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# Antimicrobial treatment of lower respiratory tract infections in the hospital setting

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Respiratory tract infections (RTIs) that may require hospitalization include acute exacerbations of chronic bronchitis (AECB), community-acquired pneumonia (CAP), and hospital-acquired pneumonia (HAP), which includes ventilator-associated pneumonia (VAP). Healthcare-associated pneumonia (HCAP) is treated similar to HAP and may be considered with HAP. For CAP requiring hospitalization, the current guidelines for the treatments of RTIs generally recommend either a β-lactam and macrolide combination or a fluoroquinolone. The respiratory fluoroquinolones (levofloxacin, gatifloxacin, moxifloxacin, and gemifloxacin) are excellent antibiotics due to high levels of susceptibility among gram-negative, gram-positive, and atypical pathogens. The fluoroquinolones are active against >98% of *Streptococcus pneumoniae*, including penicillin-resistant strains. Fluoroquinolones are also recommended for AECB requiring hospitalization. Evidence from clinical trials suggests that levofloxacin monotherapy is as efficacious as combination ceftriaxone-erythromycin therapy in the treatment of patients hospitalized with CAP. For early-onset HAP, VAP, and HCAP without the risk of multidrug resistance, ceftriaxone, ampicillin-sulbactam, ertapenem, or one of the fluoroquinolones is recommended. High-dose, short-course therapy regimens may offer improved treatment due to higher drug concentrations, more rapid killing, increased adherence, and the potential to reduce development of resistance. Recent studies have shown that short-course therapy with levofloxacin, azithromycin, or telithromycin in patients with CAP was effective, safe, and tolerable and may control the rate of resistance.


Lower respiratory tract infections (RTIs) are the main cause of death due to infectious disease in the United States.[1] RTIs treated in the hospital include severe cases of acute exacerbations of chronic bronchitis (AECB) and community-acquired pneumonia (CAP) as well as hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP) and healthcare-associated pneumonia (HCAP). Pneumonia alone is the sixth most common cause of death, with 2 to 3 million cases of CAP and 45,000 deaths occurring each year.[1] About 300,000 cases of HAP occur annually, and HAP has an attributable mortality rate of approximately 33% to 50%.[2] Chronic obstructive pulmonary disease (COPD), which is characterized by AECB, results in approximately 119,000 deaths per year in the United States.[3]

Direct costs of RTIs such as AECB are estimated to cost US$1.2 billion for patients aged ≥65 years and $419 million for patients <65 years.[4] The cost of care for CAP is estimated between $8.4 billion and $9.7 billion dollars annually.[5] Finally, HAP results in $2 billion of direct costs annually.[2] In total, these add up to over $12 billion annually. In 1997 the cost to US employers of patients with respira-

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tory infections was $112 billion, including direct costs of medical treatment and indirect costs of time lost from work.[6]

The decision to admit a patient with either CAP or AECB to the hospital is based on the severity of symptoms. For patients with CAP, the American Thoracic Society (ATS) and the Texas Academy of Family Physicians recommend using the Patient Outcomes Research Team (PORT) Severity Index (PSI) as a guideline to stratify patients.[7,8] The index uses demographic factors, coexisting conditions, and physician and laboratory findings to divide patients into 5 risk classes. It is recommended that patients in the fourth and fifth classes (i.e., those with the most severe illness) be hospitalized.[7] ATS guidelines note that the PSI should be used in conjunction with good clinical judgment, taking into consideration risk factors for a complicated course as well as potential nonmedical reasons for admission.[8] However, the PORT approach may oversimplify the process of risk stratification of individual patients even when their severity of illness is profoundly different.[8] Additionally, it gives heavy emphasis on age as a variable, requiring physicians to collect more data for younger patients to categorize them in a risk group. Finally, PORT scores do not include rare clinical conditions such as severe neuromuscular disease as factors in the prediction rules, thus affecting final scores.[8] PORT scores also are cumbersome to obtain and difficult to use.

The validity of the PSI system to determine treatment in outpatient care versus hospitalization was confirmed in a low-risk subset of CAP patients.[9] For selected patients, outpatient care was as safe and effective as hospitalization. Further support for the use of PSI in guiding the admission decision for low risk CAP patients was seen in separate studies in hospitals in Canada and the United States, which resulted in admission of fewer low-risk patients without compromising the effectiveness of treatment or well-being of the outpatients.[10,11]

The decision to admit a patient with COPD who is experiencing an AECB is based on the number of symptoms and risk factors. Symptoms include shortness of breath, increased sputum production, and increased sputum purulence. Risk factors for hospitalization include percentage of predicted forced expiratory volume in 1 minute ($FEV_1$), ischemic heart disease, and mucous hypersecretion.[7]

Inappropriate antibiotic therapy, or overuse and/or misuse of antibiotics, is a common occurrence that may increase a patient's duration of stay in the hospital, and may predispose patients to increased resistance to a class of antibiotics.[12,13] A study in the United States on excessive antibiotic use in acute respiratory infections involving the upper and lower respiratory tract showed that 55% of the total prescriptions in 1998 were prescribed in excess.[12] Additionally, inappropriate initial antibiotic therapy may increase hospital mortality rates for patients in hospital intensive care units (ICUs). For example, a retrospective study in France for the outcomes of VAP patients between 1992 and1997 found initial antibiotic therapy was appropriate in 49.5% of patients (N = 111). The study concluded that, in comparison with appropriate initial antibiotic treatment, inappropriate initial antibiotic treatment could increase the duration of stay and the crude hospital mortality in VAP patients for patients with equal severity of illness at the time of VAP diagnosis.[13]

As described below, major recommendations set forth by various healthcare groups aim at avoiding unnecessary and inappropriate therapy, particularly when selecting initial antibiotic treatment options for a patient admitted with an RTI.

## The Council for Appropriate and Rational Antibiotic Therapy Criteria

A number of health organizations, including the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), are currently spearheading efforts to reduce the incidence of antibiotic resistance.[14–16] The WHO emphasizes the importance of choosing the correct drug at the correct dose for the correct duration of treatment to control resistance. In today's environment, many treatment options are available. The Council for Appropriate and Rational Antibiotic Therapy (CARAT) has defined the following 5 core criteria to assist clinicians in determining the right drug, right dose, and right duration of treatment to improve outcomes and decrease the risk of future resistance: (1) evidence-based results; (2) therapeutic benefits; (3) safety; (4) optimal drug for optimal duration; and (5) cost-effectiveness. This article discusses the application of these criteria to the management of CAP and AECB due to bacteria, or acute bacterial exacerbations of chronic bronchitis (ABECB), in the hospital setting.

### Evidence-based results

#### Management of CAP in the hospital setting

The importance of appropriate treatment is underlined by the data: each year in the United States there are 45,000 deaths, 10 million physician visits, and 500,000 hospitalizations due to CAP. Among hospitalized patients with CAP, the average mortality is approximately 14%.[1,17] However, better management may help to improve patient care.

Despite efforts to control antibiotic resistance, which is believed to be caused mainly by the overuse and misuse of antibiotics, patients with RTIs are frequently treated with antibiotics that are incorrect, suboptimal, or unwarranted.[18] The CARAT guidelines recommend determining a need for antimicrobial treatment before prescribing antibiotics.

A number of established guidelines provide evidence-based recommendations for treatment (**Table 1**).[1,8,19,20] The ATS, the British Thoracic Society (BTS), and the Infectious Diseases Society of America (IDSA) all recom-