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In the time of strategies to end tuberculosis, prevention is better than treatment

Ana Paula Santos[1,2], Denise Rossato Silva[3], Fernanda Carvalho de Queiroz Mello[1]

In 2015, the World Health Organization (WHO) launched the End TB Strategy, which included among its goals a 95% reduction in the incidence of tuberculosis worldwide by 2030.[1] Achieving that ambitious goal will require early diagnosis and treatment of active disease, in order to interrupt the chain of transmission of *Mycobacterium tuberculosis* (Mtb), as well as preventive measures. The Brazilian National Plan to End Tuberculosis as a Public Health Problem,[2] proposed by the Brazilian National Ministry of Health, also has, among its priorities, preventive treatment against tuberculosis.

Latent tuberculosis infection (LTBI) occurs when a person is infected with Mtb but does not manifest active disease.[3] This condition has been considered a priority because it is key to achieving the goals of the WHO and the Brazilian National Ministry of Health. It is particularly important for health care professionals, who are susceptible to nosocomial Mtb infection and are at risk for LTBI.[4]

The WHO defines health care professionals as people engaged in the promotion, protection, improvement, and care of the health of the population in a given location.[5] The following factors have been associated with a higher risk of LTBI among primary health care professionals in Brazil[6]: being over 50 years of age; not having a BCG vaccine scar; having a history of smoking; working as a nurse, nursing technician, or community health agent; and not having used an N95 mask on a regular basis in the workplace.

In the article by Lima et al.,[7] published in this issue of the *Jornal Brasileiro de Pneumologia*, the authors used the QuantiFERON-TB Gold In-Tube assay (QFT-GIT; QIAGEN, Hilden, Germany) to assess the incidence of LTBI among primary health care professionals in two Brazilian cities with a high incidence of tuberculosis: Vitória and Manaus.

The QFT-GIT is an IFN-gamma release assay (IGRA) and quantifies, through an immunoenzymatic test (ELISA), the levels of this cytokine released by memory T lymphocytes after stimulation of a whole blood sample with Mtb-specific antigens; it is one of two alternatives for the diagnosis of mycobacterial infection, the other being the tuberculin skin test (TST).[3]

The main advantage of an IGRA over the TST is the fact that it is not influenced by previous BCG vaccination or by infection with nontuberculous mycobacteria, which gives the method high specificity. The other advantages are as follows: the simplicity of training for blood collection; absence of the reading bias present in the application of the TST by the health professional; direct testing of a biological sample, which reduces the risk of adverse effects; and the operational advantage of not requiring patients to return for the reading of the result. However, its high cost (in comparison with that of the TST), the need for blood collection, the fact that serial testing in not recommended, and the high frequency of indeterminate results, as well as the need for a well-equipped laboratory and careful handling of the samples to maintain lymphocyte viability, are considered limiting disadvantages.[8]

Lima et al.[7] found that the QFT-GIT conversion rate in the population studied was lower than that reported in other studies involving similar samples; that is, primary health care professionals in countries with a high incidence of tuberculosis.

In addition to the limitations described by the authors, such as the high proportional losses to follow-up and the absence of a gold standard for the diagnosis of LTBI, there is a lack of standardization of the QFT-GIT for conducting serial tests, in view of the possibility of spontaneous conversion and reversal. The QFT-GIT has also been criticized for having such a high cost, which limits its utility in countries with limited resources.

Data on the serial use of IGRAs are scarce, and it must be determined whether the identified conversions were true or whether they reflected only dynamic immunological processes, difficulties in the reproducibility of the test, or simply variations from person to person.[9] In a survey conducted in Canada, the number of QFT-GIT conversions was higher than expected and was not accompanied by a comparable number of TST conversions. In addition, occupational exposures were unrelated to the high number of QFT-GIT conversions, which suggests that these results do not reflect recent Mtb infection.[9]

Regarding the cost and effectiveness aspects, Loureiro et al.[10] found the QFT-GIT to be the test that correctly classified the largest number of individuals with LTBI among professionals at primary health care clinics in Brazil. However, the test had the lowest cost-effectiveness when the authors applied an analytical model, considering a hypothetical cohort.

The Lima et al. study[7] indicates a future application of QFT-GIT in health care professionals: that of identifying conversions after occupational exposure. However, it showed limitations, such as the high proportional losses to follow-up in the sample, as well as questions about the serial use of an IGRA and the use of a method that is still quite costly. However, at a time when the prevention of active tuberculosis has been exalted, the use of alternatives to the TST that are more specific for the identification of LTBI should be seen as imperative,

1. Instituto de Doenças do Tórax, Universidade Federal do Rio de Janeiro – UFRJ – Rio de Janeiro (RJ) Brasil.
2. Hospital Universitário Pedro Ernesto, Universidade do Estado do Rio de Janeiro – UERJ – Rio de Janeiro (RJ) Brasil.
3. Faculdade de Medicina, Universidade Federal do Rio Grande do Sul – UFRGS – Porto Alegre (RS) Brasil.

especially in high-risk populations, who are potential links in the chain of disease transmission. Studies aimed at improving understanding of the serial results of the test, in accordance with the guidelines of the End TB Strategy[1] and the Brazilian National Plan to End Tuberculosis,[2] should be encouraged, as should proposals for improving adherence to the QFT-GIT protocols and for reducing its cost.

REFERENCES

1. World Health Organization [homepage on the Internet]. Geneva: World Health Organization [cited 2019 Dec 26]. The END TB strategy. [Adobe Acrobat document, 20p.]. Available from: http://who.int/tb/End_TB_brochure.pdf
2. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. Plano nacional pelo fim da tuberculose como problema de saúde pública. Brasília: Ministério da Saúde; 2017.
3. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. Protocolo de vigilância da infecção latente pelo *Mycobacterium tuberculosis* no Brasil. Brasília: Ministério da Saúde; 2018.
4. Uden L, Barber E, Ford N, Cooke GS. Risk of Tuberculosis Infection and Disease for Health Care Workers: An Updated Meta-Analysis. Open Forum Infect Dis. 2017;4(3):ofx137. https://doi.org/10.1093/ofid/ofx137
5. World Health Organization [homepage on the Internet]. Geneva: World Health Organization [cited 2019 Dec 26]. Counting health workers: definitions, data, methods and global results. [Adobe Acrobat document, 20p.]. Available from: https://www.who.int/hrh/documents/counting_health_workers.pdf
6. Prado TND, Riley LW, Sanchez M, Fregona G, Nóbrega RLP, Possuelo LG, et al. Prevalence and risk factors for latent tuberculosis infection among primary health care workers in Brazil. Cad Saude Publica. 2017;33(12):e00154916. https://doi.org/10.1590/0102-311x00154916
7. Lima OC, Souza FM, Prado TN, Andrade RLM, Maciel ELN. Analysis of the incidence of latent Mycobacterium tuberculosis infection among primary health care professionals in two Brazilian capitals. J Bras Pneumol. 2020;46(2):e20190201.
8. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Departamento de Vigilância das Doenças Transmissíveis. Manual de Recomendações para o Controle da Tuberculose no Brasil. Brasília: Ministério da Saúde; 2018.
9. Zwerling A, Benedetti A, Cojocariu M, McIntosh F, Pietrangelo F, Behr MA, et al. Repeat IGRA testing in Canadian health workers: conversions or unexplained variability? PLoS One. 2013;8(1):e54748. https://doi.org/10.1371/journal.pone.0054748
10. Loureiro RB, Maciel ELN, Caetano R, Peres RL, Fregona G, Golub JE, et al. Cost-effectiveness of QuantiFERON-TB Gold In-Tube versus tuberculin skin test for diagnosis and treatment of Latent Tuberculosis Infection in primary health care workers in Brazil. PLoS One. 2019;14(11):e0225197. https://doi.org/10.1371/journal.pone.0225197