

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

# Chronic Cough Due to Acute Bronchitis ACCP Evidence-Based Clinical Practice Guidelines

Sidney S. Braman, MD, FCCP

Background: The purpose of this review is to present the evidence for the diagnosis and treatment of cough due to acute bronchitis and make recommendations that will be useful for clinical practice. Acute bronchitis is one of the most common diagnoses made by primary care clinicians and emergency department physicians. It is an acute respiratory infection with a normal chest radiograph that is manifested by cough with or without phlegm production that lasts for up to 3 weeks. Respiratory viruses appear to be the most common cause of acute bronchitis; however, the organism responsible is rarely identified in clinical practice because viral cultures and serologic assays are not routinely performed. Fewer than 10% of patients will have a bacterial infection diagnosed as the cause of bronchitis. The diagnosis of acute bronchitis should be made only when there is no clinical or radiographic evidence of pneumonia, and the common cold, acute asthma, or an exacerbation of COPD have been ruled out as the cause of cough. Acute bronchitis is a self-limited respiratory disorder, and when the cough persists for > 3 weeks, other diagnoses must be considered.

Methods: Recommendations for this review were obtained from data using a National Library of Medicine (PubMed) search dating back to 1950, which was performed in August 2004. The search was limited to literature published in the English language and human studies, using search terms such as "cough," "acute bronchitis," and "acute viral respiratory infection."

Results: Unfortunately, most previous controlled trials guiding the treatment of acute bronchitis have not vigorously differentiated acute bronchitis and the common cold, and also have not distinguished between an acute exacerbation of chronic bronchitis and acute asthma as a cause of acute cough. For patients with the putative diagnosis of acute bronchitis, routine treatment with antibiotics is not justified and should not be offered. Antitussive agents are occasionally useful and can be offered as therapy for short-term symptomatic relief of coughing, but there is no role for inhaled bronchodilator or expectorant therapy. Children and adult patients with confirmed and probable whooping cough should receive a macrolide antibiotic and should be isolated for 5 days from the start of treatment; early treatment within the first few weeks will diminish the coughing paroxysms and prevent spread of the disease; the patient is unlikely to respond to treatment beyond this period.

Conclusion: Acute bronchitis is an acute respiratory infection that is manifested by cough and, at times, sputum production that lasts for no more than 3 weeks. This syndrome should be distinguished from the common cold, an acute exacerbation of chronic bronchitis, and acute asthma as the cause of acute cough. The widespread use of antibiotics for the treatment of acute bronchitis is not justified, and vigorous efforts to curtail their use should be encouraged. (CHEST 2006; 129:95S–103S)

Key words: acute bronchitis; acute cough; acute upper respiratory tract infection; acute viral respiratory infection; chest cold

Abbreviations: RSV = respiratory syncytial virus; SARS = severe acute respiratory syndrome

A cute bronchitis has been the term used for an acute respiratory infection that is manifested predominantly by cough with or without phlegm production that lasts for up to 3 weeks. The absence of an infiltrate on the chest radiograph rules out pneumonia as a cause of acute cough and sputum production. Cough with or without phlegm produc-

tion can also be part of the common cold syndrome, which is a benign self-limited illness of all age groups. The *common cold* is a conventional term for a mild upper respiratory illness, the hallmark symptoms of which are nasal stuffiness and discharge, sneezing, sore throat, and cough.<sup>2</sup> At times, these symptoms are also accompanied by constitutional

symptoms such as fever, muscle aches, and fatigue. The prevalence of cough due to the common cold is as high as 83% within the first 2 days of illness,<sup>3</sup> and because the common cold and acute bronchitis share many of the same symptoms the clinical distinction between acute and chronic bronchitis and the common cold is difficult, or at times impossible, to make. Cough associated with the common cold is an upper airway cough syndrome that is often associated with throat clearing and the sensation of postnasal drip. The presumed lower airway cough of acute bronchitis also, at times, is accompanied by an upper airway cough syndrome, which has previously been referred to as *postnasal drip syndrome*, further compounding the difficulties in diagnosis.

Acute bronchitis is one of the most common diagnoses made by primary care clinicians and emergency department physicians. Unfortunately, most previous controlled trials guiding the treatment of acute bronchitis have not vigorously differentiated acute bronchitis and the common cold, and also have not distinguished between an acute exacerbation of chronic bronchitis and acute asthma as a cause of acute cough. This is in part due to the lack of a uniform definition for acute bronchitis.<sup>4,5</sup> In studies of acute bronchitis, acute asthma was misdiagnosed as acute bronchitis in approximately one third of the patients who presented with acute cough.<sup>6,7</sup> For those patients who have had at least two similar doctor-diagnosed episodes of acute bronchitis in the past 5 years, 65% can be identified as having mild asthma.<sup>8</sup> Because the clinical picture of both disorders is frequently quite similar, the only diagnostic tool that the clinician can rely on is a prospective evaluation of the patient to see whether the "acute bronchitis" is an isolated event or a predictor of a chronic disease such as asthma.

Acute bronchitis has been considered to be a self-limited respiratory disorder, and when the cough persists for > 3 weeks other diagnoses must be considered, including postinfectious cough, upper airway cough syndrome due to a variety of rhinosinus conditions, asthma, and gastroesophageal reflux disease. Most patients with acute bronchitis are otherwise healthy and are considered to have "uncomplicated" acute bronchitis. Those with underlying lung disease (eg, COPD or bronchiectasis), congestive heart failure, or a compromised immune system (eg, AIDS or chemotherapy) are considered to be at high

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (www.chestjournal.org/misc/reprints.shtml).

Correspondence to: Sidney S. Braman, MD, FCCP, Division of Pulmonary and Critical Care Medicine, Rhode Island Hospital, 595 Eddy St, Providence, RI 02903; e-mail: sidney\_braman@brown.edu risk for complications of acute bronchitis and are not included in this discussion.

Recommendations for this review were obtained from data using a National Library of Medicine (PubMed) search dating back to 1950, which was performed in August 2004. The search was limited to literature published in the English language and human studies, using search terms such as "cough," "acute bronchitis," and "acute viral respiratory infection."

## RECOMMENDATION

1. In a patient with an acute respiratory infection manifested predominantly by cough, with or without sputum production, lasting no more than 3 weeks, a diagnosis of acute bronchitis should not be made unless there is no clinical or radiographic evidence of pneumonia and the common cold, acute asthma, or an exacerbation of COPD have been ruled out as the cause of cough. Quality of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A

## PREVALENCE

In the United States, cough is the most common symptom that results in an office visit to a physician, and acute bronchitis is the most common diagnosis given.9 Each year an episode of acute bronchitis is reported in up to 5% of the general population. The majority of these patients seek medical attention, and this accounts for > 10 million office visits per year.9-11 Acute bronchitis leads to 10 ambulatory visits per 1,000 people per year.<sup>12</sup> The major reason for seeking care is for symptom relief, and one survey<sup>10</sup> of adults showed that 66% of those who sought care did so in the first week of illness, and that 88% did so within 2 weeks. When asked, most individuals label an acute illness that causes cough and sputum production as a "chest cold"; considerably fewer suggest the diagnosis of "bronchitis." Because colds, upper respiratory infections, and bronchitis have been targeted as conditions that are associated with excessive antibiotic prescription use in the general medical community, and much of this problem is fueled by public expectation, the descriptive term used with patients may be very important. When asked, a greater proportion of patients thought that therapy with antibiotics was important for recovery from acute bronchitis (44%) compared with chest colds (11%).10

## **PATHOGENESIS**

Respiratory viruses appear to be the most common cause of acute bronchitis. The organism responsible for acute bronchitis is rarely identified in clinical practice because viral cultures and serologic assays are not routinely performed. Fewer than 10% of patients will have a bacterial infection diagnosed as the cause. Even when prospectively investigated, <sup>13,14</sup> an organism has been identified in only 16 to 30% of cases.

The viruses that have been identified in patients with acute bronchitis include those that are known to involve the lower respiratory tract, such as influenza B, influenza A, parainfluenza, and respiratory syncytial virus (RSV). Influenza occurs in distinct outbreaks each year, and because of its rapid spread it causes considerable morbidity in the general population. The most frequently reported symptoms of influenza are weakness (94%), myalgia (94%), cough (93%), and nasal congestion (91%). Individuals with influenza are more likely than those with influenzalike illness to have baseline cough (93% vs 80%, respectively), fever (68% vs 40%, respectively), and cough and fever together (64% vs 33%, respectively). 15 When influenza is circulating within the community, the presence of both cough and fever within 48 h of symptom onset is a strong predictor of influenza infection. RSV has also been recognized as a substantial cause of morbidity and mortality in adults, especially in the elderly. Attack rates are very high in households with small children, 16 and in geriatric wards, senior day care settings, and nursing homes.<sup>17,18</sup> In one outbreak, the clinical and serologic attack rates were 61.2% and 75%, respectively, with intense coughing reported by 96%.<sup>17</sup> In surveillance studies of influenza-like illnesses in adults in general practice, RSV has been identified as the causative agent in 20% of patients compared to 30% for influenza.19

Another emerging infection that must be considered in patients with an acute influenza-like illness is severe acute respiratory syndrome (SARS), which was first defined by the World Health Organization in mid-March 2003. This viral illness is a highly infectious disease due to a novel coronavirus, the SARS-associated coronavirus. The infection was first seen in humans in China in November 2002 but has spread worldwide. Exposed health-care workers are at high risk of infection; in the Toronto outbreak, 77% of the patients were exposed to SARS in the hospital setting.<sup>20</sup> Nonproductive cough was seen in 69% of patients, with documented fever in 85%, myalgias in 49%, and dyspnea in 42%; only 2% had rhinorrhea. In a report from Taiwan,21 74% of patients developed cough at a mean (± SD) time of

 $4.5\pm1.9$  days after the onset of fever. Fifty-nine percent of these patients had an infiltrate that was consistent with pneumonia seen on the chest radiograph on admission to the hospital. This incidence rose to 98% of the patients during the hospital stay. Information on future outbreaks of the SARS virus can be found at www.who.int/csr/sars/archive/en/.

Viruses that are predominantly associated with upper respiratory tract infection, including coronavirus, rhinovirus, and adenovirus, have also been implicated as causes of acute bronchitis.1 The predominant symptoms with these infections are nasal congestion, rhinorrhea, and pharyngitis. The bacteria that have been causally linked to acute bronchitis in otherwise healthy individuals include only Mycoplasma pneumoniae, Chlamydophila pneumoniae, Bordetella pertussis, and Bordetella parapertussis.1 Prospective surveys<sup>22</sup> of healthy adults and adolescents with a cough lasting  $\geq 5$  days have shown that M pneumoniae and C pneumoniae are rare causes (<1%). Greater incidences have been described in community outbreaks of acute illnesses, and outbreaks among military personnel and on college campuses.<sup>23–25</sup> In these settings, as many as 36% of patients showed evidence of mixed infections with viruses and M pneumoniae, C pneumoniae, or B pertussis.<sup>25</sup> While the importance of other bacterial pathogens in the pathogenesis of acute uncomplicated bronchitis has been suggested,<sup>26</sup> there are few data to support this. In patients with chronic bronchitis, there is evidence that bacteria such as Streptococcus pneumoniae, Moraxella catarrhalis, and Haemophilus influenzae play a role during an acute exacerbation of cough and sputum production.<sup>27</sup> However, an acute exacerbation of chronic bronchitis is a different disease than acute bronchitis. Because these three organisms may inhabit the upper airways of healthy adults, their presence in sputum cultures in patients with acute uncomplicated bronchitis may signify colonization and not acute infection.<sup>28</sup> The concept that acute bacterial bronchitis in healthy adults may be caused by these organisms remains unproven.

The cause of cough in the putative diagnosis of uncomplicated acute bronchitis is likely multifactorial, and begins with mucosal injury, epithelial cell damage, and the release of proinflammatory mediators. <sup>29</sup> Transient airflow obstruction <sup>14,30,31</sup> and transient bronchial hyperresponsiveness <sup>14,16,32–34</sup> can be seen in approximately 40% of previously healthy individuals with an acute viral respiratory tract infection, and a reversibility of FEV<sub>1</sub> > 15% has been demonstrated in 17% of patients. <sup>30</sup> Patients with documented *M pneumoniae* or *C pneumoniae* infections have significantly lower FEV<sub>1</sub> values and a greater degree of reversibility than those with viral

etiologies.<sup>30</sup> In most patients with acute bronchitis, the airflow obstruction and bronchial hyperresponsiveness resolve within 6 weeks. In some patients, particularly in those with recurrent attacks of presumed uncomplicated acute bronchitis, asthma, and not acute bronchitis, may be the cause of the recurrent symptoms and abnormal airway reactivity.<sup>35</sup> In other patients, the symptoms of acute bronchitis may persist for > 3 weeks, and a diagnosis of asthma becomes apparent. Whether acute bronchitis caused by *C pneumoniae*, *M pneumoniae*, or viruses is a risk factor for the development chronic persistent asthma has been suggested but not established.<sup>36,37</sup> The answer to this question will require large prospective population studies.

## RECOMMENDATION

2. In patients with the presumed diagnosis of acute bronchitis, viral cultures, serologic assays, and sputum analyses should not be routinely performed because the responsible organism is rarely identified in clinical practice. Quality of evidence, low; benefit, intermediate; grade of recommendation, C

## **DIAGNOSIS**

The diagnosis of acute bronchitis is established in a patient who has the sudden onset of cough, with or without sputum expectoration, and without evidence of pneumonia, the common cold, acute asthma, or an acute exacerbation of chronic bronchitis. Because pneumonia is not usually a self-limited disease and has considerable morbidity and mortality when not adequately treated, the distinction between these two respiratory infections is particularly important. This is especially pertinent in the elderly population, in which a high index of suspicion is necessary because pneumonia in persons in this age group is associated with a lower prevalence of respiratory and nonrespiratory symptoms at the time of presentation.<sup>38</sup> Four prospective studies<sup>39–42</sup> in younger and older adults have evaluated the patient medical history and physical examination for accurately diagnosing radiographically confirmed pneumonia. These studies and an evidence-based and qualitybased review<sup>43</sup> have concluded that the absence of the following findings reduces the likelihood of pneumonia sufficiently to obviate the need for a chest radiograph: (1) heart rate > 100 beats/min; (2)respiratory rate > 24 breaths/min; (3) an oral body temperature of > 38°C; and (4) chest examination findings of focal consolidation, egophony, or fremitus. Purulent sputum was not an accurate distinction between pneumonia and acute bronchitis; moreover, there were no serum markers that could be used with sufficient accuracy for a presumptive diagnosis of pneumonia.

Specific epidemiologic evidence from family and community contacts may be important to the diagnosis of acute bronchitis. For example, linkage to a confirmed case of pertussis or a cough with severe paroxysms, the typical whooping sound, or posttussive vomiting strongly suggest *B pertussis* infection. Similarly, epidemiologic evidence from outbreaks in specific populations, such as military personnel and college students, may suggest a diagnosis of *M pneumoniae* or *C pneumoniae* infection. In most patients, the diagnosis of acute bronchitis is a clinical diagnosis, and no specific etiologic agent is discovered.

# RECOMMENDATION

3. In patients with acute cough and sputum production suggestive of acute bronchitis, the absence of the following findings reduces the likelihood of pneumonia sufficiently to eliminate the need for a chest radiograph: (1) heart rate > 100 beats/min; (2) respiratory rate > 24 breaths/min; (3) oral body temperature of > 38°C; and (4) chest examination findings of focal consolidation, egophony, or fremitus. Quality of evidence, low; benefit, substantial; grade of recommendation, B

## TREATMENT

A review of the literature suggests that many patients with a diagnosis of acute bronchitis have not received a correct diagnosis and that their acute cough is more likely due to acute asthma, an acute exacerbation of chronic bronchitis, or even the common cold. The recommendations made in this section are provided from the best available original studies, metaanalyses, and, when available, the Cochrane Database of systematic reviews. Although studies were randomized, double-blinded, and placebo-controlled, asthma and acute exacerbation of acute bronchitis were not adequately ruled out.

# Antibiotics

Most reports<sup>44</sup> have shown that between 65% and 80% of patients with acute bronchitis receive an antibiotic despite the evidence that, with few exceptions, they are ineffective. Elderly patients

are particularly likely to receive unnecessary antibiotic coverage, and more than one-half of prescriptions are for extended-spectrum antibiotics. 45 This trend to rely on broad antibiotic coverage has also been seen in the general population.<sup>46</sup> In cigarette smokers, it has been reported<sup>5,44</sup> that > 90% of patients with acute bronchitis receive an antibiotic; yet, there is no evidence that smokers without COPD are in more need than nonsmokers. This has led to a national campaign to reduce antibiotic use for this indication. 47,48 There have been a large number of randomized trials<sup>49-59</sup> (Table 1), several published reviews of randomized trials, and several metaanalyses on the effects of antibiotics on the duration and severity of cough and the duration of illness putatively due to acute bronchitis. 47,48 The conclusion of this large body of data is that because acute bronchitis is primarily a viral illness, routine treatment with antibiotics is not justified. 47,48 Because many patients with acute bronchitis expect to receive an antibiotic, office or clinic time must be set aside to explain the decision not to use these agents, and the potential harm of using unnecessary antibiotics to the individual and to the community at large. 10,47

#### RECOMMENDATIONS

- 4a. For patients with the putative diagnosis of acute bronchitis, routine treatment with antibiotics is not justified and should not be offered. Quality of evidence, good; benefit, none; grade of recommendation, D
- 4b. For these patients, the decision not to use an antibiotic should be addressed individually and explanations should be offered because many patients expect to receive an antibiotic based on previous experiences and public expectation. Quality of evidence, expert opinion; benefit, intermediate; grade of recommendation, E/B

An exception to recommendation 4 comes with cases of acute bronchitis caused by suspected or confirmed pertussis infection. Treatment with erythromycin (or trimethoprim/sulfamethoxazole when a macrolide cannot be given) is necessary. The isolation of a person with an active case for 5 days is a necessary precaution (see the section on postinfectious cough).

# RECOMMENDATION

5. Children and adult patients with confirmed and probable whooping cough should receive a macrolide antibiotic and should be isolated for 5 days from the start of treatment; early treatment within the first few weeks will diminish the coughing paroxysms and prevent spread of the disease; the patient is unlikely to respond to treatment beyond this period. Level of evidence, good; net benefit, substantial; grade of evidence, A

# **Bronchodilators**

Although one study<sup>60</sup> concluded that patients using inhaled β-agonists were as likely to report a productive cough at 7 days as those receiving placebo, this has not been a consistent finding. A Cochrane review on the use of \beta-agonists for the treatment of acute bronchitis,61 reporting on five trials in adults, concluded that β-agonists are not recommended for treatment in cases of uncomplicated acute bronchitis. The overall summary statistics of the Cochrane review did not reveal any significant benefit from the use of either oral or inhaled β<sub>2</sub>-agonists on daily cough scores or the number of patients still coughing after 7 days. However, subgroups of patients with airflow obstruction at baseline and wheezing at the onset of the illness did show some benefit. Tremor, nervousness, and shakiness were more common in the treatment groups. The effect of orally inhaled anticholinergic agents on the cough of acute bronchitis has not been studied and therefore cannot be recommended based on the evidence.

## RECOMMENDATIONS

- 6a. In most patients with a diagnosis of acute bronchitis,  $\beta_2$ -agonist bronchodilators should not be routinely used to alleviate cough. Quality of evidence, fair; benefit, none; grade of recommendation, D
- 6b. In select adult patients with a diagnosis of acute bronchitis and wheezing accompanying the cough, treatment with  $\beta_2$ -agonist bronchodilators may be useful. Quality of evidence, fair; benefit, small/weak; grade of recommendation, C

## Antitussives

The use of codeine or dextromethorphan to reduce cough frequency or severity has not been systematically studied in double-blind, placebo-controlled studies in patients with acute bronchitis. Because they can be effective in patients with chronic bronchitis, it is reasonable to presume that they would be effective for patients with acute bronchitis. Studies on the use of these agents for the cough due to colds or acute viral respiratory illnesses

Table 1—Studies of the Effect of Antibiotics on Cough Symptoms or Other Outcomes in Patients With Acute Bronchitis\*

Drug	Study/Year	Patients, No.	Age,† yr	Population	Dosing	Results	p Value
Erythromycin vs placebo	Hueston <sup>60</sup> /1994	46	18–65	Acute bronchitis	250 mg po qid $\times$ 10 d	Reduction in frequency of cough	NS
						Reduction in mucus production	NS
	Brickfield et al <sup>59</sup> / 1986	52	18–65	Acute bronchitis	333 mg tid $\times$ 7 d	Increased side effects Cough symptoms significantly better on days 3, 5, and 6; magnitude of benefit not given	NS ≤ 0.5
	Dunlay et al <sup>58</sup> / 1987	63	43.5	Acute bronchitis	333 mg tid $\times$ 10 d	Cough symptoms; data not shown	NS
	Brickfield et al <sup>59</sup> / 1986	52	18–65	Acute bronchitis	333 mg tid $\times$ 7 d	Cough symptoms; data shown graphically	< 0.05
	Dunlay et al <sup>58</sup> / 1987	63	43.5	Acute bronchitis	333 mg tid $\times$ 10 d	Day/night cough symptoms	NS
	King et al <sup>57</sup> /1996	91	$37 \pm 13.7$	Acute bronchitis	250 mg qid × 10 d	Cough frequency; data not reported	NS
Immediate or delayed antibiotics vs placebo	Dowell et al <sup>56</sup> / 2001	191	39	Acute cough	Immediate antibiotics (14 d) vs 1 wk delayed antibiotics	Recovery from cough; data in graph form	NS
Trimethoprim- sulfamethoxazole vs placebo	Franks and Gleiner <sup>55</sup> /1984	67	39	Acute bronchitis	160/800 mg bid $\times$ 7 d	Presence of nighttime cough 56% treatment, 84% placebo	0.03
						Daytime cough frequency Presence of cough 93%	NS 0.05
						treatment, 99% placebo	
Amoxicillin- clavulanic acid vs placebo	Gottfarb and Brauner <sup>54</sup> /1994	52	2.65; 0.58–7	LRI	$20 \text{ mg/kg/d} \times 7 \text{ d}$	Recovery from cough at 7 d in 71% vs 22%	0.002
Amoxicillin/ ambroxol vs amoxicillin	Peralta et al <sup>53</sup> / 1987	24	59.6 ± 8	Bronchitis	500/30 mg tid × 10 d	Cough symptoms similar	NS
						Cough clearance improved by 90%	$\leq 0.001$
Doxycycline vs placebo	Scherl et al <sup>52</sup> / 1987	39	30	Bronchitis	100 mg bid $\times$ 1 d then 100 mg qd $\times$ 6 d	No. of days of cough reduced from 15 to 9.4	NS
	Stott and West <sup>50</sup> / 1976	212	NR (14+ yr)	Bronchitis	100 mg bid $\times$ 1 d, then 100 mg qd $\times$ 9 d	Daytime cough score similar Nighttime cough score	NS NS
	Verheij et al <sup>51</sup> /	158	NR (18+ vr)	Bronchitis or	200 mg qd $\times$ 1 d, then	similar Percent with cough	110
	1994		1111 (10 1 y1)	URI	$100 \text{ mg qd} \times 9 \text{ d}$	Ö	
	Williamson <sup>49</sup> /	74	33.4	Bronchitis or	200 mg qd $\times$ 1 d, then	Cough duration	0.5
	1984			URI	$100 \text{ mg qd} \times 6 \text{ d}$	Interrupted sleep	NS

<sup>\*</sup>NS = not significant; LRI = lower respiratory tract infection; URI = upper respiratory tract infection; NR = not reported. †Values are given as the mean  $\pm$  SD or range.

have shown mixed results and are not recommended for routine use $^{62-65}$  (see the section on cough suppressant and pharmacologic protussive therapy). Some studies have shown these agents to be successful in reducing subjective cough scores. In one

study,<sup>63</sup> 710 adults with an acute upper respiratory infection and cough were given a single dose of 30 mg of dextromethorphan hydrobromide or placebo, and objective cough assessment was conducted using continuous cough recordings. Cough was signifi-

cantly reduced during a 4-h observation period. Because the cause of the cough in many of these subjects was likely due to acute bronchitis, it would be reasonable to offer an empiric trial of an antitussive agent for severe coughing during the acute illness.

## RECOMMENDATION

7. In patients with a diagnosis of acute bronchitis, antitussive agents are occasionally useful and can be offered for short-term symptomatic relief of coughing. Quality of evidence, fair; benefit, small/weak; grade of recommendation, C

# Mucokinetic Agents

There have been no consistent favorable effects shown with expectorant and mucolytic agents on the cough associated with acute bronchitis in several therapeutic trials. <sup>66</sup> The trials have shown conflicting results, and the number of trials in each group of drugs is small. These preparations appear to be safe, based on the reported side effects. Expectorants, which fall into this category of drug, are sold as over-the-counter medications; they have gained widespread use in the general population.

### RECOMMENDATION

8. In patients with a diagnosis of acute bronchitis, because there is no consistent favorable effect of mucokinetic agents on cough, they are not recommended. Quality of evidence, fair; benefit, conflicting; grade of recommendation, I

# SUMMARY OF RECOMMENDATIONS

- 1. In a patient with an acute respiratory infection manifested predominantly by cough, with or without sputum production, lasting no more than 3 weeks, a diagnosis of acute bronchitis should not be made unless there is no clinical or radiographic evidence of pneumonia and the common cold, acute asthma, or an exacerbation of COPD have been ruled out as the cause of cough. Quality of evidence, expert opinion; benefit, substantial; grade of recommendation, E/A
- 2. In patients with the presumed diagnosis of acute bronchitis, viral cultures, serologic assays, and sputum analyses should not be routinely performed because the responsible organism is rarely identified in clinical

- **practice.** Quality of evidence, low; benefit, intermediate; grade of recommendation, C
- 3. In patients with acute cough and sputum production suggestive of acute bronchitis, the absence of the following findings reduces the likelihood of pneumonia sufficiently to eliminate the need for a chest radiograph: (1) heart rate > 100 beats/min; (2) respiratory rate > 24 breaths/min; (3) oral body temperature of > 38°C; and (4) chest examination findings of focal consolidation, egophony, or fremitus. Quality of evidence, low; benefit, substantial; grade of recommendation, B
- 4a. For patients with the putative diagnosis of acute bronchitis, routine treatment with antibiotics is not justified and should not be offered. Quality of evidence, good; benefit, none; grade of recommendation, D
- 4b. For these patients, the decision not to use an antibiotic should be addressed individually and explanations should be offered because many patients expect to receive an antibiotic based on previous experiences and public expectation. Quality of evidence, expert opinion; benefit, intermediate; grade of recommendation, E/B
- 5. Children and adult patients with confirmed and probable whooping cough should receive a macrolide antibiotic and should be isolated for 5 days from the start of treatment; early treatment within the first few weeks will diminish the coughing paroxysms and prevent spread of the disease; the patient is unlikely to respond to treatment beyond this period. Level of evidence, good; net benefit, substantial; grade of evidence, A
- 6a. In most patients with a diagnosis of acute bronchitis,  $\beta_2$ -agonist bronchodilators should not be routinely used to alleviate cough. Quality of evidence, fair; benefit, none; grade of recommendation, D
- 6b. In select adult patients with a diagnosis of acute bronchitis and wheezing accompanying the cough, treatment with β<sub>2</sub>-agonist bronchodilators may be useful. Quality of evidence, fair; benefit, small/weak; grade of recommendation, C
- 7. In patients with a diagnosis of acute bronchitis, antitussive agents are occasionally useful and can be offered for short-term symptomatic relief of coughing. Quality of evidence, fair; benefit, small/weak; grade of recommendation, C

8. In patients with a diagnosis of acute bronchitis, because there is no consistent favorable effect of mucokinetic agents on cough, they are not recommended. Quality of evidence, fair; benefit, conflicting; grade of recommendation, I

#### REFERENCES

- 1 Gonzales R, Sande M. Uncomplicated acute bronchitis. Ann Intern Med 2000; 133:981–991
- 2 Terho H, Asko J. The common cold. Lancet 2003; 361:51-59
- 3 Curley F, Irwin R, Pratter M, et al. Cough and the common cold. Am Rev Respir Dis 1988; 138:305–311
- 4 Verheij T, Hermans J, Kaptein A, et al. Acute bronchitis: general practitioners' views regarding diagnosis and treatment. Fam Pract 1990; 7:175–180
- 5 Oeffinger K, Snell L, Foster B, et al. Treatment of acute bronchitis in adults: a national survey of family physicians. J Fam Pract 1998; 46:469–475
- 6 Thiadens H, Postma D, de Bock G. Asthma in adult patients presenting with symptoms of acute bronchitis in general practice. Scand J Prim Health Care 2000; 18:188–192
- 7 Jonsson J, Gislason T, Gislason D, et al. Acute bronchitis and clinical outcome three years later: prospective cohort study. BMJ 1998; 317:1433–1434
- 8 Hallett J, Jacobs R. Recurrent acute bronchitis: the association with undiagnosed asthma. Ann Allergy 1985; 55:568–570
- 9 Schappert S. Ambulatory care visits to physicians offices, hospital outpatient departments, and emergency departments, United States, 1997. Hyattsville, MD: National Center for Health Statistics, 1997
- 10 Gonzales R, Wilson A, Crane L, et al. What's in a name? Public knowledge, attitude, and experiences with antibiotic use for acute bronchitis. Am J Med 2000; 108:83–85
- 11 Adams P, Hendershot G, Marano M, eds. Current estimates from the National Health Interview Survey, United States, 1996. Hyattsville, MD: US Department of Health and Human Services, Public Health Service, Office of Health Research, Statistics, and Technology, National Center for Health Statistics, 1999
- 12 Armstrong G, Pinner R. Outpatient visits for infectious diseases in the United States: 1980 through 1996. Arch Intern Med 1999; 159:2531–2536
- 13 Jonsson J, Sigurdsson J, Kristonsson K, et al. Acute bronchitis in adults. How close do we come to its aetiology in general practice? Scand J Prim Health Care 1997; 15:156–160
- 14 Boldy D, Skidmore S, Ayeres J. Acute bronchitis in the community: clinical features, infective factors, changes in pulmonary function and bronchial reactivity to histamine. Respir Med 1990; 84:377–385
- 15 Monto A, Gravenstein S, Elliot M, et al. Clinical signs and symptoms predicting influenza infection. Arch Intern Med 2000; 160:3243–3247
- 16 Hall C, Geiman J, Biggar R, et al. Respiratory syncytial infections within families. N Engl J Med 1976; 294:414–419
- 17 Agius G, Dindinaud G, Biggar R. An epidemic of respiratory syncytial virus in elderly people: clinical and serologic findings. J Med Virol 1990; 30:117–127
- 18 Treanor J, Falsey A. Respiratory viral infections in the elderly. Antiviral Res 1999; 44:79–102
- 19 Zambon M, Stockton J, Clewley J, et al. Contribution of

- influenza and respiratory syncytial virus to community cases of influenza-like illness: an observational study. Lancet 2001; 358:1410-1416
- 20 Booth C, Matukas L, Thomlinson G, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. JAMA 2003; 289:2801–2809
- 21 Liu CL, Lu YT, Peng MJ, et al. Clinical and laboratory features of severe acute respiratory syndrome vis-a-vis onset of fever. Chest 2004; 126:509–517
- 22 Wadowsky R, Castilla E, Laus S, et al. Evaluation on Chlamydia pneumoniae and Mycoplasma pneumoniae as etiologic agents of persistent cough in adolescents and adults. J Clin Microbiol 2002; 40:637–640
- 23 Vincent J, Cherry J, Nauscheutz W, et al. Prolonged afebrile nonproductive cough illnesses in American soldiers in Korea: a serologic search for causation. Clin Infect Dis 2000; 30:534– 539
- 24 Davis S, Suter R, Strebel P, et al. Concurrent outbreaks of pertussis and *Mycoplasma pneumoniae* infection: clinical and epidemiologic characteristics of illness manifested by cough. Clin Infect Dis 1995; 20:621–628
- 25 Jackson L, Cherry J, Wang S, et al. Frequency of serologic evidence of Bortetella infections and mixed respiratory infections with other respiratory pathogens in university students with cough illness. Clin Infect Dis 2000; 31:3–6
- 26 Henry D, Ruoff G, Rhudy J, et al. Effectiveness of short-course therapy (5 days) with cefuroxime axetil in treatment of secondary bacterial infections of acute bronchitis. Antimicrob Agents Chemother 1995; 39:2528–2534
- 27 McCrory D, Brown C, Gelfand S, et al. Management of acute exacerbation of COPD: a summary and appraisal of published evidence. Chest 2001; 119:1190–1209
- 28 Hirschmann J. Antibiotics for common respiratory tract infections in adults. Arch Intern Med 2002; 162:256–264
- 29 Polito A, Proud D. Epithelia cells as regulators of airway inflammation. J Allergy Clin Immunol 1998; 102:714–718
- 30 Melbye H, Kongerud J, Vorland L. Reversible airflow limitation in adults with respiratory infection. Eur Respir J 1994; 7:1239–1245
- 31 Williamson H. Pulmonary function tests in acute bronchitis: evidence for reversible airflow obstruction. J Fam Pract 1987; 25:251–256
- 32 Hall W, Hall C, Speers D. Respiratory syncytial virus infection in adults: clinical, virologic, and serial pulmonary function studies. Ann Intern Med 1978; 88:203–205
- 33 Hall W, Hall C. Clinical significance of pulmonary function tests: alterations in pulmonary function following viral respiratory infection. Chest 1979; 76:458–465
- 34 Little J, Hall W, Douglas RJ, et al. Airway hyperreactivity and peripheral airway dysfunction in influenza A infection. Am Rev Respir Dis 1978; 118:295–303
- 35 Hallett J, Jacobs R. Recurrent acute bronchitis: the association with undiagnosed bronchial asthma. Ann Allergy 1985; 55:568–570
- 36 Hahn D. Chlamydia pneumoniae and the "Dutch Hypothesis." Chest 2002; 122:1510–1512
- 37 Hahn D, Dodge R, Golubjatnikov R. Association of Chlamydia pneumoniae (strain TWAR) infection with wheezing, asthmatic bronchitis, and adult-onset asthma. JAMA 1991; 266:225–230
- 38 Metlay J, Schulz R, Li Y, et al. Influence of age on symptoms at presentation in patients with community-acquired pneumonia. Arch Intern Med 1997; 157:1453–1459
- 39 Gennis P, Gallagher J, Falvo C, et al. Clinical criteria for the detection of pneumonia in adults: guidelines for ordering chest roentgenograms in the emergency department. J Emerg Med 1989; 7:263–268

- 40 Diehr P, Wood R, Bushyhead J, et al. Prediction of pneumonia in outpatients with acute cough: a statistical approach. J Chronic Dis 1984; 37:215–225
- 41 Heckerling P, Tape T, Wigton R, et al. Clinical prediction rule for pulmonary infiltrates. Ann Intern Med 1990; 113: 664–670
- 42 Singal B, Hedges J, Radack K. Decision rules and clinical prediction of pneumonia: evaluation of low-yield criteria. Ann Emerg Med 1989; 18:13–20
- 43 Metlay J, Kapoor W, Fine M. Does this patient have community acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA 1997; 278:1440–1445
- 44 Linder J, Sim I. Antibiotic treatment of acute bronchitis in smokers. J Gen Intern Med 2002; 17:230–234
- 45 Steinman M, Sauaia A, Masseli J, et al. Office evaluation and treatment of elderly patients with acute bronchitis. J Am Geriatr Soc 2004: 52:875–879
- 46 Steinman M, Landefeld C, Gonzales R. Predictors of broadspectrum antibiotic prescribing for acute respiratory tract infections in adult primary care. JAMA 2003; 289:719–725
- 47 Gonzales R, Brrtlett J, Besser R, et al. Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis: background. Ann Intern Med 2001; 134:521–529
- 48 Snow V, Mottur-Pilson C, Gonzales R. Principles of appropriate antibiotic use for treatment of acute bronchitis in adults. Ann Intern Med 2001; 134:518–520
- 49 Williamson HA Jr. A randomized, controlled trial of doxycycline in the treatment of acute bronchitis. J Fam Pract 1984; 19:481–486
- 50 Stott NC, West RR. Randomised controlled trial of antibiotics in patients with cough and purulent sputum. BMJ 1976; 2:556-559
- 51 Verheij TJ, Hermans J, Mulder JD. Effects of doxycycline in patients with acute cough and purulent sputum: a double blind placebo controlled trial. Br J Gen Pract 1994; 44:400–404
- 52 Scherl ER, Riegler SL, Cooper JK. Doxycycline in acute bronchitis: a randomized double-blind trial. J Ky Med Assoc 1987; 85:539–541
- 53 Peralta J, Poderoso JJ, Corazza C, et al. Ambroxol plus amoxicillin in the treatment of exacerbations of chronic

- bronchitis. Arzneimittelforschung 1987; 37:969-971
- 54 Gottfarb P, Brauner A. Children with persistent cough: outcome with treatment and role of Moraxella catarrhalis? Scand J Infect Dis 1994; 26:545–551
- 55 Franks P, Gleiner JA. The treatment of acute bronchitis with trimethoprim and sulfamethoxazole. J Fam Pract 1984; 19: 185–190
- 56 Dowell J, Pitkethly M, Bain J, et al. A randomised controlled trial of delayed antibiotic prescribing as a strategy for managing uncomplicated respiratory tract infection in primary care. Br J Gen Pract 2001; 51:200–205
- 57 King DE, Williams WC, Bishop L, et al. Effectiveness of erythromycin in the treatment of acute bronchitis. J Fam Pract 1996; 42:601–605
- 58 Dunlay J, Reinhardt R, Roi LD. A placebo-controlled, double-blind trial of erythromycin in adults with acute bronchitis. J Fam Pract 1987; 25:137–141
- 59 Brickfield FX, Carter WH, Johnson RE. Erythromycin in the treatment of acute bronchitis in a community practice. J Fam Pract 1986; 23:119–122
- 60 Hueston WJ. Albuterol delivered by metered-dose inhaler to treat acute bronchitis. J Fam Pract 1994; 39:437–440
- 61 Smucny J, Flynn C, Becker L, et al. Beta2-agonists for acute bronchitis. Cochrane Database Syst Rev (database online). Issue 1, 2004
- 62 Lee P, Jawad M, Eccles R. Antitussive efficacy of dextromethorphan in cough associated with acute upper respiratory infection. J Pharm Pharmacol 2000; 52:1139–1142
- 63 Pavesi L, Subburaj S, Porter-Shaw K. Application and validation of a computerized cough acquisition system for objective monitoring of acute cough. Chest 2001; 120:1121–1128
- 64 Freestone C, Eccles R. Assessment of the antitussive efficacy of codeine in cough associated with the common cold. J Pharm Pharmacol 1997; 49:1045–1049
- 65 Tukiainen H, Karttunen P, Silvasti M, et al. The treatment of acute transient cough: a placebo-controlled comparison of dextromethorphan-β2 sympathomimetic combination. Eur J Respir Dis 1986; 69:95–99
- 66 Schroeder K, Fahey T. Over-the-counter medications for acute cough in children and adults in ambulatory settings. Cochrane Database Syst Rev (database online). Issue 4, 2004