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Tuberculosis Update

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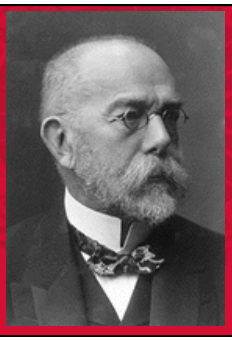
Global Tuberculosis Institute

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Tuberculosis Epidemiology

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The Global Impact of TB

	Estimated incidence, 2015	Estimated number of deaths, 2015
All forms of TB	10.4 million (8.7–12.2million)	1.4 million* (1.2 – 1.6 million)
HIV-associated TB	1.2 million (1.0–1.2 million)	0.4 million
Multidrug-resistant TB MDR/RR-TB	580,000 (520,000–640,000)	250,000 (160,000–340,000)

Approximately 1/3 of the world (2 billion people) is infected with *M.tb*

* Excluding deaths attributed to HIV/TB

Source: WHO Global Tuberculosis Report 2016

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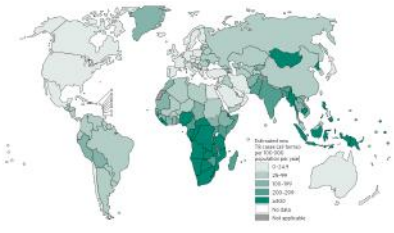
Estimated TB Incidence Rates, 2015



30 high burden countries account for 87% of incident TB cases

Source: WHO *Global Tuberculosis Report, 2016*

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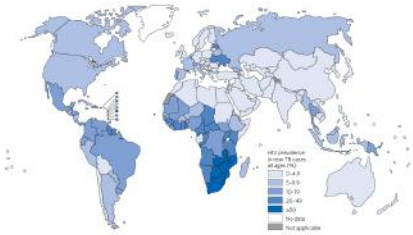
Estimated HIV Prevalence in New & Relapsed TB Cases, 2015



Source: WHO *Global Tuberculosis Report, 2016*

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Worst Case TB Scenarios

- Co-infection between TB and HIV
- Multi-drug resistant TB (MDR TB)
  - Resistance to isoniazid and rifampin
- Extensively drug resistant TB (XDR TB)
  - MDR TB plus resistance to any fluoroquinolone and at least one second line injectable agent
- Totally drug resistant TB

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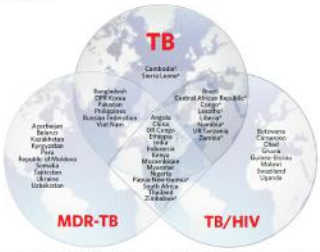
Countries in the three TB high-burden country lists that will be used by WHO during the period 2016–2020, and their areas of overlap



Source: WHO *Global Tuberculosis Report, 2016*

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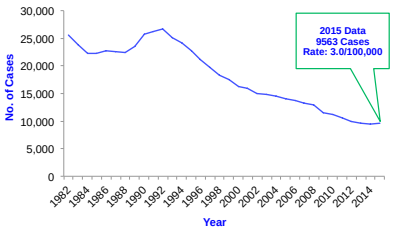
Reported TB Cases, United States, 1982–2015*



Salinas J, Mindra G, Haddad M, et al. Leveling of Tuberculosis Incidence, 2013-2015; MMWR Morb Mortal Wkly Rep 2016;65:273–78

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Rate* of TB Cases, by State/Area – United States, 2013†

* Per 100,000 population
† Data are provisional.

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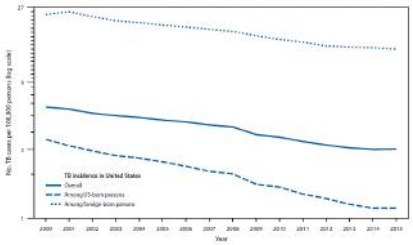
Number & Rate* of TB Cases Among U.S.-born and Foreign-born Persons, by Year Reported – United States, 2000-2015



Salinas J, Mindra G, Haddad M, et al. Leveling of Tuberculosis Incidence, 2013-2015; MMWR Morb Mortal Wkly Rep 2016;65:273–78

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Foreign-born Persons with TB, Top Countries of Origin — United States, 2015

Country	# cases	% Foreign-born	US Rate
Mexico	1,250	19.7	10.4
Philippines	819	12.9	46.9
Vietnam	513	8.1	47.8
India	578	9.1	23.9
China	424	6.7	24.9

*Salinas J, Mindra G, Haddad M, et al. Leveling of Tuberculosis Incidence, 2013-2015; MMWR Morb Mortal Wkly Rep 2016;65:273–78

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TB Transmission and Pathogenesis

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M. abscessus	M. conceptionense	M. gilvum	M. moriokaense	M. senegalense
M. agri	M. [illegible]	M. goodii	M. mucogenicum	M. senuense
M. alvei	M. confluentis	M. hackensackense	M. murale	M. seoulense
M. aichiense	M. conspicuum	M. hassiacum	M. neoaurum	M. septicum
M. angelicum	M. cosmeticum	M. hiberniae	M. neworleansense	M. setense
M. arupense	M. diernhoferi	M. hodleri	M. nonchromogenicum	M. shimoidei
M. asiaticum	M. doricum	M. holsaticum	M. novocastrense	M. simiae
M. aurum	M. duvalii	M. houstonense	M. palustre	M. smegmatis
M. austroafricanum	M. elephantis	M. immunogenum	M. parafortuitum	M. szulgai
M. avium subsp. silvaticum	M. fallax	M. interjectum	M. paraseoulense	M. terrae
M. boenickei	M. flavescens	M. intermedium	M. peregrinum	M. thermoresistibile
M. branderi	M. fluoranthenivorans	M. intracellulare	M. [illegible]	M. tokaiense
M. brisbanense	M. fortuitum	M. kansasii	M. phlei	M. triplex
M. brumae	M. frederiksbergense	M. kubicae	M. phocaicum	M. triviale
M. canariasense	M. [illegible]	M. kumamotonense	M. porcinum	M. tuberculosis
M. chelonae	M. gadium	M. lacus	M. pulveris	M. tuberculosis $H_{37}Rv$
M. chimaera	M. gallinarum	M. manitobense	M. [illegible]	M. vaccae
M. chitae	M. gordonae	M. marinum	M. ratisbonense	M. wolinskyi
M. chubuense	M. gordonae	M. massiliense	M. rhodesiae	M. xenopi
M. celatum	M. gastri	M. monacense	M. scrofulaceum	

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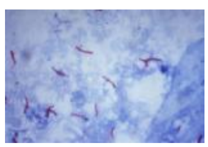
TB Transmission

Types of Mycobacteria

- *M. tuberculosis* causes most TB cases in U.S.
- Mycobacteria that cause TB:
  - *M. tuberculosis*
  - *M. bovis*
  - *M. africanum*
  - *M. microti*
  - *M. canetti*
- Mycobacteria that do not cause TB
  - e.g., *M. avium complex*



M. tuberculosis

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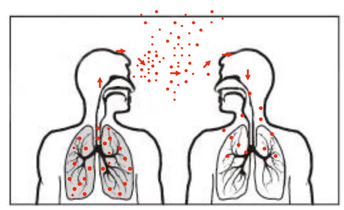
TB Transmission



Dots in air represent droplet nuclei containing *M. tuberculosis*

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TB Transmission

- Probability that TB will be transmitted depends on:
  - Infectiousness of person with TB disease
  - Environment in which exposure occurred
  - Length of exposure
  - Virulence (strength) of the tubercle bacilli
- The best way to stop transmission is to:
  - Isolate infectious persons
  - Administrative, environmental, respiratory protection controls
  - Provide effective treatment to infectious persons as soon as possible

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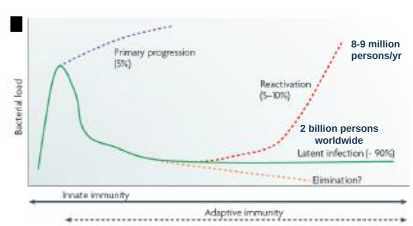

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Testing for TB Infection

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Testing for TB Infection

- Limited by inability to identify *Mycobacterium tuberculosis* in people with latent infection
- Diagnosis is indirect and based on detecting host immune response to infection
  - Tuberculin skin test (TST)
  - Interferon gamma release assays (IGRA)

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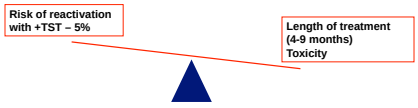
TB Testing

- Measures cell-mediated immunity via delayed type hypersensitivity response to TB antigens
- Not able to accurately predict risk of reactivation



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Tipping the Scale: Targeted Testing for TB Infection

- Identify groups at highest risk for testing:
  - High prevalence of latent infection
  - More likely to reactivate or progress to disease once latently infected
- Reduce screening groups at low risk to lessen false positives
  - Low risk groups likely to be exposed in future (e.g., HCW) is one exception
- Decision to test = decision to treat

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High Prevalence of TB Infection

- Close contacts of patients with TB disease
  - Over half lifetime risk of reactivation occurs in 1-2 years post-conversion
- Foreign-born (*recent immigrants <5 years*)
  - In one series, 43% of foreign-born cases with TB disease had no indication for testing by current guidelines, 65% had been in US > 5 years
- Injection drug users
- Homeless
- Prisoners
- Other epidemiologically defined high-risk groups, may vary based on area

Horsburgh and Rubin, NEJM, 2011;
Cain and Macenzie, CID, 2008;
Walter et al., CID 2008

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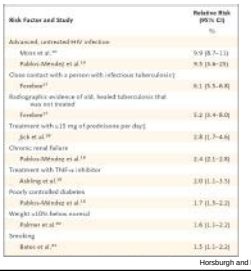
Risk for Progression from TB Infection to TB Disease



Horsburgh and Rubin, NEJM, 2011

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Approved tests for LTBI

QuantiFERON®-TB Gold In-Tube
(Cellestis) measures interferon gamma

Tuberculin Skin Test

T-SPOT®.TB test
(Oxford Immunotec) measures peripheral blood mononuclear cells that produce interferon gamma

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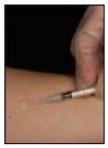
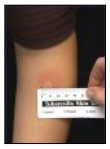
Tuberculin Skin Test

- Inject 0.1 ml of 5 TU PPD tuberculin solution intradermally on volar surface of lower arm
- Produce a wheal 6 to 10 mm in diameter
- Measure reaction in 48 to 72 hours
- Measure induration, not erythema
- Forearm: Transversely to the long axis of the forearm
  - Record in mm
- Ensure trained health care professional measures and interprets the TST





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Interpretation of TST Results

INDURATION DIAMETER	INDIVIDUAL RISK FACTORS
≥5 mm	**Positive test result for:** • Persons with HIV infection. • Recent contacts of persons with active TB disease. • Persons with evidence of old, healed TB lesions on chest X-rays. • Persons with organ transplants and other immunosuppressed persons, including those receiving prolonged corticosteroid therapy (the equivalent of >15 mg/d of prednisone for one month or more) and TNF-α blockers.
≥10 mm	**Positive test result for:** • Persons who have immigrated within the past 5 years from areas with high TB rates* • Injection drug users. • Persons who live or work in institutional settings where exposure to TB may be likely, such as hospitals, prisons, homeless shelters, SROs, and nursing homes. • Mycobacteriology laboratory personnel. • Persons with clinical conditions associated with increased risk of progression to active TB, including: silicosis; chronic renal failure; diabetes; more than 10% below ideal weight or BMI < 18.5; gastrectomy/jejunoileal bypass; some hematologic disorders (such as leukemia and lymphomas); and certain cancers (such as carcinomas of the head, neck, or lung, leukemias, and lymphomas). • Children < 5 years, and children or adolescents exposed to adults in high-risk categories. • Persons with prolonged stay in areas with high TB rates*
≥15 mm	**Positive test result for:** • Persons at low risk for active TB disease for whom testing is not generally indicated.

nyc.gov/health

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Interferon Gamma Release Assays (IGRAs)

- Approved by FDA
  - QuantiFERON®-TB GOLD In Tube (QFT-GIT)
  - T-SPOT®.*TB*
- *In vitro* blood test
- Use antigens not found in BCG or most nontuberculous mycobacteria (ESAT-6, CFP-10, TB7.7)
- More specific, less cross-reaction with NTM
- Can cross-react with *M. kansasii, M. marinum, M. szulgai*

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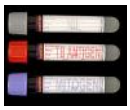
QuantiFERON®-TB Gold In Tube (QFT-GIT)

1. Blood Collection

2. Tube Shaking

3. Incubation / Shipping



www.cellestis.com

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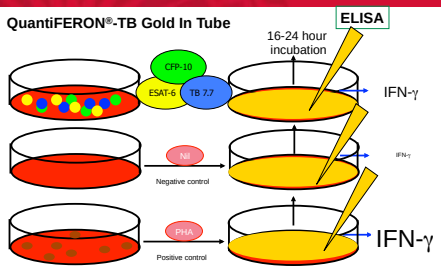
QuantiFERON®-TB Gold In Tube



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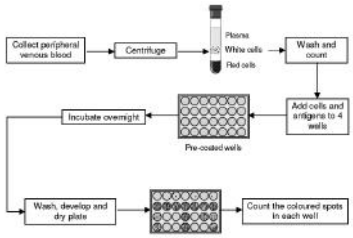
T-Spot®.*TB*



Each spot=one reactive effector T-cell

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IGRA Results

QFT-GIT

- Positive (≥ 0.35 IU/mL)
- Negative (< 0.35 IU/mL)
- Indeterminate
  - Low mitogen
  - High nil
- Failed
  - Inadequate blood volume
  - Broken tube
  - Delayed incubation

T-SPOT.TB

- Positive (≥ 8 spots)
- Negative (≤ 4 spots)
- Borderline (5-7 spots)
- Invalid
  - Low mitogen
  - High nil
- Failed
  - Inadequate blood volume
  - Broken tube
  - Delayed incubation

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IGRA Sensitivity and Specificity

Based on published meta-analyses:

- Overall sensitivity:
  - T-SPOT: **90%**
  - QFT-GIT: **80%**
  - TST: **80%**
- Specificity:
  - IGRAs: **>95%** in low-TB-incidence settings; not affected by BCG vaccination
  - TST: **97%** in populations not vaccinated by BCG; ~**60%** in populations receiving BCG (varies depending on timing of BCG administration)

Summarized in Pai et al, Clinical Microbiology Reviews, 2014

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Screening Guidelines for TB Infection

Risk Group	U.S. Guideline
Close contacts of persons with infectious TB	TST or IGRA, but not both
Persons who may not return for TST reading because of circumstances (e.g., homelessness or injection-drug use) or logistic difficulties	IGRA preferred
Immunosuppressed persons (e.g., those infected with HIV or receiving treatment with prednisone or TNF-α inhibitor)	TST or IGRA; use both if first is negative and suspicion is high
Foreign-born persons	Screening only for those who have immigrated in past 5 yr; use TST or IGRA, but not both
BCG vaccine recipients (if they belong to another risk group)	IGRA preferred
Health care workers (screening program)	TST or IGRA, but not both
Children <5 yr old	TST preferred
Other risk groups	TST or IGRA, but not both

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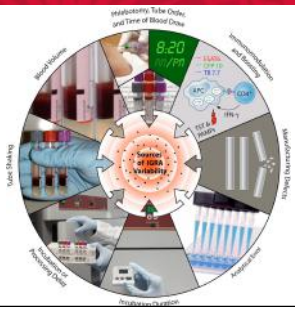

Pai, M.; Denkinger, C.M.; Kik, S.V.; Rangaka, M.X.; Zwerling, A.; Oxlade, O.; Metcalfe, J.Z.; Cattamanchi, A.; Dowdy, D.W.; Dheda, K.; Banaei, N. (2014). Gamma Interferon Release Assays for Detection of Mycobacterium tuberculosis Infection. Clinical Microbiology Reviews 27(1), 3-20.

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Cut-points, wobble and the borderline zone

- People with values near the cut-point are more likely to have a change from (-) to (+) or (+) to (-)
- Most conversions among HCWs in low TB incidence settings appear to be false positive (IGRA 6-9 x compared to TST)
- Repeat testing of apparent converters warranted

Dorman, AJRCCM 2014 189(1): 77

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IGRA Summary

- IGRAs are a significant advancement because of high specificity and operational advantages to TST
- Like TST, it is not a perfect test. Cases will be missed if relying exclusively on an IGRA result
- Training, QA and maintaining IGRA proficiency of laboratory are feasible, achievable, and may be preferable to maintaining TST proficiency of thousands of clinic personnel
- Cost-benefit advantage

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Clinical Review & Education

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Latent Tuberculosis Infection in Adults
US Preventive Services Task Force Recommendation Statement

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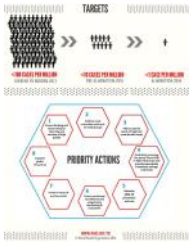
Action Framework for TB Elimination in Low-Incidence Countries



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Treatment of Latent TB Infection

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Treatment Challenges

- Lengthy treatment leading to limited adherence
- Adverse effects influencing patient and provider agreement
- Need for monitoring during treatment

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Pre-Treatment Evaluation

Before initiating treatment:

- Rule out TB disease
  - Wait for culture result if specimen obtained
  - Assess/evaluate for symptoms
- Determine prior history of treatment for TB infection or TB disease
- Assess risks and benefits of treatment
  - Active liver disease
- Ascertain current and previous drug therapy and side effects
- Counsel and educate patient

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Baseline Medical Evaluation

- Medical history
  - History of TB or HIV treatment
  - TB exposure
  - Risks for drug toxicity
    - e.g., alcoholism, liver disease, pregnancy
  - Complete medication list
- Chest x-ray
  - Rule out TB disease
- Laboratory tests
  - CBC and chemistry panel, if indicated
  - 3 sputum samples for AFB smear, culture, & DST if TB symptoms or findings on chest x-ray

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Treatment Regimens for TB Infection

Drugs	Months of Duration	Interval	Minimum Doses	Rating (Evidence)
INH	9*	Daily	270	AII
		2x wkly**	76	BII
INH	6	Daily	180	BI
		2x wkly**	52	BII
RIF	4	Daily	120	BII
INH-RPT	3	Weekly**	12	AI†

*Preferred

** Intermittent treatment only with DOT

† Recommendations not yet rated

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Laboratory Evaluation

- Baseline labs indicated for:
  - Persons with HIV infection
  - Pregnant & postpartum women (up to 2-3 mos. after delivery)
  - Individuals with history/risk of liver disease
    - Heavy alcohol use, chronic hepatitis, history of IDU, on ≥2 meds or medications for other medical conditions
  - Consider in older individuals with other chronic medical conditions/medications prior to INH-RPT
- Repeat monthly until stable
- Ongoing patient education about adherence and adverse drug reactions

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Diagnosis and Treatment of TB Disease

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LTBI vs. TB Disease

Latent TB Infection (LTBI)	TB Disease (in the lungs)
Inactive, contained tubercle bacilli in the body	**Active**, multiplying tubercle bacilli in the body
TST or blood test results usually positive	TST or blood test results usually positive
Chest x-ray usually **normal**	Chest x-ray usually **abnormal**
Sputum smears and cultures **negative**	Sputum smears and cultures may be **positive**
No symptoms	**Symptoms** such as cough, fever, weight loss
Not infectious	**Often infectious** before treatment
Not a case of TB	**A case** of TB

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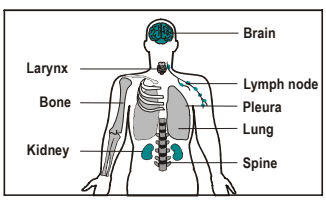
Sites of TB Disease

Bacilli may reach any part of the body, but common sites include:



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Sites of TB Disease

	Location	Frequency
Pulmonary TB	**Lungs**	**Most TB cases are pulmonary**
Extrapulmonary TB	**Places other than lungs such as:** **• Larynx** **• Lymph nodes** **• Pleura** **• Brain** **• Kidneys** **• Bones and joints**	**Found more often in:** **• HIV-infected or other immunosuppressed persons** **• Young children**
Miliary TB	**Carried to all parts of body, through bloodstream**	**Rare**

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Diagnosis of TB

- Diagnosis follows "*Suspicion*"
- When should we "*Think TB*"?
  - Who is at risk for TB?
  - Is TB presenting differently than in the past?
- How do we make the diagnosis?
- And…are there new ways to improve diagnostic capacity?

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Diagnosis: Define Groups at-Risk

Epidemiology of recent cases

- In US, know your populations
  - Majority of cases is non-US born; from high prevalence countries
  - Community-specific (*e.g.*, homeless, substance abusers, Asian, …)
  - Children from high-prevalence groups
- Medical risk factors *(if infected)*
  - HIV 7-10%/yr
  - Diabetes ? 4%/yr
  - ESRD 10-20%/yr
  - Immunosuppressive therapies – including *organ transplant recipients*, *anti-TNF-α agents*, *chronic steroids*
  - Age
- Recent transmission *versus* reactivation

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Diagnosis of TB

- History (personal)
  - TB risks?
  - Symptoms
    - Specific to system involved
      - *e.g.*, cough (pulmonary), chest pain (pericardial), neck swelling, …

      and/or
    - Nonspecific (*constitutional*)
      - *e.g.*, fever, weight loss, night sweats, fatigue, …
    - May be absent - *up to 25%*
- Physical examination
  - Findings specific to system involved; constitutional
- TST or IGRA?
  - Approx. 75% sensitive in TB disease - may *support* diagnosis
- Chest radiograph

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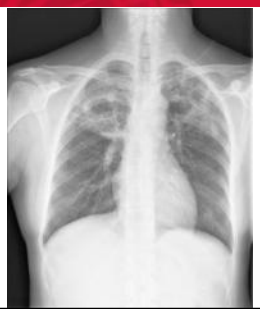

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TB is a Clinical Diagnosis

- Most clinicians will initiate multi-drug therapy *if the disease is suspected on clinical grounds*
  - But many cases go undiagnosed until a laboratory reports a positive culture
- How is that diagnosis confirmed?
  - *In the laboratory*

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Standard Mycobacteriology Laboratory Tests

- Smear/stain for *acid-fast* organisms
  - Sputum, sterile fluids, tissue
- Culture for identification of organism
  - Includes speciation
  - Drug susceptibility studies (DST)
- Nucleic acid amplification (NAA)

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Molecular DST

- Molecular assays for INH, RIF most common
- Detect polymorphisms associated with drug resistance
  - Performed on clinical specimens or culture isolates
  - Results available within 1-2 days
- In-house assays
  - Molecular beacons, pyrosequencing, RT-PCR
- Commercial assays
  - HAIN and INNO-LIPA line probe assays; Xpert® MTB/RIF
- Some Issues
  - None is FDA-approved

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Treatment of Tuberculosis
2016 ATS/CDC/IDSA Statement

- 6 month regimen for drug-sensitive TB
- Initial phase (2 months) with 4 drugs
- Continuation phase (4 months) with 2 drugs
- Prolonged therapy for some patients
- Directly observed therapy (DOT) is standard of care

Induction Phase	Continuation Phase	Extension
4 Drugs: Rifampin Isoniazid Pyrazinamide Ethambutol 8 weeks	2 Drugs: Isoniazid Rifampin 18 weeks	Consider prolonging therapy for cavitary TB, slow culture conversion, TB meningitis, TB osteomyelitis

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Regimens for Drug Sensitive Pulmonary TB

Initial phase			Continuation phase				Rating* (evidence)†	
Regimen	Drugs	Interval and doses‡ (minimal duration)	Regimen	Drugs	Interval and doses‡§ (minimal duration)	Range of total doses (minimal duration)	HIV–	HIV+
1	INH RIF P Z A EMB	Seven days per week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk)¶	1a	INH/RIF	Seven days per week for 126 doses (18 wk) or 5 d/wk for 90 doses (18 wk)¶	182–130 (26 wk)	A (I)	A (II)
			1b 1c**	INH/RIF INH/RPT	Twice weekly for 36 doses (18 wk) Once weekly for 18 doses (18 wk	92–76 (26 wk) 74–58 (26 wk)	A (I) B (I)	A (II)# E (I)
2	INH RIF P Z A EMB	Seven days per week for 14 doses (2 wk), then twice weekly for 12 doses (6 wk) or 5 d/wk for 10 doses (2 wk),¶ then twice weekly for 12 doses (6 wk)	2a 2b**	INH/RIF INH/RPT	Twice weekly for 36 doses (18 wk) Once weekly for 18 doses (18 wk)	62–58 (26 wk) 44–40 (26 wk)	A (II) B (I)	B (II)# E (I)
3	INH RIF P Z A EMB	Three times weekly for 24 doses (8 wk)	3a	INH/RIF	Three times weekly for 54 doses (18 wk)	78 (26 wk)	B (I)	B (II)
4	INH RIF EMB	Seven days per week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk)¶	4a	INH/RIF	Seven days per week for 217 doses (31 wk) or 5 d/wk for 155 doses (31 wk)¶	273–195 (39 wk)	C (I)	C (II)
			4b	INH/RIF	Twice weekly for 62 doses (31 wk)	118–102 (39 wk)	C (I)	C (II)

Definition of abbreviations: EMB = Ethambutol; INH = isoniazid; PZA = Pyrazinamide; RIF = rifampin; RPT = rifapentine.
* Definitions of evidence ratings: A = preferred; B = acceptable alternative; C = offer when A and B cannot be given; E = should never be given.
† Definition of evidence ratings: I = randomized clinical trial; II = data from clinical trials that were not randomized or were conducted in other populations; III = expert opinion.
‡ When DOT is used, drugs may be given 5 days/week and the necessary number of doses adjusted accordingly. Although there are no studies that compare five with seven daily doses, extensive experience indicates this would be an effective practice.
§ Patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31 week; either 217 doses [daily] or 62 doses [twice weekly]) continuation phase.
¶ Five-day-a-week administration is always given by DOT. Rating for 5 day/week regimens is AIII.
# Not recommended for HIV-infected patients with CD4+ cell counts <100 cells/µl.
** Options 1c and 2b should be used only in HIV-negative patients who have negative sputum smears at the time of completion of 2 months of therapy and who do not have cavitation on initial chest radiograph (see text). For patients started on this regimen and found to have a positive culture from the 2-month specimen, treatment should be extended an extra 3 months.

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Objectives of TB Therapy

- Kill actively multiplying bacteria (Initial phase)
  - Improve symptoms & prevent death
  - Prevent transmission to others
  - Prevent emergence of resistance
- Sterilize disease sites (Continuation phase)
  - Cure the disease
- Drugs differ in their activity against TB
  - Bactericidal
  - Bacteriostatic/Sterilizing

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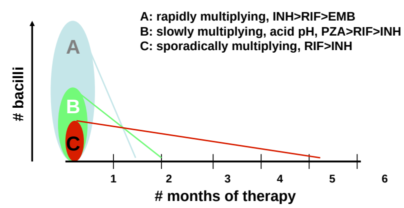
Hypothetical Model of TB Chemotherapy

M. Iseman, D. Mitchison

3 anatomic/metabolic populations of bacilli in cavitary TB

A: rapidly multiplying, INH>RIF>EMB
B: slowly multiplying, acid pH, PZA>RIF>INH
C: sporadically multiplying, RIF>INH



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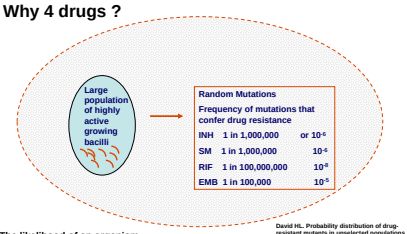
Why 4 drugs ?



David HL. Probability distribution of drug-resistant mutants in unselected populations of *Mycobacterium tuberculosis*. *Appl Microbio l970;20:810-14.*

The likelihood of an organism spontaneously resistant to 2 antibiotics is the product of their probabilities *i.e., for Isoniazid & Rifampin 1 in 10^{-14} , for 3 drugs IRE 1 in 10^{-20})*

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Treatment of TB: Risk Factors for Relapse

Cavity?	Culture (+) at 2 months? Yes	No
Yes	21.8%	6.2%
No	5.0%	2.1%

Extend therapy to 9 months for pts with cavitary TB *and* positive cultures at 2 months

Lancet, 2002

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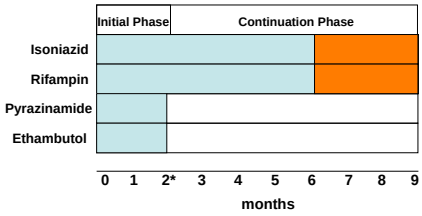
Treatment of TB: Extending Therapy



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Treatment Monitoring – components

- Microbiologic monitoring
- Clinical improvement
- Laboratory monitoring
- Radiographic improvement
- Treatment assessment

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Treatment Monitoring – microbiology

- Serial sputum smears every 2 weeks to assess early response
  - Target: Smear Conversion
- Monthly sputum for AFB smear and culture (until 2 consecutive cultures negative)
  - 2 month culture conversion is an important benchmark

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Treatment Monitoring – clinical/laboratory/ radiology

- Periodic (minimum monthly) evaluation to assess adherence and identify adverse reactions
- Repeat chest x-ray:
  - At completion of initial treatment phase for patients with initial negative cultures
  - At end of treatment for patients with culture-negative TB
  - Generally not necessary for patients with culture positive TB
- Liver function and CBC if abnormal at baseline
- Visual acuity and color vision monthly if EMB used > 2 months or doses > 15-20 mg/kg

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Treatment monitoring

- After 3 months of therapy, if cultures are positive or symptoms/radiology do not resolve, reevaluate for:
  - Drug resistance
  - Non-adherence
  - Malabsorption
- Repeat Drug Susceptibility Testing

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Responsibility for Successful Treatment:

- Goal of treatment: Cure the individual patient and minimize transmission of *M.tb*
- Successful treatment benefits the individual patient and the community
- Responsibility lies with health care provider, not only for prescribing appropriate regimen, but for ensuring successful completion of therapy

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Patient # 1 History

- VJ is a 43 y/o male pharmacy technician
- Born in India
- Immigrated to the USA on 1-30-07
- In July 2011 (7/15/11-7/23/11) he was hospitalized with complaints of fever (103º) and weight loss (10 lbs. in 1 month)
- He was found to have a right pleural effusion and reticulonodular densities and calcified RUL granulomas on CXR

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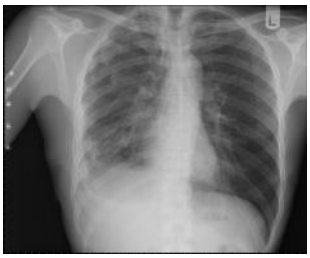
PA CXR (7/15/11)



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Patient History Cont'd

- A VATS procedure was done and a RUL lung biopsy revealed granulomatous lung disease
- PPD: 0 mm. induration
- Quanti-Feron: negative
- HIV: negative
- ESR: 96

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Treatment

- On 7-22-11 DOT was started with:
  - RIF 600 mg/d PO
  - INH 300 mg/d PO
  - PZA 1000 mg/d PO
  - EMB 800 mg/d PO
  - On the above regimen, the patient states that he felt much better and has gained approximately 8 lbs.

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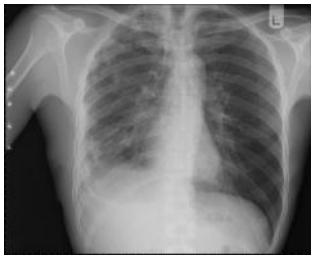
PA CXR (9-6-11)



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Case Summary

- IGRA negative, culture negative, histology suggestive of TB
- Clinically confirmed case with response to therapy

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Conclusions

- Diagnosis can only be made if considered in the differential
- TB treatment is complex and requires a multi-disciplinary and patient-centered approach
- Standardized regimens exist and have improved TB cure when high levels of adherence can be assured (i.e. D.O.T)
- Past 20 years brought forth achievements in increasing patient access to treatment and decreasing mortality
- Accelerate TB elimination in the next 20 years by addressing latent TB infection, developing new drugs and shorter treatment courses, and discover the effective vaccine