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Differences in BCG vaccination and tuberculin skin-test positivity

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We read with interest the Article by Lei Gao and colleauges,1 who estimated the prevalence of latent tuberculosis infection in rural populations in China by use of the tuberculin skin test and an interferon-γ release assay (QuantiFERON [QFT]). A key finding from the study was that in two of the four geographical sites (sites A [eastern China, plains] and C [western China, hills]), the prevalence of tuberculin skin test reactions of 10 mm or larger was much higher than QFT positivity, whereas the measurements in both tests were very similar at the other two sites (sites B [central China, plains] and D [western China, basin]). The authors1 attributed this discordance to BCG vaccination and non-tuberculous mycobacteria (NTM) exposure, and suggested that the prevalence of latent tuberculosis infection in China might be overestimated by tuberculin skin tests (28%) compared with QTF (19%), because QTF results correlated better with clinically confirmed or suspected pulmonary tuberculosis.

However, we argue that these explanations are unlikely for several reasons. First, site A had the lowest number of BCG vaccinated participants, yet showed the highest positivity rates with the tuberculin skin test, and lowest QFT rates. Conversely, site B that had the highest number of vaccinated participants showed very similar tuberculin skin test and QFT positivity rates. Second, the authors1 postulate that the high skin-test positivity result at site A might be due to NTM infections. However, available evidence shows that the effect of NTM on tuberculin skin test reactions of more than 10 mm is extremely low.2 Moreover, in 2012 a study on the prevalence of NTM in a coastal province of east China reported very low isolate rates of NTM (1·6%).3

We suggest that regional differences in BCG vaccination programmes, especially age of vaccination or revaccination, could account for the differences between tuberculin skin test reactivity and response to interferon-γ release assays. Consistent evidence shows that with the BCG vaccine administered at birth (or early during infancy) has a minimum effect on tuberculin skin test specificity, especially if the tuberculin skin test is administered 10 years or more after vaccination.2,4 By contrast, if the BCG vaccine is given after infancy or with booster shots, tuberculin skin test specificity is compromised, an effect that can persist for more than 20 years.

Therefore, one might speculate that in this study,1 the sites that showed large differences in positivity rates between the tuberculin skin test and QTF included participants vaccinated at

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an older age (≥20 years). Details about the BCG vaccination programmes for every study site, particularly age distribution of vaccination and revaccinations in addition to agreement between QFT and tuberculin skin test according to tuberculin skin test cutoff values and BCG vaccination status, would be informative. Since both tuberculin skin test and QFT measure cumulative lifetime exposure, analysing the association of positive tests with notification rates of tuberculosis over the past 40 years in the four areas would be important.

In conclusion, we believe that the study by Gao and colleagues1 provides a unique opportunity to further investigate the effect of BCG vaccination policies and trends in tuberculosis notification rates on tuberculin skin test results.

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