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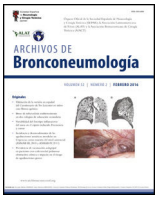

Editorial

Non-tuberculous mycobacteria: beyond the magic mountain☆

Micobacterias no tuberculosas, más allá de la montaña mágica

Tuberculosis (TB) is a disease well known for its morbidity and mortality. It infects millions of people every year and, along with the human immunodeficiency virus (HIV), is one of the leading causes of death worldwide. The incidence of TB has gradually declined in industrialized countries.[1]

In recent years, non-tuberculous mycobacteria (NTM) have taken on new importance, with an increase in the number of isolates in microbiology departments, accounting for 30%–50% of the total mycobacteria.[2]

NTM are a heterogeneous group of bacteria, widely distributed in nature, that can cause various infections in humans, most frequently pulmonary; NTM usually occurs in patients with predisposing factors for disease progression.[3] Geographical distribution varies widely, depending on the microorganism's ability to survive under certain environmental conditions and the capability of local laboratories to isolate and identify these strains.[4]

The definition, diagnosis, and management of NTM infections have been governed since 2007 by the guidelines of the American Thoracic Society/Infectious Diseases Society of America. The epidemiology of the more than 170 species of NTM described is unknown, because identification and sensitivity testing are not performed in all microbiology laboratories, and these infections are not notifiable diseases in most countries. The number of NTM infections appears to be increasing in many parts of the world. In the United States, we know that the number of cases of NTM infections is higher than that of TB. Despite this, research in this area still lags far behind TB, and many issues remain unclarified. It is still unclear why some NTM are pathogenic and others are not, and which environmental or host factors might favor infection, while the natural history of the disease and the best diagnostic and therapeutic procedures remain undetermined.[5]

The epidemiological relationship between *Mycobacterium tuberculosis* complex (MTC) and NTM infections is not yet well understood. Some studies suggest that evidence of local increases in NTM infection rates coincide with the decrease in MTC infection rates. The first hypothesis approaches the question from an immunological point of view, citing a phenomenon of cross-reactivity and immune defects favoring NTM disease, but it has not been possible to demonstrate why both diseases appear in geographically different populations.[6] The second hypothesis is that these entities are unrelated, but have a common link: an improved quality of life is associated with a decrease in MTC infection.[7] Factors related to the increase in NTM have been described, including centralized water supplies,[8] the use of showers that promotes respiratory exposure by aerosol transmission of NTM present in water,[6] some diagnostic and therapeutic procedures (bronchoscopies, dialysis fluids, especially *Mycobacterium chimaera* associated with extracorporeal membrane oxygenation for cardiac support), and cosmetic applications (mesotherapy).[3,9] Finally, it has been proposed that there may be no relationship and the phenomenon is due to a multifactorial process: improved quality of life, increased research and improved diagnostic tests for NTM, an aging population (involving a larger population with structural lung diseases, tumors, HIV, diabetes mellitus and renal failure) and changes in NTM virulence.[10]

The management of both diseases differs from a clinical, microbiological, and public health point of view. The diagnosis of TB in a baciliferous patient involves culture of the patient's respiratory sample and a contact study, an approach that carries both economic and social costs.[11] These measures are not necessary in NTM disease, although precautions must be taken in the case of *Mycobacterium abscessus* in patients with cystic fibrosis, (grade B in the 2017 British Thoracic Society recommendations).[12]

Treatment of mycobacterial diseases has been significantly complicated by increased resistance to the few available antibiotics. In the case of NTM, fewer new drugs are in development than for TB, and those that are, are mostly based on the reformulation or repositioning of other older drugs; some active drugs are also being tested against TB (bedaquiline, inhaled liposomal amikacin, ceftazidime-avibactam).[13]

Microbiological techniques are designed to optimize the detection of MTC and specific studies are only conducted in NTM cases selected for their clinical relevance. The diagnostic possibilities of most microbiology departments have increased with the availability of new technologies. Molecular diagnostic techniques are useful for rapidly differentiating between NTM and MTC diseases when the sputum smear reveals the presence of acid-alcohol-fast bacilli, as culture could take up to 45 days. MALDI-TOF mass spectrometry assists in the correct identification of these microorganisms.[14,15]

Knowledge of the epidemiological situation of NTM disease and its associated clinical factors is crucial to address this public health challenge, and to facilitate early diagnosis and treatment and increase the microbiological yield.[11] To improve this knowledge, we would need to perform molecular studies to differentiate NTM from MTC in baciliferous patients, refer all clinically relevant

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strains to reference laboratories for correct identification and sensitivity studies, and notify clinically relevant cases to the public health authorities.

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