After supper one evening, your sister-in-law calls, asking for advice. She developed a bad cough two days ago, she says, and now is coughing “nonstop,” producing yellow phlegm. Over-the-counter herbal lozenges have given her no relief. She feels sure that it’s bronchitis. She takes care of her elderly mother, who lives nearby, and is afraid of infecting her, too. Should she make an appointment with her NP, she asks you, or should she just break into a bottle of ciprofloxacin (Cipro) that had been prescribed two months earlier and that she hadn’t opened?

The average nurse might find this a familiar situation. People often consult friends and family members who are nurses when they develop an acute respiratory infection. In a recent, as-yet unpublished survey (conducted by one of us [AMH] and another colleague), 83% of 104 RNs said that they

Overview: Antimicrobial resistance: many nurses are aware of the risk but may not know that inappropriate management of acute respiratory infection contributes to it significantly. For example, more than half of antibiotics prescribed for respiratory infections are unwarranted because viruses are the cause. It is important that nurses understand antimicrobial resistance and learn how to help patients, family members, and friends manage acute respiratory infections appropriately.

Acute Respiratory Infections and Antimicrobial Resistance

Managing viral infections without the inappropriate use of antibiotics.
frequently gave advice to friends and family members on managing acute respiratory infections, and 74% said that these same people frequently asked about taking antibiotics for such infections. Nonetheless, most RNs surveyed said that they had received very little education on the management of acute respiratory infection or the appropriate use of antibiotics for acute respiratory infections. (Contact the lead author for more information on this study; see page 63.)

RESISTANCE: A GROWING PROBLEM
The overuse of antibiotics in treating acute respiratory infection—and the significant contribution of such overuse to the current crisis of antimicrobial resistance—are well documented. Experts from many leading health organizations, including the Centers for Disease Control and Prevention (CDC), the World Health Organization, and the Institute of Medicine, recognize antimicrobial resistance as one of the most serious public health threats.
In 1995 the Centers for Disease Control and Prevention (CDC) developed a campaign to reduce inappropriate antibiotic use and rising rates of antimicrobial resistance. In 2003 the campaign was branded and launched as Get Smart: Know When Antibiotics Work. The Get Smart campaign has three objectives: to promote providers’ adherence to appropriate prescribing guidelines, to decrease the demand for antibiotics for viral upper respiratory infections from healthy adults and parents of young children, and to increase adherence to antibiotic regimens prescribed for upper respiratory infections. The campaign is aimed at both the general public and health care providers because the knowledge, attitudes, and behaviors of both groups contribute to the use of antibiotics. A primary focus of the Get Smart campaign is the development and dissemination of educational materials such as fact sheets, brochures, and posters for the general public, as well as adult and pediatric “academic detailing sheets” for providers. The latter give disease-specific diagnostic and treatment guidelines for various acute respiratory infections (go to www.cdc.gov/getsmart).

Educational materials for the general public. The Get Smart campaign has also developed brochures, posters, and information sheets for a variety of audiences, including Spanish-speaking, American Indian, and Alaska Native populations. Two question-and-answer pages specifically designed for parents address runny noses and fluid in the middle ear. All of the materials are available at the campaign’s Web site and may be downloaded, copied, and distributed without alteration free of charge.

The Get Smart campaign has also supported the development of a curriculum for medical students on the appropriate use of antibiotics (a collaboration with the University of California, San Diego, and the Association of American Medical Colleges). And there are two curricula for medical residents. One is modeled after the medical school curriculum and is under development at the Oregon Health and Science University. The other curricula of the 21st century. And results from two large national studies of prescribing data indicate that ambulatory care clinicians prescribe antibiotics for acute respiratory infections 40% to 50% of the time—and the vast majority of such infections are viral. Several factors have been blamed for this inappropriate prescribing, including patients’ expectations of and requests for antibiotics and the tendency to prescribe when sinus tenderness and discolored nasal discharge are present on physical examination. Several studies indicate that antibiotic prescribing rates have decreased over the past 15 years but inappropriate prescribing still occurs and broader spectrum antibiotics are being used more frequently. Therefore, education of both prescribers and consumers is necessary to reduce overuse.

Factors contributing to antimicrobial resistance. Any use of or exposure to antibiotics, regardless of the reason for its use, can contribute to antimicrobial resistance. Antimicrobial resistance results when microbes change in ways that reduce or eliminate the effectiveness of medications to treat or prevent infections. Antibiotics are often prescribed for infections that they can’t treat, but even when they’re prescribed appropriately, nonadherence to the treatment regimen can play a role in the development of antimicrobial resistance. Patients often don’t take antibiotics as prescribed (for example, they may share them with family members, take only part of the prescribed course, or save some pills for future use), and as a result, the most resistant among the infecting bacteria survive and reproduce.

Cultural and economic factors influence patterns of antimicrobial use. For example, in Western societies, patients often expect to receive a written prescription at the end of an office visit. The prescription legitimizes the patient’s visit to the provider and, in effect, serves as an official designation that the patient is sick. Patients may ask specifically for...
antibiotics because they’ve received them previously for similar symptoms or they believe antibiotics will make them feel better, faster. Providers often feel pressure from patients to prescribe antibiotics, and they are more likely to over-prescribe antibiotics when they have a high practice volume or when they are uncertain about the patient’s condition or diagnosis.

**HEDIS performance measures.**
The CDC and the National Committee for Quality Assurance (a not-for-profit organization involved in health care improvement) have written four measures for the Healthcare Effectiveness Data and Information Set (HEDIS), the performance measurement tool used by more than 90% of the nation’s health plans. The pediatric measures, which became part of HEDIS in 2004, assess the testing of children with pharyngitis and the treatment of children with upper respiratory infections for their appropriateness. The adult measures, which became part of HEDIS in 2006 and 2008, assess providers’ avoidance of antibiotic treatment in adults with acute bronchitis and data on antibiotic prescribing practices.

**Drug-resistant Streptococcus pneumoniae risk.**
While most acute respiratory infections are viral, most cases of bacterial sinusitis, acute otitis media, and community-acquired pneumonia are caused by *Streptococcus pneumoniae*. The CDC estimates that in 2006 there were 41,400 cases (13.8 cases per 100,000 people) of invasive, potentially fatal *S. pneumoniae* infections (such as bacteremia and meningitis) in the United States. Pneumococcal infections cause substantial illness and death in the elderly, young children, and people with chronic diseases and contribute significantly to the cost of health care. Because treatment for pneumococcal infections is complicated by resistance to commonly prescribed antibiotics such as penicillin, it’s important to understand the risk factors associated with drug-resistant *S. pneumoniae* infections.

There is a strong association between recent antibiotic use and the development of drug-resistant *S. pneumoniae* infection. Patients with acute otitis media, pneumonia, or meningitis caused by resistant strains of pneumococci are much more likely to have taken antibiotics recently than are those...
infected with susceptible strains. Even when one considers other risk factors for invasive pneumococcal disease, such as recent hospitalization and underlying immunosuppressive conditions, recent antibiotic use remains the single most predictive factor for infection with resistant pneumococci.

Although further research is needed to better understand the link between antimicrobial resistance and treatment failures, Feikin and colleagues note that treatment failures because of drug resistance in S. pneumoniae have been reported in cases of meningitis and otitis media. There is also evidence of failures in macrolide treatment (for example, with azithromycin or clarithromycin) in patients whose bacteremia is caused by erythromycin-resistant S. pneumoniae. While the relationship is less clear, fluoroquinolone treatment failures (for example, with levofloxacin or moxifloxacin) have occurred among patients with fluoroquinolone-resistant pneumococcal pneumonia. β-lactam and cephalosporin failures in pneumonia treatment are more likely among patients with highly resistant rather than intermediately resistant S. pneumoniae.

**ETIOLOGY AND MANAGEMENT OF RESPIRATORY INFECTIONS**

Acute respiratory infection is a broad term covering several types of infection, including the common cold, rhinosinusitis, pharyngitis, bronchitis, otitis media, influenza, and pneumonia. CDC treatment guidelines for the first four of these (which affect virtually all people, regardless of age and other variables) will be discussed below. These recommendations apply to otherwise healthy adults and children older than two years. Keep in mind that these are general guidelines and may not apply to all patients. For example, some of the over-the-counter medications mentioned should be used with caution in people with certain chronic conditions (such as hypertension and benign prostatic hypertrophy), young children, and older adults; serious adverse events do sometimes occur with these medications. It’s important to note that over-the-counter cold and cough preparations are not approved for children younger than two years of age and that deaths have been associated with their use in this population.

The common cold, also known as a nonspecific upper respiratory infection, is probably the most frequently occurring illness in humans. Colds are acute viral infections characterized by nasal, sinus, pharyngeal, or bronchial inflammation, or a combination of these. Mild fever, body aches, fatigue, and colored nasal secretions are common. Several viral families have been linked to colds, including adenovirus, respiratory syncytial virus, and rhinovirus; however, rhinovirus is by far the most common etiologic agent and is transmitted through aerosolized particles that enter the body directly through the nose or eyes (or indirectly, from the hands to the nose or eyes). Colds typically resolve without treatment in one to two weeks, and most people report starting to feel better within one week, though symptoms sometimes persist for more than two weeks.

The most recent epidemiologic estimates of the frequency of the common cold are based on data collected from 1965 to 1981. The data indicate that the frequency of infection decreases with age, with children four years of age or younger having 4.9 colds per year, children between the ages of five and 19 years having 2.8 colds per year, adults 20 to 39 years old having 2.2 colds per year, and adults over the age of 40 having 1.6 colds per year.

The search for effective treatments to cure a cold, alleviate its symptoms, or shorten its course is ongoing. Several studies of antibiotic treatment in children and adults have shown that antibiotics don’t alter the course of the common cold. Secondary bacterial infections are a rare complication of the common cold, and prophylactic use of antibiotics does not prevent them. The current evidence doesn’t support the effectiveness of commonly used measures such as vitamin C, zinc, or echinacea supplements; warm, humidified air; or increased fluid intake. Therefore, clinicians should focus on symptom management in treating colds. Products containing first-generation antihistamines (such as brompheniramine) and decongestants (such as pseudoephedrine) have been shown to be somewhat effective in relieving coughs associated with the common cold in adults. Currently, there are no research-based recommendations for symptom relief in children. As noted above, the Food and Drug Administration (FDA) recently advised against the use of over-the-counter cough and cold preparations in children younger than two years of age; the FDA is still reviewing the safety of these products when used by children two to 11 years old.

Rhinosinusitis refers to inflammation of the nasal mucosa and the paranasal sinus cavities. Rhinosinusitis is usually a viral infection and has a similar course to the common cold. According to a CDC report, Principles of Appropriate Antibiotic Use for Acute Rhinosinusitis in Adults, bacterial rhinosinusitis is usually a secondary infection resulting from sinus obstruction or impaired mucus clearance caused by colds, allergies, and other sources of irritation or inflammation.

Differentiating viral from bacterial rhinosinusitis is difficult and can’t be done on the basis of clinical findings alone. Purulent or yellow or green nasal discharge occurs when sloughed mucosal cells and leukocytes are present in either a viral or a bacterial illness; its presence isn’t necessarily indicative of bacterial rhinosinusitis. For adults, guidelines recommend reserving a diagnosis of bacterial rhinosinusitis for those who have severe one-sided sinus pain with swelling and fever or for those with...
symptoms lasting more than seven days and who also have sinus pain and purulent nasal discharge. Pediatric guidelines recommend limiting the diagnosis of bacterial rhinosinusitis to children with severe symptoms (for example, sinus pain and fever higher than 102°F) or to those with nonspecific symptoms (for example, cough, nasal congestion) who show no improvement after 14 days.40

Regardless of the etiology of the rhinosinusitis, management in adults and children should focus on reassuring patients and their caregivers that the symptoms usually resolve spontaneously. Results of studies on the symptomatic treatment of sinusitis have been inconclusive; however, it’s probably reasonable to assume that opening the sinus passages (or both) might be helpful. In addition, sinus pain and pressure might be relieved with nonsteroidal antiinflammatory drugs (NSAIDs) or an analgesic, such as acetaminophen (Tylenol and others).41 For bacterial rhinosinusitis, both adult and pediatric guidelines recommend treatment with amoxicillin. As a general rule, clinicians should prescribe antibiotics that have as narrow a spectrum as possible while still being effective against the most likely infectious organisms—in this case, S. pneumoniae and H. influenzae.39,41

Pharyngitis (sore throat) occurs frequently in otherwise healthy adults and children and can have either infectious or noninfectious causes (such as esophageal reflux or allergy). The most common bacterial cause of infectious pharyngitis in both adults and children is group-A β-hemolytic streptococcus (GABHS), caused by Streptococcus pyogenes.42 It’s difficult to estimate the percentage of infectious pharyngitis resulting from GABHS, but experts agree that most cases of infectious pharyngitis in adults and children are viral and don’t result from GABHS.43,44,45 Studies have reported GABHS as the cause in 5% to 26% of adult cases44-46 and of 15% to 36% of pediatric cases.47,48,49

No one sign or symptom differentiates GABHS from viral pharyngitis, not even—contrary to popular belief—exudative tonsillitis (whitish spots on the tonsils) or severe throat pain. In adults and children, GABHS pharyngitis usually develops quickly and is associated with fever, sore throat, headache, and enlarged cervical lymph nodes. Runny nose, nasal congestion, and cough are rare, and their presence usually indicates a viral infection.50,51,52

The most current guideline for diagnosing GABHS pharyngitis advises clinicians to take into account a combination of clinical findings (for example, the sudden onset of sore throat, the presence of fever, or tonsillar exudate) and diagnostic tests (for example, rapid antigen tests or pharyngeal cultures). While the newer rapid antigen tests are convenient, inexpensive, and specific (95% or higher), they are associated with false negative rates of 10% to 20%. Therefore, pharyngeal cultures should be used to confirm negative rapid antigen results in children and adolescents, the age group most prone to developing GABHS pharyngitis and its sequelae (for example, rheumatic fever and glomerulonephritis). Some people are chronic streptococcal carriers and will test positive for GABHS even when they’re not acutely ill; therefore, except under special circumstances, rapid antigen testing should be done only in patients with symptoms consistent with GABHS pharyngitis.53

Penicillin remains the first-line antibiotic choice for treatment of GABHS pharyngitis; for patients allergic to penicillin, erythromycin is the first choice.42 Symptom management for both viral and GABHS pharyngitis should focus on reducing throat pain by drinking warm or cool fluids, according to personal preference, and taking acetaminophen and NSAIDs. In addition, results from two recent studies indicate that short-term use of oral glucocorticoids may be helpful in reducing the pain and swelling associated with severe pharyngitis.54,55

Acute bronchitis is marked by a sudden cough, productive or nonproductive, that has persisted for less than three weeks with no evidence of pneumonia, common cold, acute asthma, or exacerbation of chronic obstructive pulmonary disease. In most otherwise healthy patients with an acute cough, the absence of tachycardia, tachypnea, fever, and abnormal findings on chest examination indicates that pneumonia isn’t likely. Note that the presence of purulent sputum does not distinguish acute bronchitis from pneumonia.56

Acute bronchitis has been linked to several bacteria and viruses as well as noninfectious etiologies. Known viral etiologic agents include influenza viruses, picornavirus (including rhinovirus), respiratory syncytial virus, among others.35 Known bacterial etiologic agents include S. pneumoniae, Haemophilus influenzae, Moraxella catarrhalis, and Bordetella pertussis.57 Atypical etiologic agents include Chlamydia pneumoniae (also known as Chlamydophila pneu-
Other Factors Contributing to Antibiotic Treatment Failure

What if more prudent antibacterial use isn’t always enough to prevent the spread of resistance?

The mutations that make bacteria resistant to antibiotics reduce the organisms’ overall fitness. This “fitness cost” means that the energy spent on defending against antimicrobial medications makes the bacterium less competitive in other ways.

Efforts to slow the emergence of resistance through more prudent antibiotic use are rooted in the assumption that, in the absence of antibiotics, these resistant, less-fit bacteria will be unable to compete with sensitive but highly fit bacterial strains and will die off. Eventually, as this line of thinking goes, the bacterial population will revert to its original antibiotic-sensitive state. But what if this assumption isn’t always correct?

A growing body of evidence suggests that, at least in some cases, other mutations occur in resistant bacteria, helping them compensate for the fitness costs of resistance. These resistant bacteria achieve an intermediate level of overall fitness and are better able to compete with antibiotic-sensitive strains. When this occurs, resistant strains of bacteria can survive even in the absence of antibiotics.

One implication of these findings is that, even with better prescribing practices and treatment compliance, it may be difficult to prevent resistant strains of bacteria from spreading. Even bacteria that haven’t acquired resistance to antibiotics can contribute to treatment failure.

Noninherited resistance, or resistance because of phenotypic characteristics, is less well known and understood than acquired resistance, but recent research indicates that it too may be a significant factor in some treatment failures. Even when an infection is successfully treated with an antibiotic, the medication plays only a supportive role in effecting a cure. Many other factors of the host, such as age, general health, and genetic characteristics, also come into play. Likewise, in treatment failure, factors such as the host’s immune response may be more determinative of the outcome than the damage done directly by bacterial toxins.

Bacteria that are genetically sensitive to a given antibiotic can still survive in its presence, depending on the physiologic state of the bacterial cells and the physical structure of the bacterial population. For example, bacteria are usually most susceptible to antibiotics while they divide, and some bacterial cells may not be dividing or may reproduce too slowly to be affected by the medication. In other cases, a growing mass of bacteria can form a structure called a biofilm, in which some bacterial cells can be embedded too deeply to be reached by the diffusing antibiotic. Therefore, noninherited resistance may well prolong infections, make infections more difficult to treat, and promote acquired resistance.

For more on these topics, see the work of Emory University biologist Bruce R. Levin: www.biology.emory.edu/research/Levin/pubs/index.html. —James M. Stubenrauch, senior editor

REFERENCES

sis should be reported to officials at the applicable state health department, who will then assist with tracing and identifying those who should receive prophylactic treatment.62

Management of uncomplicated acute bronchitis should focus on reassuring patients and their caregivers that bronchitis is usually a viral illness that resolves in two weeks without treatment. Patients should also be advised to get an evaluation by a clinician for a persistent cough (one that lasts longer than two weeks) or a cough accompanied by extreme lethargy, anorexia, difficulty breathing, or cyanosis. Unfortunately, research efforts to date have yet to identify the best way to decrease cough. Inhaled and oral β2-receptor agonists (such as albuterol [Proventil and others]) may be of some help in cases of acute bronchitis when airflow obstruction and wheezing are present, but these medications are not recommended for routine use in acute bronchitis.13 The use of antitussive agents, such as dextromethorphan and codeine, in patients with acute bronchitis has not been thoroughly studied. Mixed results have been achieved with these medications in patients experiencing cough from the common cold.13 Until further data are available, a short trial of antitussive agents for cough associated with acute bronchitis is probably a reasonable treatment option. But expectorants and mucolytic agents (such as guaifenesin) have been shown to be of no benefit to patients with cough from acute bronchitis and are not recommended for routine use.63

NURSING MANAGEMENT

With regard to your sister-in-law’s question—should she see her NP or take previously prescribed antibiotics?—the first option is clearly the best choice. Make sure she understands that antibiotics are serious drugs to be used only for diagnosed bacterial infections, that antibiotics can produce adverse effects, and that each antibiotic targets specific microbes. Explain that taking antibiotics for viral infections has contributed to a crisis of antimicrobial resistance. Emphasize that she should not press her clinician for a prescription for an antibiotic, nor should she take any previously prescribed, leftover antibiotics. Let her know that viral infections usually last 10 to 21 days, and correct her misconception about productive coughs warranting antibiotic treatment.

Be sure to tell your sister-in-law—and any other friends and family members who have similar concerns—about the Get Smart: Know When Antibiotics Work campaign, the CDC’s effort to educate the public on antimicrobial resistance and the proper use of antibiotics. Direct her to the campaign Web site at www.cdc.gov/getsmart. It provides plenty of easy-to-understand information that will help reinforce your message.

If your sister-in-law’s cough is mild and she isn’t experiencing extreme lethargy or difficulty breathing, advise her to wait up to three weeks before seeing her health care provider, unless her symptoms worsen.

And should she make her usual visit to her elderly mother? Your sister-in-law would be wise to avoid visiting and caregiving until her cough is resolved; most acute respiratory infections, whether they’re of a viral or a bacterial origin, can be spread to others by respiratory droplets and skin contact. Regarding her use of herbal lozenges, you can inform her that they haven’t been shown to be efficacious in treating acute respiratory infections. In the meantime, she can reduce the spread to others in close contact with her by washing her hands frequently and by covering her mouth and nose with a tissue or her elbow when she sneezes or coughs.▼

Management of uncomplicated acute bronchitis should focus on reassuring patients that it is usually a viral illness that resolves in two weeks without treatment.

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GENERAL PURPOSE: To explain the phenomenon of antimicrobial resistance and guide registered professional nurses in the appropriate management of acute respiratory infections.

LEARNING OBJECTIVES: After reading the two articles on antimicrobial resistance and taking the test on the next page, you will be able to
• discuss the development of antimicrobial resistance.
• outline the etiology and manifestations of some of the most common bacterial and viral infections.
• plan the appropriate interventions for managing common bacterial and viral infections.

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To take the test online, go to our secure Web site at www.nursingcenter.com/CE/ajn.

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