Appropriate Antimicrobial Prescribing:
Approaches that Limit Antibiotic Resistance

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Since the introduction of antimicrobial agents, there has been an association between antibiotic use and the development of antimicrobial resistance. Antibiotic therapy eradicates not only pathogenic organisms but also the protective normal flora. This so-called "selective pressure" results in colonization with bacteria that are resistant to the original therapy. The result has been an increase over the past two decades in antibiotic resistance among common bacterial causes of outpatient infections. Several studies have demonstrated that a substantial portion of the antibiotics prescribed in the outpatient setting are given for viral illnesses or bacterial diseases where the benefit of antibacterial therapy is marginal. The reasons for prescribing antibiotics in these situations are related to medical and social factors. Physicians should be familiar with the clinical situations in which they should provide antibiotics and those in which they may safely be withheld. Physicians should understand the motivations of patients who are seeking antibiotics and provide education, empathy and alternative treatments. (Am Fam Physician 2001;64:999-1004.)

The development of antibiotic-resistant bacteria seems to be an inevitable consequence of using antimicrobial drugs. Antimicrobial resistance has increased since the introduction of antibiotics. Penicillin was first used in the early 1940s and by 1950, most *Staphylococcus aureus* organisms were resistant to the drug by virtue of elaboration of a penicillinase enzyme.

The emergence of a resistant population of bacteria in a patient as a result of antibiotic use generally occurs through a process termed "selective pressure." Studies using special culture techniques show that healthy persons normally harbor small numbers of bacteria that are intrinsically resistant to antibiotics.[1] The larger numbers of antibiotic-susceptible organisms usually keep resistant bacteria in check. The use of any antibiotic eliminates organisms susceptible to that drug at the site of infection and at all sites in the body into which the drug penetrates in adequate concentrations. Selective pressure occurs when the administration of an antibiotic decreases the numbers of normal flora, allowing resistant bacteria to proliferate.

When antibiotics are prescribed to large numbers of persons in a population, resistant bacteria may become the predominant organisms in that community. This situation is occurring with respiratory-tract pathogens that were once universally susceptible to antibiotics.[2] A national survey of clinically significant outpatient isolates of *Streptococcus pneumoniae*, the most common bacterial cause of most respiratory tract infections, gathered from 30 U.S. medical centers in 1994 and 1995, revealed that 23.6 percent of strains were not susceptible to penicillin. Intermediate resistance was detected in about 14.1 percent of isolates, while about 9.6 percent of strains demonstrated high-level resistance.[3] A recent study in Iceland showed a direct correlation between the use of antibiotics and the prevalence of resistant *S. pneumoniae* strains.[4]

Appropriate prescribing of antibiotics may slow the rate at which resistance becomes widespread throughout the community. A study in Finland demonstrated that erythromycin resistance among group A streptococci decreased from 16.5 to 8.6 percent over a four-year period during a nationwide program relying on national guidelines to limit the use of erythromycin.[5] Other studies in the United States show that decreased use of antibiotics for prophylaxis and treatment cor-

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related with decreasing rates of colonization with resistant organisms.[6,7]

Inappropriate Antibiotic Use

Despite the association between the increased use of antibiotics and the spread of resistant organisms in the community, antibiotic use in this country appears to be increasing. A national office-based study suggested an increase of 48 percent in antibiotic prescribing for children between 1980 and 1992.[8] The use of antimicrobials is especially prevalent in the very young and the elderly. In one study, 37 and 70 percent of children, by three and six months of age respectively, had received at least one antibiotic prescription.[9] The emergence of in vitro resistance in previously susceptible pathogens, such as *S. pneumoniae* in respiratory tract infections and *Escherichia coli* in urinary tract infections, has temporally coincided with the increase in antibiotic use.

A good portion of antibiotic use appears to be for viral or spontaneously resolving bacterial infections. The Centers for Disease Control and Prevention (CDC) estimates that about 100 million courses of antibiotics are prescribed by office-based physicians each year, and that approximately one half of those prescriptions are unnecessary.[10] Most antibiotic prescriptions in the ambulatory setting are for respiratory infections.[2] Studies evaluating physicians' prescribing patterns have found that almost 50 percent of office visits for colds and upper respiratory tract infections (URIs), and 80 percent of visits for acute bronchitis are treated with antibacterial agents.[8] This prescribing pattern persists despite the fact that antibacterial agents have no effect against a viral disease such as the common cold. Data from numerous studies show that antibacterial agents do not significantly shorten the duration of illness in acute bronchitis.[11]

Physicians continue to prescribe antibiotics despite acknowledging the association of antimicrobial use and bacterial resistance. In one study,[12] 97 percent of surveyed physicians agreed that overuse of antibiotics is a major factor contributing to antimicrobial resistance. However, an evaluation of the practice patterns of these same physicians revealed continued prescribing of antimicrobials for viral illnesses. Other potential harms of indiscriminate antibiotic prescribing include allergic reactions, adverse reactions and drug-drug interactions.[2]

Reasons for Prescribing

Patients want antibiotics, and physicians continue to prescribe them in situations where antibiotics may be withheld for many reasons. The act of prescribing an antibiotic has social and medical implications. From the patient's point of view, the prescribing of an antibiotic validates that the patient does have an illness, that a diagnosis has been made and that the illness is amenable to treatment. The fact that there is a "cure" for their problem reassures them that the illness is not serious.[13]

Patients are accustomed to receiving antibiotics for benign URIs and have come to believe, sometimes very strongly, that antibiotics demonstrate efficacy and are necessary for proper treatment of these illnesses. So convinced are patients of the efficacy of antibiotics that in one clinical trial of acute bronchitis, 60 percent of patients screened for the study refused to participate because they did not wish to be randomized to the placebo arm of the trial.[14]

The most common clinical factor causing patients to seek medical help for common infections is relief of bothersome symptoms. In one study,[15] 90 percent of patients with URIs came to the physician's office because of a persistent cough. Another two thirds of patients complained of disturbed sleep, while

nearly one half made an appointment at the urging of family and friends. Antibiotics have little effect on the rate of resolution of cough or disturbed sleep.[11]

Certain clinical features of disease may inappropriately influence physicians' treatment decisions. The presence of purulent nasal discharge is more likely to result in a physician's prescribing an antibiotic for a patient with acute bronchitis.[16] However, the purulent nasal discharge does not adequately differentiate viral from bacterial etiologies and is not associated with a worse outcome.[17-19]

The presence of cough for more than three days may also trigger an antibiotic prescription. The natural history of acute bronchitis is such that many patients cough for two to three weeks as a result of bronchial hyperresponsiveness and not as a result of persistent infection.[20] In the absence of chronic obstructive lung disease, fever and a smoking history are not indications for antibiotic therapy in patients with acute bronchitis.[17] Physicians may prescribe antibiotics in the hope of preventing more serious superinfections, but a meta-analysis of studies on antibiotic use in URIs did not show an effect of antibiotics in decreasing the incidence or severity of subsequent disease.[21]

Physicians' prescribing patterns appear to be affected by nonclinical factors in up to one half of cases.[22] In today's managed-care environment, physicians are pressed to see more patients in less time. They have insufficient time to educate patients about the ineffectiveness of antibiotics.[19] Prescribing an antibiotic may be an effective way to conclude an office visit.[13] Although some physicians believe that prescribing an antibiotic will decrease return office visits, up to one fourth of patients with URIs make a return visit within one month of the initial encounter regardless of the prescription of antibiotic agents.[11]

Although physicians often feel compelled to prescribe an antibiotic to satisfy patient demands, patient satisfaction surveys indicate that patients do not acknowledge putting such pressure on their physicians. One survey indicated that while 65 percent of patients expected to receive an antibiotic for treatment of a URI, there was no correlation between patient satisfaction and receipt of an antibiotic prescription.[23] Instead, patient satisfaction correlated highest with the quality of the physician-patient interaction. Results from focus groups indicate that patients would be satisfied if an antibiotic was not prescribed as long as the physician explained the reasons for the decision to withhold antibiotics.[24]

According to the Centers for Disease Control and Prevention, approximately 50 percent of the antibiotic prescriptions written by office-based physicians are unnecessary.

Approach to the Patient

The physician should take a well-reasoned, step-wise approach to a patient with an infection before prescribing an antibiotic *(Table 1)*. The first step is to make a tentative diagnosis based on data from the history and physical examination. Often, it is difficult to distinguish a bacterial from a viral illness by clinical features alone. Clinical and laboratory factors

TABLE 1
Steps in Approaching Patients When Considering Antibiotic Therapy

Make a tentative diagnosis based on the history and physical examination
Determine if antibiotic therapy is necessary for the given infection (see Table 2)
Choose the individual agent for the infection based on the following:
In vitro activity of the antibiotic against the most likely pathogens in the disease
Clinical trial results demonstrating efficacy and safety of the antibiotic in that disease and in patient populations similar to that of the presenting patient
Side effect profile of the drug:
Allergic reactions
Direct adverse effects of drug
Drug-drug interactions
Drug-food interactions
Use least expensive and narrowest-spectrum drug possible

TABLE 2
CDC/AAP Principles of Judicious Antibiotic Use

Diagnosis	*Principles*
Otitis media	Classify episodes of OM as acute OM or OM with effusion. Treat only proven acute OM. Although antibiotics are indicated for treatment of acute OM, diagnosis requires the following: Documented middle-ear infection Signs or symptoms of acute local or systemic illness Do not prescribe antibiotics for initial treatment of OM with effusion Treatment may be indicated if bilateral effusions persist for three months or more
Rhinitis	Antibiotics should not be given for viral rhinosinusitis. Mucopurulent rhinitis (thick, opaque or discolored nasal discharge) frequently accompanies viral rhinosinusitis. It is not an indication for antibiotic treatment unless it persists without improvement for more than 10 to 14 days.
Sinusitis	Diagnose as sinusitis only in the presence of the following: Prolonged nonspecific upper respiratory signs and symptoms (e.g., rhinorrhea and cough without improvement for more than 10 to 14 days), *or* More severe upper respiratory tract signs and symptoms (e.g., fever greater than 39°C [102.2°F], facial swelling, facial pain) Initial antibiotic treatment of acute sinusitis should use the narrowest-spectrum agent that is active against the active pathogens.
Pharyngitis	Diagnose as group A streptococcal pharyngitis using a laboratory test in conjunction with clinical and epidemiologic findings. Antibiotics should not be given to a child with pharyngitis in the absence of diagnosed group A streptococcal infection. A penicillin remains the drug of choice for treating group A streptococcal pharyngitis.
Cough illness and bronchitis	Cough illness and bronchitis in children rarely warrant antibiotic treatment. Antibiotic treatment for prolonged cough (more than 10 days) may occasionally be warranted. Pertussis should be treated according to established recommendations. *Mycoplasma pneumoniae* infection may cause pneumonia and prolonged cough (usually in children older than five years); a macrolide agent (or tetracycline in children eight years or older) may be used for treatment. Children with underlying chronic pulmonary disease (not including asthma) may occasionally benefit from antibiotic therapy for acute exacerbations.

CDC = Centers for Disease Control and Prevention; AAP = American Academy of Pediatrics; OM = otitis media.

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can be helpful in selecting subsets of patients more likely to have bacterial disease. More important than the actual microbiologic cause of the infection is knowledge of whether antibiotics will affect the course of the illness. For example, antibiotic therapy has little effect on the course of acute bronchitis caused by the bacterial pathogens *Mycoplasma pneumoniae* or *Chlamydia pneumoniae*.[25]

The second step is to decide if antibiotics are warranted for that particular infection. Antibiotics are almost never necessary for treatment of the common cold or acute bronchitis in otherwise healthy persons. *Table 2*[10]

lists the indications for appropriate antimicrobial treatment in common infections.

In the third step, the physician should evaluate the potential for side effects or drug-drug interactions. Finally, with all else being equal, the physician should choose the least expensive alternative among equally effective and safe drugs.

The physician should also address the social aspects of the illness and explain to the patient that antibacterial drugs are not effective in viral infections and emphasize that unnecessary antibiotics can be harmful in several ways *(Table 3)*. Several studies show that recent antibiotic use is a risk factor for colonization and infection with resistant organisms.[4] Unwarranted prescription of an antibiotic exposes patients to potential adverse effects of the drug. Many antimicrobial agents are costly.

Perhaps most important to patients, an antibacterial agent will not shorten the duration of bothersome symptoms. The physician should not dismiss the importance of a patient's illness and the impact of those symptoms on the daily routine. Instead, the physician should explain the natural course of the illness and what the patient can expect in terms of time to symptom resolution. Realistic patient expectations may help decrease future office visits for a resolving illness.

Patients with benign upper respiratory infections often have the inaccurate belief that antibiotics have demonstrated efficacy in and are necessary for proper treatment of their illness.

Finally, the physician should actively manage symptoms with analgesics, antipyretics and decongestants, where appropriate. Therapy with beta agonists often is effective in shortening the duration of cough in acute bronchitis when clinical evidence of bronchial hyperresponsiveness (such as wheezing or bothersome cough) is present.[26,27] The CDC Web site provides a preprinted prescription form for patients with URIs to help physicians educate patients.[28] The site also includes educational pamphlets for physicians to provide to patients and parents as part of the office visit.

Physicians may take a preemptive approach to educating patients about appropriate use of antibiotics. The American Academy of Pediatrics recommends discussing antibiotic use as part of well-child care visits. Educational materials in the office waiting room also may help disseminate the principles of judicious antibiotic use to patients. Several sites on the Internet offer posters, pamphlets, videotapes and other materials for office use.[10,29] Office personnel may be helpful in changing patient attitudes and decreasing patient demand for antibiotic therapy.

TABLE 3
Approach to Patients When Antibiotics Are Withheld

Explain to patients the probable viral nature of common respiratory infections and that antibiotics have no effect on duration of symptoms of viral infections.
Explain to patients that antibiotics are potentially harmful in the following ways:
Increased colonization and infection with resistant pathogens in patients with prior antibiotic therapy
Increased antimicrobial resistance in the community
Unwanted allergic reactions and adverse effects of antibiotics
Cost of unnecessary therapy
Empathize with patients about the effect of symptoms on their daily activities
Provide educational materials
Prescribe therapies for symptoms

The authors thank Herbert L. Muncie, M.D., Chair and Professor, Department of Family Medicine, University of Maryland School of Medicine, for assistance with the manuscript.

The authors indicate that they do not have any conflicts of interest. Sources of funding: none reported.

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