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Pharyngitis, bronchitis, and pneumonia represent the most common respiratory tract infections. With a view to establishing effective management strategies, the origins of these illnesses and the diagnostic techniques that have been developed to discover them are reviewed. Therapeutic regimens with documented efficacy are outlined with emphasis on specific rather than empiric treatment. Although many respiratory tract pathogens remain exquisitely sensitive to penicillin, the emergence of resistant strains underscores the need for safe and effective alternative therapies.

Respiratory tract infections include both the most common and the most life-threatening illnesses plaguing humankind. The ordinary "sore throat"—pharyngitis—accounts for approximately 40 million visits to physicians per year in the United States, as well as significant time lost from work. Although often considered more of a nuisance than a disease, unrecognized and/or untreated pharyngitis can lead to serious suppurative and nonsuppurative complications.

Acute bronchitis—the painful cough with sputum and possibly fever that develops after an upper respiratory infection—does not necessarily represent a bacterial infection. In contrast, persons with chronic bronchitis often experience episodes of acute infectious exacerbation of their condition, which may respond to antibiotic therapy.

The most serious of the respiratory tract infections is acute pneumonia. It is a fairly common cause of hospitalization among adults, accounting for 10 percent of adult hospital admissions per year. Acute pneumonia ranks sixth among all causes of death in the United States and should be considered a potentially fatal illness.

STREPTOCOCCAL PHARYNGITIS

Pharyngitis can be caused by a number of etiologic agents, of which about a third are viral. In as many as 40 percent of cases, attempts to identify any specific agent—viral or bacterial—will be unsuccessful. From a therapeutic standpoint, the most important pathogen in pharyngitis is group A Streptococcus, which accounts for 10 percent to 30 percent of cases. Less common causes of pharyngitis, which may require specific isolation procedures or serologic assay, include Neisseria gonorrhoeae (isolation requires Thayer-Martin medium), Corynebacterium hemolyticum (sore throat and skin rash), group C Streptococcus, Mycoplasma pneumoniae, and Epstein-Barr virus (infectious mononucleosis).

Diagnosis and treatment of streptococcal pharyngitis are clearly indicated, for a number of reasons. Several prospective, placebo-controlled trials have demonstrated that treatment decreases duration of fever and other symptoms of sore throat due to streptococcal infection [1-4]. Treatment of streptococcal sore throat also contributes to controlling and reducing the spread of such infections within families and classrooms. Clinically, prompt and appropriate treatment prevents supplicative complications—not only can bacteria spread from the pharynx to the tonsils but also to the retro- and lateral pharyngeal spaces. Even meningitis was a not-uncommon consequence of streptococcal pharyngitis before the availability of antibiotic drugs. Finally, perhaps the best recognized reason to treat group A streptococcal infections is to prevent the development of acute rheumatic fever, which
appears, after years of declining incidence, to be on the rise again in the United States.

**Diagnosis**

The standard laboratory procedure for diagnosing pharyngitis is culture of a throat swab. If the culture result is positive for group A Streptococcus, the specificity of the test is high. On the other hand, the sensitivity of the test is not as high as most clinicians would like. Cultures of two sequential specimens, for example, taken from the same patient will show identical results only about 90 percent of the time [5]. Moreover, a study conducted by Saslow and colleagues [6] showed that 24 percent of throat culture specimens failed to reveal streptococcal infection that was later identified when the patient’s tonsils were removed and examined. One of the most frustrating drawbacks of the culture method of diagnosis is the 24- to 36-hour delay before results are available. Delay also may compromise treatment efficacy; in one study, immediate institution of antibiotic drugs was associated with less incidence of morbidity than when treatment was delayed until culture results became available [3].

For these reasons, rapid tests for identifying streptococcal infection will soon become standard. Based on the use of an antibody to detect type-specific carbohydrate of group A Streptococcus in throat swabs (latex fixation or an enzyme-linked immunosassay), these tests can yield a diagnosis with both high specificity and high sensitivity within seven to 70 minutes.

**Whom to Treat**

In the absence of positive test results, the decision to treat a patient with pharyngitis is primarily based on clinical findings. Centor and colleagues [7] have performed a decision analysis based on four clinical markers of streptococcal pharyngitis: tonsillar exudates; swollen, tender anterior cervical lymph nodes; fever or history of fever; and absence of cough. If all four features are present, the chance that the infection is streptococcal ranges from 26 percent to 65 percent, if only three of the four are present, the likelihood of streptococcal infection decreases to between 11 percent and 38 percent; if none of the features is present, the infection can be assumed to be nonstreptococcal in origin.

The setting, age, and contacts of the patient help determine whether the probability of streptococcal infection is at the lower or higher end of the range. An older person who has no contact with children, for instance, will have a much lower chance of contracting streptococcal infection than a preschool youngster, or a first-grade teacher.

Decision analysis indicates that anyone with three or four clinical features indicative of streptococcal pharyngitis should be treated, without proceeding to a throat culture. If and when rapid tests become widely available, treatment without confirmation would be reasonable only when the prevalence of group A Streptococcus in the population at risk is at least 20 percent and the patient manifests all four streptococcal clinical features. In practical terms, the availability of a rapid test would virtually eliminate the question of whom to treat.

**Treatment**

Regimens of choice for treatment of streptococcal pharyngitis include oral penicillin for 10 days or a single, intramuscular injection of benzathine penicillin G. The importance of taking the oral medication for the full 10 days to prevent nonsuppurative complications should be stressed to patients. Erythromycin is an appropriate alternative for penicillin-allergic patients. Other regimens, such as cefaclor or amoxicillin plus clavulanic acid, have been used effectively to treat streptococcal pharyngitis but offer no advantages compared with penicillin.

Finally, although diagnosis and treatment of pharyngitis are usually straightforward, certain signs warrant immediate investigation. Respiratory difficulty, particularly stridor associated with sore throat in adults, may be indicative of epiglottitis due to Haemophilus influenzae. Other signs and symptoms of potentially dangerous clinical conditions include difficulty swallowing or handling secretions, severe pain without visible erythema, or a palpable mass in the pharynx. Blood in the pharynx or ear suggests an impending disastrous suppurative complication such as erosion in a carotid artery. Even untreated, the symptoms of streptococcal infection will disappear. Therefore, persistence of symptoms for more than one week also warrants further evaluation.

**ACUTE AND CHRONIC BRONCHITIS**

**Definitions**

In previously healthy persons, acute purulent bronchitis usually is not the result of a bacterial process. Rather, a productive cough, characterized by sputum, fever, and retrosternal pain on coughing, develops at the end of a typical upper respiratory tract infection. If the person is well with minimal systemic symptomology and has no underlying conditions, antibiotic treatment is generally unnecessary. Antibiotic therapy should be started, however, if cough productive of purulent sputum is protracted, and bacteria are seen on a Gram’s stained preparation of the sputum. The choice of drugs is dictated by the findings on smear and culture specimens.

A much more frequent and important type of bronchitis is acute exacerbation of chronic bronchitis. The classic definition of chronic bronchitis is almost daily production of sputum for at least three consecutive months and for two consecutive years. The origins of chronic bronchitis are cigarette smoking, inhalation of toxic substances, and possibly infection, although the role of infection usually is not clear.

Acute infectious exacerbation of chronic bronchitis describes some combination of the following: a change in sputum color, consistency, or amount; increasing cough or dyspnea; chest tightness; and general fatigue without other systemic manifestations. If the patient presents with fever and chills, the diagnosis will probably be something other than simple acute infectious exacerbation.

**Bacteriology**

The relationship between infection and exacerbation is sometimes difficult to determine. Potentially pathogenic bacteria can be isolated in most sputum specimens from persons with chronic bronchitis, even in the absence of symptoms of acute infectious exacerbation. Although it is true that Streptococcus pneumoniae is isolated in increased quantities when patients experience exacerbation [8], it is not clear in the
individual case whether culture specimen results are indicative of the normal flora for the patient or are pathogenic.

About 30 percent to 50 percent of patients with acute bronchitis will have nonencapsulated *H. influenzae* or *S. pneumoniae* (or both) as persistent colonizers of the bronchial tract. Presumably, these are the agents responsible for exacerbation. In another 25 percent to 50 percent of patients, the bronchitis will have a viral (influenza, parainfluenza, respiratory syncytial virus, rhinovirus, coronavirus) rather than bacterial origin. *Staphylococcus aureus* (often following influenza) or enteric gram-negative rods are found in 5 percent to 10 percent of cases, and, occasionally, *M. pneumoniae* is implicated based on serologies.

**Antibiotics**

Since antibiotic treatment appears to decrease the incidence of morbidity and shorten time missed from work, it is indicated in patients with acute exacerbation of chronic bronchitis [9,10].

Several regimens have been proposed and tested based on the bacteriology of bronchitis. Although none has been shown to be clearly superior, amoxicillin plus clavulanic acid, ampicillin, ceftazolin, erythromycin, tetracycline, or trimethoprim-sulfamethoxazole appear to be effective.

### PNEUMONIA

**Origins**

To initiate appropriate, life-saving therapy for acute pneumonia, it is vitally important to establish its specific origin. Clues about the cause of pneumonia can be elicited by addressing a number of questions while obtaining the history and during the physical examination (Table 1) [1].

| TABLE I Determination of the Cause of Pneumonia |
|-----------------------------------------------|
| • Is the current condition accurately termed “acute,” or is it really chronic? Is it perhaps an acute illness superimposed on several months of progressive respiratory symptoms? |
| • Is it community- or hospital-acquired? |
| • Who is the host? Young and healthy? Elderly? Is there serious underlying disease? |
| • Has there been an unusual upper respiratory or gastrointestinal infection? |
| • Is the patient a member of an at-risk group for AIDS? |
| • Is there a pleural friction rub or has there been a rigor? |
| • Is there lobar consolidation or large pleural effusions? |
| • Is the pneumonia cavitating? |

If the patient is young and otherwise healthy, he or she probably has infection with *S. pneumoniae*, *M. pneumoniae*, or a viral pneumonia. On the other hand, an elderly person is more likely to have influenza or *S. pneumoniae*, which Osler dubbed “the old man’s fricait.” Elderly people, particularly those with refractory pneumonia, also may be infected with *Mycoplasma tuberculosis*, and in those older patients who are especially debilitated, a search for gram-negative enteric organisms may be indicated.

Aspiration pneumonias and infections with possibly antibiotic-resistant *S. aureus* or gram-negative bacilli are a problem in hospitalized patients, particularly in those who have suffered seizures. Underlying alcoholism may predispose a person to *S. pneumoniae* or gram-negative organisms such as *Klebsiella*, whereas underlying diabetes increases the risk of infection with gram-negative enteric organisms or *M. tuberculosis*.

**Symposium on Cefixime**

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Patients with hemoglobinopathy, specifically children with sickle-cell disease, are particularly prone to infections with *S. pneumoniae*, *H. influenzae*, and *M. pneumoniae*.

Possible causes of pneumonia in patients with chronic lung disease include *S. pneumoniae*, *H. influenzae*, *Pasteurella multocida*, gram-negative enteric bacilli, and *M. tuberculosis*.

It is important to determine where the patient lives and whether he or she has had contact with animals. Exposure to farm animals such as cattle, goats, and sheep, for example, may be associated with Q fever, brucellosis, or anthrax. Rabbit hunters may have tularemia and exposure to birds can lead to psittacosis or histoplasmosis. People who live in semi-arid regions of the United States and in areas near the Mississippi and Ohio River valleys could have histoplasmosis or blastomycosis. Armed services personnel, travelers, and visitors who have been in Southeast Asia may be ill with tuberculosis or melioidosis.

**Diagnosis**

The patient with community-acquired purulent pneumonia classically presents with sudden pleuritic chest pain, productive cough with purulent sputum, high fever (up to 40°C), and profound shaking chills (rigors). Physical examination and chest radiograph reveal signs of lobar consolidation. The white blood cell count is elevated with an increase in circulating immature neutrophils, and lobar infiltrate is confirmed radiologically.

Acute community-acquired purulent pneumonia is most commonly caused by *S. pneumoniae* (50 percent to 90 percent). Depending on where the patient lives, 17 percent to 23 percent of these cases may be due to *Legionella pneumophila*, 2 percent to 18 percent to *H. influenzae*, and 2 percent to 10 percent to *S. aureus*. Anaerobes and non-*Haemophilus* gram-negative enteric organisms may also account for some of these community-acquired infections.

The initial diagnostic decision concerns whether the patient has acute purulent bacterial or nonbacterial pneumonia. The first step in establishing origin is obtaining a good, uncontaminated specimen for Gram's stain. If the sample is heavily contaminated with oral flora, it is unlikely to be useful and may be misleading. The adequacy of the specimen can be ascertained by the absence of squamous epithelial cells (less than five per high-power field), and the presence of neutrophils (10 to 15 per high-power field), as well as alveolar macrophages and bronchial epithelial cells. Nasotracheal or transtracheal aspiration may be necessary to obtain a good specimen of lower respiratory tract secretions. The presence of a predominant organism, particularly if found within white blood cells, suggests that it is pathogenic; aspiration pneumonia may be associated with multiple organisms.

Although the Gram's stain may suggest that the cause of a pneumonia is not bacterial by the finding of inflammatory cells and no organisms, the clinical presentation can be even more useful for distinguishing a bacterial from a nonbacterial infection. Nonbacterial pneumonia usually begins less abruptly than bacterial pneumonia, with three or four days of symptoms. Constitutional symptoms rather than respiratory tract symptoms comprise the patients' chief com-
plaints. The white blood cell count remains within normal limits. Importantly, the appearance on radiographic examination is much worse than would be anticipated based on physical examination. This constellation of symptoms suggests *M. pneumoniae*, adenovirus, Q fever, psittacosis, or *L. pneumophila*. A stain for acid-fast bacilli also is warranted because tuberculosis, although rare, is a consideration. Importantly, the appearance on radiographic examination is much worse than would be anticipated based on physical examination. This constellation of symptoms suggests *M. pneumoniae*, adenovirus, Q fever, psittacosis, or *L. pneumophila*. A stain for acid-fast bacilli also is warranted because tuberculosis, although rare, is a consideration.

Occasionally, patients with a more chronic set of respiratory symptoms will present with a nonlobar, unusual infiltrate that does not seem to fit the picture of a viral pneumonia. In this situation, it is particularly important to determine whether there are pockets of cavitation in the lesion. Although both *Pneumococcus* and *Haemophilus* can sometimes cause cavitation, its presence suggests tuberculosis, *S. aureus*, necrotizing infection due to gram-negative bacilli, or mixed anaerobic or fungal infection. Clearly, the finding of cavitation shifts the differential diagnosis of pneumonia as well as the antibiotic drugs that may be required for its treatment. Cavitation can also result from noninfectious sources, such as septic pulmonary emboli and carcinoma.

Because of the importance of recognizing necrotizing pneumonia as early as possible, investigators in Cleveland have been assessing the feasibility of a specific sputum test based on searching for elastin fibers in sputum [11,12]. Elastin fibers are found in the alveoli and terminal bronchioles; their presence in respiratory tract secretions, therefore, indicates a destructive process. These elastin fibers can be identified by dissolving the constituents of sputum with 10 percent potassium hydroxide. The presence of elastin fibers in sputum precedes both the development of cavities and the appearance of pulmonary infiltrates on radiographic examination of the chest. When the sputum test for elastin fibers is positive in an intubated or tracheostomized patient, its predictive value is 100 percent—the patient will progress to a full-blown nosocomial pneumonia [12].

Since not all nosocomial pneumonias are necrotizing, the sensitivity of the finding of elastin fibers is only 52 percent. The search for elastin fibers appears to be a generally useful adjunct for diagnosis not only in hospitalized patients but in all persons with pneumonia, particularly when symptoms do not fit the classic patterns of either bacterial or nonbacterial syndromes.

**Treatment**

Clinicians managing patients with pneumonia should strive for specific treatment based on a definite origin of the illness. Nevertheless, when obtaining sputum or interpreting the Gram's stain is difficult, an empirical regimen may be necessary.

Penicillin G is the drug of choice for *S. pneumoniae*, which remains exquisitely sensitive to that agent. Parenteral ampicillin would be appropriate treatment for infection with *H. influenzae*, although beta-lactamase-producing *H. influenzae* is presenting an increasing problem in adult patients. Initial treatment with a combination of trimethoprim and sulfamethoxazole or a third-generation cephalosporin, therefore, is a prudent choice for a serious infection presumed to be caused by *H. influenzae*.

*S. aureus* should be treated with a semisynthetic penicillin such as nafcillin. Anaerobes are exquisitely sensitive to penicillin, which is an appropriate starting regimen. If there is no clinical response, it may be useful to switch to a specific antianaerobic agent such as clindamycin. The finding of gram-negative enteric organisms on Gram's stain requires combination therapy with an aminoglycoside plus a third-generation cephalosporin. Choice of aminoglycoside should be based on the prevailing patterns of bacterial sensitivities in the hospital. Although penicillin remains a mainstay of therapy for many patients with bacterial pneumonia, the emergence of resistance should provide the impetus for discovery and testing of alternative therapies.

Although *L. pneumophila* can be diagnosed by culture or serologies, confirmation usually requires days to weeks. A diagnosis based on clinical findings is necessary, therefore, and empiric treatment should be initiated. Erythromycin can be prescribed for suspected *L. pneumophila* as well as for *M. pneumoniae*.

When empiric therapy for a seriously ill patient is clearly indicated, combination regimens, such as an aminoglycoside plus a third-generation cephalosporin, will provide the broad-spectrum coverage that ensures efficacy against possibly resistant gram-negative organisms.

In summary, the management of any respiratory tract infection—whether relatively minor or life-threatening—is most successful when an anti-infective agent is selected on the basis of a definite causative organism.

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September 16, 1988 The American Journal of Medicine Volume 85 (suppl 3A)