**Introduction**

Individuals infected with *Mycobacterium tuberculosis* develop a delayed immune response to tuberculin testing. This reaction causes a small swollen area, or induration, to appear at the site of the skin test. To determine whether a test result is negative or positive, the size of the induration...
is measured in millimeters. According to the consensus guidelines for the control of tuberculosis in Spain, a positive reaction is considered to be an induration of 5 mm or greater in individuals who have not been vaccinated against tuberculosis and in patients with pulmonary and/or extrapulmonary disease and in persons with tuberculosis infection who are at greater risk of developing active disease.2,20

The aim of this study was to analyze tuberculin reaction size in contacts with positive tuberculin skin test results and to study the association between reaction size and contact age, infection risks (degree of contact with the index patient and bacteriologic confirmation of disease in the index patient), and presence of tuberculosis disease in the contact. Patients and Methods

We reviewed contact investigation records covering a period of 7 years from the Tuberculosis Prevention and Control Center of Lleida, Spain. Contacts were defined as having tuberculosis if they met at least 1 of the following criteria: a) bacteriologic confirmation of M tuberculosis (positive sputum smear and/or culture), b) histologic findings (granulomas with caseous necrosis) in biopsy specimens in a compatible clinical picture, and c) clinical radiographic signs of tuberculosis disease and improvement attributable to anti-tuberculosis treatment. Patients with pulmonary and/or extrapulmonary disease were included in the contact investigation.

Persons who had been named by index patients as being in repeated and prolonged contact with them were included in the contact investigation. For the purpose of this study, we defined close contacts as persons who lived in the same household as the index patient or who had a close relationship with them; casual contacts were those who did not meet either of those criteria.

All the contacts analyzed had been given a Mantoux tuberculin skin test consisting of an intradermal injection of 0.1 mL of purified protein derivative (PPD) containing 2 units of PPD-RP23 with Tween 80. Between 48 and 72 hours after the injection, the skin induration was measured across the forearm as the diameter in millimeters, using the palpation method. An induration size of 5 mm or greater was considered to be a positive test result. The presence of active disease was later determined by chest radiographs, and in some cases, by a microbiologic study of respiratory secretions.

Contacts with a positive tuberculin skin reaction were included in the study although anyone who had been vaccinated against tuberculosis was excluded to avoid an interference effect. Contacts were considered to have been vaccinated if they could provide documented proof of the vaccination or had a visible scar.

We analyzed the association between reaction size in contacts with a positive skin test result and the following variables: contact age, tuberculosis transmission risk variables (degree of contact with the index patient and index patient’s sputum smear result), and presence of active disease in the contact. Reactions were classified into 3 size categories: 5 to 9 mm, 10 to 14 mm, and 15 mm or greater. Associations were analyzed using the χ² test for linear trend and statistical significance was set at a value of P less than .05.

Results

We reviewed the contact investigation records for 437 cases and studied a total of 2365 contacts. Of these, we excluded 277 (11.7%) because they had been vaccinated against tuberculosis and a further 5 because a skin test result could not be obtained. Of the remaining 2083 patients, 768 (36.9%) had a positive tuberculin skin test result and 34 (1.6%) were newly detected cases. Diagnosis of 6 of the 34 new cases was confirmed microbiologically. The mean (SD) age of the 768 contacts included in the study was 39.2 (20.3) years; 361 (47%) were men. Of the 766 contacts for whom degree of contact was known, 438 (57.2%) were close contacts, and of the 689 contacts of index patients for whom sputum smear test results were available, 517 (75%) had positive respiratory specimens.

The distribution curve for induration diameters showed that the largest percentage of patients (23.8%) had reactions measuring 15 to 19 mm; 22.1% had reactions 10 to 14 mm in diameter, and 19.1% had indurations 20 to 24 mm in size. The remaining size categories had percentages under 10%, except for the 5 to 9 mm range, in which 14.1% of the contacts were placed (Figure 1).

Reactions of 15 mm or greater were most common in contacts under 15 years of age: 6.5% of the contacts in this age group compared to 16.4% in the 15 mm or greater range (P=.029) (Table 3). No new tuberculosis cases were diagnosed in contacts with reactions of 5 to 9 mm. The percentage of new cases detected among patients with indurations 10 to 14 mm in diameter was 4.7% (8/170) and 5.3% in those with reactions measuring more than 15 mm (P=.029) (Table 3).

Discussion

Reaction size was 10 mm or greater in the majority (85.9%) of the 768 contacts with positive tuberculin skin

Figure 1. Distribution of induration diameters in contacts with positive tuberculin skin test reactions.
Tuberculin reaction size in tuberculosis patient contacts

disease.

diameter was not correlated with a greater risk of active

study that found larger reactions in this age group.19 These observations could be due to a greater prevalence of recent infection, as infection through direct contact with 

found that induration size was greater in contacts under 

contacts with a reaction of 10 mm or greater increased with age only up to 59 years. This incidence of infection by atypical mycobacteria in the study area and a decrease 

indurations are probably caused by 

Because the index patient’s sputum smear result and 

degree of contact between the patient and the contact are very closely correlated to tuberculosis transmission.25-31 we decided to analyze these 2 variables as one. We found 

that the percentage of close contacts of sputum-

All the new tuberculosis cases detected in our study population occurred in contacts with a reaction of 10 mm or greater. A similar study to ours which analyzed 3071 tuberculosis contacts also found that the number of new cases tended to increase with tuberculin reaction size.32 They reported a new case incidence of 7.8% in the 5 to 9 mm range, 11.9% in the 10 to 14 mm range, and 14.7% 

in the 15 mm or greater range.

A greater incidence of tuberculosis disease in individuals with larger reactions was also reported by 2 international controlled trials in community settings.27,34 Those studies found that the difference in the incidence of new cases was greater between individuals with reactions of 5 to 9 mm and 10 to 14 mm than between 

To explain these findings, it has been suggested that larger inductions are probably caused by 

mycobacteria or by vaccination. It is also worth noting that larger reactions are more likely to be due to recent infection and, as such, are associated with a greater risk of developing the disease.

Contradictory findings, however, were reported by a study conducted in 2 populations: close/household contacts of patients with active tuberculosis and patients that had participated in a study of pulmonary tuberculosis diagnosis.24 The authors concluded that larger reaction size in individuals with inductions greater than 5 mm in diameter was not correlated with a greater risk of active disease.

A greater incidence of tuberculosis disease in contacts under 15 years of age diagnosed with tuberculosis disease and who were close contacts of index patients with positive sputum smears increased with 

diagnosis.35 The authors concluded that larger reaction 

participated in a study of pulmonary tuberculosis 

and patients that had 

infection and, as such, are associated with a greater risk 

of developing the disease.

mycobacteria or by vaccination. It is also worth noting 

infection and smaller ones by nontuberculous 

reacted in different age groups of the general population 

as part of an epidemiological surveillance program. In 

their study, the percentage of reactions measuring 15 mm 

or greater increased with age only up to 59 years. This 

incidence of infection by atypical mycobacteria in the 

area and a decrease in infection by 

M tuberculosis.

The above findings indicate that tuberculosis contact 

investigations should be prioritized according to cost-

effectiveness. The key to success can be found in the 

application of the concentric circle strategy in an 

appropriate, timely and systematic manner.14 With regard 

to the second aim of our study, we found that larger 

reactions in contacts with positive tuberculin skin test 

results were associated with recent infection (which 

carries a greater risk of developing into active disease), 

a greater exposure to infection (close contact with an 

index patient with a positive sputum smear), and a 

diagnosis of tuberculosis disease in the contact during 

the investigation.

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<table>
<thead>
<tr>
<th>Sex</th>
<th>Positive Tuberculin Reaction</th>
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<tbody>
<tr>
<td>Male</td>
<td>165</td>
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<tr>
<td>Female</td>
<td>224</td>
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</table>

### TABLE 3

**Association Between Diagnosis of Tuberculosis Disease With Size of Tuberculin Reaction in Contacts With Positive Skin Test Results**

<table>
<thead>
<tr>
<th>Tuberculin Reaction Size, mm</th>
<th>No.</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>5-9</td>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td>10-14</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td>≥15</td>
<td>26</td>
<td>100</td>
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</tbody>
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### TABLE 1

**Association Between Age and Tuberculin Reaction Size in Contacts With Positive Tuberculin Skin Test Results**

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Variables</th>
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<tr>
<td>&lt;15</td>
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<tr>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>tuberculin reaction size, mm</td>
<td></td>
</tr>
<tr>
<td>5-9</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>101</td>
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<td>10-14</td>
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<td></td>
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<td>≥15</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>409</td>
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### TABLE 2

**Association Between Positive Tuberculin Skin Test Result in Contacts Living With Index Patients With Positive Sputum Smears and Tuberculin Reaction Size**

<table>
<thead>
<tr>
<th>Tuberculin Reaction Size, mm</th>
<th>Close Contact With Index Patients With Positive Sputum Smears</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>5-9</td>
<td>36</td>
</tr>
<tr>
<td>10-14</td>
<td>58</td>
</tr>
<tr>
<td>≥15</td>
<td>207</td>
</tr>
</tbody>
</table>

*χ² test for linear trend, P<0.05.
REFERENCES


ALSEDA MÉT AL. TUBERCULUS REACTION SIZE IN TUBERCULOSIS PATIENT CONTACTS