Reviewer's report

Title: T-cell-based diagnosis of tuberculosis infection in children in Lithuania: a country of high incidence despite high bacille Calmette-Guerin vaccination coverage

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Reviewer: Neil Schluger

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The manuscript by Hanstead et al. describes the results of a study comparing TST and T.SPOT results in a cohort of children ages 10-17 with either confirmed active tuberculosis, or in groups felt to be at high or low risk for latent tuberculosis infection. This report is from Lithuania, a moderate prevalence country for tuberculosis in which BCG vaccination is routinely administered. The authors report that there was excellent correlation between the two tests in patients with active tuberculosis, but that in other groups, correlation was poor, with far more children having positive TST than T.SPOT tests. In addition, the authors report that in a subset of patients with active tuberculosis, the number of spots in the T.SPOT assay declined with successful treatment. The authors conclude from these results that T.SPOT is at least of equal sensitivity to TST and of far greater specificity.

The study is consistent with the results of many other studies of this type, and it adds useful and much needed data on the performance of interferon gamma release assays in younger populations. However, the study is also subject to the same limitations affecting many studies of this type, and the manuscript could be strengthened if several points were addressed.

Major comments:

1. At what age do children in Lithuania receive BCG vaccine? Are all routinely vaccinated at birth? Are any children given booster doses of vaccine during the teenage years? If age of vaccination was different among children in the cohort, did the age of vaccination have an effect on the skin test result in the two groups without bacteriologically confirmed active tuberculosis?

2. Is there any way that the patients in the “high risk for TB” group could be further stratified to assess the performance of the two tests under consideration? Could the source cases be identified as have 1+, 2+, 3+, of 4+ positive sputum smears, for example? If this was done could it affect the interpretation of the results, i.e. if all the positive T.SPOT tests were in children who were contacts of 4+ smear positive cases, the interpretation of the authors regarding the specificity of the test would be stronger.

3. Is there any follow-up information available about children in the high risk group (or low-risk group) who were not treated for latent infection? Did any of
them develop active tuberculosis? If so, how was active tuberculosis defined? Did any of the children who developed active tuberculosis have either a positive TST or T.SPOT test? Did either test more accurately predict the development of active tuberculosis?

Minor comments:

1. The cases of active tuberculosis in group 1 are listed as bacteriologically confirmed. Were all cases pulmonary cases?

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests