

Approach to the Patient with Cough



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KEYWORDS

- Approach to cough • Chronic cough • Cough in the primary care setting
- Algorithm for treatment of cough

KEY POINTS

- The duration of the symptom divides cough into acute (less than 3 weeks), subacute (3–8 weeks), and chronic (greater than 8 weeks); the duration often has diagnostic implications so a careful history is key.
- Acute cough is most commonly caused by acute respiratory infections of the upper and lower airways.
- The initial evaluation for the patient with chronic cough is much reliant on a thorough history and physical examination.

INTRODUCTION

Cough is one of the most common reasons a patient may seek care in the outpatient setting, and leads to approximately 30 million clinical encounters per year in the United States alone.¹ Cough has also been observed to prompt nearly 40% of office visits to a pulmonologist.² The approach to this common and troubling symptom is discussed.

CLASSIFICATION OF COUGH

The duration of the symptom divides cough into acute (less than 3 weeks), subacute (3–8 weeks), and chronic (greater than 8 weeks); the duration often has diagnostic implications so a careful history is key. Respiratory infections are the most common cause for acute cough and may be implicated in an acute exacerbation of a chronic lung disease (eg, chronic obstructive pulmonary disease). Pulmonary embolism has rarely been noted to cause cough and should be considered if other elements of the history, signs, and symptoms rouse suspicion.³

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PATHOPHYSIOLOGY OF COUGH

Stimulation of a cough receptor initiates the cough reflex arc. Cough receptors are divided into those found in the respiratory tract and those outside of the respiratory tract. Extrarespiratory cough receptors are found within adjacent structures, such as the pericardium, esophagus, diaphragm, stomach, auditory canal, and tympanic membranes. Cough receptors are further divided into those whose reflex arc is initiated by mechanical or chemical stimuli. Chemical cough receptors are found within and outside of the respiratory tract, and are triggered by many different stimuli, which include acid, cold, heat, capsaicin/capsaicin-like compounds, and fragrances. Mechanical receptors, which are triggered by touch or displacement, typically from inhaled particulate matter, are located solely within the larynx and tracheobronchial tree. Once stimulated, impulses from cough receptors travel to the cough center in the medulla via the vagus nerve. The cough center, which is also under cortical control, then produces efferent signals via the phrenic nerve, vagus nerve, and spinal motor neurons to the diaphragm, larynx, trachea, and bronchi, and the expiratory muscles and pelvic sphincters, respectively.⁴ This coordinated effort produces a violent expulsion of air to protect the gas exchange function of the lungs.

ETIOLOGIES

Acute cough is most commonly caused by acute respiratory infections of the upper and lower airways (**Table 1**). However, when patients lack associated symptoms, such as fever, myalgias, and sore throat, hay fever or allergic rhinitis should be considered. Acute exposure to the inhalation of irritants can also cause acute cough in the right historical context.

Subacute cough, which is cough that lasts between 3 and 8 weeks, has several potential etiologies. Most commonly this follows nonspecific viral infections that have caused inflammation of the airways. Postviral cough usually improves spontaneously, but because of the prolonged symptom, there are many treatments used for alleviation. These include a trail of inhaled ipratropium, inhaled corticosteroids, or perhaps oral steroids.⁵

Bordetella pertussis may be an underrecognized cause of subacute and postinfectious cough. Diagnosis of pertussis requires a high index of suspicion. Cough of 2 weeks' duration and longer, along with coughing paroxysms, inspiratory "whoop," and posttussive emesis may suggest pertussis. These classic manifestations are less likely to be present in patients with prior immunity. Initially, culture and polymerase chain reaction testing from polyester nasopharyngeal swabs may be useful; after

Table 1 Etiologies of cough		
Acute	Subacute	Chronic
Upper respiratory tract infections	Postinfectious	Upper airway cough syndrome
Lower respiratory tract infections	cough	Gastroesophageal reflux
Hay fever, allergic rhinitis	Pertussis	Asthma
Inhalational exposure	Angiotensin-	Angiotensin-converting enzyme inhibitors
	converting	Chronic bronchitis
	enzyme	Foreign bodies
	inhibitors	Tracheobronchomalacia
		Bronchiectasis
		Lung cancer

4 weeks, only serology is useful. Generally, antibiotics are not indicated 3 weeks beyond onset of symptoms; the cough at this stage is not caused by active infection, but rather local tissue damage.⁶ Because of this, from a public health perspective the risk of transmission is decreased 3 weeks after onset of symptoms. Because the largest risk for pertussis-related morbidity and mortality is in infants and young children, it is appropriate to consider antibiotic therapy for pregnant women (or those to be in close contact with the newborn) for up to 6 weeks after onset of cough symptoms. It is also reasonable to consider treatment of those with asthma, chronic obstructive pulmonary disease, age older than 65 years, and/or immunocompromised states.⁷ Macrolides, such as a standard 5-day course of azithromycin, are the preferred treatment regimen. Vaccination is an important and effective element in the prevention of this disease.

Additionally, medications, specifically angiotensin-converting enzyme (ACE) inhibitors, may cause a subacute or chronic, nonproductive cough (in up to 15% of patients treated with ACE inhibitors).⁸ It is believed that the accumulation of bradykinin, which is typically catalyzed by ACE, may stimulate cough receptors. Generally, cough related to ACE inhibitors begins within 1 week of initiating therapy (although it can be delayed up to 6 months) and resolves within 1 week of discontinuation (although it may last up to 4 weeks).⁹ This adverse effect is more common in women and those of Chinese origin.¹⁰ Asthma does not seem to play a role. Cough returns on rechallenge with any ACE inhibitor. If the medication is still indicated, switching to angiotensin receptor antagonists, such as losartan, or other antihypertensives is advised.

Most commonly, chronic cough is caused by upper airway cough syndrome (UACS; secondary to postnasal drip), gastroesophageal reflux, or asthma.¹¹ UACS and gastroesophageal reflux may also present with subacute cough, although cough of a subacute duration is most often caused by postinfectious etiologies. Its pathogenesis is not entirely understood, but it is thought to be caused by airway inflammation and hyperresponsiveness, mucus hypersecretion, along with impaired clearance.⁵

UACS is the preferred name when referring to cough secondary to postnasal drip. The mechanism of cough is not entirely clear, although it is suspected to be secondary to stimulation of laryngeal cough receptors.⁶ The underlying causes include rhinitis (allergic, perennial nonallergic, and vasomotor), acute nasopharyngitis (“the common cold”), and sinusitis. Patients may complain of rhinorrhea, frequent throat clearing, a sensation of dripping or tickle in the back of the throat, or no symptoms at all. Visualization of secretions in the posterior nasopharynx or cobblestoning of the mucosa is suggestive. Because the history and physical examination in UACS may be elusive, empiric treatment may be the only way to confirm the diagnosis.

Asthma-related cough is generally accompanied by wheezing and dyspnea, although cough may be the only symptom in cough-variant asthma. Cough-variant asthma may eventually progress to include wheezing and dyspnea. Factors suggestive of asthma include family history of asthma; personal or family history of atopy; and worsening of cough symptoms on exposure to fumes, fragrances, dust, mold, and cold air. Cough secondary to asthma may also be seasonal or follow an upper respiratory tract infection. As is the case with typical presentations of asthma, spirometry may help reveal obstructive disease. Alternatively, spirometry is normal and bronchoprovocation may be required to demonstrate airway hyperreactivity. However, because the ability for spirometry to discern the cause of chronic cough is poor,⁹ the best way to confirm the diagnosis of cough-variant asthma is to observe improvement in symptoms with appropriate asthma therapy.

Gastroesophageal reflux is another frequent cause for prolonged cough. Patients frequently report heartburn or a sour taste in the mouth, although these symptoms

may be absent in 40% of patients whose cough is attributable to reflux.¹² Often, cough is worse when the patient is in the recumbent position because it allows for easier reflux from the stomach.¹ Although gastroesophageal reflux is thought to be related to dysfunction of the lower esophageal sphincter, laryngopharyngeal reflux (LPR) is attributed to upper esophageal sphincter dysfunction. Few patients with LPR endorse heartburn. Instead, dysphonia, hoarseness, nonproductive throat clearing, and cough are the hallmark symptoms. Laryngoscopic examination may assist in diagnosing LPR. Hoarseness in patients with significant smoking history, especially in the absence of other signs or symptoms to suggest reflux, should prompt consideration for malignancy.

Lung cancer, a feared diagnosis, is the cause in less than 2% of chronic coughs.^{8,13} Lung cancers presenting as cough are often found in the larger, central airways. The physical examination may include wheezes or focal decreased breath sounds, which could suggest tumoral obstruction of the airway. Consider lung cancer in smokers who have a new cough, a change in their usual “smoker’s cough,” or cough persisting for more than 1 month after smoking cessation.¹⁴ Survival is better in patients ultimately diagnosed with lung cancer whose initial presenting symptom is cough alone, as compared with other presentations.⁵

Chronic bronchitis is defined as cough and sputum production on most days over a 3 month period for 2 or more consecutive years (without any other cause of cough identified). It is almost universally a disease of smokers. Those with airway inflammation caused by exposure to dusts or fumes comprise the small fraction of nonsmokers with chronic bronchitis. Chronic bronchitis is a common condition, because of the prevalence of cigarette smoking. However, most smokers do not seek medical care for their cough. Sputum produced in chronic bronchitis is generally clear or white; purulent appearance (or a change in the typical appearance) often signifies respiratory infection and should be treated as such.

Recurrent airway infections and/or inflammation can lead to the development of bronchiectasis. Bronchiectasis is a cyclical condition of airway inflammation and bronchial destruction causing dilation of airways and subsequent impaired mucus clearance and secretion pooling, which in turn worsens inflammation and predisposes for infection. Cough in bronchiectasis is most often productive of copious mucopurulent sputum (which may become frankly purulent and fetid at the time of exacerbation).¹⁵ Although examination may be normal, more frequently adventitious sounds and digital clubbing are usually identified.¹⁶

Bronchiectasis may affect the lungs diffusely or in specific regions. Regional bronchiectasis is often caused by a prior severe lower respiratory tract infection, whereas multifocal bronchiectasis is often secondary to chronic infection with *Mycobacterium avium* complex, commonly seen in women middle aged and older. In a younger person, consider congenital conditions, such as cystic fibrosis or immunoglobulin deficiency.⁶

Foreign bodies can also lead to a persistent cough. Although more common in children, central nervous system impairment, traumatic endotracheal intubation, and dental procedures predispose adults to aspiration of a foreign body. This should be considered in patients with chronic cough and/or recurrent pneumonia.¹⁷ Foreign bodies may not only be limited to the tracheobronchial tree. Impaction of the auditory canal with a foreign body or cerumen may cause chronic cough via stimulation of the auricular branch of the vagus nerve (otorespiratory reflex).¹⁸

Tracheobronchomalacia (TBM) is becoming an increasingly recognized cause of respiratory symptoms, including chronic cough. TBM is a condition of excessive dynamic airway collapse, defined by a 50% reduction in cross-sectional area of the

central airways. In most adults, the cause of TBM is not known, although it is often seen with other pulmonary conditions. The cough is often of a barking quality; stridor may also be present.¹⁹ Dynamic (inspiratory and expiratory phase) noncontrast chest computed tomography (CT) is the least invasive manner to diagnose TBM, although bronchoscopy may be required.²⁰

Other uncommon causes of a chronic cough include arteriovenous malformations, retrotracheal masses, premature ventricular contractions, and psychogenic causes ("tic cough"). The more common previously mentioned diagnoses should be thoroughly ruled out before considering these.

EVALUATION

The initial evaluation for the patient with chronic cough is reliant on a thorough history and physical examination. Important historical aspects include smoking status, current medications, and concurrent symptoms. Eliciting any concerning or systemic symptoms, such as hemoptysis, weight loss, or shortness of breath, should result in a more urgent assessment, which would likely include further diagnostic testing. Additionally, the timing and aggravating and relieving activities can help to localize the potential cause of the cough.

Patients who have had chronic cough warrant a chest radiograph whether they are smokers or not. It is important to recognize that the resolution of routine chest films may not be enough to identify patients with chronic interstitial lung disease or disorders of the airways and mediastinum.²¹ In these cases, and in the cases of patients in whom other chronic lung disease is suspected or in patients with warning symptoms, such as hemoptysis or concomitant weight loss, a noncontrast CT scan of the chest should be considered.

When the history and physical examination are suggestive of one of the more common causes of cough, treatment should be initiated accordingly. However, there are data to suggest that even without evidence of a likely cause, an empiric therapeutic trial of targeted medications may be a more efficient and cost-effective strategy in the evaluation of chronic cough.^{22,23} With this in mind, one would best approach the patient with cough in a step-wise fashion. First and foremost, all active smokers should be encouraged to stop smoking with the expectation of resolution of cough within several weeks. Any patient on treatment with an ACE inhibitor should have the medication discontinued and symptoms monitored for a few weeks.

Suspected Cause

If the history and physical examination are suggestive of UACS, treatment with an antihistamine or decongestant is favored.²⁴ In cases where there is a significant component of allergic rhinitis, an intranasal corticosteroid is tried. Treatment duration should last at least 2 weeks but can be extended. If there is a partial response to treatment and UACS is strongly suspected, CT of the sinuses and ENT referral is helpful.

Alternatively, if the leading diagnosis is asthma, pulmonary function testing with spirometry should be performed and the patient should begin a 2- to 4-week trial of a combination inhaled corticosteroid-long acting beta agonist.²⁵ If there is only minimal improvement with this inhaled regimen, a course of oral steroids is considered.

When LPR or gastroesophageal reflux disease is the cause of cough, treatment should consist of once-daily proton pump inhibitor for at least 8 weeks.²⁶ Further diagnostic testing for reflux disease is controversial, but in the evaluation of cough, laryngoscopy may be helpful in providing evidence of LPR.

Unidentified Cause

When the history, physical examination, and chest radiograph do not identify a likely cause of chronic cough, an empiric strategy of treatment is suggested.²⁷ The strategy starts with treatment of UACS as discussed previously. If no improvement, one would investigate for asthma with spirometry and perhaps methacholine challenge and treat empirically. Finally, the patient should undergo a therapeutic trial for reflux.

If symptoms persist at this point, further diagnostic testing should be considered including a CT scan of the chest (if not previously ordered) and referral to a specialist for invasive procedures. These might include a referral to otolaryngology for laryngoscopy, gastroenterology for pH probe monitoring, or pulmonary medicine for inspection bronchoscopy.

When no cause is identified, treating symptomatically for cough hypersensitivity syndrome with neurologic medications, such as gabapentin, has been shown to improve quality of life in patients with persistent chronic cough.^{28,29}

SUMMARY

Cough is one of the most common presenting symptoms in the primary care setting and has a significant impact of a patient's quality of life.³⁰ A targeted approach to the assessment and treatment of cough involves identifying concerning signs and symptoms, tailoring therapies for identified etiologies of cough, and initiating an empiric and staged trial of therapy toward the most common causes in situations where no plausible diagnosis is established. Careful consideration must be paid to the potential for multiple concomitant causes of cough and, occasionally, treatment for two or more of the more common causes may be needed in coordination to eliminate the symptom completely.

CLINICS CARE POINTS

- Cough is one of the most common presenting symptoms in the outpatient setting and is classified by its duration.
- Etiologies of cough vary depending on the duration of the symptoms and are often identified by a complete history.
- While acute and subacute cough are mostly often related to an infectious etiology, chronic cough is most commonly related to post nasal drip, asthma or gastroesophageal reflux disease.
- The evaluation of chronic cough is influenced by smoking status, current medications and concurrent symptoms.
- If there is a suspected cause of chronic cough, empiric treatment for this etiology is cost-effective and can prove therapeutic.
- When there is uncertain etiology of chronic cough, further evaluation with imaging modalities, such as CT scan, laryngoscopy, bronchoscopy or pH probe monitoring may be indicated.

DISCLOSURES

The authors have nothing to disclose.

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