TB in the outpatient setting

Dr Ram Gopalakrishnan
India has a big TB problem

- WHO estimates that India accounts for 2.8 million (27%) of the 10.4 million new cases, and 29% of the 1.8 million deaths.
- Tuberculosis remained one of the top five causes of death among people aged 30–69 years.
- First, India has not adequately tackled key determinants of tuberculosis, especially malnutrition and tobacco smoking, which have been clearly linked with excess tuberculosis mortality.
- Second, India continues to under invest in health, with governmental expenditure on health being one of the lowest in the world at 1.4% of the gross domestic product.
- Third, implementation failures and a weak health system have led to suboptimal cascade of care in the public system. About half a million patients with tuberculosis in India reach tuberculosis diagnostic facilities but are either not effectively diagnosed or not started on treatment.
- While RNTCP only reports data on the number of patients who complete tuberculosis therapy, a considerable proportion of these patients relapse with tuberculosis disease within 1 year of treatment completion.
- Fourth, poor quality of tuberculosis care is a big concern in the private sector, a major provider of health services in India.

Lancet 2017 DOI: http://dx.doi.org/10.1016/S0140-6736(17)30790-0
Reducing global tuberculosis deaths—time for India to step up

- India is one of the few countries that is still reliant on intermittent tuberculosis drug regimens.
- Responding to activist petitions, in January, 2017, the Indian Supreme Court ordered the Indian Government to switch from intermittent tuberculosis therapy to an internationally accepted daily regimen.
- The Minister of Finance in India's 2017 Union Budget outlined an ambitious goal of eliminating tuberculosis by 2025.
- Subsequently, RNTCP published its new draft National Strategic Plan for Tuberculosis Elimination 2017–2025.
- National Health Policy 2017 commitment: to achieve and maintain a cure rate of >85% in new sputum positive patients for TB and reduce incidence of new cases, to reach elimination status by 2025.
Case 1

• A 32/f presents with cough, fever and weight loss for the last 3 months.

• You will order
  – Sputum AFB smear
  – Sputum AFB culture
  – Sputum for Xpert Mtb
  – Quantiferon TB Gold
  – Mantoux
  – Blood for TB PCR
Case 2

• A 18/F presents with matted, palpable nodes in the neck

• You will do
  – FNAC for cytology
  – FNAC for cytology, AFB smear
  – FNAC for cytology, AFB smear, AFB culture
  – FNAC for cytology, AFB smear, AFB culture, Xpert Mtb
  – Excision biopsy for HPE
TB - clinical aspects

• Routinely check HIV and FBS
• Quinolone use delays TB diagnosis and predisposes to quinolone resistant M.tb
  – 11 times more likely after multiple courses of quinolones (Clin Infect Dis 2009;48;1354)
  – 7 times more likely, 20% resistance if >10 days used (Am J Resp dis & Crit Care 2009;180:365)
  – Meta-analysis supports
• Indian guidelines do not support use of fluoroquinolones for CAP
• Look for TB as a cause of FUO when patient gives a history of transient response of fever to quinolones
Diagnosis

• Get a sputum AFB smear, Xpert Mtb & AFB culture, not smear alone

• Sputum AFB smear x 2 with second one on same day equivalent to traditional 3 specimens (The Lancet Infectious Diseases, Early Online Publication, 23 October 2012 doi:10.1016/S1473-3099(12)70232-3)

• Sputum AFB culture commonly not asked for!
  – Growth within 2 weeks with rapid liquid media
  – Ask for sensitivities whenever growth reported
    • WHO recommends whenever INH resistance >1%
  – Smear alone without cultures missed 45% of pulmonary and 85% of extra-pulmonary cases at Apollo (Abstract 22, CIDSCON 2011)
<table>
<thead>
<tr>
<th>Year</th>
<th>Technology</th>
<th>Turnaround time</th>
<th>Sensitivity gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before 2007</td>
<td>ZN microscopy Solid Culture</td>
<td>2-3 days 30-60 days</td>
<td>Baseline</td>
</tr>
<tr>
<td>2007</td>
<td>Liquid Culture Rapid speciation</td>
<td>15-30 days</td>
<td>+10% compared to LJ</td>
</tr>
<tr>
<td>2008</td>
<td>Line Probe Assay</td>
<td>2-4 days</td>
<td>At this time for S+ only</td>
</tr>
<tr>
<td>2009</td>
<td>LED-based FM</td>
<td>1-2 days</td>
<td>+ 10% compared to ZN</td>
</tr>
<tr>
<td>2010</td>
<td>Integrated NAAT (TB, Rif)</td>
<td>90 minutes</td>
<td>+ 40% compared to ZN</td>
</tr>
</tbody>
</table>
PCR for TB

- Use a commercial kit, not an in-house one
- Use for smear positive TB and for smear negative TB from lower resp tract specimens
- CSF – only 67% sensitivity
- Other sites of questionable value
- Never do on blood

- WHO and my recommendation: avoid in house PCR completely in the era of Xpert!
Automated TB line probe assay (Xpert MTB/RIF)

- Diagnosed 98% of all smear +ve
  - Single test diagnosed 70% of all smear neg
  - three tests 90%
- Turnaround time 2 hrs
- Also picked up 98% of rifampicin resistant isolates
- 14% of rifampicin resistant cases have sensitivity to isoniazid
- Advantages:
  - simple to do
  - not prone to cross contamination
  - minimal bio-safety hazard

1. Sputum liquifaction & inactivation with 2:1 SR

2. Transfer of 2ml after 15 min

3. Sample is automatically filtered & washed

4. Concentrates bacilli & removes inhibitors

5. Ultrasonic lysis of filter-captured organisms to release DNA

6. DNA is mixed with dry PCR reagents

7. Semi-nested real-time amplification & detection in integrated reaction tube

Time-to-result 1h 45min

Printable test result
Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance:

Xpert MTB/RIF system for the diagnosis of pulmonary and extrapulmonary TB in adults and children

Policy Update
Summary of 2013 WHO guideline on Xpert Mtb Rif

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial test</td>
<td>88</td>
<td>99</td>
</tr>
<tr>
<td>Smear negative</td>
<td>68</td>
<td>99</td>
</tr>
<tr>
<td>HIV positive</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Rifampicin resistance</td>
<td>95</td>
<td>98</td>
</tr>
<tr>
<td>Pulmonary TB in children</td>
<td>66</td>
<td>98</td>
</tr>
</tbody>
</table>

Recommended as initial test of choice in TB meningitis
False positive Xpert can be seen if history of TB treatment

- One in 7 Xpert-positive retreatment patients were culture negative and potentially false positive.
- False positivity was associated with recent previous tuberculosis, high $C_T$, and a chest radiograph not suggestive of active tuberculosis.
- Clinicians may consider awaiting confirmatory testing in retreatment patients with $C_T > 30$
This study assessed the impact of up-front Xpert MTB/RIF testing on detection of PTB and rifampicin-resistant PTB (DR-TB) cases in India.

The implementation of Xpert MTB/RIF was associated with increases in both
- notification rates of bacteriologically confirmed TB cases (aIRR 1.39)
- proportion of bacteriological confirmed TB cases among presumptive TB cases (aRR 1.33).

Xpert MTB/RIF implementation increased rifampicin resistant TB case detection by over fivefold.

Govt of India offers Xpert testing at selected hospitals for children and for suspected MDR
Genotype MTBDRplus (Hain Lifescience)

• WHO endorsed molecular line probe assay for respiratory specimens and positive cultures that detects
  – First line
    • mutations in the *rpoB* gene, which is associated with RIF resistance
    • *katG* gene and the *inhA* promoter region, which are associated with INH resistance
    • Excellent for R, 84% sens for H
  – Second line for injectables, quinolones, ethambutol
• TAT should be <7 days
Case 3

- How will you treat this patient
  - HREZ
  - HRES
  - HREZS
  - HREZ ofloxacin
  - HREZ levofloxacin
  - HREZ plus vitamin D
Standard regimen

- Isoniazid (5-10 mg/kg)
- Rifampicin (10-20 mg/kg)
- Ethambutol (15-20 mg/kg)
- Pyrazinamide (25 mg/kg)

- After first two months
  - stop pyrazinamide
  - Stop ethambutol if isoniazid sensitive
Know your ATT basics

• Always use daily regimens
• Tuberculosis Management by Private Practitioners in Mumbai, India: Has Anything Changed in Two Decades?
  – Only 6 of the 106 respondents wrote a prescription with a correct drug regimen. 106 doctors prescribed 63 different drug regimens. There was tendency to over treat with more drugs for longer durations.
  – Only 3 of the 106 respondents could write an appropriate prescription for treatment of multidrug-resistant TB.

This was a cross-sectional survey of 228 practitioners practicing in the private sector from January 2014 to February 2015 in Chennai city who saw at least one TB patient in the previous year. A median of 12 (IQR 4–28) patients with TB were seen per year. Of 10 ISTC standards evaluated, the median of standards adhered to was 4.0 (IQR 3.0–6.0). Chest physicians reported greater median ISTC adherence than other MD and MS practitioners (score 7.0 vs. 4.0, P<0.001). Only 52% of all practitioners sent >5% of patients with cough for TB testing, 83% used smear microscopy for diagnosis, 33% monitored treatment response, and 22% notified TB cases to authorities. Of 228 practitioners, 68 reported referring all patients with new pulmonary TB for treatment, while 160 listed 27 different regimens; 78% (125/160) prescribed a regimen classified as consistent with ISTC. TB management practices in India’s urban private sector are heterogeneous and often suboptimal. A 40% score is probably a fail for Chennai!
At-risk patient
Abnormal CXR
Smears negative
No other diagnosis
Positive tuberculin test

Low suspicion
No treatment

High suspicion
INH/RIF/EMB/PZA

Initial cultures negative
No change in CXR

4 months RIF +/- INH
9 months INH
2 months RIF/PZA

Initial cultures negative
Clinical/CXR improved
2 months INH/RIF

Treatment complete

Initial Evaluation
Repeat Evaluation

0 1 2 3 4 6

Time (months)
Wherever feasible, the optimal dosing frequency for new patients with pulmonary TB is daily throughout the course of therapy.

Daily dosing recommended for the intensive phase may also help in reducing acquired drug resistance, especially in patients with pretreatment isoniazid resistance.

HIV prevalent setting is when prevalence among adult pregnant women is ≥1% or among TB patients is ≥5%.

TB patients with known positive HIV status and all TB patients living in HIV-prevalent settings should receive daily TB treatment at least during the intensive phase.

For the continuation phase, the optimal dosing frequency is also daily for these patients.

In populations with known or suspected high levels of isoniazid resistance, new TB patients may receive HRE as therapy in the continuation phase as an acceptable alternative to HR (weak recommendation).
Duration of treatment

- In general, 6 months therapy adequate
- Prolong to 9-12 months if
  - bone/joint, meningeal, disseminated TB
  - cavitary disease and culture positive at 2 months
  - delayed response to therapy

Consider prolonging therapy for patients
- being >10% below ideal body weight
- being a smoker
- having diabetes, HIV infection, or other immunosuppressing condition
- having extensive disease on chest radiograph
Drug doses in children need to be higher
(Clin Infect Dis 2010;50:s184)

• Rifampicin: 10-20 mg/kg
• Isoniazid: 10 mg/kg
• Ethambutol: 20 mg/kg
• Pyrazinamide: 30 mg/kg
Duration of regimens without frontline drugs

• Without Z: 9 months
• Without H: 12 months
• Without R: 18 months
WHO and other guidelines currently recommend

- Standard first line ATT is HREZ
- Reserve quinolones
  - for toxicity to front line regimens
  - As essential component of regimens for MDR-TB
Conclusions

Empirical fluoroquinolone prescriptions for pneumonia are associated with longer delays in diagnosis and treatment of pulmonary TB and a higher risk of developing fluoroquinolone-resistant *M. tuberculosis*. 
Moxifloxacin best to replace either INH or ethambutol if toxicity

- Randomized trial looking at culture conversion at 8 weeks
  - HRZ + E: 63%
  - HRZ + moxi: 80%

- Randomized trial showed similar culture conversion at 2 months
  - REZ + H: 55%
  - REZ + moxi: 60%

Conclusion on role of quinolones as first line ATT

• In general
  – No role for routinely adding quinolones
  – No role for routinely substituting one of the front line agents with a quinolone
  – Do not help shorten 6 month regimens

• For TB meningitis
  – High dose (initially parenteral) levofloxacin has not been proven of benefit
  – Watch literature closely!
• This randomised, double-blind, placebo-controlled, superiority trial was carried out involving 247 patients at 13 sites in India.

• Treatment-naive patients who were sputum-smear positive, HIV negative, and had pulmonary tuberculosis were randomly assigned (1:1), to receive standard active tuberculosis treatment with either supplemental high-dose oral vitamin D₃ or placebo.

• Median time to culture conversion in the vitamin D group was 43·0 days versus 42·0 days in the placebo group (log-rank p=0·95).

• Perhaps Vit D more important in innate immunity in preventing progression to active TB after infection rather than after TB develops
ATT hepatotoxicity

• Defined as
  – Jaundice
  – Symptomatic with <5 fold ALT elevation
  – Asymptomatic with >5 fold ALT elevation
• Look for underlying CLD
• Z>H>R in terms of hepatotoxicity potential: Stop all three
• Treat with E + streptomycin + levo/moxifloxacin
• Once LFT recover, sequentially re-introduce R first and then H at weekly intervals
• If severe hepatitis, do not introduce Z and prolong duration to 9 months
Case

- A 32/f presents with cough, fever and weight loss for the last 3 months.
- No history of past ATT or treatment default
- Does the patient need tests for MDR-TB?
Drug resistant TB

- Isoniazid mono-resistant ~15%
- Rifampicin mono-resistant
  – treated with the shorter MDR-TB treatment regimen
- MDR (resistant to H and R) ~3%
- Pre-XDR (resistant to either injectable or quinolones)
- XDR (resistant to both injectable and quinolones)
Isoniazid resistant TB

- Continue rifampicin and ethambutol
- Continue PZA for entire duration of therapy
- Addition of quinolone optional
- Treat for 9 months

- Need better approaches
MDR -TB

• TB resistant to both rifampicin & INH
• Over the next 35 years, multidrug-resistant tuberculosis will kill 75 million people and could cost the global economy a cumulative $16.7 trillion (UK parliament)
• Need AFB culture and sensitivities
  — <3% of all patients with diagnosed tuberculosis worldwide have drug-susceptibility testing
• 3.9% of all TB globally is MDR
• More than half of cases in India and 78% of cases in China due to primary transmission (N Engl J Med 2012;366:2161)
• 7% of patients with drug sensitive tuberculosis die, but 50% with MDR die
• Only 0.5% of cases worldwide get standard of care treatment
Global epidemiology of MDR-TB
(Lancet 2009;373:1861)

• Only about a fifth of the 450,000 people estimated to have developed MDR-TB in 2012 were actually detected

• New cases
  – Worldwide 6.7% INH mono-resistant, 1.6% MDR
  – Highest prevalence in former Soviet Union countries (15%) & China (7%)
  – 15% resistant to INH in Chennai with 3% MDR
  – 1.4% MDR in Delhi

• India with 131,000 has highest no of cases
• China ranks second with 112,000 (6% new cases)
• Russia has 43,000 cases, while South Africa has 16,000 and Bangladesh 15,000

• Previously treated: 11.7% were MDR
50 isolates studied
14 (28%) of the isolates were MDR
“Tertiary care hospitals which see complicated tuberculosis patients should routinely ask for susceptibility tests whenever *M. tb* is cultured”

Suspicion of MDR-TB in clinical practice

1. H/O past ATT- complete or incomplete
2. H/O contact with MDR –TB patients
3. Persistent sputum positivity after 8 weeks ATT
4. No clinical improvement &/or deterioration despite adequate ATT for 3 months
5. Disseminated disease
6. Cavitary disease
| A. Fluoroquinolones<sup>2</sup>             | Levofloxacin  | Lfx  |
|                                          | Moxifloxacin  | Mfx  |
|                                          | Gatifloxacin  | Gfx  |
| B. Second-line injectable agents         | Amikacin      | Am   |
|                                          | Capreomycin   | Cm   |
|                                          | Kanamycin     | Km   |
|                                          | (Streptomycin)<sup>3</sup> | (S)   |
| C. Other core second-line agents<sup>2</sup> | Ethionamide   | Eto  |
|                                          | / Prothionamide | Pto  |
|                                          | Cycloserine   | Cs   |
|                                          | / Terizidone  | Trd  |
|                                          | Linezolid     | Lzd  |
|                                          | Clofazimine   | Lzd  |
| D. Add-on agents                         | Pyrazinamide  | Z    |
| (not part of the core MDR-TB regimen)    | Ethambutol    | E    |
|                                          | High-dose isoniazid | H<sup>h</sup> |
|                                          | Bedaquiline   | Bdq  |
|                                          | Delamanid     | Dlm  |
|                                          | P<sub>aminosalicylic acid</sub>    | PAS  |
|                                          | Imipenem-cilastatin<sup>4</sup>    | Ipm  |
|                                          | Meropenem<sup>4</sup>               | Mpm  |
|                                          | Amoxicillin-clavulanate<sup>4</sup> | Amx-Clv |
|                                          | (Thioacetazone)<sup>5</sup>        | (T)  |

<sup>1</sup>This regrouping is intended to guide the design of conventional regimens; for shorter regimens lasting 9-12 months the composition is usually standardised (See Section A)

<sup>2</sup>Medicines in Groups A and C are shown by decreasing order of usual preference for use (subject to other considerations; see text)

<sup>3</sup>Refer to the text for the conditions under which streptomycin may substitute other injectable agents. Resistance to streptomycin alone does not qualify for the definition of extensively drug-resistant TB (XDR-TB)<sup>(26)</sup>

<sup>4</sup>Carbapenems and clavulanate are meant to be used together; clavulanate is only available in formulations combined with amoxicillin

<sup>5</sup>HIV-status must be tested and confirmed to be negative before thioacetazone is started
Conventional MDR-TB regimens for adults & children

- A regimen with at least five effective TB medicines during the intensive phase is recommended
  - including pyrazinamide
  - four core second line TB medicines
    - one chosen from group A
    - one from group B
    - at least two from group C (in order of preference in table)
- If the minimum of effective TB medicines cannot be composed as above, an agent from group D2 and other agents from D3 may be added to bring the total to five
- further strengthened with high-dose isoniazid and/or ethambutol
WHO RECOMMENDATIONS ON THE USE OF THE SHORTER MDR-TB REGIMEN

In May 2016, WHO issued a conditional recommendation on the use of the shorter MDR-TB regimen. A flow chart outlining selection of patients on the shorter MDR-TB regimen is presented below.

CHOOSING THE MDR-TB TREATMENT REGIMEN IN PATIENTS WITH CONFIRMED RIFAMPICIN-RESISTANT OR MDR-TB

CRITERIA: Do any of the following apply?
- Confirmed resistance or suspected ineffectiveness to a medicine in the shorter MDR-TB regimen (except isoniazid resistance)
- Exposure to ≥1 second-line medicines in the shorter MDR-TB regimen for ≥1 month
- Intolerance to ≥1 medicines in the shorter MDR-TB regimen or risk of toxicity (e.g. drug-drug interactions)
- Pregnancy
- Extrapulmonary disease
- At least one medicine in the shorter MDR-TB regimen not available in the programme

NO

Shorter MDR-TB regimen

Intensive phase
Duration: 4-6 months
Composition: 4 second-line drugs

Continuation phase
Duration: 5 months
Composition: 2 second-line drugs

Supported by selected first-line TB drugs

FAILING REGIMEN, DRUG INTOLERANCE, RETURN AFTER INTERRUPTION ≥2 MONTHS, EMERGENCE OF ANY EXCLUSION CRITERION

YES

Individualised ("conventional") MDR/RR-TB regimens

Intensive phase
Duration: Up to 8 months
Composition: 4 or more second-line drugs

Continuation phase
Duration: 12 months or more
Composition: 3 or more second-line drugs

Supported by selected first-line TB drugs
FEATURES OF THE SHORTER MDR-TB REGIMEN

- Standardized shorter MDR-TB regimen with seven drugs and a treatment duration of 9-12 months
- Indicated conditionally in MDR-TB or rifampicin-resistant-TB, regardless of patient age or HIV status
- Monitoring for effectiveness, harms and relapse will be needed, with patient-centred care and social support to enable adherence
- Programmatic use is feasible in most settings worldwide
- Lowered costs (<US$1,000 in drug costs/patient) and reduced patient loss expected
- Exclusion criteria: 2nd line drug resistance, extrapulmonary disease and pregnancy.

REGIMEN COMPOSITION

4-6 Km-Mfx-Pto-Cfz-Z-H_{high-dose}-E / 5 Mfx-Cfz-Z-E

Km=Kanamycin; Mfx=Moxifloxacin; Pto=Prothionamide; Cfz=Clofazimine; Z=Pyrazinamide; H_{high-dose}= high-dose Isoniazid; E=Ethambutol
Case

- The 6 year old son of the patient with pulmonary TB is asymptomatic
- For the son, you would
  - Do nothing
  - Get a Mantoux and CXR
  - Get a Quantiferon TB Gold
Latent TB

- Defined as infection with M.tb without clinical evidence of active TB
- 40% of Indian population
- 30% of world’s population
Latent TB

- Lifetime risk of reactivation disease (Am J Crit Care & Resp Med 2010;182:420) 10% conventionally but currently 4-5.8%
- Tuberculin skin testing with PPD remains the standard method for diagnosis
- IGRA is an alternative
- Definition of positive Mantoux: >5mm induration
- Individuals with latent tuberculosis have a 79% lower risk of tuberculosis disease following reinfection compared with initial infection (Clin Infect Dis. (2012) 54(6): 784)
Mantoux

- Look for induration, not erythema
- Indicates exposure to Mtb (latent TB), not active disease
- Can be false positive due to BCG vaccine and atypical mycobacteria
- Can be false negative due to anergy
- Once positive remains so lifelong, never repeat
- Positive in 40% of the Indian population

- Not a test for active TB!
- No role for diagnosis of TB
<table>
<thead>
<tr>
<th></th>
<th><strong>TST</strong></th>
<th><strong>IGRA</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Principle</strong></td>
<td>Detects T cell mediated immunity to mycobacteria</td>
<td>Detects gamma interferon release upon exposure to purified M.tb antigens</td>
</tr>
<tr>
<td><strong>Test</strong></td>
<td>Skin test with f/u visit at 48 hrs</td>
<td>No follow up</td>
</tr>
<tr>
<td><strong>Scar</strong></td>
<td>Left if positive</td>
<td>No scar</td>
</tr>
<tr>
<td><strong>Observer error</strong></td>
<td>Often present due to confusion between induration and erythema</td>
<td>Indeterminate values may be problematic, false conversions and reversions may be seen in HCW</td>
</tr>
<tr>
<td><strong>False positives</strong></td>
<td>Due to BCG vaccine and NTM</td>
<td>Specific for M.tb</td>
</tr>
<tr>
<td><strong>Specificity in BCG vaccinated</strong></td>
<td>0.59</td>
<td>0.96</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>0.77</td>
<td>0.70 (QFN)-0.90 (Eli-spot)</td>
</tr>
<tr>
<td><strong>Predictive value for developing active TB when positive</strong></td>
<td>1.5%</td>
<td>2.7%</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>Rs</td>
<td>$$$</td>
</tr>
</tbody>
</table>
• insufficient data and low quality evidence on the performance of IGRAs in low and middle income countries
• IGRAs and the TST cannot accurately predict the risk of infected individuals developing active TB disease
• Neither IGRAs nor the TST should be used for the diagnosis of active TB disease
• IGRAs are more costly and technically complex to do than the TST
Relative to sputum smear microscopy, use of IGRA for active TB resulted in 23,700 additional true-positive diagnoses, but at the expense of 315,700 additional false-positive diagnoses and an incremental cost of 2.9 billion Indian Rupees.

Relative to Xpert MTB/RIF, use of IGRA led to 400 additional TB cases treated, 370,600 more false-positive diagnoses, 70,400 fewer disability-adjusted life years averted, and 854 million Indian Rupees in additional costs.

Using IGRAs for diagnosis of active TB in a setting like India results in tremendous overtreatment of people without TB, and substantial incremental cost with little gain in health.

These results support the policies by WHO and Standards for TB Care in India, which discourage the use of IGRAs for the diagnosis of active TB in India and similar settings.
Mantoux is 15 mm, CXR is clear

- You would
  - Start HREZ
  - Start HR for 3 months
  - Start H for 6 months
  - Do nothing, monitor child
Candidates for chemoprophylaxis

- Childhood contacts of cases
- Transplant recipients
- HIV positive
- Receiving TNF-alpha blockers
Chemoprophylaxis of latent TB

• Benefit of short course regimens lasts ~3 years only in TB endemic areas due to re-infection

• Regimens:
  – INH monotherapy for 6-9 months is standard of care
  – PZA/RIF for 2 months but hepatotoxicity is problematic
  – RIF alone for 4 mths less hepatotoxic and adherence better
  – RIF-INH for 3 months used in adults and children in UK
  – Weekly rifapentine + isoniazid for 3 months in HIV negative now approved in USA
    • 3.5% had reactions (63% had flu-like syndrome and 17% had cutaneous reactions) (Clin Infect Dis. (2015) 61 (4):527-535)
  – MDR-TB contacts:
    • Contacts of drug resistant TB: 47% have latent TB and 8% have active TB
    • ofloxacin, ethambutol, and high-dose isoniazid for 6 months effective

(Clin Infect Dis 2014 58: 381-391)
WHO recommendations for asymptomatic childhood contacts of infectious TB patients

• Above 5: IGRA or PPD followed by chemoprophylaxis if positive
• Below 5: routine chemoprophylaxis
  – INH for 6 months
  – INH-RIF for 3 months
Case

- To prevent infection to other patients and HCWs in op, you would
  - Put a surgical mask on the patient
  - Put on an N-95 mask yourself
  - Have an open ventilated room
  - Use UV light
Infection control in healthcare settings

(Clin Infect Dis 2010;50:s231)

• Outbreak of XDR-TB in South Africa was mainly nosocomial
• Healthcare workers get active TB at rate of 5.8% annually in developing countries, well above general population
• Smear negative TB is also transmissible though 4 times less likely, accounts for 13% of all cases (Clin Infect Dis 2008;47:1135)
• Surgical mask for patient reduced guinea pig infections by 56% (AJRCCM 2012): use for all patients with cough in op
• Three types of strategies:
  – Administrative controls
  – Environmental controls
  – Personal protection
Small steps..
Environmental controls

• Negative pressure and 12 air changes per hour
  – Costly, needs maintenance, may function poorly
  – Needed for inpatient rooms, bronchoscopy

• Natural ventilation
  – High ceilings, large windows, open doors & windows
  – Can provide up to 40 air changes per hour
  – Applicable to OP settings and HIV settings
  – Fails in extreme climates when windows closed

• Upper room ultra-violet light
  – Reduces airborne transmission by 70%
  – Applicable to waiting room areas
CIDSCON 2017
7th Annual Conference of Clinical Infectious Diseases Society, India
25th | 26th | 27th August, 2017
Venue: Le Méridien Nagpur, Maharashtra

Dr. V Ramasubramanian
Organizing Chairman

Dr. Ashwini Tayade
Organizing Secretary

Dr. O C Abraham
Scientific Committee Chairperson

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  - Apollo Hospitals, Chennai
  - For details go to NBE website

- **Tamil Nadu Dr. MGR Medical University:**
  - Two year fellowship
  - Apollo Hospitals, Chennai and CMC, Vellore
  - Contact institutions for details