Monaldi Archives for Chest Disease

Monaldi Archives for Chest Disease 2025; 95:3156
doi: 10.4081/monaldi.2024.3156

Novel tuberculosis skin tests for detecting latent tuberculosis infection

Jinish Doshi,[1] Kunal Deokar,[1] Priyanka Gaikwad[2]

[1]Department of Pulmonary Medicine, All India Institute of Medical Sciences, Rajkot; [2]Department of Pediatrics, All India Institute of Medical Sciences, Rajkot, India

Key words: latent TB, tuberculin skin test, C-TB test, Cy-Tb test, diaskintest.

Correspondence to: Jinish Doshi, Department of Pulmonary Medicine, All India Institute of Medical Sciences, Rajkot, India.
E-mail: jinish2209@gmail.com

Dear Editor,

We are impressed by the article titled "Latent tuberculosis diagnostics: current scenario and review" by Gupta *et al*., published in your journal [1]. The authors have reviewed the tests used for the diagnosis of latent tuberculosis (TB) infection and have given a detailed overview of the purified protein derivative (PPD)-based tuberculin skin test (TST) and interferon-γ release assays (IGRA).

We would like to draw attention to the fact that in 2022, the World Health Organization (WHO) also recommended the use of *Mycobacterium tuberculosis* (MTb) antigen-based skin tests for the diagnosis of latent TB (conditional recommendation, very low certainty of evidence). The MTb antigen-based skin tests that have been recommended by WHO include Cy-Tb test, Diaskintest, and C-test. All three tests are ESAT-6/CFP-10-based intradermal tests. The intradermal inoculation results in induration at the local skin site, causing a delayed type of hypersensitivity, which is measured after 48-72 hours [2].

The Cy-TB (erstwhile C-TB) test has been manufactured by Statens Serum Institute (Denmark) and is now being produced and marketed by the Serum Institute of India. 0.1 mL is administered *via* intradermal injection using the Mantoux technique. An induration of more than or equal to 5 mm is considered positive. The Diaskintest has been manufactured by Generium Pharmaceuticals (Russian Federation). Any induration is considered positive. The C-test or creative TST (erstwhile EC-skin test) is manufactured by Anhui Zhifei Longcom Biopharmaceutical Co. Ltd (China). An induration of more than or equal to 5 mm is considered positive.

The pooled sensitivity of the Cy-TB test and Diaskintest against the microbiological reference standard in patients with microbiologically confirmed TB was found to be 78.1%. The specificity of the Cy-Tb test, Diaskintest, and C-test with respect to IGRA has been found to be 98%, 99.1% and 95.5.%, respectively [2]. In patients with active TB, the agreement of Cy-Tb and Diaskintest with IGRA has been found to be 79.8% and 87.16% respectively [3]. They have also been found to be safe and cost-effective [2].

The advantages of the novel TB skin tests include: i) as ESAT-6 and CFP-10 are present only in MTb, the results are not affected by prior BCG vaccination and exposure to environmental non-tuberculous mycobacteria. Hence, all three tests have better specificity than the TST; ii) low cost; iii) lower resource requirement, meaning it does not require state-of-the-art infrastructure; iv) it can be administered by staff who are already trained in administering TST; v) it can be administered in a community setting; vi) it does not require venipuncture.

The disadvantages of the novel TB skin tests include: i) the result has to be interpreted after 48-72 hours, hence it requires follow-up; ii) a cold chain is required for storing the vials; iii) trained personnel are required for administration and interpretation of tests, especially in areas where TST is not routinely performed.

More data with respect to the performance of these tests in HIV-positive individuals, children, and adolescents is needed. Also, exploration of methods to prevent follow-up for interpretation of tests is needed to increase the acceptability of the tests and reduce cases lost to follow-up.

The other novel TB skin test, which is under evaluation, is the DPPD test. It uses a recombinant protein produced from a gene, *Rv0061,* which is present only in MTb. Intradermal inoculation of the protein results in a delayed type of hypersensitivity, causing skin induration. An open-label clinical trial conducted in Brazil showed that the test results correlated with those of PPD-based TST [4]. More data on the DPPD test with respect to its performance in different geographical areas, and different subpopulations, and comparison with IGRA is needed.

References

1. Gupta A, Chandra E, Anand S, et al. Latent tuberculosis diagnostics: current scenario and review. Monaldi Arch Chest Dis 2025;95:2984.
2. WHO. WHO consolidated guidelines on tuberculosis. Module 3: diagnosis. Tests for TB infection. Available from: https://iris.who.int/bitstream/handle/10665/362936/9789240056084-eng.pdf?sequence=1.
3. Krutikov M, Faust L, Nikolayevskyy V, et al. The diagnostic performance of novel skin-based in-vivo tests for tuberculosis infection compared with purified protein derivative tuberculin skin tests and blood-based in vitro interferon-γ release

assays: a systematic review and meta-analysis. Lancet Infect Dis 2022;22:250-64.
4. Badaro R, Machado BAS, Duthie MS, et al. The single recombinant M. tuberculosis protein DPPD provides enhanced performance of skin testing among HIV-infected tuberculosis patients. AMB Express 2020;10:133.

Received: 28 July 2024; Accepted: 16 September 2024; Early view: 4 November 2024.

Contributions: Jinish Doshi, Kunal Deokar: idea conception; Jinish Doshi, Priyanka Gaikwad: literature search; Kunal Deokar, Priyanka Gaikwad: manuscript preparation; Kunal Deokar, Jinish Doshi, Priyanka Gaikwad, manuscript revision.

Conflict of interest: the authors declare no potential conflict of interest.