Introduction: COPD—The Role of Infection*

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COPD, comprising emphysema and/or chronic bronchitis, with or without associated bronchospasm, is a common malady in the United States. It has been estimated that up to 15 million persons suffer from COPD and that 12.5 million have a chronic bronchitis component of their illness. The incidence of diagnosed COPD has increased by >40% since 1982, and the illness now serves as the fifth leading cause of death in the United States.

Chronic bronchitis is a clinical diagnosis characterized by the presence of cough and daily sputum production for 3 consecutive months in at least 2 consecutive years. The excessive sputum produced by the bronchitic patient is the consequence of mucus gland hypertrophy and inflammation in the airway. In addition to excessive mucus production, the patient also has associated changes in mucus composition and mucus quality. Bacterial colonization is common, being found in at least half of all patients with stable chronic bronchitis, yet the role of bacteria in this illness remains controversial and not fully defined. Patients can harbor microorganisms in lower respiratory tract secretions at times when they are healthy and at times of an exacerbation of symptoms. Thus, the mere presence of bacteria does not mean that they are pathogenic, and these organisms could simply be colonizing the airway. Generally no more than half of all exacerbations are bacterial in origin, the remainder being due to viral infection or chemical bronchitis, but bacteria could potentially serve a number of other roles. For example, even nonbacterial exacerbations can be complicated by a secondary bacterial infection. In addition, it is possible that bacteria could actually contribute to airway injury and cause a progressive loss of lung function by participating in a “vicious circle” of infection leading to inflammation, lung injury, and further infection.

The importance of bacterial infection for the COPD patient is generally underappreciated, because of the long-held belief that, from a bacteriologic perspective, all patients are the same and that the choice of one antibiotic rather than another has no impact on the course of an exacerbation or on the general direction of the illness. We are now learning that not all patients with exacerbations are the same, and various patient classification schemes have been proposed, with each patient subset being at risk for infection with a unique group of pathogens, and thus requiring specific antibiotic choices. In these classifications, antibiotic choices vary among patients because of two factors. First, there are expected differences in the bacteriologic spectrum of etiologic organisms among patients, and second, certain patients, especially those with more severe illness and comorbidity, are less able to tolerate an antibiotic failure than are others. A variety of factors can be used to define patient subsets, including age, extent of comorbid illness, duration of COPD, frequency of exacerbations in the preceding year (with at least four episodes defining patients with a high likelihood of relapse after therapy), frequency of antibiotic use (predicting the likelihood of infection with resistant pathogens), and degree of FEV₁ impairment.

In selecting an antibiotic for any given patient, it is necessary to take into account not only its bacteriologic spectrum of activity, but also its ease of use, its ability to eradicate infection rapidly, its ability to prolong times between exacerbations, its pharmacokinetic properties (penetration to site of infection, peak concentration, and time above the target organism minimum inhibitory concentration), and its documented efficacy from a health economics perspective. With proper selection, a number of both immediate and long-term benefits of therapy may follow. Short-term benefits of appropriate antibiotic selection include the following: a rapid resolution of the symptoms of exacerbation (increased sputum volume, increased sputum purulence, and increased dyspnea); a rapid return of peak flow rates; avoidance of hospitalization; an early return to work; and prevention of progression of severe airway infection into pneumonia. The long-term benefits of appropriate antibiotic use include the following: breaking the vicious cycle of airway infection, inflammation, and loss of lung function; prolonging the time between exacerbations; and prevention of secondary infection by resistant pathogens.

The impact of bronchitic exacerbations can be dramatic, but is generally not recognized by clinicians. Hospital discharge diagnoses of COPD range from the Department of Medicine, SUNY at Stony Brook, and Winthrop-University Hospital, Mineola, NY.
from 9 to 13 per thousand population per year. When acute respiratory decompensation occurs, as many as 20 to 60% of patients who are admitted to an ICU will require mechanical ventilation, with a mortality rate ranging from 10 to 30%. In one recent study, the mortality rate for patients admitted to the ICU with acute exacerbation was 24%, but the 180-day mortality rate for those older than 65 years was 47%. Although the need for mechanical ventilation did not by itself predict short- or long-term outcome, the 180-day mortality for patients admitted to the ICU was predicted by the degree of nonrespiratory organ dysfunction and by the extent of advanced respiratory system dysfunction as reflected by respiratory rate and arterial blood gas values.

The first section of this supplement addresses the question of whether all patients with exacerbations of COPD are the same. The role of infection in exacerbations is explored along with proposed classification schemes for patients, emphasizing the variability among patients with this diagnosis. Principles of pharmacologic therapy are discussed, along with suggestions for future research in this area. Future studies of antibiotic therapy for COPD will need to show that the use of subset classifications to select therapy does lead to improved patient outcome, with outcome being defined not only bacteriologically, but also from a global health economics perspective.

REFERENCES