

# Concise Review for Primary-Care Physicians

## Assessment of the Patient With Chronic Cough

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**Chronic cough, defined as cough that persists for 3 weeks or longer, is one of the most common symptoms evaluated by a primary-care physician. With the exclusion of cigarette smoking, postnasal drip, asthma, and gastroesophageal reflux are responsible for more than 80% of the causes of chronic cough. Elicitation of a thorough history and performance of a physical**

**examination will usually provide clues about the cause of chronic cough. The use of diagnostic tests including methacholine challenge, gastroesophageal reflux studies, and sinus imaging is based on clinical suspicion. Treatment of chronic cough is aimed at the underlying cause.**

*(Mayo Clin Proc 1997;72:957-959)*

Cough, an explosive expiration that clears and protects the airway, is the fifth most common symptom encountered by physicians who treat outpatients. Clinicians must be aware, however, that some patients who complain of persistent coughing may in fact be experiencing frequent throat clearing, "hawking," or symptoms of the upper respiratory tract other than cough. When the clinician is unsure whether the patient is truly describing cough, having the patient reproduce the "cough" in the office is helpful.

### MECHANISM OF COUGH

Cough reflex has five components: cough receptors, afferent nerves, cough center (medulla), efferent nerves, and effector organs (respiratory muscles and muscles in the upper airway and tracheobronchial tree). Triggering of cough receptors by chemical or mechanical factors results in stimulation of the cough center. Impulse for the cough is then transmitted through the efferent pathways to the expiratory and laryngo-tracheobronchial musculature.

Cough receptors predominate along the laryngotracheobronchial tree; however, they are also thought to exist in the nose, paranasal sinuses, ear canals and drums, pleura, stomach, pericardium, and diaphragm.<sup>1</sup> Any process that stimulates a cough receptor may cause a person to cough. Cough is under both voluntary and involuntary control.

### ACUTE VERSUS CHRONIC COUGH

Acute and self-limited episodes of cough commonly stem from viral infections of the respiratory tract and usually do

not pose a diagnostic problem. Chronic cough is generally defined as cough persisting for 3 weeks or longer.<sup>2,4</sup> In this article, we discuss the diagnostic approach to patients with chronic cough in the absence of hemoptysis, a previously known chronic respiratory disease, or obvious clues detected on a chest roentgenogram. Because a chronic cough in an immunocompromised host has a more serious connotation, it will not be discussed herein.

### CAUSES OF CHRONIC COUGH

Cigarette smoking is the most common cause of chronic cough in the general population. Cigarette smokers, however, usually do not seek medical attention for their persistent cough, which likely represents chronic bronchitis. Aside from smoking, the most common causes of chronic cough are postnasal drip, asthma, and gastroesophageal reflux.<sup>2,3</sup> These three conditions together account for 80 to 90% of the cases of chronic cough evaluated at outpatient clinics (Table 1).<sup>3</sup>

Postnasal drip is probably the most common cause of chronic cough and is diagnosed in the presence of suggestive symptoms with or without mucoid secretions visualized in the posterior pharynx. Some patients with asthma have chronic cough as a sole manifestation, and the diagnosis is based on results of spirometry with and without a bronchodilator. If the results are normal, a methacholine inhalation challenge test is performed. The diagnosis of asthma is suggested by a history of cough aggravated by exercise or exposure to cold air, irritants, or allergens. A history of intermittent wheeze or dyspnea accompanying a chronic cough is also suggestive of asthma. Similarly, in patients with gastroesophageal reflux, cough may be the sole symptom, the cause of which is the presence of acid in the distal esophagus resulting in an esophageal-tracheobronchial reflex.<sup>5</sup> Microaspiration of stomach contents may have a minor role in this manifestation. Up to one-half of patients

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*Mayo Clin Proc* 1997;72:957-959

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Table 1.—Causes of Chronic Cough

Cause	% of patients (N = 102)
Postnasal drip	41
Asthma	24
Gastroesophageal reflux	21
Chronic bronchitis	5
Bronchiectasis	4
Miscellaneous	5

Data from Irwin and associates.<sup>3</sup>

may have more than one cause for their chronic cough.<sup>3</sup> Lung cancer is a rare cause of chronic cough in the absence of suggestive abnormalities on chest radiographs.

The term "postinfectious cough" has been used to refer to cough that persists after respiratory tract infections. In some patients, transient bronchial hyperreactivity may be demonstrated. This type of cough generally fades over a period of a few months. Chronic sinusitis, interstitial lung disease, environmental agents, bronchial carcinoid, and drugs may occasionally be implicated as causes of chronic cough.<sup>2-4</sup> In particular, 5 to 20% of patients who take angiotensin-converting enzyme inhibitors have development of cough.<sup>6</sup> All commercially available angiotensin-converting enzyme inhibitors have been associated with cough. Such cough usually diminishes within 1 to 4 days after the medication has been discontinued. Occasionally, weeks may pass before improvement is noted. Angiotensin II receptor antagonists are much less likely to cause cough. Psychogenic cough is a diagnosis of exclusion but seems to exist.<sup>7</sup> In a recent article, pertussis was diagnosed on the basis of serologic criteria in 21% of 75 adults who had a persistent cough (defined as a cough lasting 2 weeks or longer).<sup>8</sup> In children, aspiration, foreign body, recurrent viral or atypical infections, cystic fibrosis, and passive exposure to cigarette smoke are additional considerations.

## DIAGNOSTIC EVALUATION

The patient's history and findings on physical examination provide a basis for the diagnostic evaluation of chronic cough. The physician should question the patient about production of phlegm, character of phlegm produced, exacerbating factors, time relationships, and associated symptoms. Examination of the patient with special attention to the lungs, ears, nose, and mouth may yield useful clues. A forced exhalation maneuver may produce a localized wheeze or diffuse wheezes suggestive of a localized airway lesion or bronchospasm, respectively. Having the patient breathe in slowly will help in auscultation of fine crackles of pulmonary fibrosis. Standard anteroposterior and lateral chest roentgenograms are usually obtained. Spirometry with or without the use of a bronchodilator may confirm the pres-

ence of asthma if reversible obstructive airway disease is present. A methacholine inhalation challenge test can be performed if the baseline spirometry value is normal. A positive methacholine inhalation challenge test result is defined as a decrease of 20% or more from the baseline value of forced expiratory volume in 1 second after inhalation of aerosolized methacholine. A positive methacholine challenge, however, indicates bronchial hyperreactivity and not necessarily asthma. For example, transient bronchial hyperreactivity may be evident after a viral infection of the upper respiratory tract. Thus, a positive methacholine challenge test result must be correlated with the clinical context and subsequent course.

Prolonged (usually 24 hours) ambulatory monitoring of esophageal pH is the most sensitive diagnostic test for detecting gastroesophageal reflux.<sup>2,3,5</sup> Radiographic examination with a barium swallow or esophagoscopy is less sensitive in diagnosing reflux. Bronchoscopy is of limited value when the chest roentgenogram shows no abnormalities and thus is rarely used in this setting. If a sinus or upper airway problem is suspected, sinus imaging and otolaryngologic consultation may be helpful.

Some investigators<sup>4</sup> suggest an algorithmic approach to the treatment of chronic cough that incorporates empiric therapy with an antihistamine-decongestant preparation before laboratory tests are performed. The rationale for this strategy is to treat postnasal drip, which seems to be the most common cause of chronic cough in this setting, and to minimize the cost of laboratory testing. This approach includes weekly follow-up visits; thus, the physician can assess the patient's response to empiric therapy and perform sequential diagnostic and therapeutic procedures.

Our initial approach is to obtain a chest roentgenogram in most patients, along with elicitation of the history and performance of a physical examination. A chest roentgenogram may be unnecessary in younger nonsmoking patients, especially if the cause of chronic cough is apparent on the initial clinical examination. If one or more causes are identified or suspected, we treat empirically with simple measures. For postnasal drip, we prescribe an antihistamine-decongestant combination drug or nasal corticosteroid spray. Nasal ipratropium bromide spray is now available. For a patient suspected of having gastroesophageal reflux, a trial of antireflux measures (including elevation of the head of the bed, low-fat foods, avoidance of chocolate and peppermint, avoidance of recumbency at least 3 hours after the evening meal, avoidance of bedtime drinks and snacks, weight control, smoking cessation, and reduction of alcohol intake) and drug therapy with an H<sub>2</sub> receptor antagonist or proton pump inhibitor is reasonable. For a patient with suspected asthma, we prefer to confirm the presence of bronchial hyperreactivity by spirometry and, if needed, methacholine challenge

testing. Treatment of asthma must be tailored to its severity. In the presence of relatively mild impairment, regular use of a corticosteroid inhaler supplemented with a short-acting  $\beta_2$ -agonist inhaler as needed generally controls the symptoms. The clinician must remember that several months of therapy may be necessary in some cases.<sup>3,4</sup>

If the cause of chronic cough is not apparent or the patient has no response to empiric treatment, further testing is performed based on clinical suspicion. Pulmonary function testing is usually done first, followed by evaluation for gastroesophageal reflux if bronchial hyperreactivity is not demonstrated. Additional evaluation including sinus imaging, otolaryngologic consultation, computed tomography of the chest, pulmonary consultation, and bronchoscopy may be considered in difficult cases. For patients with refractory cough and no apparent cause, cough suppressants such as codeine, ipratropium or corticosteroid inhaler, brief course of orally administered corticosteroids, nebulized lidocaine, or behavioral modification therapy may be helpful.<sup>9-11</sup>

### Questions About Evaluation of Chronic Cough

(See article, pages 957 to 959)

- Which one of the following is the most common cause of chronic cough in a nonsmoker who has normal findings on a chest roentgenogram?
  - Chronic bronchitis
  - Bronchiectasis
  - Postinfectious cough
  - Postnasal drip
  - Occult lung cancer
- Which one of the following statements is correct regarding a methacholine challenge test?
  - Should be performed when the baseline spirometry reveals moderate to severe airflow obstruction
  - Is considered positive when the patient coughs after inhalation
  - Is not a sensitive or specific test for hyperreactive airways disease
  - Cannot be performed when the patient is taking prednisone
  - Is considered positive when the forced expiratory volume in 1 second decreases 20% or more in comparison with the baseline value
- Which one of the following is the main pathogenic mechanism of gastroesophageal reflux (GERD)-associated cough?
  - Medication used to treat GERD induces cough
  - Acid in the distal esophagus that causes an esophageal-tracheobronchial cough reflex
  - Microaspiration of acid content
  - Hiatal hernia with GERD that causes pressure on adjacent structures
  - Recurrent aspiration pneumonia
- Which one of the following is the best initial diagnostic approach to a patient with chronic cough?
  - Methacholine challenge test
  - Gastrointestinal endoscopy-bronchoscopy
  - Twenty-four hour esophageal pH monitoring
  - History and physical examination
  - Ear, nose, and throat consultation
- Which one of the following statements is true regarding chronic cough?
  - Few patients with GERD-associated cough experience improvement with aggressive antireflux therapy
  - Corticosteroid inhalers and  $\beta_2$ -agonists are used to treat chronic cough in a patient with a positive methacholine challenge test result
  - Most nonsmokers with chronic cough have no definable cause
  - Cough receptors are present only along the tracheobronchial tree
  - Cigarette smoking is an uncommon cause of chronic cough

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Correct answers:

1. d, 2. e, 3. b, 4. d, 5. b