

Management of Acute and Chronic Cough in the Ambulatory Care Setting

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Cough is a protective physiologic reflex of the respiratory system.¹ Its function is to remove foreign objects and abnormal excessive secretions from the respiratory tract.^{1,2} Cough also can be pathologic and is a symptom of many underlying diseases. In adults in the United States, it is the fifth most common reason for visits to ambulatory care units, accounting for 30 million visits yearly.² It is also one of the most frequent reasons for children's visits to pediatricians or primary care physicians.²

Because cough is a symptom (either transient or persistent) of many underlying serious illnesses, symptomatic cough suppressant treatment alone should never be prescribed.³ Every attempt should be made to find out the exact cause (or causes) of the cough before treatment is initiated. This article reviews the most commonly encountered causes for acute and chronic cough and general principles of treatment.

PHYSIOLOGY OF COUGH

Mucociliary Transport

The healthy tracheobronchial tree is covered by a 5- to 10- μ m thick mucosal blanket.⁴ Under this blanket, the cilia of the columnar epithelium beat in a synchronized fashion 1000 to 1500 times per minute, which moves the mucus (or a foreign body) towards the pharynx. Inhabitants of urban environments inhale 10,000 microorganisms (ie, bacteria, viral particles) each day.⁵ Some inhaled microbes are trapped in the mucosal blanket, and microbes larger than 5 μ m are pushed back towards pharynx by the ciliary action. The mucosal blanket and the mucociliary transport system provide a physical, physiologic, and immunologic barrier against invading pathogens.¹ When this mucociliary transport is disturbed or when the amount of secretion increases (eg, with inflammation), coughing helps to rid the body of these secretions.

Factors that interfere with mucociliary transport include smoking; the presence of thick, viscous secretions, as seen in cystic fibrosis; aspiration of gastric contents; and trauma associated with tracheal intubation.⁵ *Haemophilus influenzae* and *Bordetella pertussis* organisms

produce toxins that paralyze the ciliary motion. Influenza viruses avoid mucociliary clearance by attaching themselves to the epithelial surface. Other viruses produce neuroaminidases, and these enzymes degrade the mucus and prevent mucosal entrapment of viruses.⁵

Physiologic Stages of Cough

In humans, cough is under both voluntary and involuntary control and is produced in 4 stages: (1) an initial deep inspiration of air (up to 2500 mL); (2) a subsequent Valsalva maneuver manifested by forceful contraction of diaphragm, chest, and abdominal wall muscles against the closed glottis for approximately 0.2 seconds, increasing the intrathoracic pressure by up to 100 mm Hg; (3) sudden opening of the glottis followed by an outward blast of air (up to 12 L/sec); and (4) prolonged inspiration.²

Cough Reflex

The cough reflex has 5 components: cough receptors, an afferent nerve (the vagus nerve), the "cough center" (an ill-defined area in the medulla), efferent nerves (recurrent laryngeal nerve, phrenic nerve, and spinal nerves), and effector organs (the diaphragm, chest, and abdominal wall muscles).² Cough receptors are located along the entire laryngotracheobronchial tree, with the greatest number in the larynx. They also are located in the nose, paranasal sinuses, pleura, diaphragm, stomach, and pericardium. The external auditory canal and ear drum also contain cough receptors, supplied by Arnold's nerve (ramus auricularis nervi vagi). The known stimulants of the cough reflex are excessive secretions, aspirated foreign body, inhaled dust particles, noxious gases, and inflammatory changes secondary to infections and allergic conditions.²

The effectiveness of cough in clearing secretions may be limited by a variety of factors, including central

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Table 1. Sounds of Cough and Clues to Etiology

Sound of Cough	Possible Etiology
Harsh or hoarse cough	Laryngitis
Whooping cough	Pertussis
Croupy cough	Laryngotracheobronchitis
Brassy cough	Tracheal compression
Loud barking cough	Hysteria
Dry cough	Pharyngitis, early pneumonia, acute bronchitis
Wet cough	Pneumonia, bronchiectasis, chronic bronchitis
Aphonia	Vocal cord paralysis
Suppressed cough	Upper abdominal or thoracic pain

Table 2. Timing of Cough and Clues to Etiology

Timing of Cough	Possible Etiology
Early morning cough	Dry cough: asthma Wet cough: chronic bronchitis
Postprandial cough	Gastroesophageal reflux disease, tracheoesophageal fistula
Worse in evening	Exposure to irritants during the day (eg, work, school)
Worse at night	Postnasal drip, asthma
Cough that disappears during sleep	Psychogenic cough

depression of the cough reflex, neuromuscular abnormalities, a low respiratory flow rate (eg, in chronic obstructive pulmonary disease) and the presence of thick mucus (eg, in cystic fibrosis).¹

CLINICAL CHARACTERIZATION OF COUGH

Cough can be characterized as single or paroxysmal, and as dry or wet (ie, producing sputum). In addition, coughs can be differentiated clinically by the sound (Table 1), by the time of day that the cough is most troublesome (Table 2), and by the characteristics of the sputum produced, if any (Table 3).⁶ These characteristics are often clues to the cough's etiology.

CONDITIONS ASSOCIATED WITH ACUTE COUGH

Acute cough is defined as any cough condition lasting up to 3 weeks.⁷ Cough may be transitory during the course of the disease or may persist throughout the disease process. Viral infection of the pharynx, larynx,

Table 3. Sputum Characteristics and Clues to Etiology

Characteristic of Sputum	Possible Etiology
Mucoid	Asthma, cystic fibrosis, chronic bronchitis
Green or yellow	Bacterial infection
Melanoptysis	Coal miner's pneumoconiosis
Resembling anchovy paste	Amebic abscess
Hemoptysis	Bronchial adenoma, bronchogenic carcinoma, bronchitis
Foul smelling	Lung abscess, bronchiectasis
Thick, viscous	Cystic fibrosis

and nasal passages is the most common cause of the acute cough in all ages.⁷ In the United States, children experience an average of 6 to 8 episodes of acute respiratory illness annually, and adults experience 2 to 3 episodes annually, accounting for 30% to 50% of work time lost and 60% to 80% of school time lost.⁸

Common Cold and Influenza

The economic burden of the common cold in the United States has been estimated at \$2 billion annually in medications and visits to physicians.⁸ It also results in loss of more than of 30 million workdays and 30 million school days annually.⁸ The common cold is a viral illness, most commonly caused by rhinovirus (60% of cases). Approximately 15% of cases are caused by a coronavirus. Parainfluenza virus, respiratory syncytial virus, adenovirus, and enterovirus are the causative agents in the remaining cases.⁵

Commonly noted symptoms include mild-to-moderate cough, nasal and postnasal drainage, nasal obstruction, and sneezing. The common cold can generally be differentiated from influenza by the absence of fever, headache, and general aches and pain. In addition, influenza is often accompanied by severe cough and chest discomfort. Although the common cold and influenza are self-limiting diseases, they may lead to acute rhinosinusitis, bronchitis, and exacerbation of bronchial asthma.

Treatment is symptomatic. Antihistamines and decongestants given within 2 to 4 days after the onset of symptoms may be helpful; however, these drugs may produce significant anticholinergic side effects after 4 days of treatment.⁹ Antibiotics should not be given, even in the presence of mucopurulent discharge, unless the mucopurulent discharge persists longer than 10 to 14 days.¹⁰

Allergic Rhinitis

Roughly 40 million Americans (5% to 22% of the US population) suffer from allergic rhinitis. Approximately 2.5% of all patient care visits to physicians are related to this condition.¹¹ Each year in the United States, more than \$1 billion are spent on drugs and 34 million work days and 824,000 school days are lost owing to allergic rhinitis.

Allergic rhinitis may be either seasonal or perennial. Seasonal allergy is related to tree pollens in early spring, grass in the late spring, and ragweed and other flowers in the summer. Perennial allergy is usually caused by dust mites and molds.

Symptoms include sneezing, nasal congestion, rhinorrhea, mouth breathing, postnasal drainage, and cough. Nineteen percent to 38% of patients with allergic rhinitis also suffer from bronchial asthma; conversely, 60% to 78% of patients with asthma also have allergic rhinitis.¹² In addition, allergic rhinitis predisposes patients to rhinosinusitis,¹³ and rhinosinusitis and asthma co-exist in 30% to 70% of patients.¹²

Treatment of allergic rhinitis is primarily symptomatic, and it includes taking either sedating first-generation antihistamines in the night or nonsedating second-generation antihistamines during the day. A decongestant may be added to this. Intranasal steroids are also very helpful. Allergy testing and hyposensitization therapy may be required in severe cases.

Rhinosinusitis

Rhinosinusitis is inflammation involving both the nasal passages and contiguous sinuses. It has been estimated that 15% of Americans suffer from rhinosinusitis annually. Thirty two million of them have acute rhinosinusitis and 2 million have chronic rhinosinusitis. In the United States, \$3 billion are spent on over-the-counter medications each year, 31 million work days and 31 million school days are lost annually, and 11.6 million physician visits are made each year for the care of rhinosinusitis.¹⁴

Viral rhinosinusitis is 20 to 200 times more common than bacterial rhinosinusitis.¹⁵ Acute bacterial rhinosinusitis occurs when the osteomeatal complex is obstructed, resulting in stagnation of mucus and secondary bacterial infection. Inflammation limited to 4 weeks is termed *acute rhinosinusitis*. Inflammation lasting for 4 to 12 weeks is termed *subacute rhinosinusitis* and inflammation lasting for more than 12 weeks is termed *chronic rhinosinusitis*. *Recurrent acute rhinosinusitis* describes an infection that recurs at least 4 times each year with each episode lasting for more than 7 to 10 days. Sudden worsening of chronic rhinosinusitis is

known as an acute exacerbation of chronic rhinosinusitis.

Rhinosinusitis is a clinical diagnosis. Symptoms of rhinosinusitis are similar to those of other upper respiratory tract infections. Cough is present in all forms of rhinosinusitis. Postnasal drainage and persistent daytime cough are common. Tenderness over the paranasal sinuses, absence or decreased light transmission upon transillumination, and presence of purulent discharge in the middle meatus are all helpful signs in diagnosing acute bacterial rhinosinusitis. Radiographs are needed only for severe or persistent infections or when surgery is indicated. Computed tomography (CT) scans are far better for imaging the sinuses than are conventional radiographs.

Clinical diagnosis of bacterial rhinosinusitis is based on the presence of symptoms (ie, cough, fever, facial swelling, and facial pain) for more than 10 to 14 days. Because antibiotics are indicated only in the treatment of bacterial rhinosinusitis, accurate diagnosis is important to avoid indiscriminate use of antibiotics. When indicated, antibiotics should be selected to cover the most common causative organisms, including *Streptococcus pneumoniae*, *H. influenzae*, and *Moraxella catarrhalis*. Nonbacterial rhinosinusitis is managed with antihistamines, decongestants, and/or intranasal steroid sprays.

Pharyngitis

Approximately 85% of pharyngitis cases are caused by viruses; the other 15% are caused by group A streptococci. Cough, rhinorrhea, hoarseness, conjunctivitis, and dysphagia are symptoms of viral pharyngitis. In streptococcal pharyngitis, cough is often absent and high fever and pharyngeal inflammation with exudate are common. An antigen-detection test and/or throat culture should be performed to differentiate the viral pharyngitis from the streptococcal form.¹⁶ Streptococcal pharyngitis should be treated with antibiotics within 9 days of onset of infection to prevent acute rheumatic fever.

Acute Bronchitis

Cough with clear or purulent sputum is the major clinical symptom of acute bronchitis.¹⁶ The cough associated with acute bronchitis usually subsides within 5 to 7 days; when it lasts longer than 2 weeks, it warrants further evaluation. In healthy adults, viruses cause nearly all cases of acute bronchitis. Only rarely does bacterial bronchitis occur in patients other than those who are immunosuppressed.¹⁶ Causative bacteria include *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *B. pertussis*. Cough secondary to *Mycoplasma*

pneumoniae infection can last up to 4 to 6 weeks and it may produce scanty mucoid sputum. Gram stain of sputum shows no or sparse microorganisms.¹⁶ Bronchitis secondary to *C. pneumoniae* may be associated with pharyngitis and laryngitis. It usually presents with low-grade fever, hoarseness, and a persistent hacking cough with or without mucoid sputum. It is more common in healthy children and young adults.¹⁶

Pertussis, otherwise known as whooping cough, is characterized by a barking cough. Although it usually occurs in childhood, it may occur in adults and should be suspected if the cough lasts longer than 3 weeks, especially in individuals who have not been immunized against pertussis. The cough in adults may be so severe that the patient has difficulty completing a sentence.¹⁶ In children, the cough is usually paroxysmal, consisting of 5 to 20 short coughs of increasing intensity followed by a distressing prolonged inspiratory whoop.

The treatment of acute bronchitis is symptomatic and includes cough suppressants. Antibiotics are indicated only in patients with prolonged cough and severe constitutional symptoms. Patients with acute bronchitis caused by *Mycoplasma pneumoniae*, *C. pneumoniae*, and *B. pertussis* require antibiotic therapy.

Community-Acquired Pneumonia

Community-acquired pneumonia is the sixth-leading cause of death in the United States and is the primary cause of death from infection. Fever, cough with purulent sputum, leukocytosis, and infiltrate visible on chest radiograph help to differentiate this condition from acute bronchitis. Community-acquired pneumonia is caused by *S. pneumoniae* in 65% of cases, *Mycoplasma pneumoniae* in 7%, *C. pneumoniae* in 9%, *H. influenzae* in 12%, and gram-negative bacilli in 1% of cases.¹⁷ The hallmark of pneumonia caused by *Mycoplasma pneumoniae* is severe disabling paroxysmal cough, the onset of which is preceded by 2 to 3 days of low-grade fever.

CONDITIONS ASSOCIATED WITH CHRONIC COUGH

Any cough persisting longer than 3 weeks is defined as chronic cough.⁸ Cigarette smoking is the most common cause of chronic cough; however, smokers generally do not seek medical help for cough alone. Postnasal drip, asthma, and gastroesophageal reflux disease (GERD) are the most common causes of cough in the outpatient setting, accounting for more than 90% of diagnoses.¹⁸ In nonsmokers with normal chest radiographs not taking an angiotensin-converting enzyme inhibitor, this percentage increased to 99.4% of diagnoses.¹⁸ Chronic cough in immunocompromised pa-

tients is not discussed here, neither are infectious causes nor other, less common causes of chronic cough.

Postnasal Drip

Postnasal drip is the most common cause of chronic cough in nonsmokers who seek medical help. It is present in 40% to 50% of cases.¹⁶ The conditions producing postnasal drip are allergic rhinitis, vasomotor rhinitis, rhinosinusitis, and nasopharyngitis. The cough is produced by stimulation of the irritant receptors in the oropharynx by the dripping mucus or pus.

Treatment of postnasal drip starts with sustained-action antihistamines and decongestants. If the patient does not improve after 1 week, intranasal steroids should be added. If the patient has not improved by the third week, a sinus CT should be obtained to look for evidence of rhinosinusitis. If rhinosinusitis is evident, antibiotics should be prescribed for up to 6 weeks. If these measures fail, an otolaryngologist should be consulted.

Asthma

Asthma is a chronic inflammatory disease of the airways. It is associated with increased airway responsiveness and variable airway obstruction, which is reversible with or without treatment. The classic asthma attack lasts up to several hours and is followed by prolonged cough. Patients with asthma may present with cough-variant asthma, which consists of cough without wheezing. The cough is dry and occurs around the clock. It is worsened by cold air, exercise, seasonal allergies, and upper respiratory tract viral infections. The cough in asthma and cough-variant asthma is caused by stimulation of the cough receptors by mechanical changes secondary to bronchoconstriction.

Most patients with asthma have a family history of asthma or other atopic conditions. Asthma is categorized clinically by severity and frequency of symptoms.¹⁹ The diagnosis is supported by improvement of asthma symptoms with β -agonist inhalation therapy and by a positive methacholine inhalation challenge test.

Guidelines for the treatment of asthma recently have been updated.¹⁹ A mnemonic for the components of an asthma treatment plan is as follows (ASTHMA)²⁰:

Activity or life style modification (stop smoking, exercise, influenza and pneumococcal vaccines)

Self-monitoring of peak flow rates

Trigger control

Health-care partnership with patient (primary care physician follow-up)

Medications (long-term controller therapy with inhaled steroids)

Action plan (written action plan)

GERD

Ten percent to 40% of cases of chronic cough are related to GERD.²¹ GERD is associated with both chronic cough and asthma, and often these patients do not have classic symptoms of GERD (eg, heartburn). GERD may be present in 34% to 89% of patients with asthma.²¹

Cough in patients with GERD stems from the presence of acid in the distal esophagus, which stimulates inflamed distal esophageal mucosal receptors to induce an esophageal-tracheobronchial reflex. Cough may be the only symptom in many patients with GERD, especially in geriatric patients. When patients with chronic cough also complain of typical heartburn, no other testing is needed and management of GERD can be started immediately.²¹ Medical antireflux therapy such as a proton pump inhibitor should be instituted; other measures to reduce acid reflux include avoiding spearmint, chocolate, hot spicy food, and tomato sauce; not eating at least 2 to 3 hours before going to bed; eating smaller, more frequent meals; and elevating the head of the bed during sleep.

When the diagnosis of GERD is not obvious, a 24-hour pH monitoring of the esophagus to document the acid reflux and a methacholine provocative study to rule out asthma are indicated.

Cigarette Smoking and Chronic Bronchitis

Cigarette smoking is the most common cause of chronic cough; however, smokers generally do not seek medical help for their cough. The cough in smokers is usually caused by chronic bronchitis. Smoking inhibits ciliary activity in both the nose and the tracheobronchial tree, decreasing mucociliary clearance. Smoking also increases mucus volume and viscosity. Cough becomes necessary to clear the mucus from tracheobronchial tree.

Chronic bronchitis is characterized by chronic cough and sputum production for at least 3 months per year for 2 consecutive years. Smoking causes enlargement of tracheobronchial mucous glands and hyperplasia of goblet cells in the small airways. These changes in turn produce excessive mucosal secretions leading to cough.

Cessation of smoking is the key to successful management of cough in patients with chronic bronchitis. Other treatments include use of bronchodilators (nebulizer or metered-dose canister) and antibiotics during acute exacerbations secondary to bacterial infection.

SYMPTOMATIC TREATMENT OF COUGH

Cough is addressed by treating the underlying pathology, and treatment principles for specific acute and chronic cough conditions are described above. General principles for the symptomatic treatment of cough are provided here. Two classes of cough medications are available: antitussives and expectorants. Antitussives are used in patients with dry cough to suppress the cough. Expectorants are used in patients with productive cough to make the cough more effective.

Antitussives

Dextromethorphan, codeine, and morphine suppress cough by increasing the threshold and/or latency of the cough center. Among these, dextromethorphan is preferred because it is as effective as codeine, but safer, with no central nervous system depressant effects and no significant drug-drug interactions. The usual adult dose is 10 to 20 mg every 4 to 6 hours. At night, the dosage may be increased to 30 mg, which extends the duration of action to up to 10 hours. Morphine is reserved for serious incurable illnesses, such as lung cancer, in which cough serves no useful purpose.

Demulcents act as antitussives by forming a protective coating over the irritated areas like pharynx. They are extremely helpful in cough conditions arising above the larynx. Acacia, licorice, glycerin, honey, and wild cherry are some of the commonly used demulcents. They are used either as lozenges or syrup.

Expectorants

Expectorants either decrease the viscosity of bronchial secretions or increase the amount of secretions. The former allows secretions to be coughed out more easily, whereas the latter exerts a demulcent effect on the bronchial epithelium. Guaifenesin is the most commonly prescribed expectorant. The usual dosage for adults is 100 to 200 mg taken 3 times daily. It has no serious side effects. Adequate hydration is the most important aspect of expectorant therapy.

COMPLICATIONS OF COUGH

Cough can lead to a number of complications related to the increases in intrathoracic, intra-abdominal, and intracranial pressure that occur during coughing. More frequently encountered complications include fractured ribs, stress incontinence, pneumothorax, retinal vessel rupture, chest and abdominal wall strain, costochondritis, and inguinal hernia (either development of a new hernia or enlargement or incarceration of an

existing hernia). Rare complications include cough-induced syncope, cough headache, bronchospasm, coronary artery disease, and emphysema.

CONCLUSION

Cough is a symptom of many underlying diseases and is a common reason for ambulatory care visits. Cough may be either acute or chronic. The most common causes of acute cough are viral infection and allergic rhinitis. The most common causes of chronic cough are smoking, postnasal drip, asthma, and GERD. Cough ideally is managed by treating the underlying condition, which can be determined in the majority of cases. Symptomatic treatment may be indicated in some cases and consists primarily of antitussive and expectorant therapy.

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