Predictive Value of Tuberculin Induration at 24 h in Healthy Schoolchildren

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Summary

Tuberculin (1 TU PPD RT23 Tween 80) was administered to 500 healthy schoolchildren, aged 5–9 years. The induration at 24 h was compared with that at 72 h. The mean (standard deviation) induration of the tuberculin reaction at the end of 24, 48 and 72 h was 4.5 (6.75), 4.4 (7.11) and 4.0 (6.91) mm, respectively. When the tuberculin reaction was 0–9 mm, a significant difference was noted between the 24- and 72-h reading ($p = 0.0001$). There was no difference in the size of the tuberculin reaction between the 24- and 72-h readings when the reaction size was $\geq 10$ mm ($p > 0.05$). Considering a tuberculin induration of < 10 mm as negative tuberculin reaction for our reference population in South India, the sensitivity, specificity, positive predictive value and the negative predictive value in our study for the 24-h reading were found to be high. The predictive value of 24-h induration was not affected by age. Reading and interpretation of tuberculin test after 24 h needs due consideration in clinical practice.

Introduction

The tuberculin test is the standard method for detecting *Mycobacterium tuberculosis* infection, with a positive test (in most circumstances) signifying infection. Conventionally, the tuberculin reaction is read after 48 or 72 h. This results in delay in the diagnosis of infection. Strict adherences to these time limits often result in prolonged hospitalization, delayed test placement, or patients interpreting their own results. Schutze, *et al.* had assessed the impact of tuberculin screening of all children during hospitalization for acute medical care and reported that nearly 30 per cent of the children were discharged before a 48-h evaluation. In our hospital, we noted that nearly 70 per cent of children screened at the outpatient department did not report for reading of the tuberculin test at 72 h (unpublished data). The present study was undertaken to study if the 24-h reading was similar to the 72-h reading. The predictive value of 24-h induration, and the influence of age and BCG scar status on the test result were also studied in these children.

Materials and Methods

This prospective cross-sectional study was conducted in four schools in the Union Territory of Pondicherry, India from September 1997 to March 1999. Written permission was obtained from the concerned authorities before the study was undertaken. All children from I to IV standard in the age group 5–9 years were included in the study. The age of the child was obtained from birth records (school admission register). The children were examined for the presence of a BCG scar and were then given the Mantoux test on the volar surface of left forearm with one TU PPD RT23 Tween 80 (BCG laboratory, Guindy, Chennai). Twenty-four hours after placement of the skin test, the maximum transverse diameter of induration was measured with a transparent plastic ruler using the pen method. The measurement of the readings was blinded by recording the readings on each day on different forms (to avoid observer bias). The data regarding the measurements were pooled together only at the end of the period of data collection. While recording the measurements, the observer was unaware of the previous day readings. At 48 and 72 h, second and third measurements were done using the same method. Children who had any clinical evidence of tuberculosis or who were receiving antituberculosis therapy were excluded from the study. Analysis of the results was done using the analysis of variance. The validity and predictive accuracy of 24-h tuberculin reading as a test as compared to the 72-h reaction was identified using the $2 \times 2$ contingency table.

Results

Out of 523 children recruited in the present study, tuberculin induration was read in 500 children. The study population included 267 female and 236 male
children. Seventy-nine per cent of the study children had a BCG scar.

Children with induration ≥ 10 mm at 72 h were considered to be tuberculin positive. Out of the 500 children, 93 (18.6 per cent) were tuberculin positive. Among those with a positive reaction, 77.4 per cent had a BCG scar. The frequency distribution of the tuberculin is given in Fig. 1.

The majority of children (360) had an induration of 0–4 mm at 24 h, which was almost the same (353 children) at the end of 72 h. Many of the children who had induration of 0–9 mm at 24 h continued to exhibit a similar reaction at 72 h (410 and 367 children respectively—89.5 per cent). Similarly, a high proportion of children who had an induration of ≥ 10 mm at 24 h (90 children) remained so at 72 h (87 children) (Table 1). The mean (standard deviation) induration of the tuberculin reaction at the end of 24, 48 and 72 h was 4.5 (6.75), 4.4 (7.11) and 4.0 (6.91) mm, respectively. The differences were not statistically significant ($p > 0.05$).

When the individual values were compared, it was found that there was no difference in the size of the tuberculin reaction at 24 and 72 h, provided the reaction was ≥ 10 mm ($F = 0.22, p > 0.05$). The size of the tuberculin reaction at 24 and 72 h were similar irrespective of the BCG status of the child. The positive and negative predictive value for a tuberculin induration of ≥ 10 mm was estimated as 96.7%.

**Fig. 1.** Frequency distribution of tuberculin reaction at 24, 48 and 72 h with internal correlation. The three columns in the groups 0–4 mm, 5–9 mm and 10+ mm indicate the number of children at 24, 28 and 72 h in the respective groups in the same order.

<table>
<thead>
<tr>
<th>Induration of the corresponding children at 72 h (mm)</th>
<th>No. of children at 24 h</th>
<th>Induration of the corresponding children at 72 h (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>360</td>
<td>353</td>
</tr>
<tr>
<td>5–9</td>
<td>50</td>
<td>31 14 5</td>
</tr>
<tr>
<td>10+</td>
<td>90</td>
<td>0 3 87</td>
</tr>
</tbody>
</table>

**Table 1.** Relationship of 24-h reading to results at 72 h
and 99.5 per cent, respectively. In children who had an initial reaction of 0–9 mm, there was significant difference between the individual readings ($F = 24.9$, $p = 0.0001$). However, the sensitivity and specificity of 0–9 mm induration at 24 h in predicting a negative reaction at 72 h was 99.3 per cent and 93.6 per cent, respectively, with a positive predictive value of 98.5 per cent and a negative predictive value of 96.7 per cent. Such a high sensitivity, specificity, positive predictive value and negative predictive value was also seen when the study population was divided into two different age groups, 5–6 years and 7–9 years, as shown in Table 2. Hence it can be concluded that a 24-h reading can be used to predict the tuberculin status as positive or negative, irrespective of the initial tuberculin induration or age of the child.

### Discussion

Current recommendations suggest that a tuberculin skin test should be read 48–72 h after administration. The rationale for this recommendation is based on dermal perivascular infiltrates and cellular movements, which occur in sensitized individuals in response to intradermal injection of tuberculin. This reaction is a variant of the type IV hypersensitivity and is characterized histologically by the initial accumulation of neutrophils (within 1–2 h) with sequential replacement by monocytes and lymphocytes commencing by 12 h and peaking by 48 h. However, recent clinical studies with purified protein derivative have shown that different timed reactions occur following intracutaneous injection of tuberculin. These include an immediate wheal and flare reaction, an erythematous reaction peaking at 6–8 h, a delayed reaction maximal at 24 h, and a further delayed reaction maximal at 48–72 h, and are possibly caused by species-specific mycobacterial antigens. The utility of these timed reactions in the identification of the tuberculin status was not well understood. The positive predictive value of reading the Mantoux tuberculin skin test in healthy adults at 24 h compared to 48–72 h was reported to be 75 per cent by Howard and Solomon. However, Ozturk, et al. found that in children the positive predictive value of any induration (≥ 1 mm) at 24 h was relatively low (63 per cent) when a cut-off of ≥ 10 mm was used to define the positive test. This rate increased to 86 per cent if the size of the induration was ≥ 5 mm at 24 h.

We have found that if Mantoux is positive at the end of 24 h, the positive predictive value of such a reaction is 96.7 per cent, which is significantly higher when compared to the above mentioned studies. Even in children who had a reaction of 0–9 mm, the tendency to remain negative was very high as indicated by the positive and negative predictive values of 98.5 and 96.7 per cent. It is possible that the difference in the individual reactions when the initial reaction was 0–9 mm could be due to a non-specific reaction to the various components in the tuberculin reagent or previous infection due to atypical mycobacteria.

It is possible that age can affect the 24-h tuberculin reading. To find the effect of age on a 24-h tuberculin reading, sensitivity, specificity, positive predictive value and negative predictive values were calculated for the age groups 5–6 years and 7–9 years. This stratification was possible because of the fact that there was a progressive increase in the prevalence of the tuberculin positivity with age. The sensitivity, specificity, positive predictive value and negative predictive values were almost the same for the various indurations between the two age groups. Hence it can be said with reasonable certainty that age does not affect the 24-h reading.

In conclusion, it is observed from our data that 24-h tuberculin skin test evaluation is an accurate measure. Focused studies are needed to ascertain the usefulness of a 24-h reading in clinical tuberculous disease.

### References


<table>
<thead>
<tr>
<th>Parameter (%)</th>
<th>5–6 years</th>
<th>7–9 years</th>
<th>5–6 years</th>
<th>7–9 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>99.3</td>
<td>99.2</td>
<td>88</td>
<td>95.7</td>
</tr>
<tr>
<td>Specificity</td>
<td>88</td>
<td>95.7</td>
<td>99.3</td>
<td>99.2</td>
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<tr>
<td>Positive predictive value</td>
<td>98</td>
<td>98.9</td>
<td>95.2</td>
<td>97.1</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>95.2</td>
<td>97.1</td>
<td>98</td>
<td>98.9</td>
</tr>
</tbody>
</table>

TABLE 2

Validity of 24-h induration in relation to 72-h reading for different age groups