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Author/s:
Volkman, T;Graham, H;Laemmle-Ruff, I;Tosif, S;Tebruegge, M;Ranganathan, S;Curtis, N

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Tosif Shidan (Orcid ID: 0000-0003-0022-1009)

Interpretation and management of discordant TST and IGRA results in children

Letter to the Editor

Authors: Thomas Volkman (1,2), Hamish Graham (corresponding author) (1,3), Ingrid Laemmle-Ruff (3), Shidan Tosif (1,3), Marc Tebruegge (3,4,5), Sarath Ranganathan (1,3), Nigel Curtis (1,3).

Affiliations

1 – Murdoch Children's Research Institute, Royal Children's Hospital Melbourne, Parkville, Victoria, Australia

2 – Paediatrics Department, Cairns Hospital, Cairns, Queensland, Australia.

3 - Department of Paediatrics, The University of Melbourne, Royal Children's Hospital Melbourne, Parkville, Victoria, Australia

4. Department of Infection, Immunity & Inflammation, UCL Great Ormond Street Institute of Child Health, University College London, London, UK.

5. Department of Paediatric Infectious Diseases & Immunology, Evelina London Children's Hospital, Guy's and St. Thomas' NHS Foundation Trust, London, UK.

There are no reported conflicts of interest

Corresponding author: Hamish Graham, Department of Paediatrics, University of Melbourne, Royal Children's Hospital Melbourne, 50 Flemington Road, Parkville, Victoria, Australia. Hamish.Graham@rch.org.au +61 3 9345 6262.

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Dear Editor,

Re: Tuberculin skin test versus interferon-gamma release assay in refugee children: A retrospective cohort study. Elliot et al.

We read with interest the retrospective analysis by Elliot et al. [1] comparing the results of tuberculin skin test (TST) and QuantiFERON Gold In-Tube assays (QFT-GIT) in refugee background children. Interpretation of TST and interferon-gamma release assays (IGRA) is a perpetual challenge for those working in child tuberculosis (TB) and immigrant health services, and we commend the authors' attempt to provide guidance. However, we have a different interpretation of the study findings and the implications for practice and policy.

As highlighted by the authors, discordant results are common and problematic. This study suggests that clinicians in the Illawarra-Shoalhaven region place greater weight on the result of IGRA than TST results. The majority (87.2% (41/47)) of TST+/IGRA- discordant children were not offered preventive therapy, compared with 12.5% (2/16) of TST-/IGRA+ patients. This indicates an assumption that TST+/IGRA- discordance reflects false-positive TST results (due to prior BCG vaccination or non-tuberculous mycobacterial exposure) rather than false-negative IGRA (due to imperfect sensitivity). We recognise that the decision to treat was primarily based on clinician perception of risk in this observational study.

However, false-positive TSTs related to BCG vaccination are uncommon. A meta-analysis of more than 240,000 subjects vaccinated with BCG in infancy (as is common for immigrant children in Australia), found that only 8.5% had a positive TST result attributable to BCG vaccination, and that the effect of BCG on TST results waned quickly over time [2]. Furthermore, immunological studies provide strong evidence that a significant proportion of TST+/IGRA- discordant patients are in fact infected with *M. tuberculosis* [3].

As the authors note, there is no gold standard for TB infection. Therefore, using IGRA as a standard against which to assess TST sensitivity is inappropriate. TST and IGRA are both imperfect screening tests for TB infection and there is compelling evidence for the limited sensitivity of IGRA in both active TB disease and latent TB infection (LTBI) [4]. The limitations of IGRA are particularly relevant for infants and young children [5], and national and international guidelines therefore continue to advise the use of TST in preference to IGRA for screening children under 5 years of age [6]. Discordant results in this age group, especially those children who have received BCG at birth, is especially problematic given that they will potentially benefit the most from preventive therapy, as they have the highest risk to progress to active TB disease

Missing LTBI and thereby the opportunity to provide preventive therapy has far greater implications in children than adults, as they are more likely to develop TB disease, especially severe disease. Based on the current evidence, the safest option for managing children with a positive IGRA or TST, including those with discordant results, is to offer preventive therapy.

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