Cough and Cold Treatments for Children:

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Despite the plethora of over-the-counter cough and cold medications designed to relieve a variety of symptoms of the common cold—primarily nasal congestion, rhinorrhea, and cough—no treatment has been shown to have any beneficial effect in children, and some may carry a substantial risk of adverse effects. Even routine symptomatic therapies such as antipyretics and humidified air may be counterproductive. Parental education is the best medicine. Parents need to understand the duration and expected symptoms of the common cold. Advise them about specific changes in symptoms (eg, rapid or labored breathing) or duration (eg, a cold lasting 10 days or more without improvement) that would warrant a re-evaluation by their child’s physician. Parents also need to be educated about the lack of proven efficacy and the potential adverse effects of available cold remedies. Saline nose drops and adequate fluids as well as antipyretics for bothersome fever may provide limited symptomatic relief, but time is still the only known cure.

Parents of young children know that colds are extremely common, especially from fall until spring. Colds account for a large number of pediatric office visits and telephone calls—particularly during "cold season." Children with rhinorrhea, cough, and fever may feel miserable. Their parents often lose sleep and time from work and want to do something to help their children get better faster. Cough and cold preparations are often seen as a likely solution. Surveys have shown that over 50% of preschoolers who had cough and cold symptoms in the previous month had been treated with 1 or more over-the-counter (OTC) cough and cold medicines.1 Unfortunately, there is little evidence that these OTC preparations have therapeutic benefit in children with colds.2 Because colds are self-limited and the symptoms are largely subjective, any treatment has the potential for a substantial placebo effect. Just because a child recovered from a previous cold after taking an OTC preparation does not prove that the drug was helpful. Many parents nevertheless remain convinced that these medications helped their child. These parents may have felt surprised and saddened recently when the Consumer Healthcare Products Association—which represents the leading makers of OTC cough and cold medicines—announced a voluntary withdrawal of such products for infants and toddlers younger than 2 years.3 This withdrawal was based on the findings of a recent FDA review that identified significant concerns about the safety of cough/cold medications in young children. OTC cough/cold medications and antihistamines are in the "top 10" for exposures reported to US poison control centers in children younger than 6 years. During 2004-2005, for example, an estimated 1519 children younger than 2 years were treated in US emergency departments for adverse events, including overdoses, associated with these medications.4 Several deaths have been attributed to toxicity of cough and cold medications, especially in children under 2 years.5,6 Last fall, federal health officials recommended that the "consult your physician" advice to parents on the labels of cold and cough medicines intended for young children be replaced by a warning not to use the medications in children under 2 years unless directed to do so by a health care provider. The panel further recommended that these medications not be used in children younger than 6 years.7 On January 17, 2008, the FDA issued its final recommendations in a public health advisory, noting that because such medications have not been shown to be safe or effective, they should not be used in children under 2 years of age.8 The FDA is continuing to review the available data for the use of cough and cold medications in children aged 2 to 11 years.

The American Academy of Pediatrics (AAP) has long held that OTC cough preparations are not indicated for use in children and supports changes in the FDA labeling requirements for children’s cough and cold preparations. Such support is based on the fact that no discernible benefits can be shown for children and that misdosing of these preparations is frequent. The potential for incorrect dosing is exacerbated by the fact that there are many multi-ingredient products available that may...
lead to confusion and unintended dosing errors by parents. In addition, children under 2 years are apparently more sensitive to the potentially fatal effects of some of these ingredients. Here we summarize the evidence about the potential benefits (or lack thereof) and possible adverse effects of various cough/cold preparations (including decongestants, antihistamines, antitussives, expectorants, and zinc) and ancillary therapies (eg, antipyretic/analgesics, herbal preparations, ipratropium, bulb suction, saline drops, and antibiotics).

OTC COUGH/COLD PREPARATIONS

The discomfort produced by the symptoms of the common cold has led to the development of over 800 OTC cough and cold medications in the United States designed to relieve a variety of symptoms—primarily nasal congestion, rhinorrhea, and cough. Antihistamines, decongestants, antitussives, expectorants, herbal remedies, and analgesics or combinations of these products are marketed in many forms. Unfortunately, little scientific evidence supports the efficacy of these products for treating cold symptoms in children. This may be because there is truly no benefit, or it may be because the benefits to be measured are largely subjective and cannot be accurately reported by children, especially those younger than 6 years. Viral colds are self-limited and the symptoms are so subjective that there is the potential for a significant placebo effect in treatment studies. Adequate blinding of patient/parent and physician is critical to eliminate the placebo effect and effectively evaluate cold therapies for children. No antiviral agents effective in treating the common cold are presently available.

Decongestants. Systemic sympathomimetic decongestants, including pseudoephedrine, phenylpropanolamine, and phenylephrine, are often used to treat nasal congestion. These agents cause vasoconstriction that persists for several hours. Pseudoephedrine and phenylpropanolamine are well-absorbed from the GI tract, but phenylephrine undergoes extensive biotransformation, which causes variable bioavailability after oral administration. Adverse effects may include tachycardia, irritability, sleeplessness, hypertension, headaches, nausea, vomiting, dysrhythmias, seizures, and dystonic reactions. Hypertensive crises can result in patients who receive monoamine oxidase inhibitor therapy.

Phenylpropanolamine has been associated with intracranial hemorrhage and stroke, leading the FDA to issue a public health advisory removing phenylpropanolamine from OTC medications in 2000. Because pseudoephedrine can be used illegally in the manufacture of methamphetamine, the availability of pseudoephedrine-containing products has been severely limited by federal law since 2005. Pseudoephedrine may be purchased in limited quantities from behind the counter only on presentation of a photo identification, with a log kept of all transactions. Both pseudoephedrine and phenylpropanolamine have been shown to be effective in adults in reducing symptoms of the common cold—including nasal congestion and sneezing—although many patients experience side effects. No studies document similar benefits in children. One study of a decongestant/antihistamine combination (phenylpropanolamine/brompheniramine) in children found no improvement in rhinorrhea, nasal congestion, or cough for those treated when compared with placebo.9

Topical decongestants, such as oxymetazoline, appear effective in reducing nasal congestion in adults, but their use is limited by the development of significant rebound congestion when the medication is discontinued after several days' use ("rhinitis medicamentosa"). Because infants are preferential nose breathers, this rebound may cause obstructive apnea. The use of topical phenylephrine during an upper respiratory tract infection (URI) did not decrease nasal obstruction and did not alter middle ear pressures significantly in a study of children 6 to 18 months of age.10 Other topical decongestants have not been studied in children.

Antihistamines. Antihistamines are commonly used to treat symptoms of the common cold, although research has clearly shown that histamine levels do not increase during the common cold and that histamine is not the chemical mediator responsible for cold symptoms. However, mean kinin levels do increase as cold symptoms increase in severity and are the mediators responsible for these symptoms. First-generation antihistamines— including triprolidine, diphenhydramine, hydroxyzine, and chlorpheniramine—are well known to affect the CNS. Adverse effects may include sedation, paradoxical excitability, dizziness, respiratory depression, and hallucination. GI and cardiovascular side effects, including tachycardia, heart block, and arrhythmias, may also occur. First-generation
antihistamines are anticholinergic and may reduce secretions and cause dry mouth, blurred vision, and urinary retention. Overdose may cause severe CNS effects, including coma, seizures, dystonia, or psychosis.

Second-generation antihistamines include terfenadine, astemizole, loratadine, and cetirizine. CNS side effects, especially sedation, are less common with these medications than with the first-generation antihistamines. Anticholinergic effects are not seen, but serious CNS or cardiovascular impairment may result from overdose.

Studies in adults suggest that first-generation antihistamines provide modest symptomatic relief. One study of chlorpheniramine in adults showed a 35% to 40% reduction in symptoms, with significantly less sneezing and higher mucociliary clearance rates, but no improvement in objective measures of nasal congestion or eustachian tube dysfunction. Patients treated with chlorpheniramine in another study reported significantly fewer objective signs of a cold and significant improvement in symptoms compared with those treated with placebo. Similarly, a multicenter placebo-controlled trial showed that chlorpheniramine decreased nasal discharge, sneezing, nose-blowing, and the duration of symptoms of the common cold in adults. It may be that the anticholinergic effects of first-generation antihistamines resulted in decreased nasal secretions and apparent benefit.

There are few well-designed studies of antihistamine use in children. In children, a randomized, double-blind, placebo-controlled trial of an antihistamine/decongestant combination (brompheniramine and phenylpropanolamine) showed no improvement in symptoms (cough, rhinorrhea, nasal congestion) in the treated group. However, half of the treated children were asleep 2 hours after treatment, and more than half of the children were better 2 days later regardless of treatment group. In another study, the incidence of acute otitis media in children with URIs did not decrease with the use of an antihistamine and decongestant combination.

**Antitussives.** Although the cough reflex is beneficial (clearing excessive secretions and maintaining airway patency), cough is a major concern of parents. A significant worsening of the patient's respiratory status from inspissation of mucous plugs may result from cough suppression and may be particularly harmful in patients with asthma, pertussis, or cystic fibrosis.

Narcotic cough syrups containing codeine or hydrocodone are thought to act centrally at the cough center in the brain stem. Even narcotic cough suppressants cannot completely suppress cough in adults. Common side effects include nausea, vomiting, constipation, dizziness, and palpitations. Respiratory depression may also occur and is directly related to the dose administered; apnea and death may result. Infants are particularly sensitive to these effects and may be at greater risk for apnea. This may result from the fact that codeine is conjugated in the liver and these pathways may not be fully developed in infants—especially in those younger than 6 months. Nalaxone can be used to reverse respiratory depression.

Dextromethorphan, a narcotic analog, has been shown to be as effective as codeine for cough suppression in adults. When used in appropriate doses, dextromethorphan has few CNS effects, but overdose can cause respiratory depression. One study reported no difference among placebo, dextromethorphan, and codeine in children aged 18 months to 12 years with cough; also, cough improved after 3 days in all children regardless of treatment group. A recent study found that when compared with placebo, neither dextromethorphan nor diphenhydramine had any significant effect on cough frequency, sleep quality, cough severity, or bothersome nature of cough in children with cold symptoms. Because there are no well-controlled studies documenting the efficacy of narcotics or dextromethorphan to treat cough in children and because serious adverse effects may result, the AAP currently recommends that pediatricians educate parents and patients about the lack of proven efficacy and the risk of adverse effects of these products.

A recent study examined the effect on a single dose of honey given at bedtime to children with cough and URIs. The effects of the honey were compared with those of either honey-flavored dextromethorphan or with no treatment. In pairwise statistical comparisons, the honey was no better than the dextromethorphan, and the dextromethorphan was no better than no treatment, but the honey was better than no treatment for reducing cough frequency and for decreasing a combined symptom score. The sample size was relatively small, however, and there are concerns about inadequate blinding and placebo effects.

Honey may represent an alternative treatment for cough that is generally safe, well tolerated, and perhaps effective, but more evidence of efficacy will be necessary before its use can be recommended. Honey is not recommended for use in children younger than 12 months.

**Expectorants.** Agents such as guaifenesin are a common ingredient in cough/cold preparations. Guaifenesin is supposed to help thin secretions, but a controlled study showed no decrease in the
volume or quality of sputum.\textsuperscript{19} When used in young adults with natural colds, patients did report a subjective decrease in sputum quantity and thickness; unfortunately, however, treatment with guaifenesin did not change cough frequency.\textsuperscript{20} Many cough and cold preparations contain both a cough suppressant and an expectorant. If both perform as advertised, the patient may have thinned secretions that he or she is unable to remove from the airway.

**Zinc.** In some studies with adults, treatment with zinc gluconate significantly decreased the duration of cold symptoms. The exact mechanism of action is unclear. In vitro, zinc inhibits rhinovirus replication and may combine with the rhinovirus to coat proteins in such a way as to prevent viral entry into the host cell.\textsuperscript{21} Treatment seems most effective if begun within 24 hours of onset and requires dosing 5 or 6 times per day. Many patients find the zinc lozenges difficult to tolerate. A similar study in children 6 to 16 years old demonstrated no benefit of zinc therapy and frequent side effects, including bad taste, nausea, irritation of the oropharynx, and diarrhea.\textsuperscript{22}

**Analgesics/antipyretics.** Aspirin and acetaminophen are commonly used to treat the fever and discomforts of the common cold. Unfortunately, studies in adults suggest that both aspirin and acetaminophen are associated with increased nasal symptoms and suppression of the host's neutralizing antibody response. Also, treatment with aspirin has been associated with increased shedding of rhinovirus.\textsuperscript{23,24}

**Herbal therapies.** Many herbal therapies, including echinacea, are marketed for relief of cold symptoms. A recent meta-analysis found that echinacea treatment decreased the likelihood of developing a cold and also reduced the duration of a cold.\textsuperscript{25} Unfortunately, such a meta-analysis is prone to publication bias, because studies that found no benefit are much less likely to be published and included in the meta-analysis. A recent well-controlled evaluation of echinacea in the prevention and treatment of experimental rhinovirus infections found no clinically significant effects on the rate of infection or severity of symptoms.\textsuperscript{26} No known benefits of such treatments have been demonstrated conclusively in randomized controlled trials. Herbal therapies are not approved by the FDA and do not undergo FDA review before marketing. In addition, there are no official standards of quality for purity of the preparations, labeling, toxicity information, and drug interaction information. There is only limited post-marketing surveillance for adverse reactions.

**Humidified air.** Adult studies abroad suggested that inhalation of steam improved nasal obstruction for up to a week following treatment and postulated that the heated humidified air inhibited rhinovirus replication, leading to symptomatic improvement. Unfortunately, studies in this country failed to show any benefit from inhaled steam; instead, the result was an increased duration of symptoms and increased nasal resistance in patients treated with steam inhalation.\textsuperscript{27} Furthermore, viral shedding of experimental rhinovirus infection is not affected by steam inhalation treatments.\textsuperscript{28} Vapor burns are a potential adverse effect of such treatment. Menthol vapor is often added to inhalation treatments to relieve nasal congestion. Objective evaluation of nasal resistance using rhinometry before and after menthol inhalation shows no consistent effect on nasal resistance, but many patients report subjective improvement in nasal airflow. The use of menthol topically may cause chemical irritation or burns and, if ingested in excess, menthol may cause nausea, vomiting, ataxia, and coma.

**Ipratropium.** This anticholinergic nasal spray effectively decreases the nasal discharge and sneezing of the common cold. It is licensed for use in children 5 years and older, but its usefulness is limited by bothersome side effects, including excessive dryness of the nose and throat, nosebleeds, and headache.

**Bulb suction/saline drops.** Bulb suction remains a mainstay of therapy for infants with cold symptoms. Saline nose drops used to humidify and loosen nasal mucus may improve the effectiveness of suctioning as a kind of reverse nose blowing. OTC saline drops are available, but parents can make their own supply at home less expensively by mixing 1/4 tsp of salt in 1 cup of water.

**Antibiotics.** Because of the viral etiology of the common cold, antibiotics have no beneficial effect on the clinical course. Antibiotics may be useful for the treatment of secondary infections, such as acute otitis media and sinusitis that may sometimes accompany or follow a cold. Furthermore, antibiotics have limited effectiveness in preventing acute otitis media among children who are otitisprone and who are treated at the onset of new cold symptoms. Antibiotics are not effective for children with uncomplicated colds. Also, indiscriminate use of antibiotics can promote the development of antibiotic-resistant bacteria.
PREVENTIVE MEASURES

Because therapeutic measures have such limited effectiveness, are there any preventive measures that can be recommended?

- **Breast-feeding.** Breast-fed children tend to have fewer colds than children who are bottle-fed. This constitutes yet another reason to recommend breast-feeding to all mothers.

- **Hand washing.** Theoretically, frequent hand washing can reduce the transmission of colds. Even physicians are often poor hand washers, so the practical value of suggesting frequent hand washing for young children is extremely limited.

- **Virucidal nasal tissues and hand lotions.** Virucidal nasal tissues are effective in the laboratory in blocking the passage of rhinovirus from one side to the other. In controlled studies among adults with rhinovirus colds, they prevent viral hand contamination during nose-blowing and subsequent spread to others via hand contamination. Unfortunately, virucidal tissues have not been shown effective in preventing transmission of colds in the real-world family setting. The usefulness of virucidal hand lotions in preventing the hand transmission of colds remains under investigation.

- **Influenza vaccinations.** Immunization is moderately effective in preventing influenza, and vaccines against respiratory syncytial virus (RSV) are in development. But with more than 100 serotypes of rhinoviruses, vaccines will not soon be available to protect against this most frequent causative agent. A humanized monoclonal antibody against RSV has limited efficacy in preventing RSV infections among extremely high-risk infants (ie, extremely premature infants with bronchopulmonary dysplasia), but the high cost makes this approach totally impractical for more general use.

**Recommendations**

Despite the desires of patients, parents, and physicians, there is currently no effective pharmacological treatment of the common cold in children. Nothing-decongestants, antihistamines, cough suppressants, expectorants, zinc, or herbal remedies—has been shown to have any beneficial effect in children and many may carry a substantial risk of side effects. Even routine symptomatic therapies such as antipyretics and humidified air may be counterproductive.

The best medicine is education. Parents need to understand the duration and expected symptoms of the common cold, and to know what specific changes in symptoms (eg, rapid or labored breathing) or duration (eg, a cold lasting 10 days or more without improvement) would warrant a re-evaluation by their child's physician. Parents also need to be educated about the lack of proven efficacy and the potential side effects of available cold remedies. Saline nose drops, adequate fluids, and use of antipyretics for bothersome fever may provide limited symptomatic relief—but time is still the only known cure.

**References:**

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