TB infection control: overview and importance

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Patterns of TB disease

• Latent tuberculosis – risk of relapse depends on immunity and strain type; risk of re-infection
• Pulmonary TB – typically cough, weight loss, fevers, haemoptysis – infectivity highest for smear positive cases
• Atypical pulmonary disease – HIV patients– detection difficult without culture or geneXpert– infectivity lower
• Non-pulmonary disease – meningitis, lymph nodes, other sites – patients not infectious
56 yo aboriginal patient, smoker presented with productive cough, fatigue, weight loss and fever
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3 weeks productive cough, one episode haemoptysis, pleuritic chest pain, night sweats, chills and rigors, fevers
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Transmission of *M. tuberculosis*  

- Almost always acquired by inhalation via airborne or droplet spread  
- Usual source is an untreated case of pulmonary *tb*  
- 25-40% of household contacts of an untreated smear positive case become infected

**Fact 1**

*Tuberculosis (TB)* is contagious and spreads through the air. If not treated, each person with active *TB* can infect an average of 10 to 15 people a year.
Droplet nuclei are inhaled. One droplet nuclei contains 3 bacilli. small that they can remain air-borne for extended periods of time. generated by during talking coughing and sneezing. Coughing generates about 3000 droplet nuclei. Talking for 5 minutes generates 3000 droplet nuclei. Sneezing generates the most droplet nuclei
Increased risk for transmission/
Increased infectiousness

coughing patient
cough-inducing or aerosol-generating procedure
failing to cover nose and mouth during coughing
cavitation on chest radiograph
high concentration of bacteria in secretions
  – smear positivity
Drug-resistant (DR)-tuberculosis

• Single drug therapy – initial response then genetic mutations arise and resistant subpopulation expands causing relapse.
• CAT1 multi-drug therapy standard- relies on INH and rifampicin susceptibility and patient compliance to avoid primary resistance
• Secondary resistance: cross transmission of a resistant strain to another person – in community or hospital. Patients on Cat1 treatment can be infected by a multidrug-R strain.
• Mixed DS and DR infections occur in around 10% of new infections- creates risk of treatment failure
MDR and XDR TB

- 3.7% of all new TB diagnoses worldwide are MDR TB
- In previously treated TB its 20%
- BRICS – Brazil, Russia, India, China and South Africa 60% of new cases/year
- Of the estimated 500000 new MDR cases per year, <7% are diagnosed and only 1 in 5 of these are appropriately treated
Impact of drug-resistant (DR)-tuberculosis

• MDR cases are resistant to INH and rifampicin
  – Renders necessity for more prolonged treatment
  – Cost of treatment X 200 that of drug susceptible TB
  – Mortality rate untreated 70%

• Without systematic detection and programmatic management of DR-TB, it replaces DS-TB and disease burden (number of cases) increases
Evidence of primary transmission of multidrug-resistant tuberculosis in the Western Province of Papua New Guinea

Christopher M Gilpin, Graham Simpson, Stephen Vincent, Terry P O’Brien, Trevor A Knight, Maria Globan, Christopher Coulter and Anastasios Konstantinos

Objective: To review patient outcomes and the molecular epidemiology of multidrug-resistant tuberculosis (MDR-TB) strains isolated from patients living in the Western Province of Papua New Guinea (PNG) seeking treatment in Australia.

Design, setting and participants: Review of all cases of MDR-TB among people living in the open border region between the Western Province of PNG and the Torres Strait Islands of Australia who presented to health clinics in the region between 2000 and 2006. All cases of suspected TB were bacteriologically confirmed at the time of presentation by the Mycobacterium Reference Laboratory in Brisbane.

Main outcome measures: Drug resistance patterns; drug use and duration; molecular typing of TB strains; patient outcomes.

Results: Between 2000 and 2006, 60 patients from the Western Province of PNG were diagnosed with TB, of which 15 had MDR-TB. Mortality was high, although no patient who was able to maintain access to supervised therapy died. All 15 MDR-TB isolates were Beijing-family strains showing the same unique mycobacterial interspersed repetitive unit (MIRU) profile, with the exception of a single strain that differed by a single repeat at one locus. Restriction fragment length polymorphism (RFLP) typing on 10 of these strains further differentiated them into two distinct clusters.

Conclusion: Transmission of MDR-TB is occurring in the Western Province of PNG. Additional resources are urgently needed to interrupt the ongoing transmission of MDR-TB from the Western Province of PNG to the Torres Strait Islands. Good supervision and management of patient treatment, which includes ensuring a regular supply of second-line anti-TB drugs, are essential elements of TB control.
Diagnosis by DST

PMGH TB Clinic PMDT Register
(n=98; MDR: 26; R-R: 49; Presumed: 18; Mono-Resistant: 5)

<table>
<thead>
<tr>
<th>Year</th>
<th>Mono-R</th>
<th>MDR</th>
<th>R-R</th>
<th>Presumed</th>
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<td>Jan-Aug-2014</td>
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<td>16</td>
<td>26</td>
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Courtesy: Dr Rendi Moke
# Diagnosis by DST

## Drug Resistant Pattern: XDR-TB

<table>
<thead>
<tr>
<th>Patient</th>
<th>H</th>
<th>R</th>
<th>S</th>
<th>Eto</th>
<th>Z</th>
<th>E</th>
<th>Ofx</th>
<th>Cm</th>
<th>Km</th>
<th>Am</th>
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<tr>
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<td>R</td>
<td>R</td>
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<tr>
<td>2 (BS)</td>
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<td>R</td>
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<td>S</td>
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<tr>
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<td>S</td>
<td>S</td>
<td>Km, Mfx, Cs, PAS, Aug/Clz</td>
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</table>

*Other drugs: Lfx, Mfx, Aug, Lzd, Clz*
PNG action 2014

• National TB drug susceptibility survey will report late 2014
• National task force set up by PM, NDOH. WHO, MSF, other NGOs involved
• Training of physicians from all Provinces this week- programmatic management of DR-TB and TB-IC – F-A-S-T strategy
• Laboratory capacity building/support; culture and DST about to restart (CPHL); lab supervision and quality assurance
**F-A-S-T** strategy for TB & DR-TB control

**Finding TB Patients:**
The most infectious TB patients are the ones that we don’t know about because they are not being treated. Undiagnosed TB patients can be in clinics, waiting areas, hospital emergency rooms, and wards that care for surgical or other medical problems. Asking all patients about TB symptoms, such as chronic cough, fever, and weight loss can lead to finding previously unsuspected TB cases, as can observing patients for cough in waiting rooms, registration areas, and admission holding areas.

**Actively:**
TB is usually diagnosed passively, occurring when patients’ symptoms lead them to seek help. However, symptoms, such as cough, fever, and weight loss can be present for a long time, be attributed to other conditions, or be overshadowed by other pressing issues. The **FAST** strategy incorporates specifically trained staff called “cough monitors” or “cough surveillance officers” whose job is to identify patients with chronic cough and other TB symptoms, and promptly collect sputum, which would ideally be sent for rapid molecular testing.

**Separating safely:**
MDR-TB patients should be moved to a well-ventilated area to prevent the transmission of MDR-TB to other patients.

**Treatment:**
Treatment is the final and most important step in preventing transmission of TB to others. Patients become non-infectious soon after starting effective TB treatment.
Finding patients-Actively-\textit{S-T}

- Administrative measures- policies and procedures, establish responsibilities
- Cough control officer(s) required!
- Screening– standard questioning of ALL admitted patients; determine risk for DR-TB as per CPHL
- HIV screening
- When indicated – PTB symptoms and/or HIV positive- rapid TB testing essential- same day sputum smear +/-geneXpert

Models of logistics & action – see published experience from South Africa and other Pacific Nations. WHO guidelines on management.
TB diagnosis: specimen types

- Sputum
- Gastric aspirate/lavage/string test
- Sterile sites- blood, fluids
- Urine
- Tissues- pleural biopsy, lymph node biopsy
Sputum specimen protocols

• Collection – instruction of patient and collection procedure; collect outside

• Two specimens recommended by WHO
  – Specimen on day of clinic followed by next morning specimen
  – Same day with two specimens and rapid diagnosis (preferred)
Mycobacterium tuberculosis
visualization using the Ziehl–Neelsen
GeneXpert-TB-RIF

• Detects TB in 2 hours
• Also detects rifampicin resistance
• Works well with a range of specimen types, but especially sputum
• More sensitive than microscopy - detects a large proportion of smear negative, culture positive cases of pulmonary TB (which often happens in advanced HIV patients);
• not as sensitive as culture
CPHL Protocol for GeneXpert testing

Xpert MTB/RIF Algorithm for DR-TB Suspects

The following patients are considered at risk for DR-TB and must be screened for drug-resistance:

A. Re-treatment cases
   (Failures, Relapse and return after default, Others: smear-negative)
B. DOTS non-converters (Cat 1 & II)
C. Symptomatic contacts of known DR-TB patients
D. TB/HIV co-infected

ALL DR-TB SUSPECTS

COLLECT 2 SPUTUM
(Spot & Morning)

PREPARE 1 SMEAR PER SPUTUM

TRANSPORT both sputum to provincial laboratory

PERFORM XPERT ASSAY ON 1 OF 2 SPUTUMS
(if 1 sputum is NEGATIVE, test smear POSITIVE sputum)

STORE second sputum where available
**F-A-Separate safely-T**

Segregation approach example

Community-based TB treatment

Hospitalized patients

General ward
Smear-negative
HIV-positive/HIV-negative

TB pavilion
Smear-positive
HIV-negative

Six isolation rooms:
Smear-positive
HIV-positive

MDR+ cases go in isolation rooms

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**Figure 1** A basic triage and separation strategy, Haiti. TB = tuberculosis; HIV = human immunodeficiency virus. All images in this
Separate safely - environmental controls

- Hospital design and patient flow - many good examples of designs that work from overseas
- Outdoor waiting areas and sputum collection areas
- Segregated buildings/wards and rooms with separate toilets
- Maximise natural ventilation
- Exhaust ventilation
- UV lighting (requires careful placement, maintenance and regular replacement)
Separate safely - Environmental control examples

Figure 2  Typical hospital room with high ceilings and tall windows in Lima, Peru.

In contrast, upper room UVGI fixtures disinfect a large volume of room air at once. Vertical air mixing, optimally aided by slow paddle fans, efficiently disinfects air in the lower room at rates difficult to achieve by mechanical ventilation alone (Figure 6).
Separate safely- protecting staff

• Educate staff – symptoms of TB, use of masks, location of TB patients etc
• Actively screen staff – regularly check for symptoms of TB
• Staff with HIV should not look after infective TB patients
• Staff who care for TB patients or enter TB wards need to protect themselves
  – particulate filtration masks (p2/n95) or respirators
  – Training required to show correct use and fit checking
  – Masks can be reused if not damaged
Masks, Respirators ...

- P2(n95) masks (respirators)
- Reusable cartridge respirators

Figure 7  Routine use of disposable and reusable masks on rounds at the PIH MDR-TB (Partners in Health Resistant Tuberculosis) Hospital, Lesotho.

The MDR-TB and HIV treatment program in Lesotho has piloted the use of a variety of non-disposable rubberized respirators, primarily to cut costs. They also tend to fit better. One non-disposable respirator costs about the same as 10–20 disposable respirators, but can be used indefinitely by replacing the disposable filter cartridges once every 6–12 months under clean conditions. There was concern initially that these...
N95 or P2 particulate masks

• “duckbill” shape
• Different types may be required to fit different facial shapes- need a range available
• Training on how to fit mask properly is essential; ‘fit check’ after putting on
• Change when moist (generally every 3-4 hrs+)
• Mask can be reused if left to dry and elastic ok; don’t share with another
Surgical masks

- Use on coughing patients to reduce aerosols
- Poor protection for staff against TB compared with particulate respirators/masks
- Beards lessen the efficacy of masks +++
**F-A-S-Treat rapidly**

- Rapid start to treatment essential to reduce infectivity
- No RIF-R – FDC (cat1) treatment
- RIF-R case – start initial MDR treatment (new PNG protocols awaited)
- [Timely culture and full drug susceptibility measurement will be required for all RIF-R/relapsed cases so that proper treatment can be designed]
Treat rapidly: How quickly to patients become non-infectious after starting treatment?

- Drug susceptible cases rapidly lose infectivity (within days) despite being culture and smear positive for longer
- MDR cases also have a short infective period ONLY IF appropriate drugs given
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References

• [www.ghdonline.org](http://www.ghdonline.org) – International discussion forums lead by experts – TB infection control and Drug-resistant TB forums
• [http://drtbnetwork.org](http://drtbnetwork.org) F-A-S-T resources, excellent training modules for DR-TB management
• [www.hicsiganz.org](http://www.hicsiganz.org), sublink Tuberculosis – access to WHO Infection control links and other key papers
• Der Spuy et al. Changing Mycobacterium tuberculosis population highlights clade-specific pathogenic characteristics. Tuberculosis 89 (2009) 120–125
• Dharmadhikari et al. Rapid impact of effective treatment on transmission of multidrug-resistant tuberculosis. INT J TUBERC LUNG DIS 2014, 18(9):1019–1025
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