

Chapter 10

Cough

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Introduction

Cough is one of the most common presentations to both primary and secondary care providers. In most cases, the cause of cough can be identified with history, physical examination, and simple diagnostic tests. Sometimes chronic cough can be challenging to diagnose and treat and will require referral to a specialist.

Decision-Making/Differential Diagnosis

Cough can be divided into acute, subacute, and chronic based on the duration of the symptom. Acute cough exists for less than 3 weeks, while chronic cough persists more than 8 weeks [1]. Acute cough is most commonly caused by upper

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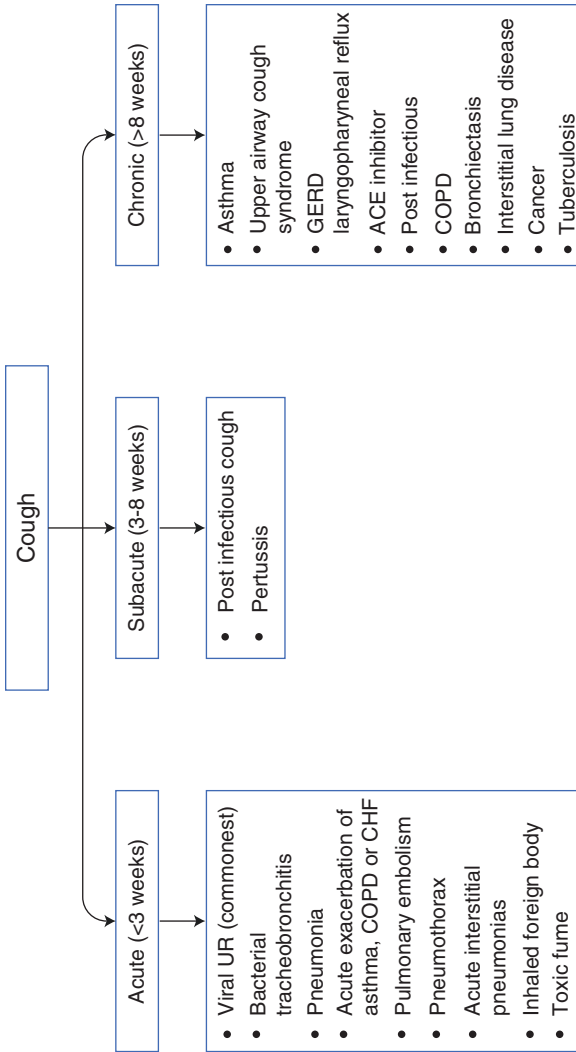


FIG. 10.1 Differential diagnosis of cough

respiratory infections. Other causes include pneumonia, bacterial tracheobronchitis, acute exacerbation of asthma, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), and pulmonary embolism (PE). It can also be an early presentation of chronic cough.

Subacute cough is most often due to postinfectious cough. *Bordetella pertussis* may play a significant role. Other etiologies overlap with chronic cough.

Chronic cough should be evaluated with a stepwise approach. After excluding the serious and obvious causes, diagnostic work-up should focus on asthma, gastroesophageal reflux disease (GERD), and rhinosinusitis (Fig. 10.1). More than one condition was found to be contributing to the persistence of chronic cough in up to 62% of patients [1].

Key History and Physical Exam

History taking should focus on the onset, duration of the cough, and presence of associated symptoms like postnasal drip, wheezing, dyspnea, and heartburn. One study suggested that the characteristics and timing of the cough are not usually helpful [2]. Significant sputum production points to an underlying pulmonary disease, e.g., bronchiectasis. Many patients report cough starting after an upper respiratory tract infection. Searching for triggers/aggravating factors including exposures, both at home and at work, tobacco use, and drugs may help identify the etiology. A history of past respiratory or heart disease should be elicited. A family history of cough can be seen in atopic patients and in those with an anatomic or neurological abnormality [3].

Acute cough is relatively easy to evaluate. When a patient presents with cough accompanied by fever, rhinorrhea, malaise, and myalgia/arthralgia with history of a sick contact and he/she looks relatively healthy, the likely diagnosis is upper respiratory infection.

Influenza has similar symptoms but is usually more severe and can only be differentiated from viruses causing common cold by specific testing. It can cause serious complications such

TABLE 10.1 CURB-65 score

Confusion
Urea >20 mg/dL
Respiratory rate \geq 30 breaths/min
Blood pressure (systolic <90 mmHg or diastolic \leq 60 mmHg)
Age \geq 65 years
1 point is assigned per criterion
0–1 points: risk of death <3%. Treat as outpatient
2 points: risk of death 9%. Consider hospitalization
\geq 3 points: risk of death 15–40%. Hospitalize and consider intensive care admission especially if 4 or 5 points

as pneumonia, acute respiratory distress syndrome, multi-organ failure, and death. Certain patients are more susceptible to poor outcomes, specifically elderly patients (>65 years) and those with chronic diseases like diabetes, heart failure, chronic pulmonary diseases including asthma and COPD, renal failure, cancer, immunosuppressive conditions, e.g., HIV, and those receiving immunosuppressive drugs [4].

The most important differential diagnosis is pneumonia. Pneumonia is usually not accompanied by rhinorrhea or other upper respiratory symptoms. Purulent sputum is commonly seen in pneumonia, but purulence is not specific to pneumonia (sinusitis and bronchitis can be also associated with purulent sputum). “Atypical pneumonia” presents often with a dry cough. Bronchial breathing or crackles can be present when auscultating the chest.

The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) recommend using a prediction score, either the CURB-65 score (Table 10.1) [5] or the pneumonia severity index (PSI) (Table 10.2) [6], to determine whether the patient can be treated as an outpatient or requires hospitalization [7]. The CURB-65 score is less well validated than the PSI but is easier to calculate [8]. Implementing the PSI results in fewer admissions without an

TABLE 10.2 Pneumonia severity index (PSI)

Sex

M (0 points)

F (-10 points)

Demographic factors

Age (1 point for each year)

Nursing home resident (10 points)

Comorbid illness

Neoplastic disease (30 points)

Chronic liver disease (20 points)

Heart failure (10 points)

Cerebrovascular disease (10 points)

Chronic renal disease (10 points)

Physical exam findings

Altered mental status (20 points)

Respiratory rate $\geq 30/\text{min}$ (20 points)Systolic blood pressure < 90 mmHg (20 points)Temperature < 35 °C (95 °F) or ≥ 40 °C (104 °F) (15 points)Pulse $\geq 125/\text{min}$ (10 points)*Laboratory and radiographic findings*Arterial pH < 7.35 (30 points)Blood urea nitrogen ≥ 30 mg/dL (20 points)Sodium < 130 mEq/L (20 points)Glucose ≥ 250 mg/dL (10 points)Hematocrit $< 30\%$ (10 points)Partial pressure of arterial oxygen < 60 mmHg or oxygen saturation $< 90\%$ (10 points)

(continued)

TABLE 10.2 (continued)

Pleural effusion (10 points)				
<i>Score</i>	<i>Risk class</i>	<i>Risk</i>	<i>Mortality rate (%)</i>	
≤50 years + no points	I	Low	0.1	Outpatient
≤70	II	Low	0.6	
71–90	III	Low	0.9	Outpatient or short hospitalization
91–130	IV	Moderate	9.3	Hospital
≥130	V	High	27	

TABLE 10.3 Differentiation among asthma, COPD, and CHF exacerbation

	Asthma	COPD	CHF
Cough	Dry/scant sputum	Purulent sputum	Frothy pink sputum
Orthopnea	+	+	+
Night symptom	Late night to early morning		Early night
Leg edema	–	–	Often
Weight gain	–	–	+

increase in adverse events [9]. Other factors should also be taken into consideration, e.g., the ability to reliably take oral medications, the patient's functional status, other comorbidities, and their social situation. Obtaining routine diagnostic tests to identify an etiologic diagnosis, e.g., blood and sputum culture, is optional for patients with community acquired pneumonia treated at home due to their low yield and small impact on clinical care [7].

Patients who are candidates for outpatient therapy and have no major comorbidities (chronic heart or lung disease,

diabetes, liver or renal disease, alcoholism, cancer, asplenia, or immunosuppression) and who have not taken antibiotics in the previous 3 months can be treated with macrolides or doxycycline. If there is a high incidence (>25%) of drug-resistant *Streptococcus pneumoniae* (DRSP) or if the patient has major comorbidities, a respiratory fluoroquinolone or a beta-lactam antibiotic (high-dose amoxicillin or amoxicillin-clavulanate is preferred; alternatives include ceftriaxone, cefpodoxime, and cefuroxime) plus either a macrolide or doxycycline is recommended [7]. The duration of treatment is a minimum of 5 days.

Acute exacerbation of asthma, COPD, or CHF is relatively easy to diagnose based on history, physical examination, and chest radiograph. All three can present with cough with dyspnea, orthopnea, and wheeze. Asthma tends to produce little sputum, while COPD exacerbation is associated with sputum (often purulent) and CHF with pink frothy sputum. Patients with asthma tend to get worse very early in the morning (Table 10.3).

The clinical presentation of PE is variable, but patients rarely present only with cough; patients also frequently complain of sudden onset dyspnea, pleuritic chest pain, hemoptysis, syncope, and symptoms of deep vein thrombosis (leg swelling and pain). Pulmonary embolism should always be included in the differential diagnosis in patients with risk factors, but these patients tend to be sicker and therefore more often visit emergency rooms rather than the outpatient office.

Other etiologies of acute cough include pneumothorax (sudden onset chest pain, dyspnea), some types of interstitial pneumonia such as acute interstitial pneumonia and hypersensitivity pneumonitis (dry cough with dyspnea), and pleural effusion (chest pain and dyspnea). The history should also reveal the presence of a foreign body or inhalation injury.

The most frequent cause of subacute cough is postinfectious cough. Severity of cough is quite variable and can be disabling in some cases (e.g., sleep disturbance, stress incontinence, post-tussive vomiting). In most cases, the patient recalls a preceding episode of fever and upper respiratory symptoms. Some report persistent nasal symptoms indicating

postnasal drip as a mechanism of cough, while severe whooping paroxysmal cough spells might suggest pertussis. Pertussis can be diagnosed by nasopharyngeal culture, polymerase chain reaction (PCR), and serology. It is important to determine the vaccination status and whether there is a possible exposure to young children to identify pertussis, where early treatment may be helpful [10].

Chronic cough is more prevalent in middle-aged females. Women have more frequent cough than men and have heightened cough reflex sensitivity. Chronic cough should be approached systematically. In up to 93% of patients, an etiology can be found [11].

The first step is to rule out the serious causes and the most common ones by history, physical examination, chest X-ray, and spirometry. The presence of weight loss, fever, night sweats, chest pain, and hemoptysis suggests serious diseases including lung cancer and tuberculosis [3]. Further work-up including sputum testing and chest computed tomography (CT) should be considered. Drug-induced cough, especially due to angiotensin-converting enzyme (ACE) inhibitors, is common (about 15%) [12] usually producing little sputum. It usually starts within 1–2 weeks after the initiation of ACE inhibitors but can be delayed up to 6 months. The cough subsides when the drug is discontinued usually within 4 weeks [13].

Bronchiectasis, COPD, and various parenchymal lung diseases can be identified by chest imaging and spirometry. Patients often have exertional dyspnea which can go unnoticed because they think it is from their smoking, so it is helpful to ask family about the patient's exercise capacity.

Localized or unilateral wheezing may suggest an endobronchial lesion (cancer or foreign body); chest CT should be ordered. The patient should be referred to a pulmonologist for bronchoscopy.

Once the obvious or serious causes are excluded, the three most frequent etiologies of chronic cough are (1) asthma, (2) GERD, and (3) rhinosinusitis [3, 14, 15]. These three conditions may present with cough and typical symptoms, but many patients have only cough; thus empirical (diagnostic) treatment is tried in many cases before an extensive work-up is undertaken (Fig. 10.2).

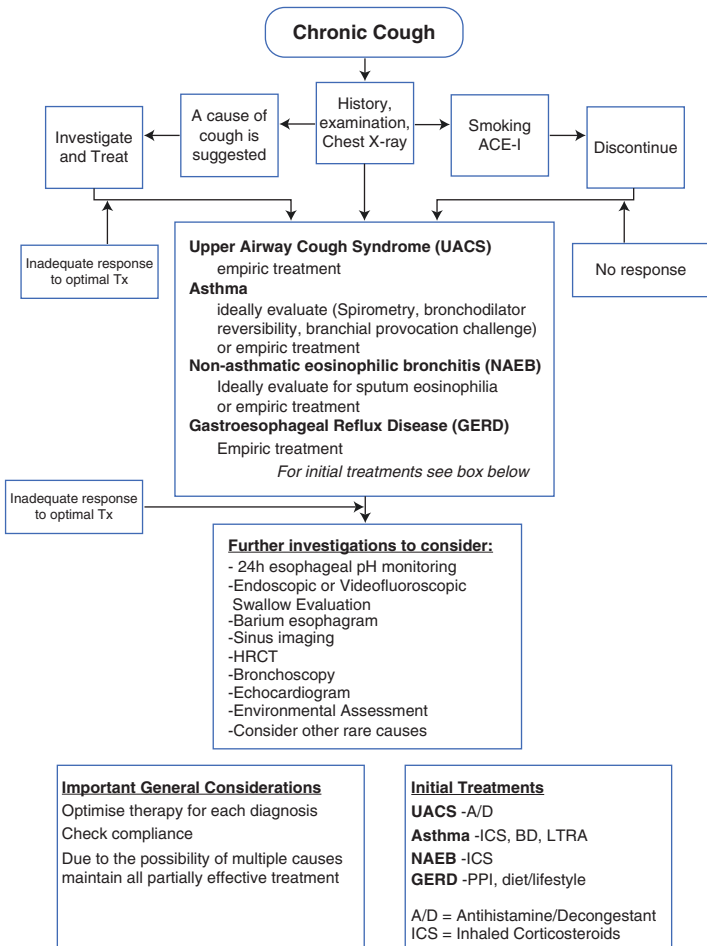


FIG. 10.2 Chronic cough algorithm for the management of patients ≥ 15 years of age with cough lasting >8 weeks. *ACE-I* ACE inhibitor, *BD* bronchodilator, *LTRA* leukotriene receptor antagonist, *PPI* proton pump inhibitor (Modified from Chest. 2006 Jan; 129(1 Suppl): 1S–23S. Irwin RS, Baumann MH, Bosler DC, et al. Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines)

Asthma usually presents with episodic dyspnea and wheezing in addition to cough. Occasionally, cough can be the only symptom, an entity known as “cough variant asthma.” A personal or family history of atopy or recent initiation of a beta-blocker can be helpful. Spirometry showing reversible airway obstruction is often seen in asthma. If the pulmonary function test is normal, a methacholine challenge test, sputum eosinophils, or elevated exhaled nitric oxide (NO) may assist diagnosis. It is important to try to identify possible triggers/allergens and encourage avoidance. Empiric treatment with inhaled steroids can be tried. Some patients may require oral glucocorticoids for 1–2 weeks [16]. Non-asthmatic eosinophilic bronchitis is difficult to distinguish from asthma clinically. Sputum eosinophilia without bronchial hyperresponsiveness is diagnostic [3].

If the patient with chronic cough has GERD symptoms, proton pump inhibitors (PPI) should be given. Empiric trial with PPI for chronic cough in the absence of GERD symptoms is controversial, and the evidence is lacking [14]. Twenty-four hour esophageal pH monitoring correlates well with cough but does not predict a response to treatment [14]. It may be indicated in patients who have failed to respond to empiric treatment and when the diagnosis is in doubt.

Patients with upper airway cough syndrome have nasal discharge, a sense of postnasal drip, or the urge to clear their throat leading to cough. Cobblestone appearance and secretions may be seen in the nasopharynx. Treatment with nasal steroids or antihistamines is recommended, especially for patients with a history of allergic rhinitis or chronic sinusitis. Saline nasal irrigation can be tried.

Uncommon causes of chronic cough include sleep apnea, chronic aspiration, recurrent tonsillitis, external ear canal processes (e.g., earwax impaction), and psychogenic. When the diagnosis remains unclear, referral to specialists (pulmonary, otolaryngology, or gastroenterology) should be considered.

Treatment

Once the etiology is found, the specific treatment can be instituted. Acute cough is usually self-limited and requires only reassurance. Patients have reported relief from the use of over-the-counter medications, e.g., dextromethorphan, menthol, and first-generation antihistamines [3]. There is no role for antibiotics except in pertussis where macrolides may decrease the duration of cough if initiated within the first 2 weeks of symptoms [10]. When influenza is suspected, treatment with antivirals should be initiated preferably within 48 h in patients who are very ill or at high risk for serious influenza-associated complications. Antiviral drugs have proven to reduce the duration of illness, ameliorate symptoms, and prevent serious complications and death [17].

As noted above, patients with chronic cough are treated empirically in many cases, but the evidence is weak, and the response rates are not perfect, creating frustration for both clinicians and patients. Symptomatic relief by antitussive medications is often suboptimal.

Clinical Pearls

- Cough should be approached based on the duration of the symptom.
- A thorough history and physical exam should give clues to the correct diagnosis in many cases.
- When patient presents with chronic cough and no other obvious symptoms, asthma, GERD, and rhinosinusitis should be considered.

Don't Miss This!

- Many serious diseases such as COPD, lung cancer, interstitial pneumonia, and tuberculosis present with cough. These should be excluded by history, physical examination, chest X-ray, and spirometry, before thinking about asthma, GERD, and rhinosinusitis.
- Weight loss, fever, night sweats, and hemoptysis suggest a serious disease like tuberculosis or cancer. Order a chest X-ray/CT and sputum for acid-fast bacilli.

- Unilateral wheezing suggests an endobronchial lesion, e.g., cancer or foreign body. Order a chest CT and refer to a pulmonologist for bronchoscopy.

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