To x-ray or not to x-ray? Screening asymptomatic children for pulmonary TB: a retrospective audit

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ABSTRACT

Objective Recent studies found that a chest x-ray (CXR) (0) has limited value in the assessment of asymptomatic adults with tuberculosis (TB) infection. We aimed to determine in asymptomatic children with a positive tuberculin skin test and/or interferon-γ release assay (TST/IGRA) whether a CXR identifies findings suggestive of pulmonary TB.

Design, setting and patients All children with TB infection (defined as TST ≥10 mm and/or positive IGRA) presenting to The Royal Children’s Hospital Melbourne during a 54-month period were included. All CXRs were reviewed by a senior radiologist blinded to the clinical details. The medical records of those with radiological abnormalities suggestive of TB were examined to identify those who were asymptomatic when the CXR was done. Demographical data were also collected.

Results CXRs were available for 268 of 330 TB-infected children, of whom 60 had CXR findings suggestive of TB. Of the 57 for whom clinical details were available, 26 were asymptomatic. Of these asymptomatic children with radiological abnormalities suggestive of TB, 6 had CXR findings suggestive of active TB, 14 had CXR findings suggestive of prior TB and 6 had isolated non-calcified lymphadenopathy. The six with findings suggestive of active TB represented 2.6% (95% CI 0.9 to 5.5%) of asymptomatic TST/IGRA-positive children with evaluable CXRs. One child with isolated hilar lymphadenopathy had microbiologically-confirmed TB.

Conclusions In contrast to the results from studies in adults, a CXR identified a small but noteworthy number of children with findings suggestive of pulmonary TB in the absence of clinical symptoms.

INTRODUCTION

In a child at risk of tuberculosis (TB), a positive tuberculin skin test and/or interferon-γ release assay (TST/IGRA) does not distinguish between latent TB infection (LTBI) and active TB.1 2 Although pulmonary TB is usually symptomatic, current guidelines recommend that asymptomatic children who have a positive TST/IGRA are screened with a chest x-ray (CXR) to exclude asymptomatic pulmonary TB.3–5 This distinction is important, as active TB requires treatment with at least three antimycobacterial antibiotics, whereas LTBI can be treated with isoniazid alone, or a combination of isoniazid and rifampicin.6

Recent studies in adults, however, question the need for a CXR in TST/IGRA-positive individuals who are asymptomatic.7 8 The diagnostic yield of a CXR in this setting has not been specifically investigated in children. We reviewed the CXRs of asymptomatic children with a positive TST/IGRA to determine what proportion had abnormal CXR findings suggestive of pulmonary TB.

METHODS

We retrospectively identified all children (0–18 years of age) who attended The Royal Children’s Hospital Melbourne (RCH) over a 54-month period (October 2006–March 2011) who had a positive TST (defined as ≥10 mm induration at 48–72 h, placed and read by specialist nurses specifically trained and certified in this procedure) and/or positive IGRA result (Quantiferon-TB Gold or Gold In-Tube assay). In our hospital, the majority of children who have a TST/IGRA comprise new arrivals from high TB prevalence countries and contacts of pulmonary TB. Data were obtained from two databases: (1) the RCH Immunisation Centre TST result database and (2) the Victorian Infectious Diseases Reference Laboratory (VIDRL) Mycobacterial Laboratory database. VIDRL is the sole provider of IGRA testing for the RCH. All IGRA were carried out routinely according to the manufacturer’s instructions.

All CXRs that were obtained within 6 months of the positive TST/IGRA in children who fulfilled the inclusion criteria were reviewed by a senior consultant radiologist, who was aware of the TST/IGRA results but evaluated the CXRs blind to any other clinical data. Features suggestive of active TB (defined as cavitation, consolidation, pleural effusion and miliary disease) or prior TB (defined as pleural thickening, fibrous scarring, calcified lymph node and calcified granuloma) were documented.7 Non-calcified hilar lymphadenopathy was documented as a separate category.

What is already known about this topic

Studies in adults found that a CXR has limited value in detecting asymptomatic pulmonary TB in patients with a positive TST/IGRA.

What this study adds

In children with a positive TST/IGRA, a CXR identified a small but not insignificant proportion of asymptomatic children with CXR findings suggestive of pulmonary TB.

The medical records of children with a CXR finding suggestive of TB were then retrieved to determine whether the patient was asymptomatic or had symptoms suggestive of pulmonary TB (cough or other respiratory symptoms, fever, weight loss or failure to thrive, night sweats). Demographical information, including BCG immunisation status and country of origin, was also collected, as well as the results of additional investigations and treatment details for all asymptomatic children.

RESULTS
We identified 330 children with TB infection on the basis of a positive TST and/or IGRA (figure 1). Of these, 268 children (81.2%) had a CXR that was available for review, of which 60 (22.4%) were reported as abnormal with non-calciﬁed hilar lymphadenopathy, or ﬁndings suggestive of prior or active TB as defined in the Methods section.

CXR ﬁndings
Of the 60 children with CXR ﬁndings suggestive of TB, 31 had symptoms suggestive of pulmonary TB, 26 were asymptomatic and for 3 children, clinical details were not available. Therefore, overall, there were 234 evaluable CXRs in TST/IGRA-positive children (excluding the 31 symptomatic children and 3 lost to follow-up).

Of the 26 asymptomatic children with CXR ﬁndings suggestive of TB, 6 had CXR ﬁndings suggestive of active TB (representing 2.6% (95% CI 0.9% to 5.5%) of the 234 total CXRs), 14 had CXR ﬁndings suggestive of prior TB and 9 had non-calciﬁed hilar lymphadenopathy (in 6 of whom this was the only abnormality) (ﬁgure 1 and table 1). Of the six children with CXR ﬁndings suggestive of active TB, three had a household contact with sputum smear-positive pulmonary TB (table 2). Only one of these six children had gastric aspirates performed, and these were negative for acid-fast bacilli. Among the six children with isolated non-calciﬁed hilar lymphadenopathy, one had gastric aspirates taken which revealed acid-fast bacilli, and a PCR test for Mycobacterium tuberculosis was positive. This was a 19-month-old non-BCG-immunised boy whose father had pulmonary TB. One other child with isolated non-calciﬁed hilar lymphadenopathy had a gastric aspirate and...
lymph node biopsy, which did not find evidence of M tuberculosis. The remaining four did not have any microbiological investigations.

**Treatment of asymptomatic children**

Of the six children who had CXR findings suggestive of active TB, five children were treated for pulmonary TB and one child was treated for LTBI. The latter was a 15-month-old girl who had consolidation on CXR. Her only identifiable risk factor was birth in a high-TB-prevalence country (Burma). At follow-up, 3 months after completing a 6-month course of isoniazid preventive therapy, she remained well. Of the 14 children who had CXR findings suggestive of prior TB, in three cases, the physician made the decision to treat for active TB. Of the six children who had isolated non-calcified hilar lymphadenopathy, one child was treated for active TB (this was the 19-month-old boy who had positive gastric aspirates for M. tuberculosis).

Overall, of the 26 asymptomatic children with CXR findings suggestive of TB for whom records were available, 17 were treated for LTBI: five had a household contact with pulmonary TB, one had a school contact with smear-positive pulmonary TB, and one had a non-household contact with smear-positive pulmonary TB. The remaining nine children were treated for active TB, of which eight (88.9%) had a known household contact with pulmonary TB.

### DISCUSSION

Our data show that a routine CXR in asymptomatic children with a positive TST and/or IGRA does identify children with CXR abnormalities suggestive of pulmonary TB despite the absence of clinical features. Importantly, the proportion (2.6%, 95% CI 0.9% to 5.5%) of asymptomatic children identified in our study whose CXR findings were suggestive of pulmonary TB is not insignificant.

Our findings contrast with two studies in adults in which CXR screening failed to identify any cases of active TB among asymptomatic healthcare workers. However, an important difference between these studies in adults and our study is that our patients had a TST/IGRA as a result of identified risk factors for TB, whereas the previous studies screened low-risk populations. There are also important differences between a study of this kind in adults and children. Children have a higher risk of progression to active TB. Moreover, those who have a positive TST/IGRA are more likely to have been recently infected, which also increases their risk of progression to active TB.

The value of CXR screening has also been raised in studies in selected paediatric populations. In a study of asylum seekers in Switzerland, 2 of 16 TST-positive children who were screened with a CXR had radiological abnormalities (not further specified), but neither was treated for pulmonary TB. In an Italian study of asylum seekers, none of the 68 TST-positive children had radiological evidence of active TB, although 7 (10.3%) had CXR abnormalities suggestive of prior TB (treatment outcomes were not reported in this study). A study of internationally adopted children in the USA reported that while 3 (3.3%) of the 90 asymptomatic TST-positive children had radiological findings consistent with pulmonary TB, none were treated for active TB and none of these 3 children developed active TB during a 2-year follow-up period. However, our results are consistent with studies in a different context in Brazil and South Africa that found that children with active TB can be asymptomatic, including up to 47% of those with culture-positive pulmonary TB.

Our study also highlights differences in the classification and management of asymptomatic children with isolated hilar lymphadenopathy. Mediastinal and hilar lymphadenopathy with or without parenchymal abnormalities (Ghon focus) is a common form of TB in children. Two studies in adults did not consider hilar lymphadenopathy in their definitions of active or prior TB, while another classified hilar lymphadenopathy as a sign of active disease. Similarly, some paediatric studies have classified hilar lymphadenopathy in an asymptomatic child as

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (years)</th>
<th>Country of birth, age arrived in Australia (other risk factors)</th>
<th>TB contact</th>
<th>BCG immunised</th>
<th>CXR abnormality</th>
<th>Microbiological confirmation</th>
</tr>
</thead>
<tbody>
<tr>
<td>M 1</td>
<td>1</td>
<td>Australia</td>
<td>Grandmother: smear-positive PTB</td>
<td>No</td>
<td>Consolidation</td>
<td>GA not done</td>
</tr>
<tr>
<td>F 5</td>
<td>Ethiopia (&lt;1 year)</td>
<td>Ethiopia (4 month visit to Ethiopia aged 5 years)</td>
<td>Sister: lymph node TB</td>
<td>Yes</td>
<td>Consolidation</td>
<td>GA not done</td>
</tr>
<tr>
<td>F 7</td>
<td>Kenya, 5 years</td>
<td>Mother: smear-positive PTB</td>
<td>Yes</td>
<td>Consolidation</td>
<td>Non-calcified hilar lymph nodes</td>
<td>GA not done</td>
</tr>
<tr>
<td>M 8</td>
<td>Australia (parents from Somalia)</td>
<td>Cousin: smear-positive PTB 'stayed with family for 1 week'</td>
<td>Yes</td>
<td>Consolidation</td>
<td>Non-calcified hilar lymph nodes</td>
<td>GA not done</td>
</tr>
<tr>
<td>M 12</td>
<td>Philippines, 10 years</td>
<td>None known</td>
<td>Yes</td>
<td>Consolidation</td>
<td>GA not done</td>
<td></td>
</tr>
</tbody>
</table>

GA, gastric aspirates; PTB, pulmonary tuberculosis.

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Table 2  Details of the six asymptomatic children with CXR findings compatible with active TB
indicative of active TB, whereas others have suggested that hilar lymphadenopathy is indicative of recent TB infection but not pulmonary disease. Data from the latter studies suggest that few children with isolated hilar lymphadenopathy develop active disease. Notably, in our study, the one child with isolated hilar lymphadenopathy who had a gastric aspirate had microbiologically-confirmed TB despite the absence of clinical symptoms.

In many instances, the decision to treat for LTBI or active TB appears to have been influenced by factors other than the CXR findings. In our study, eight of the nine children treated for active TB had a household TB contact, and five of these did not have CXR findings suggestive of pulmonary TB. Notably, only three of the nine children had gastric aspirates taken and only one child had microbiologically-confirmed pulmonary TB. However, this is not surprising, as microbiological confirmation is far less frequently achieved in children than in adults, and the decision to treat a child for active TB consequently has to be based on epidemiological risk factors, particularly a history of exposure to an infected adult, in conjunction with TST/IGRA results.

Limitations of our study include its retrospective nature. Although this resulted in a number of CXRs not being available for review, this is unlikely to have introduced selection bias. Also, all CXRs were interpreted by a single experienced consultant radiologist, an approach that provides overall consistency, but does not allow any conclusions regarding inter-observer variability.

**CONCLUSION**

Our data suggest that, in contrast to adults, a CXR remains a valuable tool in the management of asymptomatic children with a positive TST and/or IGRA, as this approach identifies a small, but not insignificant proportion of children who have pulmonary TB in the absence of clinical symptoms.

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**Contributors** AG, NR and NC were responsible for study concept and design; AG, AP, MT, TC and NC were responsible for acquisition of data; AG, MT and NC were responsible for analysis and interpretation of data; AG and NC were involved in drafting the manuscript; critical revision of the manuscript for important intellectual content was carried out by AG, AP, NR, MT, TGC, TC and NC; and NC supervised the study.

**Competing interests** None.

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**REFERENCES**


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