AMERICAN HEALTH CONSULTANTS®

Rapid Reference Card Enclosed

Inside: Reader Survey, special offer on EMTALA audio conference.

The Practical Journal for Emergency Physicians

Emergency Medicine Reports

Volume 23, Number 9 April 22, 2002

Community-Acquired Pneumonia (CAP) Antibiotic Selection and Management Update

Part I: Evaluation, Risk Stratification, and Current Antimicrobial Treatment Guidelines for Hospital-Based Management of CAP: Outcome-Effective Strategies Based on Year 2002 NCCLS Breakpoints and Recent Clinical Studies

—ASCAP (Antibiotic Selection for Community-Acquired Pneumonia) 2002 Consensus Panel Report

Author: **Gideon Bosker, MD, FACEP**, Assistant Clinical Professor, Section of Emergency Services, Yale University School of Medicine; Associate Clinical Professor, Oregon Health Sciences University, Portland.

Peer Reviewers: **Steven M. Winograd, MD, FACEP**, Attending Physician, Emergency Department, Jeannette District Memorial Hospital, Jeannette, PA, St. Clair Memorial Hospital and University of Pittsburgh Medical Center, Pittsburgh, PA; **James A. Wilde, MD, FAAP**, Assistant Professor, Emergency Medicine and Pediatrics, Research Director, Department of Emergency Medicine, Medical College of Georgia, Augusta.

A common cause for admission to the hospital, community-acquired pneumonia (CAP) is a serious, growing health problem in the United States. It has an incidence estimated at 5.6 million cases annually.[1,2] Approximately 1.7 million hospitalizations for CAP are reported each year at an annual cost of about $23 billion.[1,3] The elderly consume the majority of these expenses, account for the majority of CAP-related hospitalizations, and have longer lengths of stay. Mortality rates among the most seriously affected patients with CAP (the majority of whom are in the geriatric age group) approach 40%, and causative pathogens are identified in fewer than 50% of patients.[4] Accordingly, empiric antibiotic regimens frequently are chosen in hospitalized patients with CAP on the basis of results of clinical trials and expert panel recommendations.

Despite a general consensus that empiric treatment of CAP requires, at the least, mandatory coverage of Streptococcus pneumoniae*,* Haemophilus influenzae*, and* Moraxella catarrhalis*, as well as atypical organisms (*Mycoplasma pneumoniae*,* Chlamydia pneumoniae*, and* Legionella pneumophila*), antibiotic selection strategies for achieving this spectrum of coverage vary widely. To provide physicians and pharmacists current, evidence-supported standards for antimicrobial therapy in CAP, new treatment guidelines have been issued by a number of national panels and/or associations, including the American Thoracic Society Guidelines (2001); Infectious Disease Society of America (IDSA); the ASCAP Panel (Antibiotic Selection for Community-Acquired Pneumonia); and the Centers for Disease Control and Prevention, Drug-Resistant Streptococcus pneumoniae Therapeutic Working Group (CDC-DRSPWG).*

As might be expected, although there are consistencies among expert-endorsed recommendations, there also are variations, with some panels prioritizing one treatment strategy over another. In some cases, panel recommendations lag behind the emergence of new data that would force a reevalua-

EDITOR IN CHIEF
Gideon Bosker, MD, FACEP
Special Clinical Projects and Medical Education Resources
Assistant Clinical Professor
Section of Emergency Services
Yale University School of Medicine
Associate Clinical Professor
Oregon Health Sciences University

EDITORIAL BOARD
Paul S. Auerbach, MD, MS, FACEP
Clinical Professor of Surgery
Division of Emergency Medicine
Department of Surgery
Stanford University School of Medicine
Stanford, California

Brooks F. Bock, MD, FACEP
Dayanandan Professor and Chairman
Department of Emergency Medicine
Detroit Receiving Hospital
Wayne State University
Detroit, Michigan

William J. Brady, MD, FACEP, FAAEM
Vice Chairman of Emergency Medicine and Associate Professor,
Department of Emergency Medicine,
Associate Professor of Internal Medicine and Program Director of Emergency Medicine Residency,
Department of Internal Medicine
University of Virginia School of Medicine
Charlottesville, Virginia

Kenneth H. Butler, DO
Associate Residency Director
University of Maryland Emergency Medicine Residency Program
University of Maryland School of Medicine
Baltimore, Maryland

Michael L. Coates, MD, MS
Professor and Chair
Department of Family and Community Medicine
Wake Forest University School of Medicine
Winston-Salem, North Carolina

Alasdair K.T. Conn, MD
Chief of Emergency Services
Massachusetts General Hospital
Boston, Massachusetts

Charles L. Emerman, MD
Chairman
Department of Emergency Medicine
MetroHealth Medical Center
Cleveland Clinic Foundation
Cleveland, Ohio

Frederic H. Kauffman, MD, FACEP
Associate Professor of Medicine
Temple University School of Medicine
Philadelphia, Pennsylvania

Kurt Kleinschmidt, MD, FACEP
Assistant Professor
University of Texas Southwestern Medical Center, Dallas
Associate Director
Department of Emergency Medicine
Parkland Memorial Hospital
Dallas, Texas

David A. Kramer, MD, FACEP
Program Director,
Associate Professor
Emergency Medicine Residency
York Hospital/Penn State University
York, Pennsylvania

Larry B. Mellick, MD, MS, FAAP, FACEP
Chair and Professor
Department of Emergency Medicine
Section Chief, Pediatric Emergency Medicine
Medical College of Georgia
Augusta, Georgia

Paul E. Pepe, MD, MPH, FACEP, FCCM
Professor and Chairman
Division of Emergency Medicine
University of Texas Southwestern Medical Center
Dallas, Texas

Robert Powers, MD, MPH, FACP, FACEP
Chief and Professor, Emergency Medicine
University of Connecticut
School of Medicine
Farmington, Connecticut

David J. Robinson, MD, MS
Research Director and Assistant Professor
Department of Emergency Medicine
The University of Texas Houston Medical Center,
Director, Diagnostic Observation Center
Memorial Hermann Hospital
Houston, Texas

Steven G. Rothrock, MD, FACEP, FAAP
Associate Professor of Emergency Medicine
University of Florida College of Medicine,
Department of Emergency Medicine
Orlando Regional Medical Center
Orlando, Florida

Barry H. Rumack, MD
Director, Emeritus
Rocky Mountain Poison and Drug Center
Clinical Professor of Pediatrics
University of Colorado
Health Sciences Center
Denver, Colorado

Richard Salluzzo, MD, FACEP
Chief Executive Officer and Chief Medical Officer
Conemaugh Health System
Johnstown, Pennsylvania

Sandra M. Schneider, MD
Professor and Chair
Department of Emergency Medicine
University of Rochester School of Medicine
Rochester, New York

John A. Schriver, MD
Chief, Section of Emergency Medicine
Yale University School of Medicine
New Haven, Connecticut

David Sklar, MD, FACEP
Professor and Chair
Department of Emergency Medicine
University of New Mexico School of Medicine
Albuquerque, New Mexico

Corey M. Slovis, MD, FACP, FACEP
Professor and Chairman
Department of Emergency Medicine
Vanderbilt University School of Medicine,
Medical Director
Metro Nashville EMS
Nashville, Tennessee

J. Stephan Stapczynski, MD
Professor and Chairman
Department of Emergency Medicine
University of Kentucky Medical Center
Lexington, Kentucky

Charles E. Stewart, MD, FACEP
Emergency Physician
Colorado Springs, Colorado

David A. Talan, MD, FACEP
Chairman and Professor of Medicine
UCLA School of Medicine
Department of Emergency Medicine
Olive View/UCLA Medical Center
Los Angeles, California

Gregory A. Volturo, MD, FACEP
Vice Chairman and Professor
Department of Emergency Medicine
University of Massachusetts Medical School
Worcester, Massachusetts

Albert C. Weihl, MD
Program Director
Emergency Medicine Residency
Assistant Professor of Medicine and Surgery
Department of Surgery
Section of Emergency Medicine
Yale University School of Medicine

Steven M. Winograd, MD, FACEP
Attending Physician
Department of Emergency Medicine
Jeannette District Memorial Hospital
Jeannette, Pennsylvania;
St. Clair Memorial Hospital
Pittsburgh, Pennsylvania
University of Pittsburgh Medical Center

Allan B. Wolfson, MD, FACEP, FACP
Program Director,
Affiliated Residency in Emergency Medicine
Professor of Emergency Medicine
University of Pittsburgh
Pittsburgh, Pennsylvania

© 2002 American Health Consultants
All rights reserved

tion of current practices. For example, beginning in January 2002, the National Committee on Clinical Laboratory Standards (NCCLS) officially adopted new breakpoint minimum inhibitory concentrations (MIC) for two third-generation cephalosporins for non-meningeal sources of S. pneumoniae. *Stemming from discrepancies between microbiologic failure and clinical cure, the NCCLS reviewed and accepted revised breakpoint MICs for ceftriaxone and cefotaxime. Based on the new microbiologic standards, a drug-resistant* S. pneumoniae *(DRSP) of non-meningeal sources is defined with a breakpoint MIC of ≥ 4 mcg/mL to cefotaxime or ceftriaxone. Since the only treatment guidelines that recognized the new NCCLS breakpoints for cefotaxime and ceftriaxone are those published by the CDC-DRSPWG, the clinical implications of the revised breakpoints will be widespread as the remaining treatment guidelines reevaluate the role of third-generation cephalosporins for initial therapy of all in-patients with CAP.*

Deciphering the strengths, subtleties, and weaknesses of recommendations issued by different authoritative sources can be problematic and confusing. Because patient disposition practices and treatment pathways vary among institutions and from region to region, management guidelines for CAP in the geriatric patient must be "customized" for the local practice environment. Unfortunately, no single set of guidelines is applicable to every patient or practice environment; therefore, clinical judgment must prevail. This means taking into account local antibiotic resistance patterns, epidemiological and infection incidence data, and patient demographic features.

It also is becoming clear that outcomes in patients with CAP can be maximized by using risk-stratification criteria that predict mortality in various patient subgroups with CAP. Associated clinical findings such as hypotension, tachypnea, impaired oxygen saturation, multi-lobar involvement, elevated blood urea nitrogen (BUN), and altered level of consciousness are predictive of more serious disease, as are age and acquisition of CAP in a nursing home environment. These factors may assist clinicians in initial selection of intravenous antibiotic therapy for hospitalized patients.

Because of important advances, changes, and refinements that have occurred in the area of CAP treatment during the past year, this landmark review presents a comprehensive, state-of-the-art assessment of antimicrobial guidelines for management of the geriatric patient with CAP. Special emphasis has been given to both epidemiological data demonstrating the importance of correct spectrum coverage with specific cephalosporins (ceftriaxone) in combination with a macrolide (azithromycin) or monotherapy with a fluoroquinolone, as well as the selection of initial intravenous antibiotics for in-hospital management of CAP. In addition to antibiotic therapy, comprehensive management of the patient with CAP includes not only supportive respiratory and hemodynamic measures, but also risk-stratifying patients according to the Fine Pneumonia Severity Index (PSI) to evaluate their risk for deep venous thrombosis (DVT) and its associated, life-threatening complications. Accordingly, the ASCAP Consensus Panel has addressed the need to provide prophylaxis against venous thromboembolic disease (VTED) in immobilized patients with pneumonia, congestive heart failure (CHF), and/or respiratory failure.

In addition, a detailed analysis and comparison of two-drug (ceftriaxone plus a macrolide) approaches vs. monotherapeutic options (azithromycin or advanced generation fluoroquinolones [moxifloxacin, levofloxacin, gatifloxacin]) are provided. In this regard, although one national association (2001 American Thoracic Society Guidelines) has proposed the option of intravenous monotherapy with a macrolide for inpatient management of CAP in selected, younger patients without co-morbidity, most experts and national panels agree that hospitalized patients are at sufficiently high risk for CAP-related morbidity, complications, and mortality to require combination therapy that includes a

Emergency Medicine Reports™ (ISSN 0746-2506) is published biweekly by American Health Consultants, 3525 Piedmont Road, N.E., Six Piedmont Center, Suite 400, Atlanta, GA 30305. Telephone: (800) 688-2421 or (404) 262-7436.

Vice President/Group Publisher: Brenda Mooney
Editorial Group Head: Valerie Loner
Specialty Editor: Shelly Morrow
Marketing Manager: Schandale Kornegay
GST Registration No.: R128870672

Periodical postage paid at Atlanta, GA. **POSTMASTER:** Send address changes to ***Emergency Medicine Reports***, P.O. Box 740059, Atlanta, GA 30374.

Copyright © 2002 by American Health Consultants, Atlanta, GA. All rights reserved. Reproduction, distribution, or translation without express written permission is strictly prohibited.

Back issues: $28. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Multiple copy prices: One to nine additional copies, $323 each; 10 to 20 additional copies, $287 each.

Accreditation

Emergency Medicine Reports'™ continuing education materials are sponsored and supervised by American Health Consultants. American Health Consultants designates this continuing education activity for up to 52 hours in Category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

This CME activity was planned and produced in accordance with the ACCME Essentials.

Emergency Medicine Reports™ also is approved by the American College of Emergency Physicians for 52 hours of ACEP Category 1 credit and has been approved for 52 Category 2B credit hours by the American Osteopathic Association. Emergency Medicine Reports has been reviewed by the American Academy of Family Physicians as having educational content acceptable for Prescribed credit hours. This volume has been approved for up to 52 Prescribed credit hours. Term of approval covers issues published within one year from the beginning distribution date of 1/02. Credit may be claimed for one year from the date of this issue.

American Health Consultants (AHC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. Clinical, legal, tax, and other comments are offered for general guidance only; professional counsel should be sought for specific situations.

Subscriber Information

Customer Service: 1-800-688-2421

Customer Service E-Mail: customerservice@ahcpub.com
Editorial E-Mail: shelly.morrow@ahcpub.com

World Wide Web page: http://www.ahcpub.com

Subscription Prices

1 year *with* 52 ACEP/AMA/52 AAFP Category 1/Prescribed credits (52 AOA Category 2B credits): $494
1 year *without* credit: $359
Resident's rate $179

All prices U.S. only.
U.S. possessions and Canada, add $30 plus applicable GST. Other international orders, add $30.

For Customer Service and CME questions,

Please call our customer service department at **(800) 688-2421.** For editorial questions or comments, please contact **Shelly Morrow,** Specialty Editor, at shelly.morrow@ahcpub.com or (404) 262-5514.

THOMSON
AMERICAN HEALTH CONSULTANTS

Statement of Financial Disclosure

In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Drs. Winograd and Wilde (peer reviewers) report no relationships with companies related to the field of study covered by this CME program. Dr. Bosker (author and editor) is on the speaker's bureau for Pfizer, Aventis, Bayer, and Hoffman-La Roche. Dr. Bosker also acknowledges that he receives or has received royalties, honoraria, commissions, and other compensation relating to the sale of textbooks,consultation services, reprints of articles, and other written materials to the following pharmaceutical companies: Pfizer, Genentech, Aventis, Ortho-McNeil, Pharmacia, Hoffman La Roche, and Bayer.

cephalosporin (i.e., ceftriaxone, cefotaxime, etc.) with significant activity against S. pneumoniae*,* H. influenzae*, and* M. catarrhalis*, along with a macrolide to provide activity against atypical organisms. Moreover, one recent study suggests that CAP patient outcomes in those with bacteremic, pneumococcal pneumonia may be improved with two-drug, combination regimens as compared to monotherapeutic approaches using fluoroquinolones or other agents.[5] Detailed discussions of this important controversy and practical, antibiotic selection implications of the year 2002 NCCLS breakpoints are presented to provide evidence-based guidance in the area of empiric drug selection for CAP.*

Finally, to ensure that clinicians are current with and can apply the latest evidence-based strategies for CAP treatment to their patient populations, detailed antibiotic selection guidelines (See Table 1, ASCAP 2002 Consensus Panel Guidelines.) issued by the ASCAP Consensus Panel are provided. Drawing upon consensus panels and association guidelines, these antimicrobial protocols are linked to risk-stratification criteria and specific clinical profiles of patients presenting to the hospital or acute ambulatory setting with CAP.

—The Editor

Introduction: The ASCAP 2002 Consensus Report® Panel and Scientific Roundtable

To address the complex issues surrounding antibiotic selection and care of the hospitalized patient with pneumonia, the ASCAP Year 2002 Consensus Panel and Scientific Roundtable was convened. Its mission statement was to review, analyze, and interpret published, evidence-based trials assessing the safety and efficacy of antibiotic therapy for CAP. In addition, the ASCAP Consensus Panel was charged with developing strategies that would ensure appropriate use of antibiotics in this patient population, and with making recommendations for how patients with respiratory infections should be evaluated and managed in the inpatient setting.

Treatment guidelines generated by the ASCAP 2002 Consensus Panel, and reported in this consensus statement, were based on evidence presented from well-designed clinical trials, and focused on hospital management by the emergency physician, hospitalist, internist, critical care specialist, and/or infectious disease specialist. Detailed review and analyses of national consensus guidelines issued by the ATS, IDSA, CDC-DRSPWG, and the Year 2001 ASCAP Panel also were evaluated and included in the decision-making process. *(See Tables 2 and 3.)*

With these objectives in clear focus, the purpose of this comprehensive review, which includes the ASCAP 2002 Consensus Panel findings on assessment strategies and treatment recommendations, is to provide an evidence-based, state-of-the-art clinical resource outlining, in precise and practical detail, clinical protocols for the acute management of CAP. To achieve this goal, all of the critical aspects entering into the equation for maximizing patient outcomes, while minimizing costs, including systematic patient evaluation, disposition decision trees, and outcome-effective antibiotic therapy, will be discussed in detail. In addition, because appropriate disposition of patients with CAP has become essential for cost-effective patient management, this review includes critical pathways and treatment tables that incorporate risk-stratification tools which can be used to identify and distinguish those patient subgroups that are appropriately managed in the outpatient setting from those more appropriately admitted to the hospital for more intensive care.

Community-Acquired Pneumonia: Epidemiology, Diagnosis, and Evaluation

CAP affects 5.6 million adults annually in the United States, with 1.7 million patients requiring hospitalization.[6] It is the sixth leading cause of death overall and the most common cause of death from infection,[6,7] with an overall case-fatality rate of about 5%. Mortality is substantially greater (about 13.6%) among hospitalized patients.[8] Expert committees have published treatment guidelines intended to improve the care of pneumonia patients, but the guidelines have not been prospectively validated.[9,10] Prior studies of pneumonia guidelines have reported decreased lengths of stay, admission rates, and costs, but no change in clinical outcomes.[11-13] Expert guidelines are difficult to implement, and traditional continuing medical education has little effect on physician practice.[14-19]

The introduction of antibiotic agents dramatically reduced mortality from pneumococcal pneumonia. However, the mortality rate from bacteremic pneumococcal CAP has shown little improvement in the past three decades, remaining between 19% and 28%, depending on the population and institution studied. The aging population, increased prevalence of comorbid illnesses, human immunodeficiency virus, and increasing microbial resistance all probably have contributed to maintaining the high mortality rate despite advances in medical care. However, even allowing that some patients are seen too late to benefit from the antibiotic therapy, the continued high mortality rate, despite apparently appropriate antibiotic therapy, is cause for concern.

The annual incidence of pneumonia in patients older than age 65 is about 1%.[20] The typical presentation of pneumococcal pneumonia with fever, rigors, shortness of breath, chest pain, sputum production, and abnormal lung sounds is easy to recognize. Unfortunately, the changing epidemiology of pneumonia presents a greater diagnostic challenge, especially in the aging patient. Atypical agents or opportunistic infections in immunocompromised individuals have a much more subtle presentation. In particular, pneumonia in older patients frequently has an insidious presentation and fewer characteristic features of pneumonia, which may be confused with CHF or respiratory compromise associated with chronic lung disease.

The definitive, etiologic diagnosis of pneumonia is verified by the recovery of a pathogenic organism(s) from either the blood, sputum, or pleural fluid in the setting of a patient with a radiographic abnormality suggestive of pneumonia. In the case of atypical organisms, the diagnosis usually is made by the comparison of acute and convalescent sera demonstrating a rise in appropriate titers, or by other sophisticated techniques such as direct florescent antibody testing. The Gram's stain occasionally is helpful with establishing the diagnosis, but requires practition-

Table 1. ASCAP 2002 Guidelines — Empiric Antimicrobial Therapy of Choice for Outpatient‡ and In-Hospital Management of Patients with CAP

PATIENT PROFILE/ETIOLOGIC AGENTS	FIRST-LINE ANTIBIOTIC THERAPY†	ALTERNATIVE FIRST-LINE ANTIBIOTIC THERAPY
Otherwise Healthy < 60 years of age (Patients deemed to be suitable for outpatient/oral therapy, i.e., no systemic toxicity, high likelihood of compliance, and supportive home environment)*	Azithromycin PO	Moxifloxacin PO (preferred) *OR* Levofloxacin PO *OR* Clarithromycin *OR* Gatifloxacin PO
Otherwise Healthy > 60 years of age (Patients deemed to be suitable for outpatient/oral therapy, i.e., no systemic toxicity, high likelihood of compliance, and supportive home environment)*	Azithromycin PO	Moxifloxacin PO (preferred) *OR* Levofloxacin PO *OR* Clarithromycin *OR* Gatifloxacin PO
In-Hospital (not in intensive care unit) underlying risk factors or comorbid conditions: In-Hospital management (COPD, history of pneumonia, diabetes, etc.)	Ceftriaxone IV plus azithromycin IV†††	Moxifloxacin *OR* Levofloxacin IV *OR* Gatifloxacin IV
CAP acquired in the nursing home environment (increased likelihood of gram-negative, *E. coli, Klebsiella pneumoniae*)	Ceftriaxone IV plus azithromycin IV	Moxifloxacin *OR* Levofloxacin IV *OR* Gatifloxacin IV
CAP in the elderly individual with chronic alcoholism (Increased likelihood of *Klebsiella pneumoniae* infection)	Ceftriaxone IV plus azithromycin IV	Cefotaxime†† plus erythromycin IV *OR* Levofloxacin IV *OR* Cefepime IV plus azithromycin IV
Severe bacteremic CAP with documented *S. pneumoniae* species showing high-level resistance to macrolides and/or penicillin, but maintaining high sensitivity to extended-spectrum quinolones and cephalosporins	Ceftriaxone IV plus moxifloxacin *OR* Ceftriaxone IV plus levofloxacin IV	Vancomycin¶ plus azithromycin IV
Severe CAP complicated by structural disease of the lung (bronchiectasis): Increased likelihood of *Pseudomonas* and polymicrobial infection	Cefepime IV plus levofloxacin IV plus/minus aminoglycoside *OR* Ciprofloxacin IV plus aminoglycoside IV plus azithromycin IV	Ciprofloxacin IV plus cefepime IV plus azithromycin IV *OR* Imipenem IV plus azithromycin IV plus aminoglycoside
CAP in a patient with suspected aspiration (increases the likelihood of gram-negative and anaerobic infection**)	Ceftriaxone IV plus azithromycin IV plus clindamycin IV	Levofloxacin IV plus clindamycin IV *OR* Levofloxacin IV plus metronidazole IV *OR* Gatifloxacin IV plus clindamycin IV
Severe CAP in a compromised host with a previous hospitalization for, or who resides in, a community or facility with a high reported incidence of methicillin-resistant *S. aureus* (MRSA)***	Moxifloxacin IV plus vancomycin IV *OR* Levofloxacin IV plus vancomycin IV	Gatifloxacin IV plus vancomycin IV
CAP patient with severe pneumonia requiring ICU hospitalization***	Ceftriaxone IV plus levofloxacin IV plus/minus aminoglycoside (*Pseudomonas* strongly suspected) *OR* Ceftriaxone IV plus azithromycin IV plus/minus anti-pseudomonal agent	Cefepime IV plus aminoglycoside IV plus azithromycin IV *OR* Imipenem IV plus aminoglycoside IV plus azithromycin IV

* Oral therapy/outpatient treatment recommendations are appropriate only for those otherwise healthy patients with CAP of mild enough severity that they are judged to be suitable candidates for outpatient management with oral antibiotics.
§ Quinolones generally are restricted for use in patients > 18 years of age.
¶ If *S. pneumoniae* demonstrates complete resistance to extended spectrum quinolones (very rare), third-generation cephalosporins, and macrolides, then vancomycin may be required as part of initial therapy, although this would be necessary only in rare circumstances.
† First-line therapy recommendations take into consideration cost of the drug (which may vary from one institution to another), convenience of dosing, daily dose frequency, spectrum of coverage, side effects, and risk of drug-drug interactions.
†† Cefotaxime IV should be dosed on a q 8 hours basis when used for treatment of CAP.
††† Some institutions may use oral macrolide therapy for patients with mild-to-moderate CAP.
** When anaerobic organisms are suspected as one of the possible etiologic pathogens in a patient with CAP, clindamycin or a β-lactam/β-lactamase inhibitor (ampicillin/sulbactam, ticarcillin/clavulanate, or ticarcillin/tazobacatam) is recommended.
*** High community prevalence of, previous history of hospitalization, or increasing local incidence of methicillin-resistant *S. aureus* (MRSA) in a patient with a clinical presentation consistent with *S. aureus* pneumonia; vancomycin should be considered as component for initial therapy.
‡ Adapted from references 2, 3, 9, 12, 20-31
§§ Cefotaxime may be substituted for ceftriaxone, although ceftriaxone is preferred because of its once-daily dosing.

ers or technicians who are highly skilled in this diagnostic methodology. An adequate Gram's stain must have fewer than 25 epithelial cells per low-powered field. The finding of more than 10 gram-positive, lancet-shaped diplococci in a high-powered field is a sensitive and specific predictor of pneumococcal pneumonia. Unfortunately, the Gram's stain rarely will be helpful in determining other causes of pneumonia. The IDSA Guidelines recommend Gram's stain, whereas the ATS considers Gram's stain optional.

Transtracheal aspiration or bronchial washings are a more accurate means of obtaining specimens for Gram's stain and culture, although this procedure rarely is indicated in the outpatient setting. Overall, fewer than 50% of patients with CAP will be able to produce sputum. Of these, one-half of the sputum specimens obtained will be inadequate. When an adequate Gram's stain is obtained, however, it has a negative predictive value of 80% when compared to a sputum culture. The blood culture is helpful in about 15% of patients, while serology will establish the diagnosis in 25% of patients.[9,20] About 40% of sputum cultures will identify a pathologic organism. Bronchoscopy and thoracentesis occasionally may be necessary, but these procedures generally are reserved for seriously ill patients, particularly those who require management in the intensive care unit (ICU) setting.[3,9,21]

Signs and Symptoms. Especially in the elderly patient, the signs and symptoms of pneumonia may be mimicked by many disorders, including pulmonary embolism (PE), CHF, lung cancer, hypersensitivity pneumonitis, tuberculosis, chronic obstructive pulmonary disease (COPD), granulomatosis disease, and fungal infections. A variety of drugs also can induce pulmonary disease. Cytotoxic agents; non-steroidal anti-inflammatory drugs (NSAIDs); some antibiotics, including sulfonamides; and certain antiarrhythmics (e.g., as amiodarone or tocainide), can mimic pulmonary infection. In addition, common analgesics, including salicylates, propoxyphene, and methadone, also may precipitate acute respiratory symptoms. Such collagen vascular diseases as systemic lupus erythematosus, polymyositis, and polyarteritis nodosa may cause fever, cough, dyspnea, and pulmonary infiltrates, thereby mimicking symptoms of pneumonia. Rheumatoid arthritis can cause an interstitial lung disease, although it does not usually cause fever or alveolar infiltrates.

Initial Stabilization and Adjunctive Measures. Prompt, aggressive, and adequate supportive care must be provided to geriatric patients who present to the hospital with pneumonia. As is the case with other serious conditions, supportive care frequently must be performed in conjunction with the history, physical examination, and diagnostic testing. Among initial stabilization measures, managing the airway and ensuring adequate breathing, oxygenation, ventilation, and perfusion are of paramount importance.

Upon arrival to the hospital, oxygenation status should be assessed immediately using pulse-oximetry. Patients with an arterial oxygen saturation of less than 90% should receive supplemental oxygen, and should be considered candidates for admission, prompt evaluation, and treatment if the diagnosis is confirmed. Arterial blood gases especially are helpful in patients suspected of hypercarbia and respiratory failure. This laboratory modality may be useful in patients with COPD, decreased mental status, and fatigue. Patients with hypoxia who do not respond to supplemental oxygen, as well as those with hypercarbia accompanied by respiratory acidosis, may be candidates for mechanical

Table 2. IDSA — Year 2000 Guidelines. Empirical Selection of Antimicrobial Agents for Treating Patients with CAP

OUTPATIENTS

- Generally preferred are (not in any particular order): doxycycline, a macrolide, or a fluoroquinolone.
- These agents have activity against the most likely pathogens in this setting, which include *Streptococcus pneumoniae, Mycoplasma pneumoniae,* and *Chlamydia pneumoniae.*
- Selection should be influenced by regional antibiotic susceptibility patterns for *S. pneumoniae* and the presence of other risk factors for drug-resistant *S. pneumoniae.*
- Penicillin-resistant pneumococci may be resistant to macrolides and/or doxycycline.
- For older patients or those with underlying disease, a fluoroquinolone may be a preferred choice; some authorities prefer to reserve fluoroquinolones for such patients.

HOSPITALIZED PATIENTS

- General medical ward
- Generally preferred are: an extended spectrum cephalosporin combined with a macrolide or a β-lactam/β-lactamase inhibitor combined with a macrolide or a fluoroquinolone (alone).

INTENSIVE CARE UNIT

- Generally preferred are: an extended spectrum cephalosporin or β-lactam/β-lactamase inhibitor plus either a fluoroquinolone or macrolide.

ALTERNATIVES OR MODIFYING FACTORS

- Structural lung disease: antipseudomonal agents (piperacillin, piperacillin-tazobactam, imipenem, or cefepime) plus a fluoroquinolone (including high-dose ciprofloxacin)
- β-lactam allergy: fluoroquinolone ± clindamycin
- Suspected aspiration: fluoroquinolone with or without clindamycin, metronidazole, or a β-lactam/β-lactamase inhibitor

Note: β-lactam/β-lactamase inhibitor: ampicillin-sulbactam or piperacillin-tazobactam. Extended-spectrum cephalosporin: cefotaxime or ceftriaxone. Fluoroquinolone: gatifloxacin, levofloxacin, moxifloxacin, or other fluoroquinolone with enhanced activity against *S. pneumoniae* (for aspiration pneumonia, some fluoroquinolones show in vitro activity against anaerobic pulmonary pathogens, although there are no clinical studies to verify in vivo). Macrolide: azithromycin, clarithromycin, or erythromycin ± with or without.

Table 3. Recommended Year 2000 CDC DRSP-WG Empiric Regimens for Treating Community-Acquired Pneumonia*

Empiric treatment**	Penicillin MIC mcg/mL ≤ 0.06	0.12-1	2	4	≥ 8	Comments
Outpatients						
Macrolide (erythromycin, clarithromycin, or azithromycin)	+++	+	±	-	-	Covers atypical pathogens (*Mycoplasma* species *Chlamydia* species, and *Legionella* species)
Doxycycline (or tetracycline)	+++	++	+	-	-	Covers atypical pathogens; not FDA-approved for children younger than 8 years
Oral β-lactam (cefuroxime axetil, amoxicillin, or amoxicillin-clavulanate potassium)	+++	++	+	-	-	Does not cover atypical pathogens, alternatively cefpodoxime or cefprozil may be used
Fluoroquinolones (levofloxacin, moxifloxacin, or gatifloxacin)†	+++	+++	+++	++	++	Not first-line treatment because of concerns about emerging resistance; not FDA-approved for use in children; covers atypical pathogens
Hospitalized (Nonintensive Care Unit) Patients						
Parenteral β-lactam (cefuroxime, cefotaxime sodium, ceftriaxone sodium, or ampicillin sodium-sulbactam sodium) plus macrolide (erythromycin, clarithromycin, or azithromycin)	+++	+++	++	±	-	Ceftriaxone and cefotaxime have superior activity against resistant pneumococci in comparison with ampicillin-sulbactam and with cefuroxime.
Fluoroquinolones (e.g., moxifloxacin, levofloxacin, gatifloxacin, or trovafloxacin)†	+++	+++	+++	++	++	See previous comments about fluoroquinolones.
Intubated or Intensive Care Unit Patients‡						
Intravenous β-lactam (ceftriaxone or cefotaxime sodium) plus intravenous macrolide (erythromycin or azithromycin)	+++	+++	++	±	-	Ceftriaxone or cefotaxime are preferred over other β-lactams because of their superior activity against resistant pneumococci; clarithromycin has no intravenous formulation.
Intravenous β-lactam (ceftriaxone or cefotaxime) plus fluoroquinolone (e.g., gatifloxacin, levofloxacin, moxifloxacin, or trovafloxacin)†	+++	+++	++	++	++	Ceftriaxone or cefotaxime are preferred over other β-lactams; see previous comments about fluoroquinolones.
Fluoroquinolones (e.g., moxifloxacin, levofloxacin, gatifloxacin, or trovafloxacin)†	++	++	++	++	++	See previous comments about fluoroquinolones; efficacy of monotherapy for critically ill persons with pneumococcal pneumonia has not been established.

* FDA indicates Food and Drug Administration. Ratings estimate clinical efficacy and in vitro susceptibility among persons with pneumococcal pneumonia. In-depth information on empiric treatment of pneumonia is given by the Infectious Disease Society of America and the American Thoracic Society guidelines.

† The relative antipneumococcal activity of these agents differs slightly, with that of trovafloxacin equal or superior to that of grepafloxacin, which equals that of sparfloxacin, which is superior to that of levofloxacin. Because of new data showing an association with serious liver damage, the FDA issued a public health advisory recommending that trovafloxacin be used only for patients with serious and life- or limb-threatening infections who receive initial treatment in an inpatient health care facility and for whom physicians believe that the benefit of the agent outweighs its potential risk.

‡ Vancomycin hydrochloride may be indicated for the treatment of selected critically ill children with community-acquired pneumonia for whom coverage of drug-resistant *Streptococcus pneumoniae* must be ensured.

** Adaptations made to reflect introduction of new agents since report was published.

ventilation. This patient population also has a poorer prognosis. Support may be accomplished with either intubation and mechanical ventilation or non-invasive ventilation (bilevel positive pressure ventilation [BiPAP]). Recent studies have shown BiPAP to be successful for treatment of patients with respiratory failure due to pneumonia.[10] When this technique is available, it may avert the need for endotracheal intubation and its potential complications. Finally, patients with evidence of bronchospasm on physical exam, as well as those with a history of obstructive airway disease (asthma or COPD), may benefit from inhaled bronchodilator therapy.

Evidence of inadequate perfusion may range from mild dehydration with tachycardia to life-threatening hypotension due to septic shock. Patients with septic shock usually will show evidence of decreased tissue perfusion, such as confusion and oliguria in association with a hyperdynamic circulation. In either case, initial therapy consists of intravenous fluids (normal saline or lactated Ringer's solution) administered through a large bore IV. In elderly patients, fluid overload is a potential complication, and it is prudent to administer IV fluids with frequent assessment of clinical response.

Risk Stratification and Patient Disposition: Outpatient Vs. Inpatient Management

Determining whether to admit or discharge patients suspected of having CAP is one of the most important decisions an emergency physician, pulmonologist, or internist can make. For this reason, there have been increasing efforts to identify patients with CAP who can be treated appropriately as outpatients.[11-13,32] The disposition decision for geriatric patients with pneumonia should take into account the severity of the pneumonia, as well as other medical and psychosocial factors that may affect the treatment plan and clinical outcome.[33-35]

Patient Disposition. In the absence of respiratory distress or other complicating factors, many young adults can be treated adequately with appropriate oral antibiotic therapy. In fact, guidelines issued by the IDSA and ATS support oral antibiotic therapy in patients deemed to be at low risk for complications and/or mortality associated with CAP. This option is utilized less frequently in the case of elderly patients with CAP because comorbid conditions and other risk factors that may complicate the course of the illness frequently are present. Even following appropriate treatment and disposition, patients may have symptoms, including cough, fatigue, dyspnea, sputum production, and chest pain that can last for several months. To address the issue of patient disposition and treatment setting, a variety of investigators have proposed risk-stratification criteria to identify patients requiring hospitalization.

Among the factors most physicians use to make admission decisions for pneumonia are the presence of hypoxemia, overall clinical status, the ability to maintain oral intake, hemodynamic status, and the patient's home environment. Such factors as hypotension, tachypnea, multi-lobar involvement, elevated BUN, and confusion have been linked to inferior outcomes in patients with CAP. Using clinical judgment, however, physicians tend to overestimate the likelihood of death from pneumonia.[33] These findings have led some investigators to employ more stringent prediction rules. For example, a chest radiograph may help identify patients who are at high risk for mortality. The presence of bilateral effusions, moderate-size pleural effusions, multi-lobar involvement, and bilateral infiltrates is associated with poorer outcomes.

A landmark study outlined below presented a prediction rule (Pneumonia Severity Index [PSI]) to identify low-risk patients with CAP.[12] Using such objective criteria as patient age, coexistent medical conditions, and vital signs, patients are assigned either to a low-risk class, which has a mortality rate of about 0.1% in outpatients, or to higher-risk categories. Patients with any risk factors then are evaluated with a second scoring system that assigns individuals to one of three higher-risk categories, which have mortality rates ranging from 0.7% to 31%.[33] In addition to the factors noted in this prediction rule, patients who are immunocompromised as a result of AIDS or chronic alcohol use frequently require hospitalization.

Once the clinician has determined hospitalization is required, the need for ICU admission also must be evaluated. A variety of factors is associated with an increased risk for mortality, including increasing age (> 65 years), alcoholism, chronic lung disease, immunodeficiency, and specific laboratory abnormalities, including azotemia and hypoxemia. These patients may require admission to the ICU.

Prognostic Scoring. There have been many efforts to assess severity and risk of death in patients with pneumonia.[34,36,37] The study by Fine and colleagues has received considerable attention and is used as a benchmark by many clinicians.[33] This study developed a prediction rule, the PSI, to assess 30-day mortality in patients with CAP. The rule was derived and validated with data from more than 52,000 inpatients, and then validated with a second cohort of 2287 inpatients and outpatients as part of the Pneumonia PORT (Pneumonia Patient Outcomes Research Team Cohort) study. Subsequent evaluation and validation has been performed with other cohorts, including geriatric patients and nursing home residents.[38,39]

In this risk-stratification model, patients are assigned to one of five risk classes (1 is lowest risk, 5 is highest risk) based upon a point system that considers age, co-existing disease, abnormal physical findings, and abnormal laboratory findings. Elderly patients cannot be assigned to Class 1, as a requirement is age younger than 50 years. In older patients, age contributes the most points to the overall score. For example, it should be noted that males older than 70 years and females ages older than 80 years would be assigned to Class 3 on the basis of age alone, without any other risk factor. In the Fine study, patients assigned to Classes 1 and 2 were typically younger patients (median age, 35-59 years) and patients in Classes 3-5 were older (median age, 72-75 years).

Outpatient management is recommended for Classes 1 and 2, brief inpatient observation for Class 3, and traditional hospitalization for Classes 4 and 5.[34] For a geriatric patient to qualify for outpatient treatment based on these recommendations, he or she

would have to be younger than age 70 if male or younger than age 80 if female, and have no additional risk factors. Inpatient observation or traditional hospitalization would be recommended for all other patients based on this rule. Other studies have suggested outpatient management for Class 3 patients, but most authorities consider Class 3 patients to be appropriate candidates for hospital admission or for management in an observation unit.[12,40]

As a rule, patients considered eligible for management as outpatients must be able to take oral fluids and antibiotics, comply with outpatient care, and be able to carry out activities of daily living (ADLs) or have adequate home support to assist with ADLs. Other factors cited in previous studies, but not included in the PSI, also have been found to increase the risk of morbidity or mortality from pneumonia. These include: other comorbid illnesses (diabetes mellitus, COPD, post-splenectomy state), altered mental status, suspicion of aspiration, chronic alcohol abuse or malnutrition, and evidence of extrapulmonary disease.[9] Additional laboratory studies that may suggest increased severity of illness include white blood cell count less than 4000 or greater than 30,000; absolute neutrophil count less than 1000; elevated protime or partial thromboplastin time; decreased platelet count; or radiographic evidence of multi-lobar involvement, cavitation, and rapid spreading.[9]

Severe pneumonia may require ICU admission. In the Fine study, 6% of patients in Class 3, 11% of patients in Class 4, and 17% of patients in Class 5 required ICU admission.[33] The ATS guidelines define severe pneumonia as the presence of at least one of the following: respiratory rate greater than 30, severe respiratory failure ($PaO_2/FIO_2 < 250$), mechanical ventilation, bilateral infiltrates or multilobar infiltrates, shock, vasopressor requirement, or oliguria (urine output < 20 cc per hour). The presence of at least one of these is highly sensitive (98%) but only 32% specific for the need for ICU management.[41] It is emphasized that the above guidelines for admission should not supercede clinical judgment when assessing the need to hospitalize patients.[9,33,34,42]

Antibiotic Selection for Hospitalized CAP Patients: An Overview of Current Controversies, Issues, and Guidelines

Introduction. Antibiotic therapy is the mainstay of management for patients with CAP. It should be stated at the outset that antibiotic therapy should be initiated promptly, as soon as the diagnosis strongly is suspected or confirmed, and after appropriate microbiological studies or samples have been obtained. More and more, institutional guidelines are mandating administration of antibiotics within 4-8 hours of patient presentation to the hospital, since mortality rates rise when antibiotic administration is delayed beyond 8 hours.[43] Because the elderly are at high risk for acquiring pneumonia, many of the guidelines issued by consensus panels, clinical experts, and scientific associations, including those of the IDSA, the ATS, ASCAP Consensus Panel, and the CDCDRSP-WG, apply directly to this patient population. Therefore, these recommendations should be studied in detail to arrive at sensible, empiric pharmacotherapeutic interventions for the elderly patient with pneumonia. Although the CDC group makes no specific recommendations for geriatric patients, their guidelines apply to all adult patients; hence, their conclusions are applicable to the geriatric patient with CAP.

Consensus Panels. It should be stressed that there is no absolute or consistent consensus about precisely which drug, or combination of drugs, constitutes the most outcome-effective choice for pneumonia in patients with CAP, although a recent study suggests improved mortality rates with regimens using two-drug combinations rather than monotherapy in patients with bacteremic pneumococcal pneumonia.[5] Most panels and guideline documents agree that antimicrobial coverage must include sufficient activity against the principal bacterial pathogens *S. pneumoniae, H. influenzae,* and *M. catarrhalis,* as well as against the atypical pathogens *Mycoplasma, Legionella,* and *C. pneumoniae.* Therefore, such regimens as ceftriaxone/cefotaxime plus azithromycin, or monotherapy with advanced generation fluoroquinolones—given some qualifications regarding outcomes and resistance issues to be discussed later—have emerged as preferred options for treatment of inpatients with CAP.

Beyond this non-negotiable caveat mandating coverage for the six aforementioned pathogens, there are important differences among recommendations and expert panels for empiric treatment of pneumonia. Variations among the guidelines usually depend upon: 1) their emphasis or focus on the need to empirically cover drug-resistant *Streptococcus pneumoniae* (DRSP) species as part of the initial antimicrobial regimen; 2) their concern about using antimicrobials (fluoroquinolones) with an over-extended (too broad) spectrum of coverage; 3) their concern about the potential of growing resistance to a class (fluoroquinolones) that has agents that currently are active against DRSP species; 4) their preference for monotherapeutic vs. combination therapy; 5) when the guidelines were released (recent vs. several years old); and 6) their emphasis on drug costs (see Table 4), patient convenience, and options for step-down (IV to oral) therapeutic approaches. Clearly, these factors and the relative emphasis placed on each of them will influence antimicrobial selection for the geriatric patient with pneumonia.

With these issues and drug selection factors in mind, the most recent guidelines issued by the CDC-DRSPWG and ATS attempt to both risk-stratify and "drug-stratify" patients according to their eligibility for receiving agents as initial empiric therapy that have activity against DRSP (drug-resistant *S. pneumoniae*). Before presenting a detailed discussion of the current treatment landscape for CAP, the following points from the ASCAP expert's panel should be emphasized. First, the relative importance of *S. pneumoniae* as a cause of outpatient CAP is difficult to determine. Nevertheless, a review of the literature suggests that *S. pneumoniae* accounts for 2-27% of all cases of CAP treated on an outpatient basis.[20,44] In addition, surveillance studies have suggested that about 7% of invasive *S. pneumoniae* species in the United States show a significant degree of penicillin resistance.[45] Hence, this group estimates that only 0.14% (7% of 2%) to 1.9%

Table 4. Daily Drug Cost (WAC)*

DRUG AND DOSAGE	COST/DAY
Azithromycin IV 500 mg	$18.96
Ceftriaxone 1 gm IV qd	36.06
Levofloxacin 500 mg IV qd	33.00
Erythromycin 500 mg IV qid	5.20
Ciprofloxacin 400 mg IV bid	48.00
Cefotaxime 1 g IV tid	25.00
Tricarcillin-clavulanate 3.1 g qid	48.32

* WAC = Wholesale acquisition cost
Hospital formulary pricing guide, August 1999. WAC may not necessarily reflect actual pharmacy costs or costs associated with drug administration cost comparisons.

(7% of 27%) of outpatients with bacterial pneumonia have pneumococcal infections with levels of resistance high enough to warrant consideration of alternative treatment.

This analysis has prompted the CDC panel to conclude that, because CAP in patients who are appropriately triaged and risk-stratified generally is not immediately life-threatening and because *S. pneumoniae* isolates with penicillin MICs of no less than 4 mcg/mL are uncommon, antibiotics with predictable activity against highly penicillin-resistant pneumococci are not necessary as part of the initial regimen. From a practical, drug-selection perspective, the working group, therefore, suggests that oral fluoroquinolones are not first-line treatment in outpatients with CAP because of concerns about emerging resistance. Consequently, oral macrolide or beta-lactam monotherapy is recommended by the CDC-DRSPWG as initial therapy in patients with pneumonia considered to be amenable to outpatient management. Because atypical pathogens are an important cause of outpatient CAP, the ASCAP Consensus Panel recommends macrolides over beta-lactam monotherapy for outpatients.

It should be noted, however, that even for hospitalized (non-ICU) patients, this panel, while noting the effectiveness of monotherapy with selected fluoroquinolones, recommends the combination of a parenteral beta-lactam (ceftriaxone, cefotaxime, etc.) plus a macrolide (azithromycin, erythromycin, etc.) for initial therapy.[2] Regardless of the panel or critical pathway, one of the important consistent changes among recent recommendations for initial, empiric management of patients with CAP is mandatory inclusion of a macrolide (which covers atypical pathogens) when a cephalosporin (which has poor activity against atypical pathogens) is selected as part of the regimen. For critically ill patients, first-line therapy should include an intravenous beta-lactam, such as ceftriaxone or cefotaxime, and an intravenous macrolide, such as azithromycin (please see discussion below).

The committee issued clarifying statements about the role of fluoroquinolone monotherapy in the critically ill patient, stating that caution should be exercised because the efficacy of the new fluoroquinolones as monotherapy for critically ill patients has not been determined.[2]

Clearly, however, fluoroquinolones are an important part of the antimicrobial arsenal in the elderly, and CDC-DRSPWG has issued specific guidelines governing their use in the setting of outpatient and inpatient CAP. In general, this panel has recommended that fluoroquinolones be reserved for selected patients with CAP, and these experts have identified specific patient subgroups that are eligible for initial treatment with extended-spectrum fluoroquinolones. For hospitalized patients, these include adults for whom one of the first-line regimens (e.g., ceftriaxone plus a macrolide) has failed, those who are allergic to the first-line agents, or those who have a documented infection with highly drug-resistant pneumococci (i.e., penicillin MIC = 4 mcg/mL).[2] The rationale for this approach is discussed in subsequent sections.

Emergence of Fluoroquinolone Resistance in *S. pneumoniae*

Ironically, the only treatment guideline that recognizes the potential impact of widespread fluoroquinolone resistance also is the only treatment guideline that recommends that fluoroquinolones be reserved for selected patients with CAP (CDC-DRSPWG). With revised breakpoint MICs for cefotaxime and ceftriaxone, the percentage of resistant *S. pneumoniae* to these third-generation cephalosporins is expected to drop below 3-5% nationally. This will require clinicians to re-examine the published treatment guidelines that recommend fluoroquinolones as initial therapy for CAP.

Moreover, widespread, indiscriminate use of fluoroquinolones may be associated with rising resistance rates to selected gram-positive and gram-negative organisms. Previous assumptions that fluoroquinolones will be more clinically effective vs. DRSP than ceftriaxone or cefotaxime must be reevaluated. Based on the 2002 NCCLS guidelines, both ceftriaxone and cefotaxime are expected to provide comparable microbiologic end points and clinical cures in patients with non-meningeal *Streptococcus pneumoniae* as compared to the anti-pneumococcal fluoroquinolones. The clinician will be asked to incorporate geographic-specific resistance rates and the ecology of micro-organisms into his/her decision about how empirically to treat the patient with CAP.

When first introduced in 1987, ciprofloxacin was promoted for the treatment of respiratory tract infections, including those due to *S. pneumoniae.* Early trials demonstrated clinical success for patients with respiratory infections.[46,47] However, subsequent studies found that the use of ciprofloxacin against *S. pneumoniae* was associated with poor eradication rates both in acute exacerbations of chronic bronchitis (AECB) and pneumonia.[48-50] Reports of the development of resistance soon appeared.[51-55] Knowing the pharmacodynamics parameters of ciprofloxacin and *S. pneumoniae,* this is not unexpected. The AUC24/MIC generally accepted to be most predictive of bacterial eradication and clinical success is greater than 35.[56-59] The C_{max}/MIC ratio generally accepted to be most predictive for prevention of resistance selection is greater than 4.[60,61] Following a 750 mg oral dose of ciprofloxacin, the C_{max} is only 3 mg/L and

the AUC24 is 31 mcg/mL.[62] The MIC_{90} of *S. pneumoniae* is 1 mg/L giving a C_{max}/MIC of 3 and an AUC/MIC of 31.[63]

Although ciprofloxacin was not promoted or widely used for the treatment of CAP, it was used for the treatment of AECB at a dose of 500 mg twice daily. Eradication rates of *S. pneumoniae* in AECB varied from 63% to 90%.[64,65] This failure to eradicate was associated with the development of resistance during therapy in some patients.[64,65] This may, in part, explain the emergence of pneumococci with reduced susceptibility to the fluoroquinolones and, in particular, to ciprofloxacin.

Emergence of resistance in *S. pneumoniae* to the fluoroquinolones has been described in Canada, Spain, Hong Kong, and Northern Ireland. In Canada, Chen et al found that the prevalence of ciprofloxacin-resistant pneumococci (MIC ≥ 4 mcg/mL) increased from 0% in 1993 to 1.7% in 1997-1998 (P = 0.01).[66] In adults, the prevalence increased from 0% in 1993 to 3.7% in 1998. This was associated with an increase in the consumption of fluoroquinolones. Overall, the number of fluoroquinolone prescriptions increased from 0.8 to 5.5 per 100 persons per year between 1988 and 1997.[66] In addition to the increase in prevalence of pneumococci with reduced susceptibility to fluoroquinolones, the degree of resistance also increased. From 1994 to 1998, there was a statistically significant increase in the proportion of isolates with a MIC for ciprofloxacin of greater than or equal to 32 mcg/mL (P = 0.04).

Linares et al found an increase of ciprofloxacin-resistant pneumococci in Spain from 0.9% in 1991-1992 to 3% in 1997-1998.[67] Ho and colleagues documented a marked increase in the overall prevalence of non-susceptibility to the fluoroquinolones when comparing results of surveillance carried out in Hong Kong in 1998 and 2000.[68,69] Over a two-year period, the prevalence of levofloxacin non-susceptibility increased from 5.5% to 13.3% among all isolates and from 9.2% to 28.4% among the penicillin-resistant strains. In Northern Ireland ciprofloxacin resistance was linked to penicillin resistance. Eighteen (42.9%) of 42 penicillin-resistant pneumococci were resistant to ciprofloxacin.[70] Current rates of resistance in the United States are low.[71-74] Doern et al[72] reported ciprofloxacin resistance rates of 1.4%. The Centers for Disease Control and Prevention's Active Bacterial Core Surveillance (ABCs) program carried out during 1995-1999 reported levofloxacin resistance rates of 0.2%.[71] They have not included ciprofloxacin as one of the agents they test.

One study group reviewed 181 *S. pneumoniae* isolated in Hong Kong in 1998. Hong Kong is an area with high rates of resistance, which gives us a picture of what high levels of *S. pneumoniae* resistance can look like.[68] Within three years, the resistance of *S. pneumoniae* to fluoroquinolones has increased from less than 0.5% to ofloxacin, to 5.5% for levofloxacin. Also, 4% of penicillin-resistant isolates also were resistant to trovafloxacin, an agent that was only approved for use in October 1998, demonstrating the cross-resistance to newer quinolones. Resistance to levofloxacin and trovafloxacin was found only in isolates that also were penicillin-resistant.

One abstract detailed changes in *S. pneumoniae* resistance among different drug classes. Unfortunately, although no MICs or breakpoints are given, *S. pneumoniae* resistance grew from 0.1% to 0.6%, a growth rate over the period of about 600%. While *S. pneumoniae* grew in several antibiotic classes and among various agents, including macrolides, trimethoprim-sulfamethoxazole (TMP-SMX), and cefuroxime, the greatest growth in resistance was seen with levofloxacin.[75] In another study evaluating emergent resistance it was found that, compared to cephalosporins and combination therapy, fluoroquinolones were associated with the greatest risk for acquiring emergent resistance during therapy, had the highest treatment failure due to emergent resistance, the largest increase in treatment duration due to resistance, and the largest decrease in clinical response due to emergent resistance.[76]

Clinical Implications. Although treatment failures due to beta-lactams, macrolides, and TMP-SMX resistance in pneumococci have been reported with meningitis and otitis media, the relationship between drug resistance and treatment failures among patients with pneumococcal pneumonia is less clear.[77,78] However, fluoroquinolone resistance in pneumococci causing pneumonia in association with clinical failures, although anecdotal, has been well-described.[48-51,79,80]

Reports of the development of resistance and clinical failures appeared shortly after the introduction of ciprofloxacin in 1987.[51-55] Weiss and colleagues described a nosocomial outbreak of fluoroquinolone-resistant pneumococci.[80] Over the course of a 20-month period, in a hospital respiratory ward where ciprofloxacin often was used as empirical antimicrobial therapy for lower respiratory tract infections, 16 patients with chronic bronchitis developed lower respiratory tract infections caused by a strain of penicillin- and ciprofloxacin-resistant *S. pneumoniae* (serotype 23 F). The MIC of ciprofloxacin for all isolates was greater than or equal to 4 mcg/mL. All five patients with AECB due to the resistant strain who were treated with ciprofloxacin failed therapy. Davidson et al report four cases of pneumococcal pneumonia, treated empirically with oral levofloxacin, that failed therapy.[79] All cases were associated with the isolation of an organism that was either resistant to levofloxacin prior to therapy or that had acquired resistance during therapy. Two of the four patients had been or were on fluoroquinolones prior to initiating levofloxacin.

From these and other studies, a number of risk factors may identify the patients who are likely to be colonized or infected with a fluoroquinolone-resistant pneumococci: patients who are older than age 64, have a history of chronic obstructive lung disease, and/or a prior fluoroquinolone exposure.[66,69,71,74,81] None of the CAP position papers published since the introduction of the fluoroquinolones for the treatment of pneumococcal pneumonia has suggested that a history of previous fluoroquinolone use should be a reason for caution when using one of these antimicrobials.

Year 2002 NCCLS Breakpoints: Evidence-Based Support for Adoption of New Standards

Prior to revising the NCCLS MIC breakpoints for *S. pneumoniae,* the clinical significance of the original S, I, R breakpoints

(originally published in NCCLS document M100-S9) of the parenteral aminothiazolyl cephalosporins ceftriaxone/cefotaxime in systemic non-meningeal pneumococcal infections (N-MPI) was not fully elucidated.

To evaluate clinical outcomes in patients managed with ceftriaxone/cefotaxime, one group, during the period January 1994 through October 2000, studied 522 episodes (in 499 adult patients) of N-MPI (448 of severe pneumonia—clinical and x-ray findings together with positive blood or invasive lower respiratory tract cultures—and 74 of bacteremia from other origins). Of the 522, 74% had serious underlying diseases, 14% nosocomial, and 7% polymicrobial infections.[82] The 30-day mortality rate was 21%. Ceftriaxone/cefotaxime MICs according to NCCLS were determined by microdilution methods and Mueller-Hinton broth with lysed horse blood. The frequency distribution in terms of ceftriaxone/cefotaxime MICs of strains was S less than or equal to 0.5 mcg/mL 413 (79%), I = 1 mcg/mL 79 (15%), R = 2 mcg/mL 30 (6%); no strain with a ceftriaxone/cefotaxime MIC greater than 2 mcg/mL was found.

In ceftriaxone/cefotaxime-resistant strains the most commonly encountered serotypes were 14, 9, 23, and 6. In the 429 episodes of community-acquired pneumococcal infection (polymicrobial and nosocomial cases were excluded), they correlated the ceftriaxone/cefotaxime MICs and antibiotic therapy (prescribed according to the attending physician's criteria) with the 30-day mortality rate. In 185 episodes treated with 1 g/d of ceftriaxone (n = 171) or 1.5-2 g/8 h of cefotaxime (n = 14), the mortality rates for patients with S, I, and R strains were 18% (26/148), 13% (3/24), and 15% (2/13), respectively (P = 0.81). In the 244 patients treated with other antibiotics, the mortality rates for patients with S, I, and R strains were 18% (36/200), 12% (4/33), and 9% (1/11), respectively (P = 0.55).[82]

Hence, patients infected with pneumococci with ceftriaxone/cefotaxime MIC of 1 or 2 mcg/mL categorized as I or R by NCCLS did not show an increased mortality rate compared to S strains in N-MPI when treated with ceftriaxone (1 g/d) or cefotaxime (1.5-2 g/8h). These data support the higher breakpoints for ceftriaxone/cefotaxime by the NCCLS that went into effect in January 2002 for non-meningeal pneumococcal infections. This study demonstrates that parenteral aminothiazolyl cephalosporins such as ceftriaxone (1 g/day) or cefotaxime (1.5-2 g/8 h) work well in adult patients with systemic non-meningeal pneumococcal infections caused by strains with ceftriaxone/cefotaxime MIC up to 1 mcg/mL. Based on their limited experience, they concluded it also is probable that this observation is true for strains with ceftriaxone/cefotaxime MICs of 2 mcg/mL.

Moreover, the available data in children[83] and adults suggest the NCCLS interpretive breakpoints were appropriately modified for systemic non-meningeal pneumococcal infections, and considered susceptible up to a ceftriaxone/cefotaxime MIC of 1 mcg/mL (NCCLS publication M100-S12, which went into effect January 2002). Until further experience with isolates with ceftriaxone/cefotaxime MIC = 2 mcg/mL accumulates, the investigators strongly recommend continued monitoring of the MIC of aminothiazolyl cephalosporins in all invasive pneumococcal isolates, and assessment of clinical and bacteriological outcomes.[83]

Antimicrobial Therapy

With these considerations in focus, the purpose of this antimicrobial treatment section is to review the various recommendations, consensus panel statements, clinical trials, and published guidelines. A rational analysis of this information also will be performed, to generate a set of guidelines and protocols for specific populations as these issues relate to the geriatric patient.

Antibiotic Overview. A brief overview of agents that have been used for treatment of CAP will help set the stage for outcome-effective drug selection. *(See Table 1.)* The first-generation cephalosporins have significant coverage against gram-positive organisms. third-generation cephalosporins have increased coverage against aerobic gram-negative rods.[84] Ceftazidime has coverage against *Pseudomonas*, while cefoperazone has a somewhat higher MIC. Some of the second-generation cephalosporins, such as cefoxitin, cefotetan, and cefmetazole, provide coverage against *Bacteroides* species. Imipenem has broad coverage against aerobic and anaerobic organisms. Aztreonam provides significant coverage for gram-negative bacilli such as *Pseudomonas*.

Among the beta-lactams, the CDC-DRSPWG identifies cefuroxime axetil, cefotaxime sodium, ceftriaxone sodium, or ampicillin-sulbactam as recommended empiric agents. The group notes, however, that among these agents, ceftriaxone and cefotaxime have superior activity against resistant pneumococci when compared with cefuroxime and ampicillin-sulbactam.[2] Because it is recommended that cefotaxime be administered on a q8h basis for treatment of CAP,[2,85] and because the efficacy and safety of once-daily ceftriaxone for inpatient CAP is well-established, ceftriaxone is recommended by most experts and the ASCAP Consensus Panel as the cephalosporin of choice for management of CAP.[85]

The aminoglycosides are active against gram-negative aerobic organisms. These agents generally are used for elderly patients with severe CAP, particularly when *Pseudomonas* infection is suspected. As a rule, the aminoglycosides are combined with a third-generation cephalosporin or an extended spectrum quinolone antibiotic, monobactam, or an extended spectrum penicillin when used in these circumstances.[86]

The tetracyclines are active against *S. pneumoniae, H. influenza, Mycoplasma, Chlamydia,* and *Legionella.* There is, however, a growing incidence of *S. pneumoniae* resistance to tetracyclines.[89] These agents are alternatives to the macrolide antibiotics for empiric therapy for CAP in young, healthy adults.[88] Convenience and coverage advantages of the new macrolides, however, have thrust the tetracyclines into a secondary role for managing CAP. Clindamycin has activity against anaerobes, such as *B. fragilis*.[89,90] Its anaerobic coverage makes it a consideration for the treatment of pneumonia in nursing home patients suspected of aspiration. Metronidazole also has activity against anaerobic bacteria such as

B. fragilis. It is used in combination with other antibiotics for the treatment of lung abscesses, aspiration pneumonia, or anaerobic infections.

Appropriate and Adequate Intensity of Antimicrobial Coverage. Because macrolides and extended spectrum quinolones have indications for monotherapeutic treatment of CAP, they frequently get equal billing as initial choice agents for management of CAP. However, the macrolides and extended spectrum quinolones have clinically significant differences that should be considered in the antibiotic treatment equation for CAP. Accordingly, a careful analysis of the benefits and potential pitfalls of these agents should include a full accounting of the relevant similarities and differences. It will help emergency physicians, hospitalists, infectious disease specialists, and intensivists develop criteria that suggest the appropriateness and suitability that each of these classes may have in specific patient subgroups.

Although the previously cited six organisms (*S. pneumoniae, H. influenzae,* and *M. catarrhalis,* and atypical pathogens *Mycoplasma, Legionella,* and *C. pneumoniae)* are the most commonly implicated pathogens in elderly patients with CAP, this patient population also is susceptible to infection with gram-negative enteric organisms such as *Klebsiella, Escherichia coli,* and *Pseudomonas.* In other cases, the likelihood of infection with DRSP is high. When infection with these pathogens is likely, intensification of empiric coverage should include antibiotics with activity against these gram-negative species.[3,20,21] From a practical, antibiotic selection perspective, this requires that macrolides be used in combination with a cephalosporin such as ceftriaxone as initial, empiric therapy, or alternatively, an advanced generation fluoroquinolone.

Clinical features or risk factors that may suggest the need for intensification and expansion of bacterial and/or atypical pathogen coverage include the following: 1) increasing fragility (> 85 years of age, comorbid conditions, previous infection, etc.) of the patient; 2) acquisition of the pneumonia in a skilled nursing facility; 3) the presence of an aspiration pneumonia, suggesting involvement with gram-negative or anaerobic organisms; 4) chronic alcoholism, increasing the likelihood of infection with *Klebsiella pneumoniae;* 5) pneumococcal pneumonia in an underlying disease-compromised individual who has not been vaccinated with pneumococcal polysaccharide antigen (Pneumovax); 6) history of infection with gram-negative, anaerobic, or resistant species of *S. pneumoniae;* 7) history of treatment failure; 8) previous hospitalizations for pneumonia; 9) patient requires or has had previous ICU hospitalization for pneumonia; 10) acquisition of pneumonia in a community with high and increasing resistance among *S. pneumoniae* species; and 11) immunodeficiency and/or severe underlying disease. Many of the aforementioned risk groups also can be treated with the combination of a third-generation cephalosporin plus a macrolide, in combination with an aminoglycoside when indicated.

As emphasized earlier in this report, most consensus panels, infectious disease experts, textbooks, and peer-reviewed antimicrobial prescribing guides recommend, as the initial or preferred choice, those antibiotics that, within the framework of monotherapy or combination therapy, address current etiologic and mortality trends in CAP. As a general rule, for empiric initial therapy in patients without modifying host factors that predispose to enteric gram-negative or pseudomonal infection, they recommend those antibiotics that provide coverage against the bacterial pathogens *S. pneumoniae, H. influenzae,* and *M. catarrhalis,* as well as against atypical pathogens *Mycoplasma, Legionella,* and *C. pneumoniae*.[36]

Treatment Guidelines for CAP: Outcomes, Value, and Institutional Implementation

Based on a review of the available literature and personal communications among the panel members, the ASCAP Consensus Panel recommends implementation of institution-wide guidelines for patients with CAP. A strong case can be made for adopting such a strategy, especially when educational, process of care, and quality review/improvement measures are put into place.

In one study reviewed,[91] a pneumonia guideline developed at Intermountain Health Care included admission decision support and recommendations for antibiotic timing and selection, based on the 1993 ATS guideline.[91] The study included all immunocompetent patients older than age 65 with CAP from 1993 through 1997 in Utah; nursing home patients were excluded. The investigators compared 30-day mortality rates among patients before and after the guideline was implemented, as well as among patients treated by physicians who did not participate in the guideline program.

Overall, the research group observed 28,661 cases of pneumonia, including 7719 (27%) that resulted in hospital admission. Thirty-day mortality was 13.4% (1037 of 7719) among admitted patients and 6.3% (1801 of 28,661) overall. Mortality rates (both overall and among admitted patients) were similar among patients of physicians affiliated and not affiliated with Intermountain Health Care before the guideline was implemented. For episodes that resulted in hospital admission after guideline implementation, 30-day mortality was 11.0% among patients treated by Intermountain Health Care-affiliated physicians compared with 14.2% for other Utah physicians. The guideline used ceftriaxone without or without a macrolide such as azithromycin or clarithromycin.

An analysis that adjusted by logistic regression for age, sex, rural vs. urban residences, and year confirmed that 30-day mortality was lower among admitted patients who were treated by Intermountain Health Care-affiliated physicians (odds ratio [OR]: 0.69; 95% confidence interval [CI]: 0.49 to 0.97; P = 0.04) and was somewhat lower among all pneumonia patients (OR: 0.81; 95% CI: 0.63 to 1.03; P = 0.08). The investigators concluded that implementation of a pneumonia practice guideline in the Intermountain Health Care system was associated with a reduction in 30-day mortality among elderly patients with pneumonia.

Explanations offered by the investigators for the decreased mortality after guideline implementation include selection of more appropriate antibiotics, timing of initial antibiotic administration, and use of heparin prophylaxis against thromboembolic

disease. For example, one study[92] reported that mortality was about 25% lower among inpatients when the initial, empiric antibiotic regimen combined a third-generation cephalosporin with a macrolide compared with cephalosporins alone, whereas another investigation[41] showed a 15% reduction in mortality when antibiotics were administered within eight hours of hospitalization. The guideline that was evaluated by Intermountain Health Care recommended that antibiotics be administered before a patient with pneumonia leaves the outpatient site of diagnosis. In addition, admission orders included prophylactic heparin.

Another group conducted a comprehensive review of the medical literature to determine whether guideline implementation for CAP reduces mortality and resource costs.[93] These investigators noted that studies have shown significant changes in the processes of care after implementation of guideline recommendations for treatment of patients with CAP.[94-96] The most extensive of these studies consisted of a randomized trial that was conducted in 19 hospitals and which included 1743 patients.[12] This study design provided reasonable internal validity (i.e., it is likely that the differences in the process of care between the nine intervention hospitals and the 10 control hospitals were due to the implementation of the critical pathway). The trial's motivation was a desire to find means of cost-containment, inasmuch as the primary hypothesis was that the critical pathway would reduce the use of institutional resources without compromising the safety and efficacy of therapy.[12]

Two other studies have demonstrated an improvement in outcome after implementation of guidelines: improvement of patient response to antibacterial treatment in one[97] and lower mortality rates in the other.[98] Both studies used an uncontrolled, before-and-after design, but in one of the studies, the changes in the mortality rate in the intervention hospital were compared with data from 23 other hospitals.[98] In both of these studies, the improvement in outcome was accompanied by a reduction in the cost of care. A third study used an uncontrolled, before-and-after design to show that a quality improvement program reduced time to initiation of antibacterial treatment of patients with CAP, which is likely to improve patient outcome. However, there was no direct measurement of outcome. The reviewers conclude that the best-quality evidence about the effects of guideline implementation shows that they can be used to reduce unnecessary use of resources without compromising the quality of care or patient outcomes.[40,97]

Correct Spectrum Coverage: Outcome-Optimizing Regimens for CAP

Because beta-lactams, advanced generation macrolides, and extended-spectrum quinolones constitute the principal oral and intravenous treatment options for CAP, the following sections will discuss indications, clinical trials, side effects, and strategies for their use in CAP. The discussion will focus on antibiotics that: 1) provide, as combination therapy or monotherapy, appropriate coverage of bacterial and atypical organisms causing CAP; 2) are available for both outpatient (oral) and in-hospital (IV) management; and 3) are supported by national consensus panels or association guidelines.

Beta-Lactams: Ceftriaxone for Combination Therapy in CAP. The safety and efficacy of ceftriaxone for managing hospitalized patients with CAP has been well-established in numerous clinical trials, including recent investigations confirming its equal efficacy as compared to new generation fluoroquinolones. In this regard, one recent study attempted to determine the comparative efficacy and total resource costs of sequential IV to oral gatifloxacin therapy vs. IV ceftriaxone with or without IV erythromycin to oral clarithromycin therapy for treatment of CAP patients requiring hospitalization.[99]

Two hundred eighty-three patients were enrolled in a randomized, double-blind, clinical trial; data collected included patient demographics, clinical and microbiological outcomes, length of stay (LOS), and antibiotic-related LOS (LOSAR). Overall, 203 patients were clinically and economically evaluable (98 receiving gatifloxacin and 105 receiving ceftriaxone). It should be noted that IV erythromycin was administered to only 35 patients in the ceftriaxone-treated group, thereby putting a significant percentage (about 62%) of the ceftriaxone cohort at a "spectrum of coverage" disadvantage because of the failure to include an agent with coverage against atypical organisms. Despite this, oral conversion was achieved in 98% of patients in each group, and the investigators concluded that clinical cure and microbiological eradication rates did not differ statistically between ceftriaxone (92% and 92%) and gatifloxacin (98% and 97%).[99]

Given the concern about DRSP in hospitalized CAP patients, there has been robust debate about the effectiveness of ceftriaxone in pulmonary infections caused by DRSP. Attempting to shed light on this issue, an important study evaluating actual clinical outcomes in patients treated with beta-lactams for systemic infection outside of the central nervous system (CNS) which was caused by isolates of *S. pneumoniae* considered nonsusceptible to ceftriaxone (MIC ≥ 1.0 mcg/mL) by pre-2002 NCCLS breakpoints recently has been published by the Pediatric Infectious Diseases Section, Baylor College of Medicine.[100]

The objective of the study was to determine the actual clinical outcomes of patients treated primarily with beta-lactam antibiotics for a systemic infection outside of the CNS caused by isolates of *S. pneumoniae* nonsusceptible to ceftriaxone (MIC ≥ 1.0 mcg/mL). A retrospective review was performed of the medical records of children identified prospectively with invasive infections outside of the CNS caused by isolates of *S. pneumoniae* that were not susceptible to ceftriaxone between September 1993 and August 1999. A subset of this group treated primarily with beta-lactam antibiotics was analyzed for outcome. Among 2100 patients with invasive infections outside the CNS that were caused by *S. pneumoniae,* 166 had isolates not susceptible to ceftriaxone.

One hundred patients treated primarily with beta-lactam antibiotics were identified. From this group, 71 and 14 children had bacteremia alone or with pneumonia, respectively, caused by strains with an MIC of 1.0 mcg/mL. Bacteremia or pneumonia caused by isolates with a ceftriaxone MIC ≥ 2.0 mcg/mL occurred in six and five children, respectively. Three children with septic arthritis and one with cellulitis had infections caused

by strains with a MIC to ceftriaxone of 1.0 mcg/mL. Most were treated with parenteral ceftriaxone, cefotaxime, or cefuroxime for one or more doses followed by an oral antibiotic. All but one child were successfully treated. The failure occurred in a child with severe combined immune deficiency and bacteremia (MIC = 1.0 mcg/mL) who remained febrile after a single dose of ceftriaxone followed by 12 days of cefprozil. The investigators concluded that ceftriaxone, cefotaxime, or cefuroxime are adequate to treat invasive infections outside the CNS caused by pneumococcal isolates with MICs up to 2.0 mcg/mL. Accordingly, the NCCLS breakpoints, as of January 2002, for the beta-lactam ceftriaxone and cefotaxime were modified and up-calibrated so that currently about 95-98% of all *S. pneumoniae* species are considered sensitive to ceftriaxone, as well as cefotaxime.[10]

Observational Trends from The ARM Database: Ceftriaxone Vs. Cefotaxime for *Streptococcus pneumoniae*

The Antimicrobial Resistance Management (ARM) program was established to help individual institutions define their antimicrobial resistance problems and establish cause-effect relationships that could lead to strategic interventions. To date, the ARM program has entered more than 100 community and teaching hospitals into a web-centered database. This observational database currently has susceptability data on up to 19 different organisms and up to 46 different antibiotics. As of January 2002, the ARM program had collected data on more than 10 million total isolates, and sensitivity data on more than 60,000 separate isolates of *S. pneumoniae*.[101]

Evaluation of national *S. pneumoniae* sensitivity data for ceftriaxone and cefotaxime revealed differences between the third-generation cephalosporins. Using the pre-2002 NCCLS breakpoint MICs for ceftriaxone and cefotaxime, the ARM database demonstrated *S. pneumoniae* sensitivities to ceftriaxone and cefotaxime of 80.4% and 69.2%, respectively. Since the 2002 NCCLS breakpoint MICs were adjusted equally for ceftriaxone and cefotaxime, the observed sensitivity differences are not expected to change once the new breakpoints are superimposed from the new data.

The sensitivity differences between ceftriaxone and cefotaxime observed nationally also were seen in select geographic sections of the country. Discrepancies in *S. pneumoniae* sensitivities between ceftriaxone and cefotaxime were demonstrated in the Southeast region of the United States. However, the Northeast cohort of the ARM database showed no differences in sensitivity percentages between ceftriaxone and cefotaxime.[101]

Since the ARM program originally was designed as an observational database to use antibiogram trending to identify resistance patterns for individual hospitals, it is not capable of isolating the specific reason why national sensitivity differences exist between ceftriaxone and cefotaxime. Additionally, for similar reasons, the ARM program is not designed to identify why certain geographic sections of the United States demonstrate the discrepancies in sensitivities and others do not. However, subanalysis of the data suggests that the discrepancy between the third-generation cephalosporins did not exist through the whole database. The difference in sensitivity percentages appeared to emerge during the last half of the 1990-2000 decade. This coincides with the push to use cefotaxime on a twice-a-day basis vs. a more traditional three-times-daily dosing regimen.[101]

Since cefotaxime exerts its antimicrobial activity as a function of its time above the MIC of *S. pneumoniae,* a drop in dosing frequency from TID to BID will increase the percentage of time that the organism is exposed to subinhibitory concentrations.[102] Without any significant post-antibiotic effect, the sensitivities of cefotaxime to *S. pneumoniae* may fall. Further and more specific MIC analysis is required to determine if the reduced dosing frequency is related causally to the emergence of a sensitivity discrepancy between cefotaxime and ceftriaxone.

Advanced Generation Macrolides. The established new generation macrolide antibiotics include the erythromycin analogues azithromycin and clarithromycin.[103,104] Compared to erythromycin, which is the least expensive macrolide, the major advantages of these newer antibiotics are significantly decreased gastrointestinal side effects, which produce enhanced tolerance, improved bioavailability, higher tissue levels, and pharmacokinetic features that permit less frequent dosing and better compliance, as well as enhanced activity against *H. influenzae*.[105,106] In particular, the long tissue half-life of azithromycin allows this antibiotic to be prescribed for a shorter duration (5 days) than comparable antibiotics given for the same indications. Given the cost differences between azithromycin and clarithromycin, as well as the improved compliance patterns associated with short-duration therapy, any rational approach to distinguishing between these agents must consider prescription, patient, and drug resistance barriers.

From the outset, it is fair to say that these macrolides—especially azithromycin—to a great degree, have supplanted the use of erythromycin in community-acquired infections of the lower respiratory tract.

From the perspective of providing definitive, cost-effective, and compliance-promoting therapy, the newer macrolide antibiotics, which include intravenous azithromycin for hospital-based management, recently have emerged as some of the drugs of choice—along with the new, extended spectrum quinolones—for outpatient management of CAP.[107] When used as oral agents, they play a central role in management of pneumonia in otherwise healthy elderly individuals who do not require hospitalization.

From an emergency medicine and in-hospital management perspective, the value and desirability of macrolide therapy has been enhanced significantly by availability of the intravenous formulation of azithromycin, which has been approved for hospitalized patients with CAP. Unlike penicillins, cephalosporins, and sulfa-based agents, azithromycin has the advantage of showing in vitro activity against both atypical and bacterial offenders implicated in CAP.[25,26]

The macrolides also have the advantage of a simplified dosing schedule, especially azithromycin, which is given once daily for only five days (500 mg po on day 1 and 250 mg po qd on days 2-5). Clarithromycin requires a longer course of therapy and is

more expensive. Clarithromycin costs approximately $68-72 for a complete, 10-day course of therapy vs. $42-44 for a complete course of therapy with azithromycin.

Clarithromycin, however, is another alternative among macrolides for outpatient treatment of CAP. It is now available in once-daily formulation (1000 mg/d for 10 days) for oral use, but an intravenous preparation currently is not available. In general, the decision to use a macrolide such as azithromycin rather than erythromycin is based on weighing the increased cost of a course of therapy with azithromycin against its real-world advantages, which include a more convenient dosing schedule; its broader spectrum of coverage; its favorable drug interaction profile; and its decreased incidence of gastrointestinal side effects, which occur in 3-5% of patients taking a five-day, multiple-dose regimen.[108] The introduction of a tablet formulation permits consumption of the antibiotic without regard to food ingestion.

Azithromycin-Coagent (i.e., with Ceftriaxone) for Combination Therapy in Hospitalized CAP. Intravenous azithromycin can be used for the management of hospitalized patients with moderate or severe CAP.[27,28,109] Currently, azithromycin is the only advanced generation macrolide indicated for parenteral therapy in hospitalized patients with CAP due to *C. pneumoniae, H. influenzae, L. pneumophila, M. catarrhalis, M. pneumoniae, S. pneumoniae,* or *Staphylococcus aureus*.[25,26,109,110] This coverage would be considered correct spectrum coverage for empiric therapy of CAP in most patients. However, for hospitalized patients, who tend to have co-morbid conditions, including underlying cardiorespiratory disease, the addition of a beta-lactam (ceftriaxone/cefotaxime) is considered mandatory by the ASCAP Consensus Panel.

Azithromycin dosing and administration schedules for hospitalized patients are different than for the five-day course used exclusively for outpatient management, and these differences should be noted. When this advanced generation macrolide is used for hospitalized patients with CAP, 2-5 days of therapy with azithromycin IV (500 mg once daily) followed by oral azithromycin (500 mg once daily to complete a total of 7-10 days of therapy) is clinically and bacteriologically effective. For patients requiring hospitalization, the initial 500 mg intravenous dose of azithromycin should be given in the ED.

Like the oral formulation, IV azithromycin appears to be well-tolerated, with a low incidence of gastrointestinal adverse events (4.3% diarrhea, 3.9% nausea, 2.7% abdominal pain, 1.4% vomiting), minimal injection-site reactions (less than 12% combined injection-site pain and/or inflammation or infection), and a low incidence of discontinuation (1.2% discontinuation of IV therapy) due to drug-related adverse patient events or laboratory abnormalities.[111]

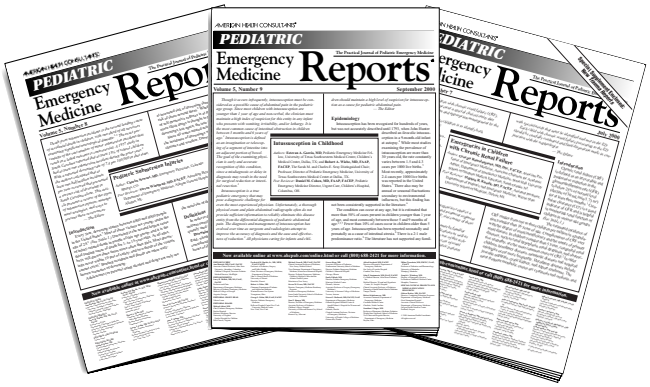
— Acknowledgement: The ASCAP 2002 Panel Members sincerely thank Dr. Donald Low, Mount Sinai Hospital and Toronto Medical Laboratories, Department of Microbiology, for his analysis, research, and contributions to the sections on emerging fluoroquinolone resistance and its clinical implications.

References

1. Sue DY. Community-acquired pneumonia in adults. *West J Med* 1994;161: 383-389.
2. Heffelfinger JD, Dowell SF, et al. A report from the Drug-resistant *Streptococcus pneumoniae* Therapeutic Working Group. Management of community-acquired pneumonia in the era of pneumococcal resistance. *Arch Int Med* 2000;160:1399.
3. Bartlett JG, Mundy M. Community-acquired pneuominia. *N Engl J Med* 1995;333:1618-1624.
4. Fine MD, Smith MA, et al. Prognosis and outcomes of patients with community acquired pneumonia. A meta-analysis. *JAMA* 1996;275:134-141.
5. Waterer GW, Somes GW, Wunderink RG. Monotherapy may be suboptimal for severe bacteremic pneumococcal pneumonia. *Arch Intern Med* 2001;161: 1837-1842.
6. Niederman MS, McCombs JS, Unger AN, et al. The cost of treating community-acquired pneumonia. *Clin Therapeut* 1998;20:820-837.
7. Medicare and Medicaid statistical supplement, 1995. *Health Care Financ Rev* 1995:16.
8. Fine MJ, Smith MA, Carson CA, et al. Prognosis and outcomes of patients with community-acquired pneumonia. *JAMA* 1995;274: 134-141.
9. American Thoracic Society: Guidelines for the Initial Management of Adults with Community-Acquired Pneumonia: Diagnosis, assessment of severity, and initial antimicrobial therapy. *Am Rev Respir Dis* 1993;148:1418-1426.
10. Confalonieri M, Potena A, Carbone G, et al. Acute respiratory failure in patients with severe community-acquired pneumonia. A prospective randomized evaluation of noninvasive ventilation. *Am J Respir Crit Care Med* 1999;160:1585-1591.
11. Hoe LK, Keang LT. Hospitalized low-risk community-acquired pneumonia: Outcome and potential for cost-savings. *Respirology* 1999;4:307-309.
12. Marrie TJ, Lau CY, Wheeler SL, et al. A controlled trial of a critical pathway for treatment of community-acquired pneumonia. *JAMA* 2000;283:749-755.
13. Dean NC, Suchyta MR, Bateman KA. Implementation of admission decision support for community-acquired pneumonia. A pilot study. *Chest* 2000; 117:1368-1377.
14. Davis DA, Thomason MA, Oxman AD, et al. Evidence for the effectiveness of CME. A review of 50 randomized controlled trials. *JAMA* 1992;268:111-1117.
15. Lomas J, Anderson GM, Domnick-Pierre KD, et al. Do practice guidelines guide practice? The effect of a consensus statement on the practice of physicians. *N Engl J Med* 1989;321:1306-1311.
16. Gleicher N. Cesarean section rates in the United States: The short-term failure of the national consensus development conference in 1980. *JAMA* 1984; 252:3273-3276.
17. Greco PJ, Eisenberg JM. Changing physician's practices. *N Engl J Med* 1993;329:1271-1273.
18. Mittman BS, Tonesk X, Jacobson PD. Implementing clinical practice guidelines. *Qual Rev Bull* 1992;18:413-422.
19. Tunis SR, Hayward RSA, Wilson MC, et al. Internists' attitudes about clinical practice guidelines. *Ann Intern Med* 1994;120:956-963.
20. Marrie TJ. Community-acquired pneumonia: Epidemiology, etiology, treatment. *Infect Dis Clinic North Am* 1998;12:723-740.
21. Bates JH, Campbell AL, et al. Microbial etiology of acute pneumonia in hospitalized patients. *Chest* 1992;101:1005-1012.
22. Fang GD, Fine M, Orloff, et al. New and emerging etiologies for community-acquired pneumonia with implications for therapy-prospective multicenter study of 359 cases. *Medicine* 1990;69:307-316.
23. Antibiotic Update 1998: Outcome-effective treatment for bacterial infections managed in the primary care and emergency department setting. *Emerg Med Rep* 1997;18:1-24.

24. Fang GD, Fine M, Orloff J, et al. New and emerging etiologies for community-acquired pneumonia with implications for therapy. *Medicine* 1990;69: 307-316.
25. Plouffe J, Schwartz DB, Kolokathis A, et al. Clinical efficacy of intravenous followed by oral azithromycin monotherapy in hospitalized patients with community-acquired pneumonia. *Antimicrob Agents Chemother* 2000;44: 1796-1802.
26. Vergis EN, Indorf A, et al. Azithromycin vs cefuroxime plus erythromycin for empirical treatment of community-acquired pneumonia in hospitalized patients. A prospective, randomized, multicenter trial. *Arch Int Med* 2000; 160:1294-1300.
27. The choice of antibacterial drugs. *Med Lett Drugs Ther* 1996;38:25-34.
28. Clarithromycin and azithromycin. *Med Lett Drugs Ther* 1992;34:45-47.
29. File TM, Dunbar L, et al. A multicenter, randomized study comparing the efficacy and safety of intravenous and/or oral levofloxacin versus ceftriaxone and/or cefuroxime in treatment of adults with community-acquired pneumonia. *Antimicrob Agents Chemother* 1997;41:1965-1972.
30. American Thoracic Society, Medical Section of the American Lung Association. *Am Rev Respir Dis* 1993;148:1418-1426.
31. American Thoracic Society. Guidelines for the initial management of adults with community-acquired pneumonia: Diagnosis, assessment of severity, and initial antimicrobial therapy. *Am Rev Respir Dis* 1993;148:1418-1426.
32. Flanders WD, Tucker G, Krishnadasan A, et al. Validation of the pneumonia severity index: Importance of study-specific recalibration. *J Gen Intern Med* 1999;14:333-340.
33. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997;336: 243-250.
34. Auble TE, Yealy DM, Fine MJ. Assessing prognosis and selecting an initial site of care for adults with community-acquired pneumonia. *Infect Dis Clin North Am* 1998;2:741-759.
35. Dean NC. Use of prognostic scoring and outcome assessment tools in the admission decision for community-acquired pneumonia. *Clin Chest Med* 1999;20:521-529.
36. Farr BM, Sloman AJ, Fisch MJ. Predicting death in patients hospitalized for community-acquired pneumonia. *Ann Intern Med* 1991;115:428-436.
37. Conte HA, Chen YT, Mehal W, et al. A prognostic rule for elderly patients admitted with community-acquired pneumonia. *Am J Med* 1999;106:20-28.
38. Ewig S, Kleinfeld T, Bauer T, et al. Comparative validation of prognostic rules for community-acquired pneumonia in an elderly population. *Eur Respir J* 1999;14:370-375.
39. Mylotte JM, Naughton B, Saludades C, et al. Validation and application of the pneumonia prognosis index to nursing home residents with pneumonia. *JAGS* 1998;46:1538-1544.
40. Atlas SJ, Benzer TI, Borowsky LH, et al. Safely increasing the proportion of patients with community-acquired pneumonia treated as outpatients. An interventional trial. *Arch Intern Med* 1998;158:1350-1356.
41. Ewig S, Ruiz M, Mensa J, et al. Severe community-acquired pneumonia. Assessment of severity criteria. *Am J Respir Crit Care Med* 1998;158: 1102-1108.
42. Marston BJ, Plouffe JF, et al. Incidence of community-acquired pneumonia requiring hospitalization. Results of a population-based active surveillance study in Ohio. The Community-Based Pneumonia Incidence Study Group. *Arch Int Med* 1997;157:1709-1718.
43. Meehan, TP, et al. Quality of care, process, and outcomes in elderly patients with pneumonia *JAMA* 1997;278:2080-2084.
44. Brentsson E, Lagergard T. Etiology of community-acquired pneumonia in outpatients. *Eur J Clin Microbiol* 1986;5:446-447.
45. Whitney CG, Barrett N, et al. Increasing prevalence of drug-resistant *Streptococcus pneumoniae* (DRSP): Implications for therapy for pneumonia. In: Programs and Abstracts of the 36th Annual Meeting of the Infectious Disease Society of America, Nov. 12-15, 1998. IDSA, Abstract 51.
46. Ball AP. Overview of clinical experience with ciprofloxacin. *Eur J Clin Microbiol* 1986;5:214-219.
47. Fass RJ. Efficacy and safety of oral ciprofloxacin in the treatment of serious respiratory infections. *Am J Med* 1986;82:202-207.
48. Davies BI, Maesen FP, Baur C. Ciprofloxacin in the treatment of acute exacerbations of chronic bronchitis. *Eur J Clin Microbiol* 1986;5:226-231.
49. Hoogkamp-Korstanje JA, Klein SJ. Ciprofloxacin in acute exacerbations of chronic bronchitis. *J Antimicrob Chemother* 1986;18: 407-413.
50. Maesen FP, Davies BI, Geraedts WH, et al. The use of quinolones in respira-

Pediatric Emergency Medicine Reports — Helping You Care for Your Youngest Patients



Nothing challenges your training and skill like caring for a sick child. Retaining those skills requires special preparation, and that's why you need a subscription to *Pediatric Emergency Medicine Reports*. Each 8- to12-page issue provides evidence-based clinical information and offers an in-depth look at a single topic.

With a paid subscription to *Pediatric Emergency Medicine Reports*, you'll benefit from all this:

Each issue is rigorously peer reviewed;

FREE—up to 30 AMA or ACEP Category 1 CME or other specialty society credit hours;

Bimonthly *Trauma Reports* supplement—earn an additional 15 CME credit hours.

FREE—sturdy binder.

Pediatrics: Updates In Emergency Medicine, Vol. 6, (a $159 value). Earn up to 16 CME credit hours with this book, FREE!

Delivery every 30 days (12 issues/year), for only $319

ORDER NOW.
Please call 1-800-688-2421 or 1-404-262-5476 (code 71210)
Visit our Web site at www.ahcpub.com

tory tract infections. *Drugs* 1987;34(Suppl 1):74-79.
51. Thys JP. Quinolones in the treatment of bronchopulmonary infections. *Rev Infect Dis* 1988;10(Suppl 1):S212-S217.
52. Cooper B, Lawlor M. Pneumococcal bacteremia during ciprofloxacin therapy for pneumococcal pneumonia [see comments]. *Am J Med* 1989;87:475.
53. Gordon JJ, Kauffman CA. Superinfection with *Streptococcus pneumoniae* during therapy with ciprofloxacin. *Am J Med* 1990; 89:383-384.
54. Lee BL, Kimbrough RC, Jones SR, et al. Infectious complications with respiratory pathogens despite ciprofloxacin therapy. *N Engl J Med* 1991;325: 520-521.
55. Perez-Trallero E, Garcia-Arenzana JM, Jimenez JA, et al. Therapeutic failure and selection of resistance to quinolones in a case of pneumococcal pneumonia treated with ciprofloxacin. *Eur J Clin Microbiol Infect Dis* 1990;9:905-906.
56. Ambrose PG, Grasela DM, Grasela TH, et al. Pharmacodynamics of fluoroquinolones against *Streptococcus pneumoniae* in patients with community-acquired respiratory tract infections. *Antimicrob Agents Chemother* 2001;45: 2793-2797.
57. Craig WA. Pharmacokinetic/pharmacodynamic parameters: Rationale for antibacterial dosing of mice and men. *Clin Inf Dis* 1998; 26:1-12.
58. MacGowan A, Rogers C, Bowker. K. The use of in vitro pharmacodynamic models of infection to optimize fluoroquinolone dosing regimens. *J Antimicrob Chemother* 2000;46:163-170.
59. Wright DH, Brown GH, Peterson ML, et al. Application of fluoroquinolone pharmacodynamics. *J Antimicrob Chemother* 2000;46: 669-683.
60. Madaras-Kelly KJ, Demasters TA. In vitro characterization of fluoroquinolone concentration/MIC antimicrobial activity and resistance while simulating clinical pharmacokinetics of levofloxacin, ofloxacin, or ciprofloxacin against *Streptococcus pneumoniae. Diagn Microbiol Infect Dis* 2000;37:253-260.
61. Thorburn CE, Edwards DI. The effect of pharmacokinetics on the bactericidal activity of ciprofloxacin and sparfloxacin against *Streptococcus pneumoniae* and the emergence of resistance. *J Antimicrob Chemother* 2001;48:15-22.
62. Gonzalez MA, Uribe F, Moisen SD, et al. Multiple-dose pharmacokinetics and safety of ciprofloxacin in normal volunteers. *Antimicrob Agents Chemother* 1984;26:741-744.
63. Mazzulli TA, Simor E, Jaeger R, et al. Comparative in vitro activities of several new fluoroquinolones and β-lactam antimicrobial agents against community isolates of *Streptococcus pneumoniae. Antimicrob Agents Chemother* 1990;34:467-469.
64. Anzueto A, Niederman MS, Tillotson GS. Etiology, susceptibility, and treatment of acute bacterial exacerbations of complicated chronic bronchitis in the primary care setting: Ciprofloxacin 750 mg b.i.d. versus clarithromycin 500 mg b.i.d. Bronchitis Study Group. *Clin Ther* 1998;20:885-900.
65. Chodosh S, Schreurs A, Siami G, et al. Efficacy of oral ciprofloxacin vs. clarithromycin for treatment of acute bacterial exacerbations of chronic bronchitis. The Bronchitis Study Group. *Clin Infect Dis* 1998;27:730-738.
66. Chen D, McGeer A, de Azavedo JC, et al and The Canadian Bacterial Surveillance Network. Decreased susceptibility of *Streptococcus pneumoniae* to fluoroquinolones in Canada. *N Engl J Med* 1999;341:233-239.
67. Linares J, De La Campa AG, Pallares R. Fluoroquinolone resistance in *Streptococcus pneumoniae* [letter]. *N Engl J Med* 1999;341:1546-1547.
68. Ho PL, Que TL, Tsang DN, et al. Emergence of fluoroquinolone resistance among multiply resistant strains of *Streptococcus pneumoniae* in Hong Kong. *Antimicrob Agents Chemother* 1999;43: 1310-1313.
69. Ho PL, Yung RW, Tsang DN, et al. Increasing resistance of Streptococcus pneumoniae to fluoroquinolones: Results of a Hong Kong multicentre study in 2000. *J Antimicrob Chemother* 2001; 48:659-665.
70. Goldsmith CE, Moore JE, Murphy PG, et al. Increased incidence of ciprofloxacin resistance in penicillin-resistant pneumococci in Northern Ireland [letter; comment]. *J Antimicrob Chemother* 1998; 41:420-421.
71. Centers for Disease Control. Resistance of *Streptococcus pneumoniae* to fluoroquinolones-United States, 1995-1999. *Morbid Mortal Weekly Rep MMWR* 2001;50:800-804.
72. Doern GV, Heilmann KP, Huynh HK, et al. Antimicrobial resistance among clinical isolates of Streptococcus pneumoniae in the United States during 1999-2000, including a comparison of resistance rates since 1994-1995. *Antimicrob Agents Chemother* 2001; 45:1721-1729.
73. Sahm DF, Karlowsky JA, Kelly LJ, et al. Need for annual surveillance of antimicrobial resistance in *Streptococcus pneumoniae* in the United States: 2-year longitudinal analysis. *Antimicrob Agents Chemother* 2001;45: 1037-1042.
74. Sahm DF, Peterson DE, Critchley IA, et al. Analysis of ciprofloxacin activity

Stay On Top of EMTALA with Audio Conference

EMTALA rules continue to change. Are you up-to-date?

Keep abreast of all the latest changes with EMTALA Update 2002, an audio conference sponsored by American Health Consultants. The conference, scheduled for Tuesday, June 4, 2002, from 2:30 to 3:30 p.m. Eastern time, will be presented by Charlotte S. Yeh, MD, FACEP, and Nancy J. Brent, RN, MS, JD. Dr. Yeh is medical director for Medicare policy at National Heritage Insurance Company. Brent is a Chicago-based attorney, with extensive experience as a speaker on EMTALA and related health care issues.

The conference will outline a new report that puts a national spotlight on inadequate ED on-call coverage. There is a growing trend of specialists refusing to take call for the ED, partly due to increased liability risks for medical malpractice and violations of EMTALA. If you don't take steps to ensure appropriate on-call coverage for your ED, you're at risk for violations and adverse outcomes. This program also will update you on any legislative efforts to compel managed care plans to reimburse hospitals for EMTALA-related services.

Each participant can earn FREE CE or CME for one low facility fee. Invite as many participants as you wish to listen to the EMTALA Update 2002 audio conference for just $249 for AHC subscribers and $299 for non-subscribers, and each participant will have the opportunity to earn 1 nursing contact hour or 1 AMA Category 1 CME credit. For more information, or to register, call American Health Consultants' customer service department at (800) 688-2421 or (404) 262-5476, go online at www.ahcpub.com, or e-mail customerservice@ahcpub.com.

against *Streptococcus pneumoniae* after 10 years of use in the United States. *Antimicrob Agents Chemother* 2000;44:2521-2524.
75. Thornsberry C, et al. Longitudinal analysis of resistance among *Streptococcus pneumoniae* (SP) isolated from 100 geographically distributed institutions in the United States during the 1997-1998 and 1998-1999 respiratory seasons. Abstract of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, Sept. 26-29, 1999.
76. Fish DN, Piscitelli SC, Danziger LH. Development of resistance during antimicrobial therapy: A review of antibiotic classes and patient characteristics in 173 studies. *Pharmacotherapy* 1995;15:279-291.
77. Deeks SL, Palacio R, Ruvinsky P, et al. Risk factors and course of illness among children with invasive penicillin-resistant *Streptococcus pneumoniae*. The Streptococcus pneumoniae Working Group. *Pediatrics* 1999;103:409-413.
78. Straus WL, Qazi SA, Kundi Z, et al. Antimicrobial resistance and clinical effectiveness of co-trimoxazole versus amoxycillin for pneumonia among children in Pakistan: Randomised controlled trial. Pakistan Co-trimoxazole Study Group. *Lancet* 1998;352:270-274.
79. Davidson RJ, Cavalcanti R, Brunton JL, et al Resistance to levofloxacin and failure of treatment of pneumococcal pneumonia. *N Engl J Med* 2002;346: 747-750.
80. Weiss K, Restieri C, Laverdiere M, et al. A nosocomial outbreak of fluoroquinolone-resistant *Streptococcus pneumoniae. Clin Inf Dis* 2001;33:517-522.
81. Ho PL, Tse W, Tsang KW, et al. Risk factors for acquisition of levofloxacin-resistant *Streptococcus pneumoniae:* A case-control study. *Clin Infect Dis* 2001;32:701-707.
82. Pallares R, Capdevila O, Liñares J, et al. Hospital Bellvitge, University of Barcelona, Spain; Clinical Relevance of Current NCCLS Ceftriaxone/ Cefotaxime Resistance Breakpoints in non-Meningeal Pneumococcal Infections. Abstract Poster, 2001.
83. Kaplan SL, Mason EO, Barson WJ, et al. Outcome of invasive infections outside the central nervous system caused by *Streptococcus pneumoniae* isolates nonsusceptible to ceftriaxone in children treated with beta-lactam antibiotics. *Pediatr Infect Dis J* 2001;20:392-396.
84. Cleeland R, Squires E. Antimicrobial activity of ceftriaxone: A review. *Am J Med* 1984;77:3.
85. ASCAP Panel (Antibiotic Selection for Community-Acquired Pneumonia). Jackson, Wyoming, Dec. 6, 2000. A Panel of emergency physicians, internal medicine specialists, and pharmacists assessing treatment guidelines for community-acquired pneumonia.
86. Mandell LA. Antibiotics for pneumonia therapy. *Med Clin N Am* 1994;78: 997-1014.
87. Gopalakrishna K, Lerner P. Tetracycline-resistant pneumococci: Increasing incidence and cross resistance to newer tetracyclines. *Am Rev Respir Dis* 1973;108:1007.
88. Mandell L. Community-acquired pneumonia: Etiology, epidemiology and treatment. *Chest* 1995;108(supp):35S-42S.
89. Edelstein P. Legionnaires' disease. *Clin Infect Dis* 1993;16:741.
90. Garrison D, DeHaan R, Lawson J. Comparison of in vitro antibacterial activities of 7-chloro-7-deoxylincomycin, lincomycin, and erythromycin. *Antimicrob Agents Chemother* 1968;1967:397.
91. Dean NC, Silver MP, Bateman KA, et al. Decreased mortality after implementation of a treatment guideline for community-acquired pneumonia. *Am J Med* 2001;110:451-457.
92. Gleason PP, Meehan TP, Fine JM, et al. Associations between initial antimicrobial therapy and medical outcomes for hospitalized elderly patients with pneumonia. *Arch Intern* Med 1999;159:2562-2572.
93. Nathwani D, Rubinstein E, Barlow G, et al. Do guidelines for community-acquired pneumonia improve the cost-effectiveness of hospital care? *CID* 2001;32:728 (1 March, 2000).
94. People G, Kapoor WN, Stone RA, et al. Medical outcomes and antimicrobial cost with the use of the American Thoracic Society guidelines for outpatients with community-acquired pneumonia. *JAMA* 1997;278:32-9.
95. Dowell SF. The best treatment for pneumonia: New clues, but no definitive answers. *Arch Intern Med* 1999;159:2511-2512.
96. Canadian Coordinating Office for Health Technology Assessment. Clinical and economic considerations in the use of fluoroquinolones: technology overview. Pharmaceuticals. Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA), 1997;10:1-13.
97. Al-Eidan FA, McElnay JC, Scott MG, et al. Use of a treatment protocol in the management of community-acquired lower respiratory infection. *J Antimicrob Chemother* 2000;45:387-397.
98. McGarvey RN, Harper IJ. Pneumonia mortality reduction and quality improvement in a community hospital. *QRB Qual Rev Bull* 1993;19:1 24-130.

ASCAP (Antibiotic Selection for Community-Acquired Pneumonia) 2002 Consensus Panel Members: Gideon Bosker, MD, FACEP, Section of Emergency Medicine, Yale University School of Medicine and Oregon Health Sciences University, ASCAP Panel Moderator and Chairman, Editor-in-Chief, *Emergency Medicine Reports;* **Charles Emerman, MD, FACEP,** ASCAP Panel Associate Chairman, Chairman, Department of Emergency Medicine, Cleveland Clinic Hospitals and Metro Health Center, Cleveland, Ohio; **Stephen Ernest, PharmD,** Clinical Pharmacist, Infectious Diseases; **John Gums, PharmD,** Professor, Departments of Pharmacology and Medicine, University of Florida, Gainesville; **Dave Howes, MD, FACEP,** Program Director and Chairman, Residency Program, Department of Emergency Medicine, University of Chicago Hospitals and Clinics, Associate Professor, Pritzker School of Medicine; **Kurt Kleinschmidt, MD, FACEP,** Associate Professor, Department of Emergency Medicine, University of Texas Southwestern Medical School, Parkland Memorial Medical Center, Dallas, Texas; **David Lang, DO,** Operations Medical Director, Department of Emergency Medicine, Mt. Sinai Medical Center, Miami, Florida; **Sandra Schneider, MD, FACEP,** Professor and Chairman, Department of Emergency Medicine, University of Rochester/Strong Memorial Hospital, Rochester, New York; and **Gregory A. Volturo, MD, FACEP,** Vice Chairman and Associate Professor, Department of Emergency Medicine, University of Massachusetts Medical School, Worcester. **Statement of Financial Disclosure:** In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Emerman receives research grants from Merck, Scios, Sepacor, and serves as a consultant for Scios. He receives honoraria from Pfizer, Cor, Merck, Scios, Pharmacia, and Roche, and owns stock in Scios. Dr. Gums receives research grants from Pfizer, Roche, Merck, and Wyeth-Ayerst. He serves as a consultant for Aventis, Roche, and Wyeth-Ayerst, and he receives honoraria from Wyeth-Ayerst, Roche, and Aventis. Dr. Kleinschmidt is a consultant for Aventis. Dr. Schneider is a stockholder in Roche and received grant funds in 1987 from Smith Kline French. Dr. Volturo receives research grants from Roche, is a consultant for Pfizer and Aventis, and receives honoraria from Roche and Pfizer.

99. Dresser LD, Niederman MS, Paladino JA. Cost-effectiveness of gatifloxacin vs ceftriaxone with a macrolide for the treatment of community-acquired pneumonia. *Chest* 2001;119:1439-1448.
100. Kaplan SL, Mason EO Jr, Barson WJ, et al. Outcome of invasive infections outside the central nervous system caused by *Streptococcus pneumoniae* isolates nonsusceptible to ceftriazone in children treated with beta-lactam antibiotics. *Pediatr Infect Dis J* 2001;20:392-396.
101. Gums JG. Abstract/poster presentation; American College of Chest Physicians (ACCP), 2001. Antimicrobial susceptibility trends from 1990-2000: Preliminary results of the antimicrobial resistance management (ARM) program. *Pharmacotherapy* 2001;21:1300-1301.
102. Fraschini F, Scaglione F. Study on the relationship between pharmacokinetics and antibacterial activity: Comparison between ceftriaxone and cefotaxime within the respiratory tract. *Chemotherapy* 1989;45:77-82.
103. Enoxacin-A new fluoroquinolone. *Med Lett Drugs Ther* 1992;34: 103-105.
104. Cooper B, Lawer M. Pneumococcal bacteremia during ciprofloxacin therapy for pneumococcal pneumonia. *Am J Med* 1989;87:475.
105. Flynn CM, et al. In vitro efficacy of levofloxacin alone or in combination tested against multi-resistant *Pseudomonas aeruginosa* strains. *J Chemother* 1996;8:411-415.
106. Dholakia N, et al. Susceptibilities of bacterial isolates from patients with cancer to levofloxacin and other quinolones. *Antimicrob Agents Chemother* 1994;38:848-852.
107. Habib MP, et al. Abstract L002. 36th Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, LA. Sept. 15-18, 1996.
108. File TM, et al. Abstract L001 (LM1). 36th Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, LA. Sept. 15-18, 1996.
109. Pfizer, Inc. Azithromycin package insert.
110. Pfizer product monograph. Azithromycin for IV injection.
111. Data on file, Pfizer, Inc. New York, NY.

Emergency Medicine Reports CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- be educated about how to correctly perform necessary diagnostic tests;
- take a meaningful patient history that will reveal the most important details about the particular medical problem discussed;
- apply state-of-the-art therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur;
- and provide patients with any necessary discharge instructions.

Physician CME Questions

67. Causative pathogens in community-acquired pneumonia (CAP) are identified in:
    A. fewer than 10% of patients.
    B. fewer than 20% of patients.
    C. fewer than 30% of patients.
    D. fewer than 40% of patients.
    E. fewer than 50% of patients.

68. Beginning in January 2002, the National Committee on Clinical Laboratory Standards (NCCLS) officially adopted new breakpoint minimum inhibitory concentrations (MIC) for two third-generation cephalosporins for non-meningeal sources of *Streptococcus pneumoniae*. They are:
    A. cefuroxime and ceftazadine.
    B. cefuroxime and ceftriaxone.
    C. ceftriaxone and cefaclor.
    D. ceftriaxone and cefotaxime.

69. At the very least, empiric coverage for CAP must provide activity against which of the following pathogens?
    A. *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*
    B. *Mycoplasma*, *Legionella*, and *C. pneumoniae*
    C. *H. influenzae*, *M. catarrhalis*, and *Mycoplasma*
    D. *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, as well as against atypical pathogens *Mycoplasma pneumoniae*, *Legionella pneumoniae*, and *C. pneumoniae*

70. Which of the following are recommended for drug resistant *S. pneumoniae* as first-line, initial empiric monotherapy in individuals with outpatient CAP by the CDC Therapeutic Working Group?

Sign Up Now to Continue Receiving Bioterrorism News

We hope you have enjoyed receiving complimentary issues of *Bioterrorism Watch* with your subscription to *Emergency Medicine Reports*. Your last free issue will be in June.

Beginning in July, *Bioterrorism Watch* will become an eight-page bimonthly subscription newsletter, which will offer both CE and CME credits. The six yearly issues combined will offer six hours of CE and CME.

We are offering *Emergency Medicine Reports* subscribers a special introductory yearly price of $99. Don't miss a single issue of *Bioterrorism Watch*. Call our customer service department today at 1-800-688-2421 or visit us online at www.ahcpub.com to continue receiving *Bioterrorism Watch* for the low yearly price of $99.

A. TMP-SMX
B. Macrolides (azithromycin, erythromycin, or clarithromycin)
C. Fluoroquinolones (levofloxacin, grepafloxicin, gatifloxacin)
D. Cephalosporins (cefaclor)

71. The CDC recommends that fluoroquinolones be reserved for selected patients with CAP, among them those in which of the following group(s)?
    A. Hospitalized adults for whom one of the first-line regimens (cephalosporin plus a macrolide) has failed
    B. Those who are allergic to the first-line agents
    C. Those patients who have a documented infection with highly drug-resistant pneumococci (i.e., penicillin MIC = 4 mcg/mL)
    D. All of the above

72. With revised breakpoint MICs for cefotaxime and ceftriaxone, the percent of resistant *Streptococcus pneumoniae* to these third-generation cephalosporins is expected to drop below:
    A. 3-5% nationally.
    B. 1% nationally.
    C. 13-15% nationally.
    D. 30-50% nationally.

73. Clinical features or risk factors that may suggest the need for intensification and expansion of bacterial and/or atypical pathogen coverage to include coverage of gram-negative organisms include the following:
    A. chronic alcoholism.
    B. older than 85 years of age, comorbid conditions, previous infection.
    C. acquisition of the pneumonia in a skilled nursing facility.
    D. the presence of an aspiration pneumonia.
    E. All of the above

74. Emergence of resistance among *S. pneumoniae* species to new generation fluoroquinolones has been reported in a number of geographic regions, including:
    A. Northern Ireland.
    B. Hong Kong.
    C. Canada.
    D. All of the above

Immediate certificate delivery

CMEweb

The Global Continuing Medical Education Resource

Exciting **site improvements** include advanced search capabilities, more bulk purchasing options, certificate printing, and much more.

With **more than 1100 hours** of credit available, keeping up with continuing education requirements has never been easier!

Choose your area of clinical interest

- AIDS/HIV
- Alternative Medicine
- Asthma
- Cardiology
- Contraception
- Critical Care
- Diabetes
- Emergency Medicine
- Geriatrics
- Infection Control
- Internal Medicine
- Medical Ethics
- Neurology
- OB/GYN
- Oncology
- Pediatrics
- Primary Care
- Psychiatric Medicine
- Radiology
- Sports Medicine
- TB
- Therapeutics
- Travel Medicine

Price per Test

As low as $5 per test with bulk purchase option.

Log onto

www.CMEweb.com

today to see how we have improved your online CME

HOW IT WORKS

1. **Log on at http://www.CMEweb.com**
2. **Complete the rapid, one-time registration process** that will define your user name and password, which you will use to log-on for future sessions. It costs nothing to register!
3. **Choose your area of interest** and enter the testing area.
4. **Select the test you wish to take** from the list of tests shown. Most tests are worth 1.5 hours of CME credit.
5. **Read the literature reviews and special articles**, answering the questions associated with each.
6. **Your test will be graded online** and your certificate delivered immediately via e-mail.

CALL **1-800-688-2421** OR E-MAIL CUSTOMERSERVICE@CMEWEB.COM

In Future Issues:

Community-Acquired Pneumonia Part II

Emergency Medicine Reports
The Practical Journal for Emergency Physicians

Community-Acquired Pneumonia Part I

ASCAP 2002 Guidelines—Empiric Antimicrobial Therapy of Choice for Outpatient and In-Hospital Management of Patients with CAP

PATIENT PROFILE/ETIOLOGIC AGENTS	FIRST-LINE ANTIBIOTIC THERAPY†	ALTERNATIVE FIRST-LINE ANTIBIOTIC THERAPY
Otherwise Healthy < 60 years of age (Patients deemed to be suitable for outpatient/oral therapy, i.e., no systemic toxicity, high likelihood of compliance, and supportive home environment)*	Azithromycin PO	Moxifloxacin PO (preferred) *OR* Levofloxacin PO *OR* Clarithromycin *OR* Gatifloxacin PO
Otherwise Healthy > 60 years of age (Patients deemed to be suitable for outpatient/oral therapy, i.e., no systemic toxicity, high likelihood of compliance, and supportive home environment)*	Azithromycin PO	Moxifloxacin PO (preferred) *OR* Levofloxacin PO *OR* Clarithromycin *OR* Gatifloxacin PO
In-Hospital (not in intensive care unit) underlying risk factors or comorbid conditions: In-Hospital management (COPD, history of pneumonia, diabetes, etc.)	Ceftriaxone IV plus azithromycin IV†††	Moxifloxacin *OR* Levofloxacin IV *OR* Gatifloxacin IV
CAP acquired in the nursing home environment (increased likelihood of gram-negative, *E. coli, Klebsiella pneumoniae*)	Ceftriaxone IV plus azithromycin IV	Moxifloxacin *OR* Levofloxacin IV *OR* Gatifloxacin IV
CAP in the elderly individual with chronic alcoholism (Increased likelihood of *Klebsiella pneumoniae* infection)	Ceftriaxone IV plus azithromycin IV	Cefotaxime†† plus erythromycin IV *OR* Levofloxacin IV *OR* Cefepime IV plus azithromycin IV
Severe bacteremic CAP with documented *S. pneumoniae* species showing high-level resistance to macrolides and/or penicillin, but maintaining high sensitivity to extended-spectrum quinolones and cephalosporins	Ceftriaxone IV plus moxifloxacin *OR* Ceftriaxone IV plus levofloxacin IV	Vancomycin¶ plus azithromycin IV
Severe CAP complicated by structural disease of the lung (bronchiectasis): Increased likelihood of *Pseudomonas* and polymicrobial infection	Cefepime IV plus levofloxacin IV plus/minus aminoglycoside *OR* Ciprofloxacin IV plus aminoglycoside IV plus azithromycin IV	Ciprofloxacin IV plus cefepime IV plus azithromycin IV *OR* Imipenem IV plus azithromycin IV plus aminoglycoside
CAP in a patient with suspected aspiration (increases the likelihood of gram-negative and anaerobic infection**)	Ceftriaxone IV plus azithromycin IV plus clindamycin IV	Levofloxacin IV plus clindamycin IV *OR* Levofloxacin IV plus metronidazole IV *OR* Gatifloxacin IV plus clindamycin IV
Severe CAP in a compromised host with a previous hospitalization for, or who resides in, a community or facility with a high reported incidence of methicillin-resistant *S. aureus* (MRSA)***	Moxifloxacin IV plus vancomycin IV *OR* Levofloxacin IV plus vancomycin IV	Gatifloxacin IV plus vancomycin IV
CAP patient with severe pneumonia requiring ICU hospitalization***	Ceftriaxone IV plus levofloxacin IV plus/minus aminoglycoside (*Pseudomonas* strongly suspected) *OR* Ceftriaxone IV plus azithromycin IV plus/minus anti-pseudomonal agent	Cefepime IV plus aminoglycoside IV plus azithromycin IV *OR* Imipenem IV plus aminoglycoside IV plus azithromycin IV

* Oral therapy/outpatient treatment recommendations are appropriate only for those otherwise healthy patients with CAP of mild enough severity that they are judged to be suitable candidates for outpatient management with oral antibiotics.

§ Quinolones generally are restricted for use in patients > 18 years of age.

¶ If *S. pneumoniae* demonstrates complete resistance to extended spectrum quinolones (very rare), third-generation cephalosporins, and macrolides, then vancomycin may be required as part of initial therapy, although this would be necessary only in rare circumstances.

† First-line therapy recommendations take into consideration cost of the drug (which may vary from one institution to another), convenience of dosing, daily dose frequency, spectrum of coverage, side effects, and risk of drug-drug interactions.

†† Cefotaxime IV should be dosed on a q 8 hours basis when used for treatment of CAP.

††† Some institutions may use oral macrolide therapy for patients with mild-to-moderate CAP.

** When anaerobic organisms are suspected as one of the possible etiologic pathogens in a patient with CAP, clindamycin or a β-lactam/β-lactamase inhibitor (ampicillin/sulbactam, ticarcillin/clavulanate, or ticarcillin/tazobacatam) is recommended.

*** High community prevalence of, previous history of hospitalization, or increasing local incidence of methicillin-resistant *S. aureus* (MRSA) in a patient with a clinical presentation consistent with *S. aureus* pneumonia; vancomycin should be considered as component for initial therapy.

‡ Adapted from references 2, 3, 9, 12, 20-31

§§ Cefotaxime may be substituted for ceftriaxone, although ceftriaxone is preferred because of its once-daily dosing.

IDSA—Year 2002 Guidelines. Empirical Selection of Antimicrobial Agents for Treating Patients with CAP

OUTPATIENTS

- Generally preferred are (not in any particular order): doxycycline, a macrolide, or a fluoroquinolone.
- These agents have activity against the most likely pathogens in this setting, which include *Streptococcus pneumoniae, Mycoplasma pneumoniae,* and *Chlamydia pneumoniae.*
- Selection should be influenced by regional antibiotic susceptibility patterns for *S. pneumoniae* and the presence of other risk factors for drug-resistant *S. pneumoniae.*
- Penicillin-resistant pneumococci may be resistant to macrolides and/or doxycycline.
- For older patients or those with underlying disease, a fluoroquinolone may be a preferred choice; some authorities prefer to reserve fluoroquinolones for such patients.

HOSPITALIZED PATIENTS

- General medical ward
- Generally preferred are: an extended spectrum cephalosporin combined with a macrolide or a β-lactam/β-lactamase inhibitor combined with a macrolide or a fluoroquinolone (alone).

INTENSIVE CARE UNIT

- Generally preferred are: an extended spectrum cephalosporin or β-lactam/β-lactamase inhibitor plus either a fluoroquinolone or macrolide.

ALTERNATIVES OR MODIFYING FACTORS

- Structural lung disease: antipseudomonal agents (piperacillin, piperacillin-tazobactam, imipenem, or cefepime) plus a fluoroquinolone (including high-dose ciprofloxacin)
- β-lactam allergy: fluoroquinolone ± clindamycin
- Suspected aspiration: fluoroquinolone with or without clindamycin, metronidazole, or a β-lactam/β-lactamase inhibitor

Note: β-lactam/β-lactamase inhibitor: ampicillin-sulbactam or piperacillin-tazobactam. Extended-spectrum cephalosporin: cefotaxime or ceftriaxone. Fluoroquinolone: gatifloxacin, levofloxacin, moxifloxacin, or other fluoroquinolone with enhanced activity against *S. pneumoniae* (for aspiration pneumonia, some fluoroquinolones show in vitro activity against anaerobic pulmonary pathogens, although there are no clinical studies to verify in vivo). Macrolide: azithromycin, clarithromycin, or erythromycin ± with or without.

Daily Drug Cost (WAC)*

DRUG AND DOSAGE	COST/DAY
Azithromycin IV 500 mg	$18.96
Ceftriaxone 1 gm IV qd	36.06
Levofloxacin 500 mg IV qd	33.00
Erythromycin 500 mg IV qid	5.20
Ciprofloxacin 400 mg IV bid	48.00
Cefotaxime 1 g IV tid	25.00
Tricarcillin-clavulanate 3.1 g qid	48.32

* WAC = Wholesale acquisition cost

Hospital formulary pricing guide, August 1999. WAC may not necessarily reflect actual pharmacy costs or costs associated with drug administration cost comparisons.

Recommended Year 2000 CDC DRSP-WG Empiric Regimens for Treating Community-Acquired Pneumonia*

Empiric treatment**	Penicillin MIC mcg/mL ≤ 0.06	0.12-1	2	4	≥ 8	Comments
Outpatients						
Macrolide (erythromycin, clarithromycin, or azithromycin)	+++	+	±	-	-	Covers atypical pathogens (*Mycoplasma* species *Chlamydia* species, and *Legionella* species)
Doxycycline (or tetracycline)	+++	++	+	-	-	Covers atypical pathogens; not FDA-approved for children younger than 8 years
Oral β-lactam (cefuroxime axetil, amoxicillin, or amoxicillin-clavulanate potassium)	+++	++	+	-	-	Does not cover atypical pathogens, alternatively cefpodoxime or cefprozil may be used
Fluoroquinolones (levofloxacin, moxifloxacin, or gatifloxacin)†	+++	+++	+++	++	++	Not first-line treatment because of concerns about emerging resistance; not FDA-approved for use in children; covers atypical pathogens
Hospitalized (Nonintensive Care Unit) Patients						
Parenteral β-lactam (cefuroxime, cefotaxime sodium, ceftriaxone sodium, or ampicillin sodium-sulbactam sodium) plus macrolide (erythromycin, clarithromycin, or azithromycin)	+++	+++	++	±	-	Ceftriaxone and cefotaxime have superior activity against resistant pneumococci in comparison with ampicillin-sulbactam and with cefuroxime.
Fluoroquinolones (e.g., moxifloxacin, levofloxacin, gatifloxacin, or trovafloxacin)†	+++	+++	+++	++	++	See previous comments about fluoroquinolones.
Intubated or Intensive Care Unit Patients‡						
Intravenous β-lactam (ceftriaxone or cefotaxime sodium) plus intravenous macrolide (erythromycin or azithromycin)	+++	+++	++	±	-	Ceftriaxone or cefotaxime are preferred over other β-lactams because of their superior activity against resistant pneumococci; clarithromycin has no intravenous formulation.
Intravenous β-lactam (ceftriaxone or cefotaxime) plus fluoroquinolone (e.g., gatifloxacin, levofloxacin, moxifloxacin, or trovafloxacin)†	+++	+++	++	++	++	Ceftriaxone or cefotaxime are preferred over other β-lactams; see previous comments about fluoroquinolones.
Fluoroquinolones (e.g., moxifloxacin, levofloxacin, gatifloxacin, or trovafloxacin)†	++	++	++	++	++	See previous comments about fluoroquinolones; efficacy of monotherapy for critically ill persons with pneumococcal pneumonia has not been established.

* FDA indicates Food and Drug Administration. Ratings estimate clinical efficacy and in vitro susceptibility among persons with pneumococcal pneumonia. In-depth information on empiric treatment of pneumonia is given by the Infectious Disease Society of America and the American Thoracic Society guidelines.

† The relative antipneumococcal activity of these agents differs slightly, with that of trovafloxacin equal or superior to that of grepafloxacin, which equals that of sparfloxacin, which is superior to that of levofloxacin. Because of new data showing an association with serious liver damage, the FDA issued a public health advisory recommending that trovafloxacin be used only for patients with serious and life- or limb-threatening infections who receive initial treatment in an inpatient health care facility and for whom physicians believe that the benefit of the agent outweighs its potential risk.

‡ Vancomycin hydrochloride may be indicated for the treatment of selected critically ill children with community-acquired pneumonia for whom coverage of drug-resistant *Streptococcus pneumoniae* must be ensured.

** Adaptations made to reflect introduction of new agents since report was published.

Supplement to Emergency Medicine Reports, April 22, 2002: "Community-Acquired Pneumonia (CAP) Antibiotic Selection and Management Update. Part I: Evaluation, Risk Stratification, and Current Antimicrobial Treatment Guidelines for Hospital-Based Management of CAP: Outcome-Effective Strategies Based on Year 2002 NCCLS Breakpoints and Recent Clinical Studies." —*ASCAP (Antibiotic Selection for Community-Acquired Pneumonia) 2002 Consensus Panel Report* Author: **Gideon Bosker, MD, FACEP**, Assistant Clinical Professor, Section of Emergency Services, Yale University School of Medicine, Associate Clinical Professor, Oregon Health Sciences University, Portland.

Emergency Medicine Reports' "Rapid Access Guidelines." Copyright © 2002 American Health Consultants, Atlanta, GA. Editor-in-Chief: **Gideon Bosker, MD, FACEP**. Vice President and Group Publisher: **Brenda Mooney**. Editorial Group Head: **Valerie Loner**. Specialty Editor: **Shelly Morrow**. For customer service, call: 1-800-688-2421. This is an educational publication designed to present scientific information and opinion to health care professionals. It does not provide advice regarding medical diagnosis or treatment for any individual case. Not intended for use by the layman.