LETTER TO THE EDITOR

Tuberculin skin test and/or interferon gamma release assay: is it still time to debate?

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Dear Editor,

It seems to be by now ascertained that both tuberculin skin test (TST) and interferon gamma release assays (IGRAs) represent the gold standard to identify latent tubercular infection (LTBI). Nevertheless, in clinical practice, often physicians misunderstand the correct value of both the methods. It must be emphasized that both TST and IGRAs demonstrate host/pathogen interaction between the immune system and Mycobacterium tuberculosis, so they can be positive both in case of LTBI and in case of disease [1]. But it's likewise obvious that the core of undoubted diagnosis of tubercular disease is cultural confirmation. Similarly, there is some confusion about the choice of one or the other test, even considering that often several physicians perform both the tests in the same patient. Such considerations, seemingly clear, aren't always reflected in real life. Therefore, a very useful clarification for clinicians is represented by a recent statement of American Thoracic Society, jointed with Infectious Diseases Society of America, and Centers for Disease Control and Prevention, that points out when, and to which subject, to perform TST and/or an IGRA [2].

First, the key point to be underlined is that it's crucial both the context and the risk of infection: the main recommendation is that individuals at low risk of infection, and/or at low risk of disease pro-

gression, should not be tested for *M. tuberculosis* infection, since the possibility of a false positive result, in such conditions, should be clearly kept in mind, and could influence a clinician's decision to treat. So, in these comditions, it's suggested to perform a second test (either an IGRA or a TST) if the initial test is positive in individuals 5 years or older. When such a procedure is performed, the person is considered infected only if both tests are positive.

Second, clinicians who treat their patients by monoclonal antibodies TNF alpha-antagonists (e.g., dermatologists, gastroenterologists, rheumatologists) must be sure, before starting therapy, that the patient is not affected by LTBI, since, in case of infection, the risk of Tb reactivation could be very high [3]. For this purpose, such kind of patients must be pre-treatment screened for LTBI, by TST, and, in case of a negative result (possible, owing to long term use of corticosteroids and immunosuppressive drugs) by an IGRA test, more sensible, independently of iatrogenic effects [4, 5]. Third, an IGRA test is more advisable than TST in the following cases: subjects 5 years or older with a high risk of infection; subjects with a history of BCG vaccination; subjects with low compliance to return in order to read TST; subjects treated by BCG for bladder cancer [6].

On the other hand, TST is preferable when the individual is a child under 5-years of age with a high risk of infection and/or the socioeconomic context is a low-income one.

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REFERENCES

- [1] Guglielmetti L., Conti M., Cazzadori A., Lo Cascio G., Sorrentino A., Concia E. Diagnostic sensitivity of QuantiFERON-TB Gold In-Tube and tuberculin skin test in active tuberculosis: influence of immunocompromission and radiological extent of disease. *Infez. Med.* 20, 1, 16-24, 2012.
- [2] Lewinsohn D.M., Leonard M.K., LoBue P.A., et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children". *Clin. Infect. Dis.* 64, 2, 111-115, 2017.
- [3] Assante L.R., Barra E., Bocchino M., Zuccarini G., Ferrara G., Sanduzzi A. Tuberculosis of the tongue in a
- patient with rheumatoid arthritis treated with methotrexate and adalimumab. *Infez. Med.* 22, 2, 144-148, 2014. [4] Goletti, D., Sanduzzi A., Delogu, G. Performance of the tuberculin skin test and interferon-gamma release assays: An update on the accuracy, cutoff stratification, and new potential immune-based approaches. *J. Rheumatol.* 91, 24-31, 2014.
- [5] Bocchino M., Bellofiore B., Matarese A., Galati D., Sanduzzi A. IFN-γ release assays in tuberculosis management in selected high-risk populations. *Expert Rev. Mol. Diagn.* 9, 2, 165-177, 2009.
- [6] Silverman M.S., Reynolds D., Kavsak P.A., Garay J., Daly A., Davis I. Use of an interferon-gamma based assay to assess bladder cancer patients treated with intravescical BCG and exposed to tuberculosis. *Clin. Biochem.* 40, 12, 913-915, 2007.