Tuberculosis in Pediatrics

13 June 2017
Tony Moody MD
Duke Pediatric Infectious Diseases

Image from the National Library of Medicine, “Profiles in Science” Collection.
Disclosures

• Advisory board member for GSK (for belimumab pregnancy registry).

• Co-founder of Grid Therapeutics (formerly Cue Biologics).

• Chief Medical Officer, DHVI.
Learning Objectives

• Choose appropriate diagnostic tests for suspected MTB disease.
• Apply proper techniques for application and reading of TSTs.
• Compare the utility of TSTs, IGRAs, and other tests.
• Use proper dosing of anti-tuberculosis drugs in pediatric patients.
Tuberculosis

first disease declared
Global Health Emergency
by WHO (1993)

estimated $\frac{1}{3}$ of humans infected
Global distribution of estimated TB incidence by rate and absolute number, 2014. The size of each bubble is proportional to the size of the country’s population. High-burden countries are shown in red.
Estimated TB mortality rates excluding TB deaths among HIV–positive people, 2014

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.


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Image courtesy of the World Health Organization Global Health Observatory Map Gallery
Estimated absolute numbers of TB cases and deaths (in millions per year), 1990–2014

- TB incidence
  - All TB cases
  - HIV-positive TB cases

- TB deaths
  - TB deaths among HIV-negative people
  - TB deaths among HIV-positive people

*a* HIV-associated deaths are classified as HIV deaths according to ICD-10.
Percentage of new TB cases with multidrug-resistant tuberculosis

- Figures are based on the most recent year for which data have been reported, which varies among countries. Data reported before the year 2000 are not shown.

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Image courtesy of the World Health Organization Global Health Observatory Map Gallery
Tuberculosis

*tuberculosis* n
disease caused by
MTB complex organisms
derived from
the Latin *tuberculum* (swelling) +
the Greek *-ωσις* (condition)
Identification of *Mycobacterium* DNA in an Egyptian Pott’s disease of 5,400 years old.

Tuberculosis

consumption
  wasting illness

Pott’s disease
  spinal osteomyelitis

King’s evil
  scrofula / lymphadenitis
By the King.

A Proclamation concerning the Kings Evil.

Hereas such people as reape to His Maiestye for healing of the Kings Evil, have in former times for home to apptach and offer their selves to the former Kings of this Realme, during the Summer time, in respect of danger, and short remissence, which other hath bene of late neglected, and such people use to repair indifferently at all times: Therefore his Maiestye doth declare and forbid, That hereafter no such person make their repair up for healing, betweene the fasts of Easter and Michaelmas, for the which although it had bene enough for his Maiestye to have signified his pleasure for recontinuing the said order into the Earcke of his Closet, or his Chirurgions in that behalfe; yet his Maiestye doubting that some such weak and unthee persons may come up from remote parts, and thereby cause trouble, as pleased out of his goodnesse, to publish this Order by his highnesse proclamation.

Given at White-hall the xxv. day of March, in the fourtie yeere of Our Reigne of Great Britaine, France and Ireland, And of Scotland the nine and fourtie.

God save the King.

Imprinted at London by Robert Barker, Printer

to the Kings most Excellent Maiestye.

Anno Dom. 1616.
Tuberculosis: Etiology?

cause
- hereditary
- punishment for sin
- bad air
- vampires
## Tuberculosis: Etiology?

<table>
<thead>
<tr>
<th>Cause</th>
<th>Cure</th>
</tr>
</thead>
<tbody>
<tr>
<td>• hereditary</td>
<td>evolve / you’re screwed</td>
</tr>
<tr>
<td>• punishment for sin</td>
<td>redemption</td>
</tr>
<tr>
<td>• bad air</td>
<td>move</td>
</tr>
<tr>
<td>• vampires</td>
<td>wooden stake</td>
</tr>
</tbody>
</table>
Tuberculosis Complex

*Mycobacterium bovis*
*Mycobacterium canetti*
*Mycobacterium microti*
*Mycobacterium tuberculosis*
Tuberculosis Complex

- fossils showing animal disease
- evidence of *M bovis* increase
  8000-4000 BCE
Hieronymus Fracastorius (Girolamo Fracastoro) (1478-1553)

1546 treatise

De contagione et de contagiosis morbis et curatione

130 years before Leeuwenhoek first saw microorganisms

Image courtesy of the Clendening History of Medicine Library, University of Kansas Medical Center
Sylvius
( Franciscus de le Boe)

defined tubercules, tuberculous cavities
Heinrich Hermann Robert Koch (1843-1910)

1882: identified *M tuberculosis*, established MTB role in cause of tuberculosis

Image courtesy of the Clendening History of Medicine Library, University of Kansas Medical Center
MTB

Aerobic
non-spore-forming
non-motile
bacillus

On Gram stain, weakly GP or ghosts
MTB

Mycolic acids
very long chain fatty acids
waxy surface

provide protection from hazards
Cording

in liquid culture TB orient parallel

MOTT orient randomly
MTB

Acid-fast
decolorization step done with acid-alcohol
bacilli retain stain
MTB

For initial stains most labs use a fluorescent stain

auramine-rhodamine

$\text{KMnO}_4$ counterstain
MTB

Requires special media for culture

Middlebrook 7H11
Löwenstein-Jensen
BACTEC
MGIT
MTB

MTB very slow growing
average replication time
15-20 hours

*E coli* replicates in about 20 minutes
## MTB

Starting with one bacterium in ideal conditions

<table>
<thead>
<tr>
<th>Time</th>
<th>MTB</th>
<th>E coli</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hour</td>
<td>1</td>
<td>4-8</td>
</tr>
<tr>
<td>1 day</td>
<td>2</td>
<td>2.3 x 10^{21}</td>
</tr>
<tr>
<td>1 week</td>
<td>1024</td>
<td>2.6 x 10^{151}</td>
</tr>
</tbody>
</table>
Primary TB (childhood)

mid lung zones
regional lymphadenitis
pleurisy with effusion
persistent cough illness
risk of hematogenous spread
Primary TB (childhood)
can look like anything
MTB—Clinical

high risk of dissemination

miliary tuberculosis
MTB—Clinical

high risk of dissemination

cerebral tuberculosis
insidious
difficult to diagnose
high risk of dissemination

cerebral tuberculosis

LP in any child < 3yo

LP if headache / signs
MTB—Clinical

• How often is disease recurrent vs. reinfection?

• How risky are biologics?

• Why is there a summer peak in Dx?
Result

Recurrence most common in first year, reinfection more common thereafter.

Figure 2. Kaplan-Meier survival estimates for relapse (n = 64), reinfection tuberculosis (n = 66), and unknown type of recurrence (n = 73) (Kolmogorov-Smirnov test for difference in relapse vs reinfection, P < .001).
Biologic Therapies in Rheumatoid Arthritis and the Risk of Opportunistic Infections: A Meta-analysis

Irene S. Kourbeti, Panayiotis D. Ziakas, and Eleftherios Mylonakis

Infectious Diseases Division, Rhode Island Hospital, and Warren Alpert Medical School of Brown University, Providence, Rhode Island

Opportunistic Infections in RA • CID 2014:58 (15 June) • 1649

**Table 2. GRADE Summary of Findings on the Effects of Biologic Agents Compared With Placebo or Disease-Modifying Antirheumatic Drugs**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative Effect (OR; 95% CI)</th>
<th>No. of Participants (No. of Studies)</th>
<th>Quality of Evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All OIs</td>
<td>1.79 (1.17–2.74)</td>
<td>20,232 (37)</td>
<td>High&lt;sup&gt;a,b,c,d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mycobacterial Ols</td>
<td>3.73 (1.72–8.13)</td>
<td>9,194 (18)</td>
<td>High&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>All viral Ols</td>
<td>1.91 (1.02–3.58)</td>
<td>6,056 (16)</td>
<td>Moderate&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>VZV Ols</td>
<td>1.51 (.71–3.22)</td>
<td>5,515 (11)</td>
<td>Low&lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>All fungal Ols</td>
<td>1.31 (.46–3.72)</td>
<td>7,507 (10)</td>
<td>Moderate&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Invasive fungal infections</td>
<td>2.85 (.68–11.91)</td>
<td>3,915 (7)</td>
<td>Moderate&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pneumocystis jirovecii pneumonia</td>
<td>1.77 (.42–7.47)</td>
<td>5,669 (8)</td>
<td>Moderate&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Attributed mortality</td>
<td>1.91 (.29–12.64)</td>
<td>3,058 (5)</td>
<td>Moderate&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**Result**
Mycobacterial OIs are the most associated; fungal second.
The Seasonality of Tuberculosis, Sunlight, Vitamin D, and Household Crowding

Tom Wingfield,1,4,5,6 Samuel G. Schumacher,1,3 Gurjinder Sandhu,3,4,5 Marco A. Tovar,1,2,3 Karine Zevallos,1,2 Matthew R. Baldwin,3 Rosario Montoya,1,2 Eric S. Ramos,3 Chulanee Jongkaewwattana,1 James J. Lewis,1,7 Robert H. Gilman,2,8 Jon S. Friedland,4,5 and Carlton A. Evans1,3,4,5

Cohort
Residents of a Peruvian shantytown

Measures
Vitamin D, TST, IGRA

Results
Infections occur during winter months, but symptoms don’t appear until the summer.
<table>
<thead>
<tr>
<th></th>
<th>Peak season</th>
<th>Rest of year</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hours without sunlight (%)</td>
<td>87.5 (87.0 - 88.0)</td>
<td>76.0 (75.5 - 76.4)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Vitamin D deficient (%)</td>
<td>63.3 (62.5 - 64.1)</td>
<td>53.1 (52.4 - 53.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Crowding (%)</td>
<td>56.4 (56.1 - 56.7)</td>
<td>50.9 (50.6 - 51.2)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>TST positivity (%)</td>
<td>60.5 (60.3 - 60.8)</td>
<td>54.4 (54.2 - 54.7)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>IGRA positivity (%)</td>
<td>56.2 (55.7 - 56.6)</td>
<td>49.1 (48.7 - 49.5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Tuberculosis diagnoses, cases, no.</td>
<td>440 (438 - 442)</td>
<td>416 (414 - 418)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Tuberculosis symptom onset, cases, no.</td>
<td>397 (396 - 399)</td>
<td>380 (378 - 381)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>
MTB—Testing

the gold standard

biopsy / specimen with culture
MTB—Testing

PPD (purified protein derivative)
Mantoux test
must be placed intradermal
Clemens Peter von Pirquet (1874-1929)

developed one of the first non-culture tests for TB

tuberculin applied to superficial abrasion on arm

Image courtesy of the Clendening History of Medicine Library, University of Kansas Medical Center
Tuberculosis

Pirquet test

"Der diagnostische Wert der kutanen Tuberkulinreaktion bei der Tuberkulose des Kindesalters auf Grund von 100 Sektionen."

Von Dr. G. v. Pirquet.

Moro test

"Ueber eine diagnostisch verwertbare Reaktion der Haut auf Einreibung mit Tuberkulinsalbe."

Von Privatdozent Dr. Ernst Moro, Oberarzt der Klinik.
Tuberculosis

Calmette-Wolff-Eisner test

MEDICINE. — Sur un nouveau procédé de diagnostic de la tuberculose chez l’homme par l’ophtalmo-réaction à la tuberculine. Note de M. A. Calmette.

Mendel-Mantoux test

Felix Mendel (1862-1925)

Zur endevenöse Applikation der Medikamente II. Die kombinirte Arsen-Tuberkulinbehandlung

*Therapeutische Monatshefte, Berlin 17: 177-188 (1903)*
Charles Mantoux (1877-1947)

**Pathologie. — Intradermo-réaction de la tuberculine.** Note de M. Ch. Mantoux, présentée par M. E. Roux.

*Comptes rendus de l’Académie des sciences, Paris* 147: 355-357 (1908)
MTB—Testing

PPD (purified protein derivative)
Mantoux test
must be placed intradermal
MTB—Testing

PPD

read 48-72 hours after placement

can be read up to 1 week later with accuracy
PPD

erythema is meaningless
induration is the key

Sokol method (ball-point pen)
Problems with TST

- requires specialized training for both placement and reading
- requires two provider visits
- false positives and negatives
- vaccine confounding
- booster phenomenon
Problems with TST

- requires specialized training for both placement and reading
- requires two provider visits
- false positives and negatives
- vaccine confounding
- booster phenomenon
Tuberculin Skin Testing in Patients with HIV Infection: Limited Benefit of Reduced Cutoff Values.


**Result**

Adult study.

Lower cutoff doesn’t capture many more.

Seems to be an all or nothing phenomenon.

**Figure 2.** Sensitivity of the tuberculin skin test (TST) for detecting tuberculosis disease among HIV-infected (*solid line*) and HIV-uninfected (*dashed line*) patients at various cutoff levels. Data are based on crude reaction size distributions.
Problems with TST

• requires specialized training for both placement and reading
• requires two provider visits
• false positives and negatives
• vaccine confounding
• booster phenomenon
The tuberculin skin test is unreliable in school children BCG-vaccinated in infancy and at low risk of tuberculosis infection.


**result**

Canadian study. BCG-vaccinated children more likely to have a positive TST.

Concludes test unreliable in 6-12 yo children.
Problems with TST

- requires specialized training for both placement and reading
- requires two provider visits
- false positives and negatives
- vaccine confounding
- booster phenomenon
Enhancing of Tuberculin Allergy by Previous Tuberculin Testing


cohort
eight villages in India

result
those with mild reactions, 8-13 mm initially, had the most increases with boosting

testing
TST using 1 TU on upper ⅓ of L forearm
some given 20 TU tests
2 mo later TST w/ 1 TU on middle ⅓ of R forearm
The Booster Effect in Two-Step Tuberculin Testing among Young Adults in Montreal

Menzies R, Vissandjee B, Rocher I, St. Germain Y.

result
boosting seen in both BCG-V +ve and –ve groups

greater effect in BCG-V gp

correlation w/ age at BCG-V

most boosters reactive to PPD-B(I)
• CDC recommends two-step testing for HCW at first screen
Desirable Properties

• no special training
• single encounter
• reduced false positives and negatives
• distinguish between MTB and other mycobacteria
IGRA

Interferon-\textbf{G}amma \textbf{R}elease \textbf{A}ssay

- reduced cross-reactivity
- lab-based test / quantitative answer
- single patient contact
- no boosting
BOVIGAM

- testing of cattle

- licensed in
  Australia & New Zealand
Evaluation of the Tuberculin Gamma Interferon Assay: Potential to Replace the Mantoux Skin Test


cohort
immigrants, HCW, patients

testing
QuantiFERON using PPDs for MTB, M bovis, M avium TST

result
64-89% concordance
71% +ve w/ smear +ve TB (Mantoux slightly better)
humans are to chimpanzees

as

*M tuberculosis* is to *M bovis*

>98% genetic identity
differences between *M. bovis* and BCG

RD1 (region of difference)

encodes for ESAT-6 & CFP10
IGRA

• relies on response to RD1 antigens

• can be negative in disease

• increasing studies in pediatrics

• multiple forms (ELISA, ELISpot)
Performance of whole blood IFN-g test for tuberculosis diagnosis based on PPD or the specific antigens ESAT-6 and CFP-10

Brock I, Munk ME, Kok-Jensen A, Andersen P. 

**cohort**
healthy volunteers
known TB +ve patients

**testing**
QuantiFERON using
PPDs for MTB, *M avium*,
ESAT-6, CFP-10

**result**
78% sensitive
100% specific in non-BCG, 89% in BCG-V
Whole blood interferon-γ release assay is a useful tool for the diagnosis of tuberculosis infection particularly among Bacille Calmette Guèrin-vaccinated children.


**result**

High rates of concordance between TST and IGRA in non-vaccinated children.

IGRA more predictive in BCG-vaccinated children.
The Utility of an Interferon Gamma Release Assay for Diagnosis of Latent Tuberculosis Infection and Disease in Children

A Systematic Review and Meta-analysis

Shingai Machingaidze, BSc,*† Charles Shey Wiysonge, MD,*† Yulieth Gonzalez-Angulo, BSc,*† Mark Hatherill, MD,*† Sizulu Moyo, MB ChB, Willem Hanekom, FCP (Paed),*† and Hassan Mahomed, MMed*†

Result
IGRA reasonably accurate in Dx of TB disease.
Impact of targeted testing for latent tuberculosis infection using commercially available diagnostics.


**result**

Testing in low incidence populations gives poor results.
Performance of QuantiFERON-TB Gold and Tuberculin Skin Test Relative to Subjects’ Risk of Exposure to Tuberculosis

Sharon E. McMullen, David A. Pegues, Frances S. Shofer, Alexandra C. Sheller, and Evelyn B. Wiener

result

In low risk college students, TST better than IGRA; for high risk, they are the same.

Figure 2. Results of tuberculin skin test and QuantiFERON-TB Gold In-Tube test by student risk of tuberculosis exposure. Abbreviations: QFT-GIT, QuantiFERON-TB Gold In-Tube; TST, tuberculin skin test.
Other Diagnostic Options

• In-house PCR tests

• Xpert MTB/RIF
Rapid Molecular Diagnosis of Pulmonary Tuberculosis in Children Using Nasopharyngeal Specimens

Heather J. Zar,1,2 Lesley Workman,1,2 Washiefa Isaacs,1,2 Jacinta Munro,1,2 Faye Black,1,2 Brian Eley,1,2 Veronica Allen,3,4 Catharina C. Boehme,5 Widaad Zemanay,3,4 and Mark P. Nicol3,4

1088 • CID 2012:55 (15 October)

<table>
<thead>
<tr>
<th></th>
<th>Definite TB 87 (16.3%)</th>
<th>Possible TB 255 (47.6%)</th>
<th>Not TB 193 (36.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IS culture positive 84 (96.6%)</td>
<td>IS culture positive 0 (0%)</td>
<td>IS culture positive 0 (0%)</td>
</tr>
<tr>
<td></td>
<td>NPA culture positive 61 (70.1%)</td>
<td>NPA culture positive 0 (0%)</td>
<td>NPA culture positive 0 (0%)</td>
</tr>
<tr>
<td></td>
<td>IS Xpert positive 64 (73.6%)</td>
<td>IS Xpert positive 5 (2.0%)</td>
<td>IS Xpert positive 0 (0%)</td>
</tr>
<tr>
<td></td>
<td>NPA Xpert positive 49 (56.3%)</td>
<td>NPA Xpert positive 7 (2.8%)</td>
<td>NPA Xpert positive 1 (0.5%)</td>
</tr>
<tr>
<td></td>
<td>Smear positive 30 (5.6%)</td>
<td>Smear positive 0 (0%)</td>
<td>Smear positive 0 (0%)</td>
</tr>
</tbody>
</table>

Result
TB Xpert on NP aspirates perhaps useful, esp if induced sputum impractical. (Gastric aspirates better.)
**Result**

Very small numbers, but results from stool and GA testing similar.
What about vaccine?
Edmond Isidore Etienne Nocard (1850-1903)

isolated virulent *M bovis* strain → ‘lait Nocard’

1901: transferred strain to Institut Pasteur

*Image obtained via en.wikipedia.org*
Jean-Marie Camille Guérin (1872-1961)

student of Nocard

joined Institut Pasteur in 1897 under Calmette

together with Calmette attenuated *M bovis*
Léon Charles Albert Calmette (1863-1933)

1908-1919: serial passage of ‘lait Nocard’ on glycerinated bile potato medium (230 x)

continued attenuation from 1919-1929

Image courtesy of the Clendening History of Medicine Library, University of Kansas Medical Center
BCG Genealogy

BCG widely distributed (1924-1926)
34 nations

1927: 26 other nations given BCG
BCG Genealogy

BCG Moreau (Brazil)
BCG Tokyo (strain 172)
BCG Danish (2 transfers) (1331)
BCG Tice (BLP)
BCG Pasteur (1173P)
Mapping the global use of different BCG vaccine strains

Nicole Ritz\textsuperscript{a,b,c}, Nigel Curtis\textsuperscript{a,b,c,*}

Tuberculosis 89 (2009) 248–251

Figure 1. BCG vaccine strains used between 2003 and 2007 worldwide. Boxes surround BCG vaccines strains that are most genetically similar. Box I includes BCG vaccine strains that were obtained from the Pasteur Institute before 1926. Boxes II are III are strains obtained at later dates.
BCG and vole bacillus vaccines in the prevention of tuberculosis in adolescence and early adult life


BCG and vole bacillus vaccines in the prevention of tuberculosis in adolescence and early adult life

BCG: World Experience

- > 2.5 billion immunizations
- given routinely to infants
- can be given PO
- quite heat stable
**Result**
Overall case number not changed, disseminated cases reduced.
Result
BCG given to LBW infants reduced all-cause mortality.

Figure 2. Cumulative mortality curves during the first year of life according to randomization group.
Result

BCG responses reduced in both HIV infection and HIV exposure.
MTB—Treatment

Isolation

MTB aerosolized into fine droplets
light enough to be suspended
air in room is infectious
1 cough = 5 min talking
MTB—Treatment

Isolation
  negative pressure room
  N95 masks / PAPR

Family should be isolated until tested
  must wear masks outside of room
MTB—Treatment

Isolation and drugs

streptomycin  amikacin
isoniazid  quinolones
pyrazinamide
rifampin
ethambutol
MTB—Treatment

isoniazid

nicotinamide analog
primarily active against MTB

hepatic toxicity

neurotoxicity (slow-acetylators)
prevented by giving pyridoxine
MTB—Treatment

pyrazinamide

nicotinamide analog

good CNS penetration

hepatic toxicity
  (compounded by INH)

reduces uric acid excretion
rifampin inhibits DNA-dependent RNA polymerase.

dye enhances metabolism of some drugs.
MTB—Treatment

ethambutol
bacteriostatic
affects mycobacterial cell wall
optic neuritis
(needs careful monitoring in children)
MTB—Treatment

streptomycin
  still an excellent drug

only available as an IM preparation
## MTB—Treatment

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pediatric Dose</th>
<th>Adult Dose</th>
<th>Daily Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>10 mg/kg (10-15)</td>
<td>5 mg/kg (4-6)</td>
<td>300 mg</td>
</tr>
<tr>
<td>Rifampin</td>
<td>15 mg/kg (10-20)</td>
<td>10 mg/kg (8-12)</td>
<td>600 mg</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>35 mg/kg (30-40)</td>
<td>25 mg/kg (20-30)</td>
<td>—</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>20 mg/kg (15-25)</td>
<td>15 mg/kg (15-20)</td>
<td>—</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>—</td>
<td>15 mg/kg (12-18)</td>
<td>1000 mg</td>
</tr>
</tbody>
</table>

Recommendations from the World Health Organization.

Figure 1. Factors to be considered in deciding to initiate treatment empirically for active tuberculosis (TB) (prior to microbiologic confirmation). Abbreviations: AFB, acid-fast bacilli; HIV, human immunodeficiency virus; IGRA, interferon-γ release assay; Mtb, Mycobacterium tuberculosis; TNF, tumor necrosis factor; TST, tuberculin skin test.
Table 2. Drug Regimens for Microbiologically Confirmed Pulmonary Tuberculosis Caused by Drug-Susceptible Organisms

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Druga</th>
<th>Intensive Phase</th>
<th>Continuation Phase</th>
<th>Comments</th>
<th>Regimen Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>INH RIF PZA EMB</td>
<td>7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)</td>
<td>INH RIF</td>
<td>7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)</td>
<td>182–130</td>
</tr>
<tr>
<td>2</td>
<td>INH RIF PZA EMB</td>
<td>7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)</td>
<td>INH RIF</td>
<td>3 times weekly for 54 doses (18 wk)</td>
<td>110–94</td>
</tr>
<tr>
<td>3</td>
<td>INH RIF PZA EMB</td>
<td>3 times weekly for 24 doses (8 wk)</td>
<td>INH RIF</td>
<td>3 times weekly for 54 doses (18 wk)</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>INH RIF PZA EMB</td>
<td>7 d/wk for 14 doses then twice weekly for 12 doses</td>
<td>INH RIF</td>
<td>Twice weekly for 36 doses (18 wk)</td>
<td>62</td>
</tr>
</tbody>
</table>
Increasing adherence for latent tuberculosis infection therapy with health department–administered therapy.


**result**

Looked at multiple variables related to therapy completion.

Only variable associated was health department DOT (>90% completed vs. 50% for self administered; OR 7.7).
Unexplained deterioration during antituberculous therapy in children and adolescents: clinical presentation and risk factors.

Thampi N, Stephens D, Rea E, Kitai I. 

**result**

Canadian case series.

Some children deteriorated during therapy; hard to distinguish from clinical failure.

Corticosteroids seemed to help a subset.
In children with Sx referable to TB (cough, wheeze, FTT) symptoms took ≥60 days to resolve on appropriate Tx.

Do not use response to Tx as proof of Dx.
TUBERCULOSIS

Don't kiss me!

Your kiss of affection
The germ of infection

Town of Hempstead, W.H. Runcie M.D., Health Officer
WPA Federal Art Project District 4