NCC Pediatrics Continuity Clinic Curriculum
Over-The-Counter Cough & Cold Medications

Goals & Objectives

1. Be able to recite the science on the use of over-the-counter cough & cold medications in children.
2. Compare and contrast the science & FDA policy on OTC pediatric cough & cold medications.
3. Know that branding alone is not a reliable indicator of the OTC medications present in a cough & cold preparation.
4. Identify risks related to multiple ingredient products and multiple caregiver administration of OTC cough & cold medication
5. State five non-pharmacologic interventions parents can implement to provide symptom relief for cough and cold symptoms.

Pre-Meeting Preparation

- Read the 2-page "Perspective" on OTC Medications (*NEJM, 2007*)
- "Over-the-Counter Medications: Update on Cough and Cold Medications" (*PIR, 2015*)
- Bring the label of a currently available pediatric cough & cold formulation for discussion with the group (no need for purchase, search Google images)

Conference Agenda

- Review quiz on OTC cough & cold medication
- Discuss the case
- Share your OTC label

Additional Information

- Read the AAP recommendations for treating the symptoms of the common cold

- "Use of antitussive medications in acute cough in young children" *(JACEP, 2021)*

- Frequently Asked Questions On Children's Cough and Cold Medicines *(FDA)*

- "What treatments are effective for common cold in adults and children?" *(BMJ, 2018)*

- Codeine: Time to Say "No"AAP Clinical Report (2016)

- "Cough and cold medicines should not be recommended for children" *(Acta Paediatrica, 2021)*

- "Efficacy of Oral Phenylephrine as a Nasal Decongestant" *(FDA Briefing, 2023)*

Original Module Greg Gorman, update 2024, C. Carr

Perspective
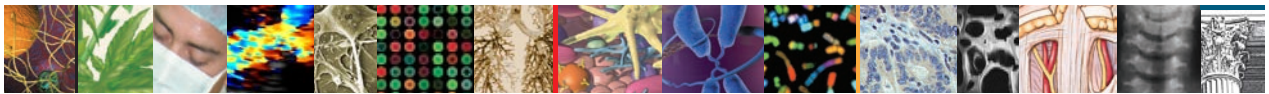
Over the Counter but No Longer under the Radar — Pediatric Cough and Cold Medications

Joshua M. Sharfstein, M.D., Marisa North, B.A., and Janet R. Serwint, M.D.

In recent weeks, over-the-counter cough and cold medications for children have received unprecedented attention from regulators, physicians, the media, and parents. This scrutiny represents a long-overdue reassessment of products that were purchased by 39% of U.S. households during the past 3 years.[1] It also reflects an important evolution in the standard of evidence for medications used in children.

Over-the-counter cough and cold preparations include various combinations of antihistamines, decongestants, antitussives, and expectorants. There is no standard for describing these products; two products marketed similarly may have different types of ingredients (see table). Consumers purchase about 95 million packages of such medication for use in children each year.[1] Within the pediatric community, however, concern over the effectiveness and safety of such drugs has been growing for more than two decades.

Since 1985, all six randomized, placebo-controlled studies of the use of cough and cold preparations in children under 12 years of age have not shown any meaningful differences between the active drugs and placebo. In 1997, the American Academy of Pediatrics noted in a policy statement on cough medications that "indications for their use in children have not been established." In 2006, the American College of Chest Physicians found that "literature regarding over-the-counter cough medications does not support the efficacy of such products in the pediatric age group."

Meanwhile, poison-control centers have reported more than 750,000 calls of concern related to cough and cold products since January 2000.[2] A recent report from the Centers for Disease Control and Prevention identified more than 1500 emergency room visits in 2004 and 2005 for children under 2 years of age who had been given cough or cold products.[3] Among other concerns are findings in children under six linking decongestants to cardiac arrhythmias and other cardiovascular events, antihistamines to hallucinations, and antitussives to depressed levels of consciousness and encephalopathy. A review by the Food and Drug Administration (FDA) identified 123 deaths related to the use of such prod-

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Ingredients and Marketing of Some of the Available Pediatric Cough and Cold Products.*		
Ingredients	**Brand Name**	**Marketed Use**
Antihistamine	Pediacare	Nighttime cough
	Triaminic	Cough and runny nose
Antitussive	Robitussin	Long-acting cough
Decongestant	Dimetapp	Decongestant
Antihistamine and antitussive	Robitussin	Long-acting cough and cold
	Tylenol Plus	Cough and runny nose
Antihistamine and decongestant	Dimetapp	Cold and allergy
	Pediacare	Nighttime multisymptom cold
	Triaminic	Nighttime cough and cold
Antitussive and decongestant	Dimetapp	Decongestant plus cough
	Pediacare	Multisymptom cold
	Triaminic	Daytime cough and cold
Decongestant and expectorant	Dimetapp	Cold and chest congestion
	Triaminic	Chest and nasal congestion
Antihistamine, antitussive, and decongestant	Dimetapp	Cold and chest congestion
	Tylenol Plus	Flu
	Tylenol Plus	Multisymptom cold
Antitussive, decongestant, and expectorant	Robitussin	Cough and cold

* The antihistamines include brompheniramine, chlorpheniramine, and diphenhydramine; the antitussive is dextromethorphan, the decongestant is phenylephrine, and the expectorant is guaifensin. All formulas of Tylenol Plus also contain acetaminophen.

pediatric over-the-counter cough and cold preparations to parents.

The fact that these medications are widely marketed and used despite the lack of evidence of efficacy can be explained in part by their regulatory history. This class of drugs was first marketed well before 1972, the year that the FDA began a comprehensive review of hundreds of over-the-counter cough and cold preparations. It obtained input from an expert advisory panel, solicited public comment on proposed rules, and prepared a monograph outlining conditions of use. In 1976, the advisory panel endorsed the use of some over-the-counter ingredients for cough or cold symptoms in adults but, in the face of "negligible or nonexistent" data on pediatric use, recommended against their marketing for children under two. For older children, it endorsed the extrapolation of doses from those recommended for adults, using a crude formula: half the adult dose for children between 6 and 11 years of age and a quarter of the adult dose for children between 2 and 5 years. Dose recommendations were calculated for children as young as 6 years for antihistamines and as young as 2 years for all other categories of cough or cold drugs. The FDA adopted these guidelines in its monograph but permitted manufacturers to market the drugs for children below these ages if labeling instructed parents to consult a doctor before use.

In the ensuing 30 years, the FDA never returned to review the effects of these preparations in young children. In March 2007, we, along with 13 other signatories, filed a petition urging the

ucts in children under six during the past several decades.[4] Serious adverse effects have been associated with accidental overdose, inadvertent misuse, and drug–drug or drug–host interactions in children given standard doses.
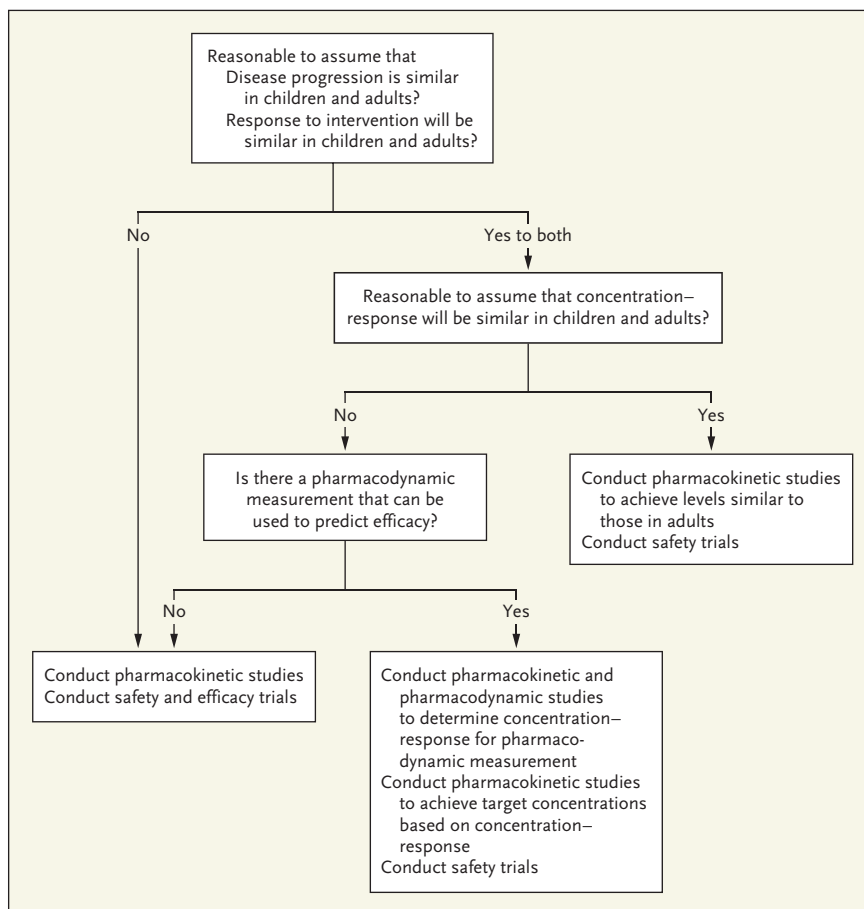
The marketing of these preparations for young children does not reflect the risks or the lack of evidence of efficacy. The Federal Trade Commission, which oversees advertising for over-the-counter products, does not have the FDA's scientific expertise for evaluating

marketing materials and does not require that advertisements show a "fair balance" between risks and benefits. Direct-to-consumer advertisements assert that preparations are safe and effective, and many state that ingredients are "pediatrician-recommended." A frequent theme is that giving children these products allows parents to relax. In fiscal year 2007, according to data provided by the Prescription Project (a policy-advocacy organization), companies spent more than $50 million marketing

FDA's Decision Tree for Determining Whether Pediatric Efficacy Studies of a Drug Are Needed.
Modified from FDA presentation, "Guidance for Industry: Exposure–Response Relationships — Study Design, Data Analysis, and Regulatory Applications," April 2003.

fects, which could not be eliminated by labeling or parent education.

More broadly, the committee debated the appropriateness of extrapolating to children data demonstrating modest efficacy in adults. Testifying for the petitioners, Wayne Snodgrass of the University of Texas Medical Branch argued against extrapolation — describing differences between adults and children in the relevant disease processes and physiology and citing recent studies, conducted as a result of the Best Pharmaceuticals for Children Act and the Pediatric Research Equity Act, that indicate that drugs approved for adult use may be ineffective, incorrectly administered, or toxic in children. Examples of prescription drugs include sumatriptan, gabapentin, and pimecrolimus. The American Academy of Pediatrics concurred, testifying that the results of pediatric drug studies "humble us on a regular basis."

The FDA presented an algorithm (see flow chart) that, in keeping with the current legal standard, permits extrapolation when there is a "similar disease progression" in children and adults and a "similar response to intervention," when it is "reasonable to assume similar concentration–response," when safety trials have been conducted, and when pharmacokinetic studies show that appropriate administration of the drug will achieve

agency to do so. We asked the FDA to issue a public statement explaining that the products have not been shown to be safe and effective for children under six, to take action against misleading marketing, and to revise its monograph accordingly. The FDA responded by convening a joint meeting of the Pediatric Committee and the Nonprescription Drug Advisory Committee on October 18 and 19, 2007. Ten days before the meeting, major manufacturers voluntarily recalled over-the-counter cough and cold preparations for children under

two and proposed adding the warning "Do not use to sedate children" to the label for antihistamines subject to the monograph.

At the meeting, there was little dispute about the lack of evidence from pediatric efficacy studies. As for safety, the manufacturers claimed that virtually all cases of serious injury or death resulted from overdose, which could be prevented through patient education. The petitioners argued that some serious adverse events have resulted from confusion and unanticipated ef-

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"levels similar to [those in] adults." Agency scientists, however, stated that pharmacokinetic data were inadequate to support extrapolation for cough and cold preparations. The manufacturers' trade association promised to conduct additional pharmacokinetic studies and said it would consider conducting efficacy studies in consultation with the FDA.

Advisory committee members expressed concern that these medications have been marketed for decades without good pediatric data, when it has long been feasible to conduct additional studies. The committee rejected the idea that pharmacokinetic data alone would be sufficient. All 22 members agreed that it was unacceptable to extrapolate data for the use of these medications in children under 2, and all but 1 member rejected extrapolation for children between 2 and 11. Instead, the group voted unanimously that pediatric clinical efficacy studies should be required. The committee voted 13 to 9 in favor of immediate action against the use of cough and cold medications in children under six.

After the meeting, the major manufacturers of these products announced that they disagreed with the committee and would continue to market these preparations for children between 2 and 5 years of age. Because the monograph is still in effect, the products and their "toddler" formu-lations are still being widely advertised to parents in ways that suggest that they are known to be safe, effective, and recommended by most pediatricians. Despite their own proposal that the use of these products for sedation be stopped, companies are

still marketing "nighttime" preparations containing sedating antihistamines. Although the FDA does not need to follow the recommendations of its advisory committees, we believe that it should immediately ask companies to remove these products from store shelves and begin legal proceedings to require them to do so. Rep. Henry A. Waxman (D-CA) and Sen. Edward Kennedy (D-MA) have recently introduced legislation to expedite this process by strengthening the FDA's oversight of the marketing and advertising of over-the-counter medications.

The agency must also respond to the broader implications of the committee's objection to extrapolating efficacy from adults to children. When it is questionable whether a drug's benefits outweigh its risks, the drug should be studied in children if at all possible. The adoption of this standard would bring benefits far beyond relief of the common cold.

Dr. Sharfstein is the commissioner of health for Baltimore; Ms. North is a medical student at the Johns Hopkins School of Medicine, Baltimore; and Dr. Serwint is a professor of pediatrics at the Johns Hopkins School of Medicine, Baltimore. The authors are the lead signers of the petition to the FDA on over-the-counter cough and cold medications.

1. Consumer Healthcare Products Association. Briefing information for the Food and Drug Administration joint meeting of the Nonprescription Drugs Advisory Committee & the Pediatric Advisory Committee. (Accessed November 14, 2007, at http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4323b1-01-CHPA.pdf.)
2. Consumer Healthcare Products Association testimony before the Food and Drug Administration (October 18, 2007). Washington, DC: American Association of Poison Control Centers, 2007.
3. Infant deaths associated with cough and cold medications — two states, 2005. MMWR Morb Mortal Wkly Rep 2007;56: 1-4.
4. Food and Drug Administration, Division of Drug Risk Evaluation. Nonprescription Drug Advisory Committee meeting: cold, cough, allergy, bronchodilator, antiasthmatic drug products for over-the-counter human use. 2007:29. memorandum. (Accessed November 14, 2007, at http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4323b1-02-FDA.pdf.)

Over-the-Counter Medications: Update on Cough and Cold Preparations

Jennifer A. Lowry, MD,* J. Steven Leeder, PharmD, PhD†

*Section of Clinical Toxicology, Division of Clinical Pharmacology, Toxicology and Therapeutic Innovations, Children's Mercy Hospital, Department of Pediatrics, University of Missouri – School of Medicine, Kansas City, MO.
†Pediatric Clinical Pharmacology, Division of Clinical Pharmacology, Toxicology and Therapeutic Innovations, Children's Mercy Hospital, Departments of Pediatrics and Pharmacology, University of Missouri-Kansas City, Kansas City, MO.

Practice Gap

Although there are benefits to the availability of over-the-counter products (eg, rapid access to effective medications, decreased utilization of the health care system, and patient autonomy), there also are risks to their use that clinicians should know and discuss with their patients and families. These include delay in seeking advice from a health care professional, increased drug-drug interactions, potential for misuse and abuse, and increased adverse effects when not used properly.

Objectives   After completing this article, readers should be able to:

1. Recognize that over-the-counter (OTC) cough and cold preparations have not been adequately studied in children younger than 6 years of age and that they are not recommended for treating the common cold.

2. Recognize the systemic effects of oral decongestants and antihistamines in infants and young children.

3. Recognize the signs and symptoms of acetaminophen and aspirin toxicity and know the management of overdose of these agents.

4. Be aware of potentially harmful additives in OTC medications.

INTRODUCTION

Over-the-counter (OTC) medications are widely marketed and frequently used to treat most health problems in adults and children. The use of symptomatic treatments, such as OTC medications for the common cold, is controversial. Children often receive analgesics, decongestants, antihistamines, expectorants, and cough suppressants during the course of their illnesses. However, these OTC products have not been proven to be safe and effective in young children. In addition, their common use puts children at risk for poisonings. Published data show no efficacy (no benefit) of OTC cough and cold preparations when compared to placebo for most ingredients in these products. After much review, the U.S. Food and Drug Administration (FDA) and the Consumer Healthcare Products

Association issued a warning against the use of OTC cough and cold products in children younger than 4 years of age. This has led to decreased unintentional ingestions reported to U.S. Poison Control Centers. Nonetheless, unintentional effects can occur, and pediatricians should understand the signs and symptoms of these adverse reactions and overdoses of medications and additives.

THE COMMON COLD

The common cold (or inflammation of the nasal passages) is a frequent manifestation of upper respiratory tract infections caused by respiratory viruses. Most of these viruses are rhinoviruses, but infection with other viruses (eg, coronavirus, respiratory syncytial virus, influenza virus, parainfluenza virus, and adenovirus) can result in similar symptoms. However, determining the virus responsible for the cold is unnecessary because a "tincture of time" results in infection resolution. Colds occur year-round, with most seen between September and May. Younger children have an average of six to eight colds annually, which decrease in number as children age and exposures to the viruses decrease. Viruses spread by aerosolization and direct contact.

The onset of symptoms usually occurs within 1 to 3 days of contact with the virus. Often, the first symptom is a sore or scratchy throat, followed by nasal congestion and rhinorrhea. By the third day of the symptoms, nasal congestion dominates. Cough may be associated with approximately 30% of common cold symptoms. Depending on the virus, fever may be present. Symptoms usually persist for 7 to 10 days; a few may last up to 2 weeks.

Management of the common cold is primarily symptomatic and supportive. Antiviral therapy is approved for respiratory syncytial virus and influenza. Antimicrobial therapy is not effective in treating viral illnesses. The use of symptomatic treatments is controversial. Efficacy may be established in adults, but this is not the case in children. However, because caregivers feel that doing something is better than doing nothing, children often receive antipyretics, analgesics, decongestants, antihistamines, expectorants, and cough suppressants during the course of the illness. For example, parents frequently treat a fever rather than focusing on a child's symptoms. Fever is a natural response to inflammation and infection but does not need to be treated unless the child appears ill. Many OTC products have not been proven to be safe and effective in young children. Further, their common use puts children at risk for poisonings because children act fast when their parents' backs are turned.

EFFICACY

Published data show no efficacy (no benefit) of OTC cough and cold preparations when compared to placebo in children for brompheniramine, diphenhydramine, chlorpheniramine, guaifenesin, clemastine, phenylephrine, codeine, phenylpropanolamine, dextromethorphan, or salbutamol (oral). (1) Only one study in children found benefit from pseudoephedrine administration, but placebo controls were not included.

A prospective randomized, double-blind, placebo-controlled trial (n=59; ages 6 months to 6 years) assessed common cold symptoms after receiving a combination product (brompheniramine and phenylephrine) at "standard" doses and placebo. (2) Using a seven-point Likert scale, patients/parents were asked to assess symptoms of runny nose, nasal congestion, cough, and sleep. No statistical difference was seen in symptoms except for higher sleep scale scores with the combination drug product. These findings are similar to other previously reported studies.

The efficacies of dextromethorphan and diphenhydramine were assessed in a single-dose night-time study (n=100; ages 2 to 16.5 years) in which patients received a fixed dose per age. (3) Using a seven-point Likert scale, no statistically significant differences were seen in symptoms assessed (cough frequency, cough severity, child or parental sleep).

A 2008 Cochrane review of 25 placebo-controlled, randomized trials assessed the efficacy of OTC products for the symptomatic treatment of cough. (4) Frequency, severity, amount of sputum, improvement in cough symptoms, patient questionnaires, and physical examination changes were assessed. Adverse effects were noted as a secondary outcome. Seven trials within the review found cough and cold medications (dextromethorphan, dextromethorphan/codeine, dextromethorphan/salbutamol, brompheniramine/phenylpropanolamine, brompheniramine/phenylephrine/propanolamine, clemastine, chlorpheniramine, and diphenhydramine) had no more efficacy than placebo. One trial of letosteine (a mucolytic) demonstrated benefit compared to placebo ($P < 0.01$). Given the unclear outcomes and limited evidence, the review concluded that there was no support for the use of OTC cough and cold medications for cough in children.

REGULATORY ACTIONS

The Durham Humphrey Amendment of 1951 authorized the FDA to classify certain drugs as available by prescription only. OTC drugs refer to "nonprescription" drugs or those that do not require a prescription. Marketing of OTC drugs is regulated by the Office of Nonprescription Products (ONP) in the Center for Drug Evaluation and Review at

the FDA., When the FDA developed a comprehensive review of OTC products, the OTC Drug Review, in 1972, an estimated 100,000 to 500,000 OTC drug products containing approximately 200 OTC active ingredients and approximately 26 OTC drug categories were being marketed.

The OTC Drug Review led to an OTC Monograph three-step rulemaking process. The first step was an Advance Notice of Proposed Rulemaking (ANPR), followed by a Tentative Final Monograph, and finally publication of the Final Monograph. The ANPR to establish a monograph for OTC cough, cold, allergy, bronchodilator, and antiasthmatic drug products along with recommendations of the advisory panel established to evaluate the products were published in the *Federal Register* of September 9, 1976 (41 FR 38312). Final rules for each type of product were published over a 10-year period between November 1985 (anticholinergics) and August 1994 (nasal decongestants). The advisory panel recommended against marketing of cough and cold preparations to children younger than 2 years of age due to negligible or nonexistent pediatric data and extrapolation of doses from adults to older children.

Final rules for antitussives, expectorants, and antihistamines were published on August 12, 1987 (52 FR 30042), February 28, 1989 (54 FR 8494), and December 9, 1992 (57 FR 58356), respectively, but the suitability of the marketed products for pediatric use was not revisited until a Citizen's Petition was filed by Joshua Sharfstein, then Commissioner of Health for Baltimore, and 15 other petitioners on March 1, 2007. Major manufacturers of OTC cough and cold products voluntarily recalled preparations for children younger than 2 years of age 10 days before a joint meeting of the Pediatric Committee and the Nonprescription Drug Advisory Committee (October 18–19, 2007) at which committee members concluded that there was no evidence that OTC medications eased cold symptoms in children younger than 12 years of age. A public hearing was held on October 2, 2008, with presentations by representatives from academia, industry, and regulatory agencies. On October 7, 2008, the Consumer Healthcare Products Association, a trade group for OTC manufacturers, announced that its members would be adding a warning against the use of OTC cough and cold products in children younger than age 4 years on product labels. This was followed the next day by a statement from the FDA supporting the industry's voluntary effort.

These changes have led to a decrease in unintentional ingestions reported to U.S. Poison Control Centers. A retrospective review of pre- and postintervention periods documented a significant decline in unintentional ingestions, therapeutic errors, health care facility referrals, and serious medical outcomes in children younger than 2 years of age. (5) Additionally, ingestions in 2- to 5-year-old children declined (Table 1).

COMMON INGREDIENTS AND FORMULATIONS

The ONP regulates the marketing of OTC medications. For products to be considered OTC, they must be regulated under a New Drug Application or the OTC drug monograph process (http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm106368. htm), which provides marketing regulations and mandates that the drug is "generally recognized as safe and effective" (GRASE). Under GRASE conditions, the product must list active ingredients, including dosage strength and form. Additional labeling requirements include the drug's indications, warnings, and directions. At times, final formulation testing is required.

The active ingredients targeted by these recommendations and labeling changes are decongestants, antitussives, expectorants, and antihistamines. Many OTC cough and cold products contain more than one of these ingredients, and similar brand names may contain varying numbers and types of active ingredients. Similarly, products with different brand names may contain the same ingredients. Common generic active ingredients are listed in Table 2.

The ideal drug should be effective, well-tolerated, stable, affordable, and (especially for children) palatable. Accordingly, in addition to active ingredients, excipients are added to OTC medications to help with formulation and palatability. These may include bulk fillers, sweeteners and flavoring agents, coloring agents, preservatives, surfactants, thickeners or suspending agents, or other miscellaneous products such as antioxidants and lubricants.

Not all excipients are inert substances; some have been shown to be potential toxicants. The Federal Food, Drug, and Cosmetic Act of 1938 was enacted after the tragedy of sulfanilamide elixir in 1937 in which an untested excipient (diethylene glycol) was responsible for the deaths of many children who consumed the pharmaceutical. The Act required manufacturers to perform safety testing of pharmaceuticals. Since that time, the FDA has become aware that certain other excipients can cause serious toxicities in OTC drug products.

Products under the OTC drug monographs (21 CFR 330.1 (e)) are required to contain "only suitable inactive ingredients which are safe in the amounts administered and do not interfere with the effectiveness of the preparation or with suitable tests or assays to determine if the product meets its professed standards of identity, strength, quality, and purity. Color additives may be used only in accordance with section 721 of the act and subchapter A." However,

TABLE 1. **Frequency of Unintentional/Therapeutic Error Ingestions of Over-the-Counter (OTC) Cough and Cold Medication (CCM) Compared With Other Pharmaceuticals**

	UNINTENTIONAL GENERAL INGESTIONS					
	2005–2006		**2009–2010**		**PERCENT CHANGE FOR OTC CCMS**	
AGE GROUP	**OTC CCMS**	**OTHER PHARMACEUTICALS**	**OTC CCMS**	**OTHER PHARMACEUTICALS**		***P***
< 2 y	15,294	295,155	9170	319,349	−40.0	< .0001
2–5 y	62,934	560,875	42,503	640,966	−32.5	< .0001
6–12 y	3100	38,873	2495	41,721	−19.5	< .0001
Total	81,328	894,903	54,168	1,002,036	−33.4	< .0001
	Therapeutic Error Ingestions					
	2005–2006		**2009–2010**		**Percent Change for OTC CCMs**	
Age Group	**OTC CCMs**	**Other Pharmaceuticals**	**OTC CCMs**	**Other Pharmaceuticals**		***P***
< 2 y	12,672	47,707	3112	53,051	−75.4	< .0001
2–5 y	21,715	49,018	11,793	57,458	−45.7	< .0001
6–12 y	9815	48,827	8958	58,087	−8.7	< .0001
Total	44,202	145,552	23,863	168,596	−46.0	< .0001

Statistically significant declines in the unintentional ingestions and therapeutic errors reported to U.S. Poison Control Centers were seen after the U.S. Food and Drug Administration changes in recommendations for use. From Mazer-Amirshahi M, et al. (5) Used with permission from Mosby, Inc.

these regulations do not account for hypersensitivity reactions to the excipients or the harm that can occur in overdoses (eg, ethanol in mouthwash).

One of the principal determinants of oral drug administration in children is the ability to actually get the drug into the body. Medications are often rejected by children because of poor taste and texture. This is a significant issue, especially when considering that taste sensation differs as a consequence of development and on an interindividual basis. Solid formulations such as tablets and capsules are not easily administered to most infants and children because of their inability to swallow them easily and safely. Finally, solid formulations limit the ability for dose titration and dosing flexibility.

With regard to dosing accuracy with oral formulations, liquids (eg, drops, solutions, syrups, suspensions, elixirs) are preferred for infants and young children. The utility of these formulations is often limited by palatability when the taste of the active ingredient(s) cannot be masked effectively. In the case of suspension formulations, improper reconstitution or resuspension before dose administration can introduce problems related to dosing accuracy. Other potential limitations of liquid drug formulations (including those that may be extemporaneously compounded by the pharmacist from drug powder or from solid dosage forms of a given drug) are related to possible problems related to drug stability, contamination

(chemical or bacterial), portability, and the need for refrigeration of some products to ensure drug stability.

Administration of liquid medications can be associated with risk if the administration device is not appropriate (eg, use of a kitchen teaspoon or dosing cup rather than a 5.0-mL dosing spoon) or the dose for the patient's age or weight is inappropriate. The low cost and convenience of oral syringes has prompted many physicians and pharmacists to dispense them with liquid medications. However, these are not available with OTC medications, and often parents rely on the dosage cup that accompanies the liquid medication, resulting in inaccurate dosing.

ADVERSE REACTIONS AND TOXICITY

Antihistamines

Diphenhydramine and other first-generation antihistamines (eg, chlorpheniramine, doxylamine, brompheniramine) antagonize histamine-induced responses at histamine-1 receptors. They are commonly used in the management of allergic disorders, motion sickness, vertigo, pruritus associated with skin disorders, and nausea as well as for sedation. They can prevent, but not reverse, histamine peripheral effects, such as urticaria, pruritus, and wheal-and-flare responses. Overdose of these medications is common.

TABLE 2. **Common Active Ingredients in Pediatric Over-the-Counter Cough and Cold Products**

ACTIVE INGREDIENT	DRUG CLASS	USUAL PEDIATRIC DOSES	ADVERSE EFFECTS AND TOXICITY
Dextromethorphan	Antitussive	2–6 y: 2.5–7.5 mg q 4–8 h 7–12 y: 5–10 mg q 4–8 h	Confusion, dysarthria, stupor, nystagmus, dystonia, coma, hallucinations, tachycardia, seizures, respiratory depression
Guaifenesin	Expectorant	> 2 y: 12 mg/kg per day divided into 6 doses 2–5 y: 50–100 mg q 4 h 6–11 y: 100–200mg Q4H	Nausea, vomiting, diarrhea, abdominal pain, nephrolithiasis
Phenylephrine hydrochloride	Decongestant	4–6 y: 2.5 mg q 4 h prn > 6–12 y: 5 mg q 4 h prn	Hypertension, angina, precordial pain, reflex severe bradycardia, peripheral vasoconstriction, arrhythmias, respiratory depression, hallucinations
Pseudoephedrine	Decongestant	< 4 y: 1 mg/kg per dose q 6 h 4–5 y: 15 mg q 4-6 h 6–12 y: 30 mg q 4-6 h	Arrhythmias, palpitations, tachycardia, bradycardia, nausea, insomnia, dizziness, psychosis, rash, urticaria
Diphenhydramine	Antihistamine	2–5 y: 6.25 mg q 4 h 6–11 y: 12.5 mg q 4 h	Hypertension, tachycardia, chest pain, confusion, constipation, diarrhea, paresthesia
Loratadine	Antihistamine	2–5 y: 5 mg > 6 y: 10 mg	Hypotension, hypertension, palpitations, tachycardia, hallucinations
Brompheniramine	Antihistamine	2–6 y: 1 mg q 4–6 h prn 7–12 y: 2–4 mg q 6–8 h prn	Palpitations, paradoxical reactions, anxiety, circulatory collapse, rash, diplopia
Chlorpheniramine maleate	Antihistamine	2–5 y: 1 mg q 4–6 h 6–11 y: 2 mg q 4–6 h	Hypotension, tachycardia, palpitations, sedations, confusion, depression, hemolytic anemia, nausea, diarrhea, constipation
Clemastine	Antihistamine	< 6 y: 0.335–0.67 mg/day divided into 2 doses 6–12 y: 0.67–1.34 mg bid	Sedation, dizziness, disturbed coordination, epigastric distress, difficult urination, hemolytic anemia, wheezing

q 4–8 h=every 4 to 8 hours, q 4 h=every 4 hours, q 6 h=every 6 hours, q 4–6 h=every 4 to 6 hours, prn=pro re nata (as needed)

The typical therapeutic dose of a sedating antihistamine may produce adverse effects in a susceptible individual and can cause delirium during topical or oral therapy. The acute toxicity of oral antihistamines is dose-dependent. Mild symptoms (somnolence, anticholinergic signs, tachycardia, nausea, vomiting) occur in 60% of patients. These are usually seen at doses less than 300 mg for diphenhydramine. Moderate symptoms (isolated and spontaneously resolving agitation, confusion, hallucinations, and electrocardiographic [ECG] disturbances) develop in 25% of patients, usually at doses between 300 and 1000 mg. Severe symptoms (delirium, psychosis, seizures, and coma) occur with larger doses (generally > 1 g ingested).

Most serum concentrations of oral antihistamines peak in 1 in 4 hours, but the peak may be prolonged in overdoses because the anticholinergic effects can decrease gastrointestinal (GI) motility and prolong the absorption phase. Antihistamines are metabolized by the liver with extensive first-pass metabolism. The half-life in therapeutic doses is 2.4 to 9.3 hours, which may be prolonged in overdoses.

Neither diagnostic tests specific to determining the ingestion of antihistamines nor specific drug measurements are readily available. Two types of urine drug screens can be used to detect the presence of antihistamines: immunoassay and gas chromatography-mass spectrometry (GC-MS). Immunoassays, which use antibodies to detect the presence of specific drugs or metabolites, are the most commonly used initial screening processes. Advantages of immunoassays include large-scale screening through automation and rapid detection. The primary disadvantage is the potential for false-positive results when detection of a drug in the same class requires a second test for confirmation. Results of immunoassays are always considered presumptive until confirmed by a laboratory-based test for the specific drug (eg, GC-MS or high-performance liquid chromatography). Tricyclic antidepressants (TCAs) are commonly found as a false-positive result on immunoassay.

Most patients experiencing antihistamine overdose only require symptomatic and supportive care. Treatment focuses on controlling agitation, maintaining the airway, reversing hyperthermia, and supporting hemodynamic function. GI

ACTIVE INGREDIENT	DRUG CLASS	USUAL PEDIATRIC DOSES	ADVERSE EFFECTS AND TOXICITY
Dextromethorphan	Antitussive	2–6 y: 2.5–7.5 mg q 4–8 h 7–12 y: 5–10 mg q 4–8 h	Confusion, dysarthria, stupor, nystagmus, dystonia, coma, hallucinations, tachycardia, seizures, respiratory depression
Guaifenesin	Expectorant	> 2 y: 12 mg/kg per day divided into 6 doses 2–5 y: 50–100 mg q 4 h 6–11 y: 100–200mg Q4H	Nausea, vomiting, diarrhea, abdominal pain, nephrolithiasis
Phenylephrine hydrochloride	Decongestant	4–6 y: 2.5 mg q 4 h prn > 6–12 y: 5 mg q 4 h prn	Hypertension, angina, precordial pain, reflex severe bradycardia, peripheral vasoconstriction, arrhythmias, respiratory depression, hallucinations
Pseudoephedrine	Decongestant	< 4 y: 1 mg/kg per dose q 6 h 4–5 y: 15 mg q 4-6 h 6–12 y: 30 mg q 4-6 h	Arrhythmias, palpitations, tachycardia, bradycardia, nausea, insomnia, dizziness, psychosis, rash, urticaria
Diphenhydramine	Antihistamine	2–5 y: 6.25 mg q 4 h 6–11 y: 12.5 mg q 4 h	Hypertension, tachycardia, chest pain, confusion, constipation, diarrhea, paresthesia
Loratadine	Antihistamine	2–5 y: 5 mg > 6 y: 10 mg	Hypotension, hypertension, palpitations, tachycardia, hallucinations
Brompheniramine	Antihistamine	2–6 y: 1 mg q 4–6 h prn 7–12 y: 2–4 mg q 6–8 h prn	Palpitations, paradoxical reactions, anxiety, circulatory collapse, rash, diplopia
Chlorpheniramine maleate	Antihistamine	2–5 y: 1 mg q 4–6 h 6–11 y: 2 mg q 4–6 h	Hypotension, tachycardia, palpitations, sedations, confusion, depression, hemolytic anemia, nausea, diarrhea, constipation
Clemastine	Antihistamine	< 6 y: 0.335–0.67 mg/day divided into 2 doses 6–12 y: 0.67–1.34 mg bid	Sedation, dizziness, disturbed coordination, epigastric distress, difficult urination, hemolytic anemia, wheezing

q 4–8 h=every 4 to 8 hours, q 4 h=every 4 hours, q 6 h=every 6 hours, q 4–6 h=every 4 to 6 hours, prn=pro re nata (as needed)

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decontamination is not essential, but if it is used, it should be undertaken within 1 to 2 hours of the ingestion. In view of the potential cardiac toxicity, observation for dysrhythmias is warranted. Agitation and hallucinations are typically treated with a benzodiazepine or antipsychotic medication. Fluids followed by vasopressors can be used to treat hypotension, but hypertension is more typical. If hypertension occurs, benzodiazepines (to control agitation) or antihypertensives may be indicated. The addition of sodium bicarbonate to the treatment may be indicated because, as with TCA overdoses, the QRS can be prolonged and place the patient at risk for serious dysrhythmias. Hemoperfusion and hemodialysis are of limited use.

Physostigmine is indicated in the presence of peripheral or central anticholinergic manifestations without evidence of significant QRS or QT prolongation. This approach is controversial because of documented adverse events with physostigmine use in patients who have ingested TCAs. In those patients, physostigmine may augment vagal effects, contributing to decreased cardiac output and conduction defects. However, in cases of pure anticholinergic overdose, physostigmine is clearly beneficial. A shorter time to recovery following agitation has been seen in patients receiving the antidote. The dose is 1 to 2 mg in adults and 0.02 mg/kg (maximum, 0.5 mg) in children administered intravenously over at least 5 minutes. The onset of action is within minutes. The dose can be repeated after 10 to 15 minutes if an adequate response is not achieved and muscarinic (eg, salivation, lacrimation, vomiting, sweating) effects are not noted. The onset of action is up to 1 hour and repeat doses may be needed. However, care must be exercised to avoid cholinergic symptoms.

Nonsedating Antihistamines

Nonsedating (second-generation) antihistamines (eg, loratadine, desloratadine, cetirizine) are long-acting selective histamine-1-receptor antagonists used in the treatment of allergic rhinitis. Somnolence, tachycardia, and headache have been reported in adult overdoses (range, 40 to 180 mg). Sinus tachycardia (150 beats/min) and respiratory alkalosis were reported in an adult following an ingestion of 300 mg, but the patient recovered completely. Extrapyramidal signs and palpitations have been reported in children following doses of greater than 10 mg. A 6-year-old child who ingested 300 mg of loratadine developed mild elevations in heart rate and blood pressure with no permanent sequelae. Sinus tachycardia has been reported in overdoses with minimal hemodynamic instability. Dysrhythmias are a rare event.

The time to peak concentration is approximately 2 hours following a single dose of the once-daily and twice-daily combination tablet formulation. Loratadine is 97% protein bound; cetirizine has minimal protein binding. Cetirizine is minimally metabolized, and loratadine is extensively metabolized in the liver. Evidence suggests that loratadine is preferentially metabolized by the cytochrome P450 isoenzyme CYP3A4 to its active metabolite. It can also be metabolized by CYP2D6 in the presence of inhibitors of CYP3A4. Desloratadine is rapidly metabolized via hydroxylation. Mean elimination half-life in normal adults for most second-generation antihistamines is 8 hours (range, 3–20 hours). The mean elimination half-life of desloratadine is 27 hours.

Treatment of overdoses is symptomatic and supportive. Significant toxicity has not been reported in patients ingesting second-generation antihistamines. There is no known antidote for these agents. Tachycardia has been reported in overdose but does not usually require intervention unless hemodynamic compromise is present. The heart rate should be monitored, and a baseline ECG may be indicated and repeated as necessary. Continuous cardiac monitoring should be instituted as needed. No routine laboratory studies are necessary, unless otherwise clinically indicated. Neurologic status also should be monitored because limited reports suggest that somnolence may develop following overdose.

Decongestants

Children experience an average of six to eight colds per year that may result in significant congestion. Parents and physicians often use decongestants (oral or topical) to help alleviate the symptoms. Because these treatments are available without a prescription, they are commonly used. Previous studies have shown that the use of decongestants in children can result in significant adverse reactions. A recent Cochrane Review failed to find any trials that proved efficacy for their use in children. Accordingly, they should not be used routinely in children.

Phenylephrine. Phenylephrine is the primary decongestant used in oral OTC products in the United States. It is a sympathomimetic agent, differing from epinephrine only in lacking a hydroxyl group in the 4 position on the benzene ring. It is a powerful postsynaptic alpha-receptor stimulant with little effect on beta-receptors in the heart. Peripheral resistance increases considerably due to constriction of most vascular beds, and both systolic and diastolic blood pressures increase. Phenylephrine is used orally as a decongestant even though evidence of its effectiveness in reducing nasal congestion is inconclusive.

Phenylephrine has 38% oral bioavailability. It is extensively metabolized in the intestinal wall and liver after oral dosing. It is renally excreted, with 2.6% eliminated as the parent compound in the urine after 48 hours. The elimination half-life is 2 to 3 hours in most patients.

With mild-to-moderate overdoses, most patients experience tachycardia, hypertension, mydriasis, insomnia, headache, and agitation. Large overdoses and severe toxicity may cause seizures, hallucinations, agitated delirium, and tachydysrhythmias, including supraventricular tachycardia and ventricular tachycardia. Vasospasm can lead to myocardial ischemia or focal cerebrovascular deficits. Severe hypertension may also result in intracranial hemorrhage or renal insufficiency. Reflex bradycardia due to significant hypertension is possible. Prolonged agitation can lead to rhabdomyolysis and hyperthermia.

Treatment is largely symptomatic and supportive. A 12-lead ECG should be obtained in all symptomatic patients. Patients with moderate-to-severe toxicity should be admitted until symptoms improve. Those with mild tachycardia, hypertension, and agitation can be treated with benzodiazepines and observed until symptoms and vital signs normalize.

Oral Decongestants of the Past. In 2000, the FDA requested a voluntary recall of phenylpropanolamine (PPA) from all manufacturers and issued a public health warning about the increased risk for hemorrhagic stroke associated with its use, particularly among women. In a case-control study, the adjusted odds ratio was 1.49 for an association between hemorrhagic stroke and PPA use within 3 days in all patients. The adjusted odds ratio increased to 1.98 in women. A similar study found an adjusted odds ratio of 16.58 (95% confidence interval 1.51 to 182.21) in women. (6) Case reports have documented similar clinical findings in children ingesting PPA overdoses.

Although pseudoephedrine is considered a safe and effective oral nasal decongestant, its use as a precursor in the manufacturing of methamphetamine has resulted in legislation to restrict its availability (2005 Combat Methamphetamine Epidemic Act). Epidemiologic data have shown that pseudoephedrine exposures in children are common, especially among those younger than 2 years of age. Because most pseudoephedrine products are in combination products, many of the exposures resulted from taking more than one combination product or use for extended periods of time. Pseudoephedrine has sympathomimetic properties, and clinical effects and toxicity are expected to be similar to those seen with phenylephrine.

Topical Decongestants. Imidazoline topical decongestants are commonly used in adults for the immediate and temporary treatment of nasal congestion. However, they are not approved by the FDA for use in children younger than age 6 years. Topical imidazolines are found in many OTC eye and nose decongestants. Products with imidazoline components are numerous and include: tetrahydrozoline, naphazoline, oxymetazoline, and xylometazoline. Imidazolines have central and peripheral alpha-2 agonist activity. However, unlike other alpha-2 agonists, they are designed to stimulate peripheral alpha-2 receptors on local vessels to achieve the intended clinical effect of vasoconstriction. Both topical and oral imidazolines have a rapid onset of action that is often prolonged.

Use of topical imidazolines in infants and inappropriate use in children and adults has had important consequences. Administration of intranasal tetrahydrozoline, especially in larger-than-recommended doses in adults and children, may cause drowsiness, hypertension, bradycardia, rebound hypotension, and possibly arrhythmias due to coronary vasoconstriction. Rebound congestion frequently occurs with prolonged use of these solutions and may prompt overuse of the drug. Unfortunately, exposures are not specific to topical applications, and significant morbidity (hypotension and bradycardia) and mortality has resulted from tetrahydrozoline ingestions in young children that necessitated intensive care management.

Antitussives/Expectorants

Cough is a normal response to irritation (eg, mechanical, chemical, or inflammatory) to the tracheobronchial tree mediated by neural reflexes from the brainstem. Cough can be the result of many process, including infection, asthma, foreign body, or other inflammatory processes. However, because of the symptomatology and the interference with daily life, children are often given cough suppressants that may adversely affect their health. Dextromethorphan and codeine are often chosen as OTC agents for their cough suppression properties, but their efficacy has not been established in children. In fact, use of these medications may be harmful in overdoses. In addition, both medications are commonly used as drugs of abuse.

Dextromethorphan. Dextromethorphan is an antitussive agent commonly used in OTC cough and cold preparations. It is the D-isomer of the codeine analog of levorphanol but has little analgesic or addictive properties. However, it does act on the cough center in the medulla oblongata by elevating the threshold for coughing. In usual doses, the drug can cause pupillary dilation but without significant reduction of respiratory rate. Dextromethorphan may cause slight elevations in blood pressure. After ingestion, the initial response occurs within 15 to 30 minutes, with an duration of effect of 5 to 6 hours. The time to peak concentration is 2 to 2.5 hours.

Dextromethorphan undergoes extensive hepatic oxidative biotransformation via cytochrome P450 2D6 (CYP2D6). The *CYP2D6* gene locus is highly polymorphic, with more than 70 allelic variants (and additional subvariants) identified. The proteins encoded by these alleles may have full, reduced, or no function, conveying a wide range of activity from none to ultrarapid metabolism. In patients who are genetically deficient in CYP2D6 activity, clearance of dextromethorphan is reduced 150-fold and can result in symptoms of toxicity.

Ingestion of less than 10 mg/kg of dextromethorphan is unlikely to produce toxicity in a child. Overdose may result in symptoms from the parent compound and active metabolites. Central nervous system (CNS) effects are most prevalent and include stupor, ataxia, nystagmus, hyperexcitability, dystonia, coma, toxic psychosis, and changes in muscle reflexes. Among other effects are respiratory depression, tachycardia, increased baseline seizure activity, and nausea and vomiting. Anecdotal reports suggest that the CNS and respiratory depressant effects of dextromethorphan can be reversed. Otherwise, treatment is symptomatic and supportive. Agitation and seizures may be treated with benzodiazepines.

Codeine. Codeine is an opiate receptor agonist that binds to the mu receptor. It is commonly used as an analgesic, with a mechanism that is speculated to stem from its conversion by CYP2D6 to morphine. In prodrugs like codeine, however, increased formation of pharmacologically active metabolites may lead to an increased incidence of adverse effects or, in extreme cases, overt toxicity. In addition, the antitussive effects of codeine may result from direct depression of the cough reflex in the medulla. In adults, studies have shown a linear relationship between codeine dose and the decrease in frequency of chronic cough. The dosing in these studies ranged from 7.5 to 60 mg/day. However, even at the highest dose, complete cough suppression was not achieved. Although codeine is a scheduled drug in all states, it has been present in OTC cough suppressants in the past. However, the available concentrations were very low, resulting in much lower efficacy.

Studies assessing the pharmacokinetic properties of codeine in children are lacking. Published recommendations suggest a dose of 1 mg/kg per day in four divided doses (not to exceed 60 mg/day), but no studies have confirmed the safety and efficacy of this dose. Codeine is absorbed within the GI tract and food has no effect on its absorption. It undergoes metabolism in the liver by CYP2D6, CYP3A4, and glucuronidation. The active metabolite of codeine is morphine, which is a product of the CYP2D6 pathway. As mentioned previously, CYP2D6 is polymorphic, which can lead to problems with codeine efficacy and safety if patients are poor metabolizers or ultrarapid metabolizers , respectively. The elimination half-life is approximately 3 hours.

Adverse reactions can occur at therapeutic doses and overdoses, depending on the pharmacogenetics. The most common adverse effects at therapeutic doses are dizziness, somnolence, nausea, and vomiting. In mild-to-moderate overdoses, euphoria, drowsiness, constipation, bradycardia, hypotension, and miosis may occur. Severe overdoses can result in respiratory depression leading to apnea, hypoxia, worsening bradycardia, and coma. Treatment is symptomatic and supportive, but the toxicity is generally responsive to naloxone unless the

codeine is ingested with other CNS depressants. Naloxone is an opioid antagonist that may be administered intravascularly, intramuscularly, subcutaneously, intranasally, or endotracheally. In children, the usual dose is 0.4 to 2 mg. In adolescents and adults, care must be exercised when administering naloxone because its use may precipitate withdrawal symptoms if the patients being treated are chronic users of opiates. A continuous infusion of naloxone can be considered if frequent boluses are required to maintain mental status and airway.

Guaifenesin. Guaifenesin is commonly used alone or in combination products as an expectorant. It is believed to act by irritating the gastric mucosa, resulting in stimulation of respiratory tract secretions. However, a recently conducted clinical trial failed to show measurable effect on sputum volume or viscosity, suggesting that the drug is unlikely to be an efficacious expectorant or mucolytic when used to treat acute respiratory tract infections.

Guaifenesin is generally well absorbed. It is hydrolyzed in the blood to an inactive metabolite, beta-2-methoxyphenoxylactic acid. The elimination half-life of the parent drug is approximately 1 hour.

The most common adverse effects are nausea, vomiting, and GI discomfort. Excessive doses of guaifenesin have resulted in renal stones containing the metabolite. This has usually occurred in patients who have intentionally ingested combination products with the purpose of using them as drugs of abuse.

Analgesics/Antipyretics

Many OTC cough and cold preparations are combination products that include an analgesic/antipyretic such as acetaminophen, ibuprofen, or aspirin. Parents may fail to recognize the individual medications in these products and choose to supplement cough and cold preparations with stand-alone antipyretics. This places children at great risk for toxicity. Clinicians should educate parents on the risks associated with combined products. **Acetaminophen.** An acute acetaminophen (APAP) overdose in children younger than 6 years of age occurs when more than 200 mg/kg is ingested in one period or if more than 200 mg/kg or 10 g (whichever is less) is ingested in children older than 6 years of age. Absorption is generally complete within 4 hours, and the Rumack-Matthew nomogram (Figure) may be used to assess the need for treatment. The nomogram is conservative because it is overly sensitive and lacks specificity to allow a safety net. Plasma concentrations of greater than 150 mcg/mL at 4 hours postingestion are considered "possibly toxic."

Clinical manifestations of APAP toxicity occur in three stages. Typical early signs and symptoms within the first 24 hours are anorexia, nausea, vomiting, malaise, pallor, and sweating. Hepatotoxicity has not yet occurred, so the patient

may be asymptomatic and laboratory test results should be normal. The ==next 24 hours reveal the onset of liver injury, and other organ system effects may occur, most commonly approximately 24 hours after ingestion but nearly universally by 36 hours.== Aspartate aminotransferase abnormalities are the most sensitive, occurring before evidence of actual liver dysfunction. GI distress, tenderness of the right upper quadrant of the abdomen, worsening of liver function laboratory results, worsening of coagulopathy, and possible renal effects occur due to hepatotoxicity. The ==third phase occurs 3 to 5 days after ingestion when liver enzymes usually peak. Signs and symptoms vary with severity of injury, ranging from asymptomatic to fulminant hepatic failure with encephalopathy, coma, and hemorrhage.== Aspartate aminotransferase/alanine aminotransferase commonly measure more than 10,000 U/L (167 μkat/L) and may continue to rise until 7 to 8 days after ingestion. Fatalities generally occur between days 3 and 5, typically due to multiorgan failure, with hemorrhage, acute respiratory distress syndrome, sepsis, and cerebral edema, but if the patient survives the acute stage, hepatic failure may not occur for 8 to 10 days. Notably, a decrease in liver enzymes after 7 to 8 days may indicate hepatic cellular death rather than improvement. Thus, it is imperative to examine liver function (eg, bilirubin, glucose, bleeding time) concurrently with the falling enzyme concentrations.

Up to 90% of acetaminophen normally undergoes hepatic glucuronide and sulfate conjugation to form active, harmless metabolites that are eliminated in urine. Approximately 5% to 15% is oxidized by the CYP2E1 pathway of the P450 mixed-function oxidase system, resulting in the formation of a highly reactive electrophile, N-acetyl-p-benzoquinoneimine (NAPQI). Toxicity is the result of glutathione depletion and formation of the NAPQI metabolite that instantly binds to cysteine-containing cellular macromolecules, especially in the liver
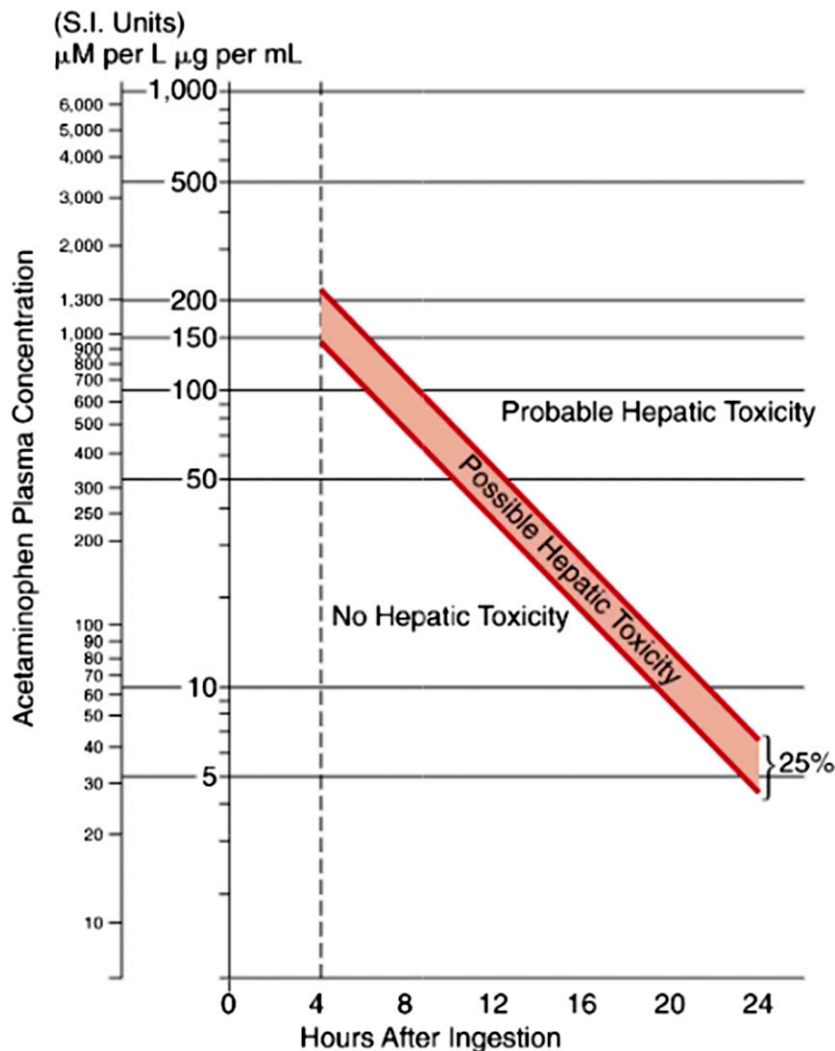

Figure. ==The Rumack-Matthew nomogram== for acetaminophen poisoning is a semilogarithmic plot of plasma acetaminophen concentrations versus time. Cautions for the use of this chart: The time coordinates refer to time after ingestion, serum concentrations obtained before 4 hours are not interpretable, and the graph should be used only in relation to a single acute ingestion with a known time of ingestion. The nomogram is not useful for chronic exposures or unknown time of ingestion and should be used with caution in the setting of coingestants that slow gastrointestinal motility. The lower solid line is typically used in the United States to define toxicity and direct treatment; the upper line is generally used in Europe. From Rumack BH, Hess AJ, eds. Poisindex, Denver, 1995, Micromedix. Adapted from Rumack BH, Matthew H. Acetaminophen poisoning and toxicity. *Pediatrics* 1975;55:871–876. Used with permission from Elsevier, Inc.

and kidneys. This covalent binding causes hepatocellular damage that can lead to necrosis and fulminant liver failure. In as many as 46% of cases with significant hepatic enzyme elevation, clinically evident renal injury may also occur. Renal P450 formation of NAPQI is the likely cause of acute proximal renal tubular necrosis after acute overdose. Cases of significant toxicity after a single acute overdose generally involve doses greater than 250 mg/kg or 15 g.

Patients either recover or develop fulminant hepatic failure, which may require liver transplantation. All survivors have 100% regeneration of the liver with no toxic sequelae. Abnormal laboratory values may resolve within days to weeks. Renal failure is reversible. Bleeding time and other coagulopathies should not be abnormal without significant hepatotoxicity. This is an important point because N-acetylcysteine (NAC) (especially intravenous NAC and the loading dose) may cause prolonged prothrombin time, which is not significant in nontoxic cases.

NAC is a glutathione precursor and aids in the conversion of NAPQI to a nontoxic metabolite. It is available in oral and intravenous form. No clear difference has been shown between oral and intravenous NAC when the antidote is administered within 10 hours. NAC should be administered intravenously to patients with vomiting or to those whose condition precludes enteral use. NAC therapy initiated within 8 to 10 hours of ingestion has almost a 100% (94%–97%) chance of preventing toxicity. Treatment after 10 hours is associated with lessening chances of preventing toxicity (eg, 64%–70% within 10–16 hours and 42%–59% within 16–24 hours). Treatment after 24 hours may not help the liver but may aid other organs such as lungs, brain, and kidneys. Young children recover better than adults. Patients with glutathione deficiency due to illness or poor diet or chronic alcoholics do worse and are especially susceptible to hepatotoxicity. Prognostic indicators of severe toxicity include an arterial pH less than 7.3, encephalopathy, prothrombin time greater than 100 seconds, and serum creatinine greater than 2.3 mg/dL (203.3 μmol/L). Delay in treatment time is also a significant risk factor for children.

Nonsteroidal Anti-inflammatory Drugs. Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used for fever and pain control. These include the combined COX-1/COX-2 inhibitors (eg, ibuprofen, naproxen, ketorolac) and selective COX-2 inhibitors (eg, celecoxib, piroxicam). OTC NSAIDs include ibuprofen and naproxen. The toxicity is primarily the result of COX-1 and COX-2 inhibition and the resultant diminished prostaglandin synthesis. There may be a direct mucosal effect as well.

There are no established lethal doses, but overall NSAID toxicity is low. Toxicity is dose-related. Children ingesting less than 200 mg/kg ibuprofen generally are asymptomatic or have mild effects. Ingestions of 400 mg/kg in children have been associated with severe toxicity. In adults, 3 g has been reported to cause mild CNS depression. Renal injury has been reported with ingestions of more than 6 g.

Depending on the amount ingested, a patient may present with effects ranging from no symptoms to CNS depression with severe metabolic acidosis. The risk of major toxicity increases with dose. CNS effects are relatively common and include changes in mood and cognition, seizures, headaches, and hallucinations. Acute renal insufficiency is rare and usually reversible after acute ingestions.

No specific diagnostic tests establish the diagnosis of NSAID exposure or toxicity. Baseline laboratory studies should include a complete blood cell count, coagulation studies that include an international normalized ratio, serum electrolytes, glucose, blood urea nitrogen, creatinine, urinalysis, liver function tests, and ECG as clinically appropriate. Asymptomatic children who have accidentally ingested more than 400 mg/kg may merit a baseline assessment of electrolytes, blood urea nitrogen, and creatinine.

Treatment is symptomatic and supportive; there is no antidote. Intravenous fluids may be necessary if the patient is volume-depleted. GI ulcers are usually not problematic in the acute overdose, and medications to address them are generally not necessary.

Aspirin. Salicylates are absorbed variably from the GI tract and absorption is largely dose-dependent (and prolonged in overdoses). They are distributed widely through the body and may be seen in increased concentrations in the CNS in toxic ingestions. They are metabolized in the liver by esterases and conjugation and undergo Michaelis-Menton elimination. As the salicylate concentration increases after an overdose, pathways for elimination become saturable and change from first-order elimination to zero-order elimination. Thus, with higher concentrations, the half-life is markedly increased. In addition, elimination is strongly dependent on urinary pH.

The mechanism of action for salicylate toxicity is uncoupling oxidative phosphorylation resulting in increased oxygen consumption and carbon dioxide production. The agent also inhibits the Kreb cycle dehydrogenases, leading to decreased production of adenosine triphosphate and increased lactate production. Ultimately, ketosis and a wide anion gap metabolic acidosis occur. Stimulation of the CNS respiratory center in the medulla leads to hyperventilation and respiratory alkalosis. Although many associate metabolic acidosis with salicylate poisoning, respiratory alkalosis predominates initially. In children, the respiratory alkalosis may be transient, and metabolic acidosis becomes significant very early in the course. Other potential effects include

hypoglycemia, pulmonary edema, hypoprothrombinemia, platelet dysfunction, GI effects, cerebral edema, and tinnitus. Lethargy, agitation, and confusion may be early findings in patients with severe toxicity, with coma and seizures possibly developing subsequently. Cerebral edema and evidence of increased intracranial pressure (papilledema, nuchal rigidity) may develop in severe cases. Cerebral edema was present on autopsy in 9 of 13 children who died after acute and chronic salicylate intoxication.

Except in certain situations, salicylate toxicity correlates poorly with serum levels. The Done nomogram is not effective in predicting toxicity and should not be used to guide treatment. Careful observation of the patient, correlation of the serum salicylate values with blood pH values, and repeat evaluation of serum salicylate concentrations every 2 to 4 hours are essential until the patient is clinically improving and has a low salicylate value in the presence of a normal or high blood pH. A concurrent blood pH should be determined when a blood salicylate is obtained because more salicylic acid leaves the blood in the presence of acidemia and enters the CSF and other tissues, increasing the toxicity. Therefore, meaningful interpretation of serum salicylate levels must take into account the effect of the blood pH on salicylate distribution. A falling serum salicylate value accompanied by a falling or low blood pH should be presumed to reflect a serious or worsening situation, not a benign or improving one.

Treatment is largely symptomatic and supportive. Laboratory studies should be obtained at least every 4 hours and include a salicylate concentration, electrolytes, glucose, and blood gas until the salicylate value is consistently falling and acid/base abnormalities are improving. Complete blood cell count and coagulopathy studies should be monitored routinely in patients with moderate-to-severe effects. Patients undergoing alkalinization may require large amounts of potassium supplementation due to renal wasting. Alkalinization is recommended to "ion trap" the salicylate ion in the kidneys and increase its elimination rather than having it reabsorbed into the body. Alkalinization can be achieved using a 1- to 2-mEq/kg bolus of sodium bicarbonate followed by maintenance fluids, with the addition of sodium bicarbonate to keep the urine pH at 7 to 8.

Activated charcoal is usually reserved for presentations within 1 hour of the ingestion, but certain circumstances may require its use later. Some medications undergo hepatic recirculation (eg, dapsone, theophylline, phenobarbital, carbamazepine, quinine); others, such as valproic acid and aspirin, may benefit from later use of charcoal. This is especially true when concentrations are rising from a presumed bezoar.

Hemodialysis is recommended for patients with high serum salicylate values (> 80 mg/dL after acute overdose, 50 to 60 mg/dL with chronic intoxication), refractory acidosis, inability to maintain appropriate respiratory alkalosis, acidemia, evidence of CNS toxicity (seizures, mental status depression, persistent confusion, coma, cerebral edema), progressive clinical deterioration despite appropriate fluid therapy and attempted urinary alkalinization, acute lung injury, inability to tolerate sodium bicarbonate (eg, renal insufficiency, pulmonary edema), refractory/profound electrolyte disturbances, or renal failure. The patient's clinical condition is more important than the serum salicylate concentration in determining the need for hemodialysis, especially in patients with chronic toxicity or delayed presentation after acute overdose. For those presenting early after acute overdose, serum concentrations approaching 100 mg/dL warrant consideration for dialysis, even with mild or moderate clinical manifestations of toxicity.

ADMINISTRATION AND ABSORPTION: THE ROLE OF EXCIPIENTS

Excipients (or additives) are used to increase the ease of administration and absorption of medications. For children, the oral administration route is preferable. Although solid forms of dosing are preferable to parents, younger children are unable to swallow tablets. Liquid preparations are easier to adjust for dosing per bodyweight. However, even after completion of a clinical trial, efficacy cannot be achieved if the child refuses to take a medication, which is why excipients (or additives) are used.

As mentioned previously, products must contain only inactive ingredients that are safe in the amounts administered and do not interfere with the clinical effectiveness. Common additives include ethanol, artificial colors, artificial sweeteners, minerals, and other agents to help with solubility and taste. OTC products that contain the inactive ingredients alcohol, calcium, magnesium, potassium, sodium, and FD&C Yellow #6 require special warning statements. In addition, alcohol must be expressed as a percent absolute alcohol per volume of product (%v/v) and be declared on the label in quantity, type, and proportion.

Ethanol

In 2012, the FDA reissued a final rule limiting the concentration limit for alcohol as an inactive ingredient in OTC products intended for ingestion. These included 0.5% alcohol for children younger than 6 years, 5% alcohol for children 6 to 12 years, and 10% for those older than 12 years. Other inactive ingredients must be listed to ensure that consumers can avoid those that may result in adverse reactions. Ethanol may also be found in other OTC products,

hypoglycemia, pulmonary edema, hypoprothrombinemia, platelet dysfunction, GI effects, cerebral edema, and tinnitus. Lethargy, agitation, and confusion may be early findings in patients with severe toxicity, with coma and seizures possibly developing subsequently. Cerebral edema and evidence of increased intracranial pressure (papilledema, nuchal rigidity) may develop in severe cases. Cerebral edema was present on autopsy in 9 of 13 children who died after acute and chronic salicylate intoxication.

Except in certain situations, salicylate toxicity correlates poorly with serum levels. The Done nomogram is not effective in predicting toxicity and should not be used to guide treatment. Careful observation of the patient, correlation of the serum salicylate values with blood pH values, and repeat evaluation of serum salicylate concentrations every 2 to 4 hours are essential until the patient is clinically improving and has a low salicylate value in the presence of a normal or high blood pH. A concurrent blood pH should be determined when a blood salicylate is obtained because more salicylic acid leaves the blood in the presence of acidemia and enters the CSF and other tissues, increasing the toxicity. Therefore, meaningful interpretation of serum salicylate levels must take into account the effect of the blood pH on salicylate distribution. A falling serum salicylate value accompanied by a falling or low blood pH should be presumed to reflect a serious or worsening situation, not a benign or improving one.

Treatment is largely symptomatic and supportive. Laboratory studies should be obtained at least every 4 hours and include a salicylate concentration, electrolytes, glucose, and blood gas until the salicylate value is consistently falling and acid/base abnormalities are improving. Complete blood cell count and coagulopathy studies should be monitored routinely in patients with moderate-to-severe effects. Patients undergoing alkalinization may require large amounts of potassium supplementation due to renal wasting. Alkalinization is recommended to "ion trap" the salicylate ion in the kidneys and increase its elimination rather than having it reabsorbed into the body. Alkalinization can be achieved using a 1- to 2-mEq/kg bolus of sodium bicarbonate followed by maintenance fluids, with the addition of sodium bicarbonate to keep the urine pH at 7 to 8.

Activated charcoal is usually reserved for presentations within 1 hour of the ingestion, but certain circumstances may require its use later. Some medications undergo hepatic recirculation (eg, dapsone, theophylline, phenobarbital, carbamazepine, quinine); others, such as valproic acid and aspirin, may benefit from later use of charcoal. This is especially true when concentrations are rising from a presumed bezoar.

Hemodialysis is recommended for patients with high serum salicylate values (> 80 mg/dL after acute overdose, 50 to 60 mg/dL with chronic intoxication), refractory acidosis, inability to maintain appropriate respiratory alkalosis, acidemia, evidence of CNS toxicity (seizures, mental status depression, persistent confusion, coma, cerebral edema), progressive clinical deterioration despite appropriate fluid therapy and attempted urinary alkalinization, acute lung injury, inability to tolerate sodium bicarbonate (eg, renal insufficiency, pulmonary edema), refractory/profound electrolyte disturbances, or renal failure. The patient's clinical condition is more important than the serum salicylate concentration in determining the need for hemodialysis, especially in patients with chronic toxicity or delayed presentation after acute overdose. For those presenting early after acute overdose, serum concentrations approaching 100 mg/dL warrant consideration for dialysis, even with mild or moderate clinical manifestations of toxicity.

ADMINISTRATION AND ABSORPTION: THE ROLE OF EXCIPIENTS

Excipients (or additives) are used to increase the ease of administration and absorption of medications. For children, the oral administration route is preferable. Although solid forms of dosing are preferable to parents, younger children are unable to swallow tablets. Liquid preparations are easier to adjust for dosing per bodyweight. However, even after completion of a clinical trial, efficacy cannot be achieved if the child refuses to take a medication, which is why excipients (or additives) are used.

As mentioned previously, products must contain only inactive ingredients that are safe in the amounts administered and do not interfere with the clinical effectiveness. Common additives include ethanol, artificial colors, artificial sweeteners, minerals, and other agents to help with solubility and taste. OTC products that contain the inactive ingredients alcohol, calcium, magnesium, potassium, sodium, and FD&C Yellow #6 require special warning statements. In addition, alcohol must be expressed as a percent absolute alcohol per volume of product (%v/v) and be declared on the label in quantity, type, and proportion.

Ethanol

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including perfumes, colognes, mouthwash, food flavorings, and hand sanitizers.

Ethanol is rapidly and almost completely (80%–90%) absorbed from the stomach and small intestine. Its peak plasma level occurs between 30 minutes and 2 hours after ingestion but may be prolonged in large overdoses. Metabolism occurs in the liver via alcohol dehydrogenase to acetaldehyde and then to acetic acid. Rather than following first-order kinetics (concentration per unit time), it follows Michaelis-Menten kinetics that involves zero-order kinetics (amount per unit time) at high concentrations. An average adult decreases ethanol by 15 to 20 mg/dL per hour. Children may metabolize ethanol more rapidly.

Mild-to-moderate toxicity can result in intoxication, ataxia, altered mental status, nausea, vomiting, and tachycardia. These symptoms may be difficult to discern, and ethanol can be the cause if taken in overdose with an OTC medication such as a cough syrup containing dextromethorphan. Large overdoses of ethanol are rare if the only source is the OTC medication, but such overdoses may result in coma, respiratory depression, hypoglycemia, and hypothermia. Children are more prone to the hypoglycemic effects due to decreased glucose reserves.

Treatment is largely symptomatic and supportive. Obtaining an ethanol value can help discern the cause of the altered sensorium if the source is an OTC product. A bedside glucose assessment should be obtained in all children and in symptomatic adolescents. Serum chemistries should be monitored. Decontamination with activated charcoal is not effective. Depending on the degree of CNS depression, patients may need airway assistance or intubation. When nausea, vomiting, or hypoglycemia is present, fluid replacement with glucose supplementation may be necessary.

Calcium

Although small amounts of calcium offer no therapeutic value, even nontherapeutic doses can change the bioavailability of drugs. Calcium salts are contraindicated in some medical conditions, such as nephrocalcinosis and metabolic conditions (eg, hypercalcemia from milk-alkali syndrome) because even small amounts can change the physiologic nature of a disease.

Sodium and Potassium

Similar to calcium, small amounts of these metals should have no clinical significance except in rare cases. Hypernatremia, hypokalemia, or systemic alkalosis has occurred with sodium or potassium bicarbonates at large therapeutic doses.

Artificial Colors and Sweeteners

Artificial colors and sweeteners are used as additives in foods, beverages, and medications for added palatability. Since 1950, the number of artificial food colors that the FDA has certified has increased more than fivefold. In addition, studies in the last few decades have found a dose association with the use of artificial colors and behavioral reactions such as hyperactivity. (7)

Summary

- Based on strong research evidence, over-the-counter (OTC) medications are used frequently to treat most health problems in adults and children, especially with cough and cold symptoms. (1,4) (Evidence Quality A)

- Based on research evidence as well as consensus from the U.S. Food and Drug Administration, the potential for misuse and abuse and increased adverse effects when not used properly has resulted in changes to recommended ages and dosing of OTC medications when used in children. (6)(8)(9) (Evidence Quality B)

- Adverse reactions to OTC medications are not uncommon in the pediatric age group, but observational studies using poison control center data show that the recommended changes have resulted in decreased reactions and risk to children. (5) (Evidence Quality C)

- Despite these findings, consistent evidence suggests that unintentional effects can occur, and pediatricians should understand the signs and symptoms of these adverse reactions and overdoses to medications and additives for appropriate diagnosis and treatment. (7)(8) (Evidence Quality B)

References for this article are at http://pedsinreview.aappublications.org/content/36/7/286.full.

Parent Resources from the AAP at HealthyChildren.org

- https://www.healthychildren.org/English/safety-prevention/at-home/medication-safety/Pages/Using-Over-the-Counter-Medicines-With-Your-Child.aspx

- Spanish: https://www.healthychildren.org/spanish/safety-prevention/at-home/medication-safety/Paginas/Using-Over-the-Counter-Medicines-With-Your-Child.aspx

Children's Robitussin®

AGES 6 & OVER

Drug Facts

Active ingredients (in each 10 ml) **Purposes**
Chlorpheniramine maleate, USP 2 mg .... Antihistamine
Dextromethorphan HBr, USP 15 mg .... Cough suppressant

Uses
- temporarily relieves cough due to minor throat and bronchial irritation as may occur with a cold
- temporarily relieves these symptoms due to hay fever or other upper respiratory allergies:
  - runny nose
  - sneezing
  - itchy, watery eyes
  - itching of the nose or throat

Warnings
Do not use
- to sedate a child or to make a child sleepy
- if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product.

Ask a doctor before use if you have
- trouble urinating due to an enlarged prostate gland
- glaucoma
- a cough that occurs with too much phlegm (mucus)
- a breathing problem or chronic cough that lasts or as occurs with smoking, asthma, chronic bronchitis or emphysema

Ask a doctor or pharmacist before use if you are taking sedatives or tranquilizers

When using this product
- do not use more than directed
- marked drowsiness may occur
- avoid alcoholic drinks
- alcohol, sedatives, and tranquilizers may increase drowsiness
- be careful when driving a motor vehicle or operating machinery
- excitability may occur, especially in children

Drug Facts (continued)

Stop use and ask a doctor if cough lasts more than 7 days, comes back, or is accompanied by fever, rash, or persistent headache. These could be signs of a serious condition.
If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- measure only with dosing cup provided
- keep dosing cup with product
- ml = milliliter
- do not take more than 4 doses in any 24-hour period

age	dose
children under 6 years	do not use
children 6 to under 12 years	10 ml every 6 hours
adults and children 12 years and older	20 ml every 6 hours

Other information
- each 10 ml contains: sodium 6 mg
- store at 20-25°C (68-77°F)

Inactive ingredients anhydrous citric acid, artificial & natural flavors, FD&C red no. 40, glycerin, lactic acid, propylene glycol, purified water, sodium benzoate, sodium citrate, sorbitol solution, sucralose

Questions or comments? Call weekdays from 9 AM to 5 PM EST at 1-800-762-4675

Use dosage cup included

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For most recent product information, visit www.robitussin.com

FPO

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NDC 63824-OTC-64

Children's Mucinex·

Multi-Symptom Cold
Expectorant
Cough Suppressant
Nasal Decongestant

Guaifenesin 100 mg
Dextromethorphan HBr 5 mg
Phenylephrine HCl 2.5 mg

✓ Stuffy Nose
✓ Cough
✓ Chest Congestion
✓ Breaks up Mucus

Very Berry
Flavor Liquid

Drug Facts

Active ingredients (in each 5 mL)	**Purpose**
Dextromethorphan HBr 5 mg	Cough suppressant
Guaifenesin 100 mg	Expectorant
Phenylephrine HCl 2.5 mg	Nasal decongestant

Uses
- helps loosen phlegm (mucus) and thin bronchial secretions to rid the bronchial passageways of bothersome mucus and make coughs more productive
- temporarily relieves:
  - cough due to minor throat and bronchial irritation as may occur with the common cold or inhaled irritants
  - the intensity of coughing
  - the impulse to cough to help your child get to sleep
  - nasal congestion due to a cold
  - stuffy nose

Warnings
Do not use in a child who is taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your child's prescription drug contains an MAOI, ask a doctor or pharmacist before giving this product.

Ask a doctor before use if the child has
- heart disease
- high blood pressure
- thyroid disease
- diabetes
- cough that occurs with too much phlegm (mucus)
- persistent or chronic cough such as occurs with asthma

When using this product
- do not use more than directed

Stop use and ask a doctor if
- your child gets nervous, dizzy or sleepless
- symptoms do not get better within 7 days or occur with fever
- cough lasts more than 7 days, comes back, or occurs with fever, rash, or persistent headache. These could be signs of a serious illness.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Directions
- do not take more than 6 doses in any 24-hour period
- measure only with dosing cup provided
- do not use dosing cup with other products
- dose as follows or as directed by a doctor
- mL = milliliter

Age	Dose
children 6 years to under 12 years	10 mL every 4 hours
children 4 years to under 6 years	5 mL every 4 hours
children under 4 years	do not use

Drug Facts

Active ingredients (in each 5 mL, 1 teaspoonful)	**Purposes**
Diphenhydramine HCl 6.25 mg	Antihistamine/cough suppressant
Phenylephrine HCl 2.5 mg	Nasal decongestant

Uses
- temporarily relieves
  - sneezing
  - itchy nose or throat
  - runny nose
  - itchy, watery eyes due to hay fever
  - nasal and sinus congestion
  - cough due to minor throat and bronchial irritation as may occur with a cold

Warnings
Do not use
- in a child under 4 years of age
- in a child who is taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if the child's prescription drug contains an MAOI, ask a doctor or pharmacist before giving this product.
- with any other product containing diphenhydramine, even one used on skin
- for the purpose of making your child sleepy

Ask a doctor before use if the child has
- heart disease
- high blood pressure
- thyroid disease
- diabetes
- glaucoma
- cough that occurs with too much phlegm (mucus)
- chronic cough that lasts, or as occurs with asthma
- a breathing problem such as chronic bronchitis

Ask a doctor or pharmacist before use if the child is taking sedatives or tranquilizers

When using this product
- do not exceed recommended dosage
- marked drowsiness may occur
- sedatives and tranquilizers may increase drowsiness
- excitability may occur, especially in children

Stop use and ask a doctor if
- nervousness, dizziness or sleeplessness occurs
- symptoms do not improve within 7 days or occur with a fever
- cough persists for more than 7 days, comes back or occurs with a fever, rash or persistent headache. These could be signs of a serious condition.

Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

Drug Facts (continued)

Directions
- may be given every 4 hours. Do not give more than 6 doses in 24 hours unless directed by a doctor.

Age	Dose
children under 4 years of age	do not use
children 4 to under 6 years of age	do not use unless directed by a doctor
children 6 to under 12 years of age	2 teaspoonfuls (10 mL)

Other information
- each teaspoonful contains: sodium 6 mg
- store at controlled room temperature 20-25°C (68-77°F)

Inactive ingredients acesulfame K, benzoic acid, citric acid, edetate disodium, FD&C blue #1, FD&C red #40, flavors, maltitol solution, propylene glycol, purified water, sodium citrate

Questions or comments?
call 1-800-452-0051 24 hours a day, 7 days a week

Triaminic® Has More Ways to Help Kids Feel Better!

Great Tasting Liquids
- Free Dosage Cup (enclosed)
- Alcohol-Free

Fast-Dissolving Softchews®
- Great Taste

Convenient Thin Strips®
- Melts in an Instant
- Easy to Give/Easy to Take
- No Mess Dosing

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NDC 0067-6344-04
See New Directions and Warnings Information

Children's Triaminic® Syrup

Night Time Cold & Cough

Diphenhydramine HCl (Antihistamine/Cough Suppressant),
Phenylephrine HCl (Nasal Decongestant)

★ Cough Relief
★ Runny, Stuffy Nose
★ Itchy Throat

Grape FLAVOR

4 FL OZ (118 mL)

Text your Program Director if you know who said "The only way to treat the common cold is with contempt."

Quick Quiz – Do it in 5 minutes

Match the OTC cough & cold medications with their characteristics

Brompheniramine _____

Guaifenesin   _____

Phenylephrine   _____

Diphenhydramine _____

Dextromethorphan _____

Chlorpheniramine _____

A. Expectorant

B. Decongestant

C. Antihistamine

D. Cough-suppressant

E. CNS stimulant when used alone; added CNS-depressant effects with anti-histamines

F. Sympathomimetic on a and beta adrenergic receptors

G. Centrally active opioid derivative

H. Linked to hallucinations in kids < 6 years old

I. Linked to CNS depression in kids < 6 years old

J. Linked to arrhythmias in kids < 6 years old

K. Acts centrally in the medulla to suppress cough

L. Reduces surface tension & viscosity of mucus

Fill in the Blank

New OTC anti-histamine labeling specifically advises that _____ is not an indication.

The OTC cough & cold medication _____ is the one linked to the most infant deaths.

What are risk factors for adverse effects of OTC cough & cold medication use in children?

Misleading marketing / Multiple ingredient products / Multiple caregivers giving medication

NCC Pediatrics Continuity Clinic Curriculum
Over-The-Counter Cough & Cold Medications

Case

You receive an urgent T-Con that Mr. and Ms. Nash need to speak with you immediately about their 12 month old son Ogden who has a terrible cold. You quickly call back and gather a history from a faculty-member who will play the part of the parent.

What physical exam maneuvers can you accomplish over the phone to help triage this patient?

The parent divulges that Ogden received one dose of Triaminic, one dose of Mucinex, and also some Zarbee's and Hyland's..

What specific medications did Ogden receive when his parent gave him Mucinex and Triaminic? Why do you think the Nash parents used the OTC medications?

How would you triage this patient?

The next morning, Ogden is your 0900 appointment. On exam, he is clinging to his father and has loud noisy breathing with no stridor or wheezing. His weight is higher than his 9 month appointment weight and on the same percentile. His respiratory rate is 21, heart rate 98, temperature 99.7 ° F, and O_2 saturation is 98% on room air. Sclera white with dried mucus in her medial canthi. No nasal flaring. Nose has moist yellow mucus in each nose, TMs are mobile and without effusion. Moist mucous membranes; no oral lesions. Heart is RR with a normal S1 and S2. Lungs have equal air movement throughout with transmitted upper airway sounds. No retractions. Cap refill is normal and skin turgor is normal with warm extremities. No rash.

What are useful cough & cold interventions that are safe to use? Ask the experienced pediatricians to recite their instructions to parents of young children with colds.

"A family is a unit composed not only of children but of men, women, an occasional animal, and the common cold"
--Ogden Nash (1902-1971)American writer of humorous poetry who won a large following for his audacious verse. 1902-1971