimation.[‡] The majority of information that is available on pediatric exposures to and poisoning from addictive substances comes from data reported by local and state poison control centers, which receive calls from parents, caregivers, and sometimes health professionals seeking advice in the wake of a suspected exposure. However, with the advent of the Internet and its unlimited resources for learning about the risks and symptoms of exposure to toxic substances, fewer people call in to ask questions or report an incident, especially if the symptoms do not appear to be particularly severe or life threatening. Indeed, while the total number of reported exposures and deaths among young children has declined or remained stable over the past 20 years, the number of reported cases with serious consequences has increased.³

† Addictive substances included in the estimate are nicotine and tobacco products, alcoholic beverages, caffeine, controlled prescription drugs (select opioids, central nervous system stimulants, and central nervous system depressants), marijuana, and other illicit drugs (heroin, cocaine, methamphetamines, hallucinogens, and club drugs).

‡ Please see the Appendix for a more detailed description of the challenges of interpreting and extrapolating from the data available from poison control centers, as collected by the AAPCC through the NPDS.



^{*} The most recent year for which comprehensive data from the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS) are available. (Please see the Appendix for more information about the AAPCC and its data).



Despite the obstacles to collecting reliable data on the prevalence of such incidents, recent developments in the proliferation of certain types of addictive substances have raised renewed concern about the growing risk of pediatric exposures. For example:

- Inconsistent regulation of non-cigarette nicotine products like e-cigarettes has been associated with a significant increase in the risk of nicotine exposures, with more than half involving children aged 5 and younger.⁴
- The well-documented increase in the use and misuse of prescription pain relievers in the U.S. was met with a 93 percent annual rate increase in unintentional exposures^{*} among children aged 5 and younger between 2000 and 2009. As prescribing practices are being reined in and public attention drawn to the opioid crisis, this trend in childhood exposures to prescription opioids is beginning to reverse.⁵
- The legalization of medical and/or recreational marijuana has been associated with a 148 percent increase between 2006 and 2013 in the rate of marijuana exposures among children aged 5 and younger.⁶ The growing popularity of marijuana edibles -- many of which are virtually indistinguishable from candies, chocolates, and pastries that are highly appealing to young children, and which can be fatal if consumed in full in one sitting -- does not bode well for reversing this trend.

Indeed, our own examination of national data from the American Association of Poison Control Centers shows a general increase over the past decade in exposures among children aged 5 and younger to nicotine, alcohol, caffeine, marijuana, and methamphetamine. Clearly the number of children who experience severe or deadly consequences from such exposures is relatively low, especially in comparison to the hundreds of people dying daily from opioid misuse and addiction. This larger group of victims of the opioid crisis certainly deserves the attention it is getting, as do the many adolescents and young adults who intentionally experiment with addictive substances and face significant risks from them. Still, the number of unintentional exposures among young children -- and the associated health consequences -- is too high to continue to be overlooked amid the growing public awareness around the costs and consequences of substance use and addiction.

We know that children exposed to toxic addictive substances are at increased risk for other injuries and life challenges, and that their families are prime targets for early, health-promoting interventions. We know that unintentional poisonings are largely preventable. We know that the best outcomes can be achieved when a comprehensive approach is taken, in which parents, other family members, educators, health professionals, policymakers, and the manufacturers and distributors of these products all do their part to ensure that no child accesses, touches, or ingests potentially toxic addictive substances. On a positive note, there is increasing movement toward enacting evidence-based practices that can protect children, such as requiring enhanced child safety packaging for certain addictive products. Furthermore, the nearuniversal concern for babies' and young children's welfare presents a compelling window of opportunity for delivering effective prevention messages to the public and for mobilizing policymakers and health care providers to do more to protect children from unintentional exposures.

This report, *Childhood Poisoning: Safeguarding Young Children from Addictive Substances*, summarizes the available research on the nature, extent, and consequences of young children's exposure to a range of addictive substances; explains why and how such exposures occur and what the barriers are to preventing them; and offers concrete recommendations for parents and other caregivers, health care professionals, policymakers, industry, and researchers to ensure that the growing availability of addictive products is met with an effective response that will protect the youngest victims of substance use and addiction.

^{*} These estimates do not include incidents of neonatal abstinence syndrome, which are symptoms of drug withdrawal that may occur among newborns exposed to opioids in utero.





The National Center on Addiction and Substance Abuse's *Childhood Poisoning: Safeguarding Young Children from Addictive Substances* was prepared by Jason Besser, MPP, and Brandie Pugh, MA, under the direction of Linda Richter, PhD, Director of Policy Research and Analysis.

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Nicotine

Key Points

- The popularity of non-cigarette nicotine products, such as electronic cigarettes, has contributed to the rise in unintentional nicotine exposures in young children.
- Liquid solutions used in electronic cigarettes and other vaping devices typically contain high concentrations of nicotine, which can be lethal in children, even in small doses.
- Many non-cigarette nicotine products are sold in colorful and attractive packaging and are available in a wide range of flavors that are highly appealing to children.
- The federal government has yet to put into effect many of the standards announced in 2016 with regard to regulating non-cigarette nicotine products.
- Some state and local governments have gone beyond federal laws and established regulations to help limit childhood exposures to nicotine products, including enacting packaging requirements in addition to child-resistant packaging, and banning flavors that appeal to children.

In December 2014, a toddler in upstate New York was found unconscious after unintentionally swallowing liquid nicotine from an electronic cigarette (e-cigarette). He was immediately rushed to the hospital, but was pronounced dead soon after. The coroner's report listed liquid nicotine exposure as the sole cause of cardiac arrhythmia, which led to the toddler's death. While children have been poisoned by nicotine prior to this incident, this was the first child in the United States to die from unintentional exposure to nicotine in e-cigarettes.¹ This tragic event, coupled with a significant increase in unintentional nicotine exposure calls to poison control centers have driven health professionals, government officials, and researchers to more closely examine this growing problem among infants and young children.²

The majority of incidents of unintentional exposure to nicotine products affects children aged 5 and younger. Of particular concern is the sharp increase in exposures to non-cigarette nicotine-containing products, like electronic nicotine delivery systems (ENDS), which include e-cigarettes and their e-liquid refill cartridges.³ Other non-cigarette nicotine products, such as dissolvable nicotine, also may be contributing to a recent surge in unintentional exposures to nicotine in young children. Dissolvable nicotine products and certain forms of nicotine replacement therapy may have a candy-like appearance that can appeal to young children.⁴





Nicotine gum



Regular gum



"Liquid nicotine is very concentrated and easily absorbed into the body...and can cause serious poisoning and death among children after even small doses."

--Gary A. Smith, MD, DrPH Director of the Center for Injury Research and Policy Nationwide Children's Hospital Columbus, Ohio

SOURCE: Lamotte, S. (2016). E-cigarette poisonings in kids skyrockets, study finds. Retrieved from CNN website: http://www.cnn.com/2016/05/09/health/ e-cigarettes-poison-kids/index.html.

The increase in nicotine exposures among young children has coincided with the growth in popularity of non-cigarette nicotine products that have varying but often high levels of nicotine concentration. While nicotine toxicity is rarely fatal, exposures involving e-cigarettes and related products more often result in adverse health effects relative to exposures involving traditional, combustible cigarettes.⁵

The American Association of Poison Control Centers (AAPCC) and individual poison control centers across the country have issued news releases and reports warning the public -- especially parents and other caregivers -- about the risks to children of exposure to these devices and their liquid nicotine.⁶

Although a child's unintentional ingestion of any product that contains tobacco or nicotine can be dangerous, the majority of the research and policy discussions in this area have focused on exposure to non-cigarette nicotine products such as e-cigarettes, e-liquids, and dissolvable nicotine.

National Data

Data on calls to poison control centers reporting incidents of nicotine exposure are collected by the AAPCC through the National Poison Data System (NPDS) (see Appendix A for more detail about the AAPCC and the NPDS).[†] An analysis of 27 years (1983-2009) of NPDS annual reports revealed 217,340 nicotine exposure calls. The majority of these calls (approximately 89 percent) involved children aged 5 and younger.⁷ Ingestion was the most common route of exposure, but children also experienced dermal, inhalation/nasal, and ocular exposure.⁸

The Centers for Disease Control and Prevention (CDC) analyzed data from U.S. poison control centers that were collected between September 2010 -- when new, unique codes were added to the coding system to specifically capture reports of e-cigarette exposures -- and February 2014. This analysis found that the number of e-cigarette exposure-related calls increased substantially during that time, from 0.3 percent to 41.7 percent, comprising a significant proportion of the total amount of monthly calls for nicotine product exposures. Notably, 51.1 percent of all e-cigarette exposures and 94.9 percent of all combustible cigarette exposures involved children aged 5 and younger.⁹

* The term "exposure" means someone has had contact with the substance in some way; for example, ingested, inhaled, or absorbed a substance by the skin or eyes, etc. Exposures do not necessarily represent poisonings or overdoses.

† Case records in the NPDS database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/ educational materials. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to poison centers and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

Rates of Nicotine Exposure*

The rise in popularity of e-cigarettes and other vaping devices appears to be associated with an increase in nicotine exposures among children aged 5 and younger. This increase can be seen in national data, as well as in data from individual states collected throughout the United States.

Another recent study that examined NPDS data on nicotine exposures looked at the time period from January 2012 through April 2015. Children aged 5 and younger accounted for an average of 729 exposure calls per month. During the study's timeframe, calls involving e-cigarettes increased by 1,492 percent. Children exposed to e-cigarettes had 5.2 times the odds of being admitted to a health care facility and 2.6 times the odds of presenting with serious effects of exposure^{*} relative to children exposed to combustible cigarettes.¹⁰

To take a broader view of reported exposures to nicotine, we examined data[†] on calls related to single-substance exposures[†] to all nicotine products (combustible cigarettes, e-cigarettes, and all other tobacco products) from January 2007 to December 2016.[§]

Reports of exposures to e-cigarettes include the device as well as the liquid nicotine. The 'other tobacco products' category consists of chewing tobacco, cigars, dissolvable nicotine, filter tips (i.e., butts), snuff, and other or unspecified types of tobacco/nicotine products.

The first graph below demonstrates reported exposures to nicotine products in all ages, and the second demonstrates reported exposures in children aged 5 and younger.

In the first graph, combustible cigarette exposures for all ages remained steady from 2007 to 2014 with an average of 5,695 calls. It was not until 2015 and 2016 where cigarette exposures increased to 6,958 and 6,699 calls, respectively.^{**} From 2011 to 2015, exposures related to the 'other tobacco products' category showed steady increases each year, whereas in 2016, the prevalence declined slightly. Additionally, the number of reported exposures to e-cigarettes for all ages increased through 2014. In 2010, there were only 29 exposure calls, but that number rose steadily until 2014 when there were 3,910 calls. Since 2014, the number of exposures has declined. In the graph examining nicotine exposures in children aged 5 and younger, the number of reported cigarette exposures remained steady until 2015, when the calls jumped to 6,556 cases. Similar to the findings described above for all ages, the number of exposures related to the 'other tobacco products' category in children aged 5 and younger increased from 2011 to 2015, and then began to decline in 2016. Moreover, e-cigarette exposures rose every year from 2010 to 2015, until a decline in 2016. This decline in 2016 could be attributed to a decreasing trend in the use of e-cigarettes in the United States over the past year.¹¹

* Including asystole/cardiac arrest, coma, seizure, and respiratory arrest.

† Based on NPDS's annual reports from the AAPCC website, in which we manually counted each exposure incident.

‡ Single-substance exposures are cases where only one substance was involved in the reported incident. In 2016, single-substance exposures made up 97 percent of all exposures among children aged 5 and younger. Data specific to cause of exposure (e.g., intentional, unintentional) are not available by age group in published and available NPDS annual reports.

ℑ The e-cigarette category was added in 2010. Because of this, rates of exposure to e-cigarettes may be underestimated since these codes may have been underutilized when first introduced.

** The AAPCC was unable to draw any conclusions about this apparent increase in 2015 and 2016 relative to previous years.





These findings coincide with those of other studies that have shown a sharp increase in e-cigarette exposure calls in children aged 5 and younger from 2010 through 2015.¹² Even with the more recent decrease in exposure calls, children aged 5 and younger still represent the majority of exposure calls for all nicotine products. They accounted for 94 percent of all cigarette exposure calls, 73 percent of all e-cigarette exposure calls, and 78 percent of all 'other tobacco product' exposure calls.



State Data

Along with the NPDS, smaller scale state-based studies have found increases in unintentional e-cigarette and liquid nicotine exposures among young children. The Washington Poison Center reported that there was more than a 1,000 percent increase from 2012 to 2014 in the number of calls related to e-cigarettes and liquid nicotine exposure. Of all these calls, the majority of exposures were considered unintentional, and 60 percent of the reported exposures were among children aged 1 to 3 years old.¹³

In California, unintentional pediatric exposures to e-cigarettes tripled over the course of one year in 2014. Children aged 5 and younger accounted for more than 60 percent of all e-cigarette exposure calls.¹⁴ A similar study in Texas examined calls to poison control centers from 2010 to 2014 and found 203 calls related to e-cigarette exposures in children aged 5 and younger. The number of reported exposures increased every year, and the majority of exposures occurred in children aged 2 and younger.¹⁵

Symptoms of Nicotine Exposure

Children experience a host of negative effects from unintentional exposure to nicotine. The severity depends on the product, quantity, dose, and means of exposure. For example, a child who drinks an entire bottle of e-liquid will experience more serious health consequences than a child who ingests a filter tip.

The chart below lists common symptoms that children may experience from exposure to nicotine. This list of symptoms derives from multiple published cases of unintentional nicotine exposure in children throughout the United States. The more severe symptoms (e.g., seizure, congestive heart failure, coma) typically occur when a child is exposed to products with a high nicotine concentration, such as that found in the liquid nicotine in e-cigarettes and other vaping products.

Symptoms of Nicotine Exposure in Children

Choking/coughing/	Lethargy ²⁸		
gagging ¹⁶ Coma ¹⁷	Muscle fasciculations (involuntary twitching) ²⁹		
Congestive heart	Nausea ³⁰		
failure ¹⁸	Pale or flushed		
Convulsions ¹⁹	appearance ³¹		
Disorientation ²⁰	Palpitations ³²		
Dizziness ²¹	Pneumonia ³³		
Gastrointestinal distress ²²	Rapid, heavy breathing ³⁴		
Headache ²³	Respiratory		
Increased blood	depression ³⁵		
pressure ²⁴	Seizure ³⁶		
Increased heart and	Vomiting ³⁷		
respiration rate ²⁵	Weakness ³⁸		
Irritability ²⁶			
Irritation/rashes (via skin and eye exposure) ²⁷			

The CDC has reported that vomiting is the most common adverse side effect of nicotine poisoning.³⁹ This helps explain why the majority of exposures have not been fatal, since vomiting limits the full absorption of nicotine⁴⁰ Considering that the most common means of exposure is ingestion,⁴¹ the acid in the stomach might also prevent nicotine from being fully absorbed into the bloodstream. While acid in the stomach and the natural vomiting reaction may account for the low mortality rate among children who unintentionally ingest products with low amounts of nicotine, it is unclear whether this natural process would facilitate recovery when higher concentrations of nicotine are ingested. Nicotine poisoning can be fatal, and typically results from paralysis of the muscles that control breathing, as well as the loss of effective blood flow to the heart and in the blood vessels.⁴²

Historically, the low likelihood of fatality from nicotine exposure may be related to the types of tobacco and nicotine products that traditionally have been accessible to children (i.e., combustible cigarettes). Mortality rates might increase now that young children are exposed to other types of products with higher concentrations of nicotine.⁴³ Data on exposure calls and hospital visits suggest that serious adverse health effects of unintentional exposure to nicotine are more likely to be found in cases where children were exposed to e-cigarettes than to combustible cigarettes.⁴⁴ While most studies examine symptoms among children who unintentionally ingested nicotine products, some children have experienced dermal (skin) exposures. An analysis of exposures to transdermal nicotine patches[†] in children aged 15 and younger found that 14 out of 36 exposures resulted in adverse health effects such as gastrointestinal pain, weakness, dizziness, lethargy, irritability, and localized rashes. These exposures were never fatal, probably because most of the exposures were to transdermal nicotine patches that had been used, which would reduce their potency.⁴⁶ The high concentrations of nicotine in e-liquid could result in whole-body toxicity,⁴⁷ and could be fatal in children if dermally absorbed.⁴⁸

Six Year Old Needs Intubation after Ingesting E-liquid

"Her pulse rate decreased to 60 beats/min and she developed vomiting, diaphoresis, disconjugate gaze,* fasciculations, obtundation,[†] and inability to control her copious secretions."

Confusing it for ibuprofen, a father of a 6-year-old girl accidentally gave the child a 10ml dose of e-liquid, causing her to ingest about 35 mg/kg of liquid nicotine. Five minutes after realizing his mistake, the father called the poison control center, and the girl was rushed to the hospital. Her immediate symptoms included going in and out of consciousness, vomiting, and jerking movements. As the girl's symptoms worsened, she was unable to listen to commands and needed to be sedated and intubated. She required overnight ventilator support to be normalized and extubated.⁴⁵ "In the past, it has been rare that a child would suffer a seriously toxic exposure to traditional tobacco products, but this has become increasingly more common with highly concentrated nicotine found in e-liquid and e-cigarettes. E-liquid, even when absorbed through the skin, can cause serious clinical effects in children."

--Michael Lynch, MD Medical Director Pittsburgh Poison Center Assistant Professor University of Pittsburgh School of Medicine

Interview on August 24, 2016

* Unpaired movements of the eyes.

- † Mental blunting with reduction in alertness and a diminished sensation of pain.
- ‡ A form of nicotine replacement therapy used as a smoking cessation aid.

Toxicity and Variations in Nicotine Dose

Current estimates of nicotine toxicity suggest that a lethal dose of orally ingested nicotine for an adult is approximately 0.5 g or more (corresponding to an oral median lethal dose of 6.5–13.0 mg/kg).⁴⁹ However, a concrete estimate of what constitutes a lethal dose, especially for children, is not known. Generally, studies have shown nicotine toxicity for children to have an estimated median lethal dose between 1 and 13 mg/ kg of body weight.⁵⁰ One bottle of liquid nicotine generally holds up to 29 mg of nicotine per ml,⁵¹ but some go up to 100 mg/ml or higher.⁵² In comparison, combustible cigarettes and cigarette butts contain nicotine levels of 5-30 mg/ml.⁵³



Discarded cigarette butts, often found in or around the homes of adults who smoke, have resulted in many exposures with minimal toxic effects (e.g., vomiting and nausea). Cigarette butts contain harmful chemicals including heavy metals, ethylphenol, and nicotine, but exposure is rarely severe or fatal.⁵⁴ Unlike cigarette butts, which are foul tasting and bitter, another nicotine product on the market that may be more deadly to children is a type of dissolvable nicotine pellet that comes in mint and cinnamon flavors. These pellets contain around 1 mg of nicotine per pellet. A young child, mistaking these pellets for candy, such as a Tic Tac,⁵⁵ could be poisoned by consuming several at a time. Consumption of an estimated 10 to 17 pellets could kill a toddler.⁵⁶ Other dissolvable nicotine products, such as nicotine strips, that have an appearance similar to Listerine strips, contain approximately 3.1 mg of nicotine per strip.⁵⁷ Given that the approximate lethal dose is between 1 and 13 mg/kg of body weight, an infant or a toddler consuming several of these nicotine strips could easily consume fatal doses of nicotine.

The chart below lists the nicotine concentration levels for most nicotine products that may be involved in a childhood unintentional exposure. Many of the products listed have a relatively stable and determined nicotine concentration level. The nicotine concentration in e-liquids, however, is less consistent. While the range of nicotine concentration in e-liquids is typically between 0 and 29 mg/ml,⁵⁸ the amount per unit can vary greatly. Some online e-cigarette retailers sell e-liquid with nicotine concentrations as high as 100 mg/ml.⁵⁹ There also are some instances where the nicotine level indicated on the bottle's label is wholly inaccurate (e.g., a bottle might say there is 30 mg/ml of nicotine when testing reveals 70 mg/ml). One study examined the nicotine content in e-liquid cartridges and found that in nearly half the cartridges analyzed, there was more than a 20 percent discrepancy between the nicotine content listed by manufacturers and the actual nicotine content in the cartridge.60 Another recent study that examined nicotine content in 35 samples of e-liquid from the most popular online manufacturers or distributors of these products found that nicotine was detected in the vast majority (91.4 percent) of the samples that were labeled as containing 0 mg/ml of nicotine.61

Nicotine Levels in Nicotine Products			
Nicotine Product	Nicotine Concentration per Product Unit (mg/g)		
Smoked Tobacco			
Cigarettes ^{* 62}	16.2-19.9		
Cigars ⁶³	6.3-15.6		
Cigarette butt ⁶⁴	5.0-7.0		
Smokeless Tobacco			
Moist snuff ⁶⁵	4.4-25.0		
Snus ⁶⁶	9.0-11.3		
Dissolvable nicotine67	3.9-8.7		
Electronic Nicotine Delivery Systems (ENDS)			
E-cigarette ⁶⁸	.05-15.4 mg		
E-liquid ⁶⁹	0.0-100.0+ mg/ml ⁺		
Nicotine Replacement Products			
Patch ⁷⁰	8.3-114.0		
Gum ⁷¹	2.0-4.0		
Lozenge ⁷²	2.0-4.0		
Nasal Spray ⁷³	0.5		

Approaches to Addressing Childhood Nicotine Exposure

Federal, state, and local governments as well as public health organizations have all taken steps to help shape tobacco and nicotine policies in the United States. The majority of these initiatives has focused on:

- Preventing the initiation of tobacco or nicotine product use;
- Helping people who already use tobacco or nicotine products quit or cut down; and
- Reducing the harmful effects caused by tobacco or nicotine product use.⁷⁴

With regard to the third priority, there has been a recent surge in interest in implementing policies to help prevent unintentional exposures to nicotine among young children.

Federal Laws and Regulations

Nearly all laws and regulations[‡] dealing with tobacco and nicotine policy in the United States emerged after the publication in 1964 of the U.S. Surgeon General's report, *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service.*⁷⁵ The report provided a comprehensive synthesis of the health risks associated with cigarette smoking.⁷⁶ Informed by the science detailed in the report, the U.S. Government became one of the first authoritative bodies to declare cigarette smoking a public health threat and act to implement laws and regulations to reduce that threat.⁷⁷

* Unfiltered and filtered U.S. brands (American Spirit, Camel, Kool Marlboro, Menthol, Newport Menthol).

 \dagger While the typical range of nicotine concentration in e-liquid is 0-29 mg/ml, studies have found concentrations as high as 75 mg/ml, 87mg/ml, 100 mg/ml, and higher.

‡ Laws are passed by legislatures (U.S. Congress for federal laws, state legislatures for state laws) and typically are enforced through the executive branch. Regulations are standards and rules adopted by administrative agencies that govern how laws are enforced.



While the report did a good job of informing the public of the health risks of smoking, it mainly discussed tobacco, and did not address the harmful effects of nicotine itself. The report also did not mention unintentional nicotine exposures.

It was not until 1988 that a U.S. Surgeon General declared nicotine to be an addictive substance.⁷⁸ As a result, the regulation of non-cigarette nicotine products lags far behind that of combustible cigarettes.⁷⁹ The same can be said for efforts to control unintentional exposures to non-cigarette nicotine products. The two federal organizations that have been most involved in regulations dealing with nicotine policy and unintentional exposures to nicotine are the U.S. Food and Drug Administration (FDA) and the Consumer Product Safety Commission (CPSC).

Food and Drug Administration (FDA)

The passage of the 2009 Family Smoking Prevention and Tobacco Control Act (TCA) was instrumental in attempting to limit nicotine exposures. The TCA granted the FDA the authority to regulate the manufacture, distribution, and marketing of certain tobacco products. The FDA was authorized to conduct inspections of tobacco product retailers to determine compliance with federal laws, and implement standards for tobacco products to protect the public health.⁸⁰

The 2009 TCA only applied to cigarettes, loose tobacco, roll-your-own tobacco, and smokeless tobacco products. All other nicotine products, including those like e-cigarettes and other vaping devices that were starting to become popular, fell outside the scope of FDA regulation. Finally, in May 2016, the FDA was authorized to extend its oversight to all tobacco and tobacco-derived products that were previously unregulated.⁸¹ This 2016 final deeming rule would expand the FDA's authority to regulate nicotine-containing products like e-cigarettes, cigars, and dissolvable nicotine, many of which had been mislabeled and debased when outside the scope of FDA regulation.



However, since President Trump appointed a new FDA commissioner, enforcement of the stricter standards from the 2016 deeming rule has been delayed.⁸² In May 2017, the FDA released a three-month extension of compliance deadlines relating to the 2016 rule.⁸³

In October 2017, the FDA released a statement that enforcement of the deeming rule would begin on August 10, 2018.⁸⁴ This means that tobacco and e-cigarette companies do not have to abide by certain required warning statements, premarket review requirements, and other provisions established in 2016 until two years later.⁸⁵ It is still not known if the FDA will enforce the standards once August 2018 comes around.⁸⁶

Even if the FDA finally does enforce the 2016 oversight rule in 2018, the broader regulatory authority of the FDA still would not apply all of the restrictions that it currently places on cigarettes to non-cigarette nicotine products.⁸⁷ Not having these restrictions may increase the chance of pediatric unintentional exposure to e-cigarettes and other non-cigarette nicotine products. For example, unlike smoked cigarettes, for which characterizing flavors other than tobacco and menthol are prohibited, there are no restrictions on the flavorings that may be included in non-cigarette nicotine products. This means that e-liquids and other non-cigarette nicotine products like little cigars can be sold in a broad range of candy-like flavors that strongly appeal to children.⁸⁸ The new rule also does not fully address the issue of warning consumers about the risks of nicotine exposure (e.g., from e-liquid solutions), particularly to young children.89

FDA Commissioner has Ties to the E-Cigarette Industry

On May 11, 2017, Scott Gottlieb, MD, was sworn in as the new FDA Commissioner.⁹⁰ At his confirmation hearing on April 5, 2017, Dr. Gottlieb refused to say whether the FDA should ban flavored e-cigarettes. When asked what flavors should be banned, he said, "I recognize there is a line here somewhere, and I don't know where that line gets drawn." Dr. Gottlieb also has been criticized for his financial ties to Kure, a vape store franchise. While he said he would recuse himself from any matters related to the company for one year from May 2016 when he resigned, there remains a conflict of interest. The Center for Tobacco-Free Kids, a public health organization, argued that not only should Dr. Gottlieb recuse himself from matters related to Kure, but also from any decision involving e-cigarettes.⁹¹

Consumer Product Safety Commission (CPSC)

The CPSC is another federal agency that plays an important role in regulating potentially toxic substances. One of the CPSC's responsibilities is to implement and enforce the landmark Poison Prevention Packaging Act (PPPA) of 1970, which required childproof packaging for particular household substances.⁹² The implementation of this Act has led to a decline among children in reported poisoning deaths from household products and certain medications.⁹³

The success of the PPPA paved the way for the Child Nicotine Poisoning Prevention Act of 2015,⁹⁴ signed into law by President Obama on January 28, 2016. The law requires liquid nicotine containers used for e-cigarettes and other vaping products to be packaged in accordance with strict child-resistant poison prevention standards.⁹⁵ All packaging must be tested on children and adults before being allowed on the

market. During the testing, young children are asked to open the container after an instructor shows them how it is done. To meet the child safety standards, young children must be unable to open the container 80 percent of the time. On the other hand, senior adults must be able to open the same package at least 90 percent of the time during testing to meet CPSC safety standards. Other than testing, the prevention standards require a restricted flow on the package to limit the amount of liquid released each time the bottle is squeezed. The law states that there can be no more than 2 ml of e-liquid released at one time from the bottle once it is opened and inverted.⁹⁶ These updated standards are a major step forward in protecting young children from unintentional nicotine exposure and poisoning.

"The approval of the Child Nicotine Poisoning Prevention Act represents significant progress in addressing an increasingly important child safety concern in our country... This bill not only addresses public health challenges posed by liquid nicotine, but more importantly, takes strides to protect a child's right to a healthy and safe home environment."

--AAPCC press release, January 12, 2016

SOURCE: American Association of Poison Control Centers. (2016). AAPCC applauds the congressional approval of the Child Nicotine Poisoning Prevention Act of 2015. Retrieved from https://aapcc.s3.amazonaws.com/pdfs/ releases/2016_AAPCC_Child_Nicotine_Poisoning_Prevention_Act_of_2015_ FINAL_ayRwGc5.pdf.

State and Local Laws and Regulations

The gaps in federal legislation governing noncigarette nicotine products have inspired state and local governments to take the initiative toward more regulation.⁹⁷ For example, while the TCA prohibited the sale of combustible cigarettes, loose tobacco, rollyour-own tobacco, and smokeless tobacco products to minors under age 18, and the 2016 FDA rule extended this to all tobacco and tobacco-derived products (including e-cigarettes), as of September 2017, eight states* have set the minimum legal age higher. Four of those states (California, Hawaii, Maine, and Oregon) have set the minimum legal age to 21.98

With regard to unintentional exposures, 21 states[†] have enacted e-cigarette retail regulations related to childresistant packaging that go beyond federal laws.⁹⁹ The chart below lists those states that have imposed requirements in addition to child-resistant packaging.

States with Packaging Requirements in Addition to Child-Resistant Packaging Related to ENDS Products (as of September 2017) ¹⁰⁰		
State	Additional Requirements	
Indiana	"E-liquid container must use a tamper evident package and label must identify nicotine content, active ingredients, among other requirements"	
Massachusetts	"Electronic smoking devices may not be opened, repackaged, or sold in smaller quantities than the smallest package distributed by the manufacturer for individual consumer use"	
Minnesota	"Liquids intended for human consumption and use in an electronic delivery device (whether they contain nicotine or not) must be sold in child resistant packaging."	
New Mexico	"E-cigarettes and nicotine liquid containers must be sold in original factory-sealed package"	
North Carolina	"Must state the product contains nicotine"	
Oregon	"Inhalant delivery systems [‡] must be sold in child-resistant packaging which is not attractive to persons under age 18, and labeled in accordance with rules adopted by the authority"	
Utah	"Required display of nicotine content on label and safety warning, among other things"	
Washington	"Liquid nicotine containers must be labeled with warnings concerning nicotine, keeping away from children, age restrictions, and must include nicotine content"	

In 2015, a study examined the effectiveness of state e-cigarette legislation related to child-resistant packaging against four benchmarks:¹⁰¹

- 1. Broad product definitions that contemplate future development in the market;
- 2. Citations to a specific packaging standard;
- 3. Stated penalties for violations; and
- 4. Express grants of authority to a state entity to enforce packaging requirements.

The study concluded that the three states to meet all four benchmarks were Indiana, Minnesota, and

Washington.¹⁰² Other states should examine these three examples of legislation as models for their own laws.

* AK (age 19-legal age of sale/distribution); AL (age 19-legal age of purchase/ possession); CA (age 21-legal age of sale); HI (age 21-legal age of sale/ distribution and purchase/possession); ME (age 21-legal age of sale/ distribution); NJ (age 19-legal age of sale/distribution); OR (age 21-legal age of sale and purchase/possession); and UT (age 19-legal age of sale/distribution).

† AK, CA, IL, IN, MA, ME, MN, MO, NC, ND, NJ, NM, NY, OR, TN, TX, UT, VA, VT, WA, WY.

‡ Inhalant is defined in the regulation as "nicotine, a cannabinoid, or any other substance that is in a form that allows the nicotine, cannabinoid, or substance to be delivered into a person's respiratory system." Another way states have regulated e-cigarettes that could potentially help limit unintentional exposures is by including e-cigarettes in statutes that define tobacco products. This would allow e-cigarettes to be regulated the same way as other tobacco products even if they do not contain tobacco. As of September 2017, 12 states^{*} and the District of Columbia have included e-cigarettes in at least one definition of tobacco products in their statutes.¹⁰³

Local governments also have taken steps toward more stringent policies. New York City and Providence, Rhode Island have passed laws banning myriads of flavors of e-liquid in 2009 and 2012, respectively. Flavors that have been banned are candy, chocolate, cocoa, dessert, any fruit, and herbs or spices. Only menthol and wintergreen are permitted. These laws have gone further than federal regulation, which only ban characterizing flavors (other than menthol) in cigarette products.¹⁰⁴

San Francisco is the latest city attempting to ban flavored e-cigarettes. The current proposal approved by the city's board of supervisors includes a ban on all flavors, as well as menthol cigarettes.¹⁰⁵ However, the proposal has been met with great backlash from tobacco companies, and a petition with over 33,000 signatures forced the board to reconsider the measure. After the petition, the board of supervisors again voted in favor of the ban in September 2017. The fate of San Francisco's e-cigarette measure will now be placed on the ballot on June 5, 2018 to see if it will be enacted into law.¹⁰⁶

Health Organizations

Several public health organizations have attempted to address unintentional nicotine exposures in young children by pushing for greater regulation and reforms to limit their occurrence.

American Academy of Pediatrics (AAP)

The AAP is a professional membership organization whose mission is to ensure that children of all ages have optimal physical, mental, and social health.¹⁰⁷ The AAP strongly supported the passage of the Child Nicotine Poisoning Prevention Act in 2016, calling for all companies to comply with the CPSC child-resistant packaging standards.¹⁰⁸ Currently, the focus of the AAP is on state advocacy. The AAP's positions with regard to nicotine control include:

- Banning all candy and fruit flavored liquid nicotine products;
- Having flow-restrictors[†] placed on the necks of all liquid nicotine vials; and
- Limiting the amount of concentrated liquid nicotine solution to amounts not lethal to young children.¹⁰⁹

American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO)

The AACR and ASCO are professional health organizations that collaboratively released a special report in 2015 examining the current landscape of ENDS products, and suggested several policy recommendations. The report stressed that more research on ENDS products is needed to better understand the health effects. It also recommended that manufacturers of ENDS products report all ingredients to the FDA, prohibit flavoring in ENDS that appeal to children, and ensure warning labels are placed on all ENDS products.¹¹⁰ These suggestions could help limit nicotine accessibility, exposures, and poisonings among young children.

 $^{^{\}dagger}$ Flow-restrictors are caps placed on vials to limit the amount of liquid nicotine released when opened.



^{*} CA, CO, HI, IN, ME, MN, NC, PA, SD, UT, WV, WY

American Heart Association (AHA)

For decades, the AHA has pushed to increase tobacco control throughout the United States. In 2015, the AHA released a policy statement in which it provided clear positions regarding the growing use of e-cigarettes. Some of these positions can help limit nicotine exposure in young children. For example, one of AHA's positions is to make sure that all state laws include e-cigarettes in their definitions of tobacco products.¹¹¹ This would help ensure that e-cigarettes are not exempt from state tobacco laws.

Other Organizations that Supported the Child Nicotine Poisoning Prevention Act

Many other organizations have expressed their support for regulating nicotine products to limit unintentional exposures among young children. The following are just some of the public health organizations that have applauded the Child Nicotine Poisoning Prevention Act:

- American Public Health Association¹¹²
- Campaign for Tobacco Free Kids¹¹³
- Consumers Union¹¹⁴
- Kids in Danger¹¹⁵
- Truth Initiative¹¹⁶

Alcohol

Key Points

- The number of unintentional exposures to alcohol in young children has increased every year since 2012.
- The widespread use of alcohol, along with the array of appealing packaging (many of which resemble packaging for non-alcoholic sweet beverages), may promote unintentional exposure to alcohol beverages among young children.
- Case studies have shown alcohol to be more dangerous for children than adults.
- There currently are no systematic approaches to preventing pediatric exposures to alcohol among young children.

Alcohol is the most widely used addictive substance in the United States. In 2015, 86.4 percent of people aged 18 and older reported consuming alcohol at some point in their lifetime, and 70.1 percent reported consuming alcohol in the past year.¹ The immense popularity of alcoholic beverages could increase the risk of alcohol exposure and poisoning in young children.² However, while exposure to alcohol is acknowledged as a public health problem in young children,³ most attention has been drawn to unintentional alcohol exposures via antiseptics, mouthwashes, and perfumes.⁴ Despite the increasing availability of sweet-flavored alcoholic beverages -many of which come in colorful packaging that might appeal to children or be confused with non-alcoholic juice or soda beverages -- few studies have addressed unintentional exposures to alcohol among young children.

The trend of marketing flavored alcoholic beverages began in the early 1980s with wine coolers,⁵ advanced in the early 1990s with alcopops,⁶ and continues to this day. In recent years, more flavors have been added to beer in an effort to expand the market to those who do not normally like the taste of beer.⁷ Spiked sparkling water was also recently introduced as a low-calorie alternative to alcoholic hard sodas.⁸ Unintentional exposures also may occur because certain alcoholic beverages resemble other types of products typically found in a home. For example, a case study reported that a parent accidentally gave a child a bottle of formula mixed with vodka instead of water.⁹





Rum and coke

Coke

Another study suggests that alcohol-containing products could be palatable to young children. Although this study was conducted with mouthwash containing alcohol, it suggests that palatability can potentially promote the consumption of alcohol in young children.¹⁰

Although exposure to alcoholic beverages among young children has not been heavily researched or documented, national poison control center data highlight the risk of childhood alcohol poisoning.¹¹

Rates of Alcohol Exposure*

Unintentional exposures to alcohol-containing household products in young children are commonly reported to poison centers in the United States. This is different from exposure to alcohol via alcoholic beverages, for which documented reports are less common. This may be because children who consume alcohol-containing products may not consume enough alcohol to have any noticeable effects (due to the unpleasant taste or because they may vomit soon after consuming it) or because, in many cases, they can safely be observed at home if they are asymptomatic.¹²

Unlike exposures to other addictive substances, there are no published national studies based on data from the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS)[†] that have examined trends in reported alcoholic beverage exposures among young children. We collected data on single-substance exposures[‡] to alcoholic beverages from the NPDS annual reports[§] from 2007 to 2016. The first graph below demonstrates reported exposures to alcohol among individuals of all ages, and the second demonstrates reported exposures in children aged 5 and younger.

In all ages, reported exposures to alcoholic beverages increased slightly from 2007 to 2012, then decreased through 2014, and increased again from 2014 to 2016.

Among children aged 5 and younger, there was a marked increase in exposures from 2007 to 2009, followed by a decline until 2012. Since 2012, the number of exposures in children this age has increased each year. In 2016, children aged 5 and younger accounted for nearly one in four (23.7 percent) of all alcohol exposure calls. While this increase in the number of exposures is concerning, an explanation for it is not readily apparent.

* The term "exposure" means someone has had contact with the substance in some way; for example, ingested, inhaled, or absorbed a substance by the skin or eyes, etc. Exposures do not necessarily represent poisonings or overdoses.

† Case records in the NPDS database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/educational materials. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to poison centers and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

 \ddagger This excludes cases where more than one substance was involved in the reported exposure incident.

§ We collected NPDS's annual reports from the AAPCC website and manually counted each exposure incident overall and among children aged 5 and younger.









Symptoms of Alcohol Exposure

Based on numerous case studies dating back to the early 1960s,¹³ outdated reviews of cases,¹⁴ hospital visits related to accidental exposures to alcoholic beverages or alcohol-containing household products,¹⁵ and more recent research on alcohol exposure via mouthwash,¹⁶ several symptoms have been documented in children with alcohol exposure. Although these are relatively uncommon, they are listed below:

Symptoms of Alcohol Exposure in Children

Brain damage17Hypokalemia*23Coma18Hypotension24Convulsions19Irritability25Death20Metabolic acidosis26Decreased mental status21Seizures27Hypoglycemia22Vomiting28

* When the blood's potassium levels are too low.



T

Alcohol generally is more dangerous for children than adults.²⁹ It is more likely to lead to hypoglycemia (i.e., low blood sugar) in children since they have smaller livers and less glycogen stores.³⁰ Alcohol-induced hypoglycemia may result in seizures, coma, and convulsions,³¹ and prolonged hypoglycemia can cause irreversible brain damage.³² Alcohol is believed to be the most common cause of hypoglycemic coma, which can have devastating and lethal effects on both children and adults.³³

A child's blood alcohol level may peak several hours after ingestion, possibly delaying identification of and intervention for alcohol poisoning by parents, caregivers, or health professionals.³⁴ With children exposed to alcohol first exhibiting symptoms of lethargy and irritability, parents and caregivers may not suspect unintentional alcohol ingestion. They might ignore these relatively common mild or moderate symptoms, or think they are brought on by other causes.³⁵

Prompt recognition and treatment are essential to counteract the effects of alcohol poisoning in young children.³⁶ In a reported case, a two-year old child died after a delay in seeking care.³⁷ A lack of clinical experience in recognizing alcohol-induced hypoglycemia³⁸ and, more generally, in relation to childhood alcohol exposures also might explain higher mortality rates in cases of alcohol poisoning among children relative to adults.³⁹

Toddler Hospitalized after Accidentally Served Alcohol at Restaurant

A 15-month old toddler was sent to the hospital after accidentally receiving and ingesting an alcoholic mixed drink at an Applebee's restaurant in Michigan. The container was mislabeled, and the waiter mistakenly served the toddler apple juice with margarita mix in it because it did not look any different from regular apple juice. After drinking some of the alcoholic beverage, the toddler experienced many symptoms including irritability, confusion, and guick bursts of sleepiness and hyperactivity. Once the mistake was realized and he was sent to the hospital, doctors found that his blood alcohol content (BAC) was 0.10. To put this into perspective, a BAC level of 0.08 is considered a DUI (driving under the influence) offense. Luckily, the toddler's symptoms subsided with no long-term adverse consequences. The mother of the toddler was told that if the toddler had consumed the entire margarita mixed drink, he likely would have died.40

Alcohol Toxicity

It is difficult to ascertain the toxicity of alcohol in children, particularly because it varies based on the child's weight, age, chronicity of exposure, rate of metabolism, hydration, and nutritional status.⁴¹ Nonetheless, the most commonly cited lethal dose of alcohol for young children is 3 grams per kilogram.⁴² However, there have been cases of children surviving incidents in which they have consumed more than this amount,⁴³ and children can have life-threatening reactions at lower doses.⁴⁴ In adults, the lethal dose of alcohol is estimated at 5 grams per kilogram.⁴⁵

T

A Case of Alcohol Poisoning in a Toddler

The National Capital Poison Center in Washington DC reported an unintentional exposure to alcohol by a 2-year-old child who drank two ounces from a bottle of vodka that he found on a coffee table. He was found unconscious by his father and was taken to the emergency room. The child was later transported by helicopter to an intensive care unit for children. The child could not breathe without medical support, and remained in a coma for several hours. The next morning, the child woke up and could breathe on his own. He was discharged from the hospital the following day. Had his father not found him when he did, the child may not have survived.⁴⁶

Approaches to Addressing Childhood Alcohol Exposure

There currently are no widespread approaches directly dealing with unintentional exposures to alcoholic beverages among young children. While the Poison Prevention Packaging Act of 1970 requires child-resistant packaging for certain mouthwashes and other antiseptics that contain alcohol,⁴⁷ there are no child-resistant packaging requirements for alcoholic beverages. The lack of child-resistant packaging laws for alcoholic beverages might increase the risk of exposures in young children.

Caffeine

Key Points

- Historically, caffeine had been found only in soft drinks and other products where it is a naturally occurring ingredient, such as coffee, tea, and chocolate. However, in recent years, caffeine has been added to numerous food and beverage products, usually without the consumer's knowledge.
- Since 2014, the number of unintentional exposures to caffeine has been increasing among children aged 5 and younger.
- Highly caffeinated energy drinks are implicated in a significant proportion of unintentional caffeine exposures among young children.
- Caffeine toxicity in children can produce serious health effects.
- The federal government's policy toward regulating caffeine is inadequate. While it has acknowledged the health risks associated with consuming high doses of caffeine, the government has done little to educate the public and prevent exposures to caffeine products among children.

Caffeine is a naturally occurring substance and stimulant of the central nervous system.¹ It is believed to be the most ubiquitous psychoactive drug currently in use, consumed in various ways by 90 percent of the world's population. In the United States alone, 80 percent of adults consume caffeine every day.² More surprisingly, 63 percent of children aged 2 to 5 consume caffeine on any given day.³ Children have normally ingested caffeine in either the form of soft drinks or food and other beverage products where caffeine is naturally occurring (e.g., chocolate, coffee, or tea).⁴ Although caffeine intake among children declined between 1999 and 2010,⁵ current consumer trends indicate that, since 2010, the consumption of food and beverages with added caffeine has been on the rise.6

Historically, caffeine was found only in food and drinks where it is a natural ingredient. That changed in the 1950s when caffeine was introduced as an additive in soft drinks.⁷ This led the U.S. Food and Drug Administration (FDA) to implement caffeine regulations to apply solely to added caffeine found in soft drinks.

However, a startling trend has emerged where caffeine is now added to many other foods and beverages, including select gums, mints, potato chips, candy bars, and even specialty water.⁸

"Existing rules never anticipated the current proliferation of caffeinated products...The gum is just one more unfortunate example of the trend to add caffeine to food. Our concern is about caffeine appearing in a range of new products, including ones that may be attractive and readily available to children and adolescents, without careful consideration of their cumulative impact."

--Michael R. Taylor, J.D. Former Deputy Commissioner for Foods and Veterinary Medicine U.S. Food and Drug Administration

SOURCE: FDA. (2013). Caffeine and kids: FDA takes a closer look. Retrieved from https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm350570.htm.

Energy drink products are another increasingly popular source of caffeine. While these drinks resemble soft drinks, they are marketed as having energizing effects due to caffeine and other additives.⁹ Energy drinks comprise a growing proportion of total caffeine consumption.¹⁰ Energy drink sales increased by 60 percent from 2008 to 2012, when it reached \$12.5 billion.¹¹ Between 2010 and 2014, sales from readyto-drink caffeinated coffee drinks increased by 48.1 percent, with growth expected to continue through 2020.¹² The European Union's Food Safety Authority produced a report in 2013 examining caffeine consumption in children. The report examined data from 16 countries between February and November of 2012 and found that 18 percent of children aged 3 to 10^{*} consumed energy drinks. The report also found that energy drink products made up the largest percentage of total caffeine intake in children compared to any other age group (energy drinks accounted for 43 percent of total caffeine consumed by children, relative to 13 percent by adolescents and 8 percent by adults).¹³

The amount of caffeine in energy drinks varies greatly. For example, while the caffeine content in a six-ounce cup of brewed coffee ranges from 77-150 mg,¹⁴ energy drinks contain between 50-505 mg of caffeine per can or bottle.¹⁵

Researchers and health care professionals have demonstrated their concern regarding the effects on children of consuming myriads of products with added caffeine. Given that children regularly consume potato chips, candy bars, and other food items to which caffeine is being added, they could unknowingly be ingesting very high doses of caffeine.¹⁶ Parents are largely unaware of the many consumable items that contain caffeine,¹⁷ the amount of caffeine in consumable products, or the dangers to children associated with caffeine consumption.¹⁸ As children unintentionally consume large doses of caffeine each day, they are at increased risk of caffeine toxicity.[†]



"Studies have demonstrated that, compared to adults, children are at increased risk for possible health effects from ingestion of even naturally occurring dosages of caffeine. And, with caffeine now appearing in so many different product types, it's possible that a young child may be at risk of ingesting caffeine from many sources in a given day without even having any sense of the exposure they are having from what they are eating and drinking. The consequences of this cumulative exposure are deserving of greater analysis, attention, and understanding."

--Margaret A. Hamburg, M.D. Former Commissioner of the FDA

SOURCE: Hamburg, M. (2013). Caffeine in food and dietary supplements: Examining safety: Remarks. Washington, DC: National Academies Press.

* Children aged 3 to 5 only accounted for 1 percent of the sample of children.

† Experiencing adverse behavioral or medical effects from caffeine.

Rates of Caffeine Exposure*

Much of the available information on childhood caffeine consumption comes from reports from parents and other caretakers, much of which may be inaccurate given the increasing and broad range of products that contain caffeine without consumers' knowledge.¹⁹ Moreover, data cited in much of the relevant literature on childhood caffeine consumption predates the widespread availability and popularity of energy drink products.²⁰ Nevertheless, recent national data have shown an increase in energy drink exposures in young children.²¹

A study that examined data from the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS)[†] from 2010 and 2011 (following the introduction of energy drink-related codes to the database in 2010) found that 46 percent of all energy drink-related singlesubstance exposures were among children aged 5 and younger (50.7 percent of exposures to nonalcoholic energy drinks were among children in this age group). The majority of these cases were classified as unintentional. Of available cases with outcome data, 28 percent resulted in minor or moderate adverse consequences. Minor effects included signs and symptoms that may have been uncomfortable, but were resolved rapidly. Moderate effects included those that were not life threatening, but had more pronounced symptoms, a longer duration, and required treatment. Although age-related outcome data were not provided specifically for energy drinks with additives (e.g., taurine, guarana, yerba mate), consumption of these products was associated with an increased likelihood of being referred to a health care facility and experiencing adverse effects. Children aged 5 and younger comprised 9.8 percent of cases of reported exposures to alcohol-containing energy drink products, and had the highest proportion of unintentional exposures. For those cases where an outcome was reported, 50 percent experienced minor to moderately serious adverse effects. Overall, among all ages, cases of exposure to energy drinks that contain alcohol resulted in more referrals to a health

care facility than cases of exposure to non-alcoholic energy drinks.²²

Another study using NPDS data that examined singlesubstance exposures to energy drinks from October 2010 to September 2013 found that more than 40 percent of the cases involved unintentional exposures among children aged 5 and younger.²³

To examine more closely trends and patterns in childhood exposure to caffeine, we present data from NPDS annual reports on single-substance exposures to all caffeine products (soft drinks, energy products, and all other caffeine products) from 2007 to 2016.[‡] The two graphs below highlight exposures to caffeine products collected from the NPDS. The first graph demonstrates reported exposures to caffeine products in all ages, and the second demonstrates reported exposures in children aged 5 and younger.

The data indicate that from 2007 to 2012, singlesubstance exposure calls for all ages involving 'other caffeine products' (or caffeine products other than energy products) steadily declined for six straight years before increasing between 2012 and 2015 (with a slight decline in 2016). The number of energy product exposure calls remained relatively steady since 2011.

* The term "exposure" means someone has had contact with the substance in some way; for example, ingested, inhaled, or absorbed a substance by the skin or eyes, etc. Exposures do not necessarily represent poisonings or overdoses.

† Case records in the NPDS database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/educational materials. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to poison centers and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

[‡] The energy drink category was added to the NPDS in 2010. Because of this, rates of exposure to energy drinks may be underestimated since these codes initially may have been underutilized.





Between 2010 and 2016, NPDS data indicate that children aged 5 and younger comprised 38 percent of all poison center calls related to the 'other caffeine products' (not energy drinks) category and 50 percent of all calls related to energy product exposure. Exposure calls related to 'other caffeine products' increased from 2007 to 2010, peaked in 2010, and slightly declined from then to 2012. Between 2012 and 2016, calls related both to 'other caffeine products' and energy products increased, with reports of energy product exposures surpassing reports for exposure to other caffeine products. This might be due to the higher caffeine levels in energy drinks compared to other caffeinated products, which might increase the likelihood that caretakers would call poison centers. The growing popularity of energy drinks also makes it more accessible to young children,²⁴ increasing the risk of unintentional exposure.



Symptoms of Caffeine Exposure

The majority of research on the effects of caffeine has been on adult populations.²⁵ These studies have shown that toxic symptoms of caffeine exposure appear relatively quickly, since peak plasma levels tend to be reached between 15 and 45 minutes after exposure.²⁶

While moderate caffeine consumption is considered to be fairly harmless among healthy adults, the effects of caffeine depend on dose, individual tolerance level, and consumption rate.²⁷ The rising popularity of energy drinks is concerning, as consuming large doses of energy drink products can lead to severe symptoms. Between 2007 and 2011, the number of emergency department (ED) visits involving energy drinks among individuals aged 12 and older doubled, from 10,068 to 20,783.²⁸ One in 10 ED visits resulted in hospitalization, with patients suffering from multiple symptoms.²⁹ Even without studies specifically examining the symptoms of caffeine toxicity in young children, available reviews on caffeine overdose, hospital visits, case studies, and exposure data can help inform our current understanding of the potential harmful effects. High levels of caffeine at any age, but especially in young children, can result in potentially serious symptoms, which can be exacerbated by preexisting health conditions.

The chart below lists common symptoms of caffeine exposure. Symptoms tend to be most severe when young children unintentionally consume high doses of caffeine.

Symptoms of Caffeine Exposure

Abdominal pain³⁰ Altered consciousness³¹ Anxiety³² Arrhythmias³³ Breakdown of muscle tissue³⁴ Death³⁵ Elevated body temperature (hyperthermia)³⁶ Excess fluid in brain (cerebral edema)³⁷ Gastrointestinal disturbance³⁸ Hallucinations³⁹ Headache⁴⁰ Heart attack (myocardial infarction)⁴¹ Heart palpitations⁴² Increased intracranial pressure43 Increased or decreased blood pressure⁴⁴ Insomnia or disturbed sleep⁴⁵ Irritability/agitation⁴⁶ Low potassium (hypokalemia)47 Muscle twitching⁴⁸ Nausea⁴⁹ Rapid breathing (tachypnea)⁵⁰ Rapid heart rate (tachycardia)⁵¹ Restlessness⁵² Rigidity⁵³ Seizures54 Tremor⁵⁵ Ventricular fibrillation⁵⁶ Vomiting⁵⁷



Caffeine toxicity and serious health effects appear to be strongly linked to the excessive consumption of caffeine via energy drinks,⁵⁸ due to the high doses of caffeine found in these products. The most severe adverse health effects of high-dose caffeine ingestion are cardiac arrhythmias or ventricular fibrillation, which can be fatal.⁵⁹

Rapid physical development during childhood might make children more vulnerable than adults to the neurological and cardiovascular effects of caffeine.⁶⁰ Moreover, children may be more likely to experience caffeine toxicity and multiple side effects from large amounts of caffeine since children typically tend to consume less than adults on a daily basis, and have a lower tolerance level than adults who habitually use caffeine.⁶¹

Similar to symptoms in adults, research suggests that caffeine toxicity in young children can manifest as emesis, tachycardia, agitation of the central nervous system, and diuresis.⁶² Children also may exhibit behavioral symptoms, such as anxiety, mood swings, restlessness, and disrupted sleep patterns.⁶³

Children with certain medical conditions, such as cardiac or seizure disorders, might be particularly vulnerable to the effects of caffeine.⁶⁴ Children taking certain medications may be at risk for more serious symptoms from exposure to high doses of caffeine. For example, the effects of caffeine consumption could be especially pronounced among the many children diagnosed with attention-deficit/hyperactivity disorder (ADHD) who take stimulant prescription medication.⁶⁵ as voluntary consumer and health care provider reports, the FDA compiled a list of serious adverse health events possibly resulting from 5-Hour Energy, Monster, and Rockstar brand energy drinks between January 2004 and October 2012. In the report, 13 deaths were associated[†] with 5-Hour Energy, five deaths were associated with Monster, and many other life-threatening symptoms resulting in hospitalization were associated with all three energy drink products.⁶⁶

Toxicity and Variations in Caffeine Dose

Although no amount of caffeine is recommended in children's diets, a 1994 study that serves as the basis for daily-recommended caffeine intake indicates that children should not exceed 45 mg of caffeine per day. Caffeine toxicity and behavioral symptoms typically present after ingestion of more than this amount of caffeine.⁶⁷ Although this study was conducted on children older than age 5, the 45 mg/day limit is the same recommended limit for children aged 4 to 6 by Health Canada, Canada's federal department responsible for the public health of its citizens. By way of comparison, recommended limits are 85 mg/day for 10 to 12 year olds⁶⁸ and 100 mg/day for adolescents.⁶⁹ It is important to note that caffeine toxicity is dosedependent, and just one energy product with caffeine levels between 50 mg and 505 mg exceeds the recommended limit for most children.

FDA's Adverse Event Reporting System Highlights Serious Effects of Energy Drinks

The Dietary Supplement and Nonprescription Drug Consumer Protection Act of 2006 required that all serious adverse events^{*} resulting from the use of dietary supplements be reported to the FDA. With these mandatory reports, as well * This law defined a serious adverse event as resulting in "death, a lifethreatening experience, inpatient hospitalization, a persistent or significant disability or incapacity, a congenital anomaly or birth defect, or that requires, based on reasonable medical judgment, a medical or surgical intervention to prevent one of those outcomes."

† This report included a disclaimer indicating that there is no definitive proof that the product mentioned in the report is the direct cause of the adverse event. It only reflects what was reported to the FDA, but does not contain a conclusion made by the FDA regarding a direct causal relationship between the adverse event and use of the product.

There may be instances where the caffeine content listed on the label of a product may not represent the caffeine content in the product. Consumer Reports magazine collected 27 top-selling energy drinks and shots to determine the caffeine content in their products and to examine the labeling of the caffeine content. The analysis found that 11 out of the 27 energy products did not even specify the amount of caffeine contained in the product. Of the 16 products that did include a precise amount, five actually contained caffeine at a level that was, on average, 20 percent higher than the amount indicated on the label.⁷⁰

The chart below lists the average caffeine concentration levels in common products that children may be exposed to unintentionally. The chart that follows presents the caffeine content in popular coffee, tea, and soft drink products from well-known food companies. Going by the 45 mg/day limit, most of the products listed would cause adverse side effects if unintentionally consumed by young children. Energy drinks, such as 5-Hour Energy, which contains 200 mg of caffeine per bottle, could cause serious and potentially life-threatening side effects if consumed by young children.⁷¹

Teen Dies after Drinking Too Much Caffeine

A 16-year old high school student from South Carolina collapsed after drinking a caffé latte, large Diet Mountain Dew, and an energy drink in a two-hour time span. About an hour after collapsing, he was pronounced dead. Coroner Garry Watts stated that the boy died from a caffeine-induced cardiac event that likely caused arrhythmia. The autopsy report revealed that the teenager was healthy, had no undiagnosed heart problems, and had no other drugs or alcohol in his system.⁷² "I think there is no place for caffeine in a child's diet until they become young adults, at age 18...And even in adults, it's important to be really careful. As in all things, caffeine should be consumed in moderation."

--Jessica Lieb, RD, LDN Nutritionist Children's Hospital of Pittsburgh University of Pittsburgh Medical Center

SOURCE: Carroll, L. (2014). Kids and caffeine may be a dangerous combination, new study suggests. Retrieved from TODAY Show website: http://www.today. com/health/kids-caffeine-may-be-dangerous-combination-new-studysuggests-1D79801666.



Average Estimated Caffeine Content in Common Products ⁷³			
Drink	Size	Caffeine Content	Product Image
Brewed Coffee	8 oz (237 mL)	95-165 mg	
Specialty Coffee (Latte or Mocha)	8 oz (237 mL)	63-126 mg	
Brewed Hot Tea*	8 oz (237 mL)	25-48 mg	
Cola	8 oz (237 mL)	24-46 mg	
Energy Drink	Shot: 1 oz (30 mL)	40-100 mg	16
	Regular: 8 oz (237 mL)	27-164 mg	Finer

* Combination of black and green tea.

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Caffeine Content in Company Products ⁷⁴			
Type of Product	Size	Caffeine Content (mg)	
Coffee			
Dunkin' Donuts Brewed Coffee	14 oz.	210	
Dunkin' Donuts Latte	14 oz.	151	
McDonalds Coffee	16 oz.	145	
Panera Bread Coffee	16 oz.	189	
Starbucks Cold Brew Coffee	16 oz.	200	
Starbucks Decaf Coffee	16 oz.	25	
Starbucks Grande Caffé Latte	16 oz.	150	
Starbucks Grande Coffee	16 oz.	330	
Iced Tea			
Arizona Iced Tea	20 oz.	38	
Fuze Iced Tea	20 oz.	20	
Lipton Iced Tea	20 oz.	48	
Soft Drinks			
Coca-Cola	12 oz.	34	
Diet Coke	12 oz.	46	
Dr. Pepper	12 oz.	41	
Mountain Dew	12 oz.	54	
Pepsi Cola	12 oz.	38	
Energy Drinks			
5-Hour Energy	2 oz.	200	
AMP Energy Drink	16 oz.	142	
Monster Energy Drink	16 oz.	160	
Red Bull	8.46 oz.	80	
Rockstar Energy Drink	16 oz.	160	
Foods			
Breyers Coffee Ice Cream	8 oz. (per scoop)	30	
Clif Energy Bars	2.4 oz. (per bar)	50	
GU Energy Gel	1 oz. (per package)	40	
Jelly Belly Extreme Sports Beans	Per 1 oz. bag	50	



Approaches to Addressing Childhood Caffeine Exposure

Unlike other addictive substances, states typically have not regulated caffeine. The responsibility of caffeine regulation resides primarily with the federal government.

U.S. Food and Drug Administration (FDA)

The FDA is the federal agency in charge of regulating caffeine. While the FDA has voiced concerns about the health risks associated with energy drinks and other caffeinated food and beverages, it has not published guidelines on caffeine consumption for children.⁷⁵ Compared to other countries, the U.S. has relatively lax regulations related to caffeine. For example, Canada's federal agency, Health Canada, has guidelines suggesting that children aged 4 to 6 should not have more than 45 mg of caffeine per day.⁷⁶

The FDA's policy toward caffeine has been inadequate ever since the substance was first regulated in 1958, when the Food Additives Amendment was added to the Federal Food, Drug, and Cosmetic Act (FFDCA) of 1938. The amendment listed caffeine in soft drinks as a "generally recognized as safe" (GRAS) additive, and indicated that it should not exceed 71 mg per 12 fluid ounces. However, the FFDCA only applies to soft drinks, and not to other caffeinated products.⁷⁷

Energy drinks, for example, are regulated differently because they can be classified either as conventional beverages or as dietary supplements. Energy drink companies that classify their products as dietary supplements do not fall under the FFDCA; instead, they are regulated by the 1994 Dietary Supplement Health and Education Act (DSHEA). The DSHEA does not limit the amount of caffeine manufacturers can add to energy products. Energy drink companies are free to add more than 71 mg per 12 fluid ounces (the FFDCA limit for soft drinks).⁷⁸ A 2006 analysis of several energy products, conducted well before the recent expansion in availability of these products, found that non-soda caffeinated beverages contained between 150-300 percent of the caffeine limit specified by the FDA for cola-type beverages.⁷⁹

Even if energy drink companies classify their products as conventional beverages, they still are allowed to add caffeine without seeking premarket approval from the FDA. The amount of caffeine in a product does not have to be revealed to the consumer because caffeine has the GRAS designation.⁸⁰ The GRAS designation makes it challenging for the FDA to address caffeine exposure in children if companies are not forced to label how much caffeine is in their products. This applies to the labeling of caffeine-containing food, beverages, and dietary supplements. However, there are different rules depending on the source of caffeine. When caffeine is derived from a natural source, it is not required to be listed on the label. When it is added to food or dietary supplements, it must be present on the list of ingredients. Still, the exact amount of caffeine does not have to be listed on the label on either food products or dietary supplements.⁸¹

The lack of proper labeling requirements render consumers -- particularly children -- vulnerable to unwittingly consuming high levels of caffeine that could pose significant health risks. Variable levels of caffeine in products that do not have warning labels not only leave adults unaware of how much caffeine they are ingesting,⁸² but also expose children to the risk of inadvertently ingesting caffeine at potentially harmful levels. With caffeine being added to multiple food products without any indication of dosage, it is impossible for parents to accurately monitor their children's caffeine intake or ensure that they do not exceed the maximum recommended daily limit of 45 mg/day.

It is safe to assume that the FDA did not foresee the explosion in products on the market containing added caffeine.⁸³ In recent years, the FDA has begun to explore and adopt stricter actions on some caffeine products, which may help limit the adverse effects of caffeine exposure in children. In 2010, the FDA sent warning letters to four manufacturers of caffeinated alcoholic beverages, stating that they recognized caffeine as an "unsafe additive" when combined with alcohol. While caffeine normally has the GRAS designation, the FDA believes it should not have the designation with alcohol, and caffeinated-alcoholic beverages are in violation of the FFDCA. Because of the FDA letters, all four manufacturers have ceased to manufacture, produce, and ship their caffeinated alcoholic beverages.84

In 2013, at the FDA's request, the Institute of Medicine assembled a science-based workshop to evaluate levels of safe caffeine consumption. The experts concluded that caffeine consumption, particularly energy drinks, could be harmful to children and that more research is needed to understand how children, especially those with underlying conditions, could be affected by caffeine.⁸⁵ After the workshop, the FDA announced it would continue to investigate the safety of caffeine intake in children and adolescents in response to the current trend of companies adding caffeine to more and more consumable products.⁸⁶

In 2015, the FDA sent warning letters to five manufacturers of dietary supplements containing powdered caffeine.⁸⁷ Powdered caffeine is extremely dangerous, and children can easily confuse powdered caffeine with sugar. Even adults can easily overdose on powdered caffeine. The FDA stated that it has not received any reports of serious adverse health events since these warning letters were issued.⁸⁸

FDA Releases Warning to Customers to Avoid Powdered Pure Caffeine

In light of two deaths attributable to the use of pure caffeine powder, the FDA issued a warning to consumers to stay away from this product,⁸⁹ and issued five warning letters to companies distributing dietary supplements containing caffeine powder.⁹⁰ The FDA warned that it is almost impossible to measure pure caffeine powder, and a lethal amount could easily be consumed. Research shows that one teaspoon of caffeine powder is equivalent to drinking 28 cups of coffee.⁹¹ Since the safe amount of caffeine for an adult is considered to be approximately 400 mg per day,⁹² powdered caffeine can be fatal in healthy adults,⁹³ and all but guarantees death in young children.

Since the FDA does not have the authority to remove caffeine powder from the market, it began building a legal case against companies that sell pure powdered caffeine and market it in bulk⁹⁴ in an attempt to persuade these companies to stop selling and marketing the product.⁹⁵ While all five companies have agreed to stop selling powdered caffeine, other manufacturers continue to sell it online.⁹⁶

Since the federal government has not officially banned pure powdered caffeine, some states have looked to regulate it themselves. Ohio passed a law banning the purchase of bulk powdered caffeine, and Illinois forbids minors from purchasing powdered caffeine.⁹⁷

Health Organizations

Some health organizations, recognizing the serious consequences caffeine consumption can have on children, have begun to address caffeine regulations and childhood caffeine exposure.

American Academy of Pediatrics (AAP)

The AAP released a clinical report in 2011 addressing the current landscape of energy and sports drinks for children and adolescents. The AAP stressed that not only should energy drinks not be consumed by children and adolescents, but neither should caffeine in general.⁹⁸ This stance may help reduce childhood caffeine exposures because parents may be less likely to purchase caffeinated products if they know the risks they can pose to children's health. After the report was published, the AAP called for increased public education regarding the negative consequences of caffeine exposure in children, stronger federal caffeine regulations, and for all energy drink products to list on the package the total amount of caffeine content in the product.⁹⁹

American Medical Association (AMA)

In 2013, the AMA issued a press release fully supporting a ban on marketing by energy drink companies to children under age 18.¹⁰⁰ The position of the AMA is that children and adolescents should not consume products with high caffeine content.¹⁰¹

The Dietary Guidelines for Americans Fall in Line with the AAP and the AMA

The Dietary Guidelines Advisory Committee submitted a scientific report on its findings on caffeine to the Secretaries of the U.S. Department of Health and Human Services (HHS) and the U.S. Department of Agriculture (USDA) in February 2015. In this report, the committee presented the evidence on the health effects of excessive caffeine intake on adults and children. It stated that it concurs with the American Academy of Pediatrics and the American Medical Association that, "until safety has been demonstrated, limited or no consumption of high-caffeine drinks, or other products with high amounts of caffeine, is advised for vulnerable populations, including children and adolescents."¹⁰²
Prescription Drugs

Key Points

- Young children are especially susceptible to the effects of opioids, which are among the most toxic substances to young children and can be lethal in small doses.
- From 2000 to 2010, there was a dramatic increase in unintentional exposures to controlled prescription drugs among young children. Since 2011, the number of exposures, with a few exceptions, has been declining steadily. Between 2013 and 2015, exposures to the opioids fentanyl, oxycodone, and buprenorphine increased among children aged 5 and younger.
- The risk of pediatric exposure to medications has been associated with increases in the availability of such medications in the home, due in large part to more lenient prescribing. In response to the opioid epidemic, curbs on prescribing practices have been enacted, which may help to account for the reversal of the trend in increasing rates of exposure.
- Strategies to reduce childhood poisonings from prescription drugs include product reformulations; child-resistant and other forms of safety packaging; and consumer, parent, and caregiver education and awareness. Expanding efforts to reduce overprescribing and educating the public about safe storage and disposal methods for controlled prescription medications can help to decrease the risk of pediatric exposure and fatalities.

The growth in prescription drug use among adults in the United States since 1999,¹ due in part to more lenient prescribing practices, resulted in greater availability of potentially addictive medications and a consequent increase in the risk of unintentional exposures to these drugs among young children.² However, recent improvements in child-resistant packaging, product reformulations, increased public awareness of the risks of unintentional ingestion, and curbs on prescribing practices in response to the opioid epidemic have all contributed to a decline in the past few years in childhood poisonings from prescription drugs.³ Still, data from both poison control centers and emergency departments (EDs) indicate that unintentional exposures to medications among children aged 5 and younger continue to be a significant problem.4

Although some ED visits for unintentional medication exposures are due to over-the-counter medications or dietary supplements, prescription drugs are implicated in approximately 50 percent of such visits among children aged 5 and younger.⁵ Opioids in particular are implicated in the highest proportion of ED visits involving prescription drugs in this age group,⁶ reflecting the particular danger these drugs pose to children.⁷

"The opioid crisis, which has been affecting our adult population, has now trickled down to our children... When adults bring these medications into their homes, they can become a danger to the children that live there. It is important that these medications are stored up, away and out of sight of kids of all ages. In a locked cabinet is best."

--Marcel Casavant, MD Medical Director Central Ohio Poison Center

SOURCE: Rettner, R. (2017). Thousands of US kids take opioid drugs accidently each year. Retrieved from LiveScience website: https://www.livescience. com/58351-kids-opioids-ingestion.html.

The Consumer Product Safety Commission (CPSC) Issues Warnings to Shed Light on the Problem of Childhood Poisonings

In 2009, the CPSC issued a news release highlighting that 9 out of 10 unintentional childhood poisonings occur at home, and that the majority of exposures are to medications and involve children aged 1 and 2 years old. The CPSC recommended that parents and caregivers actively work to keep medications in original child-resistant packaging, store products out of reach of children, and call poison control centers if they suspect an exposure or poisoning.⁸

Rates of Prescription Drug Exposure*

Given the high incidence of hospitalizations and other serious outcomes from opioid exposures,⁹ available research on exposures to prescription medications in children has focused primarily on opioids. Nevertheless, case studies, data from regional poison control centers, ED surveillance systems, and data collected from the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS)[†] shed light on the extent of unintentional poisonings from opioids in addition to other commonly misused and addictive stimulant and depressant prescription drugs.

Studies have found that rates of unintentional exposure to prescription drugs among children aged 5 and younger increased between 2000 and 2010, but tapered off by 2013.¹⁰ Most notable has been the increase in exposures to opioids at both the national¹¹ and state levels.¹² Data from ED visits and poison control centers demonstrate that the most severe exposure-related health outcomes in children tend to be from the ingestion of opioids and sedative/ hypnotics.¹³

Data from the Centers for Disease Control and Prevention's (CDC) National Electronic Injury

Surveillance System: Cooperative Adverse Drug Event Surveillance System (NEISS-CADES) from 2004-2013 indicate that 640,161 ED visits were related to unintentional exposures to medications among children aged 5 and younger. Data from 2010-2013[‡] indicate that prescription drugs accounted for 51.2 percent of ED visits, with opioids and benzodiazepines comprising the top two implicated classes of prescription drugs.¹⁴ NPDS data analyzed by the nonprofit organization Safe Kids Worldwide indicate that almost half of all calls to poison control centers in 2013 were medication-related, and that children between the ages of 1 and 4 accounted for 75 percent of all unintentional and therapeutic error medicine exposures calls. Although the majority of calls were for exposures to over-the-counter medications, among children ages 0 to 5, controlled prescription drugs such as oxycodone, methylphenidate, amphetamines, benzodiazepines, and buprenorphine were among the top 10 substances most commonly involved in exposures with more serious outcomes.¹⁵

To examine exposure rates more closely, we organized prescription drugs into the three classes of potentially addictive prescription medications[§] that pose a risk to young children: opioids, central nervous system (CNS) stimulants, and central nervous system (CNS) depressants.¹⁶

‡ NEISS-CADES data on the type of drug implicated in the ED visit were available only for these years.

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^{*} The term "exposure" means someone has had contact with the substance in some way; for example, ingested, inhaled, or absorbed a substance by the skin or eyes, etc. Exposures do not necessarily represent poisonings or overdoses.

[†] Case records in the NPDS database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/educational materials. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to poison centers and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

[§] These are classified as controlled substances by the U.S. Controlled Substances Act of 1970, which created a system for classifying illicit and prescription drugs according to their medical value and their potential for misuse.

Opioids

Analgesics or pain relievers, which include opioids and certain over-the-counter medications, are one of the most frequent substance categories involved in pediatric exposures,¹⁷ and they constitute a significant proportion of serious, life-threatening drug-related outcomes.¹⁸ Children may be especially susceptible to the detrimental effects of opioid exposure, as a single lick or taste of certain prescription opioids could be fatal.¹⁹

Exposure data on prescription opioids, collected from the Drug Abuse Warning Network's (DAWN)* national estimates of drug-related ED visits, show that accidental drug exposure among children aged 5 and younger remained relatively stable from 2004 to 2011. However, in certain drug classes, opioids in particular, there were significant increases in accidental exposures. In 2011, opioids were the most common class of drugs associated with ED visits among children aged 5 and younger, present in 25 percent of visits among children in this age group. These exposures amounted to a 225 percent increase between 2004 and 2011 in ED visits for opioid exposure among children aged 5 and younger.²⁰ Research suggests that increases in childhood exposures to opioids parallel increases in adult opioid prescriptions and adult opioid use²¹

A more recent study using NPDS data analyzed prescription opioid exposures[†] from 2000 through 2015 among children and adolescents younger than 20 years old. The study concluded that, of all the age groups,[‡] children aged 5 and younger accounted for the largest number of exposures. The number of opioid exposures in children aged 5 and younger increased by 93.2 percent from 2000 to 2009. After this large initial increase, the number of exposures in children decreased by 29.4 percent.²²

Poison Control Centers Receive 32 Calls a Day about Children Exposed to Opioids

A recent article reported that poison control centers throughout the U.S. receive 32 calls a day associated with prescription opioid exposures in children. From January 2000 to December 2015 there were 188,000 calls involving opioid prescription drug exposures in children and adolescents. Approximately 60 percent of these calls were for exposures in children aged 5 and younger.²³ It is important note that these are calls reported to poison centers, and not necessarily a census of all unsupervised exposure incidents, which may be even greater.

"While overall rates of exposure to opioids are going down, they are still too high...We need to continue to examine our prescription practices and to increase education to parents about safe ways to store these medications at home to keep them out of the hands of children."

-- Gary A. Smith, MD, DrPH Director of the Center for Injury Research and Policy Nationwide Children's Hospital Columbus, Ohio

SOURCE: Rettner, R. (2017). Thousands of US kids take opioid drugs accidently each year. Retrieved from LiveScience website: https://www.livescience. com/58351-kids-opioids-ingestion.html.

* DAWN was a public health surveillance system maintained by the U.S. Department of Health and Human Services' Substance Abuse and Mental Health Services Administration (SAMHSA), which monitored drug-related hospital ED visits in metropolitan areas and across the nation. DAWN was discontinued in 2011.

† Specific opioids included hydrocodone, oxycodone, codeine, tramadol, propoxyphene, morphine, buprenorphine, meperidine, hydromorphone, fentanyl, and oxymorphone.

‡ Age groups were 0-5 years, 6-12 years, and 13-19 years.

The current opioid epidemic has made it increasingly important to analyze current rates of opioid exposure. We collected data on single-substance exposures^{*} to 10 opioids using the NPDS annual reports from 2011⁺ to 2016. Opioids included in our analysis were hydrocodone,[‡] hydromorphone, oxycodone,[§] oxymorphone, tramadol, morphine, fentanyl, codeine, buprenorphine, and methadone. These 10 drugs may not represent all the types of opioids that children can be exposed to unintentionally; however, they currently are some of the most widely prescribed pain relievers.²⁴ The two graphs below highlight the number of exposures reported in the NPDS to all 10 opioids combined. The first graph demonstrates reported exposures to opioids in all ages, and the second demonstrates reported exposures in children aged 5 and younger. In both cases, the number of reported exposures to the opioid class of drugs has decreased from 2011 to 2016.





* Single-substance exposures are cases where only one substance was involved in the reported incident.

† The AAPCC did not collect single-substance exposure data on hydrocodone, hydromorphone, oxymorphone, fentanyl, and buprenorphine until 2010. We analyzed data starting in 2011 because rates of exposures to these opioids may have been underestimated in 2010 since these codes may initially have been underutilized. ‡ Alone or in combination (excluding combination products with acetaminophen, acetylsalicylic acid/aspirin, or ibuprofen).

I Alone or in combination (excluding combination products with acetaminophen or acetylsalicylic acid/aspirin).

The next two graphs display the number of exposures to six separate types of opioids: codeine, fentanyl, morphine, tramadol,* oxycodone/oxymorphone, and hydrocodone/hydromorphone. The first graph shows the number of cases in all ages, and the graph that follows shows cases for children aged 5 and younger. For all ages, reported exposures to the specific opioids included in the analysis have either remained relatively stable or declined slightly since 2011. However, the number of oxycodone/oxymorphone exposures increased marginally from 2014 to 2016.



Looking at exposures to the specific opioids among young children, the number of reported cases has remained relatively stable from 2011 to 2016; however, the number of exposures to oxycodone/ oxymorphone and fentanyl increased from 2013 to 2015 and then declined in 2016.



* Tramadol accounts for the largest proportion of exposures of all the opioids included in the analysis. Although the exact reason for this cannot be determined based on existing data, there is reason to believe that tramadol may be misperceived as less addictive than other opioids, and its effects may

not be as well understood. This might account both for its widespread use/ misuse and for a disproportionate number of calls to poison centers from health care providers who may be less familiar with its toxicity and adverse effects compared to other opioid medications.

The Dangers of Fentanyl

Fentanyl is a synthetic opioid that is 100 times more potent than morphine.²⁵ Transdermal fentanyl patches are strong prescription opioids, and even a used patch contains high amounts of the drug.²⁶ Children may access used patches by finding those that have been discarded or stored improperly or that have fallen off the intended user. There also have been examples of patches that have transferred from the intended wearer to a child. According to data from the U.S. Food and Drug Administration's (FDA) Adverse Event Reporting System (from 1990 to 2012) and from the Centers for Disease Control and Prevention's (CDC) National Electronic Injury Surveillance System: Cooperative Adverse Drug Event Surveillance System (NEISS-CADES) (from 2004 to 2010), 30 cases of accidental exposures to fentanyl among young children were identified. Twentyeight cases were among children aged 10 and younger, while 19 cases involved a child aged 2 or younger. Of all pediatric exposure cases, most had serious outcomes: 10 children died and 16 others required medical care or hospitalization.²⁷ It is likely that the risk of exposure in more recent years has increased with the increasing availability of fentanyl on the drug market.

The last two opioids for which we collected exposure data are buprenorphine and methadone. These two opioid medications are important to address because they are two of the three types of FDA-approved medications for the treatment of opioid addiction.²⁸ Although buprenorphine and methadone have been tremendously successful in improving the quality of care for opioid addiction,²⁹ they do have the potential to be misused, and one adverse consequence of their increasing availability is unintentional ingestion among young children.³⁰

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The graph below represents the number of exposures to buprenorphine and methadone in all ages, and the graph that follows shows the number of exposures to buprenorphine and methadone among children aged 5 and younger. As seen in both graphs, exposure to methadone declined from 2012 to 2016. Reported buprenorphine exposures declined from 2011 to 2013, but appears to have reversed course in 2013.





Children aged 5 and younger accounted for 14 percent of all methadone exposures and 44 percent of all buprenorphine exposures from 2011 through 2016. Since these medications are nearly always prescribed to adults and never to young children, this finding highlights the need to adopt better strategies to prevent unintentional exposures to these drugs in children.³¹

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Additional data from the CDC's National Electronic Injury Surveillance System: Cooperative Adverse Drug Event Surveillance System (NEISS-CADES) indicate that 68 cases involving buprenorphine product ingestion among children aged 5 and younger were identified in 2010-2011. Based on the cases from select hospitals during that time, the CDC estimated that an average of 1,499 children aged 5 and younger were evaluated in U.S. EDs each year for buprenorphine ingestions. The majority (76.8 percent) involved children aged 1 and 2 years old. Due to the risk of respiratory depression and the long half-life of buprenorphine, 58.4 percent of buprenorphine-related ingestion ED visits resulted in hospitalization. Compared to unintentional ingestions from other prescription drugs, buprenorphine accounted for a larger proportion of ED visits and hospitalizations among children aged 5 and younger (29.8 percent of ED visits and 59.5 percent of emergent hospitalizations for opioid product ingestions).*32

Central Nervous System (CNS) Stimulants and Depressants

Prevalence data on unintentional ingestions of CNS stimulants in pediatric populations are limited due in part to the fact that physicians intentionally prescribe stimulants to children with attention-deficit/ hyperactivity disorder (ADHD). ADHD is the most commonly diagnosed neurobehavioral disorder in childhood and adolescence. In 2011, the American Academy of Pediatrics lowered the age for when physicians should begin screening for ADHD in children from 6 to 4. This adjustment also coincided with a recommendation that prescription stimulants (e.g., methylphenidate) be prescribed to children between the ages of 4 and 5 if behavioral interventions do not adequately treat the disorder.³³

The NPDS collects data on the number of prescription stimulant exposures in children. One study used the NPDS data from January 2007 to December 2012 and analyzed the number of calls to poison control centers for exposures to three types of stimulants[†] among children aged 19 and younger. Children aged 5 and younger accounted for 10,421 calls over the time frame, and had the highest proportion of stimulant exposures compared to any other age group.³⁴

With regard to CNS depressants, the three main classes are benzodiazepines, non-benzodiazepine sleep medications, and barbiturates. Calls made to poison control centers regarding children aged 5 and younger for exposures to substances that fall under the NPDS generic substance category of sedative/hypnotic/ antipsychotic (which includes benzodiazepines, barbiturates, and sedatives/hypnotics) increased by 79 percent over an 11-year period, from 1,857 exposures in 2000 to 3,317 exposures in 2010.³⁵

To examine more closely national trends in prescription drug exposures among young children, we collected data on single-substance exposures to prescription stimulants and depressants from the NPDS annual reports from 2007 to 2016. The stimulants included were methylphenidate, amphetamines, and related compounds.[‡] Depressants included benzodiazepines and barbiturates. The graph below highlights reported exposures to theses prescription drugs among people of all ages, and the graph that follows highlights reported exposures to the same prescription drugs in children aged 5 and younger.

Among all ages, exposures to CNS depressants increased from 2007 to 2010. Since 2010, exposures generally have been declining. For stimulants, exposures increased every year from 2007 to 2011, and have since remained relatively steady.

* Excluding opioid-containing antitussive formulations.

 \dagger lisdexamfetamine, dextroamphetamine/amphetamine extended release, and dextroamphetamine/amphetamine immediate release.

[‡] The NPDS does not indicate the source of these stimulants. Therefore, it is possible they derived from illegal substances rather than prescription medications.



Reported exposures to CNS depressants among children aged 5 and younger increased from 2007 to 2009, and decreased every year since then. Exposures to CNS stimulants increased each year from 2007 to 2012, and has since remained relatively stable.



Symptoms of Prescription Drug Exposure

Over an 11-year period from 2000 to 2010, calls to 12 poison control centers in five states for exposures among children aged 5 and younger revealed a 53 percent increase in serious medical outcomes.* The generic substance categories of sedatives/hypnotics/ antipsychotics and analgesics, including opioids, were among the categories associated with the largest increase in serious outcomes.³⁶ Similarly, according to the NPDS, the category of sedatives/hypnotics/ antipsychotics (primarily benzodiazepines) showed the largest rate of increase from 2000 to 2013 in exposures that resulted in serious outcomes.³⁷ Over the 11-year period, opioids and cough and cold preparations each comprised 17.6 percent of all fatalities, whereas sedative/hypnotics were involved in 3.4 percent of fatalities among children aged 5 and younger.³⁸

Case reports, reported clinical outcomes from prevalence data, and pharmacological literature have outlined the most common symptoms of unintentional prescription drug exposure in young children. The symptoms are listed below for prescription opioids, CNS stimulants, and CNS depressants.

"It is notable that these ingredients [in narcotic painkillers and benzodiazepine sedatives] have relatively long durations of action and ingestion of doses intended for older patients can have serious and potentially life-threatening consequences for young children."

-- Maribeth C. Lovegrove Division of Healthcare Quality Promotion Centers for Disease Control and Prevention

SOURCE: Doyle, K. (2014). Painkillers, sedatives biggest threat when kids get into medicine chest. Retrieved from Reuters: https://www.reuters.com/article/ us-prescription-overdose-kids/painkillers-sedatives-biggest-threat-whenkids-get-into-medicine-chest-idUSKBN0HA1VH20140915.

Symptoms of Prescription Drug Exposure

Opioids

Vomiting⁷⁸

Agitation³⁹ CNS depression⁴² Coma⁴⁵ Convulsions⁴⁸ Death⁵¹ Drowsiness or lethargy⁵⁴ Hypotension (low blood pressure)⁵⁷ Miosis (pupil constriction)⁶⁰ Nausea⁶³ Respiratory depression and failure⁶⁶ Seizure⁶⁹ Slow breathing⁷² Tachycardia⁷⁵

CNS Stimulants

Agitation⁴⁰ Chorea (involuntary movement)⁴³ Disorientation⁴⁶ Hallucinations⁴⁹ Hypertension⁵² Insomnia⁵⁵ Lethargy⁵⁸ Nausea⁶¹ Palpitation⁶⁴ Restlessness/Hyperactivity⁶⁷ Seizure⁷⁰ Tachycardia (rapid heart rate)⁷³ Vomiting⁷⁶

CNS Depressants

Agitation⁴¹ Ataxia⁴⁴ Coma⁴⁷ Confusion⁵⁰ Dizziness⁵³ Drowsiness⁵⁶ Hallucinations⁵⁹ Hypertension⁶² Mydriasis (pupil dilatation)⁶⁵ Respiratory depression⁶⁸ Slurred speech⁷¹ Tachycardia⁷⁴ Vomiting⁷⁷

* Serious medical outcomes include moderate outcomes (more pronounced and prolonged symptoms than minimal outcomes, but not requiring a specific intervention), major outcomes (life-threatening symptoms), or death.

Toxicity of Prescription Drugs

Although a single pill can cause adverse symptoms or fatality in children, some classes of prescription drugs have dose-dependent effects. Developmental changes, metabolism, body composition, and other factors contribute to the risks associated with exposure, making it difficult to specify the exact dose or amount of a prescription medication that can result in pediatric toxicity.⁷⁹ Nonetheless, toxicity is largely characterized in terms of symptoms or adverse outcomes present following exposure. Toxicological information on prescription drugs in children is incomplete, given that this information typically is reported for adults only.

Opioids

In general, young children are very susceptible to the effects of opioids, which are among the most toxic substances to young children and can be lethal in small doses.⁸⁰ The bioavailability^{*} of particular formulations of opioids, and the fact that licking, sucking, or swallowing one pill can result in significant toxicity,⁸¹ make exposure to opioids particular concerning when young children are involved. In comparison to adults, unintentional opioid ingestions in children often result in a higher amount of medication per kilogram of body weight.⁸² Death from opioid overdose usually results from respiratory depression and failure.83

Two Toddlers Develop Malignant Cerebellar **Edema after Unintentionally Ingesting Prescription Opioids**

The opioid epidemic currently ravaging the United States can have serious consequences and a "trickle-down" effect on young children. A report published in July 2017 describes two cases of toddlers who accidentally ingested prescription opioids. Both children developed malignant cerebellar edema and showed symptoms of neurological decline, hydrocephalus (water on

the brain), and brain herniation. They were sent to the hospital where they needed fluid drained from their brains. Thankfully, both toddlers were quickly treated and survived. Nevertheless, these cases demonstrate the importance of recognizing the serious effects of opioid exposure in young children.84

In children, the connection between opioid dose and toxicity is not clear, in part because information on toxicity is often derived from studies on adults.85 There is limited information on toxic doses from common opioids such as morphine, oxycodone, and hydrocodone, even though deaths due to exposure to these drugs in children aged 5 and younger have been reported to poison centers.⁸⁶

A review of the literature on opioid toxicity in children suggested that utilizing available data on codeine might inform the understanding of the toxic dose of other opioids. If children consume more than 5 mg/kg of the equivalent of codeine, then they should be referred to a health care facility. For example, the analgesic dose equivalent of oxycodone to 5 mg/kg of codeine is 0.42 mg/kg, indicating that if a child ingested this amount of oxycodone or more, he or she should receive medical care.⁸⁷ Along with codeine, there also are data on pediatric toxicity from specific opioids such as methadone, buprenorphine, dextromethorphan, and fentanyl.

* The amount of a drug that enters the body's circulation.

Codeine

A retrospective study of 430 pediatric exposures to codeine in a Berlin poison center from 1976 is often cited as the basis for determining codeine toxicity in children between 1 and 6 years of age.⁸⁸ This study found that the appearance of symptoms from unintentional codeine ingestion depended on the dosage and time following exposure. In a very small percentage of children, ingestion of more than 5 mg/kg of codeine was associated with severe, life-threatening symptoms. Nonetheless, the researchers concluded that, aside from non-life-threatening symptoms (e.g., ataxia, miosis), a range of 5-15 mg/kg is generally tolerated in young children.⁸⁹

More recently, a review on opioid toxicity concluded that cases in which children consumed more than 5 mg/kg of codeine should be observed in the ED, since exceeding this amount can result in substantial toxicity.⁹⁰ Another review of codeine use in the pediatric population cited case studies and other reports that demonstrated adverse reactions in infants and children who consumed less than 2 mg/kg of codeine. Codeine toxicity in children is not straightforward and focusing on a single high dose of codeine as the cause of toxicity ignores the developmental and genetic variations in young children that place them at a higher risk of experiencing adverse reactions to even low doses of codeine.⁹¹ For example, one infant died from codeine overdose after being given 1.26 mg/kg over a six-hour period⁹² and another infant was hospitalized for a total of 6 days following the ingestion of 1.3 mg/kg of codeine.93

Methadone

Methadone can be lethal for children aged 5 and younger; there have been several cases in which children either have been hospitalized or have died from methadone exposure.⁹⁴ A review of the literature identified multiple case reports in which children experienced methadone toxicity from doses as low as 5 mg. Life-threatening toxicity also has been reported in ingestions as low as 0.5 mg/kg. Methadone is typically prescribed in a 5-mg or a 10-mg tablet or as a liquid concentration of 1 mg/mL; therefore, one tablet or dose of methadone could be fatal in young children.⁹⁵

Death from opioids generally is the result of respiratory depression, which is delayed in children exposed to methadone. Partially because of this delayed respiratory effect, young children exposed to any amount of methadone should be evaluated by a health care professional.⁹⁶ However, the standard 6-hour observation time in EDs may not allow for the detection of methadone poisoning,⁹⁷ especially if the parent or caregiver is unaware or unwilling to disclose possible methadone ingestion.98 The presence of other drugs may mask the effects of opioid exposure⁹⁹ or symptoms, and patient history may lead health care professionals to diagnose another condition.¹⁰⁰ If health care providers send children home early after the observation period prior to the onset of respiratory depression, or misdiagnose the symptoms, the delay in treatment or provision of inappropriate treatment may be fatal for children exposed to methadone.¹⁰¹

Toddler Dies after Unintentionally Ingesting Methadone

A mother was arrested in March 2015 after her 2-year-old son unintentionally ingested methadone. The child was not taken to the hospital and died several hours later. He came into contact with his mother's medication via an unsecured lock box of methadone and ingested an unknown amount of pills. The medical examiner stated that the child would have survived had he received emergency medical care. According to Debi Forrest, an education coordinator at Florida Poison Information Center at UF Health Jacksonville, "it's very, very sad to learn of a child's death in this way, especially when it could have very well been prevented by a timely call to 911 or taking them to a healthcare facility emergency department." She also emphasized the need to store medications high up, out of sight, and locked up.¹⁰²

Buprenorphine

While there are known benefits of treating adults who have opioid addiction with buprenorphine, including a decreased risk of overdose due to its ceiling effect in respiratory depression,¹⁰³ this protective effect may not apply to children.¹⁰⁴ Therefore, children are more vulnerable than adults to experiencing a fatal exposure to buprenorphine-containing products.¹⁰⁵ Even toddlers who taste or suck on a buprenorphine tablet are at risk of receiving a toxic dose, due to their receptor sensitivity and lack of developed opioid tolerance.¹⁰⁶

A toddler weighing 10 kg could experience buprenorphine overdose from even the smallest sublingual formulation available -- a single 2 mg tablet.¹⁰⁷ Nonetheless, adverse effects from exposures to buprenorphine can be dose-dependent, and cases with reported health consequences have all involved ingestions of more than 4 mg.¹⁰⁸ One case study of five children under the age of 2 exposed to between 4 and 10 mg of buprenorphine indicated that each child experienced respiratory depression.¹⁰⁹ Another study suggested that children under the age of 2 and children who have ingested 2 mg or more of buprenorphine should be referred to an ED.¹¹⁰ Due to the substantial danger of buprenorphine, children should be observed by a health care professional if they are exposed to any amount of this opioid.¹¹¹

One study found that three quarters (76.5 percent) of children aged 5 and younger exposed to buprenorphine were treated at a health care facility (compared to 41.2 percent of adults).¹¹² Another study found that 74 percent were treated at a health care facility, and the younger the child, the more likely he or she was to have experienced adverse clinical effects.¹¹³

Dextromethorphan*

The degree of toxicity of dextromethorphan is less clear than that of codeine, but available data suggest the amount typically associated with adverse effects in children. In 304 cases of unintentional exposure to cough and cold preparations, 282 of the cases

indicated an amount of dextromethorphan that was ingested, with a mean dextromethorphan dose of 2.65 mg/kg.¹¹⁴



Fentanyl

With regard to fentanyl, children who find a new or used fentanyl patch may put it in their mouth or apply it to their skin.¹¹⁵ Case studies of unintentional childhood exposure to transdermal fentanyl patches that resulted in life threatening hospitalization reported that one patient survived and another died.¹¹⁶ Opioid naïve children are vulnerable to overdose of fentanyl given its potency. An overdose of fentanyl in children can cause death by slowing breathing and increasing the levels of carbon dioxide in the blood. From 1997 to 2013, the FDA reported that there were 12 reported cases of death in children due to fentanyl.¹¹⁷ With the mounting misuse of fentanyl in recent years, an uptick in the number of fentanyl exposures in young children can be expected.

* Antitussive/cough medicine: a controlled substance.

Methylphenidate (CNS Stimulant)

Poison centers that have guidelines for methylphenidate exposure provide the recommendation that children aged 5 and younger can consume less than 2 mg/ kg without experiencing serious toxicity. Thus, it is recommended that if a child in this age group consumes more than 2 mg/kg, he or she should be referred to a health care facility.¹¹⁸

Approaches to Addressing Childhood Prescription Drug Exposures and Poisonings

Strategies to reduce childhood poisonings from prescription drugs through regulatory action include product reformulations and child-resistant packaging. Other public health approaches involve consumer, parent, and other caregiver education and awareness. Efforts to reduce and better monitor the prescribing of certain medications that are overprescribed aim to decrease their availability and the risk of pediatric exposure.

Federal and State Regulations and Initiatives

Federal and state governments have used various approaches over the years to address prescription drug exposures and poisonings in young children.

Poison Prevention Packaging Act of 1970

The U.S. Consumer Product Safety Commission (CPSC) implements and enforces the Poison Prevention Packaging Act (PPPA) of 1970, which requires childresistant packaging for particular household products. These substances are packaged in a way that makes it easy for an adult to open, but difficult for children under the age of 5 to open. The implementation of this act is largely recognized as one of the most influential changes responsible for a decrease in fatal poisonings among children aged 4 and younger from all types of potentially dangerous substances found in the home, including prescription medications.¹¹⁹ However, this Act mandates that testing of the childresistant packaging be conducted on children aged 3.5 to 4.5 years of age,¹²⁰ even though the majority of children who are unintentionally exposed to medications are 2 years of age or younger.¹²¹

It is important to note that child-resistant packaging is only effective if it is utilized properly and if the cap is properly replaced after use.¹²² There have been many examples of reported medication exposures that resulted from children accessing medication located in purses or pillboxes, or that simply have been left out in the open. In order to address unintentional exposure, manufacturers are encouraged to create containers for their products and promote strategies to make it both easy for adults and difficult for children to access the medication.¹²³ Other solutions to address the potential problems associated with child-resistant packaging with regard to preventing unintentional childhood exposures that have been introduced include educational campaigns directed toward parents and caregivers,¹²⁴ innovative packaging,¹²⁵ and product reformulations.¹²⁶ Product reformulations such as adding a bitter taste to potentially toxic substances have also been proposed as a way to curb pediatric exposures to prescription drugs,¹²⁷ but there is no evidence that such reformulations have yet been done or whether they would be effective.



Prevention of Overdoses and Treatment Errors in Children Taskforce (PROTECT)

In 2008, the CDC held a meeting for public and private stakeholders -- including public health agencies, medication manufacturers, and poison control centers -- concerning childhood medication safety. Although this task force originally was developed to address overdoses from over-the-counter medication, its scope has been extended to preventing unintentional overdoses from prescription medication as well. From this meeting, the PRevention of Overdoses and Treatment Errors in Children Taskforce (PROTECT) emerged. This task force involves stakeholders voluntarily collaborating to reduce unintentional medication overdoses in children.¹²⁸ In December 2011, PROTECT began an initiative, Up and Away and Out of Sight, which is a public awareness campaign designed to educate parents about the importance of keeping medications stored properly and out of the reach of young children.¹²⁹

In order to address existing limitations in childresistant packaging, PROTECT also encouraged the implementation of a new type of packaging specifically developed to decrease unintentional and unsupervised ingestions by young children by incorporating "passive" mechanisms of protection in addition to those required under the PPPA. These innovations are intended to limit the amount of medication that could be ingested by a child even if a child-resistant cap has not been properly re-secured.¹³⁰ For oral liquids (such as children's acetaminophen, cough and cold products, and methadone) this type of packaging includes "flow restrictors" to limit the amount of the drug product that may be delivered in order to prevent unintended access by children and other similarly vulnerable populations.¹³¹ Flow restrictors have been shown to reduce young children's ability to access liquids even when child-resistant caps are removed, and can reduce the number of calls to poison centers for high dose ingestions.¹³² In 2011, manufacturers of liquid acetaminophen voluntarily added flow restrictors to infant acetaminophen products.133

For oral solid medicines (pills), another type of packaging incorporating passive mechanisms of protection could be based on a single-dose unit, limiting the amount of medication children could ingest even if they were to be exposed to the drug.¹³⁴ For example, a 2013 study found that children were 3.5 to 8.8 times more likely to come into contact with the medication Suboxone[®] (buprenorphine/naloxone) in pill form than in a single-dose, child-resistant film formulation.¹³⁵ After the study was published, the drug's manufacturer^{*} volunteered to discontinue the sale of the medication in tablet form. While it is not known if reducing pediatric unintentional ingestions of Suboxone[®] was the manufacturer's primary intention for discontinuing the tablet form, the "unique childresistant, unit-dose packaging" should decrease unintentional childhood exposures to their products, especially given that the tablets come in a bottle of 30 pills.¹³⁶ Since children are less likely to ingest buprenorphine in a child-resistant film formulation than in a pill form, innovative packaging for high-risk prescriptions drugs could help to reduce the rates of exposures and ED visits among young children.¹³⁷



Risk Evaluation and Mitigation Strategy (REMS)

Given that research has found that the increase in opioid prescribing for adults is directly related to the increase in opioid exposures among children aged 5 and younger,¹³⁸ efforts to reduce excessive or inappropriate prescribing of controlled substances should help to reduce childhood exposures to them.

* Reckitt Benckiser Pharmaceuticals Inc.

One such effort includes the FDA's approval of a Risk Evaluation and Mitigation Strategy (REMS) directed at the prescribers of extended-release and long-acting opioids. REMS works to address prescription drug misuse and diversion by focusing on the continuing education of prescribers of prescription drugs.¹³⁹

The FDA also frequently issues warnings to manufacturers for noncompliance and alerts to the public via Drug Safety Communications.¹⁴⁰ Starting in 2005, the FDA released four warnings to patients, caregivers, and health care providers about the danger transdermal fentanyl patches pose to children, especially due to improper storage and disposal.¹⁴¹ While there are no REMS in place for short-acting opioids, REMS for transmucosal immediate-release fentanyl (TIRF) recently was implemented. The REMS for TIRF is not intended to curb the misuse of TIRF products, but rather to address other concerns, such as unintentional exposure to fentanyl products in children.¹⁴²

Statewide Prescription Drug Monitoring Programs (PDMP)

Similar to REMS, Prescription Drug Monitoring Programs (PDMPs) are statewide programs designed to track the prescribing and dispensing of controlled substances with the goal of mitigating the risks of prescription drug misuse and diversion.¹⁴³ Evaluations of PDMPs have found that they are promising strategies to reduce inappropriate prescribing¹⁴⁴ and possibly overdose-related mortality.¹⁴⁵ While opioid prescriptions have been declining since 2012, the number of PDMPs throughout the United States continues to increase.¹⁴⁶ However, because PDMPs are state based, they can vary considerably¹⁴⁷ and not all of them are in active operation.¹⁴⁸ Given their underutilization by health care providers,¹⁴⁹ there have been recent efforts to mandate that physicians use PDMPs prior to prescribing opioids.¹⁵⁰

FDA Warnings

In April 2017, the FDA issued a warning statement to the public urging against the use of any prescription drug containing codeine or tramadol by children aged 11 or younger. The FDA issued an additional warning in January 2018, stating that no child or adolescent under age 18 should be prescribed cough or cold medications that contain codeine or hydrocodone -two types of powerful opioids.¹⁵¹

Disposal of Unused Medicines and the National Take-Back Initiative

The FDA provides the public with information regarding the proper ways to dispose of unused prescription drugs.¹⁵² While certain unused medications can be thrown in the trash or flushed down the toilet, the FDA recommends that most drugs be disposed of by other means.¹⁵³ The FDA provides resources on their website regarding how to dispose of specific types of drugs, along with other tips and guidelines.

Once every six months, the U.S. Drug Enforcement Administration (DEA) implements the National Take-Back Initiative.¹⁵⁴ This initiative was created as a result of the Secure and Responsible Drug Disposal Act of 2010, and provides people the ability to safely dispose of prescription drugs free of charge at dropoff sites monitored by the DEA and state and local law enforcement.¹⁵⁵ As of October 2016, the DEA has collected 7.1 million pounds of prescription drugs since the initiative first began in September 2010.¹⁵⁶ Because studies have shown that most childhood exposures to prescription drugs occur in the home,¹⁵⁷ the take-back initiative is an excellent strategy to dispose of unused medications and prevent unintentional exposures among young children. The next national take-back day is scheduled for April 28, 2018.158

Healthy People 2020

The Healthy People 2020 campaign is a national health promotion and disease prevention initiative developed by the U.S. Department of Health and Human Services in 2010.¹⁵⁹ One of its objectives related to medical product safety is to reduce the number of ED visits due to medication overdoses among children aged 5 years and younger.¹⁶⁰ By 2020, the campaign has a target goal of reducing the number of ED visits to 29.4 visits per 10,000 children in this age group.¹⁶¹

Health Organizations

Health organizations have an important role to play in educating the public about the various dangers of prescription drug exposures, as well as influencing legislators to pass regulations to better protect children.

American Academy of Pediatrics (AAP)

Over the years, several reports have been published in the official journal of the American Academy of Pediatrics (AAP) examining the number of exposures to prescription drugs in children.¹⁶² These reports have been instrumental in uncovering the problem of unintentional exposure and getting the information out to the public. The AAP also has published press releases and collaborated with other organizations to provide tips to parents and caregivers on how to properly store and dispose of various medications and prescription drugs.¹⁶³

American Medical Association (AMA)

Similar to the AAP, the American Medical Association (AMA) has released reports promoting the safe storage of opioids and other prescription drugs.¹⁶⁴ In 2014, the AMA created the <u>Task Force to Reduce Opioid Abuse</u>. Along with the AAP, 25 other health organizations have collaborated and joined the AMA Task Force.¹⁶⁵

Some of these organizations include the:

- American College of Physicians;
- American Psychiatric Association;
- American Society of Addiction Medicine;
- American Academy of Family Physicians; and,
- American Academy of Pain Medicine.¹⁶⁶

The Task Force to Reduce Opioid Abuse provides strategies and recommendations to physicians and parents to help end the opioid epidemic. Some of these strategies include having physicians educate their patients about the risks of prescription drugs, teaching parents the proper ways to store medications, and promoting the use of state PDMPs.¹⁶⁷ In April 2017, the AMA released a report on the progress the Task Force has made, and provided additional recommendations regarding how to address the opioid epidemic. One positive reported trend was that between 2012 and 2016, the number of opioid prescriptions declined by more than 43 million throughout the United States¹⁶⁸ Since research has shown that the number of unintentional exposures to opioid medications in young children is positively related to the number of opioids prescribed to adults, limiting the number of opioid prescriptions to adults could potentially help limit the number of unintentional exposures in children.169

"These are good signs of progress, but to truly reverse the nation's opioid epidemic, we all have much more work to do. That's why the AMA Opioid Task Force urges physicians to increase their efforts and use PDMPs, enhance their education, help prevent overdose deaths by co-prescribing naloxone, and improve access to the best treatment options available."

-- Patrice A. Harris, MD, MA Former Chair, Board of Trustees American Medical Association

SOURCE: American Medical Association. (2017). Physicians' progress to reverse the nation's opioid epidemic. Retrieved from https://www.ama-assn.org/sites/ default/files/media-browser/public/physicians/patient-care/opioid-task-forceprogress-report.pdf.

Safe Kids Worldwide

Safe Kids Worldwide is a nonprofit organization whose mission is to prevent childhood injuries.¹⁷⁰ Over the years, Safe Kids Worldwide has published extensive reports examining the impact of having prescription drugs in the home. For example, recently published reports include, "Medicine Safety for Children: An In-Depth Look at Calls to Poison Centers" (2015), "The Rise of Medicine in the Home: Implications for Today's Children["] (2016), and <u>"Safe Medicine Storage:</u> <u>A Look at the Disconnect Between Parent Knowledge</u> and Behavior" (2017). All three reports provide health professionals, parents, and other caregivers essential information about the risks associated with prescription drug exposures and how to keep children safe around medicine.171



Marijuana

Key Points

- Since 2012, the number of exposures to marijuana products among young children has increased each year.
- Marijuana products are becoming more available and accessible to children due to the growing number of states that have legalized marijuana for medical and/or recreational use and due to the growing popularity of marijuana edibles.
- Marijuana edibles pose an added risk of exposure to children due to their similar appearance to nonmarijuana food products, appealing packaging, and lack of child-resistant packaging in some states that have legalized marijuana.
- Children exposed to marijuana tend to develop more severe symptoms compared to adults.
- There are many steps parents, health care professionals, and policymakers can take to limit unintentional exposures to marijuana in children. Examples include caregivers practicing safe storage, physicians being more attuned to the symptoms of marijuana exposure, and policymakers passing legislation regulating marijuana edibles.

Historically, reports of unintentional exposures to marijuana among children aged 5 and younger have been rare, and documentation of these exposures has been limited to a few case studies.¹ In the past, a key explanation for the low reported rate of unintentional exposures to marijuana was its poor palatability, which made it unappealing for children to ingest.² Until recently, marijuana was also illegal throughout the country, which restricted its availability and accessibility to young children,³ and likely contributed to parents' or other guardians' reluctance to report cases of childhood exposure for fear of social stigma or legal repercussions.⁴

Over the years, marijuana policy has changed drastically, as has the form in which marijuana can be ingested, potentially influencing the incidence of unintentional exposures in young children.

More and more states are legalizing marijuana for medical and/or recreational use, increasing its general availability and accessibility to young children. "In the case of marijuana, we might be seeing an increase in calls to poison centers or emergency department visits for unintentional childhood exposures because of increased availability, as more people have it in their homes. Also, parents may be more likely to report possible marijuana ingestion now that it is legal. Typically, increases in availability -- whether of a medication or household product -- result in increases in exposures. Take the case of laundry pods and e-cigarettes: as their availability in the home has increased, so have childhood exposures to these products."

--G. Sam Wang, MD

Assistant Professor of Pediatrics Emergency Medicine and Medical Toxicology University of Colorado Anschutz Medical Campus Children's Hospital Colorado

Interview on August 18, 2016





These policy changes have been associated with greater public acceptance and reduced stigma surrounding the use of marijuana,⁵ and a potentially diminished role of legal concerns in decisions to report cases of exposure.

Despite the logical connection between these recent changes and the potential increase in childhood exposures to marijuana products, limitations in currently available data make it difficult to document trends in exposures that may be associated with marijuana's changing legal status. There is reason to believe that such data will become available as the number of states that legalize marijuana continues to increase.⁶ Although still illegal at the federal level, as of January 2018, 29 states and Washington, DC have legalized medical marijuana, and 9 states and DC have legalized marijuana for recreational use.⁷ Many more states are considering implementing changes to marijuana's legal status⁸ or have bills pending to legalize marijuana for recreational use.⁹

Also contributing to an increase in exposures is the fact that marijuana is now marketed and sold in an array of enticing edible forms that mimic common sweets in appearance and taste (e.g., brownies, cookies, beverages, candies, and other food products), increasing their appeal to children.¹⁰



Marijuana edibles have existed prior to recent changes in marijuana's legal status, and there are case studies dating back to the 1980's documenting unintentional exposures to edible marijuana products among young children.¹¹ However, with more states legalizing marijuana for recreational use, the availability of and demand for marijuana edibles has grown,¹² raising concern about greater risk of exposure in young children.¹³ Factors That Have Increased the Risk of Exposure to Marijuana among Young Children¹⁴

- Greater availability of edible marijuana products in states with less stringent marijuana laws
- Similarities in appearance of edibles to nonmarijuana food and beverage products
- Packaging that is appealing to children
- The improper storage of marijuana products in the home and limited supervision around them
- The lack of child-resistant packaging for these products in some states





Marijuana edible brownies

Regular brownies

In Colorado, edibles comprised a large proportion of the recreational marijuana market in 2014,¹⁵ and recreational marijuana consumers in Washington State are buying more edibles each month since commercialization began in July of 2014.¹⁶ One of the primary concerns regarding edibles, particularly in terms of the risk they pose to young children, is that they have higher concentrations of THC (tetrahydrocannabinol) -- the main psychoactive ingredient in marijuana -- than other marijuana products,¹⁷ and can produce adverse clinical symptoms even in small doses.¹⁸

National and local studies indicate that state and regional poison control centers -- including those in Arizona, Colorado, New England, Oregon, and Washington -- have shown increases in marijuana exposures among young children since the legalization of marijuana, either medical or recreational.¹⁹ Research also suggests that the increase in exposures is primarily associated with the increased presence of marijuana edibles in the home.²⁰





The Demand for Marijuana Edibles in Denver Skyrockets

There has been high demand for marijuana edibles ever since recreational marijuana became legal in Colorado. The popularity of edibles has even been surprising to manufactures of marijuana products. The demand has out-paced supply, leaving many companies scrambling to produce enough edibles for consumption. Many manufacturers have decided to expand their operations and move to larger facilities. Bob Eschino, a co-owner of a major marijuana firm in Colorado, says they are "bursting at the seams" and have outgrown their new facility even before it opened.²¹

Rates of Marijuana Exposure*

The majority of available data on exposures to marijuana among young children is restricted to individual states,²² but several published studies have utilized the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS)[†] to determine the prevalence of marijuana exposures in young children.²³ These data indicate that marijuana exposures have increased in recent years, particularly in states where medical marijuana is legal.²⁴

National Data

One national study found that from 2000 to 2013 there were 1,969 calls to NPDS-participating poison control centers in which single-substance exposures[†] to marijuana among children aged 5 and younger were reported. Of these calls, 92 percent were for unintentional exposures and 83 percent occurred at the child's home. Children younger than age 3 accounted for 78 percent of exposures, and the most common route of exposure was ingestion (75 percent), followed by inhalation (14.5 percent).²⁵

During the study, there were no significant changes in the annual rate of exposures per 1 million children between the years 2000 and 2006. However, between 2006 and 2013, the rate of exposures in children increased significantly by 147.5 percent. This increase was largely attributable to states that had legalized medical marijuana. The increase was even more pronounced after the year 2009,²⁶ when the U.S. Department of Justice declared that the federal government would be less likely to prosecute those who complied with their state's medical marijuana laws.²⁷ Other studies examining trend data from the NPDS also found greater increases in unintentional exposures to marijuana among children living in states that have legalized medical marijuana relative to states that have not done so.28

"Unintentional pediatric exposures to marijuana have undoubtedly increased since the legalization of recreational marijuana...Many exposures involve edible products – things like brownies and gummy bears that would naturally appeal to children – and, in most cases, the product belonged to a parent, grandparent, neighbor, friend, babysitter, or other family member."

--G. Sam Wang, MD Assistant Professor of Pediatrics Emergency Medicine and Medical Toxicology University of Colorado Anschutz Medical Campus Children's Hospital Colorado

SOURCE: Children's Hospital Colorado. (2016). Experts research pediatric exposure to marijuana since legalization. Retrieved from https://www. childrenscolorado.org/about/news/2016/july-2016/experts-research-pediatric-exposure-to-marijuana-since-legalization/.

* The term "exposure" means someone has had contact with the substance in some way; for example, ingested, inhaled, or absorbed a substance by the skin or eyes, etc. Exposures do not necessarily represent poisonings or overdoses.

† Case records in the NPDS database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/educational materials. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to poison centers and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

[‡] These exclude cases where more than one substance was involved in the reported exposure incident.



Exposures to marijuana edibles reported to the NPDS from January 2013 to December 2015 revealed 430 single-substance exposure calls.²⁹ Not only did Colorado, Oregon, and Washington -- the leading states in recreational marijuana legalization and commercialization -- have the most exposure calls involving marijuana edibles, but also 91 percent of all such calls came from states that have legalized medical and/or recreational marijuana use.³⁰ The number of exposure calls increased over the study period and the age group comprising the largest proportion of exposures involving marijuana edibles was children aged 5 and younger, accounting for 25 percent of the calls.³¹

To examine more closely the national trends in marijuana exposures among young children, we collected data on single-substance exposures to all marijuana products^{*} from the 2007 to 2016 NPDS annual reports.[†] The first graph below shows the number of exposures to marijuana products in all ages, while the second graph shows exposures in children aged 5 and younger. Across all ages, the number of exposures to marijuana increased significantly from 2009 to 2011. From 2011 to 2013, the number of cases declined. Since 2013, calls increased steadily, until there was a drop in 2016.



Other than a slight decline from 2011 to 2012, reported marijuana exposures in children aged 5 and younger have been increasing steadily from 2007 to 2016.

* The codes for tetrahydrocannabinol (THC) homologs (i.e., synthetic cannabinoids such as K2 or Spice) and tetrahydrocannabinol (THC) pharmaceuticals were established in 2010.

t We collected NPDS's annual reports from the AAPCC website and manually counted each exposure incident overall and among children aged 5 and younger.





State Data

State-specific data documenting marijuana exposures in young children are available from states that have legalized medical and/or recreational marijuana.³² Similar to the patterns found in the national data, state data show an increase in exposures to marijuana among young children overall,³³ especially following the legalization (and commercialization) of medical³⁴ and recreational³⁵ marijuana.

Colorado

In 2012, Colorado became the first state to legalize recreational marijuana use in the United States, following its legalization of medical marijuana in 2000. One study, using data from Colorado's Rocky Mountain Poison and Drug Center (RMPDC), examined changes from 2000-2014 in marijuana exposures.³⁶ Calls related to marijuana exposures for all ages increased significantly in 2010, and again in 2014.³⁷ The greatest increases in reported marijuana exposures from 2013 to 2014 were among children aged 8 and younger and adults aged 25 and older.³⁸

According to the Retail Marijuana Public Health Advisory Committee in Colorado, the entity responsible for monitoring the effects of marijuana legalization in the state, 2001-2009 was considered the initial period of medical marijuana legalization, 2010-2013 was considered the period of "medical marijuana commercialization," and 2014 was the first year that the legalization of recreational marijuana sales was implemented.³⁹ Essentially, the first year of medical marijuana commercialization (2010) and the first year of recreational marijuana sales (2014) corresponded with the largest increase in marijuana-related exposure calls to the RMPDC.⁴⁰

Other research finds that the number of calls for single-substance exposures to marijuana among children aged 9 and younger increased significantly between 2009 and 2015.⁴¹ The median age of children exposed was 2 years old, the majority of exposures were deemed unintentional, and ingestion was the most common route of exposure.⁴² Moreover, 34 percent of marijuana exposures were from a medical marijuana product and, from 2014 to 2015, 47 percent were from a recreational marijuana product.⁴³ Of exposures in which the marijuana product was identified, 48 percent were from marijuana edibles, mostly baked goods, but also candy and popcorn.⁴⁴





Cases of children younger than age 12 presenting for unintentional marijuana exposures at a Colorado tertiary-care children's hospital emergency department (ED) from January 2005 to December 2011 were analyzed both before and after the federal government's 2009 memorandum indicating that they would not prosecute individuals or organizations complying with their state's medical marijuana laws.⁴⁵ Between January 2005 and September 2009, there were no patients younger than age 12 who presented to the ED for unintentional marijuana ingestion.⁴⁶ However, between October 2009 and December 2011, 14 patients aged 12 and younger presented to the ED for exposure to marijuana, confirmed by a positive THC urine screen.⁴⁷ The majority of these exposures were to medical marijuana and in the form of marijuana edibles.48

Oregon

In 2014, Oregon legalized recreational marijuana, and the initiative went into effect on July 1, 2015. According to the Oregon Poison Center,^{*} there were more marijuana exposure calls in 2015 than in the previous two years among all age groups.⁴⁹ In 2013, children under age 13 accounted for 12 percent of all marijuana exposure calls to the poison center. This number increased to 20 percent in 2015.⁵⁰ Data specific to children aged 5 and younger from 20142016 indicated that the number of marijuana exposure calls in young children tripled from 2014 to 2016 (14 in 2014, 25 in 2015, and 43 in 2016).^{t 51}

Washington

The first store to sell recreational marijuana in Washington opened on July 8, 2014.⁵² Washington's poison control center saw an increase in marijuana exposure calls following the commercialization of recreational marijuana, particularly among children.⁵³ Specifically among children aged 5 and younger, there were 22 calls for marijuana exposures in 2013, 34 calls in 2014,⁵⁴ and 49 calls in 2015.⁵⁵ In 2016, over 39 percent of the calls for marijuana exposures were in children younger than age 19, and 73 percent of exposures among children 5 and younger occurred in 1 to 3 year olds.⁵⁶

Symptoms of Marijuana Exposure

Along with recent changes in marijuana's legal status, there has been a rise in serious medical outcomes among young children exposed to marijuana.⁵⁷ Marijuana exposures, relative to other poisoning exposures in young children, recently have been associated with more severe clinical effects and with an increase in the utilization of health care facilities.⁵⁸ A national study found that the annual proportion of children aged 5 and younger admitted to a health care facility for unintentional marijuana exposure more than doubled between 2000 and 2013 (from 12.8 percent to 30.8 percent).⁵⁹ Another study found that children who experienced moderate or major clinical effects due to unintentional exposure to marijuana were more likely to come from states where medical marijuana was legal than from states where it was not.⁶⁰

* Serving Oregon, Alaska, and Guam.

† These data should be interpreted with caution as they derive from a broad query of raw data from the Oregon Poison Center and were not initially intended for scientific or research purposes.



The rise in more serious medical outcomes may be due to the unintentional consumption of marijuana edibles, which have a relatively high THC concentration⁶¹ or to the increasing potency over time of illicit (nonmedical)^{*} marijuana.⁶²

Acute marijuana intoxication has a well-described clinical presentation in adolescents and adults, but often is not suspected in young children and is frequently misdiagnosed.⁶³ Compared to adults, children tend to experience more severe clinical effects from marijuana exposure,⁶⁴ possibly due to children's marijuana naivety[†] and lower body mass.⁶⁵

The most common symptoms in children are neurological effects, usually presented as decreased coordination, ataxia, lethargy, sedation, difficulty concentrating, altered psychomotor activity, slurred speech, and slow reaction time.⁶⁶ Effects that are more serious are rare, but may involve respiratory depression, apnea, bradycardia (abnormally slow heartbeat), hypotonia (abnormally low muscle tone), seizures, and coma.⁶⁷ To date, there have been no reported cases of children who have died directly from marijuana exposure.[‡]

Case reports,⁶⁹ data from EDs,⁷⁰ and prevalence studies⁷¹ have reported the following symptoms of marijuana exposure in young children.

"This is extremely dangerous...When young children get ahold of these products, they can have severe reactions, including nausea, vomiting, disorientation, anxiety-like reactions, and even psychotic reactions that can make them do things they wouldn't normally do."

--Robert Glatter, MD Emergency Physician Lenox Hill Hospital

SOURCE: Rossen, J., et al. (2017). Rossen reports update: Edible marijuana that looks like candy is sending kids to the ER. Retrieved from https://www.today. com/parents/edible-marijuana-looks-candy-sending-kids-er-t94486.

* Reports on increased potency refer only to seized illicit marijuana.

† Children typically do not have any experience with marijuana exposure; as such, their bodies are not used to the substance. This could result in more severe symptoms, compared to adolescents and adults who consume a comparable amount of marijuana.

[‡] There was one reported death of an 11-month-old child who had tested positive for THC, but the autopsy stated the cause of death as myocarditis. Therefore, the role THC played in the child's death is unclear.





Symptoms of Marijuana Exposure

Abdominal pain⁷² Agitation⁷³ Ataxia74 Bradycardia/abnormally slow heartbeat⁷⁵ Coma⁷⁶ Conjunctivitis/red eye⁷⁷ Drowsiness/lethargy⁷⁸ Fever/hyperthermia⁷⁹ Hallucinations⁸⁰ Hypertension⁸¹ Hypotension⁸² Hypothermia⁸³ Hypotonia/muscle weakness⁸⁴ Mydriasis/excessive or prolonged pupil dilation⁸⁵ Nausea/vomiting⁸⁶ Nystagmus⁸⁷ Respiratory depression⁸⁸ Seizure⁸⁹ Slowly reactive pupils⁹⁰ Slurred speech⁹¹ Somnolence⁹² Stupor⁹³ Tachycardia94 Tremor⁹⁵

Symptoms of pediatric exposure to marijuana vary widely as a function of the route of consumption, the dose, and whether the child had been exposed previously.⁹⁶

Route of Consumption

The majority of unintentional marijuana exposures in children are via ingestion,⁹⁷ with rare cases of passive inhalation leading to clinically adverse outcomes.⁹⁸ A number of reports have suggested that unintentional ingestion of edibles is the main source of pediatric marijuana poisonings.⁹⁹ Since these products frequently have high levels of THC compared to marijuana buds,¹⁰⁰ even a small amount of ingested edibles has the potential to cause severe symptoms with slow onset and prolonged duration.¹⁰¹

A study examining symptoms associated with exposure to marijuana edibles found that children aged 5 and younger were more likely than adults to experience drowsiness/lethargy, ataxia, conjunctivitis, and respiratory depression, but less likely to have agitation/ irritability, confusion, dizziness/vertigo, hallucinations/ delusions, hypertension, tachycardia, and tremors.¹⁰²



Passive exposure to marijuana smoke also can cause clinical effects in children, although this is rare.¹⁰³ Marijuana smoke has similar components (e.g., carcinogens) to tobacco smoke,¹⁰⁴ which is known to have serious adverse effects when passively inhaled.¹⁰⁵ One case report described a 13-month-old child who had experienced passive exposure to marijuana smoke for several hours presenting with apathy, unresponsiveness, loss of appetite, and a mild fever.¹⁰⁶

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Dose

Although documentation of the marijuana dose consumed by a child after an unintentional exposure is rarely accurate,¹⁰⁷ there does seem to be a correlation between estimated THC and the clinical symptoms displayed in a child.¹⁰⁸ Lower doses often have more potential for adverse effects in children than in adults.¹⁰⁹ However, large quantities of ingested marijuana can cause delayed and prolonged effects, which often end within 12 hours post-exposure;¹¹⁰ there have been reports of clinical effects lasting as long as 55 hours.¹¹¹ The relatively more severe effects in infants is most likely related to the fact that a dose of marijuana ingested by a child has a greater impact than a similar dose ingested by an adult due to the smaller body mass of children¹¹² and their lack of prior exposure.113

Previous Exposure

A study comparing the clinical outcomes of acute THC toxicity in THC-naïve children (average age 3.5 years) and non-naïve children (average age 15.2 years) found differences in the symptoms and duration of THC-related effects.¹¹⁴ THC-naïve children were more likely to exhibit central nervous system effects with a longer duration of symptoms, whereas non-naïve children were more likely to experience cognitive, emotional, and gastrointestinal effects.¹¹⁵ THC-naïve children also had longer hospital stays.¹¹⁶

Marijuana Toxicity

While there have been reports of accidental deaths attributed to marijuana consumption, no reported deaths have ever been directly attributed to a marijuana overdose.¹¹⁷ Over the years, researchers have attempted to examine the lethal dose of marijuana and generally agree that the amount required for a fatal overdose is virtually impossible to consume. In 1988, Drug Enforcement Administration (DEA) Administrative Law Judge, Francis Young, released a ruling stating that the lethal dose of

marijuana is 20,000 to 40,000 times the amount of marijuana consumed in a marijuana cigarette.¹¹⁸ Other studies have shown that a person would have to ingest 1,000 times the usual dose of marijuana for marijuana ingestion to be fatal.¹¹⁹

One possible explanation for the non-lethal nature of marijuana ingestion is that the cannabinoid receptors in the human brain are not located in the areas of the brainstem that control respiration.¹²⁰ Indeed, acute toxicity from cannabinoids in adults is very rare because respiratory depression does not occur.¹²¹ However, this might not necessarily be true for children. Some case studies have reported on children suffering from respiratory depression after ingesting marijuana.¹²² More research is needed to examine how and whether the toxic or lethal dose of marijuana differs between adults and children.

Approaches to Addressing Childhood Marijuana Exposures and Poisonings

With more states legalizing medical and recreational marijuana, there are many opportunities for parents and caregivers, health care professionals, public health experts, and policymakers at all levels of government to take action to help prevent unintentional childhood exposures and poisonings related to marijuana. The following is a summary of some of the steps currently being taken to address this problem.



Health Care Professionals and Public Health Experts

Health and pediatric organizations can work to prevent unintentional childhood exposures to marijuana by affirming their position on marijuana legalization,¹²³ documenting the potential impact of marijuana legalization on children,¹²⁴ and recommending and demanding adequate legislation and regulation to protect children and the public from marijuana legalization.¹²⁵ The American College of Pediatricians,¹²⁶ the American Academy of Pediatrics,¹²⁷ and the American Academy of Child and Adolescent Psychiatry¹²⁸ do not support the legalization of recreational marijuana and caution against the medical use of marijuana, citing the harms to adolescents and children, including the risk of unintentional exposures. These organizations have documented exactly how marijuana legalization has or will adversely affect both adolescents and young children and have provided suggestions on how to minimize this impact.¹²⁹ The Oregon Medical Association (OMA), in light of reports of an increase in unintentional exposures to marijuana among young children in Oregon, submitted concerns to both the Oregon Health Authority and the Oregon Liquor Control Commission, the organizations responsible for governing medical and recreational use of marijuana, respectively.¹³⁰ The OMA, in their letters to these agencies, emphasized that the THC concentration limit in marijuana edibles should be reduced from 15 to 5 mg per serving and that edibles should be packaged and marketed in a way that is not attractive to children and placed in child-resistant, single-serving, clearly labeled packages.¹³¹

The movement toward marijuana legalization has prompted citizen groups to come forward with strong positions or campaigns against legalization, particularly for recreational use.¹³² Some of those who have voiced opposition to such legalization have cited the increase in unintentional marijuana exposures among young children in Colorado.¹³³ Public awareness campaigns such as Colorado's <u>Good to Know</u> campaign is intended to inform the public about the safe, legal, and responsible use of recreational marijuana through education, public awareness, and prevention messages.¹³⁴ Although not exclusively intended to reduce unintentional exposures among young children, some campaign content contains messages about keeping marijuana safely stored and away from children.¹³⁵ The nonprofit organization, *Smart Colorado*, which focuses on protecting youth in Colorado from marijuana, has cited unintentional exposure to marijuana among young children as one of the many unintended consequences of legalization and commercialization, and has stressed the importance of marijuana education and keeping marijuana away from children.¹³⁶

Policymakers

At the federal level, marijuana is classified as a Schedule I drug, meaning that it is considered to have no currently accepted medical use and a high potential for misuse.¹³⁷ Since marijuana use remains illegal at the federal level, laws and regulations surrounding medical and recreational marijuana are state-, county-, and city-based, and vary widely in both their stipulations and implementation.¹³⁸ Many medical and recreational laws were approved and implemented prior to the establishment of a permanent regulatory structure.¹³⁹ As a result, medical and recreational marijuana regulations have been in flux since legalization and commercialization began.¹⁴⁰ For instance, Colorado and Washington State adjusted medical marijuana regulations following the legalization of recreational marijuana.¹⁴¹ Much of these rule changes were due to concerns surrounding unintentional exposures to marijuana products, particularly among young children.142



States that are in the process of legalizing marijuana for recreational use should look to Colorado for ideas regarding how to regulate the product. Since Colorado became the first state to legalize marijuana for recreational use, it has continued to update its policies to protect children from unintentional exposures.

There is general agreement that regulations related to medical and recreational marijuana should prioritize preventing unintentional pediatric exposures by:

- Requiring child-resistant packaging;
- Eliminating packaging deemed attractive to children or requiring plain packaging with no logos or branding;
- Regulating the appearance of marijuana edibles to ensure they do not resemble candy or other sweets, prohibiting flavoring in nonedible products, or possibly banning edibles that might be attractive to children;
- Limiting the amount of THC allowed in marijuana edibles;
- Requiring clear labeling of all marijuana-containing products, with graphic warnings; and
- Implementing surveillance to monitor the impact of marijuana legalization.¹⁴³

Requiring Child-Resistant Packaging

Child-resistant packaging, as mandated by the Poison Prevention Packaging Act of 1970 (PPPA), has been successful in reducing unintentional exposures to toxic substances among young children.¹⁴⁴ It is considered one of the most commonsense strategies for preventing unintentional marijuana exposures.¹⁴⁵ Nonetheless, some state medical marijuana laws did not initially require child-resistant packaging.¹⁴⁶ Based on data showing an increase in ED visits and calls to poison control centers for unintentional exposure to marijuana among young children, Washington and Colorado became the first states to pass preventive regulations, including child-resistant packaging.¹⁴⁷ However, state implementation of these regulations did not begin until a year after they were written into law.¹⁴⁸ Due to concerns about children unintentionally consuming marijuana edibles,¹⁴⁹ Washington enacted emergency rules with preventive measures, including child-resistant packaging, until permanent rules were developed and implemented.¹⁵⁰

As of November 2017, 16 states that have legalized medical or recreational marijuana require the use of child-resistant packaging for edibles.¹⁵¹ However, not all child-resistant packaging laws are in accordance with the PPPA, and regulations vary by state. Along with child-resistant packaging, certain states require that individual serving sizes be singularly packaged, even if placed within a larger child-resistant package,¹⁵² and that all packages are re-sealable.¹⁵³

Eliminating Packaging that is Attractive to Children

Children are drawn to packages that are brightly colored, have cartoons or other illustrations, or that look like non-marijuana-infused products.¹⁵⁴ Nine states have regulations that require the use of opaque packaging, making the product less attractive to children.¹⁵⁵



Regulating Edibles that are Attractive to Children

A significant limitation of child-resistant packaging is that it only is effective if adults use it properly.¹⁵⁶ Once out of the package, many types of marijuana edibles are indistinguishable to young children from other food and drink products.¹⁵⁷ For example, children will not be able to tell a marijuana-infused gummy bear candy from a regular gummy bear candy.¹⁵⁸ Therefore, marijuana edibles -- such as gummy bears, gummy worms, and 'sour patch kids' -- may be particularly enticing to children and should be prohibited, as they pose an unnecessary risk to their health and safety.¹⁵⁹





Regular gummies

Marijuana gummies



Regular lollipops

Marijuana lollipops

In June 2016, Ohio passed a law legalizing medical marijuana, but it prohibits some edibles that are considered attractive to children.¹⁶⁰ Colorado recently signed a law prohibiting marijuana edible products that are shaped as humans, animals, or fruit, which were deemed especially enticing to young children.¹⁶¹ A bill with similar provisions passed final legislative approval in September 2017 in California. The bill would have made it illegal for companies to sell marijuana edibles in the shape of a person, animal, insect, or fruit once recreational marijuana is legalized in California.¹⁶² The bill included rules stating edibles could not be "designed to be appealing to children or easily confused with commercially sold candy or foods that do not contain cannabis."¹⁶³ However, Governor Brown vetoed the bill when it reached his desk for signature in October 2017.164

Colorado Health Department Initially Proposed a Ban on all Marijuana Edibles

In 2014, Colorado's Health Department discussed a possible ban on almost all marijuana edibles after recreational marijuana was legalized in 2012 and the state began to see a substantial increase in the number of children accidentally ingesting edibles and being sent to the hospital for unintentional exposure to marijuana. Most of these children were between 3 and 7 years old. While the Health Department recognized the risk of edible products, it ultimately decided not to impose a ban, indicating that an edibles ban might not be constitutional under Colorado's marijuana-legalization laws.¹⁶⁵

Limiting THC Levels in Edibles

Marijuana edibles pose a significant risk to children, not only because they are palatable and resemble non-marijuana-infused food products that appeal to children, but also because of their high THC potency.¹⁶⁶ Colorado's recreational marijuana permanent rules limit the serving size of recreational marijuana edibles to 10 mg of THC, and this rule was proposed as one of the ways regulations can address unintentional exposures to marijuana among children.¹⁶⁷ Oregon lawmakers proposed even lower limits on the dose, at 5 mg per serving size and 50 mg per package for recreational marijuana edibles, citing that such rules are imperative to protect children and other novice consumers.¹⁶⁸



Requiring Clear Labeling

Although it is unlikely that a child would be deterred from opening and eating a marijuana product with warnings akin to "contains THC" and "keep away from children," clear labels with these warnings would allow adults to identify potentially harmful products and might encourage them to keep them away from children.¹⁶⁹ The majority of state medical and recreational marijuana regulations require that such warnings be placed on all marijuana products.¹⁷⁰ In Washington, a new "not for kids" warning symbol was required on all edible marijuana products as of February 14, 2017.¹⁷¹ The symbol is a large stop hand with the words "not for kids" in bright red.



To examine whether labelling regulations are effective, a 2017 study conducted focus group interviews with adult consumers and nonconsumers of edibles in Denver and Seattle. The study asked questions about the usefulness, attractiveness, and comprehensibility of the labels on marijuana edibles.

The focus groups in Denver examined packages of marijuana edible gummy candy, and the focus groups in Seattle examined packages of marijuana edible chocolate bars. The findings indicated that some participants in both cities thought there was too much information, causing them not to read everything and missing important information on the labels. Others mentioned the need for clearer labels so people can know there is marijuana in the products. The study concluded that improvements are needed, and that there should be more education initiatives to help consumers and non-consumers of marijuana edibles know the difference between products.¹⁷²

Implementing Surveillance to Monitor the Impact of Marijuana Legalization

Colorado and Oregon have implemented surveillance systems to monitor the impact of marijuana legalization on public health.¹⁷³ Colorado's Retail Marijuana Public Health Advisory Committee, which was established as part of the recent legalization of recreational marijuana in the state, is responsible for conducting research and public health-related activities to routinely monitor the effects of the legalization of recreational marijuana.¹⁷⁴ The Oregon Health Authority's Public Health Division is responsible for monitoring the effects of the legalization of recreational marijuana in Oregon.¹⁷⁵ Both of these systems are responsible for examining unintentional exposures to marijuana among young children and working toward protecting children and other vulnerable populations from marijuana exposure.¹⁷⁶ They provide tips to parents on how to safely store marijuana products, and ensure they are unavailable to children. The Oregon Health Authority also provides data on marijuana consumption and exposure throughout the state. Surveillance and data collection are critical for determining whether packaging restrictions, dose limitations, educational campaigns, and other initiatives aimed at reducing childhood exposures are effective.¹⁷⁷

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Illicit Drugs

Key Points

- Illicit drugs are less easily accessible to young children than other addictive substances.
- Childhood exposures to illicit drugs can cause serious adverse effects, including death.
- Exposures to methamphetamine and cocaine among young children have been increasing, while exposures to heroin, hallucinogens, and club drugs have remained relatively stable over the past decade.
- No laws exist to prevent unintentional childhood exposures to illicit drugs. Most initiatives to reduce childhood exposures to illicit drugs have involved efforts by states to protect children from parents who misuse illicit drugs.

Compared to other addictive substances such as nicotine, caffeine, and controlled prescription drugs, illicit drugs generally are less accessible to young children because they are illegal and not as commonly used. In 2016, 1.7 percent of individuals in the United States, aged 12 years and older, reported using an illicit drug (other than marijuana)* in the past 30 days. The rates of use for each type of illicit drug are less than one percent in the population. By way of comparison, 23.5 percent reported using a tobacco product and 50.7 percent reported drinking alcohol in the past 30 days.¹ Given the relatively low rate of illicit drug use, childhood exposures to these drugs compared to other addictive substances are relatively rare. However, it is important to examine unintentional childhood exposure to illicit drugs because these substances can cause serious adverse effects, including death.²

Exposures to illicit drugs among young children typically are unintentional and usually represent the inability or failure of caretakers to safeguard these drugs properly. For example, case reports have shown that parents may leave Ecstasy pills out in the open, such as on a nightstand,³ despite the fact that these pills have a candy-like appearance and can be attractive to children.⁴ Illicit drugs also may be mixed with items that children regularly consume. One case report documented GHB[†] poisoning in two young teens that resulted from consuming a soft drink containing the drug, which had been mixed by their father.⁵



Cocaine



Powdered Sugar

* Not including the misuse of a prescription drug.

⁺ GHB (gamma-hydroxybutyric acid) is a central nervous system depressant commonly referred to as a "club drug" or "date rape" drug.

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Heroin Passed Around at a Daycare Center

In 2014, a 4-year-old girl at a daycare center in Philadelphia accidentally was given a backpack by her mother containing 249 bags of heroin, totaling 3.7 grams. According to investigators, the girl passed the packets of heroin to her classmates, believing they were candy. Children possibly exposed to the drug were brought to the hospital.⁶ While no children experienced adverse effects, this incident reveals the potential threat of accidental poisoning from illegal drugs.

One challenge to safeguarding children from accidental exposure to illicit drugs is that their manufacture and production are unregulated due to their illegal status. To maximize profits, illicit drug manufacturers and distributors sometimes dilute the substance with adulterants to increase bulk, enhance or mimic the drug's effect, or facilitate drug delivery. The adulterants may consist of relatively innocuous ingredients like sugar or caffeine, but also may involve cheaper illicit drugs like fentanyl or other toxic ingredients like strychnine.⁷ The contents of the drug may differ from how it is identified or marketed.⁸ For example, 3,4-methylenedioxy-methamphetamine (MDMA), the main ingredient in Ecstasy, is often marketed as Molly, the purest form of Ecstasy. However, Molly frequently is cut with other addictive or dangerous substances such as methamphetamine, ketamine, cocaine, dextromethorphan,* or caffeine.9

Certain drugs may be misidentified, complicating how accidental exposures among young children are handled. For example, psychedelic mushrooms can be difficult to differentiate from regular mushrooms. A recent study showed an increase in poisonings from all mushroom species, perhaps due to an increase in gastronomic and recreational use of mushrooms.¹⁰ Case reports have shown that dealers and foragers can make mistakes in determining mushroom species, and users have unintentionally consumed nephrotoxic Cortinarius mushrooms, instead of hallucinogenic mushrooms.¹¹ While it may be difficult to determine the exact type of mushroom ingested, different mushrooms have unique symptom onset times and effects, which can help determine the species ingested.¹² Difficulties in determining species can complicate treatment protocol, and lead to inaccurate data with regard to poison control calls and reported rates of exposure.



Psychedelic Mushrooms



Regular Mushrooms

* An antitussive, or cough medicine, sometimes referred to as DXM or DM.

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Rates of Exposure to Illicit Drugs*

Determining the prevalence and consequences of illicit drug exposures or poisonings in children is complicated. Caretakers, who may be worried about the legal consequences of possessing illegal drugs, might refrain from informing health professionals or poison control centers of a child's possible drug exposure, and may be inclined to lie about the cause of their child's symptoms.¹³ For example, case reports have shown that instead of admitting that their child ingested drugs, parents have claimed that their child had ingested plastic bags¹⁴ or rat poisoning.¹⁵ There also are cases in which children are exposed to illicit drugs while in the presence of non-parent family members or friends. In these cases, parents may not know of the drug exposure and do not call a poison control center.¹⁶ Childhood poisonings from illicit drugs may be missed or misdiagnosed by health professionals who do not suspect such ingestion due to misinformation provided by the parent, or because the symptoms may be obscure or reflective of other common health problems.¹⁷

Rates of unintentional exposure to illicit drugs among young children that have been reported are relatively low and, aside from case reports, rarely documented in the research literature. To examine more closely the national trends in illicit drug exposures among young children, we collected data on singlesubstance exposures[†] to illicit drugs (heroin, cocaine, methamphetamine, hallucinogens,[‡] and club drugs[§]) from the American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS)^{**} annual reports from 2007 to 2016.^{‡†} The first graph below demonstrates reported unintentional exposures to illicit drugs among individuals of all ages, and the second demonstrates reported exposures in children aged 5 and younger. Our examination of NPDS data indicate that, in all ages, exposures to heroin and methamphetamine have been on the rise since 2007. Exposures to club drugs and hallucinogens have fluctuated but remained relatively stable, while cocaine exposure declined over the past 10 years.

* The term "exposure" means someone has had contact with the substance in some way; for example, ingested, inhaled, or absorbed a substance by the skin or eyes, etc. Exposures do not necessarily represent poisonings or overdoses.

† This excludes cases where more than one substance was involved in the reported exposure incident.

[‡] Hallucinogens include lysergic acid diethylamide (LSD), mescaline/peyote, phenylcyclohexylpiperidine (PCP), psilocybin and psilocybin mushrooms, other hallucinogens, and unknown hallucinogens.

I Club Drugs include gamma-hydroxybutyric acid (GHB), and Ecstasy/MDMA (listed in NPDS annual reports as hallucinogenic amphetamine).

** Case records in the NPDS database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/educational materials. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to poison centers and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

†† We collected NPDS annual reports from the AAPCC website and manually counted each exposure incident overall and among children aged 5 and younger. Data specific to cause of exposure (e.g., intentional, unintentional) are not available by age group in published and available NPDS annual reports.





Among children aged 5 and younger, exposures to methamphetamine have increased since 2007 and exposures to cocaine have increased since 2014, whereas exposures to heroin, hallucinogens, and club drugs have fluctuated during the course of the 10-year period.



E.



Methamphetamine Exposures

The production of methamphetamine in home laboratories (i.e., "meth labs") poses a unique risk to children.¹⁸ Chemicals involved in the home production of methamphetamine, such as sulfuric acid, can cause severe burns of the skin and digestive tract as well as respiratory distress.¹⁹ During the manufacturing of methamphetamine, the drug often is airborne; methamphetamine residue has been detected on surfaces in rooms where methamphetamine is cooked²⁰ and traces have been found in food kept in the refrigerator. Methamphetamine laboratories increase children's risk of exposure if they crawl, touch their hands to their mouths, or even consume food in the house.²¹

Two separate studies of children aged 16 and younger from homes with either known or suspected manufacture of methamphetamine found that about 45 percent tested positive for methamphetamine via hair analysis.²² In one of these studies, 36 percent of the children were younger than 3-years-old.²³ In another, 48 percent were aged 4 and younger.²⁴ An additional state-level study of children removed from homes with methamphetamine labs found that 80 percent of those who received a medical exam had a documented physical or mental health issue.²⁵ This indicates that even children who are asymptomatic and have not orally ingested methamphetamine can still experience subclinical exposure,²⁶ which may contribute to health problems.

Raided Homes Often Have Illicit Drugs in Reach of Young Children

There have been many reports throughout the United States of police-raided homes containing drugs within the reach of young children. In Ohio, police found a 1-year-old child in the home along with cocaine, weapons, and packaging materials for heroin. Another home in Florida that was investigated after a shooting found six children aged 3 to 11 in close proximity to marijuana and crack cocaine, as well as a loaded AK-47 rifle. In Massachusetts, law enforcement raided a home with two 4-year-old children and collected large amounts of heroin, cocaine, and pills.²⁷

Symptoms of Illicit Drug Exposure

The nature and severity of symptoms associated with childhood exposure to illicit drugs depend on various factors including the specific drug, the age of the child, the method of exposure, and the dose of the drug exposure. Secondhand exposure can also pose a threat to children if the drug involved is smoked or inhaled.²⁸ Symptoms in young children are described below, and are separated by four types of illicit drugs: heroin, stimulants (cocaine and methamphetamine), hallucinogens, and club drugs.

Heroin

Exposure to heroin in young children has not been well documented. Although there have been many reports of unintentional exposures to various opioid prescription medications, heroin exposures are much less common in young children. When it does occur, exposure to heroin in young children is extremely dangerous. One case report described a baby who became unconscious and eventually died after accidentally swallowing heroin that was left near his cot.²⁹ Below are symptoms of heroin exposure obtained from two case reports of an 18-month old and 23-month old.

Symptoms of Heroin Exposure

Death³⁰ Unresponsiveness³¹ Vomiting³²


Stimulants (Cocaine and Methamphetamine)

Cocaine and methamphetamine are illicit stimulants that are chemically similar to amphetamine.³³ They affect both the central and sympathetic nervous systems and, like all addictive substances, increase levels of dopamine in the brain, which produces a rewarding sensation and reinforces repeated use.³⁴ Despite their similarities, methamphetamine and cocaine differ in certain important respects. Methamphetamine is a synthetic substance, whereas cocaine is derived from a plant. Methamphetamine remains in the brain longer than cocaine and produces a longer-lasting effect. Cocaine works by blocking dopamine re-uptake in the brain (allowing dopamine to remain in the neuronal synapses), whereas methamphetamine blocks dopamine re-uptake and also increases dopamine release.35

Children can be exposed to cocaine or methamphetamine via passive inhalation of vapor or dust or household products that contain traces of the drug.³⁶ There also have been cases in which children have accidentally ingested cocaine³⁷ and methamphetamine.³⁸

General symptoms of methamphetamine exposure in children overlap with adult symptoms. However, unsuspecting health professionals have mistaken methamphetamine poisoning for other serious pediatric diseases such as sepsis, intracranial lesions,³⁹ and scorpion envenomation.⁴⁰ In children older than age 8, manifestations of cocaine poisoning are similar to adults, primarily with regard to alterations in mental status; children younger than age 8 are more likely to have seizures.⁴¹ Below is a list of symptoms of unintentional exposure to cocaine and methamphetamine in young children, collected from case reports.

Symptoms of Cocaine and Methamphetamine Exposure in Children

Agitation/irritability⁴²

Apnea43

Arrhythmias44

- Ataxia45
- Choreoathetosis (involuntary movements)⁴⁶

Coma47

Death⁴⁸

Diaphoresis (excessive sweating)⁴⁹

Diarrhea⁵⁰

- Drowsiness/Lethargy⁵¹
- Dystonia⁵²
- Fever53
- Hypertension⁵⁴
- Hyperthermia⁵⁵
- Nausea⁵⁶
- Seizures⁵⁷
- Stroke⁵⁸
- Tachycardia⁵⁹
- Transient cortical blindness⁶⁰
- Unresponsiveness⁶¹
- Vomiting⁶²
- Wheezing63



Hallucinogens

Cases of unintentional childhood exposures to hallucinogenic drugs (e.g., LSD, PCP, mescaline, psilocybin, mushrooms) are not well documented.

One case report of a 5-year-old girl who mistakenly ingested an LSD (lysergic acid diethylamide) tablet thinking it was sugar indicated that she developed symptoms within 15-20 minutes. According to her uncle, the tablet she consumed contained a typical LSD dose of 100 micrograms (µg).⁶⁴ While normal LSD "trips" last 12 hours for adults,⁶⁵ this child still exhibited symptoms 30 hours after unintentionally ingesting the drug.⁶⁶ Symptoms of childhood LSD poisoning generally match adult symptoms, and can include panic, alteration in mental status, and hyperreflexia.⁶⁷

PCP (phencyclidine, also known as angel dust) also has been implicated in accidental exposures in children. PCP can be ingested or inhaled, and there are cases where children have developed symptoms following secondhand exposure. Medical professionals have misdiagnosed PCP exposure in children as meningitis or seizure disorder. Unlike adult symptoms of PCP toxicity, hypertension, hyperreflexia, and increased muscle tone are not as common in children aged 5 and younger who were unintentionally exposed to PCP.⁶⁸ Overall, reported symptoms in children are based on a small number of studies derived from relatively old case reports.

Symptoms of Hallucinogen Exposure in Children

Agitation⁶⁹

Alteration in mental status⁷⁰

Cerebellar dysfunctions,⁷¹ including nystagmus (involuntary eye movements)⁷² and ataxia (difficulty moving)⁷³

Coma⁷⁴

Depression⁷⁵

Irrational behavior⁷⁶

Irritability⁷⁷

Miosis (constricted pupil)78

Opisthotonos (body spasms)⁷⁹

Panic⁸⁰

Pupil dilation⁸¹

Psychosis⁸²

Tachypnea (rapid breathing)83

Club Drugs

Club drugs, such as GHB (gamma-hydroxybutyric acid) and Ecstasy (MDMA), rarely are associated with accidental poisonings in young children. However, if exposed, young children may experience adverse symptoms.

GHB, originally used as an anesthetic in the 1960s and 1970s, and now used to treat narcolepsy, is considered a club drug,⁸⁴ and is commonly referred to as a "date-rape" drug. The symptoms of GHB poisoning in children mimic those in adults who experience a toxic dose.⁸⁵

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Children Swallowed Toys Contaminated With GHB

In 2008, more than four million bead toys were recalled after they were found to be contaminated with GHB and to have resulted in the hospitalization of three children. The toys had a coating that converted to GHB when metabolized, putting a child who swallowed them at risk. Children exposed to GHB via these beads became dizzy, began vomiting, and eventually became comatose. All the children eventually recovered.⁸⁶

Ecstasy's psychoactive ingredient, MDMA (3,4-methylenedioxy-methamphetamine), is chemically similar to both amphetamines and hallucinogens.87 The active compound of Ecstasy releases and/ or inhibits reuptake of dopamine, serotonin, and norepinephrine,⁸⁸ the key neurotransmitters involved in addiction. While Ecstasy typically has been used recreationally in nightclubs, use in the home has been increasing.⁸⁹ Excessive dancing at nightclubs and subsequent dehydration can cause symptoms in adults that will not present in well-hydrated children.⁹⁰ Nonetheless, neurologic and cardiac symptoms predominate in many of the case reports of Ecstasy poisonings.⁹¹ Both adults and children typically experience increased heart rate, blood pressure, and temperature.⁹² Severe poisoning can lead to organ failure and death.*93 Unlike adults, neurologic symptoms in children may include seizures,94 decreased consciousness, and stupor.95

Actor's Child Accidentally Ingested Ecstasy at a Children's Party

The actor Jude Law's 2-year old daughter ingested half of an Ecstasy pill when she was at a child's birthday party in a London event space. Her mother was able to take half the pill out of her mouth to prevent her from eating the entire tablet. It is believed the tablet had been on the floor following a party the previous night. Once brought to the hospital, the child underwent a stomach pump, and would eventually stabilize.⁹⁶



Ecstasy pills



Hard candies

Cases of Ecstasy poisoning in children appear to be idiosyncratic. One case study reported that children could develop symptoms within 30 minutes of ingesting the drug.⁹⁷ Another reported that a 17-month old developed symptoms within 5 minutes of putting the tablet on her tongue (without swallowing it) and had a serum MDMA concentration of 0.30 mg/l. Poisoning symptoms are likely to present more quickly in children than in adults.⁹⁸ Children metabolize the drug faster than adults, and could have more serious symptoms.⁹⁹ Long-term neurologic effects following a single dose of MDMA/Ecstasy are not well documented in children due to the lack of cases and the inability to follow up with some of the patients.¹⁰⁰

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^{*} There are no documented child fatalities due to Ecstasy poisoning.

HEFE

Symptoms of Club Drug Exposure

Agitation¹⁰¹

Coma¹⁰²

Convulsion¹⁰³

Cyanotic (i.e., discoloration; blue or purple appearance)¹⁰⁴

Hyperreflexia¹⁰⁵

Hypertension¹⁰⁶

Hyperthermia¹⁰⁷

Incontinence¹⁰⁸

Lethargy¹⁰⁹

Muscle tension¹¹⁰

Nausea¹¹¹

Organ failure¹¹²

Pupil Dilation¹¹³

Respiratory Depression¹¹⁴

Seizure¹¹⁵

Tachycardia¹¹⁶

Tachypnea (abnormally rapid breathing)¹¹⁷

Vomiting¹¹⁸

Toxicity of Illicit Drugs

Lethal toxicity levels for children with regard to illicit drugs generally are unknown because most of the analyses have relied solely on case studies. The chart below lists the estimated acute lethal toxicity of common illicit drugs in a healthy 70 kg (154 lb.) human adult.¹¹⁹ Other than LSD and psilocybin mushrooms, the lethal dose of the other illicit drugs listed below may be lower in children.

Acute Lethal Toxicity of Common Illicit Drugs ¹²⁰	
Common Illicit Drugs	Estimated Lethal Dose
Cocaine	1200 mg
Ecstasy (MDMA)	2 g
Gamma hydroxybutyrate (GHB)	16 g
Heroin	50 mg
LSD	100 mg*
Methamphetamine	> 150 mg
Psilocybin Mushrooms	6 g

While illicit drugs affect people differently depending on factors such as absorption rate and metabolism, heroin and GHB are thought to be two of the most toxic misused drugs; they can be lethal at doses close to or less than the typical amount consumed. Cocaine and Ecstasy have shown to be lethal at 10 to 20 times the usual effective dose. The least toxic illicit drugs are LSD and psilocybin mushrooms, with an estimated 100 to 1,000 times the typical dose needed to cause death.¹²¹

Besides dose, the mode of consumption also is related to the toxicity of illicit drugs. For example, eating or drinking a substance tends to be less lethal than smoking or injecting the drug.¹²² Individual physical tolerance also plays a role in toxicity with regard to a particular drug. When children are unintentionally exposed to illicit drugs, it is usually the first time their bodies interacted with the substance. As such, their tolerance level is very low, and they could experience more severe side effects compared to adults who may have already used the drug in the past.

* Equivalent to more than 800 times the usual 'street' dose.





Approaches to Addressing Childhood Illicit **Drug Exposure**

Unlike regulations for nicotine, alcohol, or marijuana, there currently are no laws regulating illicit drugs, such as child-resistant packaging, clear labeling, or standards for the appearance of illicit drugs to ensure that they do not resemble candy or otherwise appeal to young children. Most initiatives to reduce childhood exposures to illicit drugs have focused on state-level policymakers.

State Policymakers

States have expanded the civil definition of child abuse to include situations where children are exposed to illegal drugs. The latest report released from the Child Welfare Information Gateway^{*} indicated that 34 states have listed some form of childhood exposure to illicit drugs in their criminal statutes. It is considered a felony in 20 states to possess methamphetamine in the presence of a child. In 10 states, the possession of any controlled substance is considered a felony if there is a child present.123

Health Organizations

Health organizations play an important role in educating the public about preventing pediatric exposures to illicit drugs.

The National Alliance for Drug Endangered Children (National DEC)

The National DEC is a nonprofit organization founded in 2006 that promotes the safety of children living in environments where drugs are accessible.¹²⁴ Its multidisciplinary approach involves law enforcement, medical providers, social services, and prosecutors.¹²⁵ One of the National DEC's strategies is to provide fact sheets to parents and caregivers with essential information about the signs that a child has been exposed to drugs, and strategies to prevent unintentional exposure. Two of the fact sheets produced by the National DEC include, "Drug Exposed Children: What Caregivers Should Know" and "Do You Suspect a Drug Endangered Child?"126

Prevent Child Abuse America

Prevent Child Abuse America was founded in 1972 and is one of the oldest health organizations to solely address the needs of children who have been neglected. It has chapters in all 50 states, and provides research on drug prevention and strategies to ensure healthy development in young children.¹²⁷ For example, the Prevent Child Abuse chapter in Illinois has information about symptoms of unintentional exposure to methamphetamines, the risks associated with children living in homes with methamphetamine, and who to contact if a child has been exposed to a methamphetamine lab.128

* A congressionally mandated service of the Children's Bureau of the Administration for Children and Families, U.S. Department of Health and Human Services.



Explaining Unintentional Pediatric Exposures

Key Points

- Pediatric exposures to addictive substances continue to be a serious public health problem.
- Parents and caregivers may underestimate the risks to young children of having addictive substances in the home, especially those that are legal such as nicotine, alcohol, prescription medications, and (in some states) marijuana products.
- Features associated with the natural progression of early childhood development, such as curiosity and exploration, can elevate the risks of exposure to addictive substances and poisoning events.
- Addictive substances placed in unsecured packaging or packaging that appeals to children -- along with gaps in policies regulating their marketing, packaging, and dosage -- contribute to the risk of pediatric exposures and poisonings.

Despite the growing awareness of the risks and harms associated with unintentional exposure to addictive substances, especially among young children, such exposures remain a significant and persistent public health problem.¹ In the latest annual report from the American Association of Poison Control Centers (AAPCC), almost half (46 percent) of all exposure calls to poison centers was for incidents in children aged 5 and younger.² While young children can be exposed to a wide range of toxic substances, addictive substances represent a particularly serious threat.³ With the growing availability of addictive products such as e-cigarettes, caffeinated energy drinks, marijuana edibles, and various types of opioids, understanding what exactly leads to unintentional exposures is essential for effectively preventing such occurrences and their harmful consequences.⁴

Several pathways to unintentional childhood exposures and poisonings related to addictive substances alone or in combination can account for these incidents:

- Inadequate appreciation of the risks
- Parents or other caregivers who use, misuse, or are addicted to substances
- Natural features of childhood development

- Widespread availability of addictive substances
- Unsafe product design and packaging
- Inadequate policies to address exposure risk

Inadequate Appreciation of the Risks

Parents and other caregivers may have a false sense of security when it comes to the risk to young children of having addictive substances in the home.⁵ Though parents generally perceive their home as a safe place for their children,⁶ the majority of unintentional childhood exposures occur in the home.⁷ Too often, these exposures lead to serious consequences.





One study found that emergency department visits due to adverse drug events stemming from unsupervised exposures to medication -- when a child accesses medication without caregiver permission or oversight -- were three times more likely to result in hospitalization than were ED visits for adverse drug events stemming from caregiver administration of a medication.* ⁸ In emergency department visits for medication overdoses among young children, the medications involved most often belonged to a family member such as a parent, grandparent, aunt, or uncle.⁹

Some parents and caregivers may not fully appreciate the potential risks associated with the natural course of child development or have accurate expectations of their children's capabilities and limitations at different developmental stages. For example, a parent may not recognize that a child who recently developed the ability to climb is now more likely to reach objects placed on a higher shelf, or a parent may overestimate a child's ability to understand admonitions against touching certain objects, especially if that child is demonstrating accelerated verbal skills.

As children spend a large amount of time in the home, it is important that substances are stored very carefully, which does not always happen when parents underestimate the risks and do not exercise adequate vigilance.¹⁰

Unsafe Storage Practices

When a particular substance is used frequently, storage practices often are insufficient. This is highly problematic in the case of addictive substances, given their frequent usage. Approximately half of unintentional childhood exposures occur while a product is being used or has been moved from its usual storage place.¹¹ This suggests that parents must be vigilant during the storage, usage, and transportation of potentially toxic substances. Typically, children find medicine that has been misplaced or that has fallen on the ground; they also may find it in a purse/bag/wallet, on a counter/dresser/ nightstand, or in a pillbox.¹²



One study examining consumers' perceptions of household hazardous materials found that the relative danger of particular household substances was not reflected in their storage practices (e.g., placing a substance high and out of reach vs. in an easily accessible place).¹³ Other research shows that even when stored out of reach such as in a high place, children still are frequently able to access them.¹⁴

Safe Kids Worldwide[†] conducted an online survey in 2017 of parents with children aged 5 and younger, examining their attitudes toward safe storage. The findings indicated that about 4 in 10 parents believed it was sufficient to keep medications on the counter if someone in the house takes them every day. About half the parents believed it was satisfactory to keep them on the counter or another easily accessible location when a child is sick and is prescribed medication.¹⁵

Another study published in 2017 surveyed 681 parents who had used a prescription opioid pain reliever during the past 12 months and who had at least one child between the ages of 0 and 17 years living in the home.

^{*} Adverse reactions due to allergic reactions; administration of the medication at levels greater than prescribed or recommended; medication errors; or secondary effects like choking.

[†] Safe Kids Worldwide is a nonprofit organization whose mission is to protect children of all ages from preventable injuries.



The findings revealed that safe storage of opioid medications occurred in only about one-third (32.6 percent) of households with children who were less than 7 years old. Among parents with two or more children in that age range, safe storage was reported in only 29 percent of households.¹⁶



A study that specifically investigated potential causes of exposure to buprenorphine, an opioid medication used to treat opioid addiction, found that children were most likely to access buprenorphine because it either was in sight, in a bag or purse, or not kept in the original childproof packaging. Almost all exposures (93.8 percent) occurred in the child's home and the medication always was intended for parents, other family members, or friends.¹⁷

Misunderstandings Related to Child-Resistant Packaging

While the use of child-resistant packaging does reduce the incidence of childhood poisonings,¹⁸ "child-resistant" is not equivalent to "childproof."¹⁹ Many parents falsely assume that children cannot open packages with child-resistant closures and, as a result, may not store potentially dangerous substances safely.²⁰ Child-resistant packages can malfunction, given sticky liquids or pill residue in screw threads, and some children may be able to open them even if the container is considered child-resistant.²¹ Data from a national sample of U.S. hospital emergency departments demonstrated that, of all poisonings (including prescription and nonprescription drugs, cleaning products, etc.) among children aged 5 and younger, more than half (54.7 percent) involved products that were already in compliance with the child-resistant packaging requirements of the Poison Prevention Packaging Act.²²

Child-resistant packaging does not replace the need for proper storage of potentially poisonous products and adequate supervision of young children.²³ Childresistant packaging is reliable only if the caretaker does not remove the medication from its original packaging and remembers to replace the child-resistant cap after each use.²⁴

"Many parents believe that childproof packaging can keep a child from getting into medications. However, childproof packaging is falsely reassuring, as it might slow down a child from getting into a medication, but it often does not prevent it. You really need a parent that is present, available, and watching.

Also, adults often take medications out of the original packaging for convenience, which completely eliminates the usefulness of childproof packaging. For instance, while pillboxes are very convenient for adults, they can be dangerous to children as they are very easy to open"

--Adelaide Eichman, MD Assistant Professor of Pediatrics Division of Child Advocacy Children's Hospital of Pittsburgh University of Pittsburgh School of Medicine

Interview on September 13, 2016



Confusing Messages from Parents and Other Adults

Parents may not always be clear and accurate when discussing addictive substances with their children. One of the most common examples of mixed messaging is when parents convince their children to take medicine when they are sick by telling them that the medicine tastes like candy.²⁵ Young children who are told this may be more inclined to take pills in the future thinking that they are like candy. Children are never too young to be told the exact purpose for taking medicine, and the ways in which medications should not be used.

"Children are taught that medicine is good for them when they are sick. Many children's medicines are sweetened and flavored to make them more palatable, and many parents inappropriately encourage their children to take medicines by telling them, "It tastes like candy." Children have been observed "making tea" from plants or "making pizza" with mushrooms from the yard."

-- Jeremy S. Fine, MD

SOURCE: Nelson, L. S., Lewin, N. A., Howland, M. A., Hoffman, R. S., Goldfrank, L. R., & Flomenbaum, N. E. (2011). Goldfrank's toxicologic emergencies (9th ed.). New York: McGraw-Hill.

Repeat Exposure

Up to 30 percent of children who experience one exposure will experience a repeat exposure, often involving the same substance.²⁶ This implies that parents might not reassess their supervision or storing practices to safeguard their children following an initial exposure incident. Repeat exposure could also mean that parents may not be receiving adequate educational interventions from health care professionals or other service professionals, even following an initial exposure. An analysis of poison prevention interventions found that education and low cost equipment are most effective in prompting caregivers to practice safe storage of medicines.²⁷

Parents or Other Caregivers Who Use, Misuse, or are Addicted to Substances

Children of parents with addiction or mental illness are at increased risk of unintentional exposure.²⁸ This is because addictive substances are more likely to be in the homes of people with addiction or mental illness²⁹ and because parents' caregiving abilities, including supervision and vigilance, might be compromised by their illness.

National data indicate that approximately one in eight children (8.7 million) under the age of 18 live with at least one parent who had a substance use disorder in the past year.³⁰ Parental substance use and addiction are associated with child neglect and poor supervision.³¹ Addiction is also often characterized by a compulsive use of time and money to obtain drugs,³² which may lead to a more chaotic or stressful home environment, putting children at an elevated risk of poisoning.³³ Parents or caregivers who are misusing addictive substances may be less likely to adhere to safety measures such as keeping substances in their original packaging or properly storing them out of the reach of children.³⁴ Unfortunately, due to stigma and inadequate access to treatment in the United States, most parents and caregivers with addiction do not receive the treatment and support services they need to help them manage their substance misuse, enter a sustained recovery from addiction, or improve their parenting skills and practices.



Natural Features of Childhood Development

Another crucial factor in explaining unintentional exposures among young children has to do with the children themselves.

Beyond the increased risk of poisoning among young children due to their smaller size and immature metabolic processes,³⁵ there are risk factors related to the natural progression of child development. The developmental proclivities of babies, toddlers, and young children -- including their natural curiosity and desire to explore and their lack of awareness of which items might be dangerous -- compound the problem of unintentional poisoning. Babies and toddlers are inclined to put objects in their mouths, especially as their teeth come in, to soothe teething symptoms.³⁶

The high rate of toxic ingestions in young children also is associated with their newly developed ability to explore their environment.³⁷ Studies have shown that more than 90 percent of unintentional childhood poisonings occur in the home, and that most children access addictive substances on their own, without someone else's help.³⁸ A child's ability to access a substance plays a major role in the likelihood of unintentional poisoning.³⁹ The exploratory behavior of young children makes them more vulnerable to unintentional exposures relative to older children and adolescents.⁴⁰



From 0 to 2 months, infants are first learning how to reach for and grasp objects, but must rely on their caregiver to move them around. By 11 months, children can reach, grasp, and manipulate small objects, but rarely are able to access objects

stored out of reach.⁴¹ As children get older, their development greatly influences their new ability to gain

access to objects that used to be more challenging to reach. They begin to develop fine motor skills, and become more agile, mobile, and curious.⁴² This enhanced mobility, which can increase from one day to the next, means that some addictive substances that caregivers might have believed to be out of reach for the child actually become accessible.⁴³

Young children also tend to imitate their parents' behaviors, which may include observing parents taking medicine, smoking, or drinking.⁴⁴ Unlike potentially poisonous non-drug substances, such as household cleaners, which children do not see adults ingesting, some children witness a parent or caregiver ingest addictive substances and medications,⁴⁵ and this could lead to dangerous consequences. Imitation is especially concerning if the substance is also appealing to children. Substances such as flavored e-cigarettes, attractively packaged caffeinated energy drinks or alcoholic beverages, candy-like illicit drugs, and edible marijuana products carry heightened risk of pediatric poisoning.

Lastly, the degree of pediatric exposure risk appears to relate to the sex of the child, with male children showing higher rates of unintentional exposures. This could be attributed to the tendency of young boys to be taller, more active, less compliant, and more likely to take risks than girls, giving them higher odds of accessing and consuming addictive substances.⁴⁶ Clearly, this is not always the case, and there are behavioral traits that have been identified as risk factors for poisoning in both boys and girls, including hyperactivity, impulsive risk-taking behavior, pessimistic attitude, and rebelliousness.⁴⁷ These traits might reflect the child's natural temperament, but they also can be influenced by instability in the child's home environment.⁴⁸ Parents should be aware of these risk factors and compensate for them both in how they supervise their children and in how carefully they safeguard them from potentially poisonous substances. ••••

Widespread Availability of Addictive Substances

The problem of childhood poisoning largely reflects the widespread availability of addictive substances.⁴⁹ The availability of an addictive substance is influenced in part by its popularity and the public perception of it as commonplace and/or safe.

Nicotine Products

The use of non-cigarette nicotine products (e.g., vaping, e-cigarettes) among adolescents and adults has increased dramatically in recent years.⁵⁰ New dissolvable nicotine products also have become readily available throughout the United States.⁵¹

The recent surge in the supply and popularity of these products and public perceptions regarding their safety (especially relative to cigarettes) has been met with a parallel increase in the rate of unintentional poisonings from these products in young children.⁵²

"What's most concerning is that we are getting calls about toddlers and young children taking 'puffs' from e-cigarettes, which is a learned behavior from watching their parents. Also, e-cigarettes may be appealing to children as they often have fruity or other pleasant flavorings or scents."

--Carol DesLauriers, PharmD, DABAT Director, Illinois Poison Center

SOURCE: : Illinois Poison Center. (2016). IPC warns of young children facing increased exposure to e-cigarettes. Retrieved from http://illinoispoisoncenter. org/children-facing-increased-exposure-ecigarettes.

E-Cigarette and E-Liquid Sales are Increasing Across the Globe

A report produced by the market research firm Euromonitor International found that, in just one year, global sales of e-cigarettes and e-liquids almost doubled, totaling \$6 billion in 2014. The United States accounted for close to half of these sales at \$2.8 billion. According to an analyst at the firm, low risk perceptions of e-cigarettes and the belief that they may be healthier than traditional cigarettes contribute to their widespread market growth.⁵³

Alcohol

Alcohol is ubiquitous in the United States. More people suffer from addiction to alcohol than to any other drug.⁵⁴ One in 10 children aged 17 and younger (7.5 million) live in a household with at least one parent with an alcohol use disorder.⁵⁵ The growing availability of flavored alcoholic beverages poses a new risk to children who may be attracted to the appearance and flavors of these beverages. It also might account for the increase in exposures to alcoholic beverages reported to the AAPCC among children aged 5 and younger over the past few years.

Caffeine

Caffeine is one of the most commonly consumed psychoactive substances in the world.⁵⁶ While caffeine was originally confined to foods and beverages as a naturally occurring substance and as an added component of soda, it is now added to numerous foods and beverages, with a wide range of caffeinecontaining products now on the market.⁵⁷ Energy drink products are an especially popular source of caffeine, and are highly concerning because of the high dose of caffeine in each drink. Energy drinks can contain anywhere between 50-505 mg of caffeine per can or bottle.⁵⁸ The widespread availability of caffeine in food products and energy drinks can help explain increases in reported exposures among children consuming food with added caffeine.⁵⁹ Parents generally are unaware of the ubiquity of caffeine in everyday food and beverage products, making it difficult for them to protect their children from exposure to high levels of caffeine.60



Prescription Drugs

The prevalence of prescription drug use in the adult population may be associated with the prevalence of unintentional exposures among young children.⁶¹ The number of prescriptions filled has nearly tripled from 1980 to 2014, from 1.4 billion to more than 4 billion.⁶² The Centers for Disease Control and Prevention (CDC) reports that in 2012, more than 259 million prescriptions for opioid painkillers were written -- enough for every American adult to have a bottle of pills.⁶³ Prescription depressants and opioids are almost exclusively prescribed to adults,64 but the abundance of prescription drugs in U.S. households has been associated with their increased accessibility to children.⁶⁵ Opioids and other prescription drugs continue to be readily available, posing significant risk to young children who get their hands on them.⁶⁶

The widespread availability of prescription drugs leading to unintentional pediatric exposure also can be attributed in part to the trend of more grandparents living with children. The number of grandparents considered head of household in the same home as children has more than doubled, from 2.2 million in 1980 to 4.8 million in 2014. According to data collected from children's emergency room visits, approximately 48 percent of all pediatric medication exposures were from grandparents' medications.⁶⁷

Marijuana

The use of medical or recreational marijuana is becoming increasingly common due to the recent trend toward decriminalization and legalization in many states.⁶⁸ Regardless of one's opinion about how medical and recreational marijuana should be regulated, one undeniable consequence of this trend is the increased accessibility of marijuana to young children.⁶⁹

In states where medical or recreational marijuana is legal, there is a relatively higher risk of marijuana exposure and poisoning in children.⁷⁰ For example, Colorado was the first state to legalize marijuana for recreational purposes, and it has the highest number of unintentional exposure cases among young children compared to all other states.⁷¹

Another growing problem is the greater likelihood of a child experiencing toxic effects from exposure to marijuana due to the increasing potency of marijuana products.⁷² Not only have THC* levels risen in marijuana strains,⁷³ but marijuana edibles have become more widespread and popular as well.⁷⁴ Marijuana edibles are particularly potent, containing higher concentrations of THC. High doses of THC from even small doses ingested by children can result in symptomatic exposures.⁷⁵ As the availability of and demand for marijuana edibles have grown, children are at greater risk of exposure.⁷⁶ Most unintentional marijuana exposures in young children have been associated with ingested medical marijuana, often in the form of a food product.⁷⁷

"There is a misconception that if a substance is safe for adults, then it must be safe for children. Similarly, some people conflate a substance being legal with it being benign. This latter problem is particularly a concern for a drug like marijuana, which is becoming legal in more and more states; as marijuana becomes more common, it is seen as non-threatening, which can lead to decreased vigilance on the part of a caretaker, and increased risk of a pediatric ingestion."

-- Adelaide Eichman, MD Assistant Professor of Pediatrics Division of Child Advocacy Children's Hospital of Pittsburgh University of Pittsburgh School of Medicine

IInterview on September 13, 2016

* Tetrahydrocannabinol -- the main psychoactive ingredient in marijuana.



Unsafe Product Design and Packaging

Many addictive substances are distributed in forms that are troublingly difficult to distinguish from non-addictive substances. Flavored e-cigarettes, caffeinated foods and beverages, energy drinks, marijuana edibles, and prescription pills all can be found in forms that may seem harmless and look appealing to children. These potentially toxic products may be indistinguishable from real candies, desserts, or other foods and beverages that are consumed regularly by children. The design and packaging of these products with bright colors or pleasant smells is another contributor to the risk of childhood poisonings.⁷⁸

Nicotine

More than 7,700 flavors of electronic nicotine delivery systems are on the market, including fruit and candy flavors that could be enticing to children.⁷⁹ Other non-cigarette nicotine products, such as dissolvable nicotine, easily can be confused with candy or other food products as well.



Alcohol

Similar to energy drinks, certain alcoholic products strongly resemble non-alcoholic beverages. With new products on the market, like alcoholic lemonade and fruit-flavored cocktails, children could easily encounter them in the home or at a party and ingest these potentially dangerous beverages.



Whiskey Cocktail



Lemonade

Caffeine

There is a current trend among food and beverage manufacturers to add caffeine to numerous products where it is not a natural ingredient.⁸⁰ In many cases, products with added caffeine look identical to noncaffeinated products.⁸¹ For example, a young child would have a difficult time telling the difference between caffeinated and non-caffeinated chips or candy. There also is the risk posed by the proliferation of energy drink sales and consumption.⁸² Energy drinks often resemble juices and other non-caffeinated beverages, which could lead to unintentional exposure in young children.

Caffeinated Products Look Identical to Products without Caffeine

"The gummi bears you love, infused with the energy you need"

Energy Gummi Bears are candies marketed as providing a tasty energy boost. One ounce of gummy bears, available in citrus and berry flavors, contains 32 mg of caffeine⁸³ and looks almost identical to regular, non-caffeinated gummy bears.

Extreme Sport Beans, marketed as providing "quick energy," are caffeinated jellybeans that come in many flavors, including watermelon, cherry, and pomegranate. One ounce of these jellybeans contains 50 mg of caffeine. Although this product comes with a statement indicating that it is not recommended for children, these caffeinated jellybeans are indistinguishable from regular jellybeans.⁸⁴ In both the caffeinated gummy bears and caffeinated jellybeans, the caffeine content far exceeds the recommended daily limit for young children.



Caffeine Gummy Bears

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Regular Gummy Bears





Caffeine Jellybeans

Regular Jellybeans

Prescription and Illicit Drugs

Prescription and illicit drugs can resemble popular candy products. Mints and candies such as Tic Tacs, Altoids, and Life Savers resemble prescription pills, making it difficult for children to tell the difference between them. There have been cases reported around the world of children mistaking illicit drugs for other foods, and ingesting them.⁸⁵ For example, earlier this year, a student mistakenly brought cocaine to school thinking it was a sweet, and gave the cocaine to three other students. Fortunately, the police were called right away and the children, who were immediately sent to the hospital, did not suffer any health effects.⁸⁶



Pills



Mints



Marijuana

The increasing incidence of childhood exposures to marijuana may be explained in part by the growing popularity of palatable edible marijuana products among adults.⁸⁷ These products include cookies, hard and soft candies, chocolates, brownies, popsicles, and beverages. They often are indistinguishable from non-marijuana products that young children consume regularly.⁸⁸ Even adults could have a difficult time telling the difference between marijuana edibles and regular desserts.



Regular candy





Regular hard candies

Marijuana hard candies

Inadequate Policies to Address Exposure Risk

Federal, state, and local governments have attempted to address unintentional exposures to addictive substances among young children through a variety of policies and regulations. While some attempts have been effective, including the 1970 Poison Prevention Packaging Act,⁸⁹ there has not been a comprehensive, evidence-based approach to the problem that reflects current trends in addictive substance use. The gaps in regulation, labeling, and child-resistant packaging laws can help explain why such poisonings continue to occur in unacceptably large numbers.

Nicotine

Regulations and policies directed toward non-cigarette nicotine products have lagged behind policies focused on cigarettes. There are no restrictions, at the federal level, on the types of flavoring that can be added to non-cigarette nicotine products.⁹⁰ This means that products such as e-cigarettes, other vaping devices, and hookah can come in thousands of flavors that appeal to children.

Even regulations at the state level have not adequately addressed the problem. For example, only 21 states have enacted e-cigarette retail regulations related to child-resistant packaging that go beyond federal laws.⁹¹ While states tend to have regulated nicotine products more stringently than the federal government has, most states can do more to protect children from unintentional exposure. In a study evaluating the effectiveness of state e-cigarette laws, only three states met all benchmarks for effective legislation in proper packaging of nicotine products.⁹²

Alcohol

There currently are no regulations directed at decreasing unintentional exposures to alcoholic beverages in young children. Companies manufacturing alcoholic products are free to market them with a wide array of colors and flavors that appeal to children. While there are restrictions on where alcohol can be displayed and sold, once it is purchased, children can access them, especially in the absence of child-resistant packaging requirements for alcoholic beverages.



Caffeine

Federal policy toward regulating caffeine has been and continues to be inadequate. There currently are no guidelines published by the U.S. Food and Drug Administration (FDA) regarding how much caffeine is safe for children to consume. The rise in popularity of energy drinks and other caffeine-containing products has taken the FDA by surprise.⁹³ Regardless of whether energy drinks are classified as dietary supplements or beverages, the exact amount of caffeine content in a particular product is not required to be listed on the label.⁹⁴ The lack of regulation regarding labeling could contribute to unintentional exposures to caffeine among young children because parents typically are unaware of the risks associated with children consuming caffeine.⁹⁵

Energy Drink Companies Are Circumventing Regulations

Energy drink companies Monster Energy and Rockstar Energy have decided to stop marketing their products as dietary supplements, and instead market them as beverages. According to the New York Times, these companies have made this decision amid growing concerns about the safety of energy drinks, given that companies that market products as beverages are not required to submit reports of serious adverse health events to the FDA's Adverse Event Reporting System. The marketing changes by these two companies came after several deaths and serious injuries were reported to the FDA, bringing negative attention to these products.⁹⁶

Prescription Drugs

The Poison Prevention Packaging Act of 1970 requires companies to manufacture prescription drugs in childresistant packaging.⁹⁷ Over the years, the increase in the number of children exposed to prescription drugs demonstrates the limitations of such packaging. First, tests of the efficacy of child-resistant packaging are conducted with children 3.5 to 4.25 years of age,⁹⁸ even though the majority of children who are unintentionally exposed to medications are 2 years of age or younger.⁹⁹ In addition, child-resistant packaging is effective only if it used properly.¹⁰⁰ Many cases of children exposed to prescription drugs have been reported in which the medications were not in their child-resistant container, but rather were left on a table or nightstand.¹⁰¹ It is especially dangerous when prescription drugs are in containers that hold a large number of pills because it makes keeping track of missing pills difficult. Even if the container is child-resistant, if it is not properly used, there is a much higher chance of pediatric exposure than if the drug is in a single-dose packaging unit, limiting the extent of the exposure.¹⁰² In one study, children aged 5 and younger had significantly fewer exposures to buprenorphine when it was in a single-dose, childresistant film formulation than when it was in a tablet form.103

"Often, the more convenient the packaging is for adults, the more dangerous it is for children. For example, buprenorphine comes in a Listerine-like formulation. It is in a shiny package and catches children's eyes. Just licking the wrapper can cause a child to experience opioid effects."

-- Adelaide Eichman, MD Assistant Professor of Pediatrics Division of Child Advocacy Children's Hospital of Pittsburgh University of Pittsburgh School of Medicine

Interview on September 13, 2016



Marijuana

At the federal level, marijuana remains an illegal drug.¹⁰⁴ At the state level, shifting opinions over the last decade has led to significant marijuana policy changes, with more and more states legalizing marijuana for medical and/or recreational use.¹⁰⁵ These changes in policy have contributed to increased childhood exposures to marijuana through greater availability and accessibility of the drug.¹⁰⁶

While there are many strategies that have been recommended to limit unintentional exposures in young children, not every state implements all regulations effectively and efficiently. For example, in Colorado and Washington, implementation of child-resistant packaging laws did not go into effect until a year after recreational marijuana became legal.¹⁰⁷ Some states do not even have child-resistant packaging laws for marijuana products.¹⁰⁸ Moreover, only nine states have regulations that require the use of opaque packaging for marijuana edible products.¹⁰⁹ Every other state where marijuana is legal allows companies to manufacture brightly colored packaging that could be attractive to children.

Many states also do not have any laws regulating the appearance of marijuana edibles to ensure they do not resemble candy, requiring clear labeling of all marijuana-containing products, or limiting the amount of THC allowed in marijuana edibles. Because marijuana is a Schedule I drug,* there has been a lack of research on the dosing and potency of marijuana, especially for edible marijuana, which has resulted in a lack of regulatory standards for both dosing and the potency of these products.¹¹⁰ Regulations on packaging and testing of THC concentrations have lagged behind the surge in marijuana sales.¹¹¹

Illicit Drugs

The main barrier to better safeguarding children from accidental exposure to illicit drugs is that they are illegal and therefore unregulated. Producers and distributors of illicit drugs can add other harmful ingredients and adulterants to addictive substances, making them even more dangerous for children.¹¹² Not only are these unregulated adulterants dangerous for children, but for adults as well. One of the reasons for the high death toll from the opioid epidemic is that deadly drugs, such as fentanyl, are added to heroin as well as to other illicit drugs, often without the knowledge of the person using the drug.¹¹³

* In the Controlled Substances Act of 1970, the federal government classified marijuana as a Schedule I drug along with heroin and other illicit drugs, indicating that it has the highest abuse potential and no accepted medical use.

Recommendations and Conclusions

Childhood poisoning from addictive substances is a serious public health problem, and one more way that addictive substances put the lives of young children at risk. Despite this, it is often overlooked in discussions of the countless harmful consequences of substance use and addiction.

As our nation grapples with the current opioid epidemic and the toll it is taking on adolescents, young adults, and older adults who use and misuse these drugs, it is easy to lose sight of the threat to young children of exposure to opioids and other addictive substances.



To better protect the health and safety of young children, a number of specific, research-based actions should be taken. Based on the state of knowledge and the regulatory landscape as of the publication date of this report, The National Center on Addiction and Substance Abuse presents the following recommendations for parents and other caregivers, health care professionals, policymakers, industry, and researchers to help reduce the number of exposures to and poisonings from addictive substances among young children.

Parents and Other Caregivers

Parents and other child caregivers have an important role to play in limiting unintentional exposures to addictive substances in young children. They must recognize that poisonings can happen, and take proper precautions to ensure their children's safety. Steps parents and other caregivers should take to safeguard young children from addictive substances include:

Keep all addictive substances -- including nicotine, alcohol, caffeine, prescription drugs, and marijuana and other illegal drugs -- safely stored and out of sight. The home is the primary place where young children are exposed to addictive substances. Parents and other caregivers should either lock addictive substances in a secure cabinet or store them out of reach and out of sight to ensure they are not accessible to young children. Reducing easy access in the home is the most straightforward and effective way to protect a child from unintentional exposure to a dangerous substance. Caregivers should require visitors as well as friends or relatives who host children in their homes to practice the same safety procedures with their medications and other addictive substances. With regard to prescription medications in particular, a public awareness and education program called <u>Up and Away and Out of</u> Sight -- an initiative of the



PRevention of **O**verdoses and **T**reatment **E**rrors in **C**hildren **T**askforce (PROTECT) in partnership with the Centers for Disease Control and Prevention, the Consumer Healthcare Products Association Educational Foundation, and other organizations -- seeks to remind families about the importance of safe medicine storage and provides useful tips and resources.



Limit the amount of addictive products in the home. Take steps to limit the amount of addictive substances kept in the home. This will reduce the risk of unintentional pediatric exposures, and might help reduce unhealthy substance use among other members of the household.

Set a good example. Young children imitate adults. Parents' own substance use sends a powerful message to children that ingesting addictive substances is safe. Parents and other caregivers should set an example and not use addictive substances casually in front of young children. They also should refrain from extolling the virtues of a cigarette, an alcoholic drink, a prescription pill, or other drugs in the presence of young children, which can undermine efforts to convey the direct and clear message that such items can be dangerous and should never be touched or used by a child.

Talk to children about addictive substances. It is never too early to explain to children that certain substances are dangerous and not to be touched. Obviously, the nature of the conversation should evolve as the child ages, and should always be developmentally appropriate. The Partnership for Drug-Free Kids offers <u>suggestions</u> for how to talk to children of all ages, from 2 to 25, about all kinds of addictive substances.



Stay informed. It is important for parents to be knowledgeable about addictive substances -- how they work and what their effects are on adults and children

of all ages. Parents should learn about ingredients, formulations, symptoms, and other characteristics of addictive substances that are kept in the home. Knowing the amount of caffeine in food products, understanding that e-cigarettes typically contain high doses of nicotine, and learning how to spot the difference between marijuana edibles and regular food items can aid in safeguarding children from poisonings. With regard to marijuana edibles, parents and caregivers should be aware that children have the potential to find and unintentionally consume marijuana products, particularly marijuana edibles, and that children can get sick from such exposure.¹

Call a poison control center immediately if you think there might be an exposure. If parents or other caregivers suspect that a young child may have been exposed to an addictive substance, they should seek qualified professional help as they would for any other health condition or illness. While using the internet can be helpful to learn about symptoms and information about poisoning events, the information on many websites is not necessarily accurate. The best approach is to call a poison control center. Local poison control centers are open 24 hours a day, 7 days a week, and provide extensive medical advice on exposure and poisoning events. If a child is unresponsive or having difficulty breathing, call 911 immediately. Be sure to provide honest, accurate, and detailed information about the exposure incident to help ensure that the child receives the appropriate intervention. Early intervention and treatment can help prevent serious health consequences.

"Ultimately, I recommend that parents and caregivers call a poison center if they either suspect or know their child has ingested any substance at all. Turning to the internet may provide a glimpse into how a substance might affect children, but it is not reliable. It will not take into account nuanced information, such as the age of the child, how much the child weighs, how much of the drug was ingested, if there are underlying conditions, what medications the child might be currently taking, etc. However, poison centers have trained medical professionals to help caregivers decide whether the child can be managed safely at home or should be seen by a doctor"

-- Adelaide Eichman, MD
 Assistant Professor of Pediatrics
 Division of Child Advocacy
 Children's Hospital of Pittsburgh
 University of Pittsburgh School of Medicine

IInterview on September 13, 2016

Properly dispose of prescription medications.

Know how to dispose properly of unused prescription medications, used nicotine patches and devices, and other addictive products. Some drugs can be flushed down the toilet, while others may need to be removed by others means so as not to contaminate the water supply. The U.S. Food and Drug Administration (FDA) provides online <u>resources</u> on safe disposal of different types of medicines. Getting rid of drugs that no longer are needed can prevent children from accidentally accessing and ingesting them.

Health Care Professionals

Health care professionals should be well informed about how best to safeguard children from addictive substances, how to convey key safety messages to parents and other caregivers, and how to respond in the event of an exposure. As with other health conditions, health care professionals should adopt strategies to educate children and parents and know how to assess, diagnose, and treat children who experience an unintentional exposure. To achieve these goals successfully, health care professionals should:



Ask about addictive substances in the home and counsel on safe storage and disposal. At every pediatric well or sick visit, screen for the presence of

addictive products in the home and offer concrete recommendations for proper storage -- putting them out of reach or in locked containers -- to ensure children's safety. Also, use this opportunity to provide brief interventions or referrals to treatment for parents or other caregivers who reveal symptoms of an addictive disorder. If a parent or caregiver reports the misuse of prescription or illicit opioids, prescribe naloxone for the immediate reversal of a potential opioid exposure.

Discuss the dangers of childhood poisoning with parents. Every interaction with parents is an opportunity to impart a clear message that unintentional exposures to addictive substances can occur among young children. Routinely discuss the issue with parents and describe the health risks and consequences of a poisoning event. Parents should know that addictive substances are particularly damaging to young children because children are highly sensitive to the toxins in nicotine, alcohol, and other drugs. For example, a recent study found that while doctors in Colorado discuss some issues related to marijuana use with their patients, many are still uncomfortable talking about the health effects associated with its use. This study called for additional education for health care providers so that they can become more comfortable discussing the effects and risks associated with marijuana use and exposure and how best to avoid those risks.²

Evaluate the child's diet at a checkup. During routine pediatric checkups, ask parents questions regarding their child's food and beverage intake. These checkups should include questions about caffeine consumption and parental education about the presence of caffeine in many common foods and information about the other risks of exposure to addictive substances, including nicotine, caffeinated energy drinks, and marijuana edibles.



Assess young children for possible poisoning from addictive substances in the event of unexplained symptoms. A health care professional might have difficulty detecting poisoning resulting from a child's exposure to an addictive substance. One reason for the delay of a proper diagnosis might be an unwillingness on the part of parents or other caregivers to inform health care providers that their child consumed an addictive substance. In addition, when children are exposed to an addictive substance, the effects can resemble symptoms of other illnesses, making it difficult for health care professionals to make an accurate diagnosis. Given the increasing accessibility to addictive substances among young children, a suspected exposure should be one of the primary issues health care professionals look for when a young child presents with unexplained symptoms.

For example, in states where recreational and/or medical marijuana is legal, health care professionals are in a unique position to help prevent unintentional childhood exposures.³ Historically, health care professionals did not typically suspect marijuana intoxication as the cause of a child's presenting symptoms, mostly because parents and other caregivers were reluctant to admit to possible marijuana exposure.⁴ Children presenting to health care facilities where marijuana intoxication is not suspected often receive invasive and unnecessary laboratory testing, procedures, and radiographic imaging to identify the sources of the symptoms.⁵ However, as health care professionals who work with children become more familiar with the symptoms associated with unintentional marijuana exposure, they may be more likely to recognize it and forego unnecessary and expensive diagnostic tests and treatments.⁶ This occurred in Colorado where, following the legalization and commercialization of recreational marijuana, health care professionals in a children's hospital were less likely to use extensive and invasive tests on young children presenting with symptoms of marijuana intoxication.⁷

Conduct urine drug testing. Emergency departments may not typically perform a rapid urine test for young children. Even when urine is tested, many hospitals do not always test for the content of certain drugs, which makes it difficult to see if a poisoning event in a young child is a result of an addictive substance. Any time a young child displays symptoms of a poisoning, health care professionals should conduct a routine test for addictive substances, such as cannabinoids, cocaine, opioids, and other illicit drugs.

Consider the recreational and therapeutic drug history of parents. When children are sent to an emergency department with unexplained symptoms, it is important for health care professionals to rule out the possibility that the symptoms might have resulted from a drug exposure. In some cases, collecting information from the parents about their history of substance use may help eliminate or reduce the need for more invasive investigations to determine the cause of symptoms, and could potentially limit the risk of a misdiagnosis and subsequent inappropriate treatment for a young patient.

Policymakers

Policymakers have not taken on full responsibility or engaged all the leverage points at their disposal to better safeguard children from potentially toxic addictive substances. To prevent and reduce childhood exposures, policymakers at all levels of government should:

Ban flavoring in all nicotine products. Flavored nicotine products are highly appealing to children. The gaps in the federal regulation of nicotine products have encouraged some state and local governments to develop more stringent policies. Cities such as New York City and Providence have passed laws banning nearly all flavors of liquid nicotine. Policymakers at all levels of government should follow suit. The federal government banned the sale of flavored cigarettes other than menthol, and should do the same for all products that contain tobacco or nicotine.

Ensure that liquid nicotine for electronic cigarettes and other vaping products is sold in child-resistant packaging containers and in small, nonfatal doses. Liquid nicotine for vaping products has led to the most severe nicotine-related childhood poisonings cases. What makes liquid nicotine so dangerous is that there is a much higher nicotine concentration in the liquid compared to other nicotine products. To prevent serious poisonings, standards for all liquid nicotine manufactures should be set in which these products are only permitted to contain small amounts of liquid nicotine per container, with amounts that would not be lethal if a young child accidentally ingested all the liquid in the container.

Require caffeine doses to be listed on the label of all products that contain caffeine. Manufacturers of caffeinated food products or dietary supplements are not required to list on the label the exact amount of caffeine contained in the product. The U.S. Food and Drug Administration (FDA) should update its regulations related to caffeine, and require all products and supplements with caffeine to state the amount of caffeine in the product, and to do so in a manner that would be understandable to a parent. That way, parents would be better able to monitor their children's caffeine intake and ensure that they do not exceed a safe dose of caffeine per day.

Encourage or require warnings on product labels or in package inserts. Retailers should be required to inform customers who buy addictive substances that the products can pose a threat to young children and that the products should be stored and disposed of safely. Such information should be included with all addictive products sold by retailers, including vape shops that sell nicotine products, food and beverage markets that sell alcohol or caffeinated energy drinks, pharmacies that dispense controlled prescription medications, and marijuana dispensaries that sell marijuana edibles.

Ban the sale of pure powdered caffeine. There is no reason companies should be selling pure powdered caffeine. Not only is it extremely lethal if children accidentally ingest powdered caffeine, but it is dangerous for adults as well. It is estimated that one teaspoon of powdered caffeine is equivalent to drinking 28 cups of coffee. While the FDA recommends avoiding purchasing pure powdered caffeine, it should ban it altogether. Ohio has passed a law banning powdered caffeine, and the federal government and other states should follow its lead.

Require opaque packaging for marijuana edibles.

Young children are attracted to packages that are brightly colored and have cartoons or other illustrations on them. States in which marijuana edibles are legal should require that manufacturers place edibles in darkly colored plain packages, where the actual product is not visible from outside the package. Edibles look very similar to comparable food products, and opaque packaging can help prevent young children from being able to see, and be attracted to, the marijuana edible inside the package.

Ensure that manufacturers of marijuana products follow the child-resistant packaging laws in accordance with the Poison Prevention Packaging Act (PPPA) of 1970. Marijuana labeling and packaging laws vary from state to state, but all states should adopt regulations surrounding the packaging requirements set under the PPPA. Similar to prescription drugs, all marijuana (cannabis) products should have childresistant packaging that would make it difficult for children under age 5 to access them. In addition, labels on all marijuana products should have a prominently visible warning to keep the product away from children.

Implement re-sealable child-resistant packaging laws for all marijuana edibles. Along with the recommendation that all marijuana products be placed in child-resistant packaging, the packaging should also be re-sealable. Once opened, some packages no longer are child-resistant. Ensuring the package is both re-sealable and child-resistant can prevent children from ingesting a marijuana product once it has been opened. Re-sealable packaging is especially important for marijuana products that contain multiple servings.

Ban marijuana edibles that look like regular food products. It is extremely difficult to tell the difference between most edible marijuana products and regular food and drink products. Marijuana edibles should not resemble other food products such as gummy bears, lollipops, other candy, chocolate, or brownies. Policymakers in states where recreational and medical marijuana are legal or where legalization is being considered should ban all marijuana edible products, especially those that might appeal to children.

Assure legal immunity for parents who report a childhood exposure to an illegal substance. Parents might avoid reporting a child's exposure to an illegal substance due to fear of criminal prosecution. If a parent of a child with exposure symptoms is not forthcoming about the cause of the symptoms, health care providers cannot provide quick and effective interventions. Parents should have immunity from criminal prosecution if an exposure is reported. If it is the parent's illegal substance that a child had ingested, the parent should receive appropriate health-based interventions for his or her substance use condition, rather than being punished for it.

Get the facts out through population-wide public awareness campaigns. Policymakers should implement public awareness campaigns targeted to parents, other caregivers, educators, and health care professionals that educate the public about the need to protect young children from the harms of addictive substances and how best to do so. Campaigns such as these have proven effective in reducing other public health problems and can influence public perceptions and behaviors regarding children's unintentional exposure to and consumption of addictive substances. Campaigns aimed specifically at raising public awareness of poison control centers -- what they are, how to reach them, and the services they provide -- can help to increase exposure for the most useful but vastly underutilized resources available, which are specifically designed to help prevent and address the problems outlined in this report.

Increase funding for research on caffeine's effects on young people and formulate comprehensive standards for the amount of caffeine a person can consume safely. While Canada's federal agency, Health Canada, has guidelines suggesting children aged 4 to 6 should not consume more than 45 mg of caffeine per day, the FDA currently has no guidelines on caffeine consumption for children. The FDA should publish official guidelines on the amount of caffeine that children of all ages can consume safely per day.

Fund research on better ways to prevent childhood poisoning. Policymakers should invest public funds in the development of innovative approaches to address childhood exposures to addictive substances. Funding should be dedicated to learning the causes and consequences of childhood poisoning, as well as effective solutions. Once implemented, any campaign, program, or initiative must be evaluated to ensure that it is effective, and modifications should be made as needed.

Fund improvements in data collection and surveillance techniques. The current system of collecting local and national data on exposure and poisoning events has a number of significant limitations that constrain accurate reporting of the prevalence and nature of such incidents and impede efforts to intervene where and when such interventions are needed most. One prominent example is that poison control centers base their reports of exposure and poisoning events on calls received from concerned caregivers or health care providers. Telephone calls no longer are the standard means of communication, as people increasingly feel more comfortable seeking information or help online or through apps, direct messaging, texts, and chats.

To begin to address these limitations, innovative strategies are being tested by state and local poison control centers and hospitals to improve data collection. These include encouraging state and local governments to mandate reporting of all incidents of exposure among children by emergency departments and other health care facilities via the use of electronic

medical record (EMR) systems, and developing ways for the public to communicate with the centers through means other than a telephone call. However, such efforts are constrained by a serious lack of resources. As the rate of pediatric exposures to many harmful addictive substances increases, federal and state funding of poison control centers has declined, making it difficult to implement research-based technical advances in potentially life-saving detection, screening, and intervention. With appropriate resources and funding to enhance infrastructure, technology, and public awareness, poison control centers would more than pay for themselves in avoided healthcare expenditures, as demonstrated by a comprehensive cost-benefit (return on investment) analysis, which found that such centers save an estimated \$13 for every \$1 spent on them.8

"There are a number of potential opportunities to improve data collection, both from health care facilities, such as emergency departments, and from the public. Obviously, any advances would require funding. Key benefits of the poison center system are that it is: 1) nationwide, 2) has consistent and uniform coding and documentation, and 3) has a national near-real-time surveillance database. In addition to having centralized reporting and leadership, poison centers also have a community-based presence, which allows them to identify and address specific regional trends that could otherwise be overlooked in a national database with a single collection mechanism. The local presence also allows the centers to build relationships with local and regional health care providers, policymakers, elected officials, law enforcement, etc., that enhance their connection to the community and allow for meaningful educational outreach."

--Michael Lynch, MD Medical Director Pittsburgh Poison Center Assistant Professor University of Pittsburgh School of Medicine

Email correspondence on January 24, 2018

Industry

Pharmaceutical companies, nicotine product manufacturers, pharmacies, and retailers* are directly responsible for the distribution of legal addictive substances to consumers. It is their ethical responsibility to warn people about the dangers associated with the use of their products, and to design and package their products in a way that protects children from their harms should they access them.

Even if child safety regulations are not passed by the government, the industry can adopt strategies to limit childhood exposures to addictive substances. Industries should take it upon themselves to avoid child-friendly marketing and ensure that product packaging does not appeal to children. Specific recommendations for industry to play a larger role in curbing childhood poisonings include:

Refrain from advertising or marketing addictive products in ways that appeal to children. Industries that manufacture or sell addictive substances should never market products in a way that appeals to children. Child-friendly flavors, colorful packaging, and advertisements that are attractive to children can lead to unintentional pediatric exposures and their associated health consequences.

Package addictive products in a way that protects children from harm, should they gain access to the products. Innovative methods of designing product packages to make them more child-resistant or to reduce the risk of harm if accessed by a child can reduce the number and amount of unintentional pediatric exposures and poisonings. Such methods include installing flow restrictors[†] on the packaging of oral liquid medications or e-cigarette liquid solutions, or packaging medications, marijuana edibles, or e-cigarette liquid solutions in single-dose units to limit the amount of the product children can ingest if they are exposed to these addictive substances.

* Tobacco, vaping, alcohol, and marijuana outlets in states where marijuana is legal.

† Flow-restrictors are caps placed on vials to limit the amount of a liquid substance (such as medication or liquid solutions for electronic cigarettes) that is released when opened.

Warn customers about the potential danger that nicotine, alcohol, caffeine, prescription drugs, and marijuana pose to young children. Retailers should inform customers who buy addictive substances that they can pose a threat to young children and should provide information about how best to store and dispose of them safely. Such information should be included with all addictive products sold by retailers, including vape shops that sell nicotine products, food and beverage markets that sell alcohol or caffeinated energy drinks, pharmacies that dispense controlled prescription medications, and marijuana dispensaries that sell marijuana edibles.

Researchers

Increasing our understanding of the causes and consequences of childhood poisoning and developing innovative approaches to address this health issue are critical for helping to protect young children. Researchers should help to design and implement strategies to prevent exposures, and collect and provide relevant data on the risks, prevalence, and consequences of exposures and poisonings.

Research innovative packaging techniques. Childresistant packaging regulations under the Poison Prevention Packaging Act of 1970 have reduced unintentional exposures to prescription drugs among young children. However, child-resistant packaging is not equivalent to childproof packaging, and children can still access prescribed medication. New innovative product formulations, along with innovative childresistant packaging that reduces the risk of harm even if a child accesses the product, can help limit the incidence of childhood poisonings.

Improve data collection and reporting requirements for exposures and poisoning events. The American Association of Poison Control Centers (AAPCC) is currently the only organization that collects national data on childhood poisonings based on phone calls to local poison control centers. This makes it challenging to capture the true prevalence of pediatric exposures to addictive substances. Not only do some parents not call a center when a child develops symptoms, but the AAPCC data itself have several limitations and methodological concerns (to learn more about the AAPCC and their data, please see Appendix A). Researchers should develop additional standardized data collection methods to improve the accuracy of data collected on pediatric exposures to addictive substances.

Conduct studies on the effectiveness of different prevention and intervention strategies and explore best practices for implementation. Program evaluation research is needed to ensure that existing programs are having their intended effects. Once programs are established, researchers should explore ways to ensure that effective strategies are implemented as intended in order to produce the best results possible.

"There are multiple pathways to each child poisoning event. Successful prevention efforts are achievable. They require multifaceted and multi-disciplinary efforts to discover effective prevention strategies, nimble implementation of effective programs, and attention to cost-efficiency for consumers, manufacturers, and government bodies. The effort must be team based and interdisciplinary."

SOURCE: Schwebel, D. C., et al. (2017). Unintentional child poisoning risk: A review of casual factors and prevention studies. Children's Health Care, 46(2), 109-130.

Conclusions

As is true of substance use and addiction more generally, there is no single, simple way to eliminate the risk to children of exposure to addictive substances in their environment. More troubling is that this issue barely registers for most people when considering the massive public health problem of addiction and its countless health, economic, and social consequences.

Efforts to reduce substance use and addiction in the United States typically revolve around delivering prevention messages and programs to adolescents and young adults to forestall substance use, and providing intervention and treatment services to those who already have begun to use or who have addiction. Policymakers, educators, and health professionals seeking to inform the public about the risks of substance use and addiction expound on the tremendous toll they take on the population, primarily in terms of the health, social, and financial costs incurred by those who engage in substance use. While powerful, these messages frequently are dismissed by individuals on the cusp of initiating substance use and among those deciding whether to reduce their use or seek treatment. However, even people who are relatively immune to the long list of consequences associated with using addictive substances tend to be moved by the toll they take on babies and

young children, who may experience the collateral damage not only via abuse, neglect, secondhand exposure, and an increased risk of future addiction, but also via unintentional ingestion of available substances.

Every encounter with a health care professional or social services agency is an opportunity to impart to people who engage in substance use that the young children in their lives might be put in harm's way because of the presence of addictive substances in their environment. While this message clearly will not deter most people from using addictive substances, it can help motivate people to reduce their use in the presence of young children and be more vigilant about ensuring that all addictive substances are secured, safely stored, and out of reach. Of all the harms associated with substance use and addiction. unintentional childhood exposures might just be one of the most consequential and the easiest to avoid.

As our nation tackles the opioid epidemic and hopefully develops the means to avoid future related crises, let's make protecting the youngest children a priority and ensure that every child has the opportunity to lead a full, healthy life, free from the damaging effects of addictive substances. ۲ ا

Appendix

What is the American Association of Poison Control Centers (AAPCC)?

The AAPCC is the leading nonprofit organization working with 55 poison centers across the United States to monitor incidences of poisoning. The AAPCC plays an instrumental role in tracking exposures to numerous substances, as well as helping people with poisoning emergencies. The affiliated poison centers, along with the AAPCC, provide free, year-round advice to people in all 50 states and U.S. territories. They employ toxicology specialists and other health care professionals such as doctors, pharmacists, and nurses to provide callers with information and protocols about how to handle potential exposures. All of the partnering poison centers take phone calls 24 hours a day, 7 days a week, for poisoning emergencies.¹

The AAPCC manages the National Poison Data System (NPDS), which was launched in 2006. The NPDS is a database that documents the number of phone calls that poison centers receive in relation to unintentional and intentional exposures to a wide variety substances.* Participating poison centers upload their data to the NPDS every eight minutes to allow for almost real-time monitoring of exposure calls. The phone calls received from poison centers are organized into categories, such as whether the incident involved an animal or human exposure, the age of the person exposed, the type of poisoning event, the route of exposure, and the reason for exposure. Once the data are collected and organized, the AAPCC publishes the number of cases to the public through annual NPDS reports.²

Why Did We Use the NPDS Annual Data?

The annual NPDS dataset is the only national data collected on exposures to addictive substances. The NPDS organizes exposures by age group and has a distinct category for exposures among children aged 5 and younger -- the age group that is the primary focus of this report.³ Having data separated by age groups allowed us to identify poisoning exposures among young children relative to adolescents and adults.

The NPDS collects specific information on each group of addictive substances that was included in this report, including data on nicotine, alcoholic beverages, caffeine, prescription drugs, marijuana, and illicit drugs. Each substance is further organized by type. For example, specific data are available on cigar exposures under the category of tobacco or on heroin exposures under the category of illicit drugs.⁴

The NPDS is an important resource for understanding national trends and the prevalence of exposures to addictive substances among young children. Analyzing the trends in exposures and their relationship to the availability and accessibility of addictive substances is critical for designing and implementing effective policies and strategies to safeguard children from childhood exposures, poisonings, and adverse health consequences.

* AAPCC DISCLAIMER: The term "exposure" means someone has had contact with the substance in some way; for example, ingested, inhaled, or absorbed a substance by the skin or eyes, etc. Exposures do not necessarily represent poisonings or overdoses. The American Association of Poison Control Centers (AAPCC; http://www.aapcc.org/) maintains the national database of information logged by the country's poison centers (PCs), the National Poison Data System (NPDS). Case records in this database are from self-reported calls: they reflect only information provided when the public or healthcare professionals report an actual or potential exposure to a substance (e.g., an ingestion, inhalation, or topical exposure, etc.), or request information/ educational materials. The AAPCC is not able to completely verify the accuracy of every report made to member centers. Additional exposures may go unreported to PCs and data referenced from the AAPCC should not be construed to represent the complete incidence of national exposures to any substance(s).

What Are the Limitations of the NPDS Data?

While the information collected and obtained from the NPDS is beneficial, the population estimates derived from its data should be regarded with caution. The data have several important features that limit the valid and reliable assessment of rates of pediatric exposure to addictive substances, and their generalizability:

Data are Self-Reported. The data presented in the NPDS are self-reported and voluntary. Anyone from family members to health care professionals can report potential exposures to poison centers.⁵ This makes it difficult for the AAPCC to verify the accuracy of the results submitted by participating poison centers.

Outcome Data are Limited. Once data from calls are collected, there frequently is no follow-up to the reported cases, and data regarding the outcomes of the exposure incidents are incomplete. This could be due to patients being unwilling to submit to a follow-up, a determination that the exposure was deemed nontoxic, or some other reason.⁶

Actual Exposure Cases may be Underreported.

The number of exposure cases included in the NPDS underrepresent the actual number of exposures in the United States because the NPDS only reports exposures based on calls to poison centers.⁷ Reporting an exposure to a poison center is not mandatory, and the Institute of Medicine has estimated that poison centers account for less than half of all the poisonings that occur in the United States each year.⁸

Instead of calling a center in the event of a child's exposure to an addictive substance, a parent or other concerned adult might call for emergency assistance (911), take the child directly to a doctor or hospital, search for information on the Internet, call a family member or friend to find out how and whether to respond, or do nothing but monitor the child at home.

Even in the event that a parent or other concerned adult may want to call a poison center, he or she might avoid doing so from fear of criminal prosecution if the exposure was to an illegal substance or if the adult might be charged with neglect. If the child is brought to the attention of a health care professional because the child is displaying symptoms, the health care professional might not call a poison center if an exposure is not suspected.⁹

We used the NPDS annual reports from 2007-2016 and manually counted each single-substance exposure incident for every addictive substance included in our report. This process excludes cases where two or more substances were reported in the exposure incident. For example, a case in which a young child is exposed both to cocaine and marijuana would not be included in the data we analyzed. However, multiple exposure incidents are very rare among young children. In 2016, single-substance exposures made up 97 percent of all exposures among children aged 5 and younger.

Some underreporting of exposures in the NPDS data set might have resulted from the AAPCC's introduction of new codes for categorizing data. For example, the e-cigarette, energy drink, and opioids categories were added to the data set in 2010.¹⁰ These codes might have been underutilized in the first few years following their inclusion in the database.

Missing or Incomplete Information. The NPDS annual reports do not indicate whether a reported exposure was intentional or unintentional. For our report, we assumed every exposure in children aged 5 and younger was unintentional, since it is very unlikely that a child that age would try to experiment with an addictive substance to get high. However, it is possible that a small percentage of cases were due to intentional exposures.

The NPDS annual reports also do not indicate whether a reported case was a simple exposure or a poisoning. While all poisonings are exposures, not all exposures result in actual poisonings. The AAPCC defines exposures as simply having contact with a substance in some way, including ingesting, inhaling, or absorbing the substance. Poisonings are exposures that result in an adverse health reaction.¹¹ In the analyses presented in this report, we consider every incident reported in the NPDS to be an exposure to an addictive substance.

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Caffeine

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