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Update on respiratory tract infections

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An ongoing CE program of The University of Florida College of Pharmacy
and DRUG TOPICS

Update on respiratory tract infections

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Upper respiratory tract infections (URTI or URI) are the most common acute illnesses in the general population. Symptoms often involve one or more sites of the respiratory system, including the sinuses, nasal passages, pharynx, and larynx. This results in a substantial number of visits to primary care providers, the emergency room, and ultimately the local pharmacy for either prescription medications or nonprescription symptomatic relief. Pharmacists should be familiar with the etiology and potential treatments for these infections. In doing so they may educate their patients on realistic expectations of antibiotic use, general prevention methods, and assist with referrals to a primary care provider when appropriate.

The common cold

The symptoms associated with the “common cold” are actually caused by at least five major groups of respiratory viruses, including the rhinoviruses and coronaviruses. The rhinovirus group, which is responsible for at least 50% of infections in adults, includes at least 100 types and one subtype. The genetic variation limits the ability for vaccine development as well as the body’s ability to achieve immunity against the “common cold.”

It is estimated that the economic impact of colds is \$40 billion annually in the United States. These cold epidemics occur annually, often in the winter months in

the United States. The rhinovirus infection rates also have their seasonal variations in outbreaks. The rhinovirus attack rates are greater in early fall and mid to late spring. The coronaviruses are more prominent in the winter. These trends are likely influenced by the school year and indoor crowding, which facilitates the transmission of viral respiratory secretions among individuals. Viral transmission occurs by hand and mucous membrane exposure and in some cases contaminated surfaces. Frequent hand washing and avoiding hand contact with either the nose or eyes assists in reducing transmission, but aerosol exposure may still occur with some viruses.

The average adult averages two to four episodes of “colds” yearly and children average six to eight episodes. However, adults with children also experience a greater rate due to secondary exposure. Individuals who smoke do not experience a greater number of infectious episodes, but those that occur are more severe. Most infected individuals experience the symptoms of sore throat first, then nasal discharge and congestion, sneezing, and cough, with slight elevations of temperature (<100°F) occurring more often in younger children. Most symptoms resolve within a week, but 25% of patients will experience symptoms for two weeks. Rarely do individuals go on to experience secondary bacterial infections of the sinuses or middle ear in which antibiotic therapy is required. Thus, treatment currently remains limited to symptomatic relief.

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GOAL

To educate pharmacists about the etiology and potential treatment options of upper respiratory infections, the realistic expectations of antibiotics in these infections, general prevention methods, and when referrals to a physician are appropriate.

CREDIT

This lesson provides two hours of CE credit and requires a passing grade of 70%.*

OBJECTIVES

Upon completion of this article, the pharmacist should be able to:

- ✓ 1. Associate symptoms of common respiratory illnesses with the identified infection
- ✓ 2. Identify and list the common pathogens responsible for each infectious process
- ✓ 3. Ascertain which infections need immediate antimicrobial therapy versus those that may be treated symptomatically
- ✓ 4. Identify the potential first-line treatment options available for each infection
- ✓ 5. Correlate risk factors for disease with general prevention mechanisms that may reduce outbreaks or transmission to others.

Effective therapeutic options for symptomatic relief of sore throat, congestion, and cough in adults include local anesthetics, throat lozenges, systemic or topical decongestants, such as pseudoephedrine and phenylephrine, respectively, and first-generation antihistamines, such as diphenhydramine. Recent guidelines from the American College of Chest Physicians (ACCP) state that using dextromethorphan and guaifenesin for coughing associated with colds is not effective and may increase morbidity and mortality in patients, especially in children less than 14 years of age. Codeine and homatropine (Hycodan) have also been used as cough suppressants in patients, but their effectiveness has been questioned in treating cough due to colds. Alternative therapies, such as Echinacea, zinc, humidified air, and fluid intake, have not been proven to reduce the severity of symptoms either. High-dose vitamin C (> 2 grams) in some studies has reduced the severity and duration of symptoms in some adults. Additionally, patients with comorbid conditions, particularly hypertension, should be counseled on potential adverse effects associated with pharmacological therapies, particularly oral decongestants.

Use of expectorants, antihistamines, decongestants, and cough suppressants is not recommended in children less than two years of age as a result of limited effectiveness and in some cases increased risk of adverse effects. The FDA is still reviewing the safety and effectiveness of these drugs in

children between the ages of two and 11 years and these drugs should be used with caution.

Non-pharmacological methods of symptomatic relief, such as a rubber suction bulb or saline nose drops, may be used as an alternative.

Pharyngitis

Acute pharyngitis is an inflammatory process more commonly referred to as a “sore throat.” It accounts for 19 million clinic visits annually in the United States. Pharyngitis may be a result of viral or bacterial origin. Approximately 50% of sore throats are attributed to the same viral agents linked to the common cold. Other viral agents associated with pharyngitis include influenza, Epstein-Barr virus, herpes simplex virus, and acute retroviral syndrome with human immunodeficiency virus (HIV-1). *Streptococcus pyogenes* (Group A streptococci or GAS) is frequently associated with pharyngitis and is the etiologic agent in 10% of adults and between 10% and 30% of infections in children. Streptococcal Group C is often associated with pharyngitis in college students. Streptococcal Group G, *Neisseria gonorrhoea*, *Corynebacterium diphtheriae*, and a few chlamydial species are offending pathogens in exceptional cases. The origin of the infection may be influenced by the season of the year, patient age, severity of illness, and comorbid conditions.

While symptoms are often nonspecific, the presence of exudate on the tonsils or throat, a fever greater than 100.9°, and cervical lymph node

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tenderness tend to indicate pharyngitis due to GAS in patients greater than three years of age. The presence of sore throat and cough would prompt consideration of a viral infection. For patients less than three years of age, nasal inflammation and crusting may be a presenting symptom of GAS. Diagnosis and treatment of GAS is important in order to avoid complications of acute rheumatic fever, acute glomerulonephritis, and invasive infection. Some current guidelines recommend a clinical prediction model or “scoring” system, based on symptoms to identify those patients who should be tested and treated. Others suggest a “test and treat” model by which only those who test positive by a rapid-detection method receive treatment. Diagnosis by a rapid-detection test has a reported specificity rate of 90% but offers a more variable sensitivity rate. The gold standard of detection is a throat culture, but the use of a backup throat culture after a negative rapid test is no longer recommended. In severe cases of pharyngitis, the American College of Physicians-American Society of Internal Medicine (ACP-ASIM) guidelines suggest empiric therapy, while the Infectious Diseases Society of America (IDSA) opposes this decision, citing the risks of unnecessary antibiotic use.

Treatment of GAS with antibiotics has been associated with a reduction in symptoms if therapy begins during the first 48 hours of onset. After 48 hours, there is a good likelihood for self-improvement without medical intervention. When weighing the risk of complications with the potential for self-improvement, it is important to note that therapy may be safely postponed in adults up to nine days after the onset of symptoms without the risk of complications. However, those who are treated within the first 48 hours also have a great frequency of recurrence, as it is believed that the immune response offers some future protection. Should treatment be prescribed, penicillin (250mg four times a day or 500mg twice to four times a day) remains the drug of choice for treatment of GAS pharyngitis. Antibiotic treatment offers the potential benefit of prevention of rheumatic fever, further infectious complications, and reducing the symptomatic duration and risk of transmission to others. The exception is acute glomerulonephritis, which is unaffected by therapy as it is associated with the patient’s immune response to the bacterial infection itself. Amoxicillin may be utilized as an alternative for children or others to improve tolerability. Cefdinir

(600mg daily or 300mg twice daily), macrolides (azithromycin or clarithromycin), and clindamycin all remain effective alternatives for patients with a non-anaphylactic penicillin allergy. When recommending a treatment alternative for GAS, it is important to keep in mind that erythromycin resistance has been reported in sections of the United States. The standard duration of therapy remains 10 days with the exception of azithromycin, which follows a five-day dosing course.

Sinusitis

This upper respiratory infection, also known as rhinosinusitis, is defined as inflammation of one or more of the paranasal sinuses, which is caused by viral or bacterial pathogens. Sinusitis can be further delineated into categories as acute (<four weeks), subacute (four to eight weeks), and chronic (>eight weeks). It affects over 30 million people annually and is the fifth-most common reason for antibiotic treatment. Viral pathogens include rhinovirus, parainfluenza, influenza, and coronaviruses. The most common bacterial pathogens involved in sinusitis include *Streptococcus pneumoniae* and *Haemophilus influenzae*. *Moraxella catarrhalis* and *Staphylococcus aureus* infections are also possible.

Symptoms of sinusitis can be nonspecific but usually include purulent nasal discharge, congestion of one or both nasal passages, and facial tenderness or pain over the affected sinus cavity, especially upon bending down. Other symptoms associated with sinusitis are unpleasant taste or smell, jaw or tooth pain, and headache. The gold-standard diagnostic test for bacterial sinusitis is sinus aspiration and culture. However, this is an invasive procedure and is rarely done in primary care settings. There are no other diagnostic tests to differentiate between viral and bacterial sinusitis. Viral sinusitis will usually resolve in seven to 10 days. In contrast, bacterial sinusitis usually lasts longer and may require treatment. However, 75% of bacterial sinusitis cases resolve without antibiotics in one month.

Treatment of sinusitis usually is supportive. Analgesics are used to treat facial, jaw, or tooth pain associated with the infection. Topical decongestants are sometimes more effective than systemic decongestants when treating sinusitis. However, patients with sinusitis, especially bacterial, have poor response to decongestants, and the risk

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of rebound congestion when using topical decongestants for more than three to five days is a concern. Systemic steroids have not been shown to be effective when treating sinusitis, and a recent study of 207 patients showed that nasal steroids were not effective in severe cases of acute sinusitis. The same study showed a modest benefit of nasal steroids when used early in mild cases of acute sinusitis. Antihistamines and nasal irrigation with saline have been used to treat some cases of sinusitis, but the effectiveness of these treatments is unknown. Using antibiotics to treat bacterial sinusitis is controversial. Recent reviews of the literature suggest that antibiotics are minimally to not effective in treating sinusitis. The poor effectiveness has been attributed to the poor penetration of antibiotics into closed cavities like the paranasal sinuses. The decision to use antibiotics should be based on the severity and duration of the infection and risk for complications, such as intracranial or orbital infections of suspected bacterial sinusitis. If antibiotics are deemed necessary, amoxicillin is considered first line. Acceptable alternatives include trimethoprim/sulfamethoxazole and macrolides. Antibiotics should be prescribed for 10 to 14 days. Currently there is no evidence that longer courses of antibiotics are more effective. If the patient's symptoms worsen after seven days of antibiotic treatment, the antibiotic should be changed.

Bronchiolitis

This infectious process is characterized by a fever, nasal discharge, and a dry wheezy cough that is usually "high pitched." Neutrophilic inflammation of the lung tissue is also a predominant diagnostic sign. Eighty percent of cases are caused by respiratory syncytial virus (RSV). Other viral pathogens include human metapneumovirus, rhinovirus, adenovirus, influenza, parainfluenza viruses, and enteroviruses. RSV can be further classified as group A or B and is routinely associated with young children (<two years). Children less than one and pre-term infants are at the greatest risk for severe complications, such as pneumonia and respiratory failure. Infection with RSV does not produce complete immunity, thus allowing for multiple yearly infections. Recent studies also suggest that the elderly adult populations may be another population at risk for RSV complications. RSV bronchiolitis will usually resolve in eight to 15 days, and management is mainly supportive and includes antipyretics for fever,

increased fluid intake, and saline nasal sprays. Bronchodilators have shown some effectiveness and may be prescribed. For high-risk patients or severe cases, hospital admission may be required.

Ribavirin, in aerosol form, is the only approved antiviral for RSV and is approved for use in infants. However, there have been anecdotal reports of use of ribavirin in adults. Ribavirin belongs to pregnancy category "x", thus pregnant women or those women who are not on reliable birth control as well as their male partners should not be exposed to it. Controversy exists over the effectiveness of ribavirin as studies have not shown significant benefit. Co-infection with bacteria occurs in 10%-30% of patients already infected with RSV. A chest X-ray and sputum cultures can be used to confirm co-infection. Treatment with the specific antibiotic necessary to cover the bacterial infection is appropriate in co-infected patients. Palivizumab (Synagis) and RSV immune globulin [RSV-IG] (Respigam) may be used for prophylaxis of RSV bronchiolitis in certain high-risk patient populations, but they are not indicated for treatment.

Bronchitis

The hallmark sign of bronchitis is cough. Bronchitis is classified as acute or chronic. Patients with chronic bronchitis can have acute exacerbations (AECB). Acute bronchitis has a more sudden onset and is commonly seen in otherwise healthy patients. In contrast, chronic bronchitis is part of chronic obstructive pulmonary disease (COPD) and usually develops due to long-standing lung insults, such as smoking or environmental factors. For ease of reading, acute bronchitis and AECB will be discussed separately.

Acute bronchitis is one of the most common diagnoses and is reported in 5% of the general population annually. Acute bronchitis is a poorly defined upper respiratory infection and may resemble several other respiratory infections and disorders, including acute asthma, pneumonia, severe acute respiratory syndrome (SARS), and the common cold. Differential diagnosis is essential. Acute bronchitis has two phases. In the first phase, patients will have nonspecific symptoms such as fever, malaise, and myalgias. These symptoms last from one to five days. The second phase, lasting one

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to three weeks, consists of one or more of the following: persistent cough, phlegm production, or wheezing. Airway hypersensitivity and decreased pulmonary function tests (PFTs), resembling acute asthma, are also seen during the second phase. However, unlike asthma, PFTs will usually resolve in two to three weeks. Unlike pneumonia, vital signs will be fairly normal and chest X-rays will be clear in acute bronchitis. The ACCP does not recommend routine chest X-rays if acute bronchitis is suspected.

Acute bronchitis is most commonly caused by viral pathogens. The most common viruses suspected in acute bronchitis, in order of prevalence, include influenza A and B, parainfluenza, RSV, coronavirus, adenovirus, and rhinoviruses. Human metapneumovirus (hMPV) is an emerging pathogen suspected in acute bronchitis, especially among immunocompromised patients. Bacteria cause less than 10% of acute bronchitis. *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Bordetella pertussis* have been established as bacterial causes of acute bronchitis. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* have been suspected but have not been proven to cause acute bronchitis. Patients with bacterial infections may have longer duration of symptoms and are more likely to present with wheezing than those with viral infections.

The most effective treatment of acute bronchitis is prevention. Methods to avoid acute bronchitis are: frequent hand washing, avoiding infected individuals, and updated vaccinations, especially pertussis and influenza. If a patient does develop acute bronchitis, treatment is mostly supportive. If infection with influenza is suspected or confirmed within 48 hours of onset of symptoms, treatment with antivirals such as amantadine, rimantadine, zanamivir (Relenza), or oseltamivir (Tamiflu) may be used. Amantadine and rimantadine are only effective against influenza A while zanamivir and oseltamivir are effective against both A and B strains. Studies have shown that treatment with antivirals decreases duration of illness by one day and may lead to a return to normal level of activity by half a day. Although antibiotics are frequently prescribed, studies have shown they are not effective for almost all cases of acute bronchitis, and ACCP guidelines recommend against prescribing antibiotics for routine treatment. The exception is acute bronchitis caused by *B. pertussis*. These

patients will usually present with paroxysmal cough or “whooping” cough along with choking or vomiting. These patients need to be treated within seven to 10 days of onset of symptoms with either erythromycin 250mg four times a day or 333mg three times a day for seven to 10 days. Trimethoprim/sulfamethoxazole can be used as an alternative if a patient is allergic to macrolides. The use of bronchodilators, such as albuterol, is not recommended in most cases of acute bronchitis. A recent large review of studies of bronchodilators for acute bronchitis showed these agents failed to reduce cough severity or duration. Additionally, side effects, such as tremors, tachycardia, and nervousness, were prevalent. However, ACCP guidelines do recommend using bronchodilators—specifically, beta agonists—in patients with acute bronchitis accompanied with significant wheezing. Antitussives, such as codeine and dextromethorphan, have been shown to be useful to control severe coughing associated with acute bronchitis, and ACCP recommends the occasional short-term use of these agents. Studies have failed to show benefit of using mucokinetic agents, such as guaifenesin in acute bronchitis, and therefore these agents should be avoided.

Acute exacerbations of chronic bronchitis

Patients with chronic bronchitis will have 1.5 to three occurrences of acute exacerbations of chronic bronchitis (AECB) annually. Chronic bronchitis is defined as the presence of productive cough on most days of the week for at least three months over two consecutive years. Other symptoms include shortness of breath, purulent sputum, and increased sputum tenacity. AECB is essentially acute worsening of these symptoms, unstable lung function, and worsening airflow. AECB can be classified as mild (worsening in one baseline symptom), moderate (worsening of two baseline symptoms), and severe (worsening of \geq three baseline symptoms). AECB may be infectious in nature. Viral exacerbations are frequently associated with dyspnea, sore throat, and other cold-like symptoms. Bacterial exacerbations are usually characterized by neutrophilic inflammation, such as increased sputum production or purulence. Research has shown that inflammatory markers such as interleukin-6 and -8, tumor necrosis factor-alpha, neutrophil elastase, and serum fibrinogen increase with bacterial AECB. Chest X-rays are not commonly used to diagnose AECB unless

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patients present with atypical symptoms or pneumonia is suspected.

The predominant viral pathogens involved in AECB include influenza and rhinoviruses. Other common respiratory viruses discussed previously have also been found to cause AECB. In contrast to acute bronchitis, bacteria play a larger role in AECB. *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* are the predominant pathogens found in AECB. *Pseudomonas aeruginosa* has been implicated in more severe cases of AECB. Less than 10% AECB are caused by atypical bacteria, with *C. pneumoniae* being the most predominant, followed by *Mycoplasma pneumoniae* and *Legionella pneumoniae*.

Treatment of AECB focuses on three goals: resolving symptoms quickly, lengthening the time between exacerbations, and stopping further lung damage due to infection and inflammation. In order to resolve symptoms quickly, patients should be given oxygen to help shortness of breath. If the patient is already receiving bronchodilator therapy, increasing the dose or adding a short-acting bronchodilator will also help with shortness of breath. In severe cases, adding a systemic corticosteroid, such as prednisone, may help improve lung function by decreasing inflammation. The optimal dose and duration of steroid use is to be determined, but recent studies have shown lung function improves between three to five days of steroid therapy, so one may infer that steroid therapy should be given for at least five days. Increased hydration and chest physical therapy (e.g., oscillating positive expiratory pressure) to help thin and remove sputum may also benefit patients, although studies of effectiveness have been inconclusive.

The use of antibiotics in AECB remains controversial. Most clinicians agree that antibiotics are necessary in moderate and severe cases of AECB and in those patients at high risk of relapse (e.g., AECB within past week, advanced age, chronic steroid use, severe lung damage, malnutrition). When considering treatment with antibiotics, the prescriber should consider the spectrum activity, resistance patterns of the area, tracheobronchial penetration, and cost. Increasing drug resistance by *S. pneumoniae* and poor penetration make penicillins and most cephalosporins poor choices for AECB. However, high-dose amoxicillin/clavulanate (Augmentin, 875 twice daily or 500 mg three times daily) has shown efficacy in AECB. Studies have supported

the use of fluoroquinolones and macrolides as the most effective therapies in AECB. Head-to-head studies of moxifloxacin 400 mg daily for five days or levofloxacin 500 mg for seven days versus azithromycin (Z-pack 500mg on the first day then 250mg daily for four days) showed equal efficacy. However, resistance to the macrolides by *S. pneumoniae* is increasing, and these drugs should be used judiciously. Doxycycline may be used if *M. catarrhalis* is the sole pathogen or an alternative if the patient cannot tolerate macrolides or fluoroquinolones. Depending on the antibiotic prescribed, duration of treatment should be five to 10 days, and the patient's symptoms should return to baseline. If a patient is not improving within 24 to 36 hours after initiation of antibiotic treatment, reevaluation is necessary.

Otitis media

Otitis media (or inflammation of the middle ear) is a common infection in children. At least 80% of children will receive this diagnosis at least once by three years of age. In fact, age is one of the greatest risk factors for infection, with the age of six to 24 months showing an increased prevalence. Other risk factors that also contribute include but are not limited to increased exposure to other children that may occur as a result of daycare or other siblings, cigarette smoking in the household, pacifier use, seasonal exposures to pathogens, and even ethnic origin.

Symptoms in children and infants include pulling on the ears (potentially indicating pain), irritability, ear discharge, and possible fever. These symptoms frequently follow a viral respiratory infection but may also appear in conjunction with the "cold" symptoms of nasal discharge, cough, or gastrointestinal upset as well. Symptoms of severe inner ear pain or a temperature greater than 39°C or 102.2°F may be classified as severe. Common pathogens include *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, the same pathogens often seen in other upper respiratory tract infections. It is important to note that no bacterial pathogen is identified in up to 30% of patients. Thus the treatment decision for this infectious condition is frequently empiric and symptomatic in nature.

Studies suggest that between 70%-90% of children have resolution of symptoms without antibiotic treatment in seven to 14 days. Thus antibiotic treatment in certain

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cases may initially be delayed. Yet during this time symptomatic treatment is recommended. Acetaminophen at doses of 15mg/kg every four to six hours and ibuprofen at 10mg/kg every six hours may be used to alleviate pain in children, especially during the first two days of symptoms. The use of topical otic suspension of antipyrine/benzocaine offers an alternative for pain relief. While the oral decongestants may be used in some children for congestion, they do not alter the symptoms or treat acute otitis media. Corticosteroids and antihistamines offer no therapeutic benefits in treatment either.

The recommendations for use of antibiotic treatment are based upon age and symptomatology. Those with definite infections between the ages of six months and two years and those with severe infection (indicated by symptoms) who are older than two years of age should receive antibiotics immediately. Patients who are septic or classified as immunosuppressed should also receive immediate treatment. For all others there is a “wait and see” recommendation for 48 to 72 hours—this is assuming there is a reliable caregiver involved for symptomatic monitoring. If there is a concern about the caregiver’s reliability or access to health care is in question (i.e., transportation or funding etc.), this may alter the provider’s decision.

High-dose amoxicillin (80-90mg/kg) twice daily for 10 days is the treatment of choice for those children six years or younger. The duration declines to five to seven days in patients older than seven years of age. The use of a one-time dose of azithromycin of 30mg/kg, clarithromycin 15mg/kg/day divided three times a day, or clindamycin 30-40mg/kg/day divided four times a day may also be used as therapeutic substitutions in this setting. Once treatment is offered, its effectiveness should be reassessed in 48 to 72 hours. If symptoms are not improving and adherence has been validated, a second-line option is recommended. Second-line options include high-dose amoxicillin-clavulanate at 90mg/kg, cephalosporins, or the previously mentioned macrolides. In cases of poor tolerance (i.e., vomiting) or adherence, single daily doses of 50mg/kg of ceftriaxone for three days remain a viable option. Finally, if symptoms continue, the use of clindamycin at 30-40mg/kg divided four times a day and tympanocentesis are

the last step. The use of levofloxacin, although not FDA-approved for use in children, has also been utilized with successful outcomes.

It is important to note that effusion without symptoms or effusion after treatment is not indicative of infection when there is resolution of symptoms. Oral and topical corticosteroids may assist with quicker symptomatic improvement but do not offer any additional benefits long term. Children with speech difficulties, hearing loss, or cognitive declines need to be assessed for insertion of ventilation tube surgery immediately. Removal of the adenoids may also offer some benefit for children with nasal obstruction.

A brief review of symptoms of upper respiratory tract infections may be found in **Table 1**. While infections involving the upper respiratory tract are fairly common, infections in the lower respiratory tract are often limited. Those patients with other medical conditions that alter the host immune response or increase their risk of exposure to particularly virulent pathogens are obviously at greater risk. Discussions of infections of the lower respiratory tract will be limited to community-acquired pneumonia in the outpatient setting. A

TABLE 1
Differentiation of respiratory disorders

Illness	Signs and symptoms
Bacterial throat infection	Sore throat, fever, exudate, tender anterior cervical adenopathy
Cold	Sore throat, nasal congestion, rhinorrhea, sneezing. May also have low-grade fever, chills, headache, malaise, myalgia, and cough.
Croup	Fever, rhinitis, and pharyngitis initially. Progresses to cough (may be “barking” cough), stridor, and dyspnea
Influenza	Myalgia, arthralgia, fever, sore throat, nonproductive cough, moderate-severe fatigue
Otitis media	Ear popping, ear fullness, otalgia, otorrhea, hearing loss, dizziness
Pneumonia or bronchitis	Chest tightness, wheezing, dyspnea, productive cough, changes in sputum color, persistent fever
Sinusitis	Tenderness over the sinuses, facial pain aggravated by Valsalva’s maneuver or postural changes, fever >101.5°F (38.6°C), tooth pain, halitosis, upper respiratory tract symptoms for >seven days with poor response to decongestants
Whooping cough	Initial catarrhal phase (rhinorrhea, sneezing, mild cough, sneezing) of one to two weeks, followed by one to six weeks of paroxysmal coughing

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complete review of the pneumonia guidelines may be found at the IDSA Web site at www.idsociety.org/.

Table 2
CURB-65 criteria

Clinical factor	Determination	Points
Confusion	Based on testing or disorientation to person, place or time	1
Uremia	BUN > 7mmol/L (20mg/dl)	1
Respiratory rate	≥ 30 breaths/min	1
Low blood pressure	< 90mm Hg systolic or ≤ 60mm Hg diastolic	1
Age 65 or greater	As defined	1
Total points		

Table 3
Risk factors for particular pneumonia pathogens

Risk factors	Common pathogen
Alcoholism	Streptococcus pneumoniae, oral anaerobes, Klebsiella pneumoniae, Acinetobacter species, M. tuberculosis
COPD/smoking	Haemophilus influenzae, Pseudomonas aeruginosa, Legionella species, S. pneumoniae, Moraxella catarrhalis, Chlamydia pneumoniae
Aspiration	Gram-negative enteric pathogens, oral anaerobes
Lung abscess	CA-MRSA, oral anaerobes, fungal, M. tuberculosis, atypical mycobacteria
Hotel or cruise ship within two weeks	Legionella species
Influenza active in community	Influenza, S. pneumoniae, S. aureus, and H. influenzae
Cough >two weeks with whoop or posttussive vomiting	Bordetella pertussis
Injection drug use	S. aureus, anaerobes, M. tuberculosis, S. pneumoniae

* Adjusted from Table 8 pg S46 IDSA Community-Acquired Pneumonia Guidelines, CID 2007;44 (supplement 2)

Community-acquired pneumonia

The etiology of community-acquired pneumonia (CAP) may be of either bacterial or viral origin. Common organisms in the outpatient setting include Streptococcus pneumoniae, Mycobacteria pneumoniae, Haemophilus influenzae, Chlamydia pneumoniae, and respiratory viruses. Influenza A

and B remain the leading causes of viral pneumonia, but consideration should also be given to RSV, adenovirus, parainfluenza virus, and less often other viruses. It is important to note that specific organisms may be linked with particular co-morbid conditions, specific environmental risks, or other disease states.

Twenty percent of patients with the diagnosis of CAP will be hospitalized, increasing their risk of mortality from other co-morbid conditions. Thus the decision on whether to hospitalize a patient is of significant importance. The current IDSA/ATS guidelines recommend using the CURB-65 criteria. These five objective criteria may be found in Table 2. In the primary care office CRB-65 may suffice. A patient score of zero to one suggests that the patient may be safely treated as an outpatient with a few exceptions. A score of two or greater indicates the need for admission to a hospital. Admission to the ICU is recommended for patients with a score of three or greater. (In facilities where high-level monitoring is present, this may suffice for those patients not identified as “severe.”) The guidelines note the following exceptions for hospital admission in addition to the prior objective data. These may include complications of pneumonia, exacerbation of underlying disease(s), inability to obtain or take medication in an outpatient setting, and those patients who have multiple factors that are close to the suggested cutoffs.

Identification of a specific pathogen helps to refine treatment, with the goal of reducing cost, drug adverse effects, and the development of antimicrobial resistance. Yet empiric therapy is routinely effective. It is important for the medical provider to rule out specific organisms if the patient has particular risk factors or there are particular environmental concerns. These organisms should include influenza, RSV, SARS, avian (H5N1) influenza, diseases of bioterrorism, Legionella infection, community-acquired methicillin-resistant staphylococcus aureus (CA-MRSA), Mycobacterium tuberculosis, and endemic fungal infections. Since these organisms are infrequent causes of outpatient pneumonia, sputum analysis and blood cultures are optional. Epidemiologic conditions or risk factors for specific pathogens may be found in Table 3.

Prior to choosing empiric therapy for a patient, antibiotic resistance within

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the local community should be taken into consideration. Individual risk factors for resistant *S. pneumoniae* should also be assessed. These include age <two years or >65 years, beta-lactam therapy within the previous three months, alcoholism, medical co-morbidities, immunosuppressive illness or therapy, and exposure to a child in a daycare setting.

Consideration should also be given to risk factors or symptoms of CA-MRSA. Although rare, CA-MRSA is often seen following influenza and results in cavitary infiltrates in patients who are not at risk for aspiration pneumonia.

Empiric treatment for patients who lack any previously mentioned risk factors for drug resistance includes a macrolide antibiotic or doxycycline, although the latter is less favorable. In patients with comorbidities, those who have risk factors for drug resistance, or in regions where there is a high rate (>25%) of high-level macrolide resistance, the use of a respiratory fluoroquinolone or a beta-lactam plus a macrolide is recommended. Drug selections may be found in **Table 4**.

Measures of pneumonia prevention include vaccination as well as hand and respiratory hygiene procedures. The inactivated Influenza vaccine is recommended for all patients 50 years and greater, household contacts, and healthcare workers. The intranasally administered influenza vaccine may be offered as an alternative to patients two to 49 years of age with no underlying medical conditions. The pneumococcal polysaccharide vaccine should be administered to all patients 65 years of age, smokers, as well as those patients with preexisting medical conditions to prevent the bacterial complications of bacteremia and meningitis associated with *Streptococcus pneumoniae*. A repeat vaccination is also recommended after five years. If the patient received the first dose prior to age 65, give a single revaccination at age 65 (or older)

if at least five years have elapsed since the previous dose. Respiratory hygiene should include masks or tissues to cover the mouths of patients with illness. Finally as mentioned in prior prevention discussions, smoking increases a patient's risk of acquisition of respiratory infections and their complications in addition to increasing cancer rates. A smoking cessation program should be discussed with this patient population.

Table 4
Recommended empirical antibiotics for outpatient community-acquired pneumonia

Situation	Treatment
Previously healthy & no antibiotic use within the prior three months	Azithromycin Clarithromycin Erythromycin (# Doxycycline-secondary agent)
Comorbidities (diabetes, asplenia, etc.) or use of antibiotics in the prior three months	Moxifloxacin 400mg daily Gemifloxacin 320mg daily Levofloxacin 750mg daily Or Beta-lactam PLUS macrolide High-dose amoxicillin 1g TID Or amoxicillin/clavulanate 2g BID are preferred beta-lactams (alternatives: ceftriaxone, cefpodoxime, cefuroxime)
High rates (>25%) of macrolide drug resistant <i>S. pneumoniae</i> in the community	Follow recommendations for co-morbidities or antibiotic resistance as above

TEST QUESTIONS

Write your answers on the answer form appearing on page 55 (photocopies of the answer form are acceptable) or on a separate sheet of paper. Mark the most appropriate answer.

- 1.** Which of the following does NOT increase a person's risk of acquiring a "cold?"
 - a. Working with children
 - b. Colder seasons
 - c. Crowded environments
 - d. Smoking
- 2.** Which of the following alternative therapies is effective in reducing "cold" symptoms?
 - a. Vitamin C
 - b. Echinacea
 - c. Zinc
 - d. Humidified air
- 3.** Treatment should be started within _____ in order to reduce pharyngitis symptoms due to Group A streptococcus?
 - a. 12 hours
 - b. 24 hours
 - c. 48 hours
 - d. 72 hours
- 4.** The first-line treatment for Group A streptococcus is which of the following?
 - a. Penicillin V 250mg BID for 10 days
 - b. Penicillin V 500mg BID for 10 days
 - c. Penicillin V 500mg TID for 5 days
 - d. Penicillin V 500mg QID for 5 days
- 5.** What percentage of bacterial sinusitis infections resolves without antibiotics?
 - a. 10%
 - b. 25%
 - c. 50%
 - d. 75%
- 6.** When antibiotic treatment for sinusitis is prescribed, what is the duration of therapy?
 - a. Five to seven days
 - b. Seven to 10 days
 - c. 10-14 days
 - d. 14-21 days
- 7.** Which pathogen is responsible for the majority of the dry, wheezy "high-pitched" coughs?
 - a. Respiratory syncytial virus (RSV)
 - b. Streptococcus pneumoniae
 - c. Human metapneumovirus
 - d. Influenza virus
- 8.** What is Ribavirin's pregnancy category?
 - a. B
 - b. C
 - c. D
 - d. X

TEST QUESTIONS

- 9.** Which of the following organisms is least likely to be identified in an upper respiratory tract infection?
- Pseudomonas aeruginosa
 - Streptococcus pneumoniae
 - Moraxella catarrhalis
 - Haemophilus influenzae
- 10.** A patient presents to your pharmacy complaining of a cough with a whooping sound along with nausea and vomiting. What is the most likely pathogen?
- Streptococcus pneumoniae
 - Bordetella pertussis
 - Respiratory syncytial virus (RSV)
 - Adenovirus
- 11.** Which of the following antibiotic therapies would NOT be a good choice for a diagnosis of acute exacerbations of chronic bronchitis (AECB)?
- Penicillin V 500mg BID
 - Augmentin 875mg BID
 - Moxifloxacin 400mg daily
 - Azithromycin (Z-pack)
- 12.** What percentage of children has resolution of their otitis media symptoms within seven to 14 days without antibiotic treatment?
- 10%-20%
 - 25%-30%
 - 40%-50%
 - 70%-90%
- 13.** A mother of a four-month-old baby needs antibiotics for her child's first ear infection. Which of the following treatment regimens would be a first-line option within the first 24 hours?
- "Wait and see" for 48-72 hours
 - Amoxicillin 80-90mg/kg
 - Clarithromycin 15mg/kg
 - Clindamycin 30-40mg/kg
- 14.** The mother comes back later with her seven-year-old son with the same diagnosis of otitis media. He is penicillin-allergic (rash). What is your treatment recommendation?
- "Wait and see" for 48-72 hours
 - Amoxicillin 80-90mg/kg
 - Clarithromycin 15mg/kg
 - Clindamycin 30-40mg/kg
- 15.** True or False? Topical corticosteroids assist in providing symptomatic relief of ear effusions and offer long-term benefits.
- True
 - False
- 16.** When reviewing the CURB-65 score, what is the respiratory rate cutoff that is used to calculate an additional risk factor?
- > 20 breaths/min
 - > 25 breaths/min
 - > 30 breaths/min
 - > 65 breaths/min

TEST QUESTIONS

- 17.** Your interview with a 50-year-old patient with suspected CAP provides no indication of confusion. He has a respiratory rate of 25 breaths, a BUN of 5mmol/L, and blood pressure of 87/65 mmHg. What is your assessment of his CURB-65 score and treatment option?
- His score is zero, he may be treated as an outpatient
 - His score is one, he may be treated as an outpatient
 - His score is two, he may be treated as an outpatient
 - His score is three, he should be admitted for inpatient treatment
- 18.** Thomas is a 65-year-old smoker with diabetes who was recently diagnosed with COPD. What treatment option would you recommend for his community-acquired pneumonia?
- Ciprofloxacin 500mg BID
 - Levofloxacin 500mg daily
 - Levofloxacin 750mg daily
 - Clarithromycin 500mg BID
- 19.** What is the resistance percentage used to define “high rates” of drug resistance in a community?
- 15%
 - 25%
 - 35%
 - 45%
- 20.** Which of the following vaccine(s) is/are recommended to be administered to a healthy 55-year-old male to prevent pneumonia?
- Inactivated influenza
 - Intranasally administered influenza
 - Pneumococcal polysaccharide vaccine
 - All of the following are recommended

Evaluation of CE

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	Strongly Agree	Agree	Disagree	Strongly Disagree
1. The objectives listed on page 47 were met. If not, please describe:				
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ANSWER FORM

Update on respiratory tract infections AUGUST 11, 2008

ACPE # **012-999-08-106-H04-P** Test questions start on page 53

ACPE # **012-999-08-106-H04-T**

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|-----------------------|-----------------------|------------------------|------------------------|------------------------|
| 1. a. b. c. d. | 5. a. b. c. d. | 9. a. b. c. d. | 13. a. b. c. d. | 17. a. b. c. d. |
| 2. a. b. c. d. | 6. a. b. c. d. | 10. a. b. c. d. | 14. a. b. c. d. | 18. a. b. c. d. |
| 3. a. b. c. d. | 7. a. b. c. d. | 11. a. b. c. d. | 15. a. b. | 19. a. b. c. d. |
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