Turning Off the Spigot
Reducing Nosocomial Drug Resistant TB Transmission

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TB is an airborne infection

• Every case of MDR/XDR TB prevented is one fewer patient who will require 18-24 months of difficult and expensive treatment

• Effective treatment for TB = prevention
  – but treatment alone is not enough
Reconsidering TB Transmission Control Priorities

• Institutional transmission is fueling M/XDR epidemic spread
  - Reinfection is an essential propagation component
  - Implications for:
    • importance of institutional transmission control
    • the potential for INH prevention
    • the potential for a new TB vaccine
    • the importance of community-based MDR treatment

• Prompt, effective treatment stops transmission
  - Persons with unsuspected or inadequately treated drug resistant TB cause most transmission
  - Implications for:
    • rapid diagnostics
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How is MDR acquired?

• 2008 WHO data:
  – more than 50% of MDR occurs in patients NOT previously treated
    • primary, transmitted TB
    • not acquired through poor therapy
  – Many previously treated cases are re-infected
    • also transmitted, but misclassified as “acquired”, as if poor treatment was the cause
Trends: Peru 1996-2005

% MDR-TB among new cases

% Any INH resistance among new cases

TB notification rate

Not listed in 2010 report as a country with decreasing MDR cases
MDR Trends in Tomsk and Orel 1994-2008
Importance of Transmission in Tomsk

• Retrospective study
  – role of non-adherence and default and the acquisition of multidrug resistance

• Substance abuse
  – strong predictor of non-adherence (OR 7.3 (2.89 - 18.46)
  – but non-adherence NOT associated with MDR-TB

• MDR-TB occurred
  – among adherent patients who had been hospitalized in the course of therapy compared to those treated as out-patients
    • OR 6.34 (1.34 – 29.72) – began treatment in hospital
    • OR 6.26 (1.02 – 38.35) – hospitalized later during treatment
53 XDR Patients in Kwazulu Natal, South Africa
55% had no previous TB treatment – i.e., transmitted
- most had the same “KZN” strain
67% had been hospitalized
100% had HIV co-infection
100% mortality – avg 16 days from TB diagnosis
Samara Oblast 9-yr Study


• TB among health workers:
  – TB risk: 742/100K person-years at risk
    • 10X that of general population.
  – In-patient TB facilities
    • incidence ratio of 17.7 compared general health workers
  – Implications for global TB work force
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Reinfection Drug Resistant TB in a Boston Homeless Shelter

- Proved exogenous reinfection as common in a 1983 drug resistant TB outbreak
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Treatment delivered in homes by trained, paid, community health workers

PIH introduced community-based treatment of MDR TB in Peru in 1996. Now in PIH-Lesotho, Karachi, Cambodia, and other sites - only about 10% of patients hospitalized in Lima

Highly effective, with less opportunity for institutional transmission
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Riley Experimental TB Ward, 1956-60
(reprinted as “classic” Am J Epidemiol 1995; 142:3-14)

Hundreds of sentinel guinea pigs sampled the air from a 6-bed TB ward in Baltimore
TB transmission only from untreated patients - 1

- Patients selected:
  - strongly smear positive
  - cavitary TB
- 3 of 77 patients produced 35 of 48 (73%) of GP infections that were cultured
  - all drug resistant M. tuberculosis on inadequate therapy
  - 4 month period* of no infections when drug susceptible patients were admitted to the ward.
Riley Ward – 2nd 2-year study
- included untreated patients

Relative infectivity of patients*:

- Susceptible TB
  - 61 *Untreated* (29 GPs) 100%
  - 29 Treated (1 GP) 2%

- Drug-resistant TB
  - 6 *Untreated* (14 GPs) 28%
  - 11 Treated (6 GPs) 5%

*all smear positive patients, relative to the amount of time on the ward
TB transmission only from untreated patients – Peru

Escombe 2008 Plos Medicine; 5:e188

– 97 HIV+ pulmonary TB patients exposed 292 guinea pigs over 505 days
  • 66 cult +, 35 smear +
– 122/125 GP infections due to 9 MDR patients
  • all inadequately or delayed treatment
    » 108/125 infections due to 1 MDR patient
  • 3 drug susceptible patients infected 1 guinea pig each
    » 2 had delayed treatment
    » 1 had treatment stopped
The AIR Facility
Witbank, Mpumalanga Provence, RSA
TB transmission only from untreated patients – South Africa

Airborne Infections Research (AIR) Facility – unpublished data

- All MDR patients - selected for:
  - strongly smear +
  - cavitary TB
  - recently started on therapy

- Experiment 1: 26 MDR-TB patients exposed 360 guinea pigs over 4 months
  - 75% guinea pig infected
  - 11 spoligotype patterns from GP isolates
  - All due to 3 patients later found to have had XDR-TB not on effective treatment.

- Experiment 2: 10% guinea pigs infected over 3 months
  - no XDR patients identified so far

- Experiment 3: 53% guinea pigs infected over 2 months
  - 3 XDR patients identified
Transient TB Infections observed

1. Many guinea pigs reverted their skin test back to 0 mm.
2. Guinea pigs did not show signs of TB or have histological findings at autopsy
Reinfection is an essential pathway to cavitary disease under endemic conditions

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Unsuspected, untreated TB

General Medical Ward
Orthopedic Ward
Obstetrics Ward
Psychiatric Ward
How common is unsuspected TB?
(Emerg Inf Dis 2001; 7:123-7)

• 250 of 349 pts admitted to on female ward in Lima were screened for TB over 1 year:
  - sputum
  - CXR
  - history
  - physical exam

• 40 pts (16%) had positive cultures
  - 26/40 (65%) smear positive
  - 13/40 (33%) unsuspected
  - 8/40 (20%) had MDR
    • Incl. 6/8 MDR unsuspected
      - 3/6 were smear positive
Unsuspected, untreated MDR/XDR TB
All other patients on effective treatment

TB Hospital
Potential for re-infection
Unsuspected, untreated XDR TB
All other patients on effective treatment

MDR TB Ward
Potential for re-infection
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TB Triage – PIH-Haiti

Community based TB treatment

Hospitalized patients *on treatment*

- **General ward**
  - Sm -, HIV +/-

- **TB Pavilion**
  - Sm+, HIV-

- **6 isolation rms**
  - SM+ and HIV+
Poor Hospital and Clinic Design
- need to build local capacity

One million dollar renovation of old TB hospital in Botswana
Poor design - multiple small isolation rooms off common entries
PIH Lesotho, 2007
Botsabelo MDR Hospital
Building Global Capacity

• “Building Design and Engineering for Airborne Infection Control – an International Perspective”
  – Harvard School of Public Health, Boston
    • August 2-13, 2010
    • Co-sponsored by CDC, NIH, WHO

• https://ccpe.sph.harvard.edu/request.cfm
General Air Disinfection: Upper Room Ultraviolet Fixtures

• 75% effective in recent studies
• Better locally produced fixtures needed
• Expertise needed
Room Disinfection: Open bulb Ultraviolet Lamps

Common in Russia and E. Europe
Used in empty rooms
Not likely to be effective
-> false assurance.
Room Air Cleaners – filter or UV
- generally ineffective - false assurance
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Global Health Delivery – on line

- **GHDonline.org**
  - Free MDR and TB transmission control resource
  - Discussion on topics of interest
  - Monitored by international experts
  - Resource for guidelines, documents, and consultants around the world