

# Chapter 1

## Acute Cough

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### Pathophysiology

Cough is a common symptom of many respiratory diseases and is a normal physiological response aimed at protecting the respiratory tract. It is a voluntarily induced or involuntarily activated reflex arc that can be triggered by a wide range of chemical and mechanical stimuli. First, receptors in the head, neck and chest are stimulated. This information is then transmitted to the cough centre in the medulla via the afferent limb of the vagus nerve, resulting in increased neural activity in the efferent pathway to both the respiratory musculature and airway.<sup>[1]</sup>

Cough is present in many respiratory diseases. To help guide clinical assessment, it can be useful to classify cough according to duration within the following 3 categories: acute (lasting <3 weeks), subacute (lasting 3–8 weeks) and chronic (lasting >8 weeks).<sup>[2]</sup>

Viral infections of the upper respiratory tract are the most common causes of acute cough. Some coughs may persist despite the resolution of infection; these subacute coughs are called “postinfectious.”<sup>[2]</sup> Cough due to viral infections appears to arise from stimulation of the cough reflex in the upper respiratory tract caused by postnasal drip (referred to as upper airway cough syndrome [UACS]—formerly postnasal drip syndrome), clearing of the throat or both.<sup>[3]</sup> Other frequent causes include acute bacterial sinusitis, chronic bronchitis, allergic rhinitis and rhinitis due to environmental irritants (see Table 1).<sup>[4]</sup> *Bordetella pertussis* or *B. parapertussis* infection may be suspected in patients with subacute or chronic cough, or when the cough is paroxysmal or accompanied by vomiting; referral to primary care is required in these cases.<sup>[5]</sup> Refer to urgent care if the patient’s breathing is compromised or if there is high fever, seizures, frequent vomiting episodes or the patient becomes dehydrated.

**Table 1: Causes of Cough<sup>[4]</sup>**

Common Causes of Cough	Less Common Causes of Cough
Asthma	Bronchiectasis
Chronic obstructive pulmonary disease	Cystic fibrosis
Drugs, e.g., ACE inhibitors, beta-blockers, ASA or NSAIDs in sensitive individuals	Interstitial lung disease
Environmental/occupational irritants, e.g., air pollution, cigarette smoke, asbestos	Lung cancer
Foreign body	Psychogenic cough
Gastroesophageal reflux disease	Unexplained cough (idiopathic)
Heart failure	Zenker diverticulum (esophageal pouch)
Pulmonary embolism	
Rhinitis: allergic, nonallergic	
Sinusitis	
Upper airway cough syndrome (formerly postnasal drip syndrome)	
Upper/lower respiratory tract infection (viral or bacterial): acute or postinfectious	

## 2

### Goals of Therapy

- Alleviate symptoms
- Diagnose and treat underlying cause, when possible
- Prevent complications

### Patient Assessment

An assessment algorithm for patients presenting with cough is presented in Figure 1.

### Nonpharmacologic Therapy

Although evidence is lacking, hydration with oral liquids and humidification of room air may be beneficial. Room humidifiers used as preventive measures should be well cleaned to avoid aerosolizing mould. Nasal saline irrigation can help alleviate symptoms related to nasal congestion in the context of acute upper airway infections;<sup>[6]</sup> the cough-related impact of nasal saline in UACS requires further evaluation.

Avoid exposure to inhaled irritants such as smoke, dust, pollutants and allergens.

### Pharmacologic Therapy

For comparative ingredients of nonprescription products, consult the *Compendium of Products for Minor Ailments—Cough, Cold and Allergy Products*.

Treatment of underlying conditions contributing to cough is paramount. For example, in gastroesophageal reflux disease, treatment of the reflux itself can alleviate associated cough. Smokers presenting with cough are prime candidates for discussing smoking cessation strategies.<sup>[7]</sup>

A specific treatment is not always possible. For example, there is no cure for the viral infection that causes the common cold. Despite a lack of evidence to support their use, nonspecific treatments such as nonprescription antitussives and protussives (expectorants) are frequently used in these cases depending on the presence/absence of mucus (sputum) production; their use cannot be recommended until further evidence becomes available (see Antitussives).<sup>[8]</sup>

The efficacy of drugs used in the treatment of cough has been evaluated in numerous studies including many systematic reviews.<sup>[9][10][11]</sup> They show a lack of evidence for the effectiveness of nonprescription products in terms of reducing the frequency or severity of cough in children or adults. Some studies have shown benefit; however, the positive results in these studies were often of questionable clinical relevance.<sup>[12][13][14]</sup> Overall, there is little evidence for or against the effectiveness of nonprescription cough medicines. When counselling patients on selecting products, also consider the placebo effect, which can be significant.<sup>[15]</sup>

Nonprescription agents used in the management of cough are described in Table 3.

### Antihistamines

**First-generation antihistamines** (e.g., diphenhydramine) may have a small effect on cough caused by upper respiratory tract infections.<sup>[8][9][10][11]</sup> Their anticholinergic properties may reduce postnasal drip, which is one of the mechanisms responsible for cough in the common cold. The effect is modest and side effects such as drowsiness, dry mouth and confusion may outweigh potential benefit.<sup>[16]</sup> Products containing antihistamines are no longer recommended for the treatment of acute cough until further evidence demonstrating efficacy becomes available.<sup>[8]</sup>

**Second-generation antihistamines** lack significant anticholinergic effects and therefore are not effective for acute cough unless secondary to allergic rhinitis (see Allergic Rhinitis).<sup>[8]</sup>

## Antitussives

Nonprescription **antitussives** act centrally to suppress cough.<sup>[8]</sup> The exact mechanism is unknown; however, the brainstem is thought to be the main region where antitussive agents act to inhibit motor control of cough. Antitussives are not recommended when a cough performs a useful function. If used by a patient with a productive cough, more mucus is retained.<sup>[17]</sup>

**Dextromethorphan** and **codeine** are commonly used to treat cough related to upper respiratory tract infections, although there is little evidence for efficacy.<sup>[9][10][11]</sup> Some studies have shown that they are no more effective than placebo, while others demonstrated a modest benefit.<sup>[8][18][19]</sup> Historically, dextromethorphan has been abused for its euphoric properties, while codeine carries a risk of dependence and addiction. Consequently, the American College of Chest Physicians (ACCP) 2006 guideline on the management of cough does not recommend centrally acting cough suppressants for cough secondary to upper respiratory tract infections.<sup>[20]</sup> Conversely, codeine and dextromethorphan are effective for cough due to chronic obstructive pulmonary disease (COPD), suppressing cough counts by 40–60%,<sup>[21]</sup> and may be used for short-term relief.<sup>[8]</sup>

## Expectorants

The protussive agents act peripherally. **Guaifenesin** is purported to enhance cough effectiveness by promoting the clearance of airway secretions.<sup>[8]</sup> The efficacy and safety of guaifacel and ammonium chloride have not been established. Expectorants are reported to reduce sputum viscosity, permitting more effective removal of secretions from the respiratory tract.<sup>[2]</sup> As with antitussives, there is a lack of evidence to support the efficacy of expectorants. They do not thin sputum nor increase sputum volume, even at doses higher than recommended.<sup>[17]</sup> Adequate hydration with oral liquids and inhalation of humidified air is perhaps the best protussive or “expectorant” measure.

## Other Agents

**Honey** may be an effective cough suppressant in children;<sup>[8][22][23]</sup> no studies in adults are currently available. A Cochrane review concluded that honey administered before sleep is probably better than no treatment, placebo or diphenhydramine, and no different from dextromethorphan, at relieving cough symptoms.<sup>[8][22]</sup> It is also probably better than placebo or salbutamol for reducing the duration of cough.<sup>[22]</sup> Honey has demulcent, antioxidant and antibacterial effects. It is proposed that the demulcent effect may act to decrease cough. Because of the risk of botulism, give pasteurized honey only to immunocompetent children >1 year of age.

**Zinc** lozenges have been used to alleviate cough due to the common cold. Studies evaluating the efficacy of zinc in common cold symptoms have yielded conflicting results, and 2 meta-analyses have concluded there is insufficient evidence to recommend zinc preparations.<sup>[8]</sup> In addition, zinc can be associated with unpleasant taste, mouth irritation and nausea.

Anesthetics such as **benzocaine**, **phenol** and **menthol** may reduce the sensitivity of peripheral nociceptors. They have been used as antitussives, but evidence for efficacy is poor.<sup>[24]</sup> Rarely observed side effects include tingling or irritation at the site of administration and hypersensitivity reactions.

Inflammatory pathways have been largely investigated to play a role in the pathophysiology of cough; however, **nonsteroidal anti-inflammatory drugs** (NSAIDs) were found to have no effect on cough symptoms.<sup>[25]</sup>

## Prescription Therapy

Bronchodilators such as **salbutamol** or **formoterol** are recommended only for cough due to obstructive lung disease such as asthma or COPD.<sup>[20][26][27]</sup> Following a respiratory infection, patients sometimes develop a cough for which inhaled corticosteroids could be beneficial; the potential benefit

of inhaled corticosteroids requires confirmation through further studies before making recommendations for their routine use.

For the treatment of cough secondary to another medical condition, see Allergic Rhinitis and Viral Rhinitis, Influenza, Sinusitis and Pharyngitis as well as Acute Bronchitis in the *Compendium of Therapeutic Choices*. For cough lasting >8 weeks, see Chronic Cough in Adults in the *Compendium of Therapeutic Choices*.

## Cough in Special Populations

### Children

For comparative ingredients of nonprescription products, consult the *Compendium of Products for Minor Ailments*—Baby Care Products: Cough and Cold.

Since 2008, Health Canada has required manufacturers to relabel nonprescription cough and cold medicines with certain active ingredients to indicate that they should not be used in children <6 years of age.<sup>[28]</sup> Dextromethorphan, guaifenesin and first-generation antihistamines (including diphenhydramine) contained in cough and cold products are included in the list of active ingredients in the Health Canada advisory. See Viral Rhinitis, Influenza, Sinusitis and Pharyngitis, Table 3.

Although cough and cold medicines have been used by children for many years, little evidence supports their effectiveness in this population.<sup>[11][19][29]</sup> Furthermore, Health Canada has advised against the use of these products in children <6 years of age due to reports of very rare serious side effects as well as misuse and overdose.<sup>[28]</sup> Rare but serious potential side effects include seizures, increased heart rate, decreased level of consciousness, abnormal heart rhythms and hallucinations.<sup>[28][29]</sup>

In children ≥6 years of age, **dextromethorphan** can be used to treat nonproductive cough, though evidence of efficacy in children is absent. Health Canada recommends that any cough and cold product containing codeine or other opioids (e.g., hydrocodone, normethadone) be avoided in children <18 years of age.<sup>[30]</sup>

### Pregnancy and Breastfeeding

See Pregnancy and Breastfeeding: Self-care Therapy for Common Conditions.

## Monitoring of Therapy

Table 2 contains information on monitoring therapy.

Table 2: **Monitoring of Therapy for Cough**

Symptom	Monitoring	Endpoint of Therapy	Actions if Endpoint Not Met
Cough	Patient: daily Health-care practitioner: next visit or by telephone 2–3 days later	Patient able to perform daily activities. Patient able to sleep.	Optimize nonpharmacologic measures. Change treatment.
Drowsiness (antitussive)	Patient: daily Health-care practitioner: next visit or by telephone when checking for efficacy	No drowsiness.	Change medication schedule (bedtime only) or change treatment.

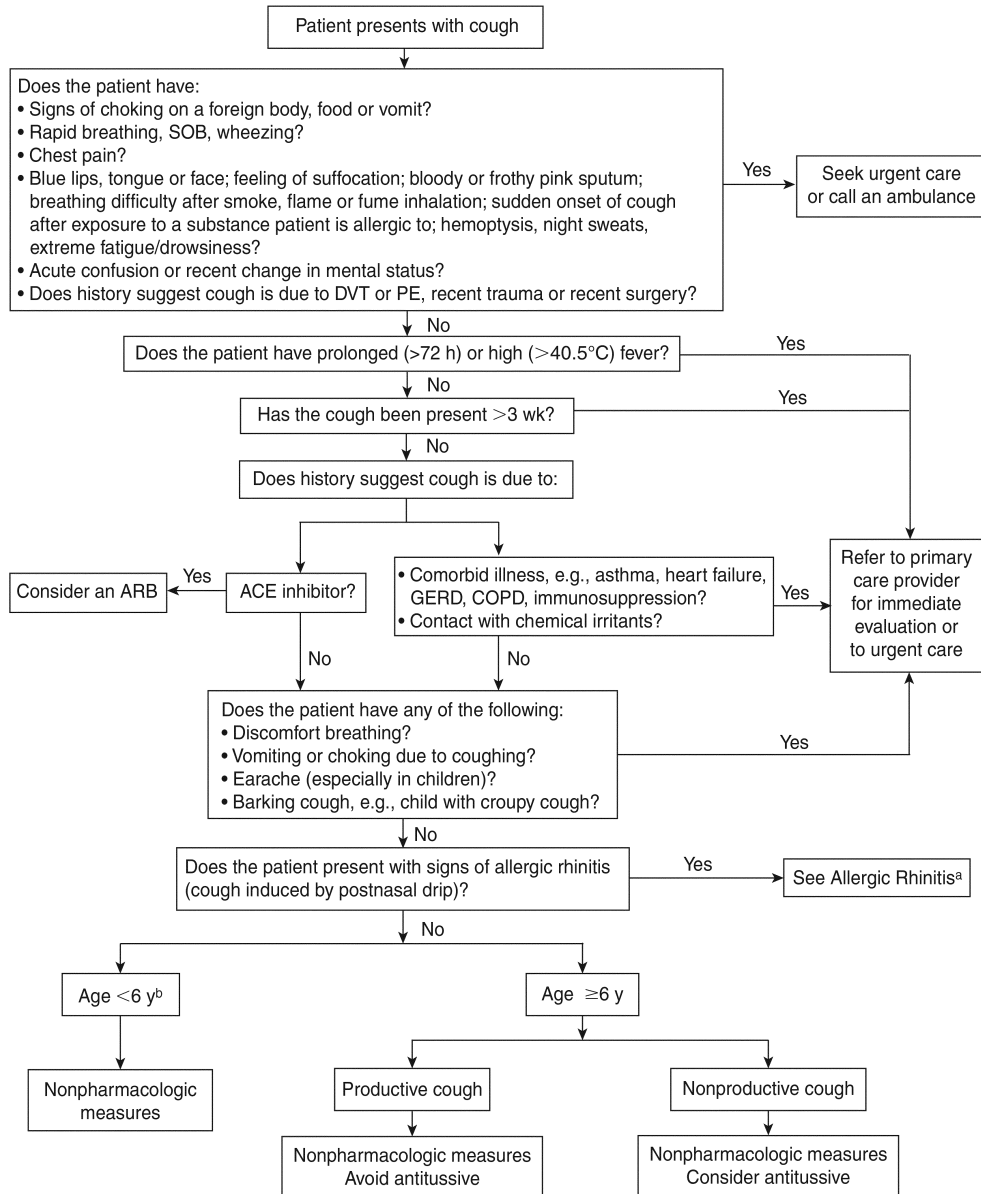
## Advice for the Patient

Advise patients regarding:

- Nonpharmacologic therapy

- Proper use of medication
- Expected results and management of side effects
- When to contact a physician (see Cough—What You Need to Know)

Figure 1: **Assessment of Patients with Cough**





<sup>a</sup> See Allergic Rhinitis.

<sup>b</sup> Cough and cold medicines are not recommended in children <6 years of age (see Cough in Special Populations, Children).

**Abbreviations:** ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease; DVT = deep vein thrombosis; GERD = gastroesophageal reflux disease; PE = pulmonary embolus; SOB = shortness of breath


Table 3: Agents for Cough

Class	Drug	Dosage <sup>[a]</sup>	Adverse Effects	Drug Interactions	Comments	Cost <sup>[b]</sup>
Antitussives	<i>codeine</i>  Combination products: Robitussin AC, generics	Adults: 10–20 mg Q4–6H PO. Maximum: 120 mg/day Health Canada recommends against the use of codeine and other opioids in children <18 y <sup>[30]</sup> For combination products, consult label for additional ingredients; follow directions on label	Drowsiness, sedation, nausea, vomiting, constipation.	CNS depressants, including alcohol, enhance CNS side effects. MAOIs: risk of serotonin syndrome. CYP2D6 inhibitors (e.g., fluoxetine, paroxetine) may inhibit conversion of codeine to its active metabolite and reduce clinical effect.	Causes less sedation than hydrocodone. Metabolized to morphine. Potential for dependence/addiction. Nonprescription codeine products always contain other ingredients.	\$
	<i>dextromethorphan</i>  Balminil DM, Benylin DM; Combination products: Robitussin DM, others	Adults and children ≥12 y: 10–20 mg Q4H PO or 30 mg Q6–8H PO. Maximum: 120 mg/day Children 6–11 y: 5–10 mg Q4H PO or 15 mg Q6–8H PO. Maximum: 60 mg/day For combination products, consult label for additional ingredients; follow directions on label	Generally well tolerated. Occasional dizziness, drowsiness, nausea.	Modulators of serotonin: risk of serotonin syndrome, e.g., SSRIs, linezolid, MAOIs (including moclobemide), sibutramine. CYP2D6 inhibitors (e.g., fluoxetine, paroxetine) may inhibit DM metabolism, resulting in increased DM levels and potential for adverse effects.	Causes less sedation than codeine and other opioids. DM has been abused for its euphoric effects.	\$
	<i>honey</i>	Adults: 15 mL daily to TID Children 1–18 y: 2.5–10 mL HS	Side effects are rare; nervousness, insomnia, hyperactivity.	No known interactions.	Only use pasteurized honey due to the risk of botulism. Due to this risk, avoid in children <1 y of age, patients who are immunocompromised or those who have structural abnormalities of the GI tract. Avoid in patients allergic to pollen. <i>Do not</i> use honey made from <i>Rhododendron</i> (e.g., <i>R. ponticum</i> , <i>R. flavum</i> , <i>R. luteum</i> ) due to risk of grayanotoxin, which is poisonous.	\$

Class	Drug	Dosage <sup>[a]</sup>	Adverse Effects	Drug Interactions	Comments	Cost <sup>[b]</sup>
Expectorants	<i>guaifenesin</i> Robitussin Mucus & Phlegm, generics	Adults and Children ≥12 y: 200–400 mg Q4H PO. Maximum: 2.4 g/day Children ≥6 y: 12 mg/kg/day in divided doses Q4H PO. Maximum: 1.2 g/day For combination products, consult label for additional ingredients; follow directions on label	Side effects are rare; dizziness, drowsiness, headache, nausea and vomiting have been reported at high doses.	No known interactions.		\$

<sup>a</sup> Cough and cold medicines are not recommended for use in children <6 years of age (see Cough in Special Populations, Children).

<sup>b</sup> Cost of 100 mL, unless otherwise specified; includes drug cost only.

 Dosage adjustment may be required in renal impairment; see Appendix I.

**Abbreviations:** CNS = central nervous system; DM = dextromethorphan; GI = gastrointestinal; MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor

Legend: \$ <\$5

## Resources

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Canadian Pharmacists Association. *Cough—What You Need to Know*. Patient handout follows  
References in this chapter.

## Suggested Readings

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## Cough—What You Need to Know

### What causes cough?

There are many possible reasons for a cough. The most common cause is a viral infection, such as the common cold or the flu. In this case, it will go away by itself in a couple of weeks. Other causes include:

- Worsening asthma
- Allergies
- Environmental irritants (air pollution, cigarette smoke)
- Side effect of certain drugs
- Other infections such as bronchitis or pneumonia

### When to see a health-care provider:

- You've had a cough lasting longer than 3 weeks
- You have difficulty breathing or chest pain
- You are coughing up bloody or coloured mucous
- You have a fever  $>40.5^{\circ}\text{C}$  or any fever lasting longer than 3 days
- Your child is  $<3$  months of age and has a cough
- Your child is between 3 and 6 months of age and has a cough and fever  $>38.5^{\circ}\text{C}$
- You have a medical condition such as asthma, chronic obstructive pulmonary disease (COPD) or heart failure

### Treatment for Cough

There is not a lot of proof that cough medicines work well. Some medicines may help control a cough (cough suppressants) while others help clear chest phlegm (expectorants). Cough suppressants should not be used if you have a cough with mucous. Talk to your pharmacist about which medicine may be right for you.

### Cough in Children

- Cough medicines are not recommended for children  $<6$  years of age. Cough medicines containing codeine and other opioids are not recommended for patients  $<18$  years of age.
- You can try a teaspoon of pasteurized honey before going to bed; remember to brush teeth afterwards. *Do not* give honey to children  $<1$  year of age or if they have an immune condition, because of the risk of botulism.