Bronchiectasis: Still an Orphan Disease?

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Nearly 2 centuries have passed since Laënnec wrote the first clinical description of a patient with bronchiectasis,1 more than 80 years since bronchography became the standard diagnostic method, and more than half a century since Reid used histological findings and bronchography to describe and classify the diverse types of bronchiectasis approximately as they are known today.2 Bronchiectasis is currently defined as the irreversible and sometimes progressive dilatation and destruction of the bronchial wall caused by a vicious pathogenic circle of impaired local defense mechanisms, infection, and airway inflammation.3 All types of bronchiectasis are characterized by predominately neutrophilic and mononuclear inflammation with scores of cellular mediators that modulate both acute and chronic inflammatory response and perpetuate the bronchial lesion.4,5 The characteristic clinical picture is chronic purulent sputum, functional impairment in the form of air flow obstruction, multiple exacerbations of an infectious type that occasionally involve atypical microorganisms,6 and dyspnea in advanced stages of the disease—all of which cause progressive deterioration of the patient’s quality of life.1,7 To this day, the etiology of bronchiectasis is unknown in half the cases.8 The present editorial is devoted to types of bronchiectasis that cannot be attributed to cystic fibrosis, an entity which is normally studied separately due to its special characteristics.

From the perspective of epidemiology, bronchiectasis has passed through various stages in its bicentennial history. Before antibiotics, the prevalence of the disease and the associated mortality rate were high: patients died before 40 years of age. The high prevalence kept pace with that of other infectious diseases that led to bronchiectasis, such as tuberculosis and necrotizing pulmonary processes.9 Later, prevalence dropped as a result of the development of preventive medicine, especially immunizations and the antibiotic arsenal.10 Scientific and commercial attention to the disease relaxed during this period of relative epidemiological calm, in which bronchiectasis was thought to be a thing of the past, condemned to extinction. At the end of the 1980s, Barker warned the scientific community in an update on the subject11 by referring to bronchiectasis as “an orphan disease,” the term established by Brewer a few years earlier for diseases abandoned by science and marketplace interests, especially with regard to the development of new treatments, as a consequence of a supposed decline in prevalence.12

Now, 15 years later, advances in science and technology and the return of old, forgotten diseases have awakened some sleeping dogs. Although even today we lack reliable studies on the real prevalence of bronchiectasis, it seems more than likely that it continues to be a major cause of morbidity and mortality in the developing world, and areas of the developed world where health care is inadequate.13 In the industrialized world, the gradual replacement of bronchography by high resolution computed tomography since the end of the 1980s,14 the resurgence of old diseases, new medical situations (with reference to pulmonary tuberculosis, the onset of the epidemic of acquired immune deficiency syndrome in the 1980s, and the advent of organ transplants and immunodepressant treatment1 for example) and, finally, the increasing longevity of the population15 have all had an impact on the current prevalence of bronchiectasis, which is probably much higher than supposed.

Nevertheless, in spite of the new epidemiological situation, the scientific community still lacks sufficient interest in bronchiectasis, especially in therapeutic innovation. In fact, only 41 clinical trials involving bronchiectasis have been indexed in MEDLINE from 1975 through the present, whereas the number is 20 times higher for pneumonia, 25 times higher for chronic obstructive pulmonary disease (COPD), and 100 times higher for asthma—remarkable differences, even taking into account the acknowledged greater prevalence among the general population of pneumonia, COPD, and asthma. More important is that from 2000 through 2004, therapeutic research for these diseases either increased (as was the case of COPD) or at least...
remained the same (as was the case of asthma and pneumonia), whereas the case of bronchiectasis was just the contrary: only 13 clinical trials were run in those 5 years, the same number as in the 2 preceding years (1998-1999). Moreover, according to the Cochrane Collaboration systematic reviews, there are hardly any studies with sufficient evidence to demonstrate a beneficial effect of drugs such as long- or short-acting beta-agonists, inhaled or oral corticosteroids, anticholinergics, certain mucolytics, methylxanthines, and other types of treatment, such as respiratory physiotherapy and noninvasive mechanical ventilation. Some of these treatments, however, continue to be administered to patients with stable bronchiectasis or with exacerbations in the same manner they are prescribed for other airway diseases for which their beneficial effect has been demonstrated. Nevertheless, such treatment “by extrapolation” should in no case be taken to be proof of efficacy. Suffice it to remember the case of DNase, a mucolytic that has proven effective in cystic fibrosis but which is not effective in bronchiectasis of other origins and which can even be dangerous. Antibiotic treatment has perhaps been the most studied therapy so far although there are still questions pending resolution concerning types of antibiotics, methods of administration, and appropriate duration. This is especially so for patients with chronic bronchial colonization by Pseudomonas aeruginosa, possibly the most devastating microorganism in terms of related morbidity and mortality and quality of life and also one of the most common ones. However, recent statistics from the British Department of Health show that bronchiectasis in fact has great impact on public health. Seventy-eight percent of patients seeking care at emergency departments due to exacerbations are hospitalized; a third of them (mean age, 60 years) are admitted to intensive care units, 6 and a third of those admitted present with exacerbations in the same manner they are treated “by extrapolation.” A significant number of exacerbations are treated in outpatient settings. These patients, however, often experience hospital readmission, with a mean hospitalization lasting a mean 10.5 days. Seventy-eight percent of patients seeking care at emergency departments due to exacerbations are hospitalized; a third of them (mean age, 60 years) are admitted to intensive care units, with a third of those admitted presenting with exacerbations in the same manner they are treated “by extrapolation.” A significant number of exacerbations are treated in outpatient settings. These patients, however, often experience hospital readmission, with a mean hospitalization lasting a mean 10.5 days.
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clinical suspicion of a disease that today is more prevalent than might be expected—a disease that has its own pathophysiologic features and therapies. Recent findings that associate bronchiectasis with other more “attractive” diseases, such as COPD, seem an excellent starting point.

REFERENCES

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