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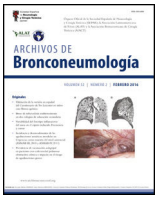

Editorial

# Bronchiectasis and Multidrug-resistant Microorganisms: The Ideal Niche?☆

## Bronquiectasias y microorganismos multirresistentes: ¿el nicho ideal?

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The worldwide increase in multidrug-resistant (MDR) pathogens has sounded alarms that are being heard beyond the health sector, and the general population is now alert to the problem. This situation has been widely recognized and publicized by the WHO, and was important enough to figure in the agenda of President Obama, who launched a message of awareness and warning regarding MDR pathogens when he addressed the scientific and general population in a unprecedented conference. In a recent publication, *The Lancet* discusses the priorities of the WHO in the research and development of new antibiotics.[1]

Multidrug resistance among respiratory microorganisms has already been observed at different times, and in different settings and circumstances. Although *Streptococcus pneumoniae* was the protagonist in community-acquired pneumonia at the end of the last century, this microorganism is no longer our principal concern, thanks to the availability of antibiotics with excellent activity and pneumococcal vaccines in the pediatric and adult population (although we must not let down the guard). Attention subsequently turned to MDR in hospitalized patients, after the publication of American reports of excessive rates of MDR infections in this population, including *Pseudomonas*, *Staphylococcus aureus*, and enterobacterias. It was not long before authors in Europe, specifically in Spain, followed suit, and while we found slightly lower rates, even a small percentage of infections caused by MDR pathogens can complicate clinical decision-making.[2] To this end, different scores have been developed in both the USA and Spain to help clinicians estimate, on the basis of the patient's risk factors, the likelihood of resistant pathogens. One such tool, published by a Spanish group, is the PES (*Pseudomonas, Enterobacteriaceae, Staphylococcus aureus*).[3] This scoring strategy is very useful, since it individualizes risk according to the patient's particular risk factors, and does not depend so much on whether the patient is referred from a hospital setting or from the community.

Concern surrounding MDR pathogens has spread from cases of acute infection to include chronic respiratory patients. Until relatively recently, bronchiectasis was an orphan disease in the field of chronic respiratory disorders. The pathological process of bronchiectasis involves structural airway damage, and is characterized by chronic infections and frequent acute exacerbations with and without pneumonia. We already know that a greater number of exacerbations and the presence of *Pseudomonas aeruginosa* are negative prognostic factors for disease progression, poor quality of life, and increased mortality. We know less from clinical studies about the real impact of the burden of multidrug resistance on the indication of antibiotic treatments and on the evolution of the disease, and this constitutes a problem in daily clinical practice. It is easy to deduce that changes in the airway itself and the need for multiple antibiotic treatments can turn our patients' airways into true "niches" for difficult-to-eradicate MDR pathogens.

The presence of MDR pathogens in bronchiectasis, already suspected from the nature of the disease, was confirmed recently in a Spanish study that found that approximately 1 in 4 exacerbations is produced by an MDR bacterium.[4] This proportion, which is close to the current rate of MDR infection in nosocomial pneumonia, highlights the magnitude of the burden of this disease, and identifies an emerging population. The risk factors for the presence of MDR pathogens are also determined in this study, and while the authors were unable to either confirm or rule out a worse long-term prognosis, the outlook is not good. Independent factors predicting an exacerbation caused by MDR pathogens were prior colonization by MDR bacteria, previous hospitalization, and chronic renal disease. As could be expected, hospitalization rates were higher in these patients, and hospitalization is associated with deterioration and worse prognosis. The presence of *Pseudomonas aeruginosa* among the resistant bacteria is of note, and the ability of these organisms to form biofilms, thus avoiding host defenses and the action of antibiotics, has been demonstrated. Curiously, very few publications are available on MDR pathogens in bronchiectasis, and no scoring systems have been developed in this disease.

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So here we have a population of patients with chronic respiratory disorders whose main characteristic is chronic infection, featuring, moreover, potentially resistant pathogens. It is also true that the most active research into the use of inhaled antibiotics is being conducted in this population. This approach, in theory, would imply less impact on the gut microbiota, although the effect on the local microbiota remains to be determined. Initial studies show that exacerbations in bronchiectasis are associated with a less diverse microbiota and a predominance of *Pseudomonas* and other bacteria.[5] It seems logical to assume that MDR pathogens that are not easily eliminated by antibiotics become more predominant in the microbiota, producing in turn more difficult-to-treat exacerbations. For this reason, if we are to manage MDR pathogens, their predominance must be determined, quantified, treated and controlled. Another possibility is that in the near future microbiota might be modified or supplemented, as is done in the gut. This approach may constitute an effective therapy that could contribute to microbiota diversity and avoid dysbiosis.

Bronchiectasis involves structural airway damage, intrinsic difficulties for bacterial eradication,[6] exacerbations, and a need for very frequent courses of antibiotics, making it an "ideal niche" for chronic infection. Our current challenge is to understand the risk factors, in order to detect the presence of MDR pathogens and indicate effective antibiotic treatment. The increase in the number of patients with bronchiectasis is of major concern; we are facing a chronic disease with frequent infections and exacerbations which offers the ideal conditions for harboring MDR pathogens. The good news is that research into local inhaled antibiotics is increasing, and knowledge of the microbiota is expanding, strategies which possibly will allow for a more holistic and innovative approach. We still have a long way to go.

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