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In reply to 'Interferon-gamma release assays have suboptimal sensitivity in both latent and active tuberculosis'

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We thank Goetzinger et al. for their interest and comments about our work.¹ They raise a number of valid points about the suboptimal performance of interferon-gamma release assays (IGRAs) in the diagnosis of tuberculous infection in pediatric populations. The tuberculin skin test (TST) and IGRA tests have known limitations for the diagnosis of latent tuberculous infection (LTBI).² We propose, as suggested by Goetzinger et al., that these tests should be interpreted in the full clinical context.

The sensitivity and specificity of TST or IGRA are the operating characteristics of these tests, and on their own, they cannot establish a diagnosis of infection or disease. Sensitivity indicates the probability of a positive result in an infected individual, but what the clinician seeks is the probability of infection given a positive test result. A positive result, however, may be either a true- or a false-positive. The optimal way to interpret diagnostic tests is to integrate these operating characteristics with the prior belief about infection in a Bayesian framework, whereby the prior belief is modified by the results of the test.³ If this modified belief surpasses a clinical threshold, then one concludes that infection is present and takes appropriate action.

In the case of tuberculous infection, prior belief about infection will be influenced by factors, including the age of the child, their exposure history, whether or not BCG-vaccinated and time of vaccination, clinical examination results, country of birth, and prevalence of tuberculosis (TB) in the local setting, among other possible risks. If the clinician believes that the likelihood of infection is high, as in a child in household contact with a TB index case, then a negative IGRA test despite a positive TST (e.g., TST ≥ 10 mm) result would not change the clinical suspicion of tuberculous infection. Similarly, if the prior belief is low because there are no major risk factors for tuberculous infection, then a positive TST or IGRA test may not be enough evidence to update the previous assessment and decide the child has LTBI.

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Conflicts of interest: none declared.

We concur with the authors that because of its limited sensitivity in children, IGRA tests should not be used to rule out infection. Relevant clinical information must be considered in context when making the diagnosis of LTBI and offering preventive therapy.

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