Becoming a TB Nurse Expert
San Antonio, Texas
July 30-31, 2008

Contact Investigation:
Evaluation and Expansion
Lynelle Phillips, RN, MPH
July 31, 2008

Contact Investigation -
Evaluation and Expansion
Lynelle Phillips, RN MPH
Heartland National TB Center
July 31, 2008
Objectives

- **Objective:** Explain the appropriate follow-up involved in monitoring contact investigations.
  - Evaluation criteria
    - CDC objectives
    - Genotyping data
- **Objective:** Discuss when to expand a contact investigation.
  - Expanding according to extent of recent transmission
  - Review of how data guides expansion
    - Contact investigation results
    - Genotyping results

Contact Investigation Principles

- Meet CDC Objectives!

**BOX 2. Recommended objectives for contact investigations, by key indicators**

<table>
<thead>
<tr>
<th>Key indicator</th>
<th>Objective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious index patients with at least one contact listed</td>
<td>90%</td>
</tr>
<tr>
<td>Contacts who are evaluated for tuberculosis disease and latent infection</td>
<td>90%</td>
</tr>
<tr>
<td>Infected contacts who begin treatment for latent infection</td>
<td>85%</td>
</tr>
<tr>
<td>Treated contacts who complete treatment for latent infection</td>
<td>75%</td>
</tr>
</tbody>
</table>
Reichler et al Evaluation of TB contact investigations

- They reviewed outcomes for 349 active TB cases and their 3824 contacts
  - 45 (13%) cases had no contacts identified
  - 2095 (55%) completed evaluation
    - 27% had no 2nd TST
    - 12% never screened
    - 6% had prior history of TB

Presence of Case Infectiousness and Contact Risk Assessment Data in Written Contact Records

Data management

- Recommended fields for including in CI data sets:
  - Prioritization of contacts (e.g. high medium low)
    - Risk factors for infection
    - Exposure duration/intensity
  - Evaluation results (e.g. Initial, follow-up, refused, etc.)
  - TB Code (0-5)

Location of Contacts:
(When found for Evaluation)

93% of positive TSTs were found while incarcerated!
Genotyping

• Use of PCR to identify genotype of tuberculosis isolates
  – Made universal in US in 2004
  – Carried out at two centers (CA, MI)
• Has led to identification of clusters and epi-links not previously recognized by traditional outbreak investigation methods
  http://www.cdc.gov/nchstp/tb/genotyping/toc.htm

Benefits of Genotyping

- Understand Transmission Patterns Better
- Identify Lab Cross Contamination
- Learn About Unsuspected Relationships and Non-Traditional Settings for Transmission
- Detect and Investigate Outbreaks Sooner
- Focus and Prioritize Contact Investigations
- Evaluate Intervention Effectiveness
- Discern Exogenous Reinfection vs Relapse
GENOTYPING FLOW

New isolate → Spoligo Spoligo MIRU → Result

Compare with prior results for same TB program

Clustered → No match

Clustered isolates (Spoligotype + MIRU)

Known link confirmed

Correlate with patient and contact information

Unsuspected transmission?

Patterns match, cluster confirmed

Patterns differ, no cluster

IS6110 RFLP
### Table 4.3. Sample genotyping laboratory report.*

<table>
<thead>
<tr>
<th>TB program name</th>
<th>Genotyping laboratory accession number</th>
<th>Date received</th>
<th>Spoligotype</th>
<th>MIRU type</th>
<th>PCR cluster designation</th>
<th>Date clustered</th>
<th>Date reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>XY</td>
<td>03AA2615</td>
<td>12/05/03</td>
<td>777776077607771</td>
<td>123326133227</td>
<td>12/12/03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XY</td>
<td>03AA2616</td>
<td>12/05/03</td>
<td>7763777777760771</td>
<td>23426163234</td>
<td>12/12/03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XY</td>
<td>03AA2617</td>
<td>12/05/03</td>
<td>700000000760771</td>
<td>23426153323</td>
<td>12/12/03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XY</td>
<td>03AA2618</td>
<td>12/05/03</td>
<td>677737607760771</td>
<td>22426143321</td>
<td>12/12/03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XY</td>
<td>03AA2619</td>
<td>12/05/03</td>
<td>7763777777760771</td>
<td>233326163224</td>
<td>XY025</td>
<td>12/12/03</td>
<td>12/12/03</td>
</tr>
<tr>
<td>XY</td>
<td>03AA2622</td>
<td>06/16/03</td>
<td>7763777777760771</td>
<td>233326163224</td>
<td>XY025</td>
<td>12/12/03</td>
<td>12/12/03</td>
</tr>
<tr>
<td>XY</td>
<td>03AA2620</td>
<td>12/05/03</td>
<td>7837777774000771</td>
<td>22426173533</td>
<td>12/12/03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>XY</td>
<td>03AA2621</td>
<td>12/05/03</td>
<td>7777777777760771</td>
<td>223125153326</td>
<td>XY004</td>
<td>12/12/03</td>
<td>12/12/03</td>
</tr>
<tr>
<td>XY</td>
<td>03AA2622</td>
<td>12/05/03</td>
<td>67777607760771</td>
<td>23426153323</td>
<td>12/12/03</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Actual report will contain additional information. See text for details.
RFLP Analysis – special request

- Lanes 1-3: school outbreak
- Lanes 4-6: sewer workers outbreak
- Lanes 7-9: family outbreak
- Lanes 10,11: family outbreak

Using genotyping data to evaluate contact investigations

- Of 481 patients with RFLP results available:
  - 240 (50%) had a unique pattern
  - 241 (50%) were in a cluster with at least one other patient
  - 155 were part of a cluster in the study area (North Holland) and study period (1998-2000) ranging from 2 – 12 patients


Aberration Detection System

- Develop formula to determine aberrant clusters – CDC
- Alert public health jurisdictions of potential outbreak
  - Expanded investigation


When to expand a contact investigation

- Expanding according to extent of recent transmission
- Review of how data guides expansion
  - Contact investigation results
  - Genotyping results
CDC Guidelines

• A “graduated” approach to contact investigations (concentric circles):
  – “If data indicate that contact with the greatest exposure have an infection rate greater than would be expected in their community, contacts with progressively less exposure are sought.”
  – Continue to expand the investigation until “the rate of positive skin test results for contacts are indistinguishable from the prevalence of positive results in the community”

Advantages and disadvantages

• Advantage –
  – Contacts with less exposure are not sought until evidence of transmission exists

• Disadvantages –
  – Exposure estimates are unreliable
  – Unaccommodated risk factors of contacts (e.g. HIV, infants)
  – Unknown prevalence of LTBI
Consider the following factors before expanding a CI:

- High- and medium- risk contacts have been identified, evaluated and Rx’d treatment
- Assess extent of recent transmission:
  - High rate of infection/disease among high-risk contacts
  - Secondary transmission
  - Unexpected TB disease in a low priority contact
  - Positive TSTs on follow-up testing
- “In the absence of recent transmission, an investigation should not be expanded to low-risk contacts”

TB in HS student

- 16 year old high school student presented with upper respiratory symptoms and fever in November 2000.
- CXR revealed upper lobe cavitary disease in early December, 2000
- Diagnosed with bronchitis and treated with “dose-pack”
TB in HS Student (2)

• Between December and May, patient’s health status steadily declined
  – Missed 48 days of school
  – Coughing up blood in class
  – 25 pound weight loss
  – Severe fatigue
• Diagnosed in May, 2001 with active TB
Contact investigation

• Patient’s contacts:
  – Dad – PPD positive – LTBI
  – Mom – PPD positive – cx positive MTB
  – 12 year-old brother – PPD positive - LTBI
  – 9 year-old brother – PPD positive – abn CXR
    – clinical MTB
  – 5-month-old brother – PPD irrelevant – abn
    CXR – tracheobronchial MTB

Data from investigation

<table>
<thead>
<tr>
<th>Persons tested</th>
<th># of students tested</th>
<th># of students TST positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Students in ≥ 3 classes</td>
<td>13</td>
<td>7</td>
</tr>
</tbody>
</table>
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<tr>
<td>Students in ≥ 3 classes</td>
<td>13</td>
<td>7</td>
</tr>
<tr>
<td>Students in periods 1,2,5-7</td>
<td>66</td>
<td>21</td>
</tr>
<tr>
<td>Students in ≥ 1 class</td>
<td>106</td>
<td>25</td>
</tr>
</tbody>
</table>

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<table>
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<td>21</td>
</tr>
<tr>
<td>Students in ≥ 1 class</td>
<td>106</td>
<td>25</td>
</tr>
<tr>
<td>All students</td>
<td>559</td>
<td>58</td>
</tr>
</tbody>
</table>


Overview of epidemiology

**Epidemiology**

“The study of the distribution and determinants of health-related states in specified populations, and the application of this study to control health problems.”

http://www.cdc.gov/excite/library/glossary.htm
**2 x 2 table**

<table>
<thead>
<tr>
<th>LTBI/MTB – yes</th>
<th>LTBI/MTB – no</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure/risk factor – yes</td>
<td>a</td>
</tr>
<tr>
<td>Exposure/risk factor – No</td>
<td>c</td>
</tr>
</tbody>
</table>

Relative Risk = \( \frac{a}{a+b} \) 
\( \frac{c}{c+d} \)

**2 x 2 table – high school outbreak**

<table>
<thead>
<tr>
<th>EXPOSURE GROUP</th>
<th>TST RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>positive</td>
</tr>
<tr>
<td>In class with index case</td>
<td>25</td>
</tr>
<tr>
<td>Not in class with index case</td>
<td>33</td>
</tr>
<tr>
<td>TOTAL TESTED</td>
<td>58</td>
</tr>
</tbody>
</table>

\( RR = \frac{25}{106} = 3.2 \) (CI = 1.26-4.93) 
\( \frac{33}{453} \)
## Data from investigation

<table>
<thead>
<tr>
<th>Persons tested</th>
<th># tested</th>
<th># TST positive</th>
<th>Relative Risk</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Students in ≥ 3 classes</td>
<td>13</td>
<td>7</td>
<td>5.7</td>
<td>3.26-10.13</td>
</tr>
<tr>
<td>Students in periods 1,2,5-7</td>
<td>66</td>
<td>21</td>
<td>4.2</td>
<td>2.6-6.75</td>
</tr>
<tr>
<td>Students in ≥ 1 class</td>
<td>106</td>
<td>25</td>
<td>3.2</td>
<td>2.0-5.18</td>
</tr>
<tr>
<td>All students</td>
<td>559</td>
<td>58</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


## High, medium, low risk contacts

- In ≥ 2 classes, RR = 5.7
- In classes 1,2,5,6,7, RR = 4.2
- In ≥ 1 class, RR = 3.2

Index case
Benefits of Genotyping

- Understand Transmission Patterns Better
- Identify Lab Cross Contamination
- Learn About Unsuspected Relationships and Non-Traditional Settings for Transmission
- Detect and Investigate Outbreaks Sooner
- Focus and Prioritize Contact Investigations
- Evaluate Intervention Effectiveness
- Discern Exogenous Reinfection vs Relapse

Table 6.1. Prioritizing genotyping cluster investigations.

<table>
<thead>
<tr>
<th>Priority (from high to low)</th>
<th>Type of cluster</th>
<th>Rationale for priority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected false-positive culture</td>
<td>Need to determine which patients do not have TB and stop treatment</td>
<td></td>
</tr>
<tr>
<td>Cluster of three or more high-risk* patients with possible epidemiologic links</td>
<td>Need to confirm or exclude recent transmission in large clusters of high-risk* patients</td>
<td></td>
</tr>
<tr>
<td>Cluster of two high-risk* TB patients with possible epidemiologic links</td>
<td>Smaller clusters less likely to yield epidemiologic links, but presence of high-risk patients deserves attention</td>
<td></td>
</tr>
<tr>
<td>Cluster of three or more low-risk TB patients with possible epidemiologic links</td>
<td>Investigation of low-risk patients less urgent than high-risk* patients, but larger clusters may deserve attention</td>
<td></td>
</tr>
<tr>
<td>Cluster of two low-risk TB patients with possible epidemiologic links</td>
<td>Investigation of smaller clusters of low-risk patients often does not yield helpful information. Investigations can, however, provide data for monitoring program performance</td>
<td></td>
</tr>
<tr>
<td>Cluster of high-risk* TB patients who have not been found to have even possible epidemiologic links</td>
<td>Low yield for establishing new epidemiologic links. Investigations can, however, provide data for monitoring program performance. Reserved for programs with sufficient resources</td>
<td></td>
</tr>
<tr>
<td>Cluster of low-risk TB patients who have not been found to have even possible epidemiologic links</td>
<td>Very low yield for establishing new epidemiologic links. Investigations can, however, provide data for monitoring program performance. Reserved for programs with sufficient resources</td>
<td></td>
</tr>
</tbody>
</table>

* "High risk" is defined as patients living in congregate settings (e.g., correctional institutions and nursing homes), persons infected with HIV or having other immunocompromising conditions, children, patients with cavities on chest radiographs or with MDR TB, and the homeless.

**Expanded contact investigation methods**

- Medical record/chart review
- Field/home visits
- Reinterviews
  - Social network
Investigation of TB in homeless-Kansas City MO

- Conducted chart reviews on the individuals in the cluster.
  - Positive or negative AFB sputum smear
  - Symptom onset dates
  - Homeless or correctional facility use
  - Foreign born
  - Other significant findings of interest
- Identified all TB cases in KC that presented with history of homelessness and requested genotyping of their isolates (added 7 to the cluster)
- Obtained incarceration histories on individuals within the cluster through the Jackson County Detention Center
- Obtained shelter histories from the City Union Mission database

Kansas City KS/MO cases by year
Steps to address outbreak

• Seeking grant funding from Western Missouri Foundation for Health
  – Administrative controls:
    • Full-time nurse to conduct communicable disease prevention and control
  – Engineering controls at the largest shelter

• Social networking project
Genotype clusters – risk groups for transmission Missouri 2004 – 2006 (some historical genotypes included)

<table>
<thead>
<tr>
<th>Genotype cluster</th>
<th># matches</th>
<th>Epidemiological link</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0-016</td>
<td>7</td>
<td>Bar – St. Genevieve</td>
</tr>
<tr>
<td>MO-006</td>
<td>14</td>
<td>Homeless shelter – St. Louis</td>
</tr>
<tr>
<td>MO-007</td>
<td>13</td>
<td>Homeless shelter – St. Louis/Greenwood MS</td>
</tr>
<tr>
<td>MO-030</td>
<td>7</td>
<td>Jail – Jasper County</td>
</tr>
<tr>
<td>MO-009</td>
<td>8</td>
<td>Homeless shelters - KC</td>
</tr>
<tr>
<td>MO-010</td>
<td>20</td>
<td>Homeless shelters – KC</td>
</tr>
<tr>
<td>MO-027</td>
<td>5</td>
<td>Bar – St. Louis County</td>
</tr>
</tbody>
</table>

Social Network Analysis

- Social Network – linkage of persons and places where *M. tuberculosis* is spread via shared air space.

- Social Network Analysis – methodology of visualizing and quantitating the relative importance of members in a social network.

- Social Network Analysis assumes there is some detectable patterning of the TB cases and their contacts in a community.

  – Connie Carpenter, MU PhD Candidate – Anthropology Dept
Social Network Analysis (cont.)

- Offers an effective way to list TB contacts and assign priorities.

- Analysis of the network can help identify important contacts (i.e., those most likely to be infected).

- Real-time monitoring of network growth may facilitate early detection of outbreaks.
“Drinkin' buddy” outbreak

1989

1991

1993

1997

1998

1999

2000

2001

RFLP testing


Index case
Clinical case
Confirmed epi link
Suspect link
Drinkin bud
Family members

Corrections
MDR TB outbreak
Missouri
001mo.H3514

RFLP testing

Corrections

Cx confirmed
Clinical case
Confirmed epi link
Suspect link
Inside DOC
Outside DOC

Always look back!
Lessons learned/After action reviews
Evaluation of a large scale TB contact investigation in the Netherlands

- In November 2004, a 25-year old male Dutch-born full-time supermarket employee...was diagnosed with sputum smear-positive cavitary TB after a 12 month history of cough
  - 12 close contacts – 3 MTB / 7 LTBI
  - 80 supermarket co-workers – 1 MTB / 46 LTBI


Results of expanded contact investigation

<table>
<thead>
<tr>
<th>Frequency of supermarket visits</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/wk</td>
<td>1/wk</td>
</tr>
<tr>
<td>2656 (20%)</td>
<td>3562 (26%)</td>
</tr>
<tr>
<td>1017/894 (4.0%)</td>
<td>50/162 (2.0%)</td>
</tr>
</tbody>
</table>

**Results of expanded contact investigation**

| Expected age-adjusted prevalence of remote TBI | 1.48% | 1.48% | 1.48% | 1.48% | 1.48% |
| Specificity TST | 90.8% | 91.1% | 90.8% | 90.8% | 90.8% |
| Number of TST | 40/167 (27%) | 50/162 (30%) | 47/165 (27%) | 61/107 (56%) | **158/343 (46%)** |
| Recent TBI, tuberculin-positive | 5/167 (3%) | 6/162 (3%) | 4/165 (2%) | 5/107 (1%) | **25/343 (7%)** |
| Recent TBI, tuberculin-negative | 35/167 (21%) | 43/162 (26%) | 43/165 (26%) | 55/107 (52%) | **133/343 (39%)** |
| Prevalence of true recent TBI | 62/2358 (2.6%) | 42/1362 (3.1%) | 127/1825 (6.9%) | 111/145 (7.6%) | **157/343 (4.5%)** |
| Incremental yield | 4/25 (16%) | 4/25 (16%) | 3/25 (12%) | 1/25 (4%) | **14/111 (13%)** |

For 62/2358 patients (2.7%); including 9/2358 with positive TST; no exposure data were available.

TST = tuberculin skin test. TBI = tuberculosis infection, including both latent infections and infections with active disease. Remote TBI: number of cases calculated as expected age-adjusted prevalence of remote TBI x number of TST.

Incremental yield: proportion of true recent infections that was identified additionally by screening contacts in the exposure category indicated.

*Significantly different from expected age-adjusted prevalence of remote infections (1.5%).

**Number of subjects needed to test by tuberculin skin testing to identify one true-positive case of recent tuberculosis infection.
Results of expanded contact investigation

Table 4. Yield and effectiveness of screening for tuberculosis infection by tuberculin skin testing among 13,343 supermarket customers, by reported frequency of visits to the supermarket.

<table>
<thead>
<tr>
<th>Frequency of supermarket visits</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1/week</td>
<td>1/week</td>
</tr>
<tr>
<td>Number of TST†</td>
<td></td>
</tr>
<tr>
<td>TB1 diagnosed (prevalence)</td>
<td></td>
</tr>
<tr>
<td>3664 (20%)</td>
<td>3352 (23%)</td>
</tr>
<tr>
<td>Sensitivity TST† [10]</td>
<td>76.6%</td>
</tr>
<tr>
<td>Specificity TST† [10]</td>
<td>98.8%</td>
</tr>
<tr>
<td>Expected age-adjusted prevalence of remote TBI</td>
<td>1.4%</td>
</tr>
<tr>
<td>Recent TBI, tuberculin-negative</td>
<td>5197 (32%)</td>
</tr>
<tr>
<td>Recent TBI, tuberculin-positive</td>
<td>5297 (32%)</td>
</tr>
<tr>
<td>Prevalence of true recent TBI</td>
<td></td>
</tr>
<tr>
<td>412/5322 (1.7%)</td>
<td>421/5322 (1.3%)</td>
</tr>
<tr>
<td>Incremental yield</td>
<td>421/5322 (1.3%)</td>
</tr>
<tr>
<td>Number needed to test†</td>
<td>421/5322 (1.3%)</td>
</tr>
</tbody>
</table>

SB of 629 persons (4.5%, including 19 with positive TST). No exposure data were available.

†Scale of 10 years (6.6%). Sensitivity TST was calculated as (expected age-adjusted prevalence of remote TBI)/total number of TST.

Prioritizing

If skin testing had been limited to shoppers who shopped at least once a week, more than half of the customers would not have been tested while 83% of MTB and 89% of true TBI would have been detected.

Blood assay testing would have improved predictive value in BCG-vaccinated shoppers

Awareness raising among local GPs could have been an alternative to mass screening

The Netherlands are currently developing a “structured protocol” for large-scale investigations


Lessons learned

- Cost-benefit
  - 500,000 Euros spent on the investigation
  - In order to detect 1 case of active TB – 1293 customers had to be tested
- 56-58% of the detected TBI cases were due to remote infection and most likely unrelated
- Prioritizing
  - If skin testing had been limited to shoppers who shopped at least once a week, more than half of the customers would not have been tested while 83% of MTB and 89% of true TBI would have been detected.
  - Blood assay testing would have improved predictive value in BCG-vaccinated shoppers
  - Awareness raising among local GPs could have been an alternative to mass screening
- The Netherlands are currently developing a “structured protocol” for large-scale investigations
Looking back – you’ll be glad you did!

- Regroup and document what worked and what did not work
  - All participants
- Lessons learned - implement change for the next investigation

References


MODHSS. (2007a). "Missouri Tuberculosis Information Summary." Retrieved April 8, 2008, from [www.dhss.mo.gov/Tuberculosis/TB06.ppt](http://www.dhss.mo.gov/Tuberculosis/TB06.ppt)


Carpenter, C (presentation) “Social Networks and TB Transmission” at Responding to a TB Event, Heartland National TB Center, April 29-May 1, 2008
References (2)


