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The Onboarding Exam: Tuberculosis Isn't Just for Healthcare Workers Anymore

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Learning Objectives

At the conclusion of this presentation learners will:

- Know the epidemiology of TB in the United States
- Know WHY IGRA is recommended over TST by all major medical associations
- Know how they can change their patients' lives and eliminate TB in the United States

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Agenda

- WHAT is TB?
  - WHERE is TB?
    - WHO has TB?
      - HOW to test for TB?

HOW to stop TB?

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HOW to stop TB?

Mycobacterium tuberculosis

Atypical bacterium, waxy coat, slow-growing

Vaccine = BCG, given to children worldwide

Infection = AIRBORNE, hangs in air

Prevalence in US = 13 million infected, 8k active disease/year

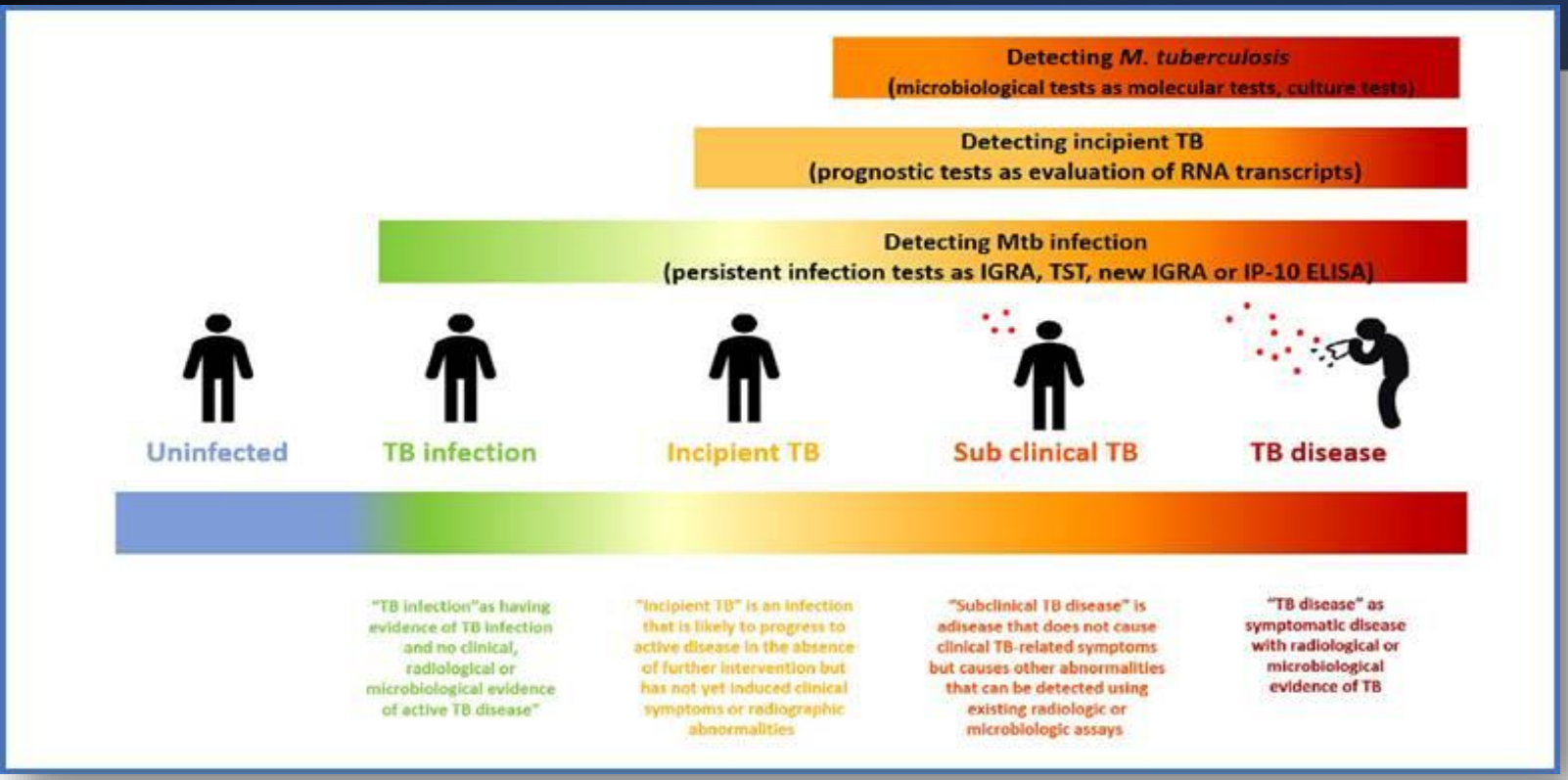
Exposure = requires time & proximity to inhale (see JOEM 2020)

Infection = pulmonary (80%) extrapulmonary (20%, mostly kids)

Disease = activates in 5-10%; 50% within <2 years from infection

Mortality in US = 13% (“consumption”)

Updated Terminology



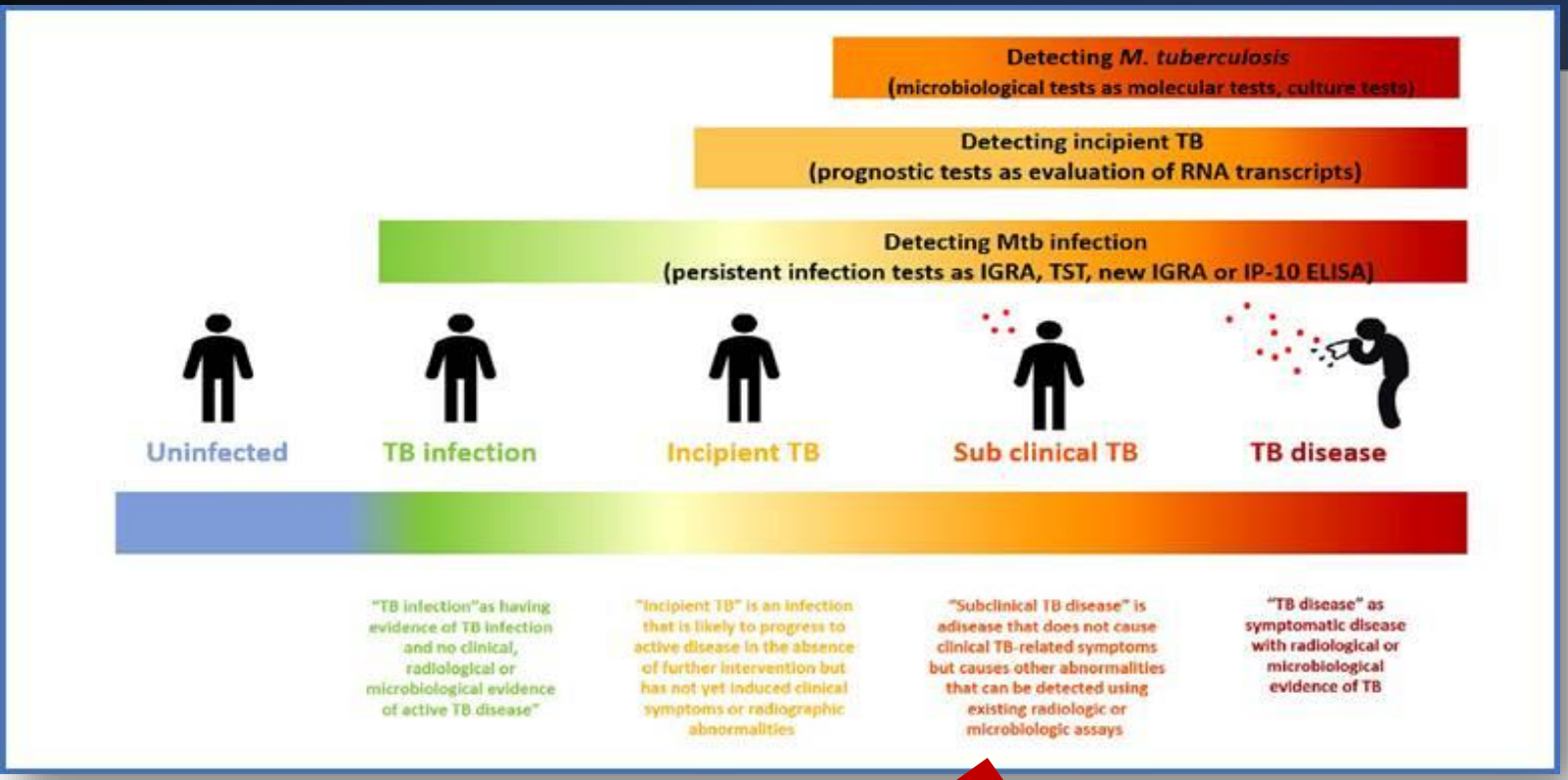
NEW LANGUAGE:

Not Latent TB -> TB infection

Not Active TB -> TB disease

Drain, P.K. et al. (2018) Incipient and subclinical tuberculosis: a clinical review of early stages and progression of infection. Clin. Microbiol. Rev.31, e00021–18.

Updated Terminology



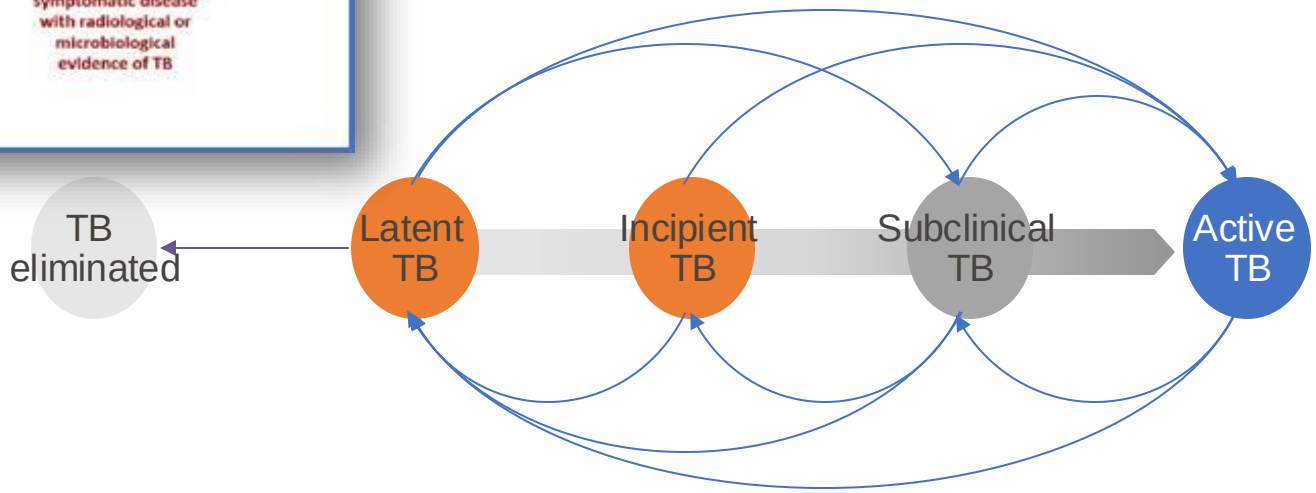
NEW LANGUAGE:

Not Latent TB -> TB infection

Not Active TB -> TB disease

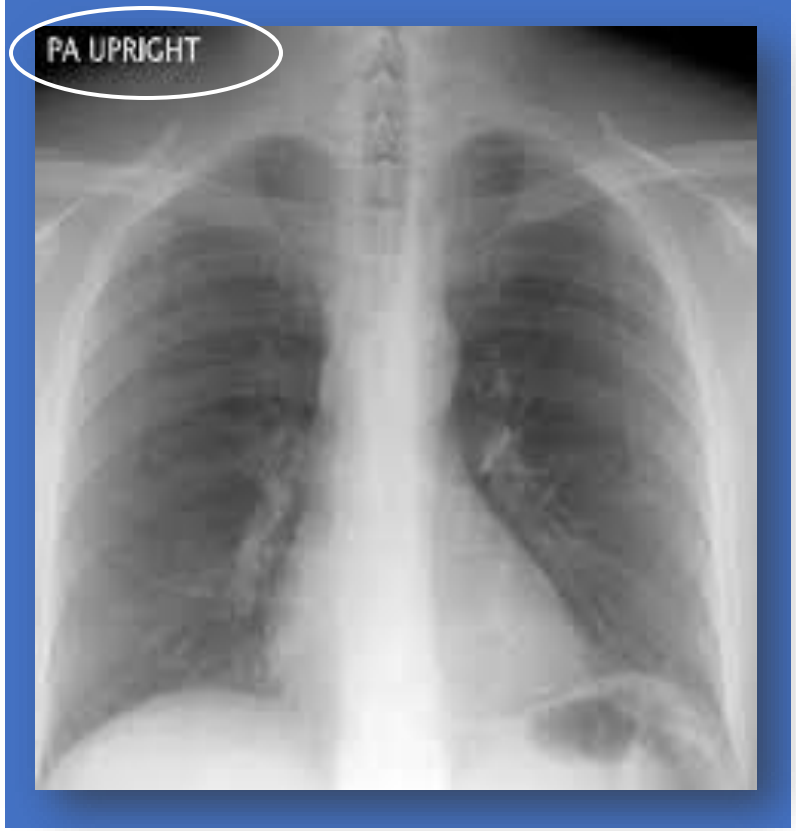
NEW CONCEPT:

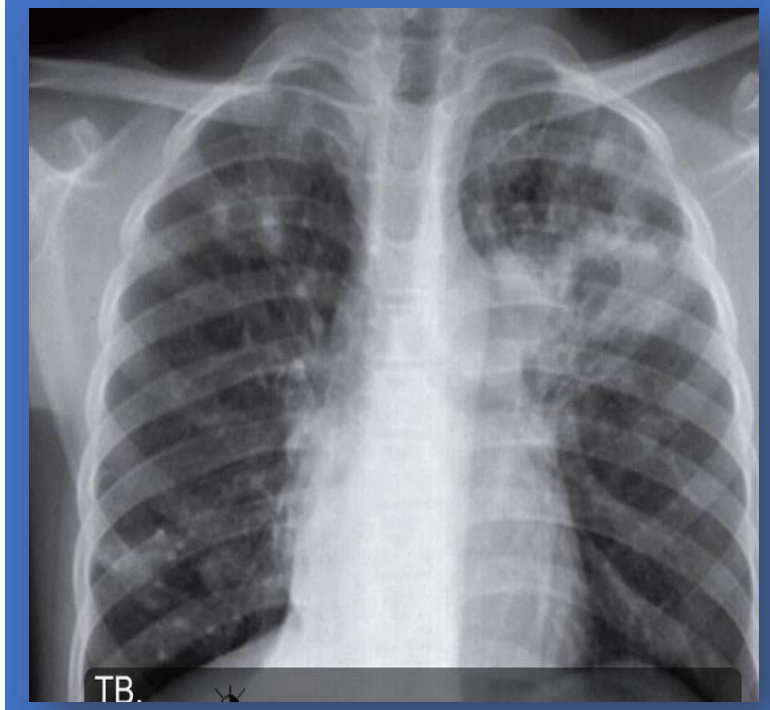
Not 2 states of infection -> Constant movement

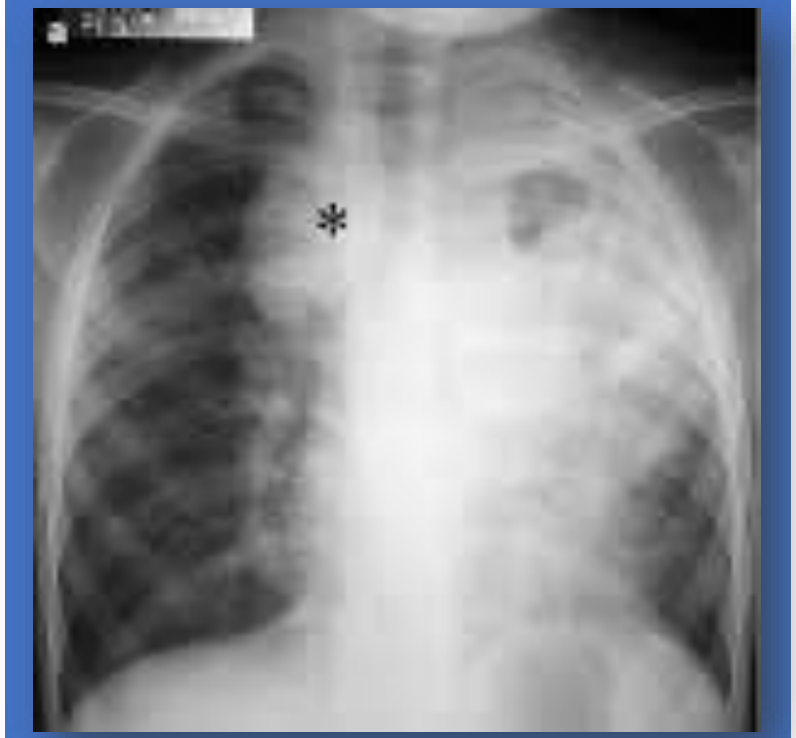


Drain, P.K. et al. (2018) Incipient and subclinical tuberculosis: a clinical review of early stages and progression of infection. Clin. Microbiol. Rev.31, e00021–18.

Infection vs. Disease







Cough > 3 weeks, fever, night sweats, hemoptysis, weight loss, fatigue*

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HOW to stop TB?

TB in the US 2022: Incidence by State

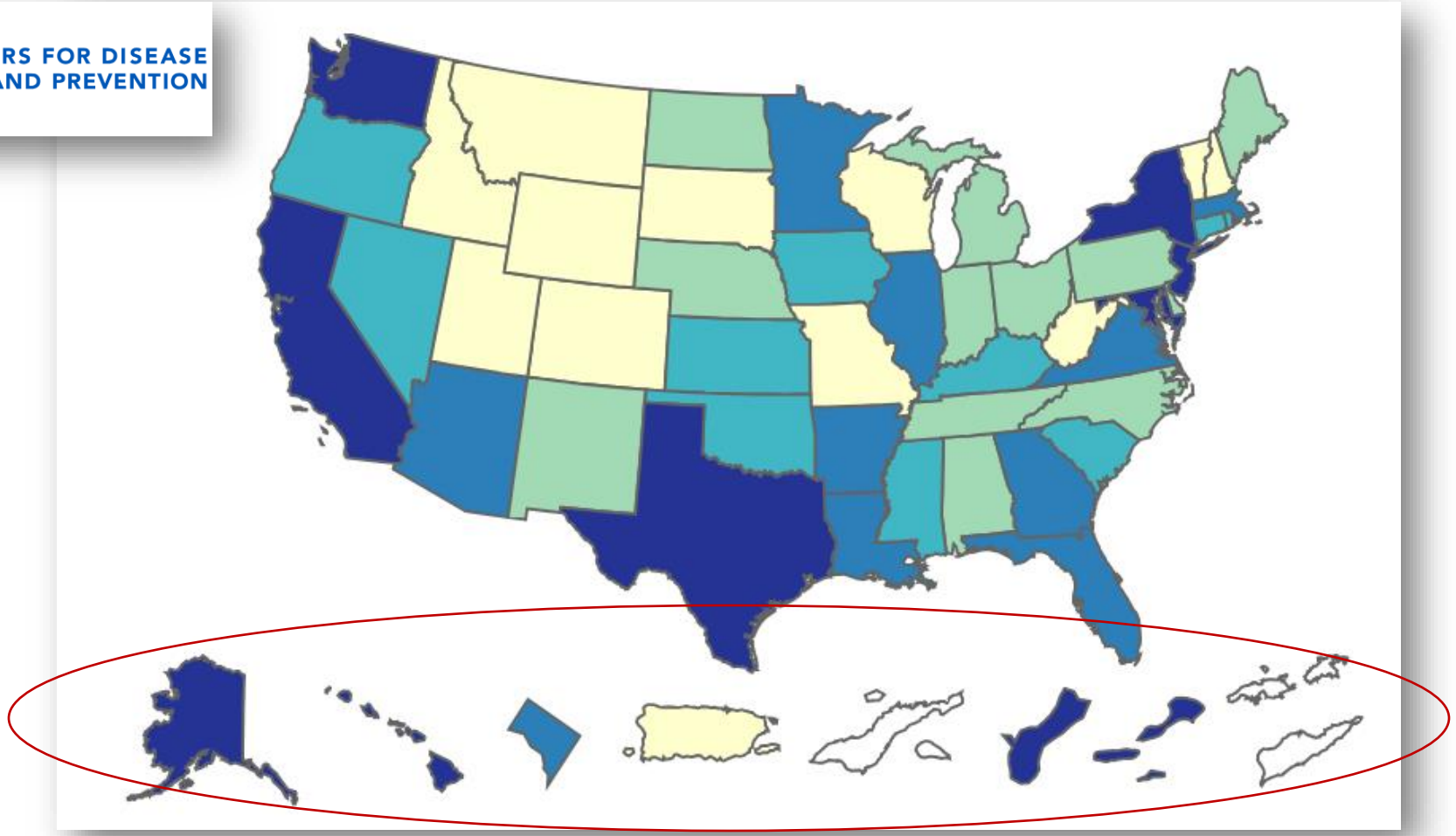
May 02, 2023

U.S. CENTERS FOR DISEASE CONTROL AND PREVENTION

States with highest INCIDENCE

vs.

States with highest PREVALENCE



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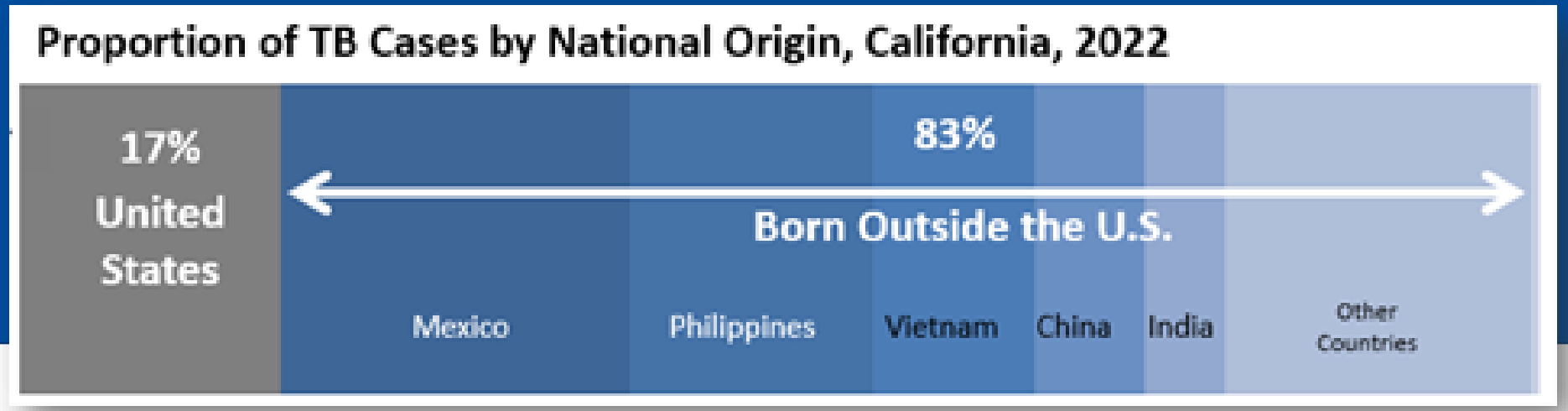
TB: Those who are infected



- >80% of TB infection is in non-US born
- >80% of active TB is from progression of TB infection to TB disease (latent to active)
- >80% of TB disease is pulmonary (20% is extrapulmonary)
- >80% of TB infection in the US is in California, Texas, Florida and New York
- USPSTF 2016, 2023; yet studies show primary care testing ~12% of FB pts

https://www.uspreventiveservicestaskforce.org/uspstf/recommendation-topics/uspstf-a-and-b-recommendations

are DIFFERENT FROM those who will progress

HIV infection (50-100x)

Substance use disorder (2-3x)

Diabetes (2-3.5x)

Rheumatoid arthritis, Crohn's disease treatments, Corticosteroids

Organ transplants (25-75x)

Silicosis (30x)

Renal Failure (10-25x)

Lobue, P. and Menzies, D. (2010) Treatment of latent tuberculosis infection: an update. Respirology 15, 603–622.

Final Recommendation Statement USPSTF

Latent Tuberculosis Infection in Adults: Screening

May 02, 2023

U.S. Preventive Services TASK FORCE

2016, 2023

- New: includes **a Clinician Summary,** "Assessment of Risk" form and section on "Screening Tests"

Recommendation Summary

Population	Recommendation	Grade
Asymptomatic adults at increased risk of latent tuberculosis infection (LTBI)	The USPSTF recommends screening for LTBI in populations at increased risk. See the "Assessment of Risk" section for additional information on adults at increased risk.	B

However, primary care's testing of non-US born = 11-12% as of 2022, per CDC

https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/latent-tuberculosis-infection-screening#citation9

Which Occupations have TB?
HCP: Where TB Isn't

2016 CDC Table 47. Primary Occupation for the Past Year

Occupation	Cases
	8,654
HCP	3.4% (96.6%)

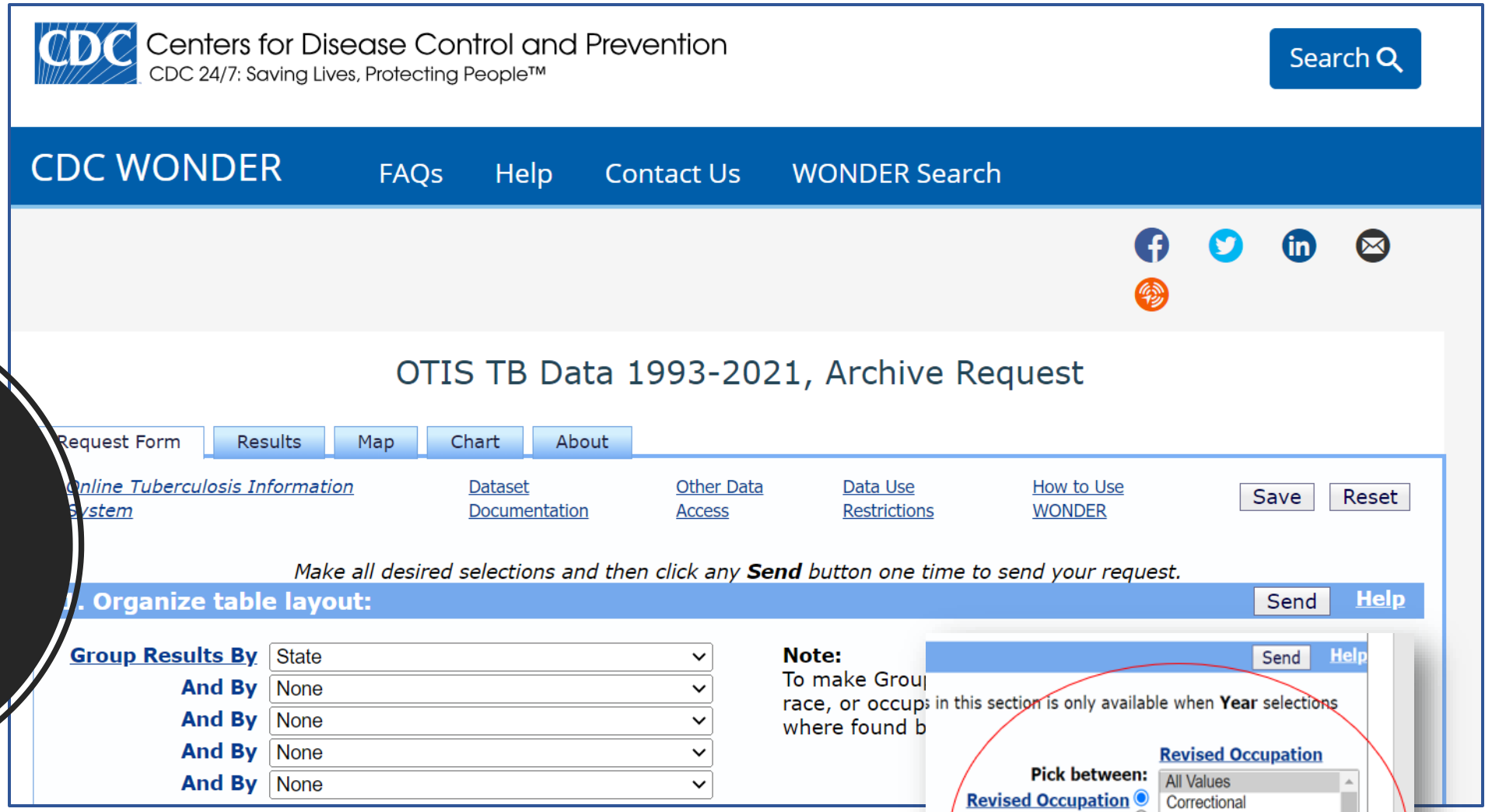
Table 1. Mean Annual Number of Active TB Cases and Rates per 100,000 Health Care Personnel (HCP) by Country of Birth Compared to All United States Residents: 2003-2007 and 2010-2016

Study Period		HCP		HCP Total	U.S. Total*	
		US-born	Non-US-born			
2003-2007	Rate	1.7	17.9	4.2	4.8	
					US-born	Non-US-born
	No. (%)	153 (36)	268 (64)	421 (100)	6,290	7,745
2010-2016	Rate	0.8	10.8	2.5	3.0	
					US-born	Non-US-born
	No. (%)	90 (28)	262 (72)	352 (100)	3,330	6,222

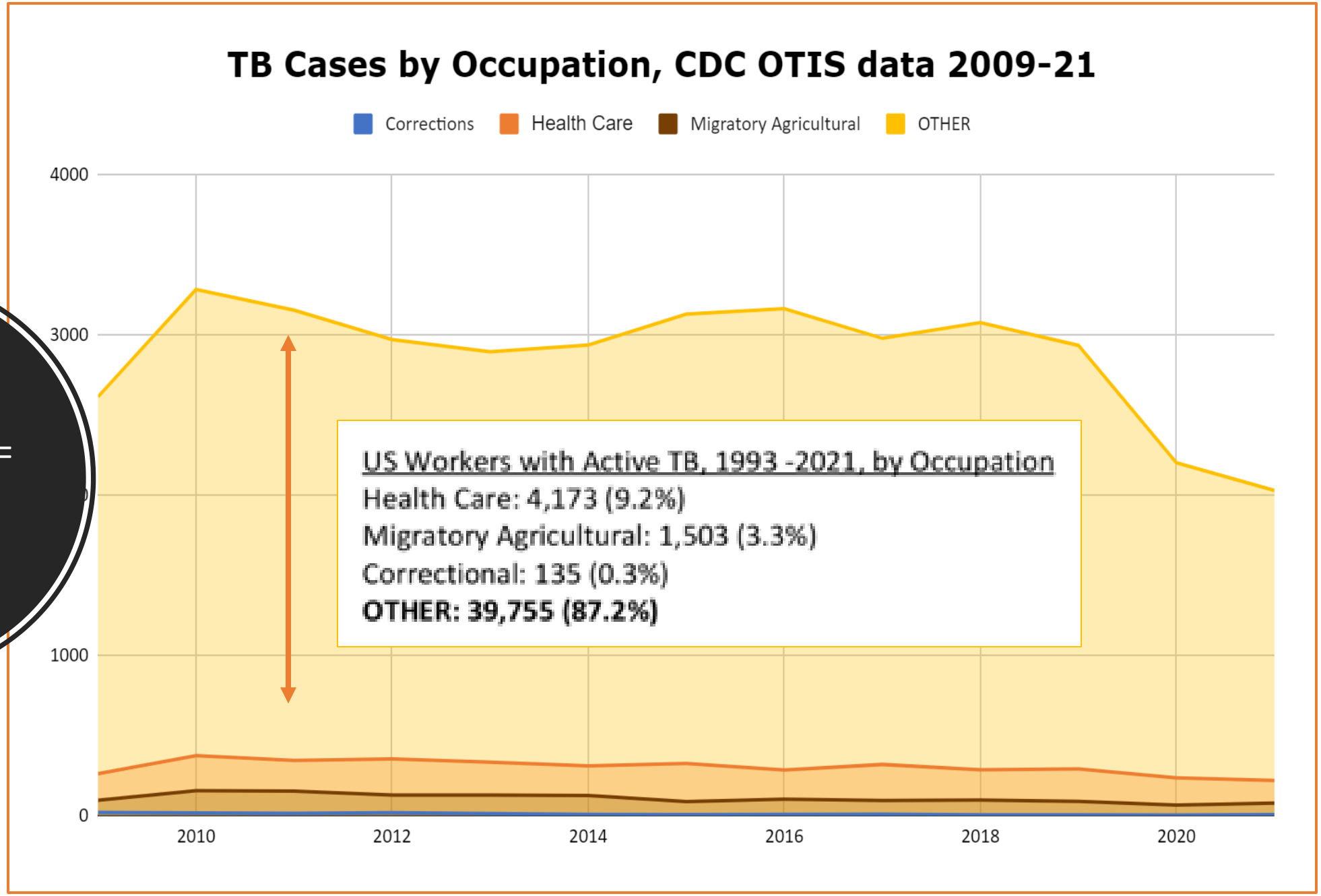
***The U.S. total number of cases (not shown) is 14,065 from 2003-2007 and 9,561 from 2010-2016.**

Sources: Lambert, et al. 2012(14) and Mongkolrattanothai, et al. 2019.(15)

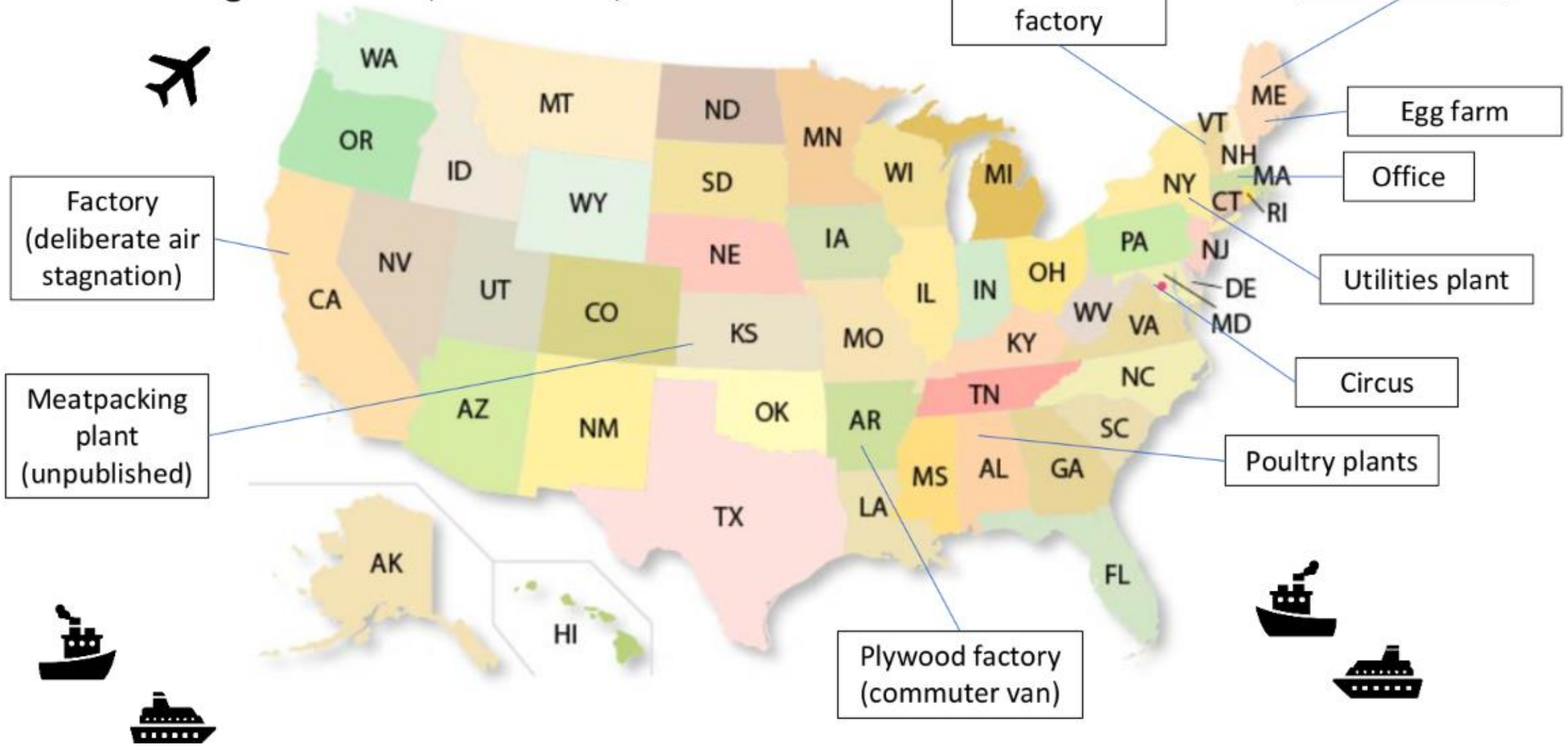
CDC Online Tuberculosis Information System



Occupation = "OTHER"!



US Worksites with Occupational TB Outbreaks
Excluding healthcare, education, and corrections



Occupational Information Network (O*NET)

O*NET OnLine (onetonline.org)

Classification

100 = near touching
75 = moderately close (arms length)
50 = shared office

Physical Proximity O*NET Descriptor

100 – Choreographers

95 – Actors

93 – Flight attendants

91 – Firefighters, Hairdressers

91 – Childcare

90 - EMT

88 – Gambling dealers

87 – Fiberglass laminators

86 – TSA screeners

85 – Meat, poultry, fish trimmers

84 – Agricultural factory

81 – Cook, Server, bartender

81 - Teacher, older grades

78 – Bus drivers

75 – Fast food counter workers

73 – Slaughterers and meat packers

64 – Office worker

61 – Retail/ cashier

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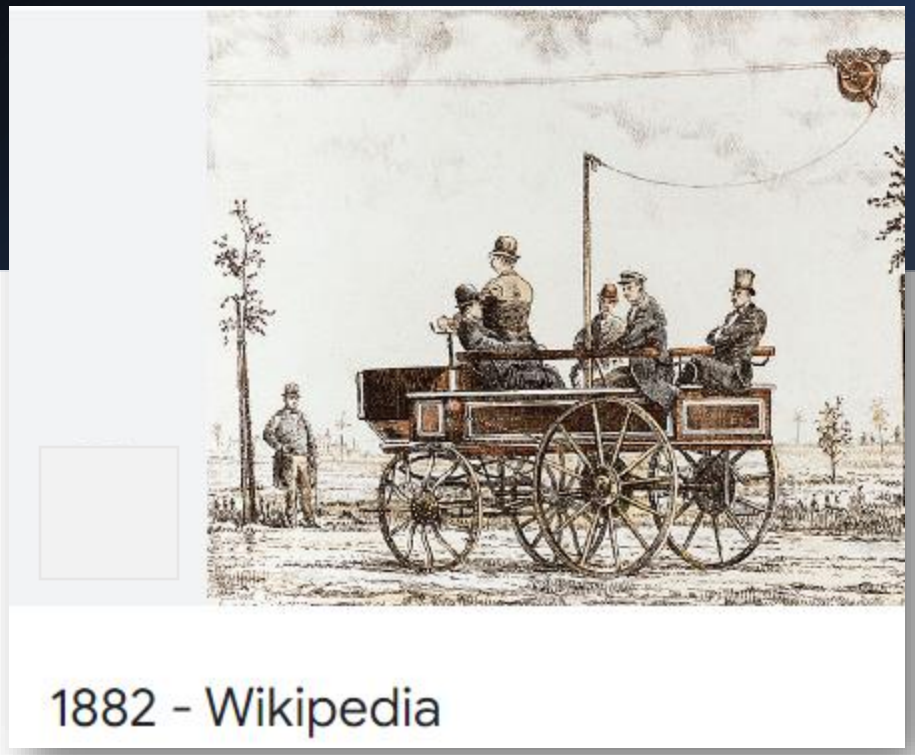
Tuberculin Skin Test: Founded 1882



"Traditional medical practices during most of the 19th century relied on symptomatic treatment, consisting primarily of bloodletting, blistering, and high doses of mineral poisons.

These medical regimens resulted in high rates of death in patients unfortunate enough to undergo treatment."

There were 38 states

Thomas Edison - first electric plant

The Anglo-Ottoman Convention of 1880 prohibits the Red Sea slave trade and gives British the right to stop slave ships in Ottoman waters

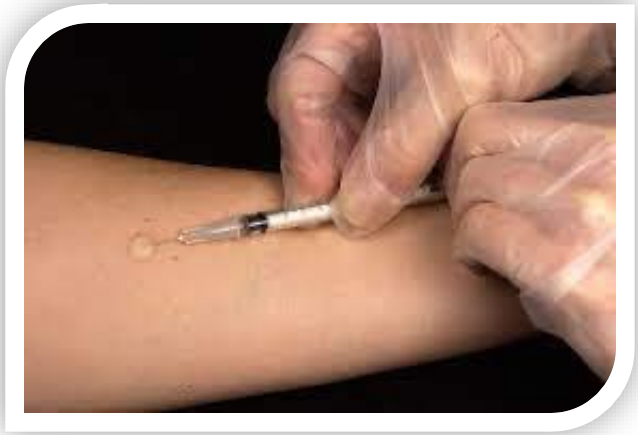
Women could not vote

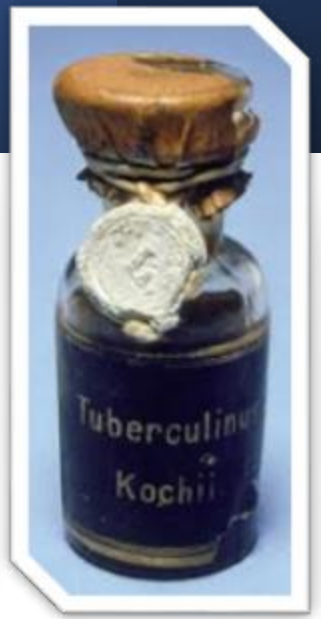
Women weren't admitted to college

Wives could not own property

Wives were property of husbands

Tuberculin Skin Test





Still widely used
Time-intensive (2-4 visits)*
- DEI
60% patient compliance[1]
Subjective reads
No controls
Manual data entry
Minimal provider training compliance
Supply problems ….
Less accurate/inaccurate =>
>60% of TST positives are false-positives!

[1] J Occup Environ Med. 2012 Jul; 54(7): 806-15

These strains all cause TST to be FALSE-positive for TB!

Tuberculosis Complex	ESAT-6 (IGRA)	CFP-10 (IGRA)	TST
M. tuberculosis	+	+	+
M. africanum	+	+	+
M. bovis	+	+	+

BCG Substrain	ESAT-6 (IGRA)	CFP-10 (IGRA)	TST
Gothenberg	-	-	+
Moreau	-	-	+
Tice	-	-	+
Tokyo	-	-	+
Danish	-	-	+
Glaxo	-	-	+
Montréal	-	-	+
Pasteur	-	-	+

Environmental Strain	ESAT-6 (IGRA)	CFP-10 (IGRA)	TST
M. abcessus	-	-	+
M. avium	-	-	+
M. branderi	-	-	+
M. celatum	-	-	+
M. chelonae	-	-	+
M. fortuitum	-	-	+
M. gordonii	-	-	+
M. intracellulare	-	-	+
M. kansasii	+	+	+
M. malmoense	-	-	+
M. marinum	+	+	+
M. scrofulaceum	-	-	+
M. szulgai	+	+	+
M. terra	-	-	+
M. vaccae	-	-	+
M. xenopi	-	-	+

★

Just because you've always done something a certain way doesn't mean it's the best way

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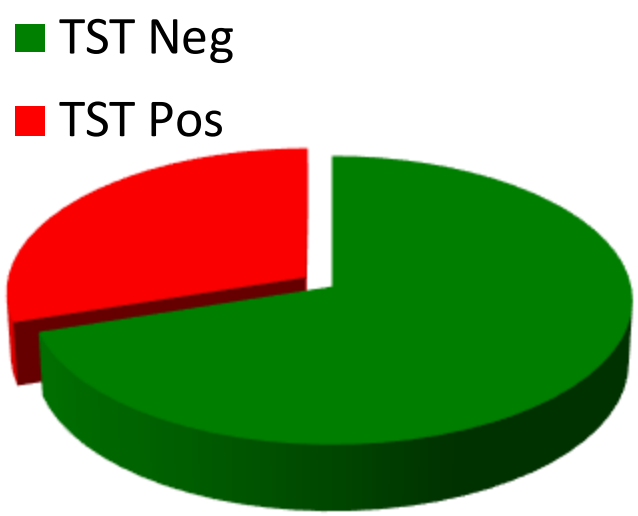
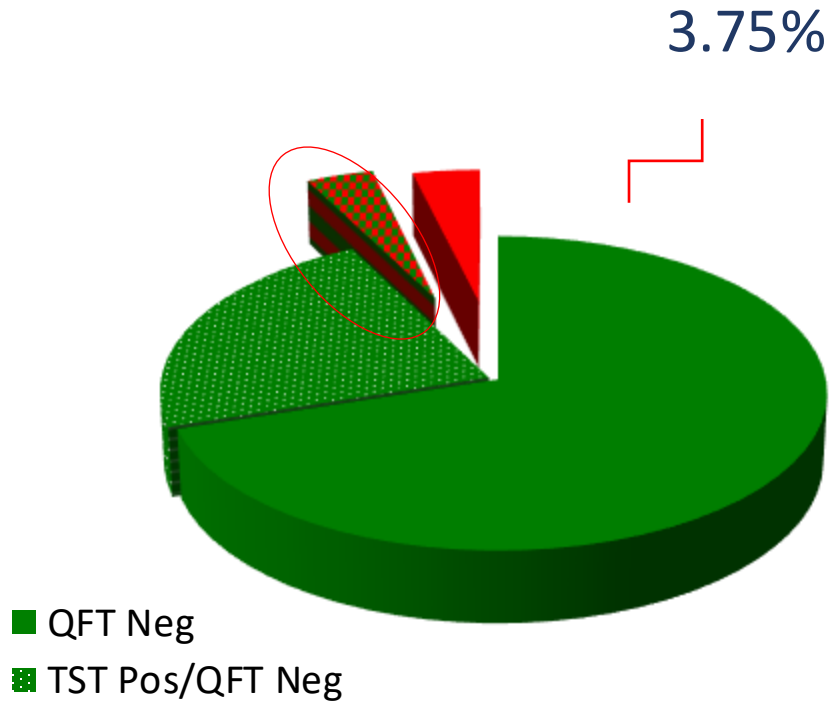
Palo Alto VA and UIC: >28,800 tests January 2009, we eliminated TST

- Pre-IGRA (TST positives)
- Who has TB?

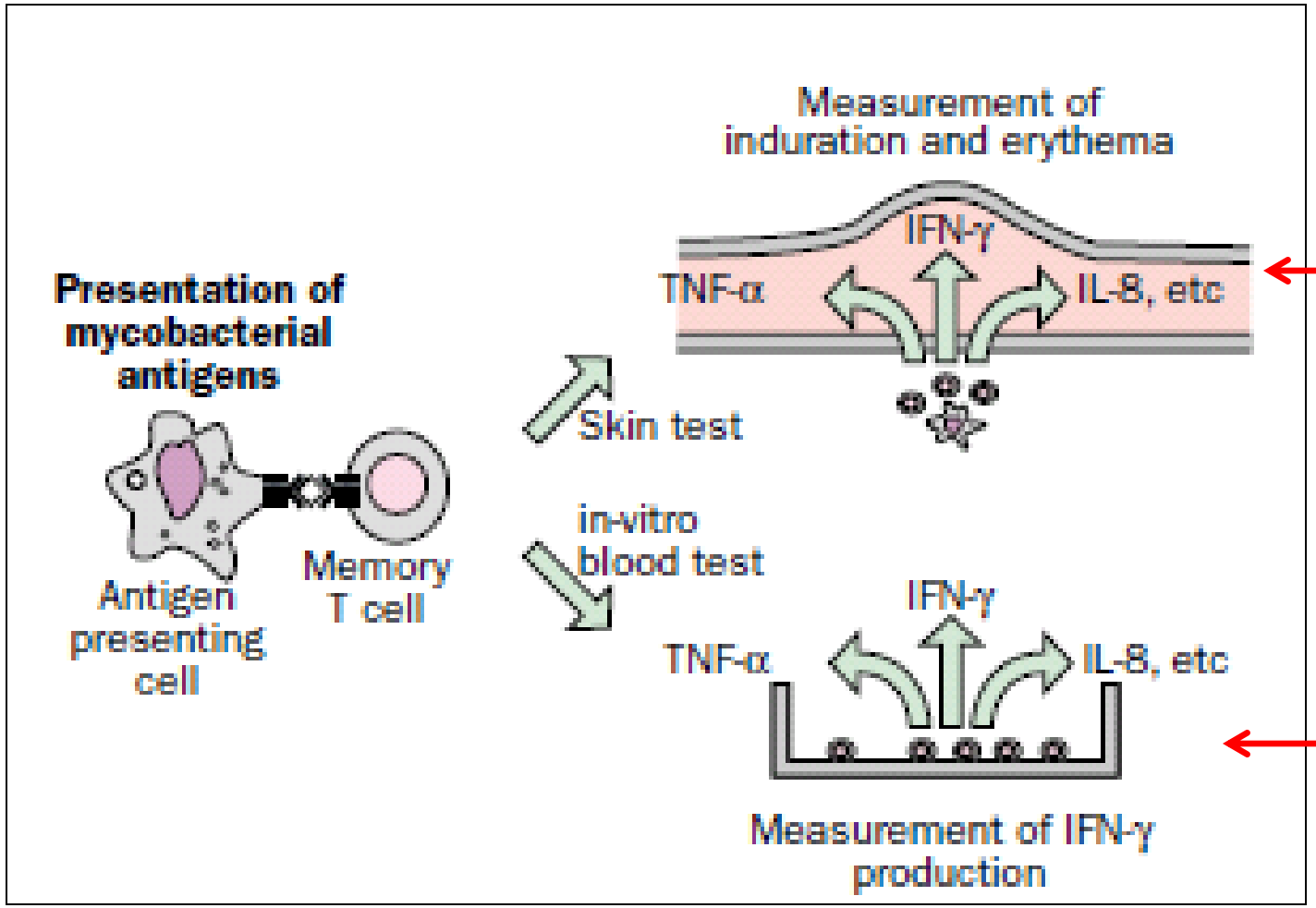


- Post-IGRA (TST positives)
- Who has TB?



*TST data calculated; QFT data actual

TST (1880) and IGRA (2005)



TST: Crude mixture of proteins

IGRA: Highly TB- specific antigens

Lancet 2000; 356: 1099-1104f

Tuberculin Skin Test (TST) vs Interferon-Gamma Release Assays (IGRAs)

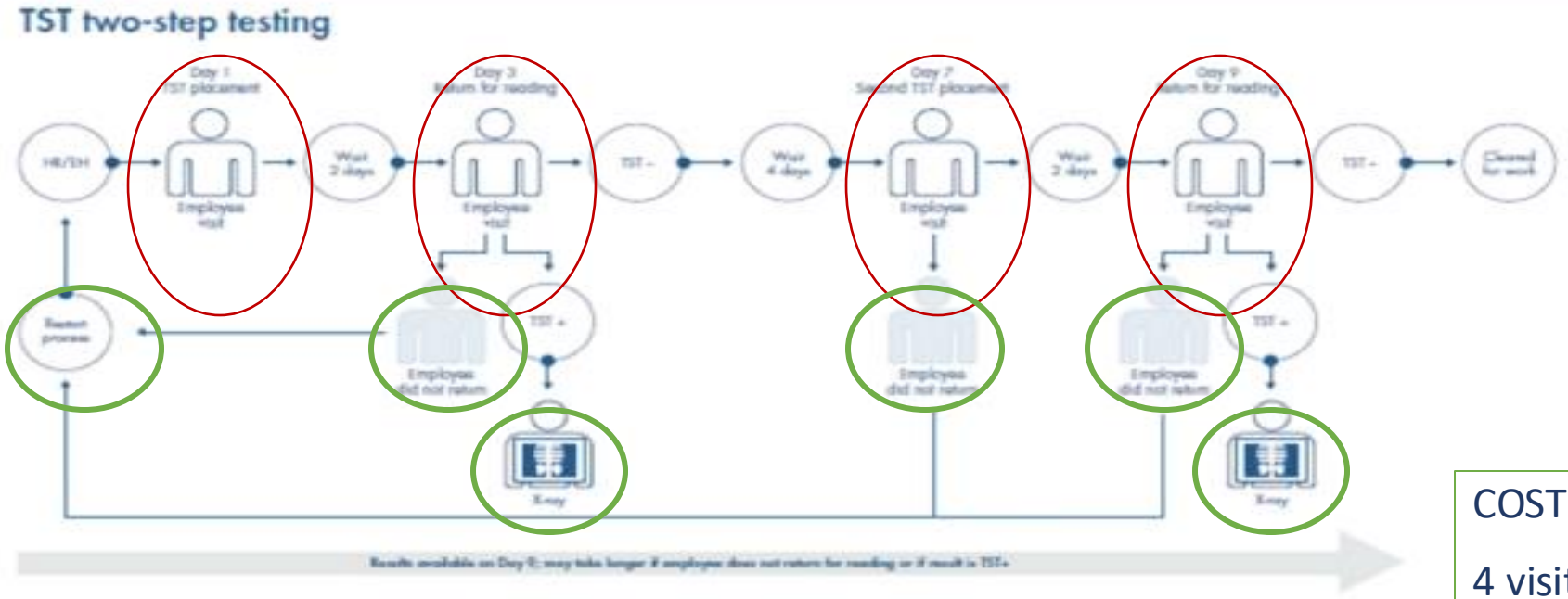
TST

- 2 - 5 visits required
- Injection into skin
- Results affected by BCG
- Results in 2-14 days
- Subjective results
- No control
- Costs unstable
- Manual data recording
- False-positive > 50%

QuantiFERON (QFT)

- **1 visit required**
- **Blood draw (4ml)**
- **Results not affected by BCG**
- **Results in 2-3 days**
- **Objective results**
- **Laboratory control**
- **Costs defined and stable**
- **EHR compatible**
- **False-positive ~3%**

TST: Lean analysis and cost myths



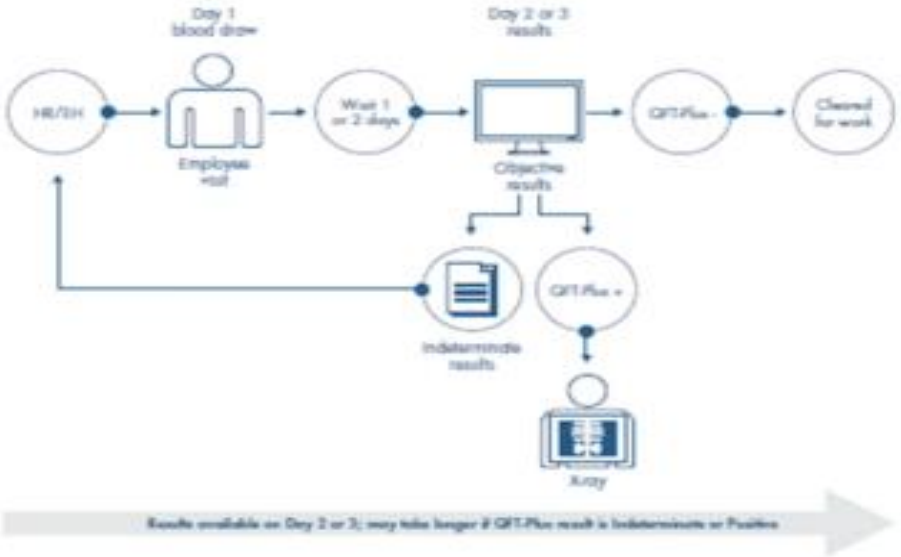


Figure 1. Onboarding new hires with QFT-Plus vs. TST two-step testing. HR – Human Resources; EH – Employee Health; EMR – Electronic Medical Record.

$

COST to UC:

4 visits:

- 4 appts made
- 4 WR vistis
- 4 nursing visits
- 4 med records
- CXR order, record

DEI: babysitters, bridge tolls, leaving work, gas/bus

Price vs. Cost TST vs. IGRA

Study	HC Segment	TST/ Patient	Overall TST Cost	% Saved	$ Saved
(Thanassi) (QFT™)	VHA	$54	$2 M	16.5%	$303 k
Lambert	Public Health	$176 - 264	$93 k - $291 k	---	---
DePerio (QFT™)	Non-BCG HCW in VA	$257	---	6.4%	$16.25/ patient
DePerio (QFT™)	BCG HCW in VA	$264	---	38.4%	$101.19/ patient
Abdalhamid	Nebraska HCWs	$726	$87 k	48.8%	$42,536 overall
Wrighton-Smith (TSPOT™)	Johns Hopkins HCWs	$53 - 72	$1.3 M		

Cost Effectiveness of Interferon Gamma Release Assay for Systematic Tuberculosis Screening of Healthcare Workers in Low Incidence Countries

Kowada, *J Hosp Inf,* Feb 2015

"The main driver for QFT being the most cost-effective strategy … has the highest specificity.

The apparent 1% higher specificity of QFT over T-SPOT increases QALYs gained and decreases the costs by decreasing inappropriate treatment."

"The superior specificity of QFT may be very important to decrease inappropriate treatment of LTBI and TB."

Which Test Do We Use?

(IDSA/CDC/ATS Guidelines 2017)

Likely to be Infected **Low** to **Intermediate** Risk of Progression (TST ≥ 10mM)	**Preferred**: IGRA where available **Acceptable**: IGRA or TST
Unlikely to be Infected (TST > 15mM)	**Testing for LTBI is not recommended** **If necessary:** **Preferred:** IGRA where available. **Acceptable**: Either IGRA OR TST **For serial testing**: **Acceptable**: Either IGRA OR TST Consider repeat or dual testing where a negative result from either would be considered **negative**[2]

Clinical Infectious Diseases

IDSA GUIDELINE

Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children

We recommend performing an IGRA rather than a TST

in individuals >5 years old who:

(1) are likely to be infected with *Mtb*,

(2) have a low or intermediate risk of disease progression,

(3) it has been decided that testing for LTBI is warranted, and

(4) have a history of BCG vaccination or are unlikely to return to have their TST read.

Testing may be obliged by law or credentialing bodies.

If diagnostic testing for LTBI is performed in individuals who are unlikely to be infected with *Mtb*:

We suggest performing an IGRA instead of a TST"

Clin Infect Dis 2017; 64: e1-e33

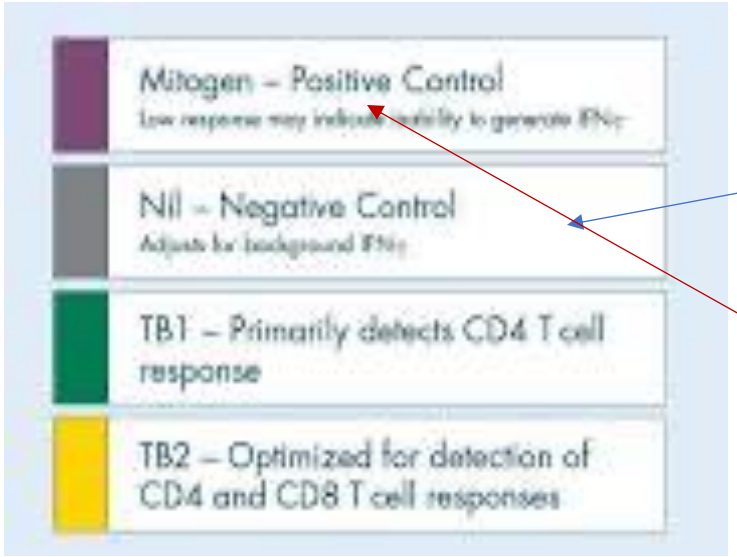
Interferon Gamma Release Assays (indirect): QFT-Plus and TB.TSPOT - Collection

Li+Hep or Na+Hep green-top tube

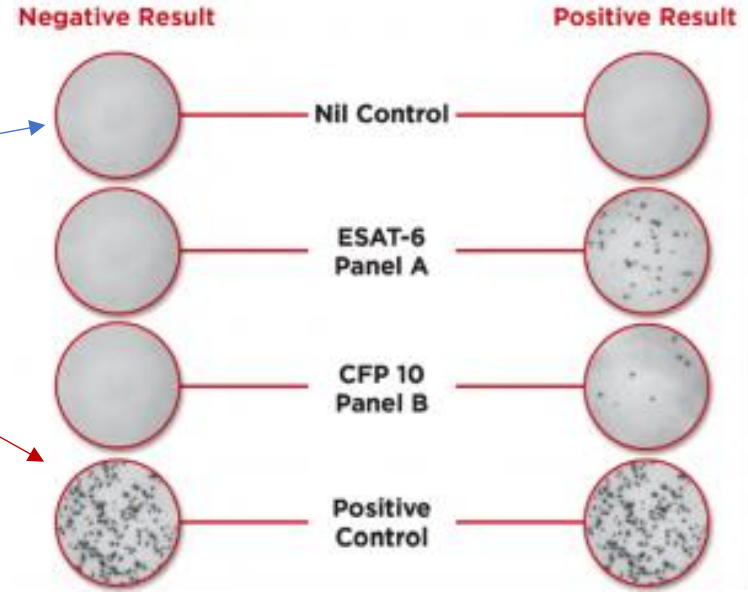
QFT = 4ML

TSPOT = 7-14ml

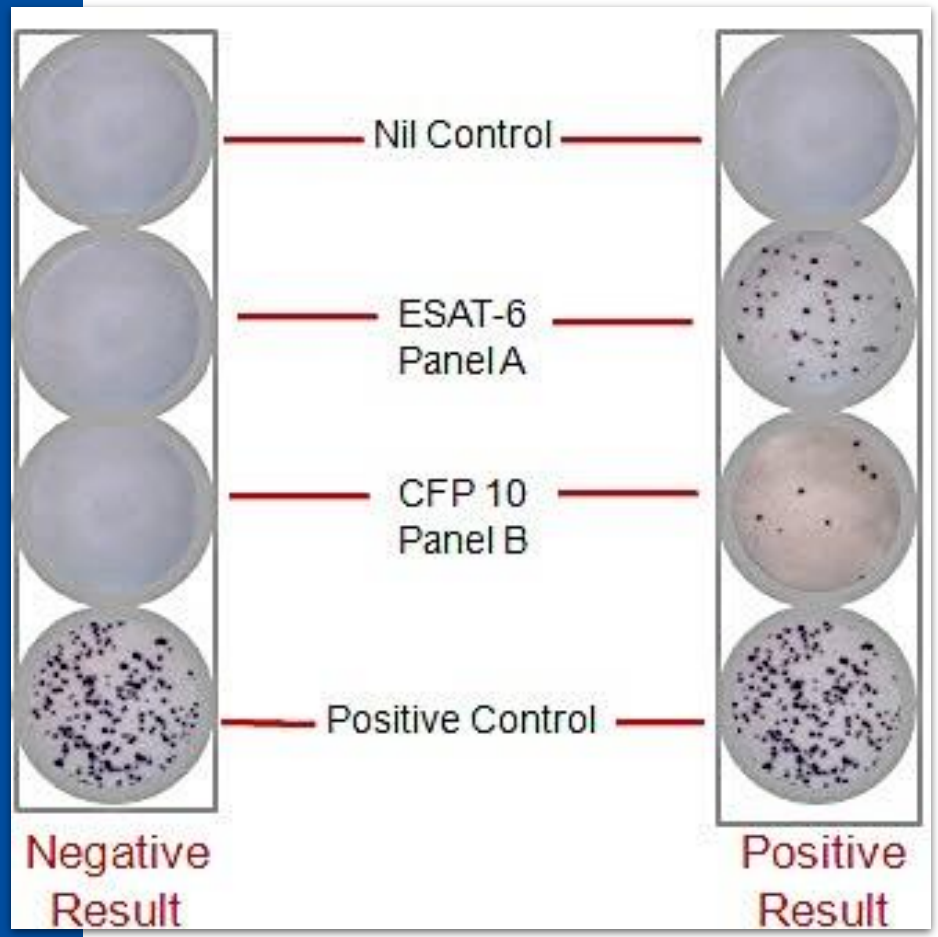
QFT



TSPOT.TB



IGRA



Ficoll Separation Assay

Manual spot count on impregnated filter paper:

- 8 spots = Positive
- 5-7 spots = Borderline
- ≤ 4 spots = Negative
- Invalid

QFT-Plus

Enzyme-Linked Immunoassay (ELISA) or Chemiluminescent Assay (CLIA)

- Nil : Negative Control, empty
- TB1 : Long-chain peptides to stimulate CD4
- TB2 : Short-chain peptides to stimulate CD4 & CD8
- Mitogen : Positive Control, phytohemagluttinin (PHA)

- ➢ 0.35 IU/ml IGRA in TB1 or TB2 = “positive”
- ➢ **INDIRECT ASSAY**

QFT-Plus

Interpretation

- Nil : Background; is subtracted from other tube values
- TB1 : ≥ 0.35 IU/ml = “positive”

- and / or -

- TB2 : ≥ 0.35 IU/ml = “positive”
- Mitogen : Check on immune system

QFT-Plus

Interpretation

Nil : Background; is subtracted from other tube values

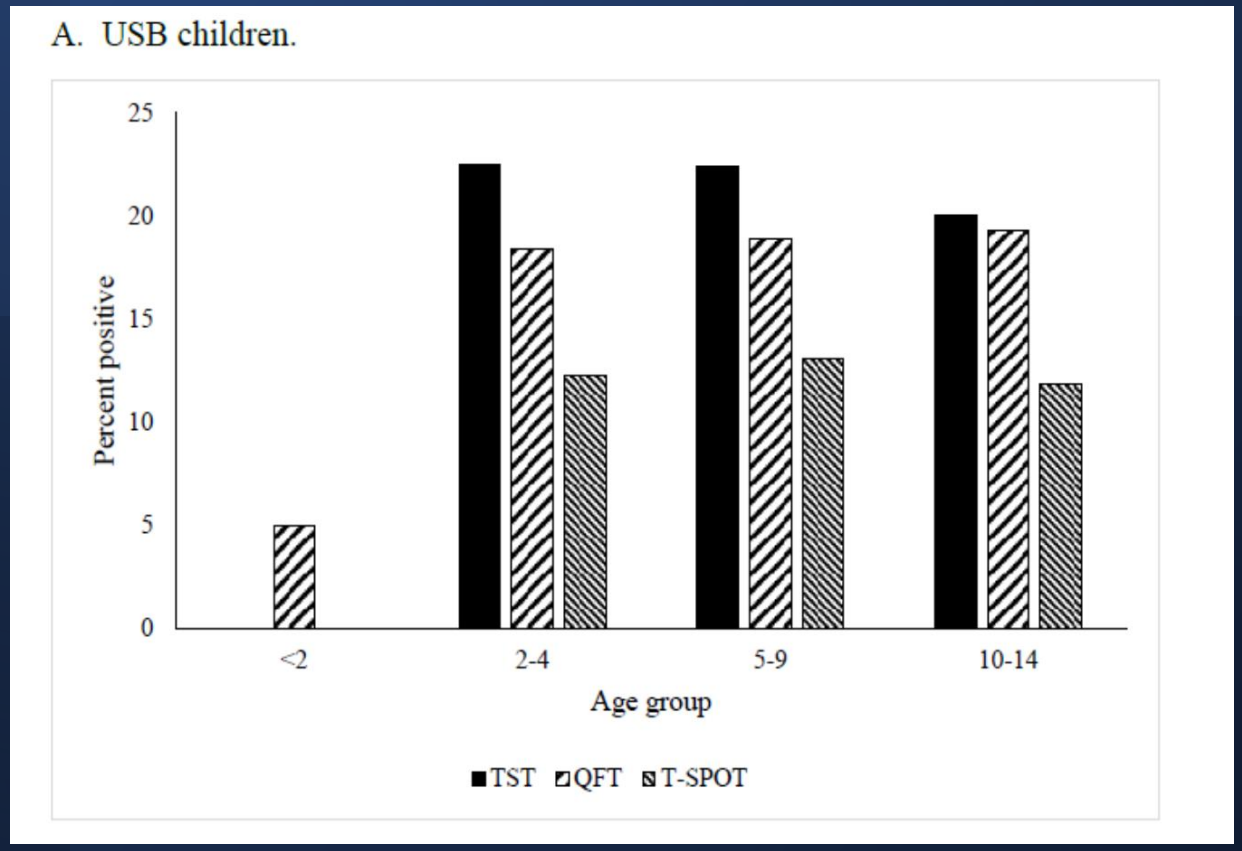
TB1 : < 0.35 IU/ml = “negative”

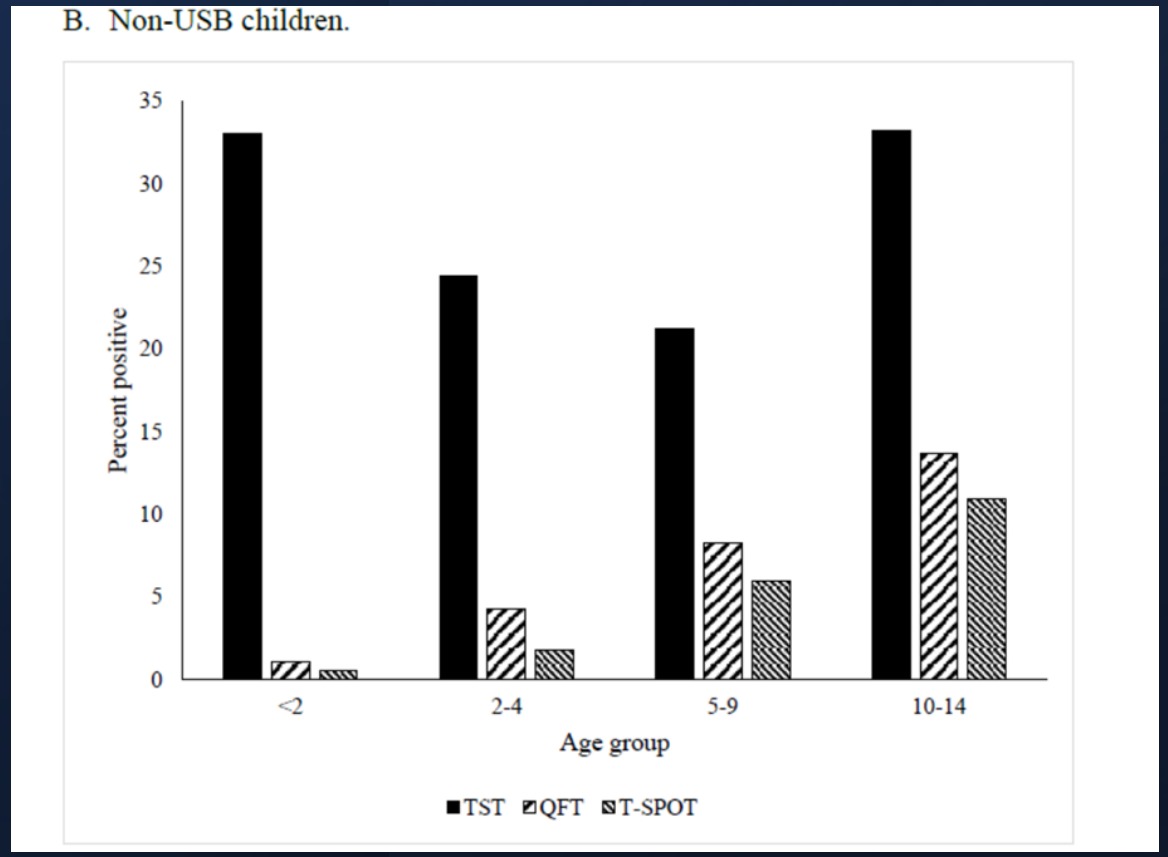
- AND -

TB2 : < 0.35 IU/ml = “negative”

Mitogen : Check on immune system

TBESC: Single Test Comparison





- Majority (69%) with all 3 test results were negative
  - 6.5% with all 3 test results positive

- Single test prevalence
  - 27.3% TST+
  - 9.3% QFT+
  - 6.8% T Spot+

Pediatrics 2020; 145(1):e20191930

TB Epidemiologic Studies Consortium, CDC

Indeterminate and/or invalid results

May 02, 2023

TBESC
TUBERCULOSIS EPIDEMIOLOGIC STUDIES CONSORTIUM-II

N=508	QFT-Plus	T-SPOT.*TB*
Indeterminate results (%)	2 (0.39%) 1 due to high nil 1 due to low mitogen	26 (5.12%) 21 borderline 5 invalid

Venkatappa TK, et al. J Clin Microbiol. 2019 Aug pii: JCM.00985-19. doi: 10.1128/JCM.00985-19.

N=21,846	QFT-GIT	T-SPOT.*TB*
Indeterminate results (%)	0.4%	0.6%

Objective evidence from the CDC:

If package inserts are followed, T-SPOT retesting will be significantly higher than QFT-Plus

Ho CS et al., Tuberculosis Epidemiologic Studies Consortium. Lancet Infect Dis. 2022 Jan;22(1):85-96

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      - ❑ HOW to test for TB?

HOW to stop TB?

A Decision to Test is a Decision to Think.

A Decision to Test is a Decision to Treat.

A Decision to Test is a Decision to Think, and then to Treat.

Task Order 18: Conversions / Reversions with TST and IGRAs

Prospective / longitudinal

4 sites: Denver, Houston, Baltimore, New York City

n = 2,500 health care workers

Design: TST, Elispot and ELISA at 0, 6, 12, 18 months

	TST	Elispot	ELISA
Baseline	5%	6%	5%
Conversions	0.9%	8.3%	6.1%
Reversions	54%	64%	57%

Dorman, Belknap et al. IGRAs and TST for Diagnosis of LTBI in Healthcare Workers; AJCCRM 199: 2014

Acceptance of Treatment: IGRA vs. TST

2,048 QFT results in HCWs

90 QFT positive

INH acceptance using IGRA increased from 11% to 52%

No. (%) of HCWs with LTBI	Before implementation (n = 45)	After implementation (n = 62)	OR (95% CI)	P
Who accepted a prescription for isoniazid	11 (24)	32 (52)	3.3 (1.3–8.0)	.008
Who took isoniazid	5 (11)	32 (52)	8.8 (3.1– 23)	.001

Sahni et al 2009. *Infect. Control Hosp. Epidemiol.*

TB Activation Occurs

The Desert Sun
PART OF THE USA TODAY NETWORK

Loma Linda VA warns veterans of possible

Barrett Newkirk, The Desert Sun 3:44 p.m. PST December 1, 2015

(Photo: Barrett Newkirk/The Desert Sun)

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The veterans hospital in Loma Linda is asking hundreds of patients to get tested for tuberculosis after an employee came down with the potentially fatal disease.

The VA Loma
to patients ea
been exposed to TB while at the Jerry L. Pettis
June 1 and Oct. 27. The letter stated that infect
was available at the hospital.

The notice was sent to 1,727 patients, said hos

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Potential Tuberculosis Exposure at VA Hospital in Palo Alto

The hospital says an employee tested positive for TB in October.

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Employee, Patient Test Positive for Tuberculosis at VA Medical Center in Mather

POSTED 7:18 PM, JUNE 22, 2016, BY SARA ZENDEHNAM, *UPDATED AT 07:17PM, JUNE 22, 2016*

Reactivation's Consequences

54 year-old female

History = born in the Philippines, BCG +, TST +

Work = RN surgical post-op unit

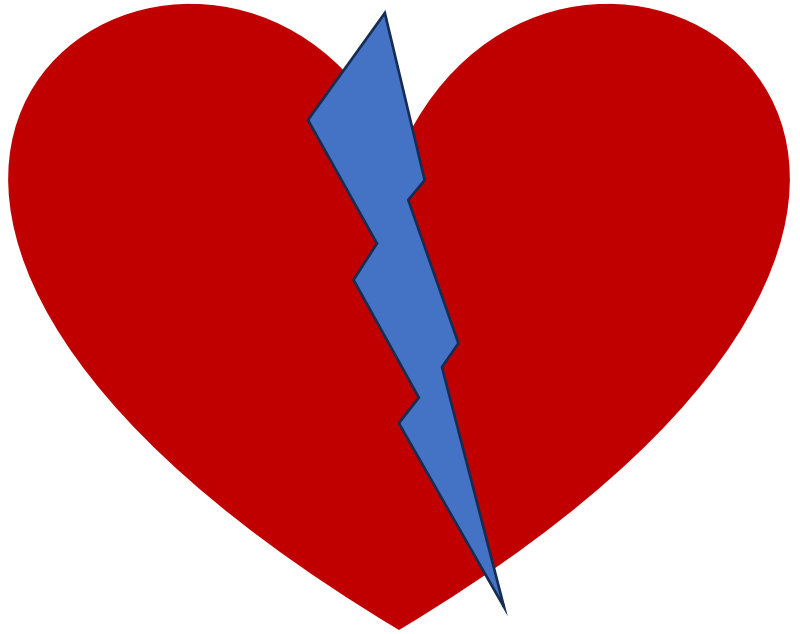
IGRA = positive 2009 – 2016

LTBI treatment = none

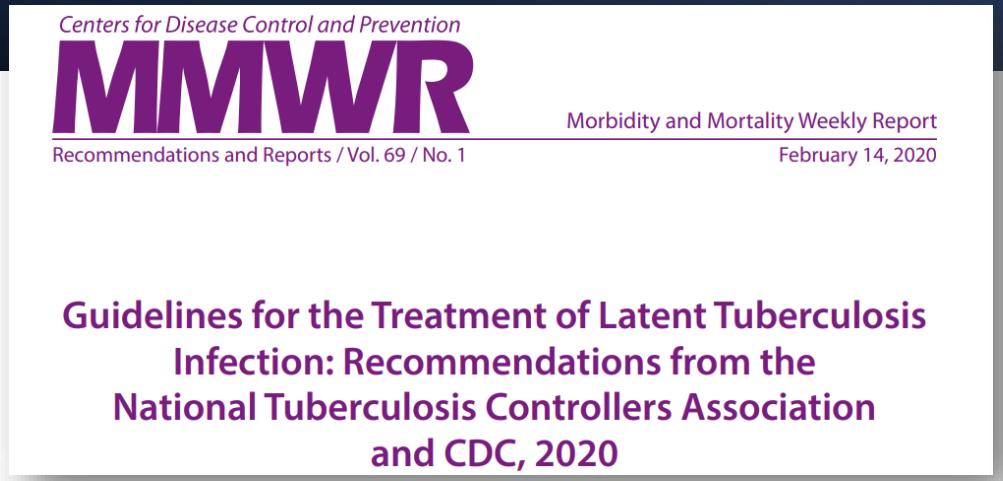
Symptoms = 4 months night sweats, fatigue, palpitations, cough

Diagnoses = menopause; URI c/ antibiotics x 3

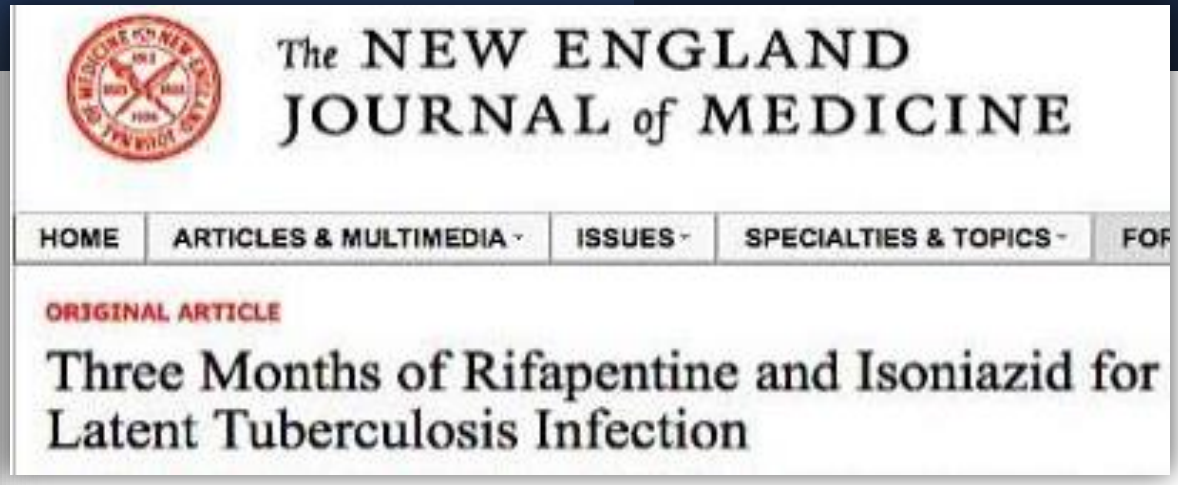
AFB Culture = positive Jan. 1, 2016



TB Disease Prevention


Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 69 / No. 1
February 14, 2020

Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020


The NEW ENGLAND JOURNAL of MEDICINE

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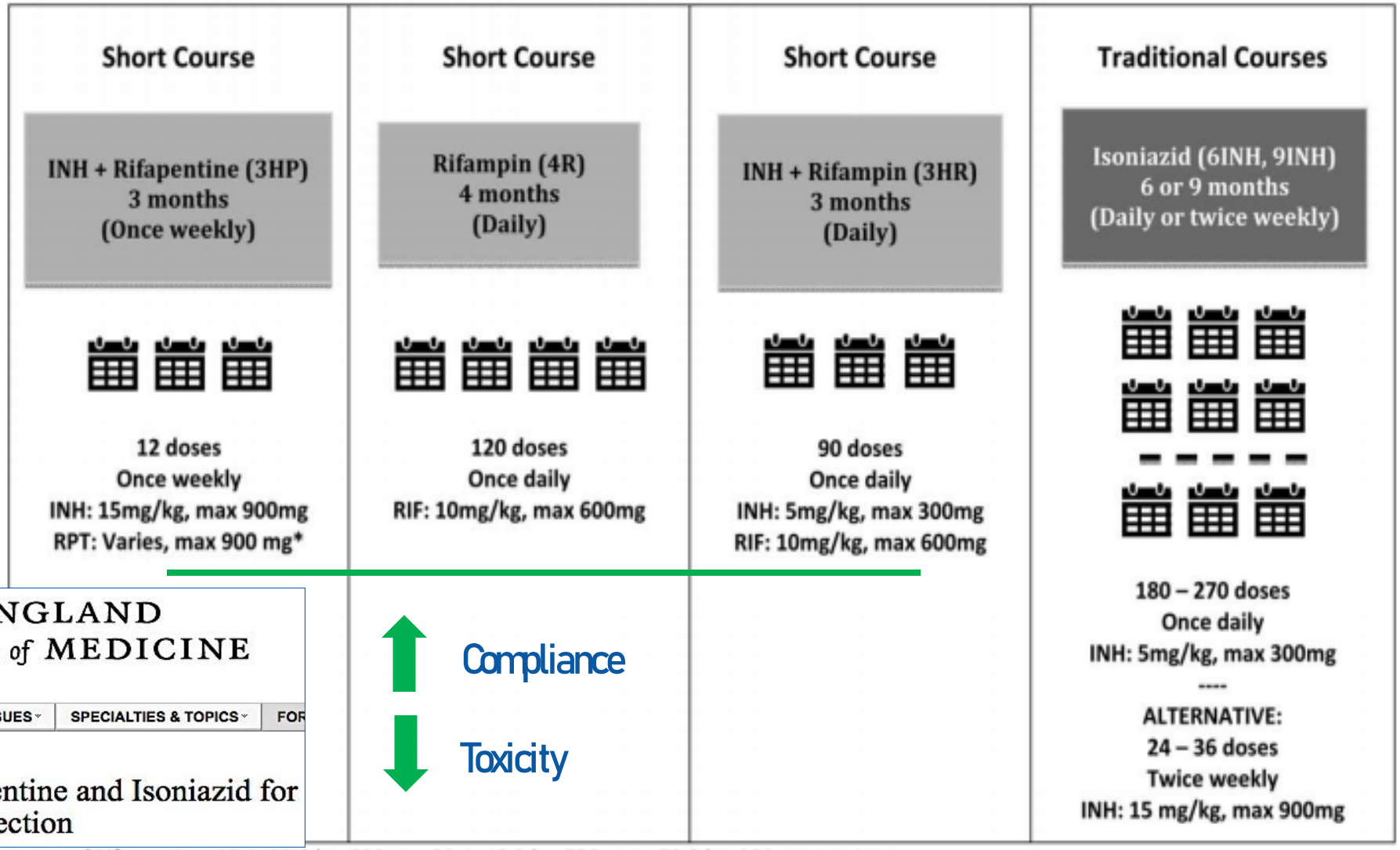
ORIGINAL ARTICLE

Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection

Priority rank	Regimen	Recommendation
Preferred	**3HP once weekly (12)**	**Strong**
Preferred	**4R daily**	**Strong**
Preferred	3HR daily	Conditional
Alternative	6H daily	Strong
Alternative	9H daily	Conditional

All HCP w/ LTBI should be encouraged to complete LTBI treatment unless contraindicated

H = isoniazid, P = rifapentine, R = rifampin



*Rifapentine: 25.1–32.0 kg, 600 mg; 32.1–49.9 kg, 750 mg; ≥50.0 kg, 900 mg maximum.

FIGURE 1. LTBI treatment options quick-reference guide, 2020. *Rifapentine: 25.1 to 32.0 kg, 600 mg; 32.1 to 49.9 kg, 750 mg; more than or equal to 50.0 kg, 900 mg maximum. See Table 4 for list of abbreviation meanings.

NTCA PROVIDER GUIDANCE:

Using the Isoniazid/Rifapentine Regimen to Treat Latent Tuberculosis Infection (LTBI)

IMPORTANT NOTE: *Rule out* **active** *TB disease in all persons prior to initiating treatment for LTBI.*

What is the 12-dose isoniazid/rifapentine regimen (aka "3HP")?

The 3HP regimen consists of 12 once-weekly doses of isoniazid (H) and rifapentine (Priftin®) (P). It provides a safe and effective treatment for LTBI. Rifapentine is a member of the rifamycin class and has many of the same drug-to-drug interactions and side effects as other rifamycins.

What are the advantages of 3HP?

- The 12-dose regimen reduces treatment time by two-thirds (9 months to 3 months) compared to isoniazid.
- Shorter treatment regimens have been shown to have higher rates of completion.
- Weekly dosing offers convenience for many individuals.
- There are lower rates of hepatotoxicity with 3HP than with daily doses of isoniazid.

What are the doses?

Drug*	Weekly Dosage	Maximum dose
Isoniazid	15 mg/kg rounded to nearest 50/100mg in patients ≥12 years	900 mg
	25 mg/kg rounded to the nearest 50/100 mg in patients 2-11 years	
Rifapentine (Priftin®)	10.0 – 14.0 kg = 300 mg	900 mg
	14.1 – 25.0 kg = 450 mg	
	25.1 – 32.0 kg = 600 mg	
	32.1 – 49.9 kg = 750 mg	

**Tablets can be crushed and administered with semi-solid food for those unable to swallow pills.*

Who is not recommended for treatment with 3HP?

- Children under 2 years of age
- Patients with potential for severe or unmanageable drug interactions, including people living with HIV or AIDS on certain antiretroviral therapy regimens
- Persons presumed infected with *M. tuberculosis* that is resistant to isoniazid and/or rifampin
- Pregnant women or women planning to become pregnant during treatment
- Patients who had prior adverse events or hypersensitivity to isoniazid or rifampin or rifapentine

ALERTS:

- Do not confuse **rifampin/rifabutin** with **rifapentine** (Priftin®).
- Patients who weigh ≥ 50kg should take 6 tablets of rifapentine and 3 tablets of isoniazid for a total of 9 pills at a time.
- Some TB experts recommend prescribing vitamin B6 with this regimen due to concerns regarding isoniazid-induced peripheral neuropathy.
- If 3HP is self-administered, it is imperative that the patient understands the directions to take all of the pills in the weekly dose at the same time. **The patient should not split doses.**
- If symptoms suggestive of a systemic drug reaction occur, the patient should stop 3HP while the cause is determined.
- Doses should be given at least 72 hours apart, and there should be no more than 3 doses in 10 days, based on the clinical trial design.
- Different from other rifamycins, rifapentine can be taken with food to increase absorption.
- Maintain adequate hydration.

What is completion of therapy?

- Completion of therapy is 12 doses taken in 16 weeks.

NOTE: *Near the end of the treatment period, the TB clinician may consider completion of therapy for LTBI with only 11 once-weekly doses within a 16-week period under rare and insurmountable circumstances in which the patient cannot take an additional (12th) dose.*

Does this regimen have to be administered via directly observed therapy (DOT)?

- DOT ensures the highest quality and safety of treatment and confirms that treatment is completed.
- The healthcare provider should choose the mode of administration, i.e., either DOT versus self-administered therapy (SAT) based on local practice and individual patient attributes and preferences. It is critically important for the clinician to assess the patient's ability to understand risks associated with treatment and procedures to follow if a side effect is suspected, as well as the risk for progression to severe forms of TB disease.

How frequently were toxicities observed with 3HP?

Hypersensitivity *including flu-like symptoms, headaches, hypotension, near-syncope/syncope*	3.8%
Rash	0.8%
Hepatotoxicity	0.4%
Thrombocytopenia	infrequent
Other toxicities	3.2%

NOTE: *Refer to the product insert for a full list of potential side effects. Most side effects occur in the first 4 weeks, although they can continue to occur throughout treatment.*

What can an adverse event include and how should I respond?

	Adverse Event		Response
Moderate to Severe	• Hypersensitivity • Hypotension • Dizziness or nausea/vomiting *(these can be prodrome to syncope)* • Syncope/fainting • Hospitalization • Life-threatening event • Flu-like syndrome *(e.g., fever, chills, headaches, dizziness, muscular pain/aches)* • Thrombocytopenia	• Shortness of breath • Wheezing • Acute bronchospasm • Urticaria • Petechiae • Purpura • Conjunctivitis • Angioedema • Shock	**Discontinue treatment** **Conduct prompt clinical assessment with appropriate lab monitoring**
Mild to Moderate	• Rash • Fever • Pruritus		**Continue to monitor the patient closely with a low threshold for discontinuing treatment**

How do I report an adverse event regarding 3HP?

- Report all adverse events to FDA MedWatch at **www.fda.gov/Safety/MedWatch/default.htm**, **1-888-INFO-FDA (1-888-463-6332)**
- Report adverse events leading to death or hospitalization to your health department. Health departments should report these adverse events to the Centers for Disease Control and Prevention at **1-800-232-4636** or **LTBIdrugevents@cdc.gov**

Are there drug-drug interactions?

Yes, there are common interactions for isoniazid and rifapentine:

- **Isoniazid** increases blood levels of phenytoin and disulfiram.
- **Rifapentine** decreases blood levels of oral or implanted hormonal contraceptives, warfarin, sulfonylureas, methadone, steroids, some cardiac medications, and certain antiretroviral therapy regimens may have serious drug interactions.

NOTE: *Use a drug interactions checker and/or refer to the product insert for a full list of drug-drug interactions.*

Whom do I contact with questions or concerns?

- Contact your local or state health department.
- NTCA has an online directory of TB programs at **http://www.tbcontrollers.org/community/statecityterritory/**

What type of monitoring do I need to do?

- Evaluate the patient at a monthly visit to identify adverse events and to assess treatment adherence.
- Some experts recommend baseline complete blood count (CBC) due to a possible adverse reaction decreasing the white blood cell count and platelet counts and comprehensive metabolic panel (CMP). Hepatitis panel may also be obtained.
- Baseline hepatic chemistry is recommended for patients with these specific conditions:
  - HIV infection
  - Liver disorders
  - In the postpartum period (≤ 3 months after delivery)
  - Regular alcohol or injection drug use

  In addition, consider baseline hepatic chemistry for older persons and for persons taking medications for chronic medical conditions.
- If baseline hepatic chemistry testing is abnormal, determine the risk vs. benefit of treatment. If a decision is made to treat, continue with subsequent hepatic chemistry testing until the patient is determined to be stable.
- If baseline hepatic chemistry is within normal limits and the treatment is self-administered, some experts recommend additional laboratory monitoring monthly to ensure that the patient does not develop hepatotoxicity.
- When or after the final dose is taken, conduct a final visit with the patient to monitor for any adverse events.

NTCA PROVIDER GUIDANCE:
USING THE ISONIAZID/RIFAPENTINE REGIMEN TO TREAT LATENT TUBERCULOSIS INFECTION (LTBI)

NOVEMBER 2018; REVISED, APRIL 2019

For references, go to **http://www.tbcontrollers.org/resources/3hp**

3HP for LTBI: 12 Days of Antibiotics!

Appendix 4. Latent Tuberculosis Infection Treatment Declination or Postponement of Treatment

I understand that:

- I have a confirmed positive tuberculosis (TB) test skin test or blood test (such as QuantiFERON® or TSpot®.*TB*), and a chest X ray that is negative for active TB disease. These show evidence that I was exposed to TB and that I have latent TB infection (LTBI).
- This LTBI is not currently communicable to others.
- LTBI can turn into active TB disease in the future, where it may become communicable to family members, patients, colleagues and the general public. The treatment of active TB disease requires multiple medications and, if untreated, can be fatal.
- Treatment of my LTBI with anti-TB medications will greatly reduce the risk of my LTBI ever becoming active TB.
- If I develop symptoms that may be active TB disease, I must immediately refrain from work and report these symptoms to a physician knowledgeable in TB diagnosis and treatment.
    - These symptoms include prolonged (>3 weeks) cough or bloody cough, drenching night sweats, unexplained weight loss and/or unexplained fevers.
- I have been encouraged to get treated for LTBI and have been given treatment information.
- I understand that by declining or postponing this treatment I continue to be at risk of developing active TB disease.

If I want to be treated for LTBI in the future, I can receive that treatment.

_____ _____

Employee Signature Date

_____ _____

Employee Printed Name Department and Location

Treatment declination option

Concluding General Principles

- The **reservoir** of TB disease, fatal, is in the untreated latent TB WORKING population
- At working age, they are generally healthy, can be identified and treated to prevent disease
- USE IGRA / QuantiFERON to diagnose latent TB
  - It's more accurate and more efficient than TST by 130 years
  - Cost, efficiency, DEI, medical accuracy, treatment acceptance
- TREAT them with short-course therapy
- EDUCATE the employers to UPDATE their FORMS to USE IGRA
- No test is 100% sensitive or 100% specific

❖ *ADVOCATING for that company and those workers to keep them safe*

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Questions?

Please submit your question in the Q&A box

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Thank you

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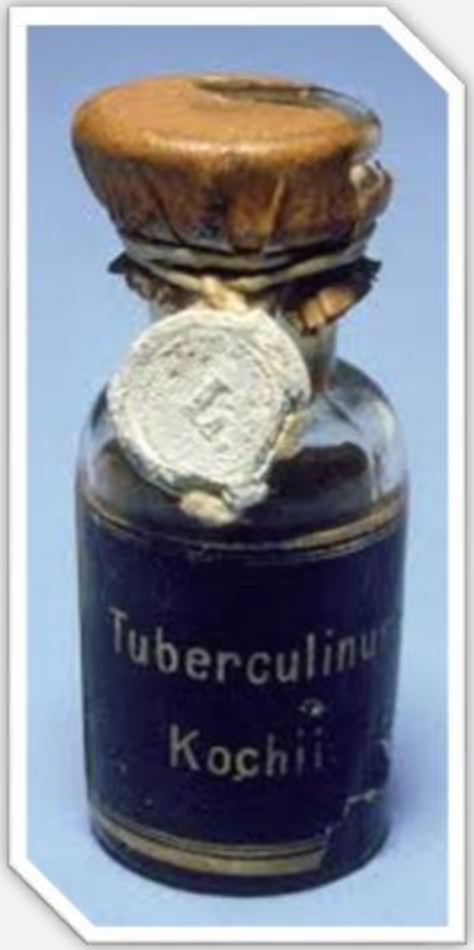
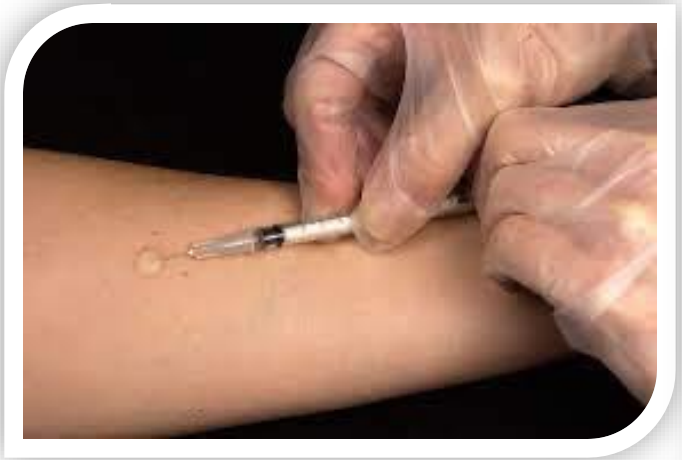
Extras

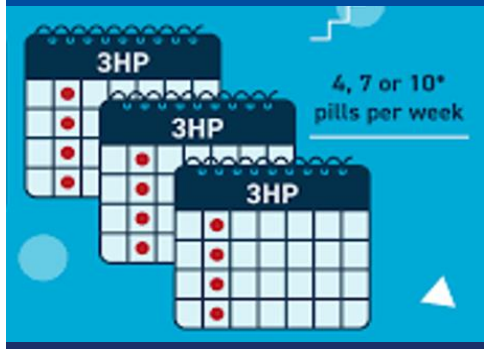
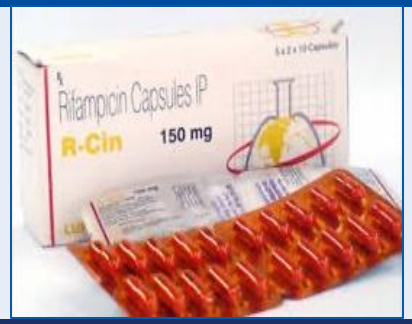
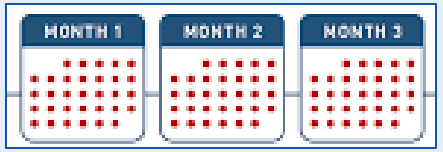
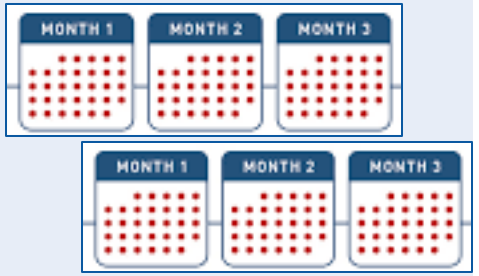
TB Tests



TST: Tuberculin Skin Test



Test-to-Treat!
Short-course regimens are here

	3HP	4RIF	3HR	6INH
				
	Once/wk x 12 weeks	Daily for 4 months	Daily for 3 months	Daily for 6 months
Medications	isoniazid (INH) + rifaPentine (weight-based dosing)	RIFampin	isoniazid (INH) + Rifampin	IsoNazid
Advantages	↑ Compliance ↓ Toxicity	↑ Compliance ↓ Toxicity	↑ Compliance ↓ Toxicity	↓ Compliance ↑ Toxicity

Retesting Recommendations

These findings have been incorporated into national guidance documents:

Pulmonary Medicine: **2012 December 30**

Delineating a Retesting Zone Using Receiver Operating Characteristic Analysis on Serial QuantiFERON Tuberculosis Test Results in US Healthcare Workers

Wendy Thanassi, Art Noda, Beatriz Hernandez, Jeffery Newell, Paul Terpeluk, David Marder and Jerome Yesavage

Journal of Occupational and Environmental Medicine: **July 2013**

ACOEM GUIDANCE DOCUMENT:

Protecting Health Care Workers from Tuberculosis, 2013

ACOEM Occupational Health Section Task Force on Tuberculosis and Health Care Workers

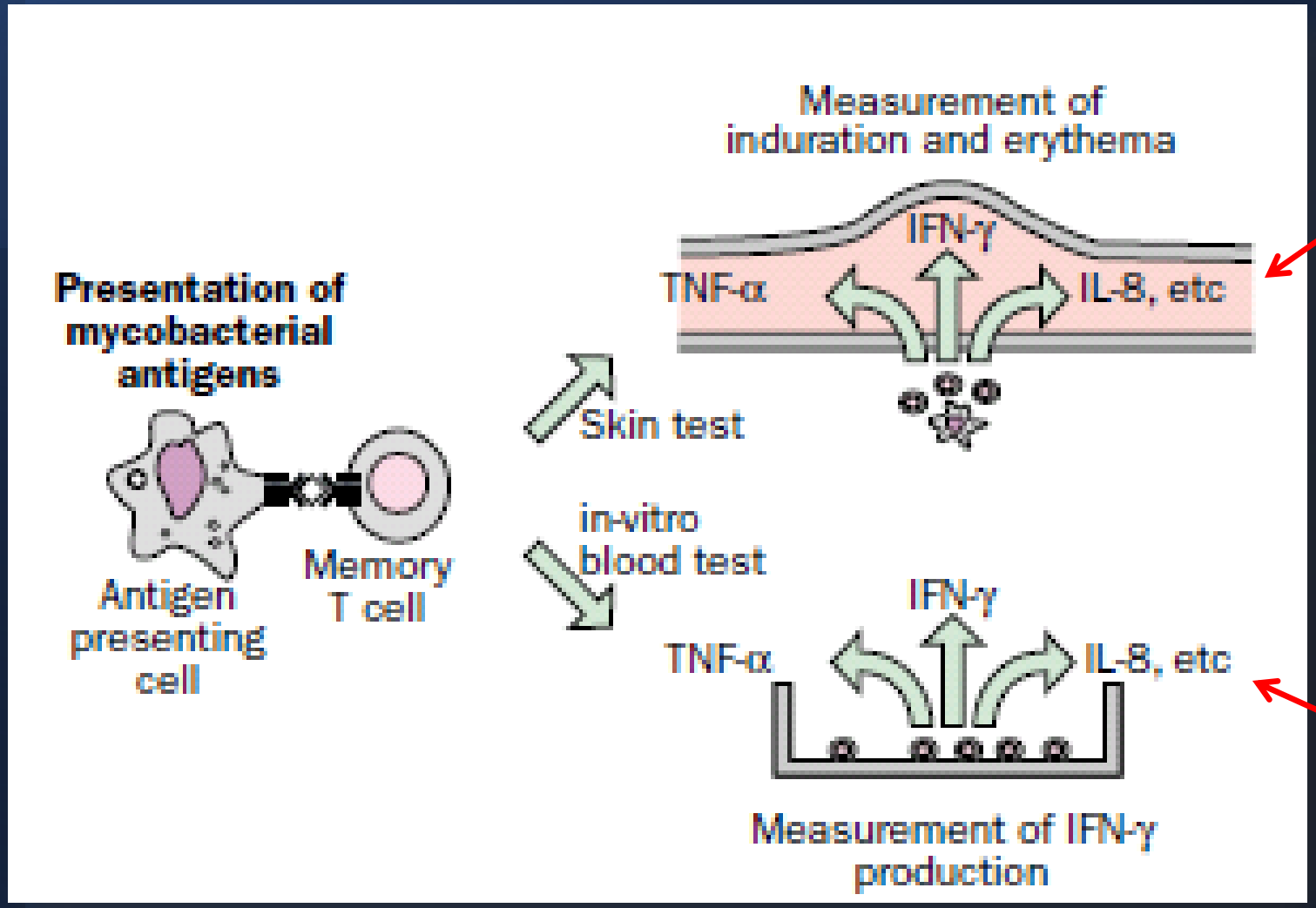
Short course LTBI treatment is less liver toxic and results in better compliance

12-dose Three months of rifapentine and isoniazid (DOT) vs INH 9 months (self-adminstered)

Duration	Disease rate (33 mo)	Compliance	liver toxicity
INH-Rifapentine	7/3986	82%	0.4%
INH 9 mo	15/3745	69%	2.7%,

Sterling et al, NEJM 2011 Dec 8;365(23):2155-66N=28,000

TST (1880) and IGRA (2005)*



Crude mixture of proteins

Highly specific antigens

Lancet 2000; 356: 1099-1104f

Comparative Performance: TST, QFT-GIT, and TSPOT.*TB*

Sensitivity (in active TB) meta-analyses	QFT	T-SPOT.*TB* **	TST
Sester et al. ERJ. 2011	80%	81%	65%
Diel et al. Chest. 2010 - Developed country	84%	89%	71.5%

Specificity (in low risk) meta-analyses	QFT	T-SPOT.*TB* **	TST
US CDC Guidelines. 2010	99%	88%	85-86%
Diel et al. Chest. 2010	99.2%	86%	ND

Note:T-SPOT positive result based on non-US cut-point of 6 spots and used blood <8 hours old

- Both IGRAs more sensitive that TST
- QFT: similar to slightly less sensitivity than **T-SPOT.*TB*** using 6-spot European cut point
- QFT: higher specificity than **T-SPOT.*TB*** using a 6-spot European cut point
- FDA rationale for 8-spot cut point: Low specificity of **T-SPOT.*TB*** **using** 6-spot cut point