

The Importance of Appropriate Treatment of Chronic Bronchitis

An interview with Antonio Anzueto, MD, Associate Professor of Medicine, University of Texas Health Science Center, Director of the Pulmonary Function Laboratories, University Hospital and the South Texas Veterans Health Care System, Audie L. Murphy Memorial Veterans Hospital Division

Epidemiology of Chronic Bronchitis

AJMC: *How prevalent is chronic bronchitis in the United States?*

Dr. Anzueto: Chronic bronchitis is highly underdiagnosed as a disease, and there are limited epidemiological studies in the United States. However, according to statistics from the National Institutes of Health, and based on extrapolation of data from the United Kingdom (UK), it is estimated that about 15 million Americans suffer from chronic bronchitis.

AJMC: *What risk factors have been identified for chronic bronchitis?*

Dr. Anzueto: By far, smoking is the major precipitating cause for chronic bronchitis. However, there is also a genetic component that can affect whether a smoker will develop severe disease. Other precipitating factors include allergens and air pollutants.

AJMC: *What is the total cost of chronic bronchitis to the health system?*

Dr. Anzueto: We don't have accurate figures regarding the extent of the disease, but the cost of treating chronic bronchitis is estimated at about \$5 billion to \$7 billion (US dollars) per year.¹

Dr. Anzueto has written extensively on all aspects of pulmonary medicine, particularly respiratory tract infection and critical care issues. He has participated in numerous panels and workshops, and lectures frequently at pulmonary symposia in this country and abroad. A physician who has been involved in various aspects of pulmonary research and the management of respiratory tract infections, Dr. Anzueto believes that patient selection and administration of the proper antibiotic is key to successful treatment of exacerbations of chronic bronchitis.

Chronic Obstructive Pulmonary Disease Nomenclature

AJMC: *In recent years, the nomenclature regarding chronic obstructive pulmonary disease and the major conditions that comprise it have changed. Can you explain how this came about?*

Dr. Anzueto: One of the major defining aspects of chronic obstructive



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tive pulmonary disease (COPD) has changed over the years. In the past, a clinician was usually able to stratify patients according to their predominant condition, whether it was chronic bronchitis, emphysema, or asthma (reactive airway disease). However, within the past 5 to 10 years it has become harder to distinguish between these 3 conditions and patients typically demonstrate aspects of all 3 conditions. Therefore, COPD may be a more correct term to use when referring to a patient who has overlapping symptoms or criteria. However, the terms acute exacerbation of chronic bronchitis (AECB) and acute exacerbation of COPD are often used interchangeably.

Acute Exacerbation of COPD

AJMC: *How does one differentiate between COPD and acute exacerbation of COPD?*

Dr. Anzueto: An exacerbation refers to any change in symptoms or worsening in functioning from the baseline. Although it may be difficult to pinpoint an exacerbation in a patient who is already short of breath or who is producing sputum, the patient himself can usually notice a change. Physicians also need to look at the larger picture—particularly how is the patient's functional status—because specific symptoms will vary from individual to individual. In addition, in recent years there has been a big emphasis to lower the threshold for treatment and to try to treat patients sooner before the disease progresses.

AJMC: *What are the risk factors for exacerbation in COPD?*

Dr. Anzueto: The major risk factors for acute exacerbation are similar in chronic bronchitis, emphysema, or asthma and include viral or bacterial infection and allergens. Viral infection is now recognized as a precipitating factor for decompensation in

patients with lung disease, primarily because it allows an overgrowth of bacteria. Because the airways are normally sterile, the presence of bacteria in the airway can produce an inflammatory response that can contribute to the precipitation of exacerbation. Allergens can trigger an exacerbation in patients with a predisposition to allergic reactions. The role of genetic factors in COPD is not clear.

Economic Impact

AJMC: *What impact does AECB have on direct healthcare costs?*

Dr. Anzueto: Data regarding the monetary costs of AECB in the United States were recently reported by Niederman et al.¹ This group calculated treatment costs based on 1994 claims data from Medicare and several medical care surveys and found total costs of \$1.2 billion for patients age 65 and older and \$419 million for those younger than 65 years of age. Treatment costs were largely attributable to hospitalization; on the average, inpatient costs were 3-fold higher than outpatient costs.

Impact on Quality of Life

AJMC: *What about the impact of AECB on indirect costs?*

Dr. Anzueto: I feel the impact of AECB on quality of life and indirect costs is an even bigger issue than monetary costs. Recent data from the UK involving mainly postal workers found that AECB was only second to back pain as the most frequent condition resulting in lost work time.^{2,3}

The best information we have regarding the impact of the disease involves outcome data from a study by Connors et al⁴ in 1996 on patients hospitalized with acute exacerbation of severe COPD. Although mortality during the hospital admission was low (11%), subsequent mortality was significantly higher (49% at 2 years). More important was the fact that, at 6

months, only 24% of patients returned to their baseline functional status. Thus, we are beginning to realize that this disease has a significant impact on quality of life.

Role of Bacteria in AECB

AJMC: *How often is AECB bacterial as opposed to viral in origin? How can one differentiate between the 2 conditions?*

Dr. Ansueto: At times it can be hard to differentiate between bacterial and viral infections. A bacterial infection is likely if there is clearly a purulent sputum or if bacterial cultures are positive. However, under the best circumstances, bacteria can be isolated only about half the time,⁵ so the true percentage is not known. In addition, there does not appear to be a direct correlation between degree of purulence and the number of bacteria present.

An important point about viral infection is that it can depress immune defenses and predispose a patient to a bacterial infection. Elegant work conducted in the 1970s and 1980s showed that significant numbers of bacteria were present following viral infection. In fact, infection with the influenza virus was shown to predispose to infection with *Haemophilus influenzae* and *Streptococcus pneumoniae*, 2 important bacterial respiratory pathogens.

AJMC: *When AECB is bacterial in origin, what are the major pathogens implicated? What role do the atypicals play?*

Dr. Ansueto: When bacteria are isolated in a case of AECB, the major pathogens include *H influenzae*, *Moraxella catarrhalis*, and *S pneumoniae*. It is only recently that the atypicals are being recognized as potential pathogens in AECB. There have been a few recent studies specifically designed to identify atypical or intra-

cellular organisms. These studies found that in 5% to 10% of cases atypical pathogens were involved. *Chlamydia* is the most frequent causative organism in a number of patients, but it has also been isolated in conjunction with *H influenzae*, so there may be a correlation between the 2 pathogens. In these studies, the intracellular organisms have been identified using a combination of serology, molecular biology, and cultures.⁶

I think it should be emphasized that clinicians have to do whatever is possible to collect sputum from these patients and evaluate the microbiologic characteristics of the exacerbations.

There is an important point that clinicians need to discuss. Clinicians know that the most frequent organisms are changing, and that there is increased resistance to the so-called "first-line" drugs. The only way that we can make sense of these data in our daily practice is by knowing the patterns of resistance in our institutions. AECB is an infectious process for which we generally don't send sputums for culture, either because the sensitivity or specificity of the specimens are low or due to the logistics related to obtaining samples. In any case, I think it should be emphasized that clinicians have to do whatever is possible to collect sputum from these patients and evaluate the microbiologic characteristics of the exacerbations.

Who Should be Treated?

AJMC: *How do you determine which patients should be treated with an antibiotic?*

Dr. Ansueto: First, I will try to stratify the patient according to risk and potential benefit. If the patient has underlying lung disease, impairment in lung function, frequent exacerbations, or comorbid conditions, I will treat with an antibiotic because this population is more likely to have a poorer outcome.

Economic and Quality of Life Impact

AJMC: *From an economic standpoint, is it better to treat or not to treat AECB with an antibiotic?*

Dr. Ansueto: We have found that use of antibiotics is a major factor affecting readmission rates in AECB, which in turn affects cost. We conducted a retrospective study of patients with AECB with documented impairment in lung function and found that patients treated with an antibiotic had a 15% rate of 2-week failure compared with a 30% rate in those who were not treated with antibiotics.⁷ These findings were independent of symptom score and disease severity. In addition, which antibiotic a clinician gives the patient is important. We found that patients receiving amoxicillin were readmitted 50% of the time, so you must use an antibiotic that is going to be effective.

Destache et al retrospectively looked at the frequency of failure and costs associated with antibiotic therapy in AECB on an outpatient basis.⁸ They divided empirical antibiotic choices into first-line (amoxicillin, co-trimoxazole, tetracyclines, or erythromycin), second-line (various cephalosporins), and third-line (amoxicillin/clavulanate, azithromycin, or ciprofloxacin) agents. Compared with patients treated with first- or second-line agents, patients treated with third-line antibiotics had the lowest failure rate and need for hospitalization. In addition, use of third-line agents prolonged the time between exacerba-

tions and was associated with lower total costs of treatment.

AJMC: *Are there any data regarding the impact of antibiotic treatment on quality of life?*

Dr. Ansueto: Data from a recent health economic study conducted by Grossman et al⁹ suggested that ciprofloxacin use was associated with a slight but not significant improvement in quality-of-life measures over conventional antibiotic therapy.

No Role in Prophylaxis

AJMC: *Is there a role for prophylactic antibiotic use in chronic bronchitis?*

Dr. Ansueto: Although prophylactic use of antibiotics plays an important role in patients with bronchiectasis, there are no data indicating that prophylactic antibiotic therapy decreases the frequency of exacerbation in COPD.

Antibiotic Therapies

AJMC: *How do you decide which therapy to use to treat AECB?*

Dr. Ansueto: Patients with AECB cannot be treated the same across the board. It is important that patients be stratified and those who will benefit the most from one therapy over another be identified. Several factors have been associated with poor outcome, including frequent exacerbations, underlying lung disease, comorbid conditions, and decreased pulmonary function. Inappropriate therapy in these patients is associated with increased hospitalization and mortality, so a clinician would want to be sure to use an effective therapy in these patients.

The agents I consider to be first line and appropriate for patients with no underlying lung disease and younger smokers without frequent exacerbations include the cephalosporins and some tetracyclines. Patients with more severe underlying

lung disease—in whom failure will have a greater impact—will receive a newer macrolide or one of the newer fluoroquinolones (levofloxacin, gatifloxacin, or moxifloxacin).

In addition, a clinician must also consider the local patterns of resistance when assigning therapy. Although very few facilities are collecting sputum samples now, we need to establish resistance databases. This is becoming more important with the changes in geographic resistance patterns we are seeing.

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