

Latent tuberculosis: the snake inside the egg

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Despite the worldwide effort to control the spread of tuberculosis (Tb), this disease continues to kill approximately 1.3 million people worldwide each year¹. A comparison of this number with the number of people killed by recent natural catastrophes reveals that Tb kills the equivalent of 4.4 Haiti earthquakes or 7 Southeast Asia tsunamis, with one large difference: such catastrophes pass and take years or decades to repeat, but Tb takes its toll almost inexorably, year after year. Brazil is among the 22 countries considered to harbor approximately 80% of all Tb cases worldwide¹⁻⁴.

These numbers convey a clear message to the healthcare and scientific communities, suggesting that the measures taken to control Tb are insufficient. Currently, most of the efforts to control Tb are directed at early diagnosis and adequate treatments for patients with active disease, approach including the Directly Observed Therapy Short-course (DOTS), with the expectation that these efforts will stop the transmission of Tb and eventually reduce the burden of this disease^{1,2,6,7}.

Although extremely important, these strategies have two relevant limitations. First, because approximately one-third of the world's population is already infected with the *Mycobacterium tuberculosis* complex, these infected individuals are already at risk of developing Tb disease, regardless of their contact with an infective person¹. Second, given the insidious nature of disease progression, most infected patients will not seek medical care until weeks, months or even years have elapsed since the beginning of the transmission period. Therefore, a single sputum smear-positive Tb patient is estimated to be able to disseminate the infection to 10-15 close contacts each year^{5,6}. Additionally, even when patients seek medical aid, the diagnosis may not be easily recognized by doctors due to the pleomorphic nature of this disease, resulting in the exposure of both healthcare workers and other patients under medical care to Tb infection^{3,8}.

We believe that it is time to be proactive, exposing and treating latent Tb before it becomes active^{5,6,9}. Among the 2 billion people estimated to harbor Tb worldwide, although most will never develop Tb disease, approximately 10% will develop

Tb disease at an unpredictable time in their lives. Although we do not know exactly who these 200 million people are, we have some important clues^{2,5,6}. We know that *M. tuberculosis* is an obligate intracellular parasite, which means that an adaptive cellular immune response is essential for the host to control the disease. Subsequently, all demographic and clinical conditions that suppress this arm of the immune reaction will enhance the risk of developing active Tb⁶.

Therefore, we can predict that a significant portion of the 10% will comprise children, malnourished individuals, human immunodeficiency virus (HIV)-infected patients, diabetics, patients with liver or kidney failure and users of anti-tumor necrosis factor alpha (TNF α), systemic corticosteroids or other immunosuppressive drugs. Thus, an important strategy for Tb control in the general population will be the identification of latent Tb carriers among those persons which can be accomplished by a tuberculin skin test, an interferon γ (IFN- γ) release assay, a physical examination and a chest radiography, to exclude active disease and evaluate signs of previous pulmonary Tb¹⁰. The treatment of latent Tb with isoniazid, rifampin or both would subsequently reduce the risk of developing active Tb disease by at least 60% for these individuals, which will eventually reduce the risk of transmission in the community¹¹.

It is noteworthy that many different medical specialties are involved in the follow-up of these patients, and thus, we must work in a coordinated manner to expose and reduce this huge one million people each year, despite the availability of a vaccine and inexpensive, effective treatments^{2,6}.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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