Topics in Primary Care Medicine

The Use of Antibiotics in Acute Bronchitis and Acute Exacerbations of Chronic Bronchitis

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"Topics in Primary Care Medicine" presents articles on common diagnostic or therapeutic problems encountered in primary care practice. Physicians interested in contributing to the series are encouraged to contact the series' editors.

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Acute bronchitis (or tracheobronchitis) is a self-limited disease with acute cough, usually productive of phlegm, and without evidence of pneumonia either clinically or by a chest x-ray film. The phlegm may be tenacious, clear, discolored, increased in amount, or foul tasting. Hemoptysis may occur. The temperature may be slightly elevated—usually not above 38.9°C (102°F)—and night sweats and fatigue are common. Shortness of breath may be worsened in patients with underlying lung disease. Occasionally there will be musculoskeletal chest wall pain, usually induced by coughing. Chest findings may include localized or diffuse crepitations and wheezes.

Laboratory tests, including sputum cultures, sputum Gram's stains, and chest roentgenograms, are not used frequently in making the diagnosis. In most instances sputum cultures (because they grow normal flora) and Gram's stains (because they show fewer than 5 leukocytes per high-powered field but no predominant organism) are not initially indicated. Chest x-ray films may be needed to help differentiate bronchitis from pneumonia. Indeed, no sign, symptom, or laboratory finding can reliably differentiate the two. An elderly patient with fever and abnormal chest findings is a case in which a chest x-ray film is useful. The absence of abnormal auscultatory findings on lung examination can exclude pneumonia with greater than 95% certainty.

Acute bronchitis may be associated with symptoms of an upper respiratory tract infection, particularly pharyngitis, although the upper respiratory tract symptoms usually fade before the cough disappears. A typical course for acute bronchitis is 7 to 14 days, although a third of patients cough for more than a month. Symptoms are more common and prolonged in cigarette smokers and in winter months.

Incidence of Acute Bronchitis

Bronchitis is a common disease. In more than 500,000 visits to general and family physicians in Virginia, acute bronchitis was the fifth most common condition diagnosed, accounting for 2.7% of all visits and 16% of visits for respiratory tract problems. In the 1980 National Ambulatory Medical Care Survey, bronchitis (unspecified) was the 7th most common condition diagnosed by general and family physicians, accounting for 1.9% of all office visits, and acute bronchitis was the 20th most common condition, accounting for another 1.1% of visits. It is estimated that in the United States acute bronchitis accounts for about 12 million physician visits a year and more than $300 million in physician visits and prescriptions. Work absences are common and probably run in the millions of days each year.

Although a diagnosis of acute bronchitis is usually made in patients without chronic lung disease, there is an association between bronchitis and asthma. Patients with a diagnosis of acute bronchitis are significantly more likely to have a previous history of asthma or atopic disease compared with controls and have a pronounced increase in subsequent visits for asthma. Indeed, the term "asthmatic bronchitis" may be appropriate to express the midrange of the spectrum that goes from acute bronchitis to asthma. In one recent study, 40% of patients with acute bronchitis but no previous history of lung disease or asthma had a forced expiratory volume in one second of less than 80% of predicted, a finding that returned to normal over a five-week period.

Chronic Bronchitis

Chronic bronchitis is defined as the production of sputum on most days for at least three months per year for more than two years. An acute exacerbation of chronic bronchitis is a clinical syndrome characterized by an increase in cough, an increased production of phlegm with altered color or tenacity, and an increased breathlessness without evidence of pneumonia—either clinically or by chest x-ray film. As with acute bronchitis, hemoptysis may occur. Wheezing is frequently present due to narrowing and obstruction in the smaller—less than 2 mm in internal diameter—airways. Most patients do not have signs or symptoms suggestive of systemic infection such as fever or leukocytosis. Increased dyspnea and chest tightness are frequently present.

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Chronic bronchitis is generally diagnosed in association with emphysema, asthma, or both. The term "chronic obstructive pulmonary disease" reflects the overlapping disorders of chronic bronchitis, emphysema, and asthma. Whereas chronic bronchitis is defined clinically, emphysema and asthma are defined by pulmonary function tests. Sorting out these three disorders in an individual patient can be a difficult task. There is a bias to make a diagnosis in male patients of emphysema and in female patients of asthma or chronic bronchitis.

The chest x-ray film in an acute exacerbation of chronic bronchitis is normal or reflects the underlying chronic obstructive pulmonary disease. Changes may range from hyperaeration and bullae characteristic of emphysema to saccules, honeycombing, and atelectasis, which can be seen in bronchiectasis. Peribronchial cuffing is sometimes seen that represents thickening of the adventitia or mucosa around the bronchi.

Incidence of Chronic Bronchitis

Because chronic bronchitis is usually diagnosed with emphysema or asthma, the frequency with which it occurs is unclear. In one cross-sectional study of a general population, 12% of adult men and 8% of adult women had symptoms of chronic bronchitis. In the Virginia study, however, chronic bronchitis was the 114th most frequent condition diagnosed, accounting for a little less than 0.2% of all visits and 1.1% of visits for respiratory problems.

Infectious Causes of Acute Bronchitis

Table 1 lists the causes of bronchitis. For acute bronchitis, almost all causes are infectious. By far the most common is viral, accounting for well over half of the diagnoses; 180 viruses have been identified as causing upper respiratory tract infections. As a guideline, a cough will develop in 50% of patients who have such an infection, and in 50% of those a productive cough characteristic of acute bronchitis will develop. The most common viral cause of acute bronchitis is probably the rhinovirus, followed by the adenovirus. Influenza virus can cause extensive destruction of the respiratory epithelium, and respiratory syncytial virus is the usual cause of bronchiolitis in young children.

The second most common cause of bronchitis, at least in young adults, is *Mycoplasma pneumoniae.* It may account for 10% to 20% of diagnoses. The true incidence is unknown, for in the absence of clinical or radiographic signs of pneumonia, cold agglutinins are often not checked (and even if checked, may be falsely negative early in the course). Complement fixation studies are available, and a fourfold rise is indicative of a recent infection. Culturing for *Mycoplasma* is difficult, but a simplified office test is under development.

Chlamydia can also cause bronchitis. Recently a TWAR—TW for Taiwan, AR for acute respiratory disease—strain of *Chlamydia psittaci* was found to be the second most common cause of pneumonia, after *M pneumoniae,* in college students, and 5% of cases of bronchitis were associated with TWAR infection. One is faced with a problem in diagnosing TWAR infections—there is no commonly available culture technique or identification test.

A smaller portion of the cases of acute infections are due to bacteria. Sputum cultures from 80% to 95% of patients with acute bronchitis will grow out only normal flora. While it is generally accepted that normal bronchi are sterile, many bacteria, including *Haemophilus influenzae* and *Streptococcus pneumoniae,* are often found further up the upper respiratory tract, making the interpretation of a sputum culture difficult. Nevertheless, *S pneumoniae* and *H influenzae* are thought to be causes of acute bronchitis, particularly in those with more systemic symptoms.

Branhamella catarrhalis (formerly called *Neisseria catarrhalis*) is a gram-negative diplococcus recently recognized as a pathogen in acute bronchitis and in acute exacerbations of chronic bronchitis. In a recent study, it was the third most common bacterial pathogen (after *S pneumoniae* and *H influenzae*). The diagnosis is suggested from a Gram's stain where it appears as a kidney bean-shaped gram-negative diplococcus.

TABLE 1.—*Common Causes of Tracheobronchitis*

External Stimuli	Viruses
Tobacco	Influenzas A and B
Cannabis	Parainfluenzae
Air pollution	Rhinoviruses
Ammonia	Respiratory syncytial virus
Chlorine	Adenoviruses
Industrial fumes, dust	Coxsackievirus
	Coronaviruses
Bacteria	Other Infectious Agents
Haemophilus influenzae	*Mycoplasma pneumoniae*
Streptococcus pneumoniae	*Chlamydia* (TWAR)
Branhamella catarrhalis	
Bordetella pertussis	

The Cause of Acute Exacerbations

Cigarette smoking is clearly the major risk factor for the development of chronic bronchitis and emphysema. In those smoking 20 cigarettes or fewer per day (light to moderate), the frequency of chronic bronchitis is about 25%; for heavy smokers (greater than a 40- to 60-pack-year history), it increases to almost 50%. A long-term smoker who stops smoking can have a definite lessening of smaller airways obstruction as well as a reduction in coughing, sputum production, and wheezing. Other less common causes of chronic bronchitis include inhaling dust and fumes, particularly chlorine and ammonia.

The role of bacterial infections in acute exacerbations of chronic bronchitis is based more on deduction than proof. Sputum cultures are more frequently positive, but their interpretation is enigmatic. Chronic colonization of the airways with unencapsulated strains of *H influenzae* and pneumococci occurs in at least half of patients. The organisms are often found in the sputum during quiescent periods, but exacerbations are associated with a quantitative increase in the number of organisms cultured.

In summary, in acute bronchitis the cause is usually viral, with *Mycoplasma* and *Chlamydia* being less frequent and bacterial causes the least likely. In flare-ups of chronic bronchitis, environmental factors—particularly cigarette smoke—are important cofactors. The infectious causes are in a different order of frequency, with viruses still being the most common, followed by bacteria—*H influenzae, S pneumoniae,* and *B catarrhalis*—with *Mycoplasma* or *Chlamydia* being the least likely.

Treating Acute Bronchitis

The treatment of acute bronchitis is still empiric. Obviously if a patient smokes, this is an opportune time for counseling. Codeine- or dextromethorphan-containing cough suppressants may be indicated in those with significant coughing spasms or nighttime cough. Glyceryl guaiacolate, potassium iodide, mucolytic agents, antihistamines, and decongestants usually are not helpful. If influenza A is suspected, starting a regimen of amantadine hydrochloride, 100 mg twice a day—or 100 mg per day in elderly patients—within the first 48 hours will ameliorate symptoms.

The role of antibiotics in the treatment of acute bronchitis or an acute exacerbation of chronic bronchitis is controversial. Patients with a diagnosis of acute bronchitis are usually administered an antibiotic—most commonly erythromycin—even though many studies and reviews state that antibiotic therapy is not indicated. Unfortunately, most trials of the use of antibiotics for treating bronchitis were not double blind and randomized. As would be expected, numerous studies comparing the use of one antibiotic with another have shown good response to either drug.

Of five randomized controlled trials (see Table 2) of antibiotic treatment of acute bronchitis, two found no benefit from a one-week course of doxycycline, one found a reduction in symptoms and time off work when patients were treated with trimethoprim and sulfamethoxazole, one found no difference with a one-week trial of erythromycin (although there was a consistent trend favoring treatment in nonsmokers), and one found significantly fewer signs and symptoms after a ten-day course of erythromycin.

The antibiotics that might be reasonable choices for therapy are listed in Table 3, along with their antibacterial spectrum. Unfortunately, none gets all the common bacterial pathogens. The choice of whether to use an antibiotic and, if so, which one still rests with clinical judgment. At this time, our recommendation is not to treat in those who are otherwise healthy and who have no significant systemic symptoms. Acute bronchitis is a self-limited condition usually caused by viruses with a course that is not dramatically changed by giving antibiotics. In those with preexisting conditions—such as diabetes mellitus or congestive heart failure—and in those who have a productive cough along with systemic symptoms, most physicians lean towards treating for one to two weeks with one of the drugs listed—with the hope of decreasing the sputum production and perhaps preventing the occasional progression towards pneumonia or respiratory failure.

TABLE 2.—*Summary of Randomized Antibiotic Trials in Patients With Acute Bronchitis*

Study	*Definition of Acute Bronchitis*	*Subjects, No.*	*Antibiotic Used and Dose*	*Results*
Stott et al (*Br Med J* 1976; 2:556-559)	Productive cough of up to 1 wk's duration and normal findings on chest examination	207	Doxycycline, 2 initially, then 1 each d × 7 to 10 d	No difference in cough or other symptoms at 1 wk
Franks and Gleiner (*J Fam Pract* 1984; 19:185-190)	Cough productive of sputum for less than 15 d without clinical evidence of pneumonia	67	TMP-SMX, 2/d × 1 wk	At 1 wk, antibiotic group had significantly less cough, less fever, and used fewer OTC drugs; there was also a trend towards fewer days off work; smoking history did not help predict responders
Williamson (*J Fam Pract* 1984; 19:481-486)	Cough and sputum production and rhonchi or history of fever	69	Doxycycline, 1/12 hr × 3, then 1 each d × 6 d	No difference in symptoms at 1 wk or thereafter; placebo group missed less work; no difference in smokers
Brickfield et al (*J Fam Pract* 1986; 23:119-122)	Cough producing sputum for 2 wk or less and no evidence of pneumonia	50	Erythromycin, 3/d × 1 wk	Symptoms tended to resolve in nonsmokers more rapidly with treatment, with less cough and sputum production (but most not significantly different); no difference for smokers
Dunlay et al (*J Fam Pract* 1987; 25:137-141)	Acute productive cough and no evidence of pneumonia	63	Erythromycin × 10 d	Patients treated had significantly less sputum and cold symptoms, took fewer cold and cough OTC drugs, and had fewer abnormalities on lung examination at 2 wk

OTC = over-the-counter, TMP-SMX = trimethoprim-sulfamethoxazole

TABLE 3.—*Oral Antibiotics Used to Treat Bronchitis*

Drug	*Sensitivities*					*Cost of 10-Day Supply, $**
	Haemophilus influenzae	*Streptococcus pneumoniae*	*Branhamella catarrhalis*	*Mycoplasma pneumoniae*	*Chlamydia*	
Tetracycline	Equivocal	Equivocal	Yes	Yes	Yes	1.00
Penicillin	No	Yes	No	No	No	1.67
Ampicillin†	Equivocal	Yes	Equivocal	No	No	3.20
Erythromycin	No	Yes	Yes	Yes	Yes	3.38
Trimethoprim-sulfamethoxazole	Yes	Yes	Yes	No	No	2.46
Cefaclor	Yes	Yes	Yes	No	No	35.84

*Average wholesale generic price in April 1988. Retail charges to patients will be higher.

†Resistant *H influenzae* and *B catarrhalis* are susceptible to the combination of amoxicillin and clavulanate potassium (wholesale price = $39.00).

Although the appropriate length of treatment for each etiologic agent has not been investigated, 10 to 14 days of erythromycin administration would be the most logical choice for acute bronchitis, especially if one is considering a mycoplasmal or chlamydial origin. It also has good penetration into sputum. For children, erythromycin estolate has greater bioavailability and fewer side effects, but its use should be avoided in adults because of cholestatic jaundice. The most common side effects of erythromycin use are gastrointestinal. The ethylsuccinate preparation or taking erythromycin with food may decrease abdominal discomfort, although no studies have shown any one group of erythromycin to have fewer side effects in adult use.

The controlled trials do not support using doxycycline, and therefore one must also be skeptical of using tetracycline. Cefaclor and an amoxicillin-clavulanate potassium combination are expensive, and controlled trials are lacking. Trimethoprim-sulfamethoxazole is a possible choice, although it is not effective against *Mycoplasma* or *Chlamydia*. Ciprofloxacin and cefuroxime, two new oral antibiotics, have a similar spectrum for respiratory tract pathogens as do trimethoprim-sulfamethoxazole and cefaclor. Their costs are similar to cefaclor's. There are no precise guidelines for monitoring therapy—a decrease in dyspnea, less sputum, and sputum that is more mucoid than purulent are reasonable guidelines. Additional therapies to be considered in those who are not responding to antibiotic therapy include bronchodilators and inhaled steroids. Hospital admission for parenteral therapy, fluid replacement, and supplemental oxygen is rarely necessary.

Antibiotic Treatment of Acute Exacerbations of Chronic Bronchitis

There have been five double-blind controlled clinical trials of the use of common oral antibiotics (tetracycline and ampicillin) in flare-ups of chronic bronchitis. Three of these showed no significant differences in any measured variable between antibiotic and placebo use, one had a trend favoring antibiotic therapy, and one had results in antibiotic-treated patients that were significantly better than using a placebo. These studies are summarized in Table 4. The most recent study found that antibiotic treatment was 13% more successful than placebo in resolving symptoms at three weeks, although more than half of the patients with placebo treatments also had resolution. Although this difference is not dramatic, there was an additional 9% difference in the deterioration—that is, treatment failures. This resulted in increased cost and morbidity and may be the best argument for antibiotic therapy.

Clinical sense dictates that there is a continuum between bronchitis and pneumonia, and a few of those with productive cough and systemic symptoms have early pneumonia. Although it is unclear how many flare-ups are causally related to bacterial infection, it makes sense to treat with antibiotics those who appear sicker or have more severe underlying disease and therefore have a greater chance of having an early bacterial pneumonia or respiratory failure. Considering that the cost of antibiotics used to treat acute bronchitis or flare-ups of chronic bronchitis probably is in the range of $100 million each year in the US, it is noteworthy that so few randomized, controlled trials have been conducted. Based primarily on judgment, we favor treating flare-ups of chronic bronchitis with trimethoprim-sulfamethoxazole if a patient has increased sputum and dyspnea. The antibiotic is relatively inexpensive, and its bacterial spectrum matches the more common lower respiratory tract pathogens. *Mycoplasma* and *Chlamydia* are much less of a concern in older patients. Antibiotic therapy has shown the clearest success in those exacerbations with the three symptoms of increased

TABLE 4.—*Summary of Randomized Antibiotic Trials in Flare-ups of Chronic Bronchitis*

Study	Definition	Patients, No.	Antibiotic and Dose	Results
Elmes et al (*Br Med J* 1957; 2:1272-1275)	Therapy was patient-initiated at onset of acute respiratory illness; all had previously met criteria for a diagnosis of chronic bronchitis	88*	Oxytetracycline, 250 mg 4 ×/d × 5 to 7 d	No significant difference in days of respiratory symptoms; antibiotic group had trend toward fewer days off work
Berry et al (*Lancet* 1960; 1:137-139)	Worsening in the past week in those with persistent or recurrent cough with diffuse physical signs in the chest, in whom CXR has excluded other diagnoses	53*	Oxytetracycline, 250 mg 4 ×/d × 5 d	Treated patients recovered sooner if moderately severe, no difference for mild attacks (statistics not given, severity based on a 0-4 subjective score)
Elmes et al (*Br Med J* 1965; 2:904-908)	Patients admitted to hospital for acute exacerbation of chronic bronchitis	56†	Ampicillin, 1 gram q 6 hr × 3 d, then 0.5 gram q 6 hr × 4 d	No difference in hospital length of stay, change in pulmonary function test results, or sputum volume
Nicotra et al (*Ann Intern Med* 1982; 97:18-21)	Patients with chronic bronchitis who had increase in symptoms of dyspnea, cough, and sputum production without evidence of pneumonia	40†	Tetracycline, 500 mg 4×/d × 7 d	No difference in spirometry, sputum volume, blood gases, or physician or patient score
Anthonisen et al (*Ann Intern Med* 1987; 106:196-204)	COPD patients with increased dyspnea, sputum production, or sputum purulence	173*	Trimethoprim-sulfamethoxazole, 2×/d; amoxicillin, 250 mg 4×/d, or doxycycline, 100 mg/d for 2 wk	Resolution of symptoms in 21 days in 68% of those treated with an antibiotic compared with 55% with a placebo (P=.01); no significant differences between antibiotics

COPD=chronic obstructive pulmonary disease, CXR=chest x-ray film

*Ambulatory.
†Patients admitted to hospital.

dyspnea, increased sputum, and sputum purulence compared with those with only one or two of these symptoms.

The question of the prophylactic use of antibiotics in patients with chronic bronchitis is unresolved. One trial of tetracycline given over the winter months showed that prophylaxis reduced by a third time off work, but this estimate had a large range of uncertainty. Prophylaxis has no effect on the decline of pulmonary function nor on the volume or purulence of sputum. Prophylactic antibiotic therapy may be useful in those selected few who have frequent exacerbations. Trimethoprim-sulfamethoxazole or ampicillin use daily or five days a week during winter months would be a logical choice. The outpatient pharmacologic treatment of chronic obstructive pulmonary disease has recently been a topic in this series (June 1985). Ipratropium, an atropinelike aerosol bronchodilator, is a new addition to the armamentarium. Avoiding irritants such as cigarette smoking is helpful, and an acute flare-up in a patient with chronic bronchitis can provide the motivation to stop smoking—the most important therapy.

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Book Review

The Western Journal of Medicine *does not review all books sent by publishers, although information about new books received is printed elsewhere in the journal as space permits. Prices quoted are those given by the publishers.*

Therapeutic Endoscopy in Gastrointestinal Surgery

Rapael S. Cuhung, MD, FACS, Professor of Surgery, State University of New York, Health Science Center at Syracuse, Director, Surgical Endoscopy Service, and Attending Surgeon, State University Hospital Veterans Administration Medical Center and Crouse Irving Memorial Hospital, Syracuse, New York. Churchill Livingstone Inc, 1560 Broadway, New York, NY 10036, 1987. 259 pages, $45.

Both the strengths and the shortcomings of this book are due to its single authorship. There are the uniformity of opinion, lack of redundancy, and good organization that go along with a single author. The writing style is excellent throughout. There is a uniform use of pertinent illustrations rather than a plethora of radiographs and endoscopic photographs that are meaningful only to the author. The recent advances in therapeutic gastrointestinal endoscopy are discussed in a most thoughtful and comprehensive manner. The organization of each of the sections lays out a brief but thorough discussion of the pathologic anatomy and pathophysiology, followed by the indications and contraindications for the procedure and a comparison with alternative operative management. The sections on results and complications of these techniques are quite good. Unconfusing algorithms of management summarize the textual material and reflect a consensus of thought of most experts in the field.

The shortcomings of the book are also due to its sole authorship. In the sections on equipment, technique, and postprocedural management, the author's bias is strongly expressed and does not necessarily represent the standard of care in endoscopy units in this country. The writer's opinions are sometimes expounded as "the truth" and alternative points of view are not explained.

In comparison with the many atlases of therapeutic endoscopy that have appeared on the market in the past two years, this work has significant value. It expresses a surgical opinion for the first time against a tide of medical opinions on therapeutic endoscopy, and this opinion is expressed concisely and with a great deal of intelligence. All told, this is an excellent, well-written, comprehensive presentation of a thoughtful surgical endoscopist's approach to therapeutic endoscopy. It is a best buy at $45 and belongs in the libraries of all physicians interested in this field.

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