Chronic Cough Due to Chronic Bronchitis
ACCP Evidence-Based Clinical Practice Guidelines
Sidney S. Braman, MD, FCCP

Background: Chronic bronchitis is a disease of the bronchi that is manifested by cough and sputum expectoration occurring on most days for at least 3 months of the year and for at least 2 consecutive years when other respiratory or cardiac causes for the chronic productive cough are excluded. The disease is caused by an interaction between noxious inhaled agents (eg, cigarette smoke, industrial pollutants, and other environmental pollutants) and host factors (eg, genetic and respiratory infections) that results in chronic inflammation in the walls and lumen of the airways. As the disease advances, progressive airflow limitation occurs, usually in association with pathologic changes of emphysema. This condition is called COPD. When a stable patient experiences a sudden clinical deterioration with increased sputum volume, sputum purulence, and/or worsening of shortness of breath, this is referred to as an acute exacerbation of chronic bronchitis as long as conditions other than acute tracheobronchitis are ruled out. The purpose of this review is to present the evidence for the diagnosis and treatment of cough due to chronic bronchitis, and to make recommendations that will be useful for clinical practice.

Methods: Recommendations for this section of the review were obtained from data using a National Library of Medicine (PubMed) search dating back to 1950, performed in August 2004, of the literature published in the English language. The search was limited to human studies, using the search terms “cough,” “chronic bronchitis,” and “COPD.”

Results: The most effective way to reduce or eliminate cough in patients with chronic bronchitis and persistent exposure to respiratory irritants, such as personal tobacco use, passive smoke exposure, and workplace hazards is avoidance. Therapy with a short-acting inhaled β-agonist, inhaled ipratropium bromide, and oral theophylline, and a combined regimen of inhaled long-acting β-agonist and an inhaled corticosteroid may improve cough in patients with chronic bronchitis, but there is no proven benefit for the use of prophylactic antibiotics, oral corticosteroids, expectorants, postural drainage, or chest physiotherapy. For the treatment of an acute exacerbation of chronic bronchitis, there is evidence that inhaled bronchodilators, oral antibiotics, and oral corticosteroids (or in severe cases IV corticosteroids) are useful, but their effects on cough have not been systematically evaluated. Therapy with expectorants, postural drainage, chest physiotherapy, and theophylline is not recommended. Central cough suppressants such as codeine and dextromethorphan are recommended for short-term symptomatic relief of coughing.

Conclusions: Chronic bronchitis due to cigarette smoking or other exposures to inhaled noxious agents is one of the most common causes of chronic cough in the general population. The most effective way to eliminate cough is the avoidance of all respiratory irritants. When cough persists despite the removal of these inciting agents, there are effective agents to reduce or eliminate cough.

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Key words: acute exacerbation of COPD; chronic bronchitis; chronic cough; cigarette cough; COPD; cough phlegm syndrome; mucous hypersecretion

Abbreviations: GOLD = Global Initiative for Chronic Obstructive Lung Disease; IL = interleukin

Chronic bronchitis is a cough phlegm syndrome. The term was introduced into the medical literature early in the 19th century and was recognized as an inflammatory disease of the airways. However, no accepted definition of this term was established until the mid-20th century following the develop-
ment of the British Medical Research Council Respiratory Questionnaire on Respiratory Symptoms. Based on responses to epidemiologic surveys, the term chronic bronchitis was defined as a disease of the bronchi that manifested by cough and sputum expectoration occurring on most days for at least 3 months of the year and for at least 2 consecutive years when other pulmonary or cardiac causes for the chronic productive cough are excluded.2–4 In 1958, a group of international experts participating in the Ciba Foundation Guest Symposium, proposed a definition of chronic bronchitis as “a condition of subjects with chronic or recurrent excessive mucous secretion in the bronchial tree.”4 Because earlier studies suggested that chronic mucous hypersecretion did not cause airflow obstruction, evidence of airflow limitation was not incorporated into these earlier definitions. In 1986, chronic bronchitis and emphysema were acknowledged in an American Thoracic Society statement5 as the two main components of COPD, which became a preferred term for both diagnoses. Evidence of expiratory flow limitation that did not change markedly over time was included in the definition of COPD.

The recently published Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines,6 sponsored by the National Heart, Lung, Blood Institute and the World Health Organization, provides a definition of COPD that differs from previous consensus statements. It does not incorporate the terms chronic bronchitis and emphysema into the definition, as does the American Thoracic Society statement. Instead, it defines COPD as a disease state that is characterized by airflow obstruction that is no longer fully reversible and is usually progressive. The disease is caused by an interaction between noxious inhaled agents (eg, cigarette smoke, industrial pollutants, and other environmental pollutants) and host factors (eg, genetic factors and respiratory infections) that results in chronic inflammation in the walls and lumen of the airways. The pathology of COPD, as well as the symptoms, the pulmonary function abnormalities, and complications all can be explained on the basis of the underlying inflammation. While the GOLD document6 does not specifically include chronic bronchitis and emphysema in the definition of COPD, it is clear that they are considered to be the predominant causes. For instance, GOLD defines the earliest stage of COPD, stage 0, by evidence of chronic cough and sputum expectoration in the absence of airflow obstruction on pulmonary function testing, not using the term chronic bronchitis.6 Because chronic cough and sputum expectoration are common in all stages of COPD, the use of the traditional definition of chronic bronchitis as cough and sputum expectoration occurring on most days for at least 3 months of the year and for at least 2 consecutive years is most appropriate. Recommendations for this section of the review were obtained from data obtained using a National Library of Medicine (PubMed) search dating back to 1950, performed in August 2004, of the literature published in the English language. The search was limited to human studies, using the search terms “cough,” “chronic bronchitis,” and “COPD.”

**Recommendations**

1. Adults who have a history of chronic cough and sputum expectoration occurring on most days for at least 3 months and for at least 2 consecutive years should be given a diagnosis of chronic bronchitis when other respiratory or cardiac causes of chronic productive cough are ruled out. Level of evidence, low; net benefit, substantial; grade of recommendation, B

2. The evaluation of patients with chronic cough should include a complete history regarding exposures to respiratory irritants including cigarette, cigar, and pipe smoke; passive smoke exposures; and hazardous environments in the home and workplace. All are predisposing factors of chronic bronchitis. Level of evidence, low; net benefit, substantial; grade of recommendation, B

**Epidemiology**

Over the past decade there has been increasing interest in the pathogenesis and management of COPD as it has been recognized that the disease is having a major worldwide impact.6 In the United States, estimates from national interviews taken by the National Center for Health Statistics,7 have shown that >16 million people are afflicted with COPD; about 14 million are thought to have chronic bronchitis, while 2 million have emphysema.7 It has been suggested that these statistics underestimate the prevalence of COPD by as much as 50%, as many patients underreport their symptoms and their conditions remain undiagnosed. On the other hand, the accuracy of a self-reported diagnosis of chronic bronchitis and a physician-confirmed diagnosis of
chronic bronchitis have been questioned. Using a longitudinal population study, patients were surveyed for self-reported chronic bronchitis or physician-diagnosed chronic bronchitis. The survey asked about symptoms of chronic cough and sputum production and the timing of these symptoms. Seventeen percent of current smokers, 12.4% of former smokers, and 6% of never-smokers met the criteria for chronic bronchitis. The vast majority of people (88.4%) who reported a self-reported or physician-confirmed diagnoses of chronic bronchitis did not meet the standard criteria. The overdiagnosis of chronic bronchitis by patients and physicians may be very common. Because the term bronchitis is often used as a common descriptor for a nonspecific and self-limited cough, many patients assume that they have had chronic bronchitis. In the Third National Health and Nutrition Examination Survey, using surveys, physical examinations, and pulmonary function testing, more accurate prevalence estimates have been made. Using World Health Organization definitions, it has been shown that 23.6 million adults (13.9% of the adult population) have COPD. Chronic bronchitis is among the most frequent causes of cough found in community surveys.

**Etiology**

In developed countries, cigarette smoking is responsible for 85 to 90% of cases of chronic bronchitis and COPD. Cigarette smoke is composed of a complex mixture of >400 particles and gases; the specific etiologic role of each of these constituents has not been established. Many studies have confirmed the association of cigarette smoking, chronic cough, and low lung function. The incidence of chronic bronchitis is directly proportional to the number of cigarettes smoked. Other risk factors for chronic mucus hypersecretion that have been identified are increasing age, male gender, childhood respiratory infections, frequent lower respiratory tract infections, occupational exposures, and asthma. Pipe and cigar smoking are also risk factors for both complications even in the absence of former cigarette smoking. The prevalence of chronic cough in the Third National Health and Nutrition Examination Survey was reported in subjects without airflow obstruction and in those with undiagnosed airway obstruction. Cough was found in 9.3% of subjects and sputum production was found in 8.3% of subjects without airflow obstruction. The study also confirmed the observation that these symptoms are more common in subjects with more severe airflow obstruction. In those subjects with mild airflow obstruction, cough was found in 16.0% of those surveyed and sputum production in 17%. With severe airflow obstruction, using the GOLD staging criteria, the prevalence of cough increased to 49% of patients, and sputum production was found in 39.5% of patients.

The identification of chronic cough and sputum production due to occupational exposures is not commonly made by clinicians; yet, it has been estimated that in as many as 15% of patients with chronic bronchitis and COPD, occupational exposure is the cause. There are a number of epidemiologic associations of workplace hazards and chronic bronchitis. The diagnosis is usually made by finding a history of exposure in individuals who have no other identifiable cause of cough. This is often difficult because many workers are smokers or are exposed to second-hand smoke. Other workers, such as those exposed to organic dusts, may present with chronic cough and a history of asthma-like symptoms without airway eosinophilia, reversible airflow obstruction, or bronchial hyperresponsiveness. This occurs with chronic exposure to cotton (byssinosis), jute, hemp, flax, sisal, wood, and various grains. There is a growing body of literature that has demonstrated that specific occupational exposures are associated with the symptoms of chronic bronchitis and, at times, airflow obstruction, which are comparable to moderate cigarette smoking. The list of agents includes the following: coal; manufactured vitreous fibers; oil mist; cement; silica; silicates; osmium; vanadium; welding fumes; organic dusts; engine exhausts; fire smoke; and second-hand cigarette smoke. While the prevalence of passive smoke exposure in the workplace has been decreasing as laws banning smoking in public places have been established, it is still a problem in many communities around the world. Often, nonsmokers are exposed to cigarette smoke in the home environment as well. Involuntary exposure to tobacco smoke is strongly associated with chronic cough and sputum production, even in young adults who have been screened for other risk factors. The risk increases significantly with an increasing duration of daily exposure. Another important exposure in the home environment that increasingly has been recognized as a cause of chronic bronchitis and fixed airflow obstruction in underdeveloped countries is exposure to the fumes of cooking fuels, especially in enclosed spaces with poor ventilation.

**Recommendation**

3. Smoke-free workplace and public place laws should be enacted in all communities.
Pathology and Pathophysiology

The inflammatory mechanisms of chronic bronchitis and COPD have been extensively reviewed. Structural changes of the airways have been described in otherwise healthy smokers even as young as 20 to 30 years old. BAL studies in such subjects have shown an increase in the number of neutrophils and macrophages; both play an important role in perpetuating the inflammatory process of chronic bronchitis. Bronchial biopsy specimens from former smokers show inflammatory changes that are similar to those in the active smoker, suggesting that inflammation may persist in the airway once established. A number of extracellular signaling proteins called cytokines are important in the pathogenesis of COPD because they are thought to mediate the tissue damage and repair that are induced by cigarette smoking. Increased quantities of certain proinflammatory cytokines including interleukin (IL)-8, IL-1, IL-6, and tumor necrosis factor-α, and the anti-inflammatory cytokine IL-10 have been found in the sputum of smokers with chronic bronchitis, and even further increased quantities of these cytokines have been found during acute exacerbations.

Other structural changes in the airways of smokers include mucous gland hyperplasia, bronchiolar edema, smooth muscle hypertrophy, and peribronchiolar fibrosis. These changes result in a narrowing of the small airways (<2 mm). There is a progressive worsening of pathologic changes when smokers with mild COPD and smokers with more severe disease are compared.

Neurogenic mechanisms may play an amplifying role in the pathogenesis of chronic bronchitis. Sensory airway nerves contain tachykinins such as substance P, neuropeptide A, and neuropeptide B that are released in the airways in association with inflammation. These tachykinins have been found in the sputum of patients with chronic bronchitis, and are known to augment airway secretions.

The presence of a gel-like mucus in the airways of healthy people is essential for normal mucociliary clearance. The mucus is eliminated by the action of mucociliary clearance to the hypopharynx, where it is swallowed and rarely noticed. Normally, about 500 mL of sputum is produced each day, and it is usually not noticed. Smokers with chronic bronchitis produce larger amounts of sputum each day, as much as 100 mL/d more than normal. This results in cough and sputum production. The excess mucus occurs as a result of an increase in the size and number of the submucosal glands and an increase in the number of goblet cells on the surface epithelium. Mucous gland enlargement and hyperplasia of the goblet cells are, therefore, the pathologic hallmark of chronic bronchitis. Goblet cells are normally absent in the small airways, and their presence there (often referred to as mucous metaplasia) is important to the development of COPD. In the larger airways in patients with chronic bronchitis, there is a reduction in the serous acini of the submucosal glands. This depresses local defenses to bacterial adherence, because these glands are known to produce microbial deterrents such as lactoferrin, antiproteases, and lysozyme. Other epithelial alterations that are seen in patients with chronic bronchitis are a decrease in the number and length of the cilia, and squamous metaplasia. The mucociliary abnormalities of chronic bronchitis cause the formation of a continuous sheet or blanket of mucus lining the airways instead of the discreet deposits of mucus seen in normal airways. The pooling of secretions also may occur. This provides an additional cause of bacterial growth, which in turn causes a release of toxins that are further damaging to the cilia and epithelial cells. Bacterial exoproducts are known to stimulate mucus production and slow ciliary beating, to impair immune effector cell function, and to destroy local Igs. This cycle is especially seen in current smokers, as opposed to former smokers.

Based on these extensive observations regarding the pathogenesis of chronic bronchitis, it is recognized that the cause of cough in patients with chronic bronchitis is multifactorial. Airway inflammation and excessive bronchial secretions are likely to activate the afferent limb of the cough reflex. There is evidence that the cough receptors are heightened in patients with chronic bronchitis as it has been demonstrated that capsaicin induced cough is increased. When airflow obstruction is present, it often leads to an ineffective cough as a result of decreased expiratory flow, and this coupled with impaired mucociliary clearance results in the further retention of secretions and a vicious cycle of chronic recurrent coughing. Even in the absence of airflow obstruction and with a short smoking history, impaired mucociliary clearance has been shown in young smokers. This occurs because of abnormal clearance in the small airways. Patients with advanced disease and evidence of airway obstruction have mucus retention in the small peripheral airways and larger central airways. This cycle is further worsened during episodes of acute viral and bacterial infections, which are common in patients with chronic bronchitis.
AIRWAY INFECTION/ACUTE EXACERBATION OF CHRONIC BRONCHITIS

Patients with chronic bronchitis have a greater frequency of acute respiratory infections than those without bronchitis, and with symptoms of an acute upper respiratory infection they are more likely to have signs of infection in the lower airways than are healthy control subjects. During these attacks or exacerbations, cough and sputum production increase and the sputum may become purulent. The exacerbations may also cause worsening shortness of breath; therefore, clinicians should be aware that other conditions such as heart failure and pulmonary embolism could mimic an acute exacerbation of chronic bronchitis. While there is no uniformly accepted definition of an acute exacerbation of chronic bronchitis, most have acknowledged that this condition is due to a sudden deterioration in the condition of a stable patient with symptoms of increased sputum volume, sputum purulence, and/or worsening of shortness of breath due to acute tracheobronchitis. An exacerbation is often preceded by symptoms of an upper respiratory tract infection. An important element of this definition is that causes of respiratory deterioration other than acute tracheobronchitis, such as pneumonia, pulmonary embolism, exacerbation of bronchiectasis, pneumothorax, and congestive heart failure, are excluded. Evidence of a viral infection is found in approximately one third of episodes. Common viral infections in the outpatient setting are rhinovirus, coronavirus, influenza B, and parainfluenza. Viral respiratory infections predispose the airways to bacterial superinfection because they interfere with mucociliary clearance, impair bacterial killing by pulmonary macrophages, and increase the risk of aspirating secretions containing bacteria from the upper airways. Whether bacterial overgrowth or infection alone, in the absence of acute viral infection, is the cause of an acute exacerbation of chronic bronchitis has been controversial. During stable periods, many patients with chronic bronchitis, and especially current smokers, are colonized with bacteria such as Streptococcus pneumoniae, Moraxella catarrhalis, and Haemophilus influenzae, and these same organisms have been found in patients during an acute exacerbation. However, the molecular typing of sputum isolates has shown that acute exacerbations of COPD are frequently associated with a new strain of a preexisting organism. This supports a causative role for bacteria in the acute exacerbations of COPD. Although most such episodes of acute exacerbations of chronic bronchitis are self-limited, they are associated with substantial decrements in the quality of life and impose a considerable financial burden on the health-care system.

Recommendation

4. Stable patients with chronic bronchitis who have a sudden deterioration of symptoms with increased cough, sputum production, sputum purulence, and/or shortness of breath, which are often preceded by symptoms of an upper respiratory tract infection, should be considered to have an acute exacerbation of chronic bronchitis, as long as conditions other than acute tracheobronchitis are ruled out or are considered unlikely. Level of evidence, expert opinion; net benefit, substantial; grade of recommendation, E/A

PROGRESSIVE AIRFLOW OBSTRUCTION

The role of chronic mucous hypersecretion and cough in the pathogenesis of airflow obstruction has been another area of controversy. The lack of association between chronic mucous hypersecretion and pulmonary function decline or mortality has been reported in a number of studies. Other studies have examined this question, and have shown an association between chronic mucous hypersecretion and overall mortality as well as mortality from COPD. The association between chronic mucous hypersecretion and the development of COPD also has been established. Both an excessive FEV1 decline and an increased rate of hospitalization have been shown in patients with established COPD who have cough and excessive mucous production. It is likely that this is due to recurrent bronchial infections.

COMORBID ILLNESSES

It should always be kept in mind that when the character of the cough changes for prolonged periods in a patient with chronic bronchitis, the possibility of bronchogenic carcinoma or another complication should be considered. Prospective studies of middle-aged cigarette smokers have shown that the incidence of lung cancer in this group is very high.

TREATMENT

While the most effective treatment of chronic cough due to chronic bronchitis is the avoidance of
respiratory irritants, often patients refuse to avoid them or find it impossible to do so because of conditions at home or in the workplace. The use of pharmacologic therapy at times may be helpful, but the evidence that these agents are effective often comes from clinical trials that do not evaluate cough as a primary outcome. The use of these agents in the treatment of stable patients with chronic disease and for episodes of acute exacerbation of chronic bronchitis will be reviewed. An American College of Chest Physicians/American College of Physicians-American Society of Internal Medicine evidence-based report on the treatment of acute exacerbations of COPD is a useful guideline.

AVOIDANCE

The most effective means for controlling cough and sputum production in patients with chronic bronchitis is the avoidance of environmental irritants. During an acute exposure to respiratory irritants at home or in the workplace, patients may experience symptoms of increased cough, sputum production, and shortness of breath that are similar to those of an exacerbation due to infection. With respect to chronic cough, several nonrandomized trials have studied the effect of smoking cessation on this troubling symptom. Cough has been shown to disappear or markedly decrease in 94 to 100% of patients after smoking cessation, and in approximately half of the subjects this occurred within 1 month. The Lung Health Study investigated the effects of smoking cessation in smokers with mild-to-moderate airflow obstruction. It was a 5-year randomized prospective trial of intensive smoking intervention compared to a control group of smokers who received usual care. At the end of 5 years, 22% of those in the intervention group had stopped smoking for the entire study period. The beneficial effects, including a reduction of chronic cough and sputum production, occurred in the first year of smoking cessation. It was sustained throughout the entire study period. Ninety percent of those patients who had chronic cough at the beginning of the study and stopped smoking reported no cough by the end of the study. Similar findings were reported regarding sputum production. However, in patients with more severe degrees of airflow obstruction chronic cough is more likely to persist despite the avoidance of cigarettes or other respiratory irritants.

RECOMMENDATION

5. In patients with chronic cough who have chronic exposure to respiratory irritants, such as personal tobacco use, passive smoke exposure, and workplace hazards, avoidance should always be recommended. It is the most effective means to improve or eliminate the cough of chronic bronchitis. Ninety percent of patients will have resolution of their cough after smoking cessation. Level of evidence, good; net benefit, substantial; grade of recommendation, A

ANTIBIOTICS

The use of antibiotics for treatment of an acute exacerbation of chronic bronchitis is recommended as it has been shown to shorten the course of the illness. The use of antibiotics is most effective in patients with purulent sputum and in those with a greater severity of illness that includes all three of the cardinal symptoms (i.e., increased cough; increased sputum volume; and increased dyspnea) and in those with more severe airflow obstruction at baseline.

An opinion expressed by the US Food and Drug Administration in November 2002 suggested that the randomized placebo-controlled trials of antibiotic therapy for the acute exacerbation of chronic bronchitis that have been conducted over the past 40 years have been methodologically flawed and that a definitive decision regarding antibiotic use cannot be reached. However, based on a metaanalysis of nine studies, which included randomized controlled trials, therapy with antibiotics is recommended, especially in those patients with more severe illness. The effect that antibiotics have on cough during an acute exacerbation of COPD has been investigated. There is no significant effect on cough clearance or cough frequency when compared to therapy with a placebo. On the other hand, older trials studying the usefulness of prophylactic therapy with antibiotics to reduce the frequency and/or severity of attacks have shown a small but statistically significant effect in reducing the number of days of illness during an acute exacerbation of chronic bronchitis. However, therapy with antibiotics is currently not recommended for stable patients with chronic bronchitis because of concerns about antibiotic resistance and the potential side effects of the drugs.

RECOMMENDATIONS

6. In stable patients with chronic bronchitis, there is no role for long-term prophylactic therapy with antibiotics. Level of evidence, low; benefit, none; grade of recommendation, I

7. In patients with acute exacerbations of
chronic bronchitis, the use of antibiotics is recommended; patients with severe exacerbations and those with more severe airflow obstruction at baseline are the most likely to benefit. Level of evidence, fair; net benefit, substantial; grade of recommendation, A

Bronchopulmonary Hygiene

The use of bronchopulmonary hygiene physical therapy for chronic bronchitis recently has been the subject of review. The clinical benefits of postural drainage and chest percussion have not been proven, and their use in stable patients with chronic disease or during an acute exacerbation of chronic bronchitis cannot be recommended.

Recommendations

8. In stable patients with chronic bronchitis, the clinical benefits of postural drainage and chest percussion have not been proven, and they are not recommended. Level of evidence, fair; net benefit, conflicting; grade of recommendation, I

9. In patients with an acute exacerbation of chronic bronchitis, the clinical benefits of postural drainage and chest percussion have not been proven, and they are not recommended. Level of evidence, fair; net benefit, conflicting; grade of recommendation, I

Bronchodilators

The effects of therapy with short-acting inhaled β-agonists in patients with chronic bronchitis have been extensively studied and have been shown to improve pulmonary function, breathlessness, and exercise tolerance. There is some evidence that chronic cough improves with the regular use of a short-acting inhaled β-agonist, but the results in the literature are not consistent. The long-term effects of ipratropium bromide therapy have been evaluated in stable patients with chronic bronchitis. With this agent, patients coughed fewer times, and their cough was less severe. In addition, the volume of sputum expectorated decreased significantly. On the other hand, trials of a once-daily regimen of inhaled anticholinergic tiotropium in patients with COPD showed significant bronchodilatation and relief of dyspnea when compared to placebo, but no effect on cough using diaries to assess daily symptom scores.

The use of oral theophylline for the treatment of COPD has declined over the last several decades because of concerns over side effects, especially in elderly patients, and issues regarding interactions with other drugs. Therapy with oral theophylline does improve cough in stable patients with chronic bronchitis. During an acute exacerbation of chronic bronchitis, there is good evidence that bronchodilator therapy improves outcomes; however, the effect on cough has not been systematically studied.

Recommendations

10a. In stable patients with chronic bronchitis, therapy with short-acting β-agonists should be used to control bronchospasm and relieve dyspnea; in some patients, it may also reduce chronic cough. Level of evidence, good; net benefit, substantial; grade of recommendation, A

10b. In stable patients with chronic bronchitis, therapy with ipratropium bromide should be offered to improve cough. Level of evidence, fair; net benefit, substantial; grade of recommendation, A

10c. In stable patients with chronic bronchitis, treatment with theophylline should be considered to control chronic cough; careful monitoring for complications is necessary. Level of evidence, fair; net benefit, substantial; grade of recommendation, A

11. For patients with an acute exacerbation of chronic bronchitis, therapy with short-acting β-agonists or anticholinergic bronchodilators should be administered during the acute exacerbation. If the patient does not show a prompt response, the other agent should be added after the first is administered at the maximal dose. Level of evidence, good; net benefit, substantial; grade of recommendation, A

12. For patients with an acute exacerbation of chronic bronchitis, theophylline should not be used for treatment. Level of evidence, good; net benefit, none; grade of recommendation, D

Mucokinetic Agents and Corticosteroids

There is limited evidence to justify the use of mucokinetic agents or inhaled corticosteroids to control cough in patients with chronic bronchitis. Combined therapy with a long-acting β-agonist and an inhaled corticosteroid has been shown to reduce the exacerbation rate in patients with COPD and also to reduce cough in long-term trials in patients.
with COPD. Therapy with inhaled corticosteroids are recommended when airflow obstruction is severe or very severe (ie, FEV₁ < 50%) and when there is a history of frequent exacerbations of chronic bronchitis. The beneficial effects of expectorants have not been proven for the treatment of cough in patients with chronic bronchitis. The oral mucolytic agent N-acetylcysteine has been studied in stable patients with chronic bronchitis, and it has been shown to improve overall symptoms and to reduce the risk of exacerbations. It is not approved for use in the United States. The use of oral corticosteroids in patients has been discouraged. There is no evidence of benefit in stable patients with chronic bronchitis, and the well-known side effects will preclude any long-term trials in the future.

Therapy with mucokinetic agents is not useful during an acute exacerbation of chronic bronchitis. There is considerable evidence that patients who have an exacerbation of COPD will benefit from systemic therapy with corticosteroids. Studies of the effect of therapy with corticosteroids on acute exacerbations of chronic bronchitis have not specifically evaluated cough as an outcome. Treatment failure and lung function (FEV₁) have been the most frequently assessed end points. In the largest trial, there was equivalence between an 8-week trial and a 2-week trial of corticosteroids. Because of the significant potential for side effects with these agents, a 2-week trial is recommended.

**Recommendations**

13. For stable patients with chronic bronchitis, there is no evidence that the currently available expectorants are effective and therefore they should not be used. Level of evidence, low; net benefit, none; grade of recommendation, I

14. In stable patients with chronic bronchitis, treatment with a long-acting β-agonist when coupled with an inhaled corticosteroid should be offered to control chronic cough. Level of evidence, good; net benefit, substantial; grade of recommendation, A

15. For stable patients with chronic bronchitis and an FEV₁ of < 50% predicted or for those patients with frequent exacerbations of chronic bronchitis, inhaled corticosteroid therapy should be offered. Level of evidence, good; net benefit, substantial; grade of recommendation, A

16. For stable patients with chronic bronchitis, long-term maintenance therapy with oral corticosteroids such as prednisone should not be used; there is no evidence that it improves cough and sputum production, and the risks of serious side effects are high. Level of evidence, expert opinion; net benefit, negative; grade of recommendation, E/D

17. For patients with an acute exacerbation of chronic bronchitis, there is no evidence that the currently available expectorants are effective, and therefore they should not be used. Level of evidence, low; net benefit, none; grade of recommendation, I

18. For patients with an acute exacerbation of chronic bronchitis, a short course (10 to 15 days) of systemic corticosteroid therapy should be given; IV therapy in hospitalized patients and oral therapy for ambulatory patients have both proven to be effective. Level of evidence, good; net benefit, substantial; grade of recommendation, A

**Antitussive Agents**

Occasionally, the cough of chronic bronchitis is so troublesome that temporary cough suppression is required. When needed, codeine and dextromethorphan (but not pipazethate) are effective for treating cough in patients with chronic bronchitis. While studies have shown that they suppress cough counts by 40 to 60%, these studies were conducted with very small patient populations.

**Recommendation**

19. In patients with chronic bronchitis, central cough suppressants such as codeine and dextromethorphan are recommended for short-term symptomatic relief of coughing. Level of evidence, fair; benefit, intermediate; grade of evidence, B

**Summary of Recommendations**

1. Adults who have a history of chronic cough and sputum expectoration occurring on most days for at least 3 months and for at least 2 consecutive years should be given a diagnosis of chronic bronchitis when other respiratory or cardiac causes of chronic productive cough are ruled out. Level of evidence, low; net benefit, substantial; grade of recommendation, B

2. The evaluation of patients with chronic cough should include a complete history regarding exposures to respiratory irritants including cigarette, cigar, and pipe smoke;
passive smoke exposures; and hazardous environments in the home and workplace. All are predisposing factors of chronic bronchitis. Level of evidence, low; net benefit, substantial; grade of recommendation, B

3. Smoke-free workplace and public place laws should be enacted in all communities. Level of evidence, expert opinion; net benefit, substantial; grade of recommendation, E/A

4. Stable patients with chronic bronchitis who have a sudden deterioration of symptoms with increased cough, sputum production, sputum purulence, and/or shortness of breath, which are often preceded by symptoms of an upper respiratory tract infection, should be considered to have an acute exacerbation of chronic bronchitis, as long as conditions other than acute tracheobronchitis are ruled out or are considered unlikely. Level of evidence, expert opinion; net benefit, substantial; grade of recommendation, E/A

5. In patients with chronic cough who have chronic exposure to respiratory irritants, such as personal tobacco use, passive smoke exposure, and workplace hazards, avoidance should always be recommended. It is the most effective means to improve or eliminate the cough of chronic bronchitis. Ninety percent of patients will have resolution of their cough after smoking cessation. Level of evidence, good; net benefit, substantial; grade of recommendation, A

6. In stable patients with chronic bronchitis, there is no role for long-term prophylactic therapy with antibiotics. Level of evidence, low; benefit, none; grade of recommendation, I

7. In patients with acute exacerbations of chronic bronchitis, the use of antibiotics is recommended; patients with severe exacerbations and those with more severe airflow obstruction at baseline are the most likely to benefit. Level of evidence, fair; net benefit, substantial; grade of recommendation, A

8. In stable patients with chronic bronchitis, the clinical benefits of postural drainage and chest percussion have not been proven, and they are not recommended. Level of evidence, fair; net benefit, conflicting; grade of recommendation, I

9. In patients with an acute exacerbation of chronic bronchitis, the clinical benefits of postural drainage and chest percussion have not been proven, and they are not recommended. Level of evidence, fair; net benefit, conflicting; grade of recommendation, I

10a. In stable patients with chronic bronchitis, therapy with short-acting β-agonists should be used to control bronchospasm and relieve dyspnea; in some patients, it may also reduce chronic cough. Level of evidence, good; net benefit, substantial; grade of recommendation, A

10b. In stable patients with chronic bronchitis, therapy with ipratropium bromide should be offered to improve cough. Level of evidence, fair; net benefit, substantial; grade of recommendation, A

10c. In stable patients with chronic bronchitis, treatment with theophylline should be considered to control chronic cough; careful monitoring for complications is necessary. Level of evidence, fair; net benefit, substantial; grade of recommendation, A

11. For patients with an acute exacerbation of chronic bronchitis, therapy with short-acting β-agonists or anticholinergic bronchodilators should be administered during the acute exacerbation. If the patient does not show a prompt response, the other agent should be added after the first is administered at the maximal dose. Level of evidence, good; net benefit, substantial; grade of recommendation, A

12. For patients with an acute exacerbation of chronic bronchitis, theophylline should not be used for treatment. Level of evidence, good; net benefit, none; grade of recommendation, D

13. For stable patients with chronic bronchitis, there is no evidence that the currently available expectorants are effective and therefore they should not be used. Level of evidence, low; net benefit, none; grade of recommendation, I

14. In stable patients with chronic bronchitis, treatment with a long-acting β-agonist when coupled with an inhaled corticosteroid should be offered to control chronic cough. Level of evidence, good; net benefit, substantial; grade of recommendation, A

15. For stable patients with chronic bronchitis and an FEV₁ of < 50% predicted or for those patients with frequent exacerbations of chronic bronchitis, inhaled corticosteroid therapy should be offered. Level of
16. For stable patients with chronic bronchitis, long-term maintenance therapy with oral corticosteroids such as prednisone should not be used; there is no evidence that it improves cough and sputum production, and the risks of serious side effects are high. Level of evidence, expert opinion; net benefit, negative; grade of recommendation, E/D

17. For patients with an acute exacerbation of chronic bronchitis, there is no evidence that the currently available expectorants are effective, and therefore they should not be used. Level of evidence, low; net benefit, none; grade of recommendation, I

18. For patients with an acute exacerbation of chronic bronchitis, a short course (10 to 15 days) of systemic corticosteroid therapy should be given; IV therapy in hospitalized patients and oral therapy for ambulatory patients have both proven to be effective. Level of evidence, good; net benefit, substantial; grade of recommendation, A

19. In patients with chronic bronchitis, central cough suppressants such as codeine and dextromethorphan are recommended for short-term symptomatic relief of coughing. Level of evidence, fair; benefit, intermediate; grade of evidence, B

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