Contact tracing in pulmonary and non-pulmonary tuberculosis

P. MANDAL¹, R. CRAXTON², J.D. CHALMERS¹, S. GILHOOLEY², I.F. LAURENSON³, C. McSPARRON², J. STEVENSON⁴ and A.T. HILL¹,²

From the ¹Centre for Inflammation Research, University of Edinburgh, Queen’s Medical Research Institute, 47 Little France Crescent, Edinburgh, EH16 4TJ, ²Department of Respiratory Medicine, ³Department Microbiology, Royal Infirmary of Edinburgh, 51 Little France Crescent, Old Dalkeith Road, Edinburgh EH16 4SA and ⁴Health Protection Team, Waverley Gate, 2-4 Waterloo Place, Edinburgh EH1 3EG, UK

Address correspondence to Dr P. Mandal, Department of Respiratory Medicine, Royal Infirmary of Edinburgh, University of Edinburgh, Queen’s Medical Research Institute, 47 Little France Crescent, Edinburgh EH16 4TJ, UK. email: pallavimandal@googlemail.com

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Summary

Aim: The aim of our study was to determine the effectiveness of contact tracing for both pulmonary and non-pulmonary tuberculosis (TB).

Methods: The authors studied contact tracing in South East of Scotland, Edinburgh TB Clinic, UK, for 3 years. New index cases of both pulmonary and non-pulmonary TB were identified from reviewing TB nurses records. Pulmonary involvement was excluded from all non-pulmonary cases. Active TB was diagnosed as per the national TB guidelines. Latent TB was diagnosed based on history, tuberculin skin test and interferon γ release assay. TB contacts were identified from reviewing TB nurses notes on index TB patients.

A positive screening episode was defined as identification of either active or latent TB in a contact following relevant investigations.

Results: Total number of positive screening episodes for pulmonary TB was 43.1% and non-pulmonary TB was 26.1%. Of these, 78.8% were household contacts and 21.2% were casual contacts.

Conclusion: Contact tracing in low-prevalence TB countries, for both pulmonary and non-pulmonary TB, is an essential intervention to identify and reduce the number of infected patients that will progress to active disease. This is the key for effective TB control.

Introduction

Tuberculosis (TB) is the second leading cause of death due to infectious diseases in the world, despite recent advances in diagnosis and treatment.¹,² In 2010, the World Health Organization (WHO) estimated that there are ~10 million new cases of TB and an estimated 1.8 million deaths occur each year due to TB although TB is a potentially curable disease.³ In most European countries, non-Caucasians account for a large proportion of TB patients, varying from 9% to 76%.⁴ The WHO aims to ‘stop and reverse’ the incidence of TB and reduce by 50% the mortality and prevalence of TB as compared to 1990.⁵ The STOP TB Strategy and the WHO guidelines for effective TB control provide a framework for TB control, especially in countries that have a high TB incidence.⁶

About 10% of infected individuals develop signs and symptoms of active TB over a lifetime.

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A majority of immunocompetent people are able to either eliminate TB or contain it in a latent state. The risk of developing TB is highest in the first and second year after infection, with the risk decreasing thereafter.

Controlling TB involves identifying and treating active disease as well as appropriate contact tracing. Although contact tracing investigations are resource intensive, they are imperative for success of TB control programmes. Contact tracing for cases of active TB is standard practice in most countries.

In 2008, a survey of the national policies for active case finding in TB was carried out, across European countries. This survey found that there was some discrepancy in active case finding policies across Europe, but all countries screened close contacts of smear positive index cases.

The UK is a low-incidence country for TB. In 2009, England was reported to have 16 cases of TB per 100,000 of the population. To help achieve the goal of STOP TB Strategy by 2050, as set out by the WHO, appropriate contact tracing in low-endemic country will help reduce the global burden of latent disease as well as promptly identify those with active disease. National guidelines in the UK, recommend routine contact tracing of pulmonary and non-pulmonary TB to identify latent TB, active TB and those that require Bacille Calmette-Guérin (BCG) vaccination. Contact tracing for non-pulmonary TB is, however, not universally practiced.

The aim of our study was to assess the efficacy of contact tracing for both pulmonary and non-pulmonary TB.

**Methods**

This study was performed at the South East of Scotland (SES) TB Contact Tracing Clinic, Edinburgh, UK, over a 3-year period from January 2008 to December 2010. The SES TB Clinic in Edinburgh receives referrals from primary care as well as two other hospitals in National Health Service (NHS) Lothian. NHS Lothian has two TB specialist nurses (funded by Public Health) who are based at the SES TB clinic. The study included all contacts of index patients with active TB aged ≥18 years. Since there were only six cases that were co-infected with human immunodeficiency virus (HIV), they were excluded from the study.

New index patients with a diagnosis of pulmonary and non-pulmonary TB were identified over this period, from reviewing TB nurse records. Pulmonary involvement was excluded in all non-pulmonary cases. Active TB was diagnosed in accordance with the national guidelines. Latent TB was diagnosed based on history, tuberculin skin test (TST) and interferon γ release assay (QuantiFERON® Gold ‘in tube’ test (QGT)). Standard treatment for pulmonary and non-pulmonary TB was in accordance with the national guidelines. Latent TB was treated with 6 months isoniazid unless a contact of an index case with drug-resistant TB. If so, the latent TB treatment was guided by sensitivity testing from the index case.

As per the National Institute for Health and Clinical Excellence (NICE) guidelines, household contacts of all cases of active TB were screened. At our centre, we screen both household and casual contacts, independent of cumulative exposure. There is a lack of an objective definition of close contacts but generally contacts with a cumulative total exposure to a smear positive case of TB exceeding 8 h within a restricted area are deemed, as close contacts. Household contacts are those who share a bedroom, kitchen, bathroom or sitting room with the index case. Casual contacts include mostly workplace contacts.

New immigrants to Edinburgh are referred by Public Health to the SES TB Clinic, where patients are triaged and are screened as per the NICE new entrant TB screening guidelines.

On identification of TB contacts, a history was taken including prior BCG vaccination. If symptomatic, sputum was sent for TB cultures and chest X-ray performed. For others, a TST was performed. If TST was positive (≥15 mm if prior BCG; ≥6 mm if no prior BCG), patients had QGT. If QGT was positive, patients were treated for latent TB, once active TB was excluded.

A positive screening episode was defined as identification of either active or latent TB in a contact following investigations described above.

**Statistical analysis**

All data were analysed using SPSS. For demographically, data are presented as median (interquartile range). Adjustment for potential confounders was achieved using multivariable logistic regression. Multivariable regression models were constructed by including demographic (age, gender and ethnicity of both index cases and contacts), smear positivity with active TB, index case pulmonary TB or not, prior BCG and casual or close contacts as independent variables. Model fit was assessed using the Hosmer–Lemeshow goodness-of-fit test (P > 0.05 indicates adequate model fit). Results are presented as adjusted odds ratio (AOR) with 95% confidence intervals (CIs). A P-value of < 0.05 was considered statistically significant.
Results

Over a 3-year period, we identified 275 index cases (Figure 1). Of these, 160 were pulmonary and 115 were non-pulmonary TB.

Baseline characteristics

Index patients: of the 275 index patients identified, 59.6% were male and median age was 37 years (interquartile range 28–59 years). One hundred and sixty patients had pulmonary and 115 non-pulmonary TB. One hundred and eighteen patients were of the Indian subcontinent, 102 Scottish, 20 Afro-Caribbean and 35 were of other origin.

Contacts: 732 contacts were identified of which 108 (14.7%) declined screening. Six hundred and twenty-four contacts were screened of which 50.2% were male. Of the 732 contacts, 55.1% were close contacts and median age was 32 years (interquartile range 19–48 years). Two hundred and ninety-four were Scottish, 238 of the Indian subcontinent, 38 Afro-Caribbean and 54 were of other origin. Contacts who had prior BCG were 66.3% and who had co-morbidities were 6.9% (mainly diabetes, hypertension and asthma).

We have presented our results as pulmonary or non-pulmonary, based on the site of TB infection in the index case (Figure 2).

Pulmonary TB

A total of 160 index patients of pulmonary TB were identified. Patients were either able to provide sputum samples or had a bronchoalveolar lavage. Of the 160 patients, 88 (55%) were smear positive and 72 (45%) smear negative.

Smear positive pulmonary TB

A total of 267 contacts were identified of which 224 were screened and 43 declined screening. Active TB was identified in 19 (15.9%) and latent TB in 50 (36.25%) from screening 88 index patients. Ten had BCG vaccination. The total positive screening episode for smear positive pulmonary TB was 48.8% (Figure 2).

Smear negative pulmonary TB

A total of 193 contacts were identified of which 167 were screened and 26 declined screening. Active TB was identified in 5 (6.9%) and latent TB in 21 (29.2%) from screening 72-index patients. Seven had BCG vaccination. The total positive screening episode for smear negative pulmonary TB was 24.3% (Figure 2).

Figure 1. Flow chart showing TB case finding in SES Clinic 2008–2010.
screening episodes for smear negative pulmonary TB was 36.1% (Figure 2).

Number of smear positive contacts needed to screen, to identify a case of active TB was 16 and for latent TB it was 7.7. For smear negative TB, the numbers need to screen to identify active and latent TB were 33.4 and 7.9, respectively.

Overall, the total number of positive screening episodes for pulmonary TB was 69 (43.1%). Active TB was identified in 19 (11.9%) and latent TB was identified in 50 (31.2%) patients (Figure 3).

Non-pulmonary TB

A total of 115 index patients of non-pulmonary TB were identified. Two hundred and seventy-two contacts were identified of which 233 were screened and 39 contacts declined screening.
From screening 115 index patients, active TB was identified in 5 (4.3%) and latent TB in 25 (21.7%) (Figure 2). Fourteen had BCG vaccination.

Number of non-pulmonary TB contacts needed to screen to identify a patient of active TB was 44.6 and it was 8.9 for latent TB.

Total number of positive screening episodes for non-pulmonary TB was 30 (26.1%) (Figure 3).

Ethnicity

Over the 3-year period, we recorded the ethnicity of the contacts identified. Indian subcontinent included India, Pakistan and Bangladesh. In the ‘other’ group, we included Eastern European and mixed ethnic origin.

The percentage of TB cases identified for each ethnic origin over 2008, 2009 and 2010 are shown in Figure 4.

Overall, in the 3 years of contact tracing, of the 99 contacts identified to have either active or latent TB, 46.4% were of the Indian subcontinent, 26.3% were Scottish, 14.1% Afro-Caribbean and 13.2% were of other origin (including Eastern European, mixed ethnic origin).

Mycobacterial interspersed repetitive units typing

Of the 19 cases identified to have active TB (from contact tracing), Mycobacterial interspersed repetitive units (MIRUs) typing was available for 15 cases. Of these 15 cases, exact MIRU matching was found in 6 cases, 4 (26.7%) were from pulmonary and 2 (13.3%) from non-pulmonary index case. All contacts found to have exact matches with the index cases were close contacts.

Screening of household vs. casual contacts

Of the 99 TB cases (both active and latent TB) identified from contact tracing, 78 (78.8%) were household and 21 (21.2%) were casual contacts. In the pulmonary group, of the 69 contacts identified to have active or latent TB, 76.8% were close and 23.2% were casual contacts. In the non-pulmonary group, of the 30 contacts identified to have active or latent TB, 75% were close contacts and 25% were casual contacts.

Patients at risk of developing TB

In a multivariable logistic regression, only independent risk factor for a positive screening episode was being a contact of a smear positive case. Contacts who were Caucasian and younger were less likely to have a positive screening episode (Table 1).

Discussion

In this study of contact tracing in TB over a 3-year period, we showed that contact tracing for non-pulmonary TB is as essential as pulmonary TB. Over a quarter of screening episodes for non-pulmonary TB cases resulted in a diagnosis of active or latent TB among the contacts. Our study validates the current NICE14 guidance of TB contact tracing, which recommends screening of non-pulmonary TB contacts. This guidance is not universally adhered to in the UK and many guidelines

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Independent predictors</th>
<th>AOR (95 CI%)</th>
<th>P-value</th>
<th>Hosmer–Lemeshow Goodness-of-fit test P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall TB</td>
<td>Age of TB contacts</td>
<td>0.98 (0.97–0.99)</td>
<td>0.009</td>
<td>0.8</td>
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<tr>
<td></td>
<td>Caucasian (TB contact)</td>
<td>0.33 (0.21–0.54)</td>
<td>&lt;0.0001</td>
<td></td>
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<tr>
<td></td>
<td>Smear positivity of index case</td>
<td>1.79 (1.14–2.80)</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

Figure 4. Ethnicity of contacts identified to have active or latent TB.

Table 1 Multivariable regression identifying risk factors for active or latent TB
internationally do not recommend screening of non-pulmonary TB contacts. Screening of contacts is essential in non-pulmonary TB although the index case is not infectious. Pick up rate for MIRU typing in our cohort was 40%. It has been hypothesized transmission of disease in contacts is either in communities or families that are ethnically at high risk or in groups living in a high-density housing or live in a community where frequent trips are made to the Indian subcontinent. Our data support this hypothesis as non-Caucasian contacts were at a significantly increased risk of active or latent TB even after adjustment for potential confounders in a multivariable analysis.

In our study, we found that the only independent risk factor for developing either active TB or latent infection was being a contact of a smear positive index case. Caucasians and younger contacts were less likely to develop active or latent TB in our study cohort. The lack of clear risk factors for developing active TB or latent infection among contacts highlights the difficulties of identifying which patients to screen. This uncertainty is reflected in international guidelines as there seems to be inconsistency in active case finding. It is also unclear whether screening should be limited to household contacts or whether casual contacts are also at risk. The Concentric Circle Approach (CCA) as recommended by the Centres for Disease Control and Prevention (CDC) suggests testing contacts in order of their exposure time.

We found that screening of casual contacts identified TB in those with smear negative pulmonary TB and non-pulmonary TB. The current NICE guidelines recommend contact tracing of casual contacts only if the index case is smear positive or if the host is immunocompromised. The number of non-household contacts was small in our study but 21.2% of those found to have active or latent disease in this study were casual contacts. It is difficult for us to conclude from our study that casual contacts should be routinely screened. The cost effectiveness of contact tracing of all casual contacts in both pulmonary and non-pulmonary TB, in a low-endemic country, will need to be evaluated. For practical purposes, screening of casual contacts should perhaps be limited to instances where active disease has been identified in close contacts or where susceptible casual contacts have already been identified.

In 1990, WHO estimated that a third of the world’s population (1.7 billion people) are infected with Mycobacterium tuberculosis and since then the figures have not significantly changed. In the UK, the data from 2009 showed that there has been further rise in the incidence of TB in the UK, with over 9000 new cases being diagnosed in 2009. To achieve the goal of eliminating TB by 2050, we have to prevent infection by vaccination, treat active disease and contain transmission of disease as well as reduce the number of infected patients progressing to active TB.

New index cases of TB need to be promptly assessed to evaluate the urgency of contact tracing. In addition to efforts to enhance protective immunity by vaccination before infection, the size and increased risk of the latent TB population indicate a crucial role for interventions that would reduce disease progression in individuals who have already been exposed to infection. To impact on the burden of identifying and treating latent disease, more specific and sensitive tests are required that can distinguish between active and latent disease.

In low-endemic countries like UK, contact tracing and early treatment of latent infection are vital steps to control TB. The main aim of contact tracing in TB is to help identify new TB cases or latent TB infection in contacts. All active cases need to be promptly treated and those with latent infection should be offered preventive therapy. This will help reduce further transmission and mortality and morbidity in newly diagnosed TB cases.

**Limitations**

First, this was a retrospective single centre study, in a low-endemic country and secondly, due to small numbers, we had to exclude patients co-infected with HIV.

**Conclusion**

Contact tracing in low-prevalence TB countries, for both pulmonary and non-pulmonary TB, is an essential intervention to identify and reduce the number of infected patients that will progress to active disease. This is the key for effective TB control.

**Conflict of interest:** None declared.

**References**


