gaps in the prevention of tuberculosis infection and disease

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U HALLBAUER
DEPT PAEDIATRICS AND CHILD HEALTH
UNIVERSITY FREE STATE
12% TB in children <15 years

In some communities: 35%

Community with high incidence and prevalence of disease -> ongoing transmission in community
Transitions in Tuberculosis

Susceptible → Exposed
Exposed → Infected
Infected → Diseased
Diseased → Infectious
Infectious → Sick
Sick → Accessed care
Accessed care → Recognized
Recognized → Diagnosed
Diagnosed → Treated
Treated → Completed
Completed → Cured

Each transition has a measurable probability

Probability varies with the situation

From Don Enarson
Childhood TB...

A child with TB is a marker of recent transmission in the community.
Reverse contact tracing important.

Children who progress to TB disease after household exposure developed preventable disease.

Rapid progression from infection to disease occurs in children.

Exposure and TB disease in children 5-15 years may be higher than among children < 5 years, but there is less disease.

25% children infected with HIV estimated to have TB.
Limit exposure: Infection control
◦ Education: cough etiquette
◦ Ventilation
◦ Identify and treat adults: Case reporting
◦ UV lights

Prevent infection -> disease
◦ Vaccine
◦ Preventive treatment for individuals at risk of developing active TB disease (young age, malnutrition, HIV, chemotherapy, high dose steroids)
◦ Contact tracing and screening of children: IPT if not diseased

Early case detection: prevent extensive disease and possible further spread
◦ Adequate treatment

“A deterioration in the control of TB thus immediately hurts the youngest generation” (Rieder, 1997)
Vaccine: BCG = Bacille Calmette-Guérin: live attenuated M bovis

*Neonatal BCG* (settings of high TB endemicity) prevents disseminated forms of TB: meningitis and miliary TB, especially in infants and young children.

Does not prevent infection.

In South Africa: high TB and high HIV burden -> still give BCG.

Protection of HIV exposed uninfected children and HIV uninfected children.

*Not used:*

Exception: HIV infected mother, newborn symptomatic.

Revaccination does not add increased protection.

Not used in low incidence countries (< 5 sputum +ve TB patients/100 000).

*Development of new vaccine*
Globally: 66% child TB cases detected

Interpretation  Our model has shown that the incidence of paediatric tuberculosis is higher than the number of notifications, particularly in young children. Estimates of current household exposure and cumulative infection suggest an enormous opportunity for preventive treatment.
Where do we look for these infectious cases?

From Don Enarson
Who is most infectious?

![Graph showing percentage of infection]

- **Smear positive**
  - Same house: 25%
  - Outside house: 10%

- **Smear negative**
  - Same house: 0%
  - Outside house: 0%

*From Don Enarson*
**Epidemiological terms**

**Case: mother**

**ADULT Source case**

Infectiousness: proximity, duration, bacterial load

**Case: grandfather**

**Diseased CHILD**

**Index case**

**CHILD: Non-infected CHILD: Infected**

**Treated: cured**

**Reverse contact tracing**

**Case finding**

**IPT**

**Reactivation after ‘cure’**

[Children are reservoir for future disease]

**stays well**
Time-related risk

Phase of disease
I  Hypersensitivity
II Miliary TB and TBM
III Lymph node disease / Pleural effusion
IV Adult-type disease

From Ben Marais

HIV-infected  PERSISTENT RISK OF REACTIVATION DISEASE
TB in children: Important concepts

- TB in children is different to TB in adults
- Children are more susceptible to develop TB disease than adults
- Children have more extra-pulmonary disease than adults
- Shorter period from infection to disease

- Primary infection of children should be prevented if possible
# Age specific risk for disease development following primary infection

<table>
<thead>
<tr>
<th>Age at primary infection</th>
<th>Risk of disease following primary infection</th>
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<tbody>
<tr>
<td></td>
<td>Immune competent</td>
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<tr>
<td>&lt;1 year</td>
<td>No disease 50%</td>
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<tr>
<td></td>
<td>Pulmonary disease (Segmental) 20-40%</td>
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<tr>
<td></td>
<td>TBM or miliary disease 10-20%</td>
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<tr>
<td>1-2 years</td>
<td>No disease 70%</td>
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<tr>
<td></td>
<td>Pulmonary disease (Segmental) 10-20%</td>
</tr>
<tr>
<td></td>
<td>TBM or miliary disease 5-10%</td>
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<tr>
<td>2-5 years</td>
<td>No disease 95%</td>
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<tr>
<td></td>
<td>Pulmonary disease (Segmental) 5%</td>
</tr>
<tr>
<td></td>
<td>TBM or miliary disease 0.5%</td>
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<tr>
<td>5-10 years</td>
<td>No disease 98%</td>
</tr>
<tr>
<td></td>
<td>Pulmonary disease (Segmental, effusion or adult type) 2%</td>
</tr>
<tr>
<td></td>
<td>TBM or miliary disease &lt;0.5%</td>
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<tr>
<td>&gt;10 years</td>
<td>No disease 80%</td>
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<tr>
<td></td>
<td>Pulmonary disease (adult type) 10-20%</td>
</tr>
<tr>
<td></td>
<td>TBM or miliary disease &lt;0.5%</td>
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Marais BJ  Int J TB Lung Dis 2003
Risk of disease in child TB contact

Smear positive contact case: pulmonary TB; smear negative also risk for infection

Prolonged close contact (mother and infant / toddler)

Household contact
  ◦ WHO: active tracing and screening of all children <5yrs who are household contacts of sputum +ve (and –ve) adults
  ◦ In only 50% children with TB is there a known contact with TB
  ◦ In high incidence TB setting, >40% exposure are with non-household contacts

Time and spatial intervals
  ◦ Might be difficult to relate to specific source case, high background endemicity of TB
  ◦ Time: within few weeks up to one year
  ◦ Often recent, can find adult source
How to screen

Depending on resources:

1. **Clinical assessment**: History (contacts, any symptoms, clinical examination)
2. **Tuberculin skin test (TST)**
3. **Chest x-ray**: if abnormal, Rx (2HRZ 4HR)

**Tuberculin skin test**
- Hypersensitivity reaction against tuberculin
  - = infection ≠ illness

Possible false negative result influenced by:
- malnutrition
- immunocompromised state
- overwhelming TB
- measles

Add names of contacts to TB treatment card of the TB patient
Contacts of index case: Purpose of screening

1. Identify contacts (all ages) with undiagnosed TB disease
2. Provide preventive therapy for contacts without TB disease who are susceptible to develop TB disease after recent infection
   - All children <5 yrs age
   - HIV infected children, any age
3. Evaluate for active disease
   - All children <5 yrs age
   - Symptomatic children, any age
   - Children with known or suspected immunocompromising conditions (esp HIV, diabetes)
   - Child contacts of index cases with drug-resistant TB (proved or suspected)
Symptom-based screening approach to child contact management

Child in close contact with source case of smear-positive pulmonary TB

Under 5 years of age
- Well: 6H, if becomes symptomatic, Evaluate for TB disease
- Symptomatic: Evaluate for TB disease

Under 5 years or over
- Well: No preventive treatment if HIV-negative
- Symptomatic: Evaluate for TB disease

Data on prevention

Studies on contact tracing

Proportion of cases identified by contact tracing

Proportion of cases completing IPT

HIV-infected children on IPT

Proportion of cases on IPT who developed TB disease
Isoniazid preventive therapy: IPT

< 5 YEARS OF AGE

NO TB DISEASE

ALL HIV-INFECTED CHILDREN

IRRESPECTIVE OF AGE

◦ Likelihood of TB infection is high
◦ Risk of TB disease is high
◦ TST is not required prior to progression or commencing INH prophylaxis

INH 10mg/kg/d (7-15mg/kg/d) for at least 6 months

Follow-up every 2 months until treatment complete - critical

• Check adherence
  (20%; 26% in studies CT 2006)
• Check effectiveness

Reduces TB disease risk by 2/3 or more with 90% adherence

No risk of INH resistance to TB, even if diagnosis of active TB (TB disease) was missed

Should be part of formal monitoring and assessment program.

Actually is treatment for latent TB infection.
Gap: policy - practice

Patients: knowledge and understanding suboptimal

HCW’s: knowledge and understanding suboptimal; migration of HCW’s

Weak health care system

Lack of resources

Costs

Transport

IS THERE A GAP, IS IT GETTING SMALLER?
– direct indicators of quality of service
  ➢ Immunisation coverage
  ➢ TB treatment outcomes
  ➢ Proportion of children of a contact screened
  ➢ Proportion of adherent children
  ➢ Proportion of children developing TB disease
Prevention of TB disease in vulnerable populations after exposure
Prophylaxis – source case with drug-resistant TB

Name of source case
Intensive contact and vulnerable contact individual
Risk of disease outweighs risk of adverse effects of prophylactic drugs
Get DST pattern of organism of source case
Select appropriate drug combination

REFER TO EXPERIENCED CLINICIAN
DR-TB VASTLY UNDERESTIMATED: GLOBALLY AND SA
Infection control

Public:
At health care facility: safe health care and attendance without fear of contracting TB
HCW: safe working environment
Raise awareness in community
Attendance at congregate settings
At home

Political, institutional, financial commitment
WHO guidelines on infection control (2009)
Factors that increase TB transmission
Inhalation of one droplet with 1-3 viable bacteria suffices for infection to occur

- smear positive sputum (30 000 – 50 000 organisms / ml)
- smear negative sputum (~1000 organisms / ml), prolonged contact
- lung cavitation, esp upper lobe
- frequent / forceful cough
- not covering cough
- forceful exhalation manoeuvres: singing, shouting
- high volume, low viscosity sputum
- prolonged duration symptoms
- no / inadequate therapy
- airway instrumentation (in children: esp miliary or laryngeal disease)
Cover your cough
PREVENTION OF TB: Infection control in the health care setting
administrative measures

Think TB : Greater risk awareness
Cough etiquette
Keep adults and children separate in outpatient setting
Keep adults (HCW’s, mothers, visitors) with symptoms of TB separate
Assess adults and treat soon
Masks (surgical) for sick persons
Identify infectious children (cavitary pulmonary TB, smear positive TB)
Local facility guidelines
A functioning TB health system: Diagnosis, treatment and adequate referral available
PREVENTION OF TB: Infection control in the health care setting engineering measures

- Adequate isolation facilities, own rooms
- Ventilation in the clinic and ward
- Safe sputum collection
- UV radiation
PREVENTION OF TB: Infection control in the health care setting
personal measures

HCW personal protection:
◦ Availability of masks for HCW’s (N-95): proper use, models and fit
◦ know your HIV status
◦ avoid working in high risk area

Contact (of HCW) investigation
Preventing the spread of TB
community messages

- Ventilation in the home
- No smoking
- Cough etiquette (cover your cough)
- Diagnose and treat adults with TB disease
- Ensure compliance to treatment (DOT)
- Personal protection of exposed persons (masks for sick persons)
FACTORS contributing to nosocomial spread of TB

EASILY RECTIFIED

- Lack of simple administrative measures
- Poor ventilation, inappropriate building design
- High patient load, long waiting times, crowded clinics and wards
- TB patients (and visitors) should never share facilities with young children (eg neonatal wards, children with malnutrition)
- Screen pregnant, breastfeeding women
- Isolate children with smear +ve or cavitary TB
- Unsuspected TB in adults visiting (eg family member) or caring (eg HCW’s) for sick children
FACTORS contributing to nosocomial spread of TB

MORE DIFFICULT TO ADDRESS

- Poor adherence to TB treatment
- Weak health care systems
- Lack of implementation of IPT and ART
- Shortage human resources
- Inadequate education of HCW’s
- Inadequate understanding of patients
- Poverty and stigmatization
Reverse contact screening of adults
(mothers, visitors, HCW’s)

1. Symptom screening
   KENYA: Missed TB disease if used alone in HIV-infected pregnant women
   +ve symptom screen: 20% (3/38 presumptive TB on CXR)
   - ve symptom screen: 80% (7/149 presumptive TB on CXR)

2. Chest x-ray

3. Sputum smear microscopy +/- culture or rapid molecular test
   (Xpert MTB/RIF)
References

7. Cruz AT, Starke JR. A current review of infection control for childhood tuberculosis. Tuberculosis 2011;91:S11-S15