

Evaluation and Management of Acute Bronchitis

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Summary

In this chapter, acute bronchitis will be discussed in the context of the otherwise healthy child or adult. Patients with previous asthma, chronic obstructive pulmonary disease (COPD), heart disease, and diabetes are not included in this discussion. Infant lower respiratory tract illnesses, including bronchiolitis, are also beyond the scope of this chapter. Recent evidence-based guidelines have focused on adults but are also broadly applicable to older children and adolescents.



Definition of Bronchitis

A precise, reproducible, and clinically useful definition of acute bronchitis has proven elusive. Some studies have included only patients with a productive cough, but this excludes many patients with an otherwise identical clinical presentation. Current definitions do not include sputum as a necessary criterion for the definition of acute bronchitis.^{1,2} Macfarlane et al² have proposed a practical and reproducible definition of *acute lower respiratory tract illness* that has practical utility in the primary care setting (Table 9-1). The diagnosis of acute bronchitis requires ruling out the presence of clinically significant pneumonia.

Another term, *wheezy bronchitis*, has been employed to describe the common occurrence of wheezing in children with an acute lower respiratory tract infection. Less well known is the fact that *at least 15 to 30 percent* (some studies have reported 40 to 60 percent) of adults with acute bronchitis also wheeze and/or have objective evidence of reversible airway obstruction.³ This high prevalence justifies the use of the term *acute asthmatic bronchitis* to describe adults with signs and symptoms of acutely reversible airway obstruction (bronchospasm) in the setting of a nonpneumonic acute lower respiratory tract infection.³ Such symptoms include complaints of

Table 9-1

Definition of Acute Bronchitis

- Previously well patients not under supervision or management for an underlying disease—for example, patients with asthma, chronic obstructive pulmonary disease, heart disease, and diabetes are excluded.
- Diagnosis of acute lower respiratory tract infection requires all of the following:
 - (a) An acute illness present for 21 days or less
 - (b) Cough as the cardinal symptom
 - (c) At least one other lower respiratory tract symptom (sputum production, dyspnea, wheeze, chest discomfort/pain)
 - (d) No alternative explanation—for example, not sinusitis, pharyngitis, or a new presentation of asthma

SOURCE: Reproduced from Macfarlane,² with permission from the BMJ Publishing Group.

wheezing, chest tightness, and shortness of breath, particularly with a nocturnal component. In many cases, troublesome nocturnal symptoms are often the main reason that patients visit the doctor in search of relief.



Acute Bronchitis in the Age of Antibiotic Resistance

As currently implemented, the management of acute bronchitis is misguided and probably does more harm than good, mainly because antibiotics are prescribed routinely despite evidence that they are not beneficial to most patients with this condition. In the past this antibiotic misuse could be shrugged off as a small price to pay for giving the impression that “everything possible” was being done. Now, however, the emergence

of antibiotic-resistant bacterial pathogens as a direct result of antibiotic overuse requires radical reassessment of current management by both patients and physicians.

New guidelines have recently been developed that have the potential to improve the process of care for acute bronchitis.^{1,4,5} These guidelines emphasize that antibiotics should not be prescribed routinely for uncomplicated acute bronchitis because the results of most randomized, controlled trials do not support the benefit of antibiotics for this condition.

An exciting but still speculative future prospect, suggested by an emerging body of research, is the determination that a subset of acute bronchitis will develop into chronic bronchitis and asthma. This research also implicates specific bacterial pathogens as potentially responsible for chronic respiratory sequelae of acute bronchitis. Although the therapeutic applications of this research are as yet unknown, primary care physicians are in an ideal position to observe, document, and research the earliest manifestations of chronic respiratory diseases that later become severe, debilitating, or fatal. Thus, in the future, the evaluation and management of acute bronchitis may become important to the early recognition, management, and perhaps even prevention of severe chronic respiratory conditions such as COPD and asthma.



Pathophysiology

Gonzales and coworkers have suggested that the clinical features of uncomplicated acute bronchitis develop in sequential phases.¹ The acute phase results from direct inoculation of the tracheobronchial epithelium by an infectious agent, followed by cytokine release and acute inflammation that produces variable constitutional symptoms, such as fever, myalgias, and malaise. These symptoms may last 1 to 5 days, depend-

ing on the infectious agent. Infection with rhinovirus, for example, may be associated with few constitutional symptoms, whereas infection with the influenza virus may cause severe constitutional symptoms lasting 3 to 5 days. A distinguishing clinical feature of acute bronchitis due to *Chlamydia pneumoniae* is the presence of several weeks of low-grade symptoms prior to seeking care.⁶

The pathogenesis of the protracted phase of uncomplicated acute bronchitis has not been formally studied. However, extensive knowledge from the study of the virus-mediated pathogenesis of asthmatic inflammation serves as a basis for extrapolation.⁷ According to Gonzales,¹ the protracted phase of uncomplicated acute bronchitis results from hypersensitivity of the tracheobronchial epithelium and airway receptors, leading to bronchial hyperresponsiveness and cough, often in association with phlegm and/or wheeze. Bronchial hypersensitivity does not appear to be related to any specific pathogen. Instead, it is probably a result of a combination of host factors that may include respiratory epithelial dysfunction, adrenergic-cholinergic tone imbalance, and IgE-mediated histamine release. Several studies document that uncomplicated acute bronchitis is often (but not invariably) associated with abnormalities of pulmonary function that are usually transient but may last several months. While there is no hard and fast rule on how long one should observe a patient with persisting symptoms after an episode of acute bronchitis before concluding that the symptoms have become chronic, a reasonable approach is to wait a minimum of a month after an acute episode of bronchitis illness before progressing to evaluation for other conditions.⁸

Microbiology of Acute Bronchitis

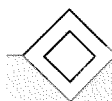
Most episodes of uncomplicated acute bronchitis are triggered by respiratory viral infections.¹ The viruses that are most often isolated include

influenza A and B, parainfluenza, and respiratory syncytial virus, which target the lower respiratory tract, and rhinovirus, adenovirus, and coronavirus, which also target the upper respiratory tract. *Bordetella pertussis* and *B. parapertussis* can also cause acute bronchitis, even in previously immunized adults. Their recognition usually depends on an enhanced awareness during an epidemic and use of appropriate cultures, as recommended by local public health laboratories.

Mycoplasma pneumoniae can cause acute bronchitis, although it has been thought to contribute to 5 percent or less of cases. Likewise, acute *C. pneumoniae* infection has been shown to cause, in general, approximately 5 percent of acute bronchitis.^{6,9} A recent prospective study of the incidence, etiology, and outcome of adult lower respiratory tract infections reported a higher proportion of cases associated with evidence for *M. pneumoniae* (7.3 percent) and *C. pneumoniae* (17 percent) infection.² In this study, whether antibiotic treatment was prescribed or withheld in cases of bronchitis associated with atypical pathogens did not seem to affect the outcome as measured by the need to revisit a clinician.

A high prevalence of serologic evidence for possible chronic *C. pneumoniae* infection has been reported in acute bronchitis. Falck et al¹⁰ found evidence for *C. pneumoniae*-specific IgA antibodies in a quarter of patients with acute bronchitis. IgA antibodies may be found in recent secondary infection, and persistent detection of IgA suggests chronic infection, since the half-life of IgA is short (less than 1 week). In a larger study from the same group, IgA antibodies were associated with a "naso-pharyngeal-bronchial syndrome," defined as a constellation of persisting upper and lower respiratory tract illness symptoms.¹¹ In a case control study using asymptomatic adults as controls, Huitinen et al¹² reported that *C. pneumoniae*-specific IgA antibodies were associated with both acute bronchitis and asthma, but that only asthma was associated with antibodies directed against

chlamydial heat-shock protein 60 (hsp60). Since antibodies against chlamydial hsp60 are associated with the chronic inflammatory sequelae of other chlamydial diseases such as trachoma, pelvic inflammatory disease, and tubal infertility, these data suggest (but do not prove) that chronic inflammation in some cases of asthma also may be related to chlamydial infection. These preliminary findings should not, however, be used as justification for antibiotic use in uncomplicated acute bronchitis. The association between atypical infections and asthma is now an active area of research, and more information should be forthcoming.



Epidemiology

The epidemiology of uncomplicated acute bronchitis has not received as much attention as the epidemiology of other respiratory illnesses.¹³ Large surveys of morbidity in general practice carried out in England and Wales between 1970 and 1999 found that the age-specific incidence of acute bronchitis assumed a U-shaped distribution, with the highest incidence in infants, a nadir in the 15- to 25-year age group, and then a progressive increase in incidence throughout adulthood.^{14,15} In early childhood, acute bronchitis tends to cluster with pneumonia and asthma, whereas a different group of children are diagnosed with acute upper respiratory illnesses (tonsillitis, otitis media, and the common cold).¹⁶ Studies in adults indicate that women are more likely than men to be diagnosed with acute bronchitis and that most diagnoses occur during the winter months.^{2,15} In a stable suburban English population presenting over 1 year with acute lower respiratory tract infections, the incidence in otherwise healthy adults was 64 per 1000 for women compared to 44 per 1000 for men.² It is interesting that these age- and sex-

specific incidence patterns for the epidemiology of acute bronchitis are the same as those for asthma.¹⁷

Diagnosis

Differential Diagnosis

Acute asthmatic bronchitis must be distinguished from chronic asthmatic bronchitis. This is a term applied to patients in whom the diagnoses of chronic bronchitis and asthma coexist or are difficult to distinguish. The textbook definition of chronic bronchitis also includes chronic sputum production for at least 3 months of the year for 2 consecutive years. The possibility that these chronic conditions arise following acute bronchitis will be addressed later in this chapter.

In addition to chronic bronchitis and asthma, other acute problems can mimic acute bronchitis. The most important of these to distinguish is pneumonia. Uncomplicated acute bronchitis is a self-limited illness, whereas pneumonia can be more severe and even fatal. The standard for diagnosing pneumonia is chest radiography,¹⁸ but this test is not universally available in primary care settings and is expensive. Thus, many primary care providers do not routinely obtain a chest radiograph to evaluate a patient with a cough. When the diagnosis of pneumonia is suspected, however, clinicians need to be aware that while no individual clinical finding or combination of findings can rule out the possibility of pneumonia,¹⁸ further diagnostic testing is usually not necessary unless the patient's vital signs are abnormal (i.e., heart rate > 100 beats/minute, respiratory rate > 24 breaths/minute, and oral body temperature > 38°C) or findings other than wheezing are present on chest examination (focal consolidation, such as rales, egophony, or fremitus).¹ In making the decision about further diagnostic testing to rule out

pneumonia, the clinician must also consider the possibility of an atypical presentation of pneumonia (without the cardinal vital sign abnormalities) in the elderly and the possible presence of influenza bronchitis (with vital sign abnormalities), depending on the epidemic milieu.

Another possibility that should not be overlooked is that of a lung cancer with localized obstruction of a proximal bronchus. Patients with lung cancer may present with a wheezy cough but often have other systemic symptoms such as weight loss, appetite changes, or night sweats. For high-risk patients, such as smokers or those exposed to occupational agents associated with increased rates of cancer, a new cough associated with systemic signs of malignancy should prompt an evaluation for a bronchial tumor. Similarly, patients who are at risk for lung cancer or who have hemoptysis should be considered for further evaluation.

Treatment/Management

Recent evidence-based guidelines for the management of uncomplicated acute bronchitis emphasize the importance of ruling out more severe disease (mainly pneumonia), limiting the use of antibiotics, and focusing on communication, patient education, and symptomatic relief of this usually self-limited condition.

Role for Antibiotics

Antibiotics should not be considered routine treatment for patients with uncomplicated acute bronchitis. Several evidence-based reviews (summarized in reference 5) of existing randomized, controlled trials of antibiotic versus placebo in uncomplicated acute bronchitis have concluded that there is little or no consistent benefit from antibiotics. In particular, giving antibiotics

with the aim of reducing the risk of later pneumonia is unwarranted. Regarding the improvement in acute symptoms such as cough, malaise, or time to return to work, conclusions are hampered by the paucity and poor quality of data and by the lack of uniformity in entry and outcome criteria.

The one uncommon circumstance in which antibiotics are indicated is the suspicion of pertussis, which requires a high probability of exposure and a supportive local public health laboratory to aid in diagnosis.⁵ Regardless of the limitations of current studies, it is clear that the benefit, if any, of antibiotics in relieving symptoms of acute bronchitis is minimal and that antibiotics should not be regarded as first-line therapy.

The majority of physicians prescribe antibiotics as their first choice for treatment of patients with uncomplicated acute bronchitis.¹⁹ In the United States and the United Kingdom, the probabilities are between two-thirds and three-quarters that an adult primary care outpatient presenting with acute bronchitis will receive a prescription for an antibiotic.^{20,21} The antibiotic prescribing rate for acute bronchitis in children is equally high.²² How this state of affairs evolved is obscure, but it probably resulted from a complex interaction among other factors: a "do everything possible" philosophy on the part of physicians associated with a training effect on patients to equate antibiotics with relief of symptoms. Fortunately, quality improvement initiatives can be successful in stemming the tide of inappropriate prescribing of antibiotics.²³

Although inappropriate prescribing of antibiotics has been documented for a long time, the recent increase in the prevalence of antibiotic-resistant bacteria has made the lowering of inappropriate antibiotic use an urgent priority.²⁴ It is hoped that decreased prescribing of antibiotics will result in a generalized lower prevalence of bacterial antibiotic resistance, as demonstrated for group A streptococci after decreased consumption of macrolide antibiotics.²⁵ Unfortunately, depending on the underlying molecular

mechanisms, restriction of antibiotic use does not always result in decreased resistance.²⁶

In addition to antibiotic resistance, other phenomena are also thought to be linked to excessive antibiotic use. Some suspect that injudicious antibiotic use can result in alterations of microbial flora, causing infectious diseases such as antibiotic-associated diarrhea (*Clostridium difficile*) and uncomplicated cystitis in young women.²⁷ Another note of concern in using antibiotics unnecessarily comes from a recent finding that antibiotics administered to infants during the first 6 months of life may increase the risk for subsequent asthma, possibly by disrupting the development of immune responses against gut flora that protect against asthma.^{28,29}

Additional reasons to avoid unnecessary prescribing of antibiotics are listed in Table 9-2. Among these are adverse reactions to and financial costs of antibiotics. Focusing on the prescribing of antibiotics as the primary treatment for acute bronchitis may also have the unintended adverse consequence of diverting attention from more useful symptomatic treatments.

One caveat to this discussion on antibiotics is that few studies have been done to evaluate effective treatment strategies for acute bronchitis. One expert in the field has commented that uncomplicated acute bronchitis is a "homely" disease that is not deemed worthy of significant

Table 9-2

Reasons to Avoid Antibiotic Prescribing in Acute Bronchitis

- Development of antibiotic resistance in the community
- Increased risk for subsequent infections and (possibly) asthma
- Side effects
- Allergic reactions
- Financial cost to the patient
- Financial cost to the health care system
- Training patients to expect antibiotics
- Diverting attention from useful symptomatic treatments

attention.³⁰ All told, fewer than 1000 patients worldwide with uncomplicated acute bronchitis have been randomized to antibiotic/placebo trials. The largest study of antibiotic therapy in acute bronchitis had a total of only 207 participants and was conducted more than a quarter-century ago. The small number of study participants makes it difficult to identify subgroups for whom antibiotics may be beneficial. In fact, the only study in the last 25 years to have enrolled more than 100 patients found that a subgroup of patients 55 years of age or older taking doxycycline had a significantly shortened illness duration compared to those taking placebo.³¹ Consequently, the available data supporting current recommendations against the routine use of antibiotics in acute bronchitis do not exclude the possibility that some patients might benefit from antibiotic treatment. However, at this time it is impossible to identify this potential subgroup on clinical grounds alone, except to note that patients age 55 years or older who feel ill might benefit from doxycycline.³¹

Furthermore, none of the randomized trials performed to date address the question of whether chronic sequelae of acute bronchitis are influenced by treatment.³ While these studies do not deal with patients with acute bronchitis, it is interesting to note that tetracycline antibiotic treatment of acute exacerbations of chronic bronchitis has been shown to be associated with fewer subsequent relapses when compared to cephalosporins and beta-lactam antibiotic therapy.³² Whether this finding also applies to relapses or other sequelae of uncomplicated acute bronchitis has not been studied systematically.

Symptomatic/Supportive Care

The most important insight into the successful management of acute bronchitis in recent decades is the observation that a significant proportion of patients with this condition have evidence of reversible airway obstruction^{33,34} and that treatment with inhaled bronchodilators,³⁵⁻³⁷

but not with oral bronchodilators,^{38,39} is beneficial to relieve symptoms. The effectiveness of bronchodilators in relieving the symptoms of acute bronchitis is not surprising, since the protracted phase of uncomplicated acute bronchitis, at least in a subgroup of patients, involves airway hyperresponsiveness and cough.

It is unclear whether all patients with uncomplicated acute bronchitis will benefit from inhaled bronchodilators or whether only the subgroup with signs and/or symptoms of hyperreactive airways will derive symptomatic benefit. The preponderance of evidence favors the latter possibility. Melbye and colleagues found that only a subgroup of patients showed improvement when treated with fenoterol. Patients who came to their physician with either over 7 days of symptoms, wheezes found on auscultation, evidence of reversible airway obstruction after bronchodilator treatment, or a forced expiratory volume in 1 s (FEV₁) less than 80 percent of predicted showed improvement in their symptoms at day 2 with inhaled fenoterol; no effect was observed in patients with normal lung findings.³⁵ On the other hand, Hueston found that wheezing was not predictive of response to inhaled bronchodilators, but his study did not report on pulmonary function.³⁶ The evidence favors the use of inhaled bronchodilators in the subgroup of patients with signs or symptoms of bronchial hyperreactivity, although more studies are needed to confirm this possibility.

Antitussives such as dextromethorphan or codeine probably have some benefit in reducing cough severity during the protracted phase of acute bronchitis.

Communication with Patients

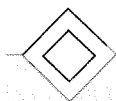
Many patients with acute bronchitis come to their physician to rule out the possibility of pneumonia, to be reassured that they will get better, and to seek relief from disturbed sleep or to address other, less predictable concerns that need to be identified.⁴⁰ Instead of routine

prescribing of an antibiotic, a clinical examination, some reassuring words (if appropriate), and information on the etiology and natural history of acute bronchitis (for example, a quarter of patients are still coughing after 3 weeks⁴¹), along with a statement that symptomatic treatments are more beneficial than antibiotics, are all that the patient needs. Patients also can be informed that there is only about a 1 in 20 chance that their bronchitis is due to bacteria that are susceptible to antibiotics. Therefore, while an antibiotic might help, the probability is low. Reconsultations for acute lower respiratory tract illness can be reduced by strategies that include information.⁴² Furthermore, patient satisfaction with a visit for acute bronchitis depends more on patient education and adequate physician-patient communication than on antibiotic prescribing, even for patients who expect to receive an antibiotic.⁴³

Other Approaches

Avoidance of known triggers (cold air, dust, or allergens) and environmental humidification are reasonable options. *Consumer Reports* has published a useful guide for patients ("What to Do about a Cold or Flu," January 1999, pp. 14-15) that includes a table of symptoms linked to a list of over-the-counter remedies.

A proposed algorithm for the evaluation and management of acute cough illness is presented in Figure 9-1.



Chronic Sequelae of Acute Bronchitis

Uncomplicated acute bronchitis may be associated with chronic sequelae. Table 9-3 illustrates the typical clinical presentations of acute bron-

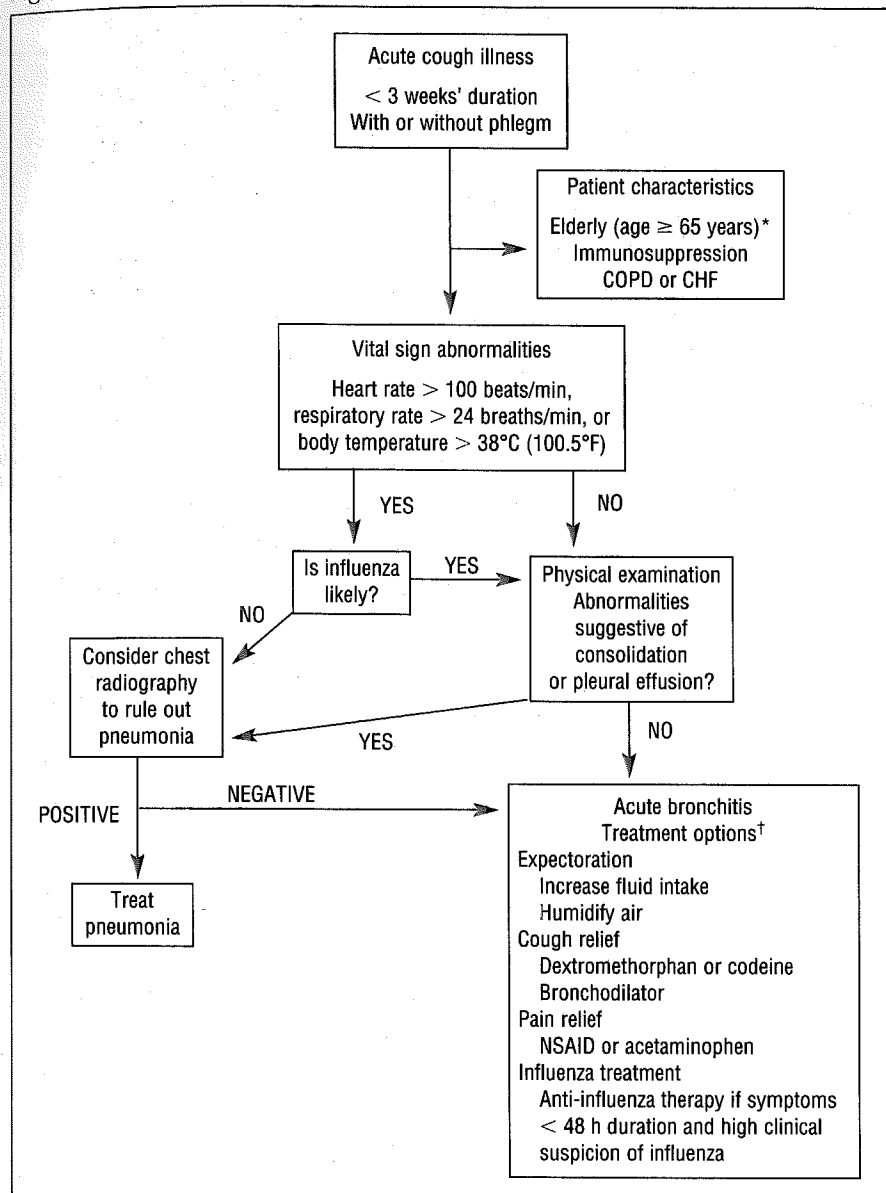
chitis (A), chronic asthma (B), and COPD (chronic asthmatic bronchitis) (C). These clinical diagnoses are usually regarded as three separate clinical entities. However, it would probably be more appropriate to regard each of them as a particular clinical manifestation of the same disease process at a different stage of development. In the particular example described in Table 9-3, the clinical scenarios involve the same patient, who was encountered over a 17-year time period.

Chronic Asthma

Often, patients with adult-onset asthma report that it began after an acute lower respiratory tract illness, usually described as acute bronchitis, pneumonia, or an influenza-like illness. This presentation for adult-onset asthma is common enough that it has been formally studied and given the descriptive term *infectious asthma*.⁴⁴ Prospective, population-based epidemiologic studies consistently report that asthma in all age groups is significantly associated with a history of preceding lower respiratory tract illnesses.⁴⁴ In most of these epidemiologic studies, a history of previous lower respiratory tract illness is more significant than atopy as an associated factor. In fact, a recent comprehensive review of all population-based asthma studies has concluded that less than half of asthma cases, whether of childhood or adult onset, can be attributed to atopy and that other mechanisms for the development of asthma need to be investigated.⁴⁵

A role for acute respiratory viral infection (particularly respiratory syncytial virus) as a precipitating cause for childhood asthma is being actively investigated,⁴⁶ and emerging evidence supports the possibility that acute *C. pneumoniae* infection, and to a lesser extent *M. pneumoniae* infection, may initiate chronic asthma in adults.⁴⁷ What quantitative contribution these infections may make to the incidence of asthma is unknown. It is also unknown whether specially designed antibiotic treatments will have

Figure 9-1



*Pneumonia in elderly persons, those with immunosuppression, and those with chronic obstructive pulmonary disease (COPD) or congestive heart failure (CHF) often presents atypically. A high index of suspicion is warranted when evaluating cough illness in these patients, even when vital signs and chest examination appear normal.

† Consider pertussis treatment if the patient has known exposure to pertussis. Follow local health department testing guidelines; pending results, treat with erythromycin for 14 days. NSAID = nonsteroidal anti-inflammatory drug.

From Gonzales and Sande,¹ with permission.

Table 9-3

Typical Presentations for Acute Bronchitis and Other Similar Conditions

A. *Acute bronchitis*

- 55-year-old male developed rhinorrhea, nasal congestion, sore throat, cough, and low-grade fever (100°F)
- Diagnosed with acute bronchitis after chest x-ray showed no infiltrate
- Treated with an antihistamine-decongestant combination and erythromycin 250 mg q.i.d. for 1 week

B. *Chronic asthma*

- 55-year-old pipe-smoking male with no previous history of chronic respiratory complaints or clinical allergies
- Presented with a 2-month history of cough, wheeze, and shortness of breath following a "cold"
- History that erythromycin treatment for "bronchitis" resulted in some improvement, but then symptoms relapsed and persisted
- Symptoms were improved by oral theophylline, an injection of epinephrine, and inhaled albuterol
- FEV₁ was 87 percent predicted without a bronchodilator response (FEV₁/FVC = 72 percent)
- His symptoms worsened, and 3 weeks later his FEV₁ was 27 percent predicted; after steroid bursts and hospitalization, his FEV₁ improved to 119 percent predicted

C. *COPD*

- 71-year-old ex-smoking male with a diagnosis of "COPD with asthma"
- Current medications:
 - Theophylline CR 300 mg t.i.d.
 - Albuterol 2 puffs q.i.d.
 - Brethine 5 mg t.i.d.
 - Prednisone 10 mg/day alternating with 5 mg/day
- Fairly well-controlled symptoms, but having occasional exacerbations
- Stable pulmonary function (FEV₁/FVC = 40–48 percent)
- Comorbidities:
 - Chronic sinusitis
 - Osteopenia
 - Atraumatic lumbar compression fractures
 - Posttraumatic glaucoma
- Died suddenly in ventricular fibrillation; no postmortem performed

ABBREVIATIONS: FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; COPD, chronic obstructive pulmonary disease.

any potential to favorably alter the natural history of infectious asthma. It is known, however, that the standard courses of antibiotics currently used for the treatment of uncomplicated acute bronchitis do not have any benefit in chronic asthma.⁴⁷

Chronic Bronchitis

Recently, evidence for chronic *C. pneumoniae* infection has been found in lung tissue from patients with COPD⁴⁸ and emphysema.⁴⁹ Nearly half of the young adults sampled were also

found to contain *C. pneumoniae* in lung specimens,⁴⁸ which raises the possibility that lung carriage of *C. pneumoniae* is common in adults and increases with age. This could contribute to the pathogenesis of obstructive lung diseases such as asthma and COPD. Since many people are infected, yet only some develop disease, genetic or other susceptibility factors must also be operating. As with chronic asthma, therapeutic interventions require further research.



Summary

The diagnosis and management of uncomplicated acute bronchitis should be simple and straightforward. Treatment for uncomplicated acute bronchitis should emphasize communication and provision of information and symptomatic remedies. Antibiotics should be reserved for the rare instances of complications or persistence of illness. Major challenges to implementation appear to involve behavioral factors, mainly resistance on the part of physicians to change current practices and on the part of patients to accept the recommended changes. An important emerging aspect of the management of uncomplicated acute bronchitis relates to evidence that this condition can lead to chronic sequelae, such as asthma and COPD. Current medical practice does not include guidelines for dealing with the chronic sequelae of acute bronchitis.

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