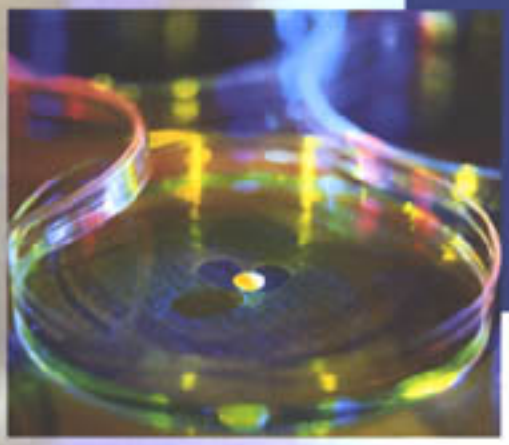

Clinical Dialogues: Antibiotic-Resistant Respiratory Tract Bacteria

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1 HOUR OF CME/CE CREDIT FOR PAs AND NPs

WELCOME!

This issue of **Clinical Dialogues** is another in a series of Continuing Education newsletters developed to inform nurse practitioners and physician assistants about the challenges posed by community-acquired respiratory tract infections—and to provide the latest clinical information about managing these infections. **In this issue, we describe the newly updated guidelines for managing community-acquired pneumonia in immunocompetent adults.** Our Editorial Board has reviewed the new guidelines, focusing on the recommendations that may affect your approach to treating this increasingly common condition.

We look forward to receiving your completed posttest and evaluation forms. In addition, we hope you'll take a moment to forward your comments about **Clinical Dialogues**—and any specific questions that you would like us to address in future issues. Please contact us by email at: clinicaldialogues@veritasime.com.

AAPA Approved CME

New Guidelines for Treating Community-Acquired Pneumonia (CAP) in the Era of Antibiotic Resistance

Learning Objectives

After reading this article, the participant should be better able to:

1. Explain the 3-step process for determining the initial site of treatment for patients with community-acquired pneumonia (CAP).
2. Describe the initial empiric therapy recommended for suspected bacterial CAP in outpatients and inpatients.
3. Identify the laboratory and agent-specific tests used to diagnose CAP.
4. Recall the pathogen-specific therapies currently recommended for CAP.

More than 4 million adults in the United States are diagnosed with community-acquired pneumonia (CAP) every year, and as many as 1 million require hospitalization. As the population ages, this incidence continues to increase, especially among patients with 5 specific comorbidities: chronic obstructive pulmonary disease, asthma, diabetes mellitus, neoplastic disease, and cerebrovascular disease. (File et al 2001; Halm and Teirstein 2002)

During the past decade, treatment of CAP has changed rapidly due to the rise of atypical pathogens, increased antibiotic resistance, and the introduction of new antimicrobial agents. (Ben-David and Rubinstein 2002) In response, the Infectious Diseases Society of America (IDSA) published guidelines for CAP in 1998, revised them in 2000, and updated them in 2003. (Bartlett et al 1998; Bartlett et al 2000; Mandell et al 2003)

The new update of the CAP practice guidelines introduces revised diagnostic and management strategies. "One of the most significant changes from the previous guidelines is that there are more specific recommendations about individualizing antimicrobial therapy based on stratification of the patient by 2 factors—prior use of antibiotics and presence of comorbid conditions," said Thomas M. File Jr, MD, of Summa Health System in Akron, Ohio, one of the guideline authors and a member of the **Clinical Dialogues** Editorial Board. The new guidelines recommend that a macrolide alone is adequate to manage CAP in patients who have previously been healthy and have not received antibiotics for any reason within the preceding 3 months. The guidelines rely less heavily on fluoroquinolones, which have been associated with increasing resistance.

The sections that follow summarize these revised CAP recommendations and the changes in practice management they entail.

Update: Initial Site of Treatment Decision

Selecting the initial site of treatment—home or hospital—is one of the most important clinical decisions for managing patients with CAP; often, it determines the choice of antibiotic agents, route of administration, intensity of medical observation, and use of medical resources.

Recommendation: The initial site of treatment should be based on a 3-step process: (1) assessment of preexisting conditions that compromise the safety of home care; (2) calculation of the Pneumonia PORT (Pneumonia Outcomes Research Team) Severity Index (PSI) with recommendations for home care for risk classes I, II, and III; and (3) clinical judgment.

Step 1 involves assessing potentially destabilizing preexisting conditions, such as severe hemodynamic instability, acute hypoxemia or chronic oxygen dependency, and the inability to take oral medication.

Method of Participation

Read this newsletter, complete the CME posttest and evaluation, and fax or mail the form to the Veritas Institute for Medical Education at the address listed. You will receive a certificate within 2 weeks. There is no certificate processing fee.

Intended Audience

This activity has been designed for physician assistants and nurse practitioners who provide care to patients with respiratory tract infections.

Effective Dates

January 2004 through December 31, 2004

Accreditation/Designation Statements

Physician Assistants—This program has been reviewed and is approved for a maximum of 1 hour of clinical Category 1 (Preapproved) CME credit by the American Academy of Physician Assistants (AAPA). Approval is valid for one year from the issue date of January 2004. Participants may submit the self-assessment form at any time during that period.

This program was planned in accordance with the AAPA's CME Standards for Enduring Material Programs and for Commercial Support of Enduring Material Programs.

Nurse Practitioners—This program has been granted 1.0 contact hour of continuing education (which includes 1.0 hour of pharmacology) by the American Academy of Nurse Practitioners. Approval is valid through December 31, 2004.

Disclosure Statements

All editorial board members have received honoraria from the Veritas Institute for Medical Education, Inc. for their involvement in this program.

Dr File is the recipient of research grants from Abbott Laboratories, Bayer, Bristol-Myers Squibb Company, GlaxoSmithKline, and McNeil Consumer & Specialty Pharmaceuticals. He is a consultant for Aventis Pharmaceuticals, Bayer, Bristol-Myers Squibb, GlaxoSmithKline, McNeil, Pfizer Inc, and Wyeth Pharmaceuticals. He is a member of the speakers bureaus of Abbott, GlaxoSmithKline, McNeil, Merck, Pfizer, and Wyeth. Dr Lipsky is a consultant and speakers bureau participant for Aventis and Bayer. Dr Taylor and Mr Deziel have nothing to disclose.

Information presented in this program does not include the unlabeled use(s) of drugs/products.

Provider

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Step 2 involves calculating the pneumonia PSI, which stratifies patients into 5 severity classes. Patients in classes I through III usually do not require hospitalization; those in classes IV and V generally should be hospitalized.

Step 3 involves clinical judgment regarding the patient's overall health and suitability for home care. Mitigating factors for Step 3 include frail physical condition, severe social or psychiatric problems compromising home care (including a history of substance abuse), and an unstable living situation or homelessness. Your clinical judgment should supersede decisions based solely on the PSI.

Initial Empiric Therapy for Suspected Bacterial CAP

Streptococcus pneumoniae is the most common pathogen associated with CAP, accounting for 20% to 60% of cases in North America. Other pathogens include *Haemophilus influenzae* (3% to 10% of cases), *Moraxella catarrhalis* (1% to 2% of cases), and "atypical" pathogens such as *Legionella, Mycoplasma pneumoniae, Chlamydophila pneumoniae* (*Chlamydia pneumoniae*). (File et al 2001) Although ideally the most appropriate antibiotic treatment would be selected after identifying the infecting pathogens, pathogens are often not identified at the time of diagnosis. Therefore, treatment is usually empiric. (Bartlett et al 2000)

The new recommendations for initial empiric therapy for suspected bacterial CAP in immunocompetent adult outpatients and inpatients are shown in Table 1. Rising resistance among *S pneumoniae* has spurred changes in the choice of agents commonly used. For example, penicillin resistance (including intermediately resistant strains) among *S pneumoniae* isolates has risen to approximately 25% to 35% in the United States. (File and Hadley 2002) The new guidelines specify:

- For previously healthy patients who have not recently been on antibiotics and have mild infection that can be safely treated in the outpatient setting, the recommended empiric treatment is a macrolide or doxycycline. Fluoroquinolones (gatifloxacin, gemifloxacin, levofloxacin, and moxifloxacin) are not recommended as first therapy for these patients, but they are appropriate options for outpatients who have comorbid medical conditions or have recently been on a ß-lactam or macrolide antimicrobial.
- Empiric therapy of suspected bacterial superinfection of influenza should provide activity against *S pneumoniae, Staphylococcus aureus,* and *H influenzae* with antibiotics such as amoxicillin-clavulanate, cefpodoxime, cefprozil, cefuroxime, or a fluoroquinolone used for respiratory infections.
- A macrolide plus a ß-lactam (eg, ampicillin/sulbactam or a cephalosporin) or one of the fluoroquinolones cited above may be used as monotherapy for patients with CAP who are admitted to a hospital ward. A ß-lactam plus either an advanced macrolide (eg, azithromycin) or a respiratory fluoroquinolone is recommended for empiric therapy for patients with CAP admitted to an intensive care unit (ICU).
- Telithromycin, which has not yet received FDA approval, may have a role as an alternative to macrolides for treatment of patients with CAP.

Table 1. Initial Empiric Therapy for Suspected Bacterial Community-Acquired Pneumonia (CAP) in Immunocompetent Patients*

Patient variable	Preferred treatment options
Outpatient	
Previously healthy	
No recent antibiotic therapy	A macrolide[a] or doxycycline
Recent antibiotic therapy[b]	A respiratory fluoroquinolone[c] alone, an advanced macrolide[d] plus high-dose amoxicillin,[e] or an advanced macrolide plus high-dose amoxicillin-clavulanate[f]
Comorbidities (COPD, diabetes, renal or congestive heart failure, or malignancy)	
No recent antibiotic therapy	An advanced macrolide[d] or a respiratory fluoroquinolone
Recent antibiotic therapy	A respiratory fluoroquinolone[c] alone or an advanced macrolide plus a β-lactam[g]
Suspected aspiration with infection	Amoxicillin-clavulanate or clindamycin
Influenza with bacterial superinfection	A β-lactam[g] or a respiratory fluoroquinolone
Inpatient	
Medical ward	
No recent antibiotic therapy	A respiratory fluoroquinolone alone or an advanced macrolide plus a β-lactam[h]
Recent antibiotic therapy	An advanced macrolide plus a β-lactam or a respiratory fluoroquinolone alone (regimen selected will depend on nature of recent antibiotic therapy)
ICU	
Pseudomonas infection is not an issue	A β-lactam[g] plus either an advanced macrolide or a respiratory fluoroquinolone
Pseudomonas infection is not an issue but the patient has β-lactam allergy	A respiratory fluoroquinolone, with or without clindamycin
Pseudomonas infection is an issue[i]	Either (1) an antipseudomonal agent[j] plus ciprofloxacin, or (2) an antipseudomonal agent plus an aminoglycoside[k] plus a respiratory fluoroquinolone or a macrolide
Pseudomonas infection is an issue but the patient has β-lactam allergy	Either (1) aztreonam plus levofloxacin,[l] or (2) aztreonam plus moxifloxacin or gatifloxacin, with or without an aminoglycoside
Nursing home	
Receiving treatment in nursing home	A respiratory fluoroquinolone alone or amoxicillin-clavulanate plus an advanced macrolide
Hospitalized	Same as for medical ward and ICU

*Mandell et al. *Clin Infect Dis.* 2003.

NOTE. COPD, chronic obstructive pulmonary disease; ICU, intensive care unit.

a Erythromycin, azithromycin, or clarithromycin.

b That is, the patient was given a course of antibiotic(s) for treatment of any infection within the past 3 months, excluding the current episode of infection. Such treatment is a risk factor for drug-resistant *Streptococcus pneumoniae* and possibly for infection with gram-negative bacilli. Depending on the class of antibiotics recently given, one or other of the suggested options may be selected. Recent use of a fluoroquinolone should dictate selection of a nonfluoroquinolone regimen, and vice versa.

c Moxifloxacin, gatifloxacin, levofloxacin, or gemifloxacin (oral gemifloxacin only, which was approved by the US Food and Drug Administration on 4 April 2003 and which is the only fluoroquinolone approved for multidrug-resistant *S pneumoniae*, not yet marketed).

d Azithromycin or clarithromycin.

e Dosage, 1 g po t.i.d.

f Dosage, 2 g po b.i.d.

g High-dose amoxicillin, high-dose amoxicillin-clavulanate, cefpodoxime, cefprozil, or cefuroxime.

h Cefotaxime, ceftriaxone, ampicillin-sulbactam, or ertapenem; ertapenem was recently approved for such use (in once-daily parenteral treatment), but there is little experience thus far.

i The antipseudomonal agents chosen reflect this concern. Risk factors for *Pseudomonas* infection include severe structural lung disease (eg, bronchiectasis), and recent antibiotic therapy or stay in hospital (especially in the ICU). For patients with CAP in the ICU, coverage for *S pneumoniae* and *Legionella* species must always be ensured. Piperacillin-tazobactam, imipenem, meropenem, and cefepime are excellent β-lactams and are adequate for most *S pneumoniae* and *Haemophilus influenzae* infections. They may be preferred when there is concern for relatively unusual CAP pathogens, such as *Pseudomonas aeruginosa*, *Klebsiella* species, and other gram-negative bacteria.

j Piperacillin, piperacillin-tazobactam, imipenem, meropenem, or cefepime.

k Data suggest that elderly patients receiving aminoglycosides have worse outcomes. (Gleason et al, 1999)

l Dosage for hospitalized patients, 750 mg q.d.

Recommended Laboratory and Agent-Specific Tests

The new guidelines continue to recommend chest radiography as the gold standard for routine evaluation of all patients with suspected pneumonia. (File et al 2001) For hospitalized patients with CAP, laboratory test recommendations still include a complete blood count; testing for serum blood urea nitrogen, glucose, electrolytes, liver function, and oxygen saturation; two pretreatment blood cultures; and an expectorated sputum Gram stain and culture.

Recommendations have changed for tests for the specific agents below:

- *Streptococcus pneumoniae.* The pneumonococcal urinary antigen assay is termed an acceptable augmentation of the standard diagnostic methods: blood culture and sputum Gram stain and culture. The assay can be advantageous in providing rapid results similar to those for a sputum Gram stain.
- *Legionella.* Any patient hospitalized with enigmatic pneumonia should be tested for *Legionella* species, especially if the patient requires ICU admission or fails to respond to a ß-lactam—or if there has been an epidemic of legionnaires' disease.
- *Chlamydophila pneumoniae (Chlamydia pneumoniae).* *C pneumoniae* pulmonary infection may be diagnosed through the demonstration of a 4-fold increase in IgG titer, or single IgM titer of ≥1:16, by means of a microimmunofluorescence serologic test, isolation in tissue culture, or a polymerase chain reaction (PCR) assay of respiratory secretions using reagents of the highest validity.
- Influenza virus. A rapid antigen detection assay is recommended for quick identification of this pathogen for epidemiologic purposes and/or treatment.
- Category A agents of bioterrorism. The recommended tests for inhalation anthrax are blood culture and chest computed tomography (CT) scan; for pneumonic plague, blood culture and Gram stain and culture of sputum samples; for tularemic pneumonia, culture of blood and sputum or pharynx in a biocontainment level 3 laboratory.
- Severe Acute Respiratory Syndrome (SARS). Clinical and epidemiologic features are the recommended diagnostic criteria for SARS. Diagnostic studies for the coronavirus may also be included. For laboratory confirmation, recommended virologic studies are: (1) culture for SARS coronavirus, (2) antibody detection during the acute phase of illness or any time after onset, or (3) detection of SARS coronavirus RNA confirmed by second PCR assay, using a second sample of the specimen or a different set of primers.

Pathogen-Specific Therapy for CAP

When testing has identified specific pathogens in patients with CAP, new treatment recommendations include:

- *S pneumoniae.* Cefotaxime or ceftriaxone are the preferred parenteral agents for treating pneumococcal pneumonia without meningitis for strains with reduced susceptibility to penicillin, but with minimum inhibitory concentrations (MICs) of cefotaxime or ceftriaxone of <2 µg/mL.

  For oral treatment of pneumococcal pneumonia involving susceptible strains, amoxicillin is preferred. If culture data show that the patient has pneumococcal pneumonia with bacteremia without evidence to support infection with a copathogen—and the isolate is penicillin-susceptible—a ß-lactam (penicillin G or amoxicillin) alone may be used. If the isolate is penicillin-resistant, cefotaxime, ceftriaxone, or a respiratory fluoroquinolone or other agent indicated by in vitro testing may be used.
- *Legionella.* Treatment for legionnaires' disease is appropriate when there is epidemiologic evidence of this disease, despite negative diagnostic test results. In hospitalized patients, the preferred treatment is azithromycin or a fluoroquinolone. For patients who do not require hospitalization, acceptable antibiotics include erythromycin, doxycycline, azithromycin, clarithromycin, or a fluoroquinolone.
- Influenza virus. Treatment within 48 hours after symptom onset is effective using amantadine, rimantadine, oseltamivir, or zanamivir in patients with influenza A, and using oseltamivir and zanamivir in patients with influenza B. These drugs are not recommended for uncomplicated influenza with a duration of symptoms of >48 hours, but they may be used to reduce viral shedding in hospitalized patients or patients with influenza pneumonia.
- Herpesviruses. Pneumonia caused by varicella zoster virus or herpes simplex virus should be treated with parenteral acyclovir.
- Other viruses. No antiviral agents have established efficacy for treating adults with pulmonary infections involving parainfluenza virus, respiratory synctial virus, adenovirus, metapneumovirus, the SARS agent, or hantavirus.

Additional Recommendations

The new guidelines specify that antibiotic therapy for hospitalized patients with CAP should be initiated within 4 hours after registration. A new recommendation adds smoking cessation as a goal for hospitalized CAP patients who smoke.

New discharge criteria recommend that during the 24 hours before discharge to the home, the patient should have no more than 1 of the following characteristics (unless this represents the baseline status):

- Temperature >37.8°C
- Pulse >100 beats/min
- Respiratory rate >24 breaths/min
- Systolic blood pressure <90 mm Hg
- Blood oxygen saturation <90%
- Inability to maintain oral intake

New CAP Prevention Guidelines

Vaccination against influenza and pneumococcus infection is the most important method for preventing pneumonia in older adults. Based on a systematic review of numerous randomized trials and cohort studies, the authors of the new CAP guidelines now recommend that:

- Administration of inactivated influenza vaccine for everyone >50 years, and for others at risk for influenza complications. Household contacts of high-risk persons should also receive inactivated influenza vaccine. The injected inactivated vaccine is the preferred formulation for most persons. The intranasally administered live, attenuated vaccine (FluMist™) is an alternative for some persons aged 5 to 49 years who have no chronic underlying diseases.
- Influenza vaccine should be offered to patients as they are being discharged from the hospital, and to outpatients who present for treatment during the fall and winter.

- Annual influenza immunization is recommended for health care workers in inpatient and outpatient settings and long-term care facilities.

Pneumococcal vaccine polyvalent (Pneumovax®) is recommended for persons aged >65 years and for those with selected high-risk concurrent diseases, among others.

Research Update: Early Mobilization of Patients Hospitalized With CAP

Patients hospitalized for acute myocardial infarction, total knee replacement, and many other procedures recover more quickly with early ambulation. To determine if early mobilization has similar benefits for hospitalized adults with community-acquired pneumonia (CAP), researchers at the Division of Infectious Diseases, Washington University School of Medicine (St. Louis) studied 458 patients with CAP who were admitted to general medical units in three Midwestern hospitals.

Patients were randomly assigned to usual care (n=231) or intervention with early mobilization (n=227). The intervention was defined as sitting out of bed or ambulating for at least 20 minutes during the first 24 hours of hospitalization, with progressive mobilization each subsequent day. Both groups were similar in age, gender, disease severity, door-to-drug delivery time, and IV-to-po switchover.

Hospital length of stay was significantly shorter for the early mobilization group (mean 5.8 days vs 6.9 days for the usual care group). The adjusted absolute difference in hospital stay was 1.1 days (95% confidence interval, 0.0 to 2.2 days). The groups showed no differences in adverse events or other secondary outcomes.

The authors conclude that early mobilization of adults with CAP reduces overall hospital length of stay and use of institutional resources, without increasing the risk of adverse outcomes.

Source: Mundy LM, Leet TL, Darst K, Schnitzler MA, Dunagan WC. Early mobilization of patients hospitalized with community-acquired pneumonia. *Chest.* 2003;124:883-889.

Check These Websites

Not sure about the latest evidence-based recommendations on antibiotic use? Need good patient education materials? Two of the best Internet resources on antibiotic use and resistance are:

Centers for Disease Control and Prevention
www.cdc.gov/drugresistance/general/index.htm
This website provides information about the CDC's "Campaign to Prevent Antimicrobial Resistance in Healthcare Settings," and the "Campaign for Appropriate Antibiotic Use in the Community." There is general information for healthcare personnel and patients on preventing the spread of antimicrobial resistance, as well as technical fact sheets, clinical guidelines, practice tips, surveillance data, scientific publications, and links for more in-depth information.

Food and Drug Administration
www.fda.gov/oc/opacom/hottopics/anti_resist.html
The FDA's website offers general background information on antibiotic resistance, recommendations, and strategies, as well as numerous links to information available from other organizations.

Case Study

Is Antibiotic Therapy Appropriate for This Patient?

Case: A 42-year-old woman with no underlying conditions indicated that she had felt achy for 2 weeks. Over the preceding 5 days, she had noted headache, chills, fever, shortness of breath, and nonproductive cough. On examination, her temperature was 38.3°C (100.9°F); blood pressure 144/88 mm Hg; pulse rate 96 beats per minute; and respiratory rate 16 breaths per minute. Pulse oximetry showed arterial oxygen saturation of 95% on room air. Auscultation of the lungs revealed localized rhonchi of the right lower lung field. Her mental status was within normal limits.

What is your suspected diagnosis? Is antibiotic therapy appropriate?

Discussion: This patient had some manifestations that would suggest the presence of pneumonia: the low-grade fever and localized auscultatory findings. A confirmatory chest x-ray film revealed a right lower lobe infiltrate.

As previously noted (p 2), patients with community-acquired pneumonia can be assigned to 1 of 5 risk classes (from low risk, class I, to high risk, class V). This patient has no preexisting conditions that would compromise safety of home care and fits the class I criteria, so she can be safely treated as an outpatient. According to recent guidelines, antimicrobial therapy directed toward pneumococci, *M pneumoniae*, and *C pneumoniae* would be most appropriate. Since this woman was a nonsmoker with no history of exposure to children, *H influenzae* might be less likely. Also, a viral origin is possible. Appropriate antimicrobial therapy would include a macrolide or doxycycline, as there were no risk factors for drug-resistant pneumococcus.

The patient was treated with an oral macrolide as part of an antimicrobial efficacy study. Of interest, her sputum PCR assay was positive for *C pneumoniae*. With antimicrobial therapy, her symptoms resolved.

Source: File TM Jr, Bartlett JG, Bernstein A, Martinez FJ. Management of community-acquired pneumonia: an appropriate-use tool. *Infect Med.* 2001;18:462-472.

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