13

Acute Cough

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CONTENTS

CASE PRESENTATION

KEY CLINICAL QUESTIONS

LEARNING OBJECTIVES

Introduction

PATHOPHYSIOLOGY

DIFFERENTIAL DIAGNOSIS

DIAGNOSIS

TREATMENT

FUTURE DIRECTIONS

REFERENCES

CASE PRESENTATION

A 62-year-old man, Mr. M., comes to your office with a chief complaint of a cough. He states that it started about 1 week ago with a "runny nose and scratchy throat." The cough is dry, nonproductive, and is interfering with the patient (and his wife) being able to get a full, restful night's sleep. Mr. M. denies any other symptoms, such as headache, sinus pressure, chest pain, and shortness of breath, but thinks that he may have had a fever "off and on the last few days." He has taken Tylenol® and has been drinking fluids, but his cough won't go away. The patient is requesting an antibiotic to "get this thing kicked out of my system." Mr. M. states that he is "tired of people at work looking at me like I have the plague."

Mr. M.'s past medical history is significant for hypertension and type 2 diabetes mellitus. Both his blood pressure and blood sugars have been under good control and are treated with lisinopril/hydrochlorothiazide and metformin, respectively. He takes an occasional ibuprofen for "aches and pains that come with

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aging." Family history is significant for a father, brother, and uncle with hypertension and a mother with diabetes. Mr. M. works full time as a postal employee, quit smoking 10 years ago (35 packs per year history), drinks occasionally, and has never used street drugs. He exercises by walking in his job as a mail carrier and has been married for 37 years with three grown, healthy children.

KEY CLINICAL QUESTIONS

- 1. What are the possible etiologies of this patient's cough?
- 2. What other history is necessary to rule out any serious causes of acute cough?
- 3. What is the proper evaluation for this patient?
- 4. Should this patient be treated with antibiotics or other prescription medications?

LEARNING OBJECTIVES

- 1. Understand the pathophysiology of cough.
- 2. Recognize the main etiological causes and symptomology of acute cough illness.
- 3. Become familiar with guidelines for the diagnosis of patients with acute cough illness.
- 4. Understand of the main treatment modalities available for acute cough illness.

INTRODUCTION

According to the Centers for Disease Control and Prevention, cough is one of the main reasons for patients to visit their physician or the emergency department. A Centers for Disease Control and Prevention survey of outpatient departments in US hospitals reported that 10.2% of the 84.6 million visits were owing to symptoms referable to the respiratory system, cough being the principal motivator for the visit. This same survey showed that the primary diagnoses for these patients were acute upper respiratory infections (URIs) (1). In 2002, cough was responsible for bringing 3 of the 110 million patients to emergency departments in the United States—11.8% of which had diagnoses of ill-defined conditions and diseases of the respiratory system (2). Another study conducted to examine the epidemiology of and recent trends in outpatient visits for infectious disease, reported that approximately 200 out of every 1000 office visits were related to URIs (3).

Even more striking is the economic impact cough has in the United States. One study showed the cost of non-influenza-related viral respiratory tract infection to be about \$40 billion annually in direct (health care resources, cost of over-the-counter [OTC] medications, outpatient physician visits, use of prescription medications) and indirect (productivity losses, absenteeism work) costs (4). A 1997 study concluded that the annual cost per capita employer expenditures for patients with respiratory infections totaled \$4397. The study reported estimates of

the total of financial burden to employers to be a whopping sum of \$112 billion spent on medical costs and lost time from work (5).

The individual "cost" of cough can be high as well. There are many "cough complications" that can become problematic to patients: perceiving something is wrong (98%), exhaustion (57%), feeling self-conscious (55%), insomnia (45%), lifestyle change (45%), musculoskeletal pain (45%), hoarseness (43%), excessive perspiration (42%), and urinary incontinence (39%) (6). Cough and its causes have a detrimental impact on individuals and on our health care resources.

PATHOPHYSIOLOGY

Cough is the result of the cough reflex, which can simply be described as a sudden rapid expulsion of air whose main purpose is to clear the airways from inhaled foreign bodies and to enhance mucociliary clearance in cases of impaired ciliary function and excessive mucus production (6). Cough is induced by inflammation or irritation of the larynx, trachea, or bronchi. (To review the physiology of the cough reflex, please *see* Chapter 14.)

Cough is a symptom whose physical characteristics (dry, productive, whooping, staccato, and so on) can often give valuable clues to the disease underlying this symptom (7). Furthermore, an effective cough depends on the ability to achieve high gas flows and velocities through the airways. Expiratory or inspiratory muscle weakness, disordered chest wall motion, altered mucus rheology, and altered mucociliary function all may affect coughing and must be kept in mind when evaluating a patient with pre-existing conditions (6).

Cough is classified into categories using time as its chief differentiator. Acute cough is defined as any acute, self-limiting episodes of cough lasting less than 3 weeks. Chronic cough is a persistent cough lasting longer than 8 weeks. Subacute cough defines the period of time between acute and chronic—a 3- to 8-week intermediate period (6,8,9). Although all coughs go through an "acute" phase, this chapter focuses on the most common and life-threatening causes of acute cough. The chronic causes of cough, such as gastroesophageal reflux disease, chronic obstructive pulmonary disease (COPD), asthma, postnasal drip, and cystic fibrosis, are addressed in Chapter 14.

DIFFERENTIAL DIAGNOSIS

Cough can literally be caused by hundreds of disease processes and agents—an overwhelming task to address in one chapter. One way of tackling this problem is to separate the possible etiologies into age groups. In this section, we will look at causes of acute cough in adults and children and the special circumstances to keep in mind when developing a differential diagnosis for these different age groups.

	<u> </u>
Virus	Bacteria
Rhinovirus	Streptococcus pneumonia
Adenovirus	Haemophilus influenza
Coronavirus	Staphylococcus aureus
Influenza A	Bordetella pertussis
Influenza B	Mycoplasma pneumonia
Parainfluenza	Chlamydia pneumonia
Respiratory syncytial virus	Pseudomonas pneumonia
Cocksackie A21	Legionella pneumonia

Table 1 Agents of Respiratory Illness

Adult Acute Cough

Published studies on the spectrum and frequency of causes of acute cough do not exist, but overwhelming clinical experience indicates that postnasal drip syndrome because of URIs is the most common cause (6). For adults, acute cough is most commonly seen in the common cold, acute bacterial sinusitis, acute bronchitis, pertussis, COPD exacerbations, allergic rhinitis, and environmental irritant rhinitis (6,8–10). Less common causes for acute cough are asthma, congestive heart failure, pneumonia, aspiration syndromes, and pulmonary emboli (6,8,9).

The most common etiology of the common cold or rhinosinusitis is viral in origin (6,8,9). The top suspects are usually rhinovirus, adenovirus, and coronavirus (see Table 1). Patients with the common cold present with an acute respiratory illness characterized by symptoms such as rhinorrhea, sneezing, nasal obstruction, postnasal drip, with or without fever, lacrimation, irritation of their throat, and a normal chest exam (9).

Bacterial rhinosinusitises are sometimes difficult to clinically differentiate from their viral cousins. URI are suggestive of a bacterial cause when they have at least two of the following signs and symptoms: a maxillary toothache, purulent nasal secretions, abnormal findings on transillumination of any sinus, poor response to nasal decongestants, and a history of discolored nasal discharge (6,9). Table 1 also contains the most likely agents in bacterial URIs.

Acute bronchitis is an acute cough syndrome, predominately caused by the viruses and less commonly by the bacteria listed in Table 1. Rhinovirus infection is the most common and can lead to exacerbations in asthma, COPD, and cystic fibrosis (8). The mechanism of this cough is a transient bronchial hyperresponsiveness and the primary symptoms of this process include phlegm production and wheezing (8,10,11).

Cough resulting from allergic rhinitis or environmental irritant rhinitis is caused by inflammation of the respiratory passages by some agent to which the patient is sensitive. There are countless numbers of irritants that cause this condition and they may be unique from patient to patient. Some of the more common agents are dog and cat hair, pet dander, dust mites, pollens, molds, and feathers. These irritants cause excess mucus production and postnasal drip, which triggers the cough reflex. A good history can identify these mechanisms as the culprits for the cough (6).

Pertussis infection is present in up to 10 to 20% of adults with cough illness of longer than 2 to 3 weeks (10). It initially presents as a URI during the catarrhal stage before involving the lower respiratory tract in the paroxysmal stage of the illness. No clinical features distinguish pertussis from nonpertussis infection in adults who were immunized against pertussis as children (6,10).

As stated earlier in this section, acute cough can be the presenting manifestation of life-threatening disease such as pneumonia, congestive heart failure, pulmonary emboli, or aspiration (6). In-depth discussion of these diseases is beyond the scope of this chapter, but ruling out pneumonia is the primary objective in evaluating adults who have acute cough with comorbidities (nursing home resident, elderly, immunocompromised, and so on) and for whom asthma is unlikely. About 5 to 10% of adult patients with acute tracheobronchitis develop bacterial infection deep in the lungs (8). In adults without comorbidities, the main agents causing pneumonia are *Streptococcus pneumonia*, *Haemophilus influenza*, and *Moraxella catarrhalis*, and in young adults, *Mycoplasma pneumonia*.

It is especially important to have a high index of suspicion for pneumonia in the elderly and immunocompromised patients with acute cough because the classics signs and symptoms that accompany this disease sometimes do not express themselves. The abnormalities that would reveal the possible presence of pneumonia are a heart rate of more than 100 beats per minute, respiratory rate of more than 24 breaths per minute, or oral body temperature higher than 38°C (6,8,9). The most common agents in elderly patients listed in order of frequency are *S. pneumonia*, *H. influenza*, Gram-negative agents, *Staphylococcus aureus*, *Chlamydia pneumonia*, *M. pneumonia*, *Legionella pneumonia*, and respiratory viruses (8,9,12). For persons who are immunocompromised, especially persons with HIV, *Pneumocystis carinii* and *Mycoplasma tuberculosis* should be considered (6).

Child Acute Cough

At least 90% of children with cough have a respiratory tract infection caused by common cold, croup, bronchitis, bronchiolitis, whooping cough, or pneumonia (13). The most common etiologies of acute cough appear to be the common cold and environmental irritants (6).

Families of children with recurrent episodes of cough frequently bring their children to their health care provider because it can be quite a disturbing and disruptive symptom to both the family and child. Although persistent moist or productive cough requires investigation, isolated nonproductive cough in the absence of evidence of airway obstruction or other evidence of systemic disease may not be abnormal (14). There is evidence to suggest that persistent cough in children is more likely related to exposure to indoor and outdoor atmospheric pollution than to atopy associated with asthma (14).

As in adults, the most common cause of the common cold is virus. Rhinovirus is the top culprit, responsible for 25 to 40% of the cases (14) and occurring in the early fall months (15). Parainfluenza peaks in the late fall, respiratory syncytial virus in the early winter, and influenza in the late winter/early spring (15). Children experience 3 to 8 colds per year and 10 to 15% have at least 12 colds per year, usually associated with attendance at day care center (14). As in adults, the symptoms usually include rhinorrhea, cough, sore throat, with or without fever, malaise, myalgias, and mucopurulent nasal discharge. As a result of immature immune systems, infants may present with symptoms slightly different than older children, including high fevers, irritability, decreased feeding, and sleeping patterns (14).

One study showed that 5 to 13% of the viral respiratory tract infections will become complicated by acute bacterial sinusitis. In children, 80% of bacterial rhinosinusitis are preceded by a viral respiratory tract infection, whereas 20% are complications from allergic rhinitis (16). The leading causes are *S. pneumonia*, *H. influenza*, and *M. catarrhalis*. As in adults, the presence of mucopurulent nasal drainage with unilateral or maxillary face pain, fever, headache, or maxillary or periorbital swelling, most likely have a cough because of this bacterial infection (16).

Croup is a URI that typically occurs in children ages 1 to 5 years and is characterized by respiratory obstruction with a characteristic barking cough with hoarseness and inspiratory stridor (13). The etiology is most commonly parainfluenza virus and tends to occur the autumn. Bronchitis or tracheobronchitis, as in adults, is a syndrome involving the lower respiratory tract in which there is transient bronchial hyperresponsiveness. The primary symptom is a cough productive of phlegm and is most often caused by viral agents.

Bronchiolitis epidemics tend to occur in winter and spring with respiratory syncytial virus being implicated in many cases. It has a very similar presentation to asthma, with coughing and wheezing being the primary symptoms. Whooping cough is characterized by distinctive paroxysms of cough with vomiting and episodes of apnea in young children (13).

Community-acquired pneumonia is one of the most serious infection-producing coughs in infants and children with an annual incidence of 34 to 40 cases per

Table 2 Common Causes of CAP

Age	Common causes
Birth to 20 days	Escherichia coli
·	Group B Streptococcus
	Listeria monocytogenes
3 weeks to 3 months	Chlamydia trachomatis
	Streptococcus pneumonia
	Adenovirus
	Influenza virus
	Parainfluenza viruses 1, 2, 3
	Respiratory syncytial virus
4 months to 5 years	Chlamydia pneumonia
	Mycoplasma pneumonia
	S. pneumonia
	Adenovirus
	Influenza virus
	Parainfluenza virus
	Rhinovirus
	Respiratory syncytial virus
5 years to adolescence	C. pneumonia
	M. pneumonia
	S. pneumonia

Modified from ref. 17.

CAP, community-acquired pneumonia.

1000 children in Europe and North America (17). The etiology is age-dependant. Table 2 shows the most common causes for the specific age group. The strongest predictors of pneumonia in children are fever, cyanosis, and more than one of the following signs of respiratory distress: tachypnea, cough, nasal flaring, retractions, rales, and decreased breath sounds. Children without fever or symptoms of respiratory distress are unlikely to have pneumonia (17,18).

Another cause of acute cough in children that can be potentially life threatening is the inspiration of a foreign body (6). This particular etiology should be on top of a differential list, especially with children 6 months to 3 years of age.

As with adults, there may be acute cough as an indicator of the onset of a more chronic condition in a child. Congenital malformation, reactive airway disease, asthma, cystic fibrosis, congestive heart failure and gastroesophageal reflux disease need to be kept in the differential diagnosis of a child with acute cough (18). These conditions tend to produce a more chronic cough in children and are discussed in Chapter 14.

DIAGNOSIS

In children or adults, a clinical approach is recommended for the initial evaluation of acute cough (6,8,9,13,14). As with all other evaluations, this approach consists of history and physical exam. In addition, keeping in mind the estimated frequency of conditions, based on the epidemiological data as well as clinical experience is key to a successful diagnosis (6,9). Most patients who present to their physician with a cough of less than 3 weeks' duration, rhinorrhea, sneezing, nasal obstruction, postnasal drip, with or without fever, lacrimation, irritation of their throat, and a normal chest exam will most likely have a viral respiratory infection (6,8,9).

In the diagnosis of a patient with acute cough, the important questions become the following:

- 1. Is this acute cough is a symptom of something that may be life threatening to the patient?
- 2. Is this a high-risk patient for which I have to look at less common causes for acute cough?
- 3. Does this patient have any symptoms besides acute cough that raise a red flag?

The evaluation of the seriousness of a patient's condition begins as the soon as the practitioner enters the room with observations such as the patient's disposition, breathing pattern, and speech patterns (Table 3). High-risk patients, such as the very young, elderly, nursing home patients, and the immunocompromised, receive an automatic high index of suspicion for a more in-depth look.

Normal history questions should include: past medical history (conditions, medications, hospitalizations, and so on); recent immunizations (pneumovax, influenza); and social history (tobacco, alcohol, drugs, recent travel, occupation, environmental exposures). Red flags in the history of present illness and physical exam such as fever, shortness of breath, orthopnea, tachypnea, tachycardia, pleuritic chest pain, rales, rhonchi, mucopurulent nasal discharge, sinus pain and pressure, and mental status changes should trigger further exploration beyond the simple clinical evaluation. Complete blood count, Chem 7, and chest X-rays would be warranted in many cases to determine if a more malevolent process than the common cold is at work. It cannot be overstressed that ruling out pneumonia is a primary objective in evaluating high-risk adults.

In the case of infants and children important information to find out in the history would include prenatal and birth history, growth and development, hospitalizations, immunizations, day care attendance, exposure to infectious agents, family history, antibiotic treatment within the previous month, recent travel, recent choking episodes and changes in feeding, and sleeping and diapering patterns (6,17,18). Red flags on the physical exam that warrant further investigation would be fever, cyanosis, pallor, dehydration, tachycardia, grunting, nasal

organ and symptoms of a line i meatening cough		
Adults/children	Infants/young children	
Position—lying down/sitting?	Irritable/crying?	
Coloring?	Inconsolable?	
Affect/mood?	Listlessness? Moving?	
Level of distress?	Able to produce a smile?	
Breathing rapidly?	Working to breathe?	
Sweating/shivering?	Coloring?	
Able to talk without effort?	Sweating/shivering?	

Table 3
Signs and Symptoms of a Life-Threatening Cough

flaring, mucopurulent nasal discharge, rales, retractions, tachypnea, use of accessory muscles for breathing, and wheezing (6,13,17,18).

As in adults, when history and physical exam indicate it, complete blood count, Chem 7, and chest X-rays would be helpful in determining the more serious causes of cough, especially pneumonia.

TREATMENT

As a first line in therapy, most practitioners will recommend OTC medications as a way of initially addressing acute cough. These OTCs include antitussives, expectorants, mucolytics, antihistamines, antihistamine—decongestion combinations (Table 4). Practitioners will typically recommend a trial of these OTCs and if the patient does not improve or worsens, he or she will then look to other causes for the illness.

No good evidence for or against the effectiveness of OTC medications for acute cough exists. Even when randomized, control trials treating adults and children with acute cough had significant results, the effect size was small, there was doubt of clinical relevance, or there were conflicting results between trials in each medication group (8,19,20). Most preparations, however, appear to be safe based on those studies reporting side effects (8,19,20).

Despite the predominately viral cause of acute cough, antibiotics are frequently prescribed to children and adults (4,10,11). At times, patients expect and demand a medicine that will alleviate or end their symptoms and many times practitioners give into this pressure. Antibiotic prescriptions for acute bronchitis, which are primarily viral and cause an acute cough illness, range from 50to 80% (11). Because of the lack of efficacy and low complication rates, antibiotic treatment of children with URIs is not supported by current evidence from randomized trials (21). Specifically, randomized, placebo-controlled trials conducted in the past 25 years have failed to support the role of antibiotics in the treatment of

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Category	OTC medication
Antitussives	Dextromethorphan
	Codeine
Expectorants	Guaifensin
Mucolytics	Bromohexine hydrochloride
Antihistamines	Loratidine
	Chlorpheniramine
	Bromopheniramine
Decongestants	Pseudoephedrine

Table 4
Examples of Commonly Used OTC Medications

OTC, over the counter.

acute bronchitis, either in the reduction of severity of symptoms (acute cough) or the duration of this condition (10,11). Meta-analysis of these trials report no impact of antibiotics on illness duration, activity limitation, or work loss, but have shown that the inhaled bronchodilator albuterol decreases the duration of the cough (8,10,11).

Figure 1 shows one proposed algorithm for the evaluation and management of adults with acute cough illness (10). Although the end point on the right side of this flow chart is "acute bronchitis," common cold or URI with its appropriate treatment can easily be substituted.

The treatment of other common causes of acute cough are summarized below:

- 1. In allergic rhinitis/environmental irritant, the simple treatment is avoiding the offending allergens or agents and using an antihistamine, such as loratidine, to alleviate symptoms (9).
- 2. In acute bacterial sinusitis, treatment includes dexbrompheniramine plus pseudoephedrine, oxymetazoline and an antibiotic directed against *S. pneumonia* and *H. influenza* (8,9).
- 3. In the case of COPD exacerbation, the recommendations are an antibiotic directed against *S. pneumonia* and *H. influenza*, systemic corticosteroids tapered over 2 weeks, continuous O₂ if PaO₂ is 55 mmHg or less or SaO₂ is 88% or less, and ipratropium plus albuterol treatments (9).
- 4. In acute bronchitis, it is recommended to treat acute cough with dextromethorphan or codeine, a bronchodilator, nonsteroidal anti-inflammatory drugs or acetaminophen for pain relief. Because one of the most common causes of acute cough is the influenza virus, a flu vaccine will help prevent the condition in the first place. If influenza is suspected as the cause, the antiviral amantidine or rimantidine can be used but must be initiated within 48 hours of diagnosis (10,11).
- 5. For *Bordetella pertussis* infections, a 14-day course of erythromycin or bactrim is the recommended treatment for acute cough (9).

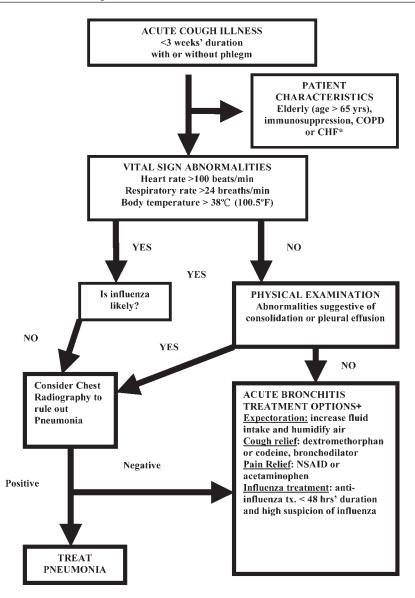


Fig. 1. Evaluation and treatment of acute cough.

Finally, prevention and prophylaxis is an important component in the care of our patients, especially our elderly and at-risk patients. Annual immunization against influenza is standard practice for these two groups. Vaccination against *S. pneumonia* with the Pneumovax® is also recommended for at-risk groups and will help to prevent many of the acute cough illnesses described earlier (8).

FUTURE DIRECTIONS

There is much work to be done to address the symptom of acute cough and provide effective means to alleviate patient suffering from this malady. First and foremost, there needs to be further study to fully define the scope and causes of the problem. Much of the information in this chapter is based on clinical experience only. Although this experience is valuable, published studies on the frequency and spectrum of causes of acute cough in both adults and children are needed.

Although there is an array of OTC medications that may help to improve the effectiveness of cough or shorten its duration, large, randomized, controlled clinical studies documenting improvement in patient morbidity and mortality are lacking (6,8-10,19-21). Lost work days, absenteeism from school, money spent on ineffective OTC treatments, and time and resources wasted in emergency departments and primary care offices would be significantly curtailed if we could identify effective self-care treatments with rigorously designed studies. Future studies using outcome measures that can be easily assessed in a primary care setting and that produce clinically meaningful results, such as patient satisfaction, relief of nighttime disturbance, side effects, or time to return to normal daily activities, are needed (6,9,19,20).

According to clinical experience, viruses are the chief agent causing the URIs that lead to the acute cough illness. Although the OTC options for treatment try and reduce the severity of certain symptoms, they do nothing to address the underlying cause of the URI—the virus. There are five treatments under development that target the most common viruses implicated in non-influenza-related URI, including three virus capsid-binding agents: pleconaril, pirodavir, and tremacamra (4). It is an exciting prospect for practitioners to possibly have a therapeutic option someday that actually addresses the etiology of the acute cough by reducing the viral load.

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