

The Tuberculin Skin Test and Risk of Tuberculosis: Size Is Not the Only Issue

To the Editor: We read with interest the excellent articles by Salinas et al¹ and Alsedà and Godoy² recently published in *Archivos de Bronconeumología*. As in other studies undertaken in Spain,³ both establish that in contact investigation of tuberculosis cases the trend is toward finding new diagnoses of tuberculosis as the diameter of the tuberculin induration increases.¹⁻³ However, we should like to comment on a recent study we have carried out.

We evaluated 742 contacts of patients with tuberculosis, in accordance with the guidelines of the Spanish Society for Pulmonology and Thoracic Surgery (SEPAR).^{4,5} All tuberculin skin test reactions of 5 mm or greater were therefore considered positive for the unvaccinated group and for vaccinated individuals who had close or frequent contact with smear-positive cases. Similarly, all indurations of 14 mm or more were considered positive for the remaining vaccinated subjects. All individuals with a negative tuberculin skin test, including the vaccinated group and subjects aged over 65 who had been retested within 7 to 10 days, were tested after 12 weeks. A chest radiograph and microbiologic studies of sputum were carried out on all contacts who were immunodeficient or symptomatic if a positive tuberculin skin test was detected by a physician experienced in treating tuberculosis. Tuberculin skin tests were performed by nurses with considerable experience in contact tracing who, in accordance with recommendations,⁵ recorded the size of the induration and also vesicular or necrotic reactions on the surface of the wheal caused by the test. This assessment was made before the results of the radiologic and microbiologic studies were known.

Tuberculin skin tests were positive for 280 contacts (37.7%), of whom 266 were persons with tuberculosis infection and 14 (1.9%) were persons with tuberculosis disease. Forty-seven (16.8%) had vesicles, bullae, and necrosis, and 37 were cases of tuberculin conversion. The mean (SD) induration diameter was 13.0 (4.9) mm for the infected individuals and 13.5 (3.1) mm ($P=.6$) for the patients with tuberculosis disease. The Table sets out the tuberculin skin test results, classified into 3 levels according to induration size. Tuberculin reactions involving vesicles or necrosis were found in 6 patients with active

disease (42.9%) and in 41 infected individuals (15.4%) ($P=.007$). After adjustment by logistic regression, the presence of vesicles or necrosis remained an independent predictor of tuberculosis (odds ratio, 3.3; 95% confidence interval, 1.0-10.4; $P=.03$).

Although in our study we found tuberculin skin test reactions of 10 mm or more for the patients with active disease compared with the infected individuals (92.9% versus 75.6%), these differences were not significant ($P=.13$), unlike in the aforementioned studies. This might be attributable to the fact that the size of our series was smaller than in other studies, in which several thousand contacts were included.¹⁻³ However, other authors have also found no relation between the diameter of the induration and the presence of illness or infection.⁶ Vidal et al³ also failed to find any correlation when they considered only the proportion of individuals with a reaction of at least 14 mm.

In the light of these findings, we believe that vesiculation or necrosis in reaction to a tuberculin skin test for contacts of patients with tuberculosis is not as uncommon as some authors have reported⁷ and this should be considered in studies of this kind, as it is likely to increase the specificity of the test.⁵ When 2 individuals have a reaction of the same diameter, the presence of vesicles or necrosis can increase the probability of active tuberculosis. However, after searching the MEDLINE database, we found no evidence of similar studies having specifically analyzed this aspect to support our results. When indurations were biopsied in a very recent study, bullae were mentioned in the histopathologic reports in 7 of the 30 cases of active tuberculosis.⁸ However, none were found in the 18 cases of latent tuberculosis and the microscopic findings of the biopsy were significantly different between the patients with active disease and those without. As with the proposal that larger indurations are more likely to arise from a true infection, while a higher percentage of smaller reactions could be attributable to mycobacterial infections or antituberculosis vaccination,¹⁻³ much the same can occur with vesicular tuberculin reactions. Similarly, it is more likely that large and very large tuberculin reactions are attributable to more recent infections, with the greater risk of subsequently developing the disease.²

Although the diameter and appearance of the skin reaction are important at the time of study for predicting the risk of presenting and developing tuberculosis in the future, we should not forget that many other factors are involved, such as intensity of contact and the presence of bacilli in the respiratory secretions of the index case, in addition to the age and risk factors of the contact. These factors should also be considered when tracing the contacts of patients with tuberculosis.¹⁻⁵

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TABLE
Tuberculin Skin Test Results, Classified Into 3 Levels, in Individuals With Tuberculosis Infection and Persons With Tuberculosis Disease

Diameter of the Tuberculin Skin Test Reaction, mm	Infected Individuals (n=266)	Individuals With the Disease (n=14)	P
5-9	65 (24.4%)	1 (7.1%)	.19
10-14	96 (36.1%)	7 (50.0%)	.29
≥15	105 (39.5%)	6 (42.9%)	.85