Household Considerations in the Management of Children with DR-TB: Contact Tracing and Infection Control.

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Wednesday
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www.drtbnetwork.org
Objectives

• To illustrate the impact of a case of DR-TB on a household
• To discuss the epidemiology of DR-TB in household contacts
• To review the need for active case finding for household contacts of persons with DR-TB and strategies to employ
• To discuss preventive therapy regimens for children exposed to DR-TB
• To review community-based infection control measures
Case Example

- PM is a 46 year-old man diagnosed with MDR-TB after 10 months of symptoms and a failed treatment regimen of HREZ.
- He is started hospitalized and started on a regimen of Z-KM-LFX-Ethio-CS after his DST shows resistance to INH-RIF-EMB.
- After three months in the hospital, plans are being made for his discharge home.
- He will be moving back to his family home in a rural area.
- A health center has been found where he can receive DOT and his injection and plans are made for him to follow-up once a month at the district health center.
Case example (continued)

• One of the nurses at the health center where he will be going calls to say she is worried about the family, that they are “very poor” and that she thinks that they are at risk for becoming infected with MDR-TB
Questions

1. What would you tell the nurse about the risk of developing MDR-TB among household members?

2. What additional action steps should be taken for this family?
Cascade in Childhood DR-TB

- Susceptible
- Exposed
- Infected
- Diseased
- Sick
- Diagnosed
- Treated
- Cured
Multiple studies have shown that DR-TB can be spread within households.

- Teixera et al (2001): 4% of 133 contacts of MDR-TB patients developed MDR-TB during follow-up, similar to rates seen in PS-TB.
- Becerra et al (2011): 359 of 4503 (7.9%) household contacts developed active TB over a period of 4 years.
- Grandjean et al (2011) found that there was a TB disease incidence of 2360 per 100,000 contact follow-up years in the first three years after exposure.
Tuberculosis burden in households of patients with multidrug-resistant and extensively drug-resistant tuberculosis: a retrospective cohort study

*Mercedes C. Becerra, Sasha C Appleton, Molly F. Franke, Katiuska Chalco, Fernando Arteaga, Jaime Bayona, Megan Murray, Sidney S. Atwood, Carole D. Mitnick*

<table>
<thead>
<tr>
<th>Year</th>
<th>Overall</th>
<th>Index XDR</th>
<th>Index MDR</th>
<th>Adjusted hazard ratio (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence rate per 100 000 person-years</td>
<td>Cases</td>
<td>Person-years</td>
<td>Incidence rate per 100 000 person-years</td>
</tr>
<tr>
<td>Year 1</td>
<td>3165</td>
<td>140</td>
<td>4423</td>
<td>4252</td>
</tr>
<tr>
<td>Year 2</td>
<td>1092</td>
<td>47</td>
<td>4303</td>
<td>2714</td>
</tr>
<tr>
<td>Year 3</td>
<td>764</td>
<td>30</td>
<td>3927</td>
<td>1816</td>
</tr>
<tr>
<td>Year 4</td>
<td>1112</td>
<td>25</td>
<td>2247</td>
<td>2734</td>
</tr>
<tr>
<td>Overall (years 1-4)</td>
<td>1624</td>
<td>242</td>
<td>14 900</td>
<td>2928</td>
</tr>
</tbody>
</table>

*Adjusted for household clustering.

**Table 3: Incidence of active tuberculosis in household contacts during 4-year follow-up period**
• 25 total studies
• Evaluated a median of 111 household contacts of patients with DR-TB
• Pooled yield of 7.8% for active DR-TB and 47.2% for LTBI
• 50% concordance with exact same DST pattern of source case; higher rates of concordance seen when looking at strains
• Majority of cases detected within 1 year of source case identification
DST concordance among household contacts

• Use caution when interpreting results from meta-analysis and studies done in which patients who did not receive early diagnosis and therapy, as “amplification” may occur.

• Parr and colleagues (2014) found that while only 36.6% of contacts matched the exact pattern of the index case, almost 90% of them shared the same strain of DR-TB.

Clin Infect Dis 2014; 58: 392-95
Case discussion (continued)

- A household evaluation and contact tracing visit is arranged and a community health nurse goes to visit the family.
- She finds that the family has 3 small shacks on a compound and an outdoor latrine.
- The patient shares one of the shacks with his wife and three children ages 5 and a half, 8 and 11 years.
- The other shack is occupied by his sister, her husband and their twin sons, both age 2 years.
The three children of the source patient are at school at the time of the evaluation, so the nurse asks if they have any signs or symptoms of TB and is told no, although one has asthma.

One of the two year-old boys in the other shack has diarrhea and is not gaining weight.

The nurse places a TST skin test on both of the children.

The nurse completes the contact tracing form, gives them family information about TB, and asks that the twin boys come to clinic in 48 hours to have their skin tests read.
Questions

3. What other information should the nurse have obtained?

4. What steps could have been taken to improve the contact tracing process?
Contact Evaluation: Need for Best Practices

- Need to define “household”
- Most contact tracing is done on a “one time only” basis, with minimal information obtained on household
- Contact tracing tends to focus on children under the age of 5 and those with HIV who are currently in the household and present at the visit
- Lack of careful follow-up for contacts in settings where TB programs are overwhelmed
Household definitions

• WHO (2012): “A person who shared the same enclosed living space for one or more nights or for frequent or extended periods during the day with the index case during the 3 months before commencement of the current treatment episode.”

• WHO recommends contact evaluation of ALL household contacts of DR-TB patients
• Definition 1: ‘All dwellings on the same plot of land that share the same residential address’
• Definition 2: ‘A person or a group of related or unrelated persons, who live together in the same dwelling unit, who share the same housekeeping arrangements, and who have the same eating arrangement
• Very different yields
Age-related risk

- Epidemiology shows highest risks in children under the age of 5 and in those with HIV infection (Marais et al. 2004)
- Older children (ages 5-14) have been shown to have rates of MDR-TB similar to those seen in children under the age of 5, even in the absence of HIV infection (7.8% older versus 6.5% younger, Amanullah et al, 2014)
- Yield of contact tracing in older children may be higher in terms of actual numbers, depending on the age distribution of the population
- Little is known about adolescents although small data series suggest late presentation may be occurring in this group (Isaakidis et al., 2013; Moyo et al., 2014)
The natural history of childhood intra-thoracic tuberculosis: a critical review of literature from the pre-chemotherapy era

B. J. Marais,* R. P. Gie,* H. S. Schaaf,* A. C. Hesseling,* C. C. Obihara,* J. J. Starke,† D. A. Enarson,‡ P. R. Donald,* N. Beyers*

Disease Progression (Percent)

Age in Years

PTB
Disseminated
• All patients diagnosed with MDR-TB patients at large referral center in Pakistan had multiple contact evaluation visits
• Community health workers/home visits were part of the initial contact evaluation strategy
• Monthly screening for a year
• Among 133 children aged under 15 years in 40 households, 7.5% had TB disease
Problems with contact tracing

- Low priority for TB programs
- Often done only once
- Often relies on patient presenting to clinic
### Characteristics of source cases identified (n=1261)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; n=1205; 95.6%)</td>
<td>35 (27-44)</td>
</tr>
<tr>
<td>Gender (n=1259; 99.8%)</td>
<td>Male 693 (55.0)</td>
</tr>
<tr>
<td>HIV status (n=1094; 86.8%)</td>
<td>Positive 585 (53.5)</td>
</tr>
<tr>
<td>Smear status (n=1041; 82.6%)</td>
<td>Positive 488 (46.9)</td>
</tr>
<tr>
<td>District</td>
<td></td>
</tr>
<tr>
<td>Khayelitsha</td>
<td>190 (15.1)</td>
</tr>
<tr>
<td>Klipfontein</td>
<td>178 (14.2)</td>
</tr>
<tr>
<td>Northern</td>
<td>76 (6.0)</td>
</tr>
<tr>
<td>Southern</td>
<td>153 (12.1)</td>
</tr>
<tr>
<td>Tygerberg</td>
<td>179 (14.2)</td>
</tr>
<tr>
<td>Western</td>
<td>166 (13.2)</td>
</tr>
<tr>
<td>Eastern</td>
<td>152 (12.1)</td>
</tr>
<tr>
<td>Mitchell’s Plain</td>
<td>167 (13.2)</td>
</tr>
<tr>
<td>DST (n=1259; 99.8%; GenoType® MTBDRplus)</td>
<td></td>
</tr>
<tr>
<td>MDR</td>
<td>1143 (90.8)</td>
</tr>
<tr>
<td>XDR</td>
<td>116 (9.2)</td>
</tr>
<tr>
<td>Days from sputum to Rx (n=1183); median (IQR)</td>
<td>37 (24-57)</td>
</tr>
</tbody>
</table>
## Expected number child contacts

<table>
<thead>
<tr>
<th></th>
<th>Khayelitsha</th>
<th>Other sub-districts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of child contacts per index case</strong></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Number of index cases</strong></td>
<td>190</td>
<td>190</td>
</tr>
<tr>
<td><strong>Children identified</strong></td>
<td>190</td>
<td>380</td>
</tr>
</tbody>
</table>
## Comparison between hospital and decentralised care

<table>
<thead>
<tr>
<th></th>
<th>Khayelitsha</th>
<th>Other sub-districts</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of children seen</td>
<td>38</td>
<td>115</td>
<td>153</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Index cases with</th>
<th>Khayelitsha</th>
<th>Other sub-districts</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children not identified</td>
<td>159</td>
<td>976</td>
<td>1,135</td>
</tr>
<tr>
<td>Children identified</td>
<td>31 (16.3%)</td>
<td>95 (9.7%)</td>
<td>126 (10.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>190</td>
<td>1,071</td>
<td>1,261</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Khayelitsha</th>
<th>Other sub-districts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to evaluation (days IQR)</td>
<td>71 (37-121)</td>
<td>90 (56-132)</td>
</tr>
</tbody>
</table>
Reasons for not attending

• Physical challenges:
  – The local clinic is easier to go to, but to go to Tygerberg Hospital is sometimes difficult to get there because of money we don’t have.
  – The weather plays a role if you have to go to the MDR-TB clinic because you must wait at the taxi rank or bus stop and sometimes it takes two to three rides to get there
• Attitudes of clinic staff:
  – The sisters at the clinic sometimes take very long to give the letter
  – I just feel some of the staff at the clinic is inexperienced
• Concerns about the appointment itself:
  – I feel uncomfortable because my child is very small and some adults—I could hear how they say that some of them don’t take their medication
  – I had sleepless nights when I first heard I must take my child to the clinic, I even thought my child was going to die; I didn’t know what the doctor was going to say
• Personal issues:
  – I feel some parents just don’t take their children to the clinic because they just don’t care. They don’t take their children’s health seriously
Reasons for not attending

### TABLE 1
Characteristics of children, households, main carers and source cases of children referred as contacts of multidrug-resistant tuberculosis

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Did not attend appointment median [IQR] or n (%)</th>
<th>Attended appointment median [IQR] or n (%)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, child, months</td>
<td>35 [25–51]</td>
<td>36 [23–53]</td>
<td>1.38 (0.62–3.05)</td>
<td>0.35</td>
</tr>
<tr>
<td>Male child</td>
<td>26 (52)</td>
<td>22 (44)</td>
<td>2.82 (1.21–6.59)</td>
<td>0.01</td>
</tr>
<tr>
<td>Coloured ethnicity</td>
<td>30 (60)</td>
<td>17 (34)</td>
<td>3.81 (0.37–39.4)</td>
<td>0.33</td>
</tr>
<tr>
<td>Child HIV-infected (n = 88)</td>
<td>3/40 (7.5)</td>
<td>1/48 (2.1)</td>
<td>1.61 (0.52–4.97)</td>
<td>0.58</td>
</tr>
<tr>
<td>Mother main carer for child</td>
<td>44 (88)</td>
<td>41 (82)</td>
<td>0.91 (0.39–2.14)</td>
<td>0.83</td>
</tr>
<tr>
<td>Years of education of main carer</td>
<td>10 [8–11]</td>
<td>10 [8–11]</td>
<td>0.48 (0.21–1.09)</td>
<td>0.07</td>
</tr>
<tr>
<td>Main carer without any paid work</td>
<td>34 (68)</td>
<td>35 (70)</td>
<td>0.31 (0.06–1.64)</td>
<td>0.27</td>
</tr>
<tr>
<td>Main carer looks after other children</td>
<td>20 (40)</td>
<td>29 (58)</td>
<td>0.61 (0.27–1.37)</td>
<td>0.23</td>
</tr>
<tr>
<td>Male main carer</td>
<td>2 (4)</td>
<td>6 (12)</td>
<td>3.78 (1.29–11.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Male source case</td>
<td>19 (38)</td>
<td>25 (50)</td>
<td>1.40 (0.42–4.11)</td>
<td>1.00</td>
</tr>
<tr>
<td>Mother source case</td>
<td>17 (34)</td>
<td>6 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Household LSM score</td>
<td>6 [6–8]</td>
<td>7 [6–8]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarettes smoked in house</td>
<td>36 (72)</td>
<td>26 (52)</td>
<td>2.37 (1.01–5.57)</td>
<td>0.04</td>
</tr>
<tr>
<td>Alcohol drunk in house</td>
<td>27 (54)</td>
<td>27 (54)</td>
<td>1.00 (0.45–2.20)</td>
<td>0.80</td>
</tr>
<tr>
<td>Illegal drug use in house</td>
<td>10 (20)</td>
<td>9 (18)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IQR = interquartile range; OR = odds ratio; CI = confidence interval; HIV = human immunodeficiency virus; LSM = living standard measure.

### TABLE 2
Financial and travel implications of accessing care for child contacts of multidrug-resistant tuberculosis

<table>
<thead>
<tr>
<th>Implication</th>
<th>Did not attend appointment median [IQR] or n (%)</th>
<th>Attended appointment median [IQR] or n (%)</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance to MDR-TB clinic, km (n = 82)</td>
<td>5 [4–8]</td>
<td>6 [2–14]</td>
<td></td>
<td>0.77</td>
</tr>
<tr>
<td>Time taken to travel to MDR-TB clinic, min (n = 93)</td>
<td>60 [45–90]</td>
<td>45 [25–60]</td>
<td></td>
<td>0.0002</td>
</tr>
<tr>
<td>Cost of travel to MDR-TB clinic, SAR</td>
<td>40 [20–60]</td>
<td>18.5 [4–50]</td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>More than one minibus taxi required to get to MDR-TB clinic, n (%)</td>
<td>26 (52)</td>
<td>13 (26)</td>
<td>3.08 (1.28–7.41)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

IQR = interquartile range; OR = odds ratio; CI = confidence interval; MDR-TB = multidrug-resistant tuberculosis; SAR = South African Rand.

*Pub Health Action 2012; 2: 71-75*
Table 3: Perceptions of disease among parents/caregivers of children referred as contacts of MDR-TB

<table>
<thead>
<tr>
<th>Positive responses to the following questions</th>
<th>Not attending n (%)</th>
<th>Attending n (%)</th>
<th>OR (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you have confidence in the medical staff at your local clinic?</td>
<td>33 (66)</td>
<td>41 (82)</td>
<td>0.43 (0.16–1.10)</td>
<td>0.07</td>
</tr>
<tr>
<td>Do you have confidence in the medical staff at the MDR-TB clinic?</td>
<td>48 (96)</td>
<td>49 (98)</td>
<td>0.49 (0.04–5.67)</td>
<td>1.00</td>
</tr>
<tr>
<td>Does the weather affect your decision on whether to attend appointments at the MDR-TB clinic?</td>
<td>16 (32)</td>
<td>13 (26)</td>
<td>1.34 (0.56–3.21)</td>
<td>0.51</td>
</tr>
<tr>
<td>Do you consider MDR-TB a disease that can kill you?</td>
<td>43 (86)</td>
<td>38 (76)</td>
<td>1.94 (0.68–5.50)</td>
<td>0.31</td>
</tr>
<tr>
<td>Do you consider MDR-TB a disease that can be treated successfully?</td>
<td>46 (92)</td>
<td>50 (100)</td>
<td>—</td>
<td>0.12</td>
</tr>
<tr>
<td>Do you think that people in your community with MDR-TB are discriminated against?</td>
<td>24 (48)</td>
<td>25 (50)</td>
<td>0.92 (0.42–2.03)</td>
<td>0.84</td>
</tr>
<tr>
<td>Do you feel that employers in your community discriminate against people with MDR-TB?</td>
<td>37 (74)</td>
<td>28 (56)</td>
<td>2.24 (0.94–5.30)</td>
<td>0.06</td>
</tr>
<tr>
<td>Are you concerned about the risk of being infected with MDR-TB while waiting at the MDR-TB clinic?</td>
<td>30 (60)</td>
<td>19 (38)</td>
<td>2.45 (1.07–5.60)</td>
<td>0.03</td>
</tr>
<tr>
<td>Do you think that your child would take anti-tuberculosis medicines every day without a problem?</td>
<td>27 (54)</td>
<td>34 (68)</td>
<td>0.55 (0.24–1.26)</td>
<td>0.15</td>
</tr>
<tr>
<td>Are you concerned about the side effects of the anti-tuberculosis medicines for the child?</td>
<td>30 (60)</td>
<td>24 (48)</td>
<td>1.63 (0.73–3.62)</td>
<td>0.23</td>
</tr>
<tr>
<td>Do you feel that you have to wait a long time to be seen at your local clinic?</td>
<td>28 (56)</td>
<td>17 (34)</td>
<td>2.47 (1.07–5.69)</td>
<td>0.03</td>
</tr>
<tr>
<td>Do you feel that you have to wait a long time at the MDR-TB clinic?</td>
<td>11 (22)</td>
<td>10 (20)</td>
<td>1.13 (0.43–2.97)</td>
<td>0.81</td>
</tr>
<tr>
<td>Do you think that parents should be responsible for preventing children from getting MDR-TB?</td>
<td>46 (92)</td>
<td>45 (90)</td>
<td>1.28 (0.32–5.11)</td>
<td>1.00</td>
</tr>
<tr>
<td>Out of ten, for you how important a priority is it to have your child assessed in the MDR-TB clinic? Median [IQR]</td>
<td>10 [10–10]</td>
<td>10 [10–10]</td>
<td>—</td>
<td>0.37</td>
</tr>
</tbody>
</table>

MDR-TB — multidrug-resistant tuberculosis; OR — odds ratio; CI — confidence interval; IQR — interquartile range.
Reverse Contact Tracing

Adult

Child

Child

Adult
• Routine chest radiography of all mothers of 163 children investigated for possible TB

• Sputum culture from those mothers with suspicious chest radiographs

• Active pulmonary TB in 12 (10 per cent) of the mothers of the 117 children with TB
Tuberculosis among Families of Children with Suspected Tuberculosis and Employees at a Children’s Hospital

Andrea T. Cruz, MD, MPH;1,2
Denise Medina, RN, COHN-S;3
Elaine M. Whaley, RN, BSN, CIC;4
Kathy M. Ware, RN, BSN, CIC;4
Tjin H. Koy, MT(ASCP), MPH, CIC;4
Jeffrey R. Starke, MD2,4

- Only 7 (12%) of 59 children treated for TB were potentially contagious
- 10 (17%) were accompanied by contagious adults
- Screening caregivers was more cost-effective than performing employee contact investigations, with one-sixteenth the cost ($5,470 vs $88,323) and requiring screening of 35 times fewer persons
Case discussion (continued)

• The mother of the two year-old twins brings both boys to the clinic for follow-up of their TSTs

• The nurse reading the TSTs notes that they are "negative" and tells the mother the children have not been exposed to TB

• She refers to child with diarrhea and weight loss to the MCH clinic where the child is given ORS and de-wormed
5. What should have been done for the child with diarrhea?

6. What should have been done for the two year-old who had no symptoms?

7. What should have been done for the 5 and a half year-old child?
Utility of the TST

- TST sensitivity against confirmed active TB only ~80%
- Impossible to measure sensitivity for LBTI due to no reference standard
- Likely to be as poor or worse

(Int J Tubercul Lung Dis 2011; 15: 1018-1032)
Suggestions for management of DS-TB by WHO (no need for TST)

If HIV-infected give preventive therapy
Management of Child Contacts of MDR-TB Cases

1. **Child exposed to source case with MDR tuberculosis disease**

2. **Does the child have tuberculosis disease?**
   - **Yes**
     - **Start treatment**
     - Obtain microbiological samples
     - Start treatment for MDR tuberculosis disease
   - **No**
     - **Assess risk of infection**
       - TST/IGRA
       - Severity of disease in source case
       - Proximity and intensity of contact
       - Duration of contact
     - **Assess risk of disease progression**
       - Age of child
       - HIV status and degree of immunosuppression
       - Nutritional status
       - Other immunodeficiency
   - **Assess likelihood of infection with MDR strain**
     - Local prevalence of tuberculosis
     - Likelihood of other source case(s)
     - Intensity of interaction with source case(s)
     - Age of child
   - **Progression likely with MDR strain**
     - Consider MDR tuberculosis preventive treatment
     - Follow up for a minimum of 12 months, irrespective of treatment decision
   - **Progression likely with susceptible strain**
     - Treat with isoniazid (10 mg/kg) daily for 6 months

Management of Child Contacts of MDR-TB Cases

- If the source case is rifampicin resistant, and if this diagnosis was made by GeneXpert, consider MDR until drug susceptibility is confirmed by line probe assay (LPA) or DST
- The MDR TB preventative regimen depends on the national program
- Examples include:
  1. Fluoroquinolone and high dose INH
  2. Fluoroquinolone, high dose INH and EMB
  3. Fluoroquinolone and EMB
  4. High dose INH alone
  5. Fluoroquinolone alone
Child in contact with infectious DR source case*  

History and examination by doctor, measure and record weight

- Child has symptoms or signs of TB** or faltering weight
  - Investigate child with CXR (AP and lat), TST and microbiological samples; refer to specialist for consideration of MDR-TB treatment

- Child is asymptomatic, growing well, and has no clinical signs of TB
  - Child is younger than five years or is HIV-infected
    - Record treatment in register
  - Child is older than five years and is HIV-uninfected
    - Reassure family and request return if any concerning signs or symptoms arise

- Source case isoniazid mono-resistant TB
  - Provide rifampicin (15mg/kg daily) for 4 months

- Source case rifampin mono-resistant TB***
  - Provide isoniazid (15-20mg/kg) daily for 6 months

- Source case MDR-TB but susceptible to ofloxacin
  - Provide MDR-TB preventative regimen****

- Source case MDR-TB and resistant to ofloxacin
  - Provide isoniazid (15-20mg/kg) daily for 6 months

Monthly collection of medications with review by nurse, measure and record weight

MDR-TB contacts Review at 3, 6, 9 and 12 months by doctor

If any concerning symptoms, signs or faltering weight, investigate with CXR (AP and lat), TST and microbiological samples and refer to specialist
• Prospective cohort study (Cape Town 1994-2000)
• Infected (n=61) and non-infected (n=44) children <5 years of age
• Household contact with adults with pulmonary MDR TB (n=73)
• All infected children and all children <2 years of age offered preventive therapy.
• Significant risk difference of 15% (95% CI -27% to -4%) between treated and untreated children
• Retrospective study in Brazil (1988 and 1992)
• Close contacts (n=218) of retreated patients with MDR-TB (n=64)
• Some contacts received isoniazid preventive therapy while others did not
• The risk of developing active TB disease was not significantly lower in the treated group
• Risk difference: 4% (95% CI: -3% to 12%)
Two outbreaks in Chuuk, Federated States of Micronesia (July 2008)
Five MDR-TB patients identified
232 contacts identified
  15 MDR-TB
  119 LTBI with positive TST - offered LTBI PT
14 of the 119 cases refused the treatment
LTBI PT was initiated in a total of 105 contacts
All therapy was directly observed
Fluoroquinolone-based regimen
Ninety-three of the 105 completed MDR-TB PT
No cases of MDR TB disease among those who initiated MDR-TB PT
28 contacts developed MDR TB disease out of those not given PT
MDR-TB child contacts in Cape Town

- 186 children
- Median age: 34 months
- TST positive: 73/183 (40%)
- HIV positive: 9/179 (5%)
- 6 months HEO
## Adverse events

<table>
<thead>
<tr>
<th>Condition</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint, muscle or bone pain</td>
<td>178</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Skin Rashes</td>
<td>140</td>
<td>40</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Itchy skin</td>
<td>147</td>
<td>33</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>153</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Sleeping/mood</td>
<td>170</td>
<td>8</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Lethargy</td>
<td>183</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Visual problems</td>
<td>186</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>155</td>
<td>30</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>170</td>
<td>15</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Jaundice</td>
<td>186</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Loss of appetite/nausea</td>
<td>150</td>
<td>15</td>
<td>19</td>
<td>2</td>
</tr>
</tbody>
</table>

*Clin Infect Dis 2013; 57: 1676-84*
Outcome

• 219 patient years of observation time
• One child died (0.5%; most likely of sudden infant death syndrome)
• Six developed incident TB (3.2%)
• The rate for poor outcome was 31.9 outcomes (95%CI 12.8-65.9) per 1000 years of patient follow up

Clin Infect Dis 2013; 57: 1676-84
## Outcome

<table>
<thead>
<tr>
<th>Age</th>
<th>Events</th>
<th>Years of observation</th>
<th>Incidence</th>
<th>Rate Ratio</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;12 months</td>
<td>2</td>
<td>175.5</td>
<td>11.4 (1.4-41.1)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0-12 months</td>
<td>5</td>
<td>43.5</td>
<td>114.9 (37.3-268.2)</td>
<td>10.1 (1.65-105.8)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Source cases</th>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>2</td>
<td>152.4</td>
<td>13.1 (3.28-52.5)</td>
<td>1.0</td>
<td>-</td>
</tr>
<tr>
<td>Multiple</td>
<td>5</td>
<td>56.4</td>
<td>88.6 (36.9-213.0)</td>
<td>6.75 (1.11-70.9)</td>
<td>0.036</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HIV status</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>5</td>
<td>201.5</td>
<td>24.8 (8.1-579.1)</td>
<td>1.0</td>
<td>-</td>
</tr>
<tr>
<td>Positive</td>
<td>2</td>
<td>7.6</td>
<td>263.8 (31.9-950.6)</td>
<td>10.6 (1.01-64.9)</td>
<td>0.049</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adherence</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>2</td>
<td>164.3</td>
<td>12.2 (1.5-44.0)</td>
<td>1.0</td>
<td>-</td>
</tr>
<tr>
<td>Poor</td>
<td>5</td>
<td>54.8</td>
<td>91.3 (29.6-212.9)</td>
<td>7.50 (1.23-78.7)</td>
<td>0.026</td>
</tr>
</tbody>
</table>

*Clin Infect Dis 2013; 57: 1676-84*
• The twin boy continues to lose weight and is eventually hospitalized with severe diarrhea and wasting
• An HIV test is positive and the child undergoes extensive work-up at a charity hospital. He is found to have GI MDR-TB with the same resistance pattern as his uncle and is started on therapy
• The child’s mother has had to get a job as a cleaning woman and she has placed her other twin in crèche. She would like to place her other son in the same crèche when he is out of the hospital, but she has been told he cannot come there because he will spread MDR-TB to the other children
Questions

8. What is the most important infection control measure that should be taken to prevent the spread of MDR-TB from this child to others?
Importance of Infection Control

• General household/community infection control principles
• Infection control issues for children diagnosed with DR-TB
• Infection control should ALWAYS include contact tracing (including reverse contact tracing)
• Maximize safety while minimizing stigma
Most transmission of TB occurs prior to the diagnosis and initiation of therapy
General Household and Community-Based Infection Control

• Education and avoidance of stigma important
• Very low risk of transmitting if on appropriate therapy due to high concentration of antimycobacterials in aerosolized particles
• Avoid bed sharing
• Natural ventilation and UV
• Spend time outside

Nardell et al., 2012, ATS
Dramatic Increase in antibiotic concentration as respiratory droplets evaporate into droplet nuclei

Infection control in households of drug-resistant tuberculosis patients co-infected with HIV in Mumbai, India

T. Albuquerque,¹ P. Isaakidis,¹ M. Das,¹ P. Saranchuk,² A. Andries,¹ D. P. Misquita,³ S. Khan,¹ S. Dubois,¹ C. Peskett,¹ M. Browne²

- Project based in a poor urban area in Mumbai
- 29 households of DR-TB patients
- Early detection and prompt initiation of therapy
- Windows, fans, outdoor time, improved ventilation
- Measure successfully applied in a challenging setting

Pub Health Action 2014; 4: 35-41
Infection Control Issues for Children with DR-TB

- Children usually have lower bacillary burden than adults and are less likely to transmit
- Children more likely to have EPTB and are also less likely to transmit
- Isolation of children, forcing them to mask, keeping them home from school and other activities likely unnecessary from an IC point of view and may be very damaging from a developmental and emotional point view
Conclusions

• DR-TB affects multiple members of families and contacts, and rates of transmission are similar to those seen with pan-susceptible TB
• Household contact tracing is a high yield procedure for finding persons with DR-TB infection and disease
• Contact tracing procedures need to be strengthened to include multiple visits, extended follow-up, and special screening mechanisms for children (who may have atypical signs and symptoms)
Conclusions

• Preventive therapy for DR-TB household contacts has been shown to be beneficial, but only in a small number of observational studies

• Infection control measures can be implemented in the community and household, with a goal of maximizing safety while reducing stigma
Thank you!
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