Chapter 7
Optimal Antibiotic Use in Severe Community-Acquired Pneumonia

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7.1 Introduction

Community-acquired pneumonia (CAP) is the main cause of death due to infectious disease in the developed countries. Although the incidence is not available in most countries, it represents more than 600,000 hospital admissions in the United States (Barlett et al. 2000) and 50,000 in the United Kingdom each year (Hirani and Macfarlane 1997). The cost is higher for nonsurvivors than for survivors (around $7,500 of an in-hospital case) (Fine et al. 1997).

Since the use of penicillin, the mortality rates of severe CAP have not decreased significantly despite advances in antimicrobial therapy and technical improvements in the ICU. Fine et al. (1997) reported that only 10% of hospitalized patients are admitted to ICU, and that the mortality rate in intubated patients reaches 40%. This mortality rate depends on the interaction between the host factors (age, comorbidities, genetic predisposition, and immunocompromise), microorganism characteristics, and optimal antibiotic use (Luján et al. 2006) (Fig. 7.1). In a recent study, Waterer et al. (2001a,b) suggest that CAP patients with septic shock appear to have different genotypes than those with hypoxemic respiratory failure without shock.

The constant increase in the number of elderly and immunocompromised patients (those receiving steroids, organ transplant recipients, HIV patients), the better survival rates of patients affected by chronic illness, and the need for appropriate empirical antibiotics administration are reasons that justify continuing research, focused on improving the diagnosis, defining risk factors that influence outcome, and assessing new therapies.

Usually, at the time of initiation of the empirical antibiotic treatment, the responsible microorganism is not identified. In the last decade, different societies (Infectious Disease Society of America – IDSA, American Thoracic Society – ATS, and British Thoracic Society – BTS) have published guidelines to help physicians in the management of CAP (Barlett et al. 2000; ATS 1993; BTS 2001).

Several studies (Malone and Shaban 2001; Dean et al. 2006; Mortensen et al. 2004) on patients with severe CAP (SCAP) have emphasized the importance of appropriate empirical therapy in reducing disease-related mortality; however, the optimal regimen has not been well defined from large case series. The use of
empiric antimicrobial therapy concordant with international guidelines is associated with decrease mortality among patients with CAP. One study reported a 4.4-fold reduction in mortality if the ATS therapy guidelines were followed (Malone and Shaban 2001). Other authors have observed similar results (Dean et al. 2006; Mortensen et al. 2004). However, these studies have limitations, such as the use of administrative databases, focus on specific patient groups, such as those with bacteremic pneumococcal pneumonia (Waterer et al. 2001a,b; Baddour et al. 2004), or low risk of mortality (Brown et al. 2003). Recently, our group (Bodí et al. 2005) reported the first study to evaluate the impact of the adherence to IDSA guidelines for severe episodes of CAP admitted to ICU. Multivariate analysis found associations between higher mortality rate and age, APACHE II score, immunocompromise, and nonadherence to IDSA guidelines for antibiotic treatment. Interestingly, adherence to IDSA guidelines was the only potentially modifiable factor for improving the prognosis of ICU patients with SCAP.

Considering the few information about treatment of critically ill patients with SCAP, we focused this chapter on the antimicrobial treatment of a subgroup of patients admitted to ICU due to SCAP, specially, on the optimal antibiotic use.

### 7.2 Antibiotic Therapy: New Concepts

Until now, the in vitro susceptibility of the microorganisms was considered the reference aspect for the antibiotic efficacy for pneumonia (Pea and Viale 2006), and was used to define the concept of “appropriate therapy.” Indeed, other factors must be considered to achieve what we call “appropriate,” “adequate,” or “optimal” antibiotic therapy for pneumonia (Rello and Mallol 2006) (Fig. 7.2). The “appropriate”