

## **Tuberculosis series**

Denise Rossato Silva<sup>1,a</sup>, Fernanda Carvalho de Queiroz Mello<sup>2,b</sup>, Afrânio Kritski<sup>3,c</sup>, Margareth Dalcolmo<sup>4,d</sup>, Alimuddin Zumla<sup>5,e</sup>, Giovanni Battista Migliori<sup>6,f</sup>

Tuberculosis is the leading cause of death from a single infectious agent, ranking above HIV/AIDS. An estimated 10.4 million people fell ill with tuberculosis in 2016, 6.3 million new cases of tuberculosis having been reported. In that same year, there were an estimated 1.3 million tuberculosis deaths among non-HIV-infected individuals and an estimated 374,000 tuberculosis deaths among HIVinfected individuals. The World Health Organization (WHO) End TB Strategy established targets for the 2016-2035 period, including a 90% reduction in tuberculosis-related deaths and an 80% reduction in tuberculosis incidence (new cases per year) by 2030. Globally, the tuberculosis incidence and mortality rates are falling; however, the disease continues to be an important public health issue.(1) Therefore, for the celebration of the World TB Day on March 24th, this issue of the JBP features six articles focusing on tuberculosis, including three editorials and three review articles. This tuberculosis series has the objective of highlighting advances in our understanding of many topics related to tuberculosis.

In 2017, the Brazilian National Ministry of Health issued a document outlining a plan for the elimination of tuberculosis—the Plano Nacional pelo Fim da Tuberculose como Problema de Saúde Pública (Brazilian National Plan to End Tuberculosis as a Public Health Problem)—which was designed with a view toward achieving the goal of reducing, by 2035, the incidence of tuberculosis to < 10 cases/100,000 population and tuberculosis-related mortality to < 1 death/100,000 population. (2) Appropriately, the first editorial in this series is an overview of efforts to eliminate tuberculosis in Latin America. Strategies and approaches have been developed to implement all the three pillars of the WHO End TB Strategy, and the initial results are encouraging.(3-5)

It is well known that the third pillar of the WHO End TB Strategy focuses on intensified research and innovation.(1) The Rede Brasileira de Pesquisas em Tuberculose (REDE-TB, Brazilian Tuberculosis Research Network) is a private, nonprofit nongovernmental organization concerned not only with assisting in the development of new drugs, new vaccines, new diagnostic tests, and new strategies to control tuberculosis but also with the validation of these technological innovations, prior to

their commercialization in the country or incorporation into the Brazilian National Tuberculosis Program. The second editorial provides a general review of the role of the REDE-TB in implementing the WHO End TB Strategy. (6)

The third editorial in this tuberculosis series reports on recently published literature reviews related to the diagnosis and treatment of tuberculosis. (7) In a review article, the tuberculosis series will also address some of the risk factors associated with tuberculosis, including diabetes, smoking, alcohol use, and illicit drug use. Those conditions are associated with tuberculosis infection and the progression to active tuberculosis, as well as contributing to poor tuberculosis treatment results. In addition, tuberculosis can lead to complications in disease course and management of some diseases, like diabetes. It is therefore important to identify these comorbidities in tuberculosis patients in order to ensure better management of both conditions.(8-13)

Another review article will cover tuberculosis in children. Pediatric tuberculosis requires special attention, especially because it represents recent transmission of Mycobacterium tuberculosis and the failure of disease control in the community. Investigation of children suspected of having tuberculosis is difficult, and there is a lack of appropriate diagnostic tools. The treatment of tuberculosis in children is also challenging. (14)

The final article in this tuberculosis series is a review on new and repurposed drugs to treat multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis. Drug-resistant tuberculosis is a growing global health threat. In 2016, there were 600,000 new cases of infection with rifampin-resistant strains, of which 490,000 were cases of multidrug-resistant tuberculosis.(1) The review summarizes what has been achieved to date, as far as new and repurposed drugs are concerned, with a special focus on delamanid, bedaquiline, pretomanid, clofazimine, carbapenems, and linezolid.(15-22)

Therefore, we believe that this tuberculosis series, dedicated to the celebration of the World TB Day, offers a valuable overview of the various aspects of tuberculosis control. We hope that this series will give rise to new ideas for research.

<sup>1.</sup> Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, - UFRGS - Porto Alegre (RS) Brasil.

<sup>2.</sup> Instituto de Doenças do Tórax, Faculdade de Medicina, Universidade Federal do Rio de Janeiro – UFRJ – Rio de Janeiro (RJ) Brasil.

<sup>3.</sup> Programa Acadêmico de Tuberculose, Hospital Universitário Clementino Fraga Filho, Instituto de Doenças do Tórax – HUCFF-IDT – Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro (RJ) Brasil.

<sup>4.</sup> Centro de Referência Hélio Fraga, Fundação Oswaldo Cruz, Rio de Janeiro (RJ) Brasil.

<sup>5.</sup> Division of Infection and Immunity, University College London and NIHR Biomedical Research Centre, UCL Hospitals NHS Foundation Trust, London, United Kingdom.

<sup>6.</sup> WHO Collaborating Centre for TB and Lung Diseases, Fondazione Salvatore Maugeri, Istituto di Ricovero e Cura a Carattere Scientifico – IRCCS – Tradate, Italia.

a. D http://orcid.org/0000-0003-0230-2734, b. D http://orcid.org/0000-0003-3250-6738; c. D http://orcid.org/0000-0002-5900-6007; d. D http://orcid.org/0000-0002-6820-1082; e. D http://orcid.org/0000-0002-5111-5735; f. D http://orcid.org/0000-0002-2597-574X



## **ACKNOWLEDGMENTS**

This paper is part of the European Respiratory Society/ Latin-American Thoracic Association and European Respiratory Society/Brazilian Thoracic Association collaborative projects.

## **REFERENCES**

- World Health Organization [homepage on the Internet]. Geneva: World Health Organization; c2017 [cited 2017 Feb 16]. Global tuberculosis report 2017. [Adobe Acrobat document, 147p.]. Available from: http://www.who.int/tb/publications/global\_report/ gtbr2017\_main\_text.pdf
- Brasil. Ministério da Saúde [homepage on the Internet]. Brasília: o Ministério; [cited 2017 Feb 16]. Brasil livre da tuberculose. Plano nacional pelo fim da tuberculose como problema de saúde pública. 1st ed; 2017 [Adobe Acrobat document, 40p.]. 2017. Available from: http://portalarquivos.saude.gov.br/images/pdf/2017/fevereiro/24/ Plano-Nacional-Tuberculose.pdf
- Lönnroth K, Migliori GB, Abubakar I, D'Ambrosio L, de Vries G, Diel R, et al. Towards tuberculosis elimination: an action framework for low-incidence countries. Eur Respir J. 2015;45(4):928-52. https://doi. org/10.1183/09031936.00214014
- Rendon A, Fuentes Z, Torres-Duque CA, Granado MD, Victoria J, Duarte R, et al. Roadmap for tuberculosis elimination in Latin American and Caribbean countries: a strategic alliance. Eur Respir J. 2016;48(5):1282-1287. https://doi.org/10.1183/13993003.01549-2016
- Duarte R, Silva DR, Rendon A, Alves TG, Rahabi MF, Centis R, et al. Eliminating tuberculosis in Latin America: making it the point. J Bras Pneumol. 2018;44(2):73-76.
- Kritski A, Dalcomo MP, Mello FCQ, Carvalho ACC, Rossato D, Oliveira MM, et al. The role of the Brazilian Tuberculosis Research Network in national and international efforts to eliminate tuberculosis. J Bras Pneumol. 2018;44(2):77-81.
- Mello FCQ, Silva DR, Dalcolmo MP. Tuberculosis: where are we? J Bras Pneumol. 2018;44(2):82.
- Imtiaz S, Shield KD, Roerecke M, Samokhvalov AV, Lönnroth K, Rehm J. Alcohol consumption as a risk factor for tuberculosis: meta-analyses and burden of disease. Eur Respir J. 2017;50(1). pii: 1700216. https://doi.org/10.1183/13993003.00216-2017
- Muñoz-Torrico M, Caminero-Luna J, Migliori GB, D'Ambrosio L, Carrillo-Alduenda JL, Villareal-Velarde H, et al. Diabetes is Associated with Severe Adverse Events in Multidrug-Resistant Tuberculosis. Arch Bronconeumol. 2017;53(5):245-250. https://doi.org/10.1016/j. arbr.2016.10.003
- Muñoz-Torrico M, Caminero Luna J, Migliori GB, D'Ambrosio L, Carrillo-Alduenda JL, Villareal-Velarde H, et al. Comparison of bacteriological conversion and treatment outcomes among MDR-TB patients with and without diabetes in Mexico: Preliminary data. Rev Port Pneumol (2006). 2017;23(1):27-30.
- Altet N, Latorre I, Jiménez-Fuentes MÁ, Maldonado J, Molina I, González-Díaz Y, et al. Assessment of the influence of direct tobacco smoke on infection and active TB management. PLoS One. 2017;12(8):e0182998. https://doi.org/10.1371/journal.pone.0182998
- 12. Slama K, Chiang CY, Enarson DA, Hassmiller K, Fanning A, Gupta P,

- Ray C. Tobacco and tuberculosis: a qualitative systematic review and meta-analysis. Int J Tuberc Lung Dis. 2007;11(10):1049-61.
- Silva DR, Muñoz-Torrico M, Duarte R, Galvão T, Bonini EH, Arbex FF, et al. Risk factors for tuberculosis: diabetes, smoking, alcohol, and the use of other drugs. J Bras Pneumol. 2018;44(2):145-152.
- Carvalho ACC, Cardoso CAA, Martire T, Migliori GB, Sant'Anna CC. Epidemiological aspects, clinical aspects, and prevention of pediatric tuberculosis from the perspective of the End TB strategy. J Bras Pneumol. 2018;44(2):134-144.
- Tiberi S, Sotgiu G, D'Ambrosio L, Centis R, Abdo Arbex M, Alarcon Arrascue E, et al. Comparison of effectiveness and safety of imipenem/clavulanate- versus meropenem/clavulanate-containing regimens in the treatment of MDR- and XDR-TB. Eur Respir J. 2016;47(6):1758-66. https://doi.org/10.1183/13993003.00214-2016
- Tiberi S, Payen MC, Sotgiu G, D'Ambrosio L, Alarcon Guizado V, Alffenaar JVV, et al. Effectiveness and safety of meropenem/ clavulanate-containing regimens in the treatment of MDRand XDR-TB. Eur Respir J. 2016;47(4):1235-43. https://doi. org/10.1183/13993003.02146-2015
- Tiberi S, D'Ambrosio L, De Lorenzo S, Viggiani P, Centis R, Sotgiu G, et al. Ertapenem in the treatment of multidrug-resistant tuberculosis: first clinical experience. Eur Respir J. 2016;47(1):333-6. https://doi. org/10.1183/13993003.01278-2015
- Borisov SE, Dheda K, Enwerem M, Romero Leyet R, D'Ambrosio L, Centis R, et al. Effectiveness and safety of bedaquilinecontaining regimens in the treatment of MDR- and XDR-TB: a multicentre study. Eur Respir J. 2017;49(5). pii: 1700387. https://doi. org/10.1183/13993003.00387-2017
- Dalcolmo M, Gayoso R, Sotgiu G, D'Ambrosio L, Rocha JL, Borga L, et al. Effectiveness and safety of clofazimine in multidrugresistant tuberculosis: a nationwide report from Brazil. Eur Respir J. 2017;49(3). pii: 1602445. https://doi.org/10.1183/13993003.02445-2016
- Tadolini M, Garcia-Prats AJ, D'Ambrosio L, Hewison C, Centis R, Schaaf HS, et al. Compassionate use of new drugs in children and adolescents with multidrug-resistant and extensively drug-resistant tuberculosis: early experiences and challenges. Eur Respir J. 2016;48(3):938-43. https://doi.org/10.1183/13993003.00705-2016
- 21. Tiberi S, Sotgiu G, D'Ambrosio L, Centis R, Arbex MA, Alarcon Arrascue E, et al. Effectiveness and Safety of Imipenem-Clavulanate Added to an Optimized Background Regimen (OBR) Versus OBR Control Regimens in the Treatment of Multidrug-Resistant and Extensively Drug-Resistant Tuberculosis. Clin Infect Dis. 2016;62(9):1188-90. https://doi.org/10.1093/cid/ciw088
- Silva DR, Dalcomo M, Tiberi S, Arbex MA, Munoz-Torrico MM, Duarte R, et al. New and repurposed drugs to treat multidrugand extensively drug-resistant tuberculosis. J Bras Pneumol. 2018;44(2):153-160.