T CELL-BASED DIAGNOSIS OF TUBERCULOSIS INFECTION

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Diagnosis and treatment of latent TB infection is a cornerstone of TB control in developed countries which, until now, has relied on the century-old tuberculin skin test. The first clinically significant output of basic science TB research is T cell-based diagnosis of TB infection. These new blood tests measure the T cell interferon-gamma response to two *M. tuberculosis* antigens as a marker of infection. The absence of these proteins from BCG gives the new tests higher diagnostic specificity than the skin test by avoiding false-positive results due to the antigenic cross-reactivity of tuberculin PPD with BCG. Diagnostic sensitivity hinges on the read-out for measuring T cell responses: whole blood ELISA or enzyme linked immunospot (ELISpot). However, the absence of a gold standard for latent TB infection precludes direct quantification of diagnostic sensitivity. Correlation of test results with TB exposure (the key determinant of *M. tuberculosis* transmission) and extrapolation of test performance in active TB have therefore been used as surrogates. On these measures, ELISpot has higher sensitivity than the skin test, especially in HIV co-infected people and young children, while ELISA and skin test seem to have similar sensitivity, although published data are limited. Control of latent TB infection targets people at high risk of progression to TB, which includes all recently infected contacts and people with suppressed or immature (i.e. young children) cellular immune systems. The future impact of the new tests therefore depends critically on their performance in these vulnerable groups and will be discussed in the context of recent European guidelines. The role of the new tests to improve diagnostic evaluation of patients with suspected active TB will also be reviewed and discussed.