EDUCATIONAL OBJECTIVES

Goal: To provide pharmacists with an overview of management options for the most common causes of cough in outpatient settings.

After participating in this activity, pharmacists will be able to:

- Describe the major etiologies of cough in adult and pediatric primary care settings.
- Summarize the pharmacology of commonly prescribed medications for cough symptoms.
- Describe the place in therapy of medications commonly prescribed for cough symptoms for both adult and pediatric patients.
- Discuss essentials of pharmacist triage for the patient with cough.

Abstract

Cough is the most common presenting symptom encountered in the ambulatory care setting. It can range from mild to severe, adversely affecting quality of life. Assessment of the underlying cause(s) of the cough should be the first step of the treatment plan, as cough is not a medical condition in itself but rather a symptom of an underlying condition or disease process. Various cough medications are popular with both healthcare providers and patients but their efficacy in various conditions is questionable and safety concerns exist. This article provides an overview of the most common causes of cough and a review of commonly prescribed antitussives and expectorants. This article also summarizes pertinent aspects of the 2006 American College of Chest Physicians guideline for the management of cough as they apply to primary care settings.

MTM essentials for cough management

Devra K. Dang, PharmD, BCPS, CDE, FNAP
ASSOCIATE CLINICAL PROFESSOR, UNIVERSITY OF CONNECTICUT SCHOOL OF PHARMACY, STORRS, CONN.

Faculty: Devra K. Dang, PharmD, BCPS, CDE, FNAP
Dr. Dang is an associate clinical professor at the University of Connecticut School of Pharmacy, Storrs, Conn.

Disclosure of Discussions of Off-Label and Investigational Uses of Drugs: This activity may contain discussion of unlabeled/unapproved use of drugs in the United States and will be noted if it occurs. The content and views presented in this educational program are those of the faculty and do not necessarily represent those of Drug Topics or University of Connecticut School of Pharmacy. Please refer to the official information for each product for discussion of approved indications, contraindications, and warnings.
Cough is the most common presenting symptom in primary care.1-3 The duration and severity of cough range from self-limiting and mild to chronic and severe. Given the common nature of cough as a presenting symptom, the complexity of diagnosis and treatment is sometimes underappreciated by healthcare professionals, leading to suboptimal management. A number of guidelines from various countries exist, including the comprehensive, evidence-based “Diagnosis and Management of Cough” from the American College of Chest Physicians (ACCP) in the United States, hereafter referred to as the ACCP guideline.4 This guideline was published in 2006 and included 36 sections. The guideline was in the process of being updated at the time of writing. The information provided in this article is from the 2006 version.

Cough is a protective mechanism to clear the airway of inhaled or aspirated irritants and sputum. The cough reflex arc consists of an afferent sensory limb (consisting of the vagus, trigeminal, and glossopharyngeal nerves) in the respiratory tract, the cough center in the medulla of the brainstem, and an efferent limb innervating not just the larynx and tracheobronchial tree but also the intercostal, diaphragm, abdominal, and pelvic muscles.5 The cough receptors in the afferent limb are sensitive to a wide variety of mechanical, chemical, inflammatory, and immunological stimuli.5 Cough can also be voluntarily suppressed, indicating that areas outside the brainstem, such as the cortex, are also involved.5

The most common causes of chronic cough in immunocompetent patients who are not smokers or taking ACE inhibitors are upper airway cough syndrome, asthma, nonasthmatic eosinophilic bronchitis, and GERD.

Overview of common causes and treatment of cough in adults
Upper airway cough syndrome
UACS, called postnasal drip syndrome before the publication of the 2006 ACCP guideline, is caused by increased sensitivity and inflammation of the airway after a URI. This postinfectious cough is caused by increased sensitivity and inflammation of the airway after a URI.9

Coughing can also be voluntarily suppressed, indicating that areas outside the brainstem, such as the cortex, are also involved.5

This series kicked off in April and May with MTM essentials for asthma management—Part 1 and Part 2. In June and July, the focus shifts to MTM essentials for chronic obstructive pulmonary disease (COPD) management. The August CE activity is a primer on inhalers and nebulizers. In September, pharmacists have the opportunity to learn about allergic rhinitis management. In October, the CE activity covers MTM essentials for cold, flu, and sinusitis management. The November CE activity includes drug-induced pulmonary disease recognition and management and idiopathic pulmonary fibrosis. The series concludes in December with a focus on MTM essentials for cough management.

The series also offers application-based and practice-based activities in 2016.
guideline, is the most common cause of chronic cough. Patients may report feeling postnasal drainage, a tickle in the throat, and/or nasal congestion or rhinorrhea. Interestingly, some patients with UACS do not subjectively feel the postnasal drip and therefore do not report this during the history and evaluation. There is no objective test to determine whether the postnasal drip is the cause of the cough.

UACS can be caused by a number of rhinosinus conditions, including bacterial and fungal sinusitis, allergic and nonallergic rhinitis, and rhinitis medicamentosa. If the cause is known, therapy should be directed toward treating the underlying cause (e.g., allergen avoidance and antihistamine or intranasal corticosteroid for allergic rhinitis). Empiric therapy with a first-generation antihistamine-decongestant combination can be quite effective, and the patient’s response to therapy can confirm the diagnosis of UACS.

**Asthma**

This is the second most common cause of chronic cough in adults, as well as a common cause of cough in children. All patients with asthma experience cough as a symptom at some point, and cough is the only presenting symptom in a subset of asthma patients (cough-variant asthma). The ACCP guideline recommends that cough in an asthmatic patient be treated with standard therapy for asthma, including inhaled corticosteroids and bronchodilators. In patients with cough that is refractory to these medications, a leukotriene receptor antagonist may be added before proceeding to (short-term) oral corticosteroid therapy.

**Nonasthmatic eosinophilic bronchitis**

NAEB is distinguished from asthma in that it is not associated with bronchial hyperresponsiveness or with abnormal spirometry. It is diagnosed by the presence of eosinophils in the sputum, after other common causes of chronic cough have been ruled out, and may be due to an inhaled allergen or irritant. Avoidance of these allergens/irritants is the best treatment; inhaled corticosteroid therapy to treat the chronic cough can also be used. Oral corticosteroid therapy may be needed if the cough persists with high-dose inhaled corticosteroid treatment.

**Gastroesophageal reflux disease**

The proposed mechanisms of GERD-induced cough are aspiration of esophageal content into the lower respiratory tract and direct acid reflux into the lower esophagus, stimulating vagus nerve-mediated cough reflex. The diagnosis of GERD-induced cough in adults is typically made after the other causes of chronic cough (smoking, ACE inhibitor use, UACS, asthma, and NAEB) have been ruled out. Some patients do not experience the typical GERD gastrointestinal symptoms and only experience chronic cough (silent GERD). The ACCP guideline recommends that patients with chronic cough due to GERD be treated with dietary and lifestyle modification and acid suppression therapy. An adequate time period (one to three months) should be given before therapy is reassessed, as it may take two to three months to see improvement in the cough in some patients.

**Common cold**

This is the most common etiology of cough in the general population, and a large variety of over-the-counter (OTC) products designated for the management of cough and cold exist. Many patients self-treat with an OTC product containing guaifenesin, dextromethorphan, or a combination of the two, but neither drug has demonstrated efficacy in this clinical scenario. A 2014 Cochrane systematic review of OTC medications for acute cough in children and adults in community settings concluded that “there is no good evidence for or against the effectiveness of OTC medicines in acute cough.” The authors stated that “this lack of evidence of effectiveness also has implications for regulatory bodies and brings into question how these products can continue to be promoted using language that implies that their effectiveness is not in doubt.”

It has been postulated that the cough associated with the common cold is most likely due to postnasal drip, and so the ACCP guideline recommends treatment with a combination of a first-generation antihistamine and a decongestant (pseudoephedrine). This combination decreased cough, cough severity, throat clearing, and postnasal drip in patients with uncomplicated common cold in a double-blind, placebo-controlled study. The mechanisms of first-generation antihistamines in the treatment of cough due to the common cold are not completely understood, but their anticholinergic (decreased nasal mucus secretion) and sedative effects are potential contributors. They may also decrease nerve transmission relating to the control of cough in the central nervous system.

---

**Pause & Ponder**

What are the most popular cough products prescribed/taken at your practice setting, and are these products used according to the recommendations made in the ACCP cough guideline?
mines are not effective for cough due to the common cold.\textsuperscript{15,16}

The ACCP guideline additionally noted that, based on a randomized, double-blind, placebo-controlled study, naproxen can also be used to treat cough due to the common cold. The proposed mechanism for this nonsteroidal anti-inflammatory drug is that inflammation due to a viral URI can lead to increased sensitivity of the afferent limb of the cough reflex arc.\textsuperscript{16}

 Despite the publication of the comprehensive ACCP cough guideline in 2006, the popularity of cough products containing dextromethorphan, guaifenesin, and codeine for treatment of the self-limiting cough associated with a viral URI among both patients and healthcare professionals remains high approximately 10 years later. Many patients report symptomatic relief with these products, despite several randomized, controlled clinical trials that demonstrated no greater efficacy compared to placebo. It has been postulated that the effect of cough medications is due to several components, including the drug itself, the physiological components of the medication formulation having a demulcent effect, and the placebo effect.\textsuperscript{19} Many cough medications are formulated as a syrup, and the syrupy liquid and its content (eg, sugar, honey, lemon) are thought to encourage salivation and swallowing and to coat sensory nerve endings, which may suppress a dry, nonproductive cough.\textsuperscript{19} These physiological components may also increase airway secretions, which can have an expectorant effect for a productive (wet) cough.\textsuperscript{20} A strong placebo effect has also been demonstrated in studies with antitussives; the mean placebo response (calculated as a percentage of the change in cough demonstrated by the active treatment arm) across six studies was 85%.\textsuperscript{20} Additionally, acute and subacute coughs are self-limiting, and the cough will likely resolve on its own even without the medication.\textsuperscript{19}

\textbf{Drug-induced cough}

A drug-induced cause is important to consider in patients with either acute or chronic cough. The November 2015 continuing education article in this respiratory medication therapy management series provides a detailed description of drug-induced pulmonary reactions.\textsuperscript{21} Given the prevalence of hypertension, diabetes, coronary artery disease, and heart failure in the United States, the most common cause of cough that pharmacists will likely encounter is from ACE inhibitors. A review of the literature reported that the prevalence of cough is 5% to 20% in patients treated with ACE inhibitors. A more recent review of randomized controlled trials concluded that the incidence of ACE-induced cough, as well as the withdrawal rate because of this adverse drug reaction, is much greater than what is described in the FDA-approved product labeling.\textsuperscript{22} For example, the incidence and withdrawal rate for enalapril from the literature are 11.48% and 2.57%, respectively, while those reported in the product labeling are 1.3% and 0.1%, respectively. The authors also posited that the real-world percentages are likely to be even higher than study data.\textsuperscript{22}

The cough caused by an ACE inhibitor is a dry, persistent cough that occurs within a few hours to several months after the first dose.\textsuperscript{23} The cough is not dose-dependent and women, nonsmokers, and Chinese patients appear to be at higher risk.\textsuperscript{23} The incidence of ACE inhibitor-induced cough in Chinese patients has been reported to be as high as 44%.\textsuperscript{24}

As with the evaluation of cough in general, a thorough history should be obtained to rule out other potential etiologies. Discontinuation of the medication typically leads to resolution of the cough within one to four weeks, but the cough may linger for as long as three months in some patients.\textsuperscript{23} In practice, many clinicians switch the patient to an angiotensin receptor blocker (ARB), as these agents have many of the same treatment indications as the ACE inhibitors. This approach is a sound one, but another option also exists. A randomized, double-blind trial showed that approximately 30% of patients who had experienced cough with two previous ACE inhibitors did not have the same reaction when treated with a third ACE inhibitor.\textsuperscript{23} A repeat attempt with another ACE inhibitor is endorsed as a grade A recommendation by the 2006 ACCP cough guideline\textsuperscript{22} and may be particularly useful for patients who are unable to afford the higher cost of ARBs.

\begin{table}
\centering
\begin{tabular}{|l|}
\hline
\textbf{Upper respiratory tract infection including common cold} \\
\textbf{Upper airway cough syndrome (previously called postnasal drip syndrome)} \\
\textbf{Allergic rhinitis} \\
\textbf{Nonasthmatic eosinophilic bronchitis} \\
\textbf{Drug-induced cough (most commonly caused by angiotensin-converting enzyme inhibitors)} \\
\textbf{Cardiac causes (eg, heart failure)} \\
\textbf{Bronchiectasis} \\
\textbf{Bronchiolitis and other nonbronchiectatic suppurrative airway disease} \\
\textbf{Tuberculosis} \\
\textbf{Intestinal lung disease} \\
\textbf{Lung cancer} \\
\textbf{Aspiration} \\
\textbf{Inhaled irritants (eg, exposure to second-hand smoking, occupational exposure)} \\
\textbf{Somatic cough syndrome and tic cough} \\
\textbf{Unexplained (refractory) chronic cough} \\
\hline
\end{tabular}
\caption{Potential Etiologies of Cough in Adults*}
\end{table}

\textsuperscript{*Not an all-inclusive list.

Source: Ref 7,8
Commonly prescribed antitussives and expectorants

Medications used in the treatment of cough have traditionally been categorized as cough suppressants (antitussives) and expectorants. Theoretically, antitussives suppress nonproductive coughs (also called dry or nuisance coughs) and expectorants thin sputum and make a cough that is productive (also referred to as a wet cough) easier to expectorate. Antitussives are further classified by their site of action. The centrally acting antitussives are thought to act on the cough center in the medulla to increase the cough threshold, whereas the peripherally acting antitussives suppress cough by acting on the peripheral pulmonary receptors.

Antitussives

Dextromethorphan is the d-isomer of the opioid analgesic levorphanol. At recommended doses for the treatment of cough, it is well tolerated and does not have analgesic, sedative, respiratory depressant, or addictive effects. Dextromethorphan’s active metabolite dextrophan is a strong antagonist of the N-methyl-D-aspartate (NMDA) receptor and possesses properties similar to those of phencyclidine (PCP) and ketamine; dissociative hallucinations can occur with these agents. Psychosis, tachycardia, lethargy, ataxia, hypertension, and mydriasis can also occur. An alarming increase in the abuse of dextromethorphan (so called “robotripping”), especially by adolescents, has been reported over the past two decades.

Dextromethorphan is a popular ingredient in both prescription and OTC cough products. It is available in a wide variety of formulations, including liquid, liquid-filled capsules, orally disintegrating strips, lozenges, and tablets. OTC formulations of dextromethorphan products provide dosing for adults and children aged as young as four years for the treatment of cough due to the common cold. However, as noted previously, the ACCP guideline recommends that this type of cough in adults be treated with a first-generation antihistamine-decongestant combination. Centrally acting antitussives such as dextromethorphan and codeine are not recommended because of their questionable efficacy in treating cough due to a URI. Of note, the author of a 2009 review article on antitussives reported that he was unable to find any published English-language studies that demonstrated the efficacy of dextromethorphan or codeine in cough due to the common cold. The ACCP guideline does recommend that these agents can be considered for the short-term symptomatic relief of chronic bronchitis in adults. Some clinicians have proposed that codeine’s analgesic and sedative effects may be useful in the management of painful cough.

As with other opioids, sedation, nausea, vomiting, constipation, respiratory depression, and potential abuse are potential adverse reactions associated with codeine use, but the risk of these events occurring may be lower compared to more potent opioids. The dosing of codeine for cough suppression is lower than that required to achieve analgesia and can be as low as less than 15 mg per dose.

In July 2015, the FDA announced that it is investigating the safety of using codeine-containing medications to treat cough and cold in children aged younger than 18 years because of the potential for serious adverse events, including respiratory depression. The FDA warned that children with breathing problems are at an increased risk of serious adverse drug reactions with codeine. The European Medicines Agency has prohibited the use of codeine to treat cough and cold in children aged younger than 12 years and has recommended against its use in children and adolescents aged between 12 and 18 years who have respiratory conditions.

Other opioids, mainly hydrocodone and morphine, have also been used for

### TABLE 2

**POTENTIAL ETIOLOGIES OF COUGH IN CHILDREN AGED 14 YEARS AND YOUNGER**

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute upper respiratory tract infection</td>
</tr>
<tr>
<td>Upper airway cough syndrome</td>
</tr>
<tr>
<td>Asthma</td>
</tr>
<tr>
<td>Protracted bacterial bronchitis</td>
</tr>
<tr>
<td>Bordetella pertussis infection</td>
</tr>
<tr>
<td>Chronic suppurative lung disease (eg, cystic fibrosis)</td>
</tr>
<tr>
<td>Tobacco smoke</td>
</tr>
<tr>
<td>Medications (angiotensin-converting enzyme inhibitors, asthma medications)</td>
</tr>
<tr>
<td>Inhaled foreign body</td>
</tr>
<tr>
<td>Psychogenic cough</td>
</tr>
<tr>
<td>Otogenic cough</td>
</tr>
</tbody>
</table>

*Not an all-inclusive list.

Source: Ref 41, 42

Dextromethorphan’s efficacy in children found that the drug was no more effective than placebo.

Codeine is an opiate that is indicated for both pain and cough and is available in a variety of liquid formulations, typically coformulated with guaifenesin, pseudoephedrine, or a first-generation antihistamine. Cough formulations containing no more than 200 mg of codeine per 100 milliliters or per 100 grams are classified as schedule V controlled substances. Codeine has been called the gold standard by which other antitussives are compared based on animal models and older studies in humans demonstrating its effectiveness. However, more recent studies reported that codeine was no more effective than placebo in both adults and children. As previously discussed, the ACCP guideline states that centrally acting antitussives can be considered for the short-term symptomatic relief of chronic bronchitis in adults. Some clinicians have proposed that codeine’s analgesic and sedative effects may be useful in the management of painful cough.

As with other opioids, sedation, nausea, vomiting, constipation, respiratory depression, and potential abuse are potential adverse reactions associated with codeine use, but the risk of these events occurring may be lower compared to more potent opioids. The dosing of codeine for cough suppression is lower than that required to achieve analgesia and can be as low as less than 15 mg per dose.

In July 2015, the FDA announced that it is investigating the safety of using codeine-containing medications to treat cough and cold in children aged younger than 18 years because of the potential for serious adverse events, including respiratory depression. The FDA warned that children with breathing problems are at an increased risk of serious adverse drug reactions with codeine. The European Medicines Agency has prohibited the use of codeine to treat cough and cold in children aged younger than 12 years and has recommended against its use in children and adolescents aged between 12 and 18 years who have respiratory conditions.

Other opioids, mainly hydrocodone and morphine, have also been used for
the management of cough. These are potent opiates, and in light of the risks of significant side effects and addiction with these agents, they are typically reserved for cases of severe, intractable cough due to a severe underlying condition such as lung cancer.34,35

Peripheral acting antitussives include benzonatate, levodropropizine, and moquisiteine. Both levodropropizine and moquisiteine have demonstrated efficacy in controlling cough due to acute and chronic bronchitis and COPD.6 However, neither drug is available in the United States. Benzonatate is chemically related to tetraaine, an anesthetic. It suppresses cough by producing an anesthetic effect on the pulmonary stretch receptors of the afferent limb of the cough reflex arc.36 The ACCP guideline does not specifically discuss benzonatate and only states that peripherally acting cough suppressants are not recommended for cough due to a URI.6 In a recent systematic review and meta-analysis of treatments for chronic unexplained or refractory cough, benzonatate was not found to be more effective than placebo in one study and was not found to be more effective than opioids in two others.37

Benzonatate has FDA-approved dosing for adults and children aged older than 10 years.38 It is relatively well tolerated; the most commonly reported adverse drug reaction is nausea. The capsules should be swallowed whole, as mouth, tongue, and throat numbness can occur if they are chewed or otherwise broken. Choking is also a risk with these capsules.38 In 2010, the FDA warned that deaths from accidental ingestion of benzonatate by children aged younger than 10 years have been reported. Benzonatate’s round/oval, liquid-filled gelatin capsules may be attractive to children. Overdose can occur with ingestion of just one to two capsules in children aged younger than two years of age and restlessness, tremors, convulsions, coma, and cardiac arrest may occur, with signs and symptoms occurring within 15 to 20 minutes after ingestion and death occurring within hours.38 Overdoses have also been reported in adolescents and adults.38 The product labeling also states that isolated incidents of bizarre behavior, including mental confusion and visual hallucinations, have been reported when benzonatate was taken in combination with other prescribed medications.38

Expectorants

The potential efficacy of expectorants is in the management of a productive cough. Guaifenesin is the only FDA-approved expectorant available in the United States. This agent’s purported mechanism is in increasing the volume and reducing the viscosity of bronchial secretions, making it easier for the patient to cough up the sputum.39 Studies of guaifenesin’s efficacy in acute and chronic cough in adults are conflicting, with several studies showing efficacy in acute URI but others showing no difference compared to placebo.6,15 The 2006 ACCP guideline states that medications that alter mucus characteristics are not recommended for cough suppression in patients with chronic bronchitis and that an antihistamine-decongestant combination is recommended for cough due to the common cold.6 A 2009 study found that guaifenesin inhibits cough-reflex sensitivity in adult patients with acute viral URI, suggesting that guaifenesin may have an antitussive as well as an expectorant effect.39

Guaifenesin is available in single-ingredient and multi-ingredient products and in tablet and liquid formulations. It is typically coformulated with dextromethorphan or

### Table 3

**Recommended Pharmacologic Treatment of Cough in Adults (2006 American College of Chest Physicians Cough Guideline)**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Drug treatment</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common cold</td>
<td>First-generation antihistamine-decongestant (pseudoephedrine) combination</td>
<td>Second-generation antihistamines are ineffective</td>
</tr>
<tr>
<td></td>
<td>Naproxen</td>
<td></td>
</tr>
<tr>
<td>Upper airway cough syndrome</td>
<td>Specific therapy directed at underlying cause, if known</td>
<td></td>
</tr>
<tr>
<td></td>
<td>First-generation antihistamine-decongestant (pseudoephedrine) combination as empiric therapy</td>
<td></td>
</tr>
<tr>
<td>Acute bronchitis</td>
<td>Antitussives for short-term symptomatic relief “are occasionally useful”</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mucokinetic agents are not recommended</td>
<td></td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td>Central cough suppressants such as codeine and dextromethorphan for short-term symptomatic relief of coughing</td>
<td>No evidence that expectorants are effective and therefore not recommended</td>
</tr>
<tr>
<td></td>
<td>Inhaled ipratropium bromide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Long-acting beta-2 agonist plus inhaled corticosteroid to control chronic cough in stable patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Short-acting beta-2 agonist to control bronchospasm and relieve dyspnea may reduce chronic cough in stable patients</td>
<td></td>
</tr>
<tr>
<td>Nonasthmatic eosinophilic bronchitis</td>
<td>Inhaled corticosteroid (if avoidance of allergen or sensitizer is not possible)</td>
<td>Determine and treat underlying cause of postinfectious cough first</td>
</tr>
<tr>
<td></td>
<td>Oral corticosteroid if cough is persistent or severe despite use of high-dose inhaled corticosteroid</td>
<td></td>
</tr>
<tr>
<td>Postinfectious cough</td>
<td>For postinfectious cough not due to bacterial sinusitis or early in a pertussis infection, while the optimal treatment is not known:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inhaled ipratropium bromide</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inhaled corticosteroid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Short-term oral corticosteroid if cough is severe</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Centrally acting antitussive as last resort</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>Treat according to asthma guidelines</td>
<td></td>
</tr>
</tbody>
</table>

**Source:** Ref 4
codeine and/or an oral decongestant in both prescription and OTC products. Guaifenesin is generally well tolerated at recommended doses, with the most common adverse reactions being nausea, vomiting, and gastrointestinal discomfort.

**Cough in children**

Similar to the evaluation of cough in adults, the first step in the management of cough in children is obtaining a thorough medical history and physical exam. Children with chronic cough should be evaluated with a chest radiograph and spirometry (if the child is old enough to do so). The etiologies of cough in children are somewhat different than in adults (Table 2).

Acute cough in children is most commonly due to a URI. Chronic cough in children, which is defined as a cough lasting more than four weeks, is most commonly due to asthma and asthma-like symptoms, protracted bronchitis, or UACS. GERD as an underlying cause accounts for less than 5% of cases. Pertussis infection, inhaled foreign body, chronic suppurative lung disease, nonasthmatic eosinophilic bronchitis, tobacco smoke, psychogenic cough, and otogenic cough are other potential causes. If the underlying cause is known, therapy should be directed toward treating this condition (eg, inhaled corticosteroid for asthma). However, the results of drug treatment in adults cannot be extrapolated to children. For example, a Cochrane systematic review concluded that empiric antihistamine therapy cannot be recommended for children with chronic cough given “minimal, if any” efficacy and the potential for adverse drug reactions. The ACCP guideline advises against using cough suppressants and other OTC cough medications because of an increased risk of morbidity and mortality, especially in young children. Adolescents aged 15 years and older may be treated according to the guidelines for adults.

In 2007 and 2008, the FDA warned that OTC cough and cold medications should not be used for infants and children aged younger than two years because serious and potentially life-threatening side effects, including death, convulsions, tachycardia, and decreased levels of consciousness, have been reported. The agency emphasized that there are no data regarding the effectiveness of OTC products in children aged younger than two years. In response, manufacturers of OTC cough and cold products announced in 2008 that they would voluntarily withdraw formulations that referred to "infants" and would also revise product labeling to state that the medications should not be used in children aged younger than four years.

Even though the labeling of the OTC cough medications dextromethorphan and guaifenesin contains dosing instructions for children aged as young as four years, the American Academy of Pediatrics (AAP) has stated that OTC cough and cold medications are not effective for children aged younger than six years. The AAP states that honey, staring with one-half to one teaspoon, can be given to children aged older than one year to ease nighttime cough and sleeplessness. Corn syrup may be substituted if honey is not available. A recent study of 300 children aged one to five years with acute URI and nocturnal cough found that honey was more effective than placebo in improving subjective (parent-reported) measures of nocturnal cough, child sleep, and parental sleep.

**The American Academy of Pediatrics has stated that OTC cough and cold medications are not effective for children aged younger than six years.**

Pharmacists have a potentially large role to play in the management of this very common medical condition, especially given that community pharmacists are the most accessible healthcare professionals. An evaluation of potential drug-induced causes of cough should be considered in the management of both acute and chronic cough. Pharmacists should also discuss the lack of efficacy of various OTC products for the management of cough in adults and children and any potential safety concerns, especially in young children. Patients should be advised that many OTC cough and cold products contain several ingredients, increasing the possibility of a drug-drug or drug-disease interaction (eg, a first-generation antihistamine in a patient with benign prostatic hyperplasia). Many patients self-treat their chronic cough but should be aware that doing so may delay diagnosis and treatment of the underlying cause of the cough. Conversely, cough due to an acute mild URI in an immunocompetent nonsmoking person is generally self-limiting and typically requires only adequate hydration and rest, not treatment with various OTC products. Pharmacists can also assist in the selection of appropriate drug treatment for common conditions associated with cough (Table 3) and can engage in smoking cessation education, as both first- and second-hand smoking can lead to chronic cough.

**Conclusion**

The management of this very common condition is multifaceted and complex. Taking a thorough history, including a medication and smoking history, is a crucial step in the evaluation of cough. Therapy should be directed toward treating the underlying cause of the cough, not just masking the symptom.

The references are available online at www.drugtopics.com/cpe.
1. A chronic cough is one that has been present for  
a. Three or more weeks  
b. Four or more weeks  
c. Eight or more weeks  
d. 12 or more weeks

2. Which of following is the most common cause of acute cough in both adults and children?  
a. Upper respiratory tract infection  
b. Heart failure  
c. Gastroesophageal reflux disease  
d. Inhaled foreign bodies

3. Which of the following is a common cause of chronic cough in adults but not in children?  
a. Asthma  
b. Upper airway cough syndrome  
c. Bronchitis  
d. Gastroesophageal reflux disease

4. The 2006 ACCP cough guideline recommends that cough due to the common cold in adults be treated with ________.  
a. Guaiifenesin and dextromethorphan combination  
b. Dextromethorphan only  
c. A first-generation antihistamine and an oral decongestant  
d. A second-generation antihistamine and an oral decongestant

5. Robotripping refers to abuse of high doses of  
a. Diphenhydramine  
b. Guaiifenesin  
c. Dextromethorphan  
d. Codeine

6. In a patient experiencing ACE inhibitor-induced cough, management option(s) include  
a. Discontinuation of the offending ACE inhibitor and changing to an ARB  
b. Continuation of the offending ACE inhibitor and suppressing the cough with an antitussive  
c. Discontinuation of the offending ACE inhibitor and changing to a different ACE inhibitor  
d. Either a or c

7. Which of the following medications is structurally related to tetracaine and can cause numbness of the mouth, tongue, and throat if the capsule is broken?  
a. Guaiifenesin  
b. Dextromethorphan  
c. Codeine  
d. Benzonatate

8. Dextromethorphan  
a. Works in the brainstem to increase the cough threshold  
b. Anesthetizes pulmonary stretch receptors  
c. Increases sputum volume and decreases sputum viscosity  
d. Disrupts the cough-reflex arc

9. Codeine  
a. They are safe and effective.  
b. They are safe but have not been proven effective.  
c. They are recommended for children aged two years and older.  
d. None of the above.

10. Guaiifenesin  
a. Short-term symptomatic relief of cough in acute bronchitis  
b. Short-term symptomatic relief of cough in chronic bronchitis  
c. The common cold  
d. A and B

11. Benzonatate  
a. Inflammation of the respiratory tract may contribute to the therapeutic effect.  
b. Avoidance of allergens or irritant  
c. Inhaled anticholinergic  
d. Expectorant  
e. All of the above.

12. Which of the following is true regarding the use of OTC cough and cold medications in young children?  
a. They are safe and effective.  
b. They are safe but have not been proven effective.  
c. They are recommended for children aged two years and older.  
d. None of the above.

13. According to the 2006 ACCP cough guidelines, dextromethorphan and codeine can be used in which of the following conditions?  
a. Short-term symptomatic relief of cough in acute bronchitis  
b. Short-term symptomatic relief of cough in chronic bronchitis  
c. The common cold  
d. A and B

14. In the management of cough due to nonasthmatic eosinophilic bronchitis, which of the following is effective?  
a. Avoidance of allergens or irritant  
b. Inhaled anticholinergic  
c. Expectorant  
d. All of the above.

15. In the evaluation of cough, which of the following statements is true?  
a. A thorough history and physical examination is an important first step.  
b. A potential drug-induced cause should be investigated.  
c. More than one cause for the cough may be present.  
d. All of the above.

16. Which of the following statements regarding codeine is true?  
a. It has a well-deserved reputation as the gold standard cough medication given its strong efficacy in treating many cough conditions.  
b. The FDA is investigating the safety of using codeine-containing medications to treat coughs and colds in children aged younger than 18 years because of the potential for serious adverse events.  
c. It is most effective when combined with dextromethorphan.  
d. All of the above.

17. Benzonatate is FDA approved for children older than  
a. Six years of age  
b. Eight years of age  
c. 10 years of age  
d. 12 years of age

18. Which of the following statements regarding the treatment of cough due to the common cold is true?  
a. Inflammation of the respiratory tract may play a role in causing the cough.  
b. There is a strong placebo effect in cough studies.  
c. The vehicle for the cough medication (eg, syrup) can act as a demulcent and contribute to the therapeutic effect.  
d. All of the above.

19. The most common cause of a subacute cough is  
a. A cardiac condition  
b. Postinfectious cough  
c. Psychogenic cough  
d. None of the above

20. Pharmacist’s role in the evaluation and management of cough involves:  
a. Assessment for a drug-induced cause  
b. Smoking cessation education  
c. Educating patients on the efficacy, or lack thereof, of cough medications  
d. All of the above.


References


