TB Screening and Diagnosis

Douglas B. Hornick, MD

Pulmonologist w/ Infectious Attitude
Division of Pulm/Crit Care/Occ Med
UI Carver College of Medicine

Disclosures: None

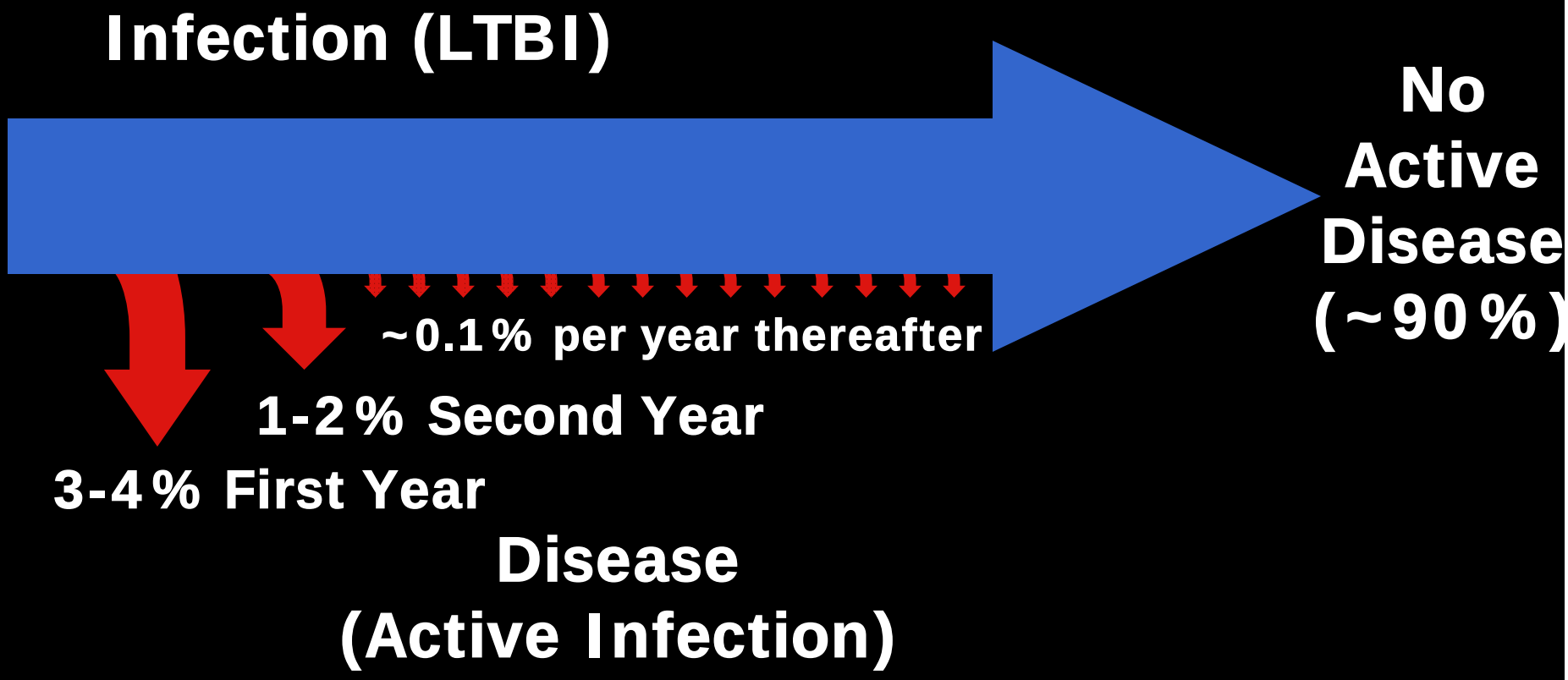
Objectives

- Rural (US) TB epidemiology indicates treating LTBI is an appropriate strategy
- Describe Screening for LTBI: TST and IGRA
- Describe current treatment for LTBI
- Describe monitoring recommendations

TB Nomenclature

- Latent TB Infection (~90% TB infections):
  - Positive TST (or IGRA eg, QFT-G)
  - No symptoms
  - Negative or chronic CXR changes
  - Can not transmit disease to others.
- Active TB Infection (~10% TB infections):
  - TST (or IGRA) may be positive
  - Symptoms present
  - CXR changes & sputum smear positive in most cases
  - Disease transmission to others
- Treatment for both latent and active infections
- Avoid terms: Prophylaxis, Preventive therapy

TB Pathogenesis
Progression to Disease



Epidemiology of Tuberculosis
TB in Foreign-Born Immigrants to US

- Proportion of TB cases foreign-born increased from <25% to 57% (1986-2006)
- US-born TB cases decreased by 45% (1993-2006)
- ~70% MDR TB occur among Foreign-born
  - Anticipate XDR TB & TDR TB
- SE Asians, Sub-Saharan Africans, & Latin Americans
- Concentrated in NY, NJ, Ca, Fl, IL, Tx
- Active cases most often arise from prior infection
- ~55% occur within 5 yrs of immigration

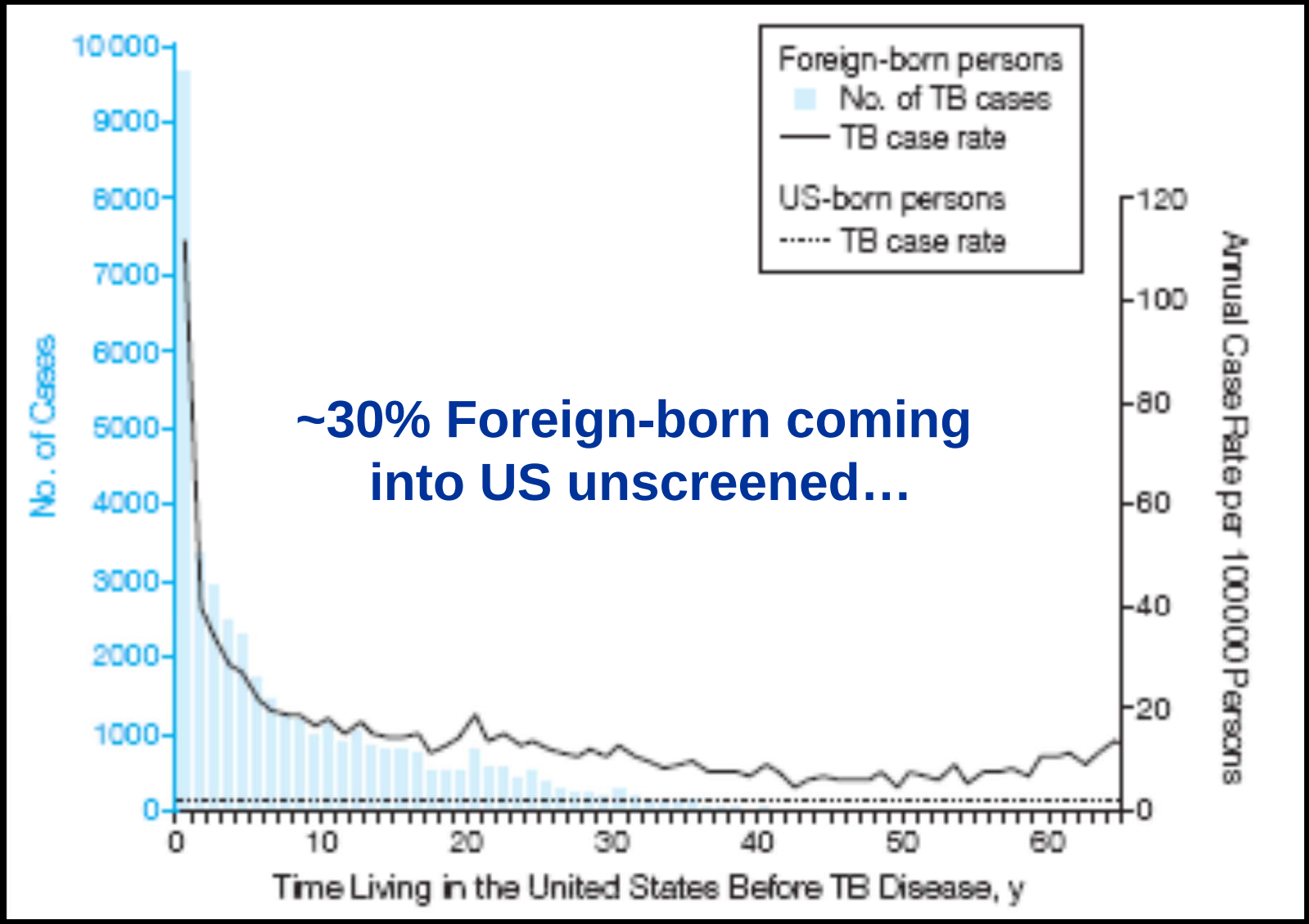
  ≤ 2 yrs in US 75/100,000

  > 2 yrs in US 16/100,000

CDC; Cain et al: *JAMA* 2008

Foreign-Born ⇒ US

TB Cases & Case Rates vs. Years in US



Cain et al: *JAMA* 2008

Refugee & Immigrant TB Screening

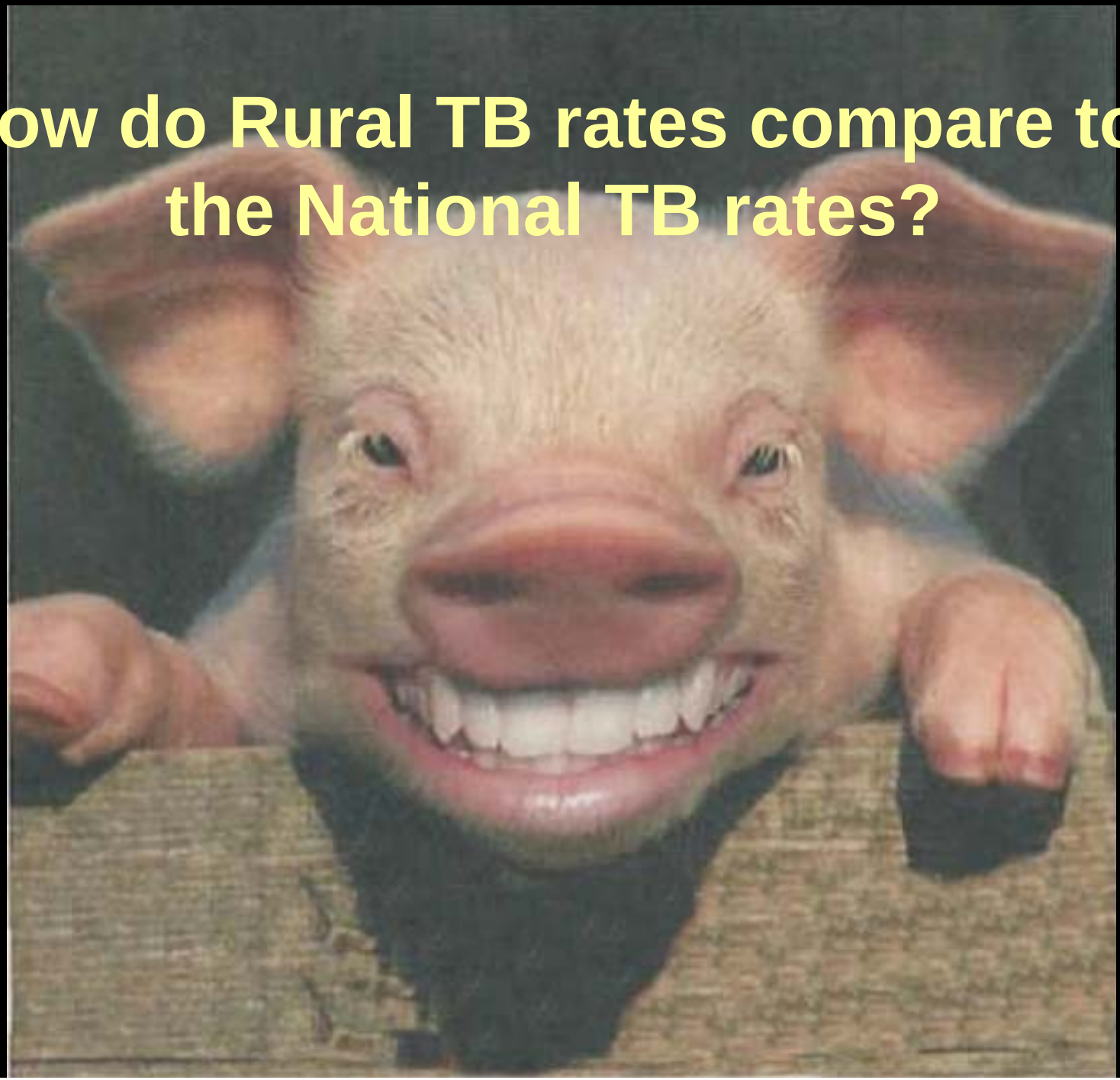
- Within Country of Origin
  - Adults: Evaluated for Active TB only
  - Children (<15 yrs) & TB contacts screened (TST) in some countries but no LTBI Rx
- Arrival within US
  - TB Suspects are expected to f/u w/ local health dept (not mandated)
  - Applicants for adjustment of status evaluated for LTBI (Rx not mandated)
- Not evaluated…Estimates ~30%
  - Visitors, Temp Workers, Undocumented
  - Student visa

Immigration process doesn't deal with LTBI for you…

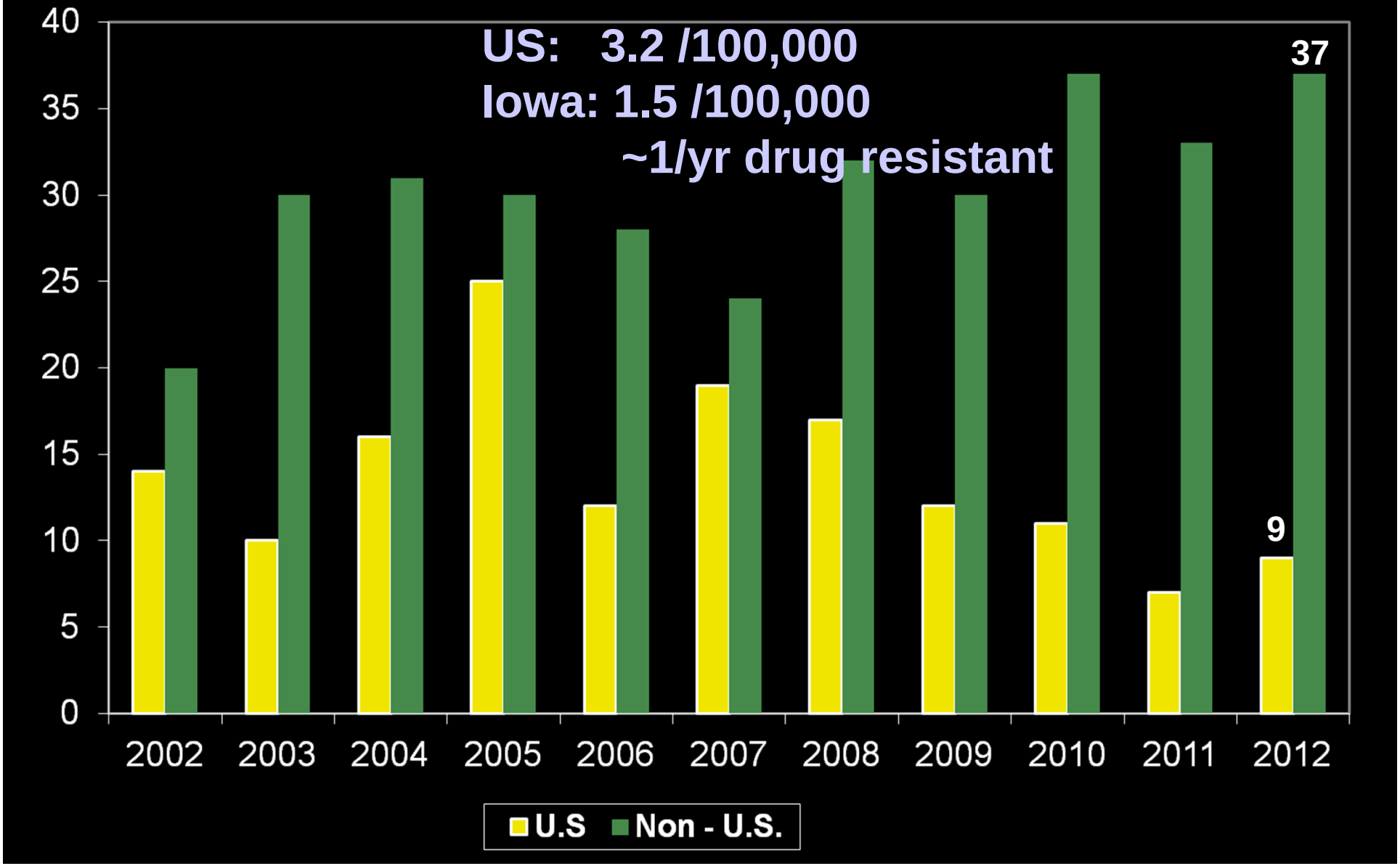
“Tuberculosis is a social disease with medical implications”

–Sir William Osler

How do Rural TB rates compare to the National TB rates?



US *vs*. Foreign-Born TB Cases – Iowa 2012



Focus of TB Control in the US: Targeted Testing & Rx for LTBI

- Few cases due to transmission from other active cases (↓ HIV related cases)
- High rates of TB among foreign-born immigrants to US (including rural locales) from high incident countries
- "Targeted tuberculin testing" is the theme of the LTBI guidelines
- One of the main targets must be the foreign-born immigrants from high incident countries

Relative TB Risk

Risk Factor	Risk Estimate (vs. control w/ +TST)
Advanced HIV	**9.9**
Anti-TNF Rx	**7.9**
Old, healed TB	**5.2**
Diabetes mellitus	3.1
Tobacco abuse	2.7
Chronic Renal Failure	2.4
Silicosis	1.7
Underweight (10% < IBW)	1.6
Gastrectomy	1.4

Horsburgh. *NEJM* 2004; Gossec. *Ann Rheum Dis* 2009
Jeon. *PLoS Med* 2008; Lin. *PLoS Med* 2007

Targeted TB Testing
Decision to Test = Decision to Treat

- Patients at highest risk for progression to active TB
- Patients with medical conditions that increase risk for active TB
- Patients in whom active TB is more prevalent

Targeted TB Testing
Decision to Test = Decision to Treat

- **Patients at highest risk for progression to active TB**
- Patients with medical conditions that increase risk for active TB
- Patients in whom active TB is more prevalent

Targeted TB Testing
Decision to Test = Decision to Treat

Patients at highest risk for progression to active TB

- HIV infection, or risk factors for HIV infection
- Receiving TNFα antagonist for RA or Crohn's
- Fibrotic lesion on CXR c/w prior pulmonary TB
- Close contact of persons with infectious TB (e.g, pulmonary, laryngeal TB)
- New TB infection (TST conversion within prior 2 years)
- IV drug abuser (HIV negative)

Targeted TB Testing
Decision to Test = Decision to Treat

- Patients at highest risk for progression to active TB
- **Patients with medical conditions that increase risk for active TB**
- Patients in whom active TB is more prevalent

Targeted TB Testing
Decision to Test = Decision to Treat
Medical conditions ↑ risk for progression to active TB

- **Diabetes mellitus**
- Tobacco abuse (NEW)
- Silicosis
- Jejunoilieal bypass surgery or gastrectomy
- Solid organ transplant (e.g. renal, heart)
- Chronic renal failure/hemodialysis
- Head/neck carcinoma
- Hematologic malignancies (e.g. leukemia, Hodgkin's)
- Immunosuppressed, particularly steroid treatment (≥15 mg/day, ≥ 1 month)
- Substantial weight loss: >10% ideal body weight

Targeted TB Testing
Decision to Test = Decision to Treat

- Patients at highest risk for progression to active TB
- Patients with non-HIV medical conditions that increase risk for active TB
- **Patients in whom active TB is more prevalent**

Targeted Skin Testing
Decision to Test = Decision to Treat
Patients in whom active TB is more prevalent

- Recent arrivals (< 5 years) from high TB prevalence countries (Africa, SE Asia, Pacific Isles, Latino, E. Europe, Russia)

- Resident or employee of high-risk congregate settings: prisons/jails, nursing homes/other long term facilities, hospitals/other health care facilities, residential facilities for AIDS patients, and homeless shelters

- Mycobacteriology lab workers

Case S. B.

- 56 yo female
- Asymptomatic
- TST+ (estranged husband had TB 20 years ago)
- On no drugs, no HIV risk factors, no EtOH
- Chest x-ray unremarkable

What is the diagnosis?

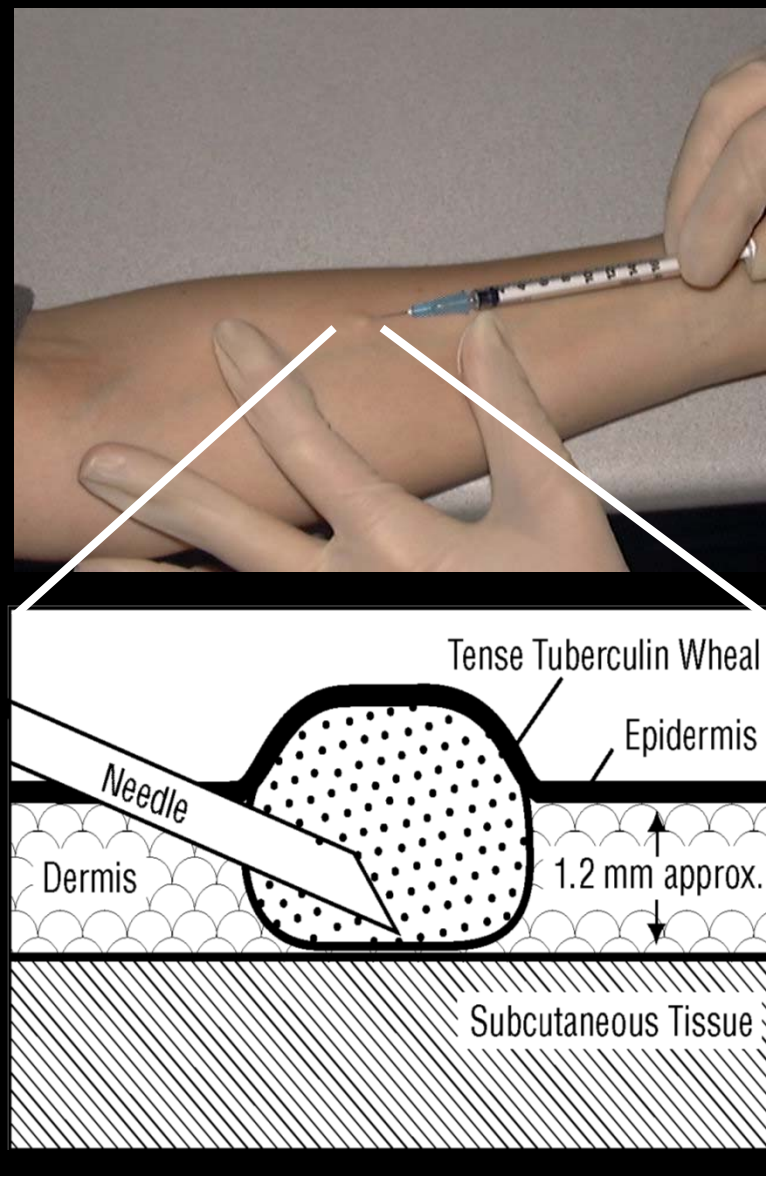
Latent TB Infection (LTBI)
New technology replacing old…

Mantoux Tuberculin Skin Test (TST)

- Standard (old) method of skin testing for *M. tuberculosis* infection
- Produces delayed-type hypersensitivity reaction
- TST is useful for..
  - Detecting LTBI
  - Contact investigation: Determining how many people in a group are infected
  - Evaluating persons who have symptoms of active TB

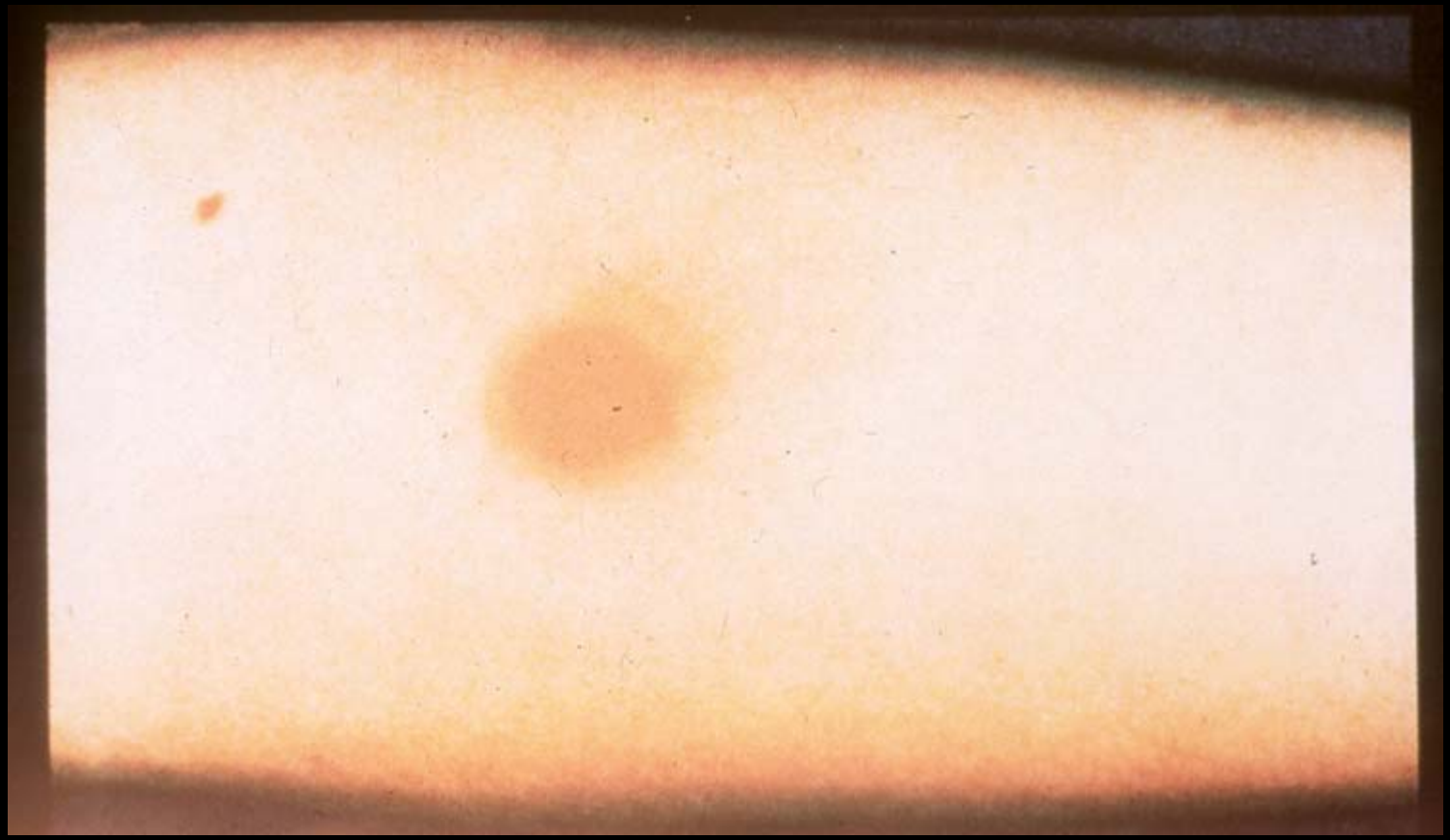
Administering the TST

- Inject 0.1 ml of 5 TU PPD tuberculin solution intradermally on volar surface of lower arm using a 27-gauge needle
- Produce a wheal 6 to 10 mm in diameter



Low (Old) Tech…TST

Delayed-type Hypersensitivity Reaction @ 48-72 hrs



- Positive: 18 mm **Induration**
- A positive test may be measured up to 7 days out
- A negative reaction can be read accurately @ 48-72 hrs

Reading a TST

- Measure induration, not erythema by 48 to 72 hours
- Record induration size in millimeters, in addition to interpretation (“negative” or “positive”)
- Ensure trained health care professional measures & interprets the TST
- Educate patient & family about the significance of a positive test

TST Interpretation

Positive classification based on pre-test probability of TB:

- ≥ 5 mm = positive
  - HIV positive
  - Household or close contact to patient with infectious, active TB
  - CXR consistent with old/healed TB
  - Organ transplant or other immunosuppressed patient
- ≥ 10 mm = positive
  - Foreign born (e.g. Africa, SE Asia, Hispanic, India, China, E Europe)
  - IV drug abusers
  - Residents or employee of high risk congregate setting
  - Non-immunosuppressive medical conditions known to increase risk of active TB
  - Mycobacteriology lab workers
- ≥ 15 mm = positive
  - Persons in regions of low TB incidence

Limitations for TST

- **Interpretation variability; False positives: NTM, BCG…**
- **BCG Vaccine effect on TST Interpretation**
  - Induces 3-19 mm TST reaction in 1st few mos.
    - Reaction wanes significantly by 10 years
    - Reaction size does not correlate with protection
  - Positive TST most likely due to TB infection:
    - Persons from regions of high TB prevalence (eg. hispanic, asian)
    - Large reaction (>15 mm)
  - **Prior BCG, should be Tested and Treated if positive**
- **Booster Phenomenon**
  - False negative TST, becomes positive as a result of skin testing
  - Most common situations:
    - Initial TB infection many years previous
    - Prior BCG immunization
  - Two Step Skin Testing (TST x 2, one week apart)
    - Elderly nursing home population
    - Prior BCG immunization

LTBI Testing Upgrade… Interferon Gamma Release Assay (IGRA)

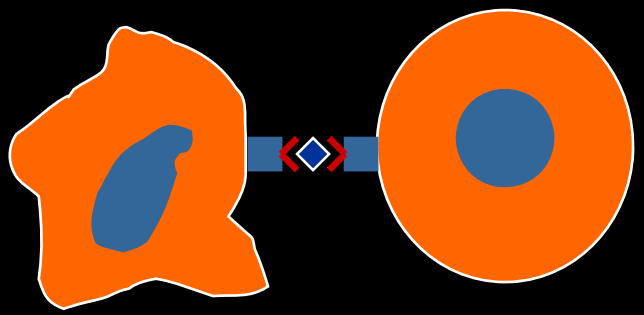
Measures interferon-gamma (IFN-γ) released by lymphocytes in response to specific TB antigens: ESAT-6, CFP-10

- QuantiFERON® Family:
  - QuantiFERON® -TB test 1999
  - QuantiFERON® - TB Gold 2005
  - QuantiFERON® - TB Gold In-Tube (GIT) 2007
    Added 3rd antigen TB7.7 (RD4) & travel time
- T-Spot.*TB*® Aug 2008:

TST vs IGRA

Presentation of TB antigens

- TST (Multiple = PPD)
- IGRA (Specific = ESAT-6, CFP-10)



Antigen Presenting Cell

Memory T-Cell

TST

IFN-γ

TNF-α

IL-8, etc.

IGRA

IFN-γ

TNF-α

IL-8, etc.

IGRA Results include control wells

- Negative (Nil) – no antigen (subtract from pt value)
- Positive – mitogen stimulation

Andersen P et al: *Lancet* 2000;356:1099

IGRA vs TST

IGRA

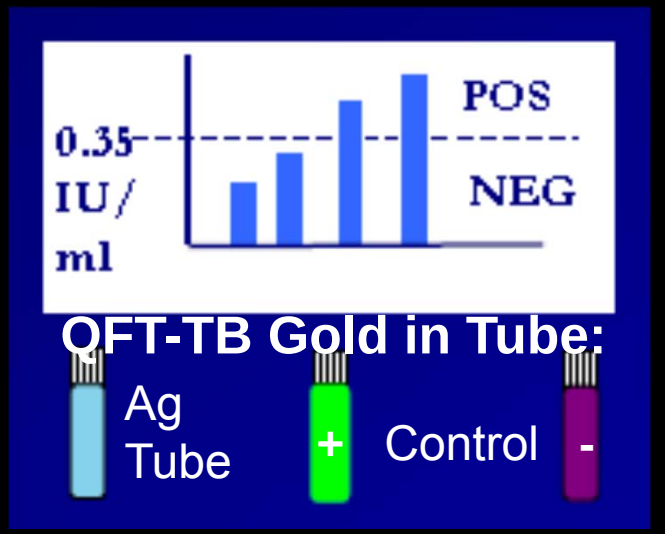
- *In vitro*
- Specific antigens
- Unaffected by BCG
- No boosting
- One patient visit
- No inter-reader variability
- One standard result for all

TST

- *In vivo*
- Multiple antigens
- BCG affects results
- Boost occurs
- Two pt visits
- Inter-reader variability
- Different thresholds based on risk

QFT vs T-Spot.TB

- Quantiferon TB (QFT): Whole blood incubated w/ TB specific antigens. ELISA measures IFN- γ release



- T-Spot.TB: Lymphocytes (T) incubated w/ specific antigens. ELISPOT-method counts IFN-γ releasing cells

IGRA Interpretation

	Positive	Negative	Gray Zone	Indeterminate
QFT-TB Gold & IT version	≥0.35*	<0.35*	None	Controls fail: •High Nil •Mitogen response
T Spot.TB	≥8 spots*	<8 spots*	5-7 spots*	Same as above

*TB Ag – Nil, assuming appropriate control response

IGRA CDC Guidelines 2010

- IGRA may substitute for TST
- IGRA preferred:
  - BCG vaccinated persons
  - Clients unlikely to return for TST reading
  - Low risk persons
- TST preferred in children <5
- Clinical judgment required when interpreting IGRA among immunosuppressed, children <5, & TB suspects
- Lab should be reporting quantitative results

Indeterminate IGRA Results

- Poor response to mitogen that resolves with repeat assay
  - Delayed specimen processing
  - Technical errors
- Persistent poor response to mitogen
  - Anergy from immunosuppression
  - May occur in healthy persons
- High background IFN-γ levels (high NIL response)
  - Often persistent, reasons unclear
  - IGRA not useful

Interpreting IGRA Results

- Contact investigation: If initial IGRA negative, Repeat test at 8-10 wks as one would with TST
- IGRA conversion = change from neg to positive
- Indeterminate result: Repeat IGRA or do nothing (don't recommend TST generally)

<u>Areas of uncertainty:</u>

- Quantification of IGRA conversion (serial testing)
- Possible quantitative assessment of Rx response

Host Factors Creating False Negative TST & IGRA

- HIV (low CD4, no HART)
- <10 wks since TB infection
- Other infections (viral, fungal, bacterial)
- Lymphoma
- Live virus vaccination (eg, measles, smallpox)
- Immunosuppressive Rx
- Overwhelming TB (eg, miliary TB)
- Age (newborn, very old)

TST False Positives

- Cross reaction w/ NTM or BCG
- Immediate hypersensitivity misinterpreted as positive
- TST product switch (Tubersol vs Aplisol)

IGRA False Positives

- Cross reaction NTM: *M kansasii*, *M szulgai*, & *M marinum*
- Product failure such as endotoxin traces in tubes
- Lab error

Can IGRA Replace TST?

- Contact investigation: YES
- BCG vaccine Hx: YES
- Low risk person: yes
- Screening homeless & other unreliable persons: YES
- Serial Testing: Yes, but…

Real Life with IGRA

- Significant reduction in positive rate vs TST
- Increased frequency of retesting

- Serial testing issues:
  - Unexpected positives that require further review (eg, repeat testing, assessing quantitative results)
  - “Wobblers” = results hovering around cut point

LTBI: TST & IGRA ≠ Gospel

- Reassess TB risk factors
- Review symptoms
- Review CXR… evidence suggest old TB (Upper lobe fibrosis, Gohn lesion, Hilar Ca^{++})

- LTBI Rx decision should be based on complete certainty that active TB not present

Key Recent References

CDC. Updated Guidelines for Using IGRAs to detect M tuberculosis infection, US 2010. *MMWR Recommendations and Reports* June 25, 2010

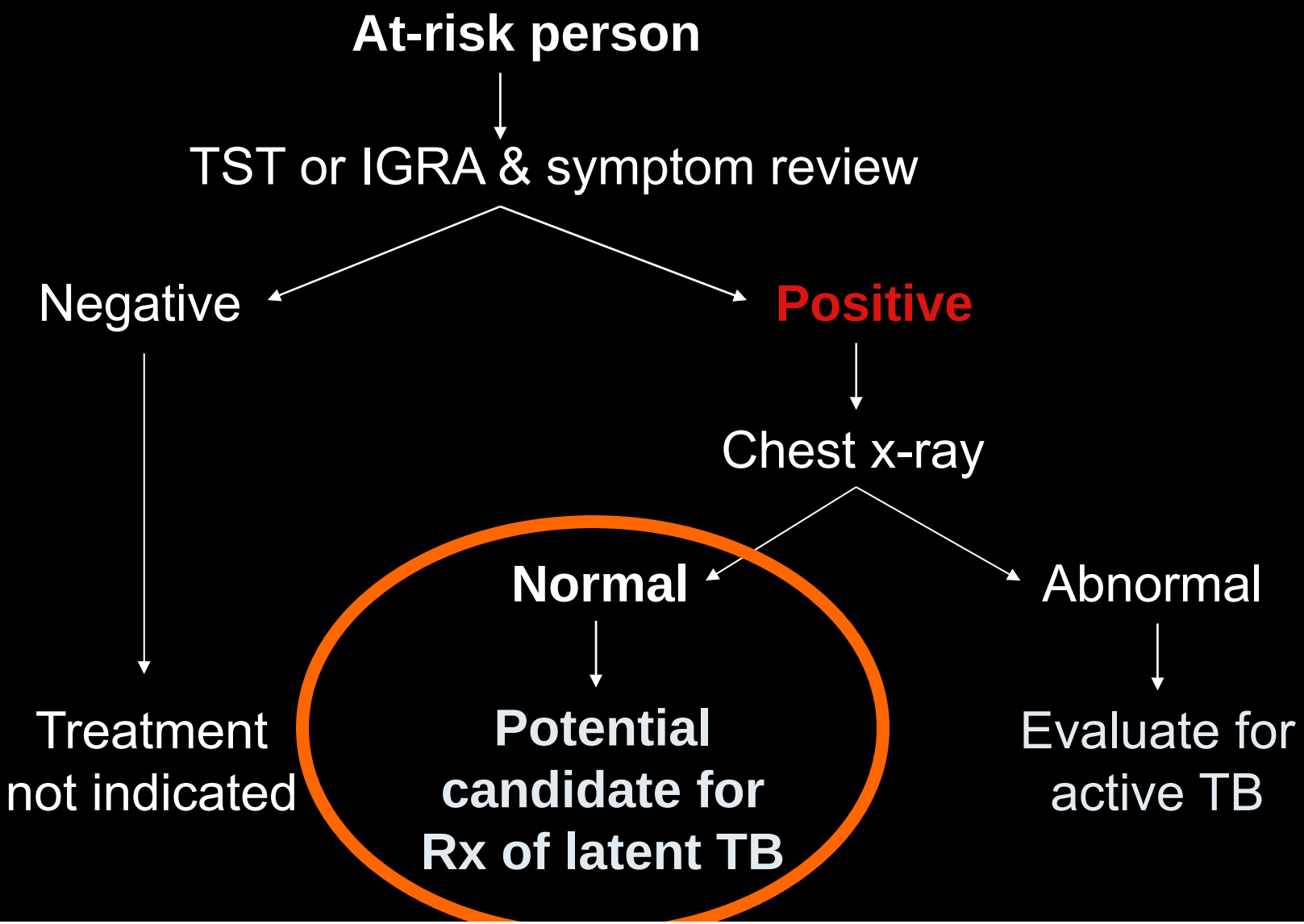
Pai M et al. Systematic Review: T-Cell–based Assays for the Diagnosis of Latent TB Infection: An Update. *Ann Intern Med* 2008; 149:177-184.

Is This Really True?

- Apples, not Caffeine, are more efficient at waking you up in the morning
- You burn more calories sleeping than you do watching TB
- Donkeys kill more people annually than plane crashes and/or shark attacks…

So watch your ASS…

Tuberculosis Screening Flowchart



…Back to SB, the case of LTBI

- Obtained:
  - ✓TST (Mantoux) Positive
  - ✓Chest x-ray Negative

- Do you need sputum smear and culture?

Only if suspicious for active disease
<u>Not</u> necessary in asymptomatic patient, positive TST, normal CXR

What Treatment for S. B.?

Optimal LTBI Rx…

- Short as possible to enhance completion rates (programmatic advantages)
- Minimally toxic

Treatment of Latent TB Infection
HIV Neg. & Pos. Adults
(Dept of Public Health provides meds)

1. **Daily INH for 9 months (270 doses w/in 12 mos)*,+**
2. **Daily INH for 6 months (100 doses w/in 9 mos)+**
   Exclude any w/ old healed fibrotic TB lesions on CXR
3. 1*,+ or 2+ above, administered as DOT, twice weekly
   76 doses w/in 12 months or 52 doses w/in 9 months
4. Daily rifampin for 4 months (120 doses w/in 6 m)
   Alternative for those who are known contacts with INH resistant TB or INH not feasible

Completion = Total # doses, not duration alone

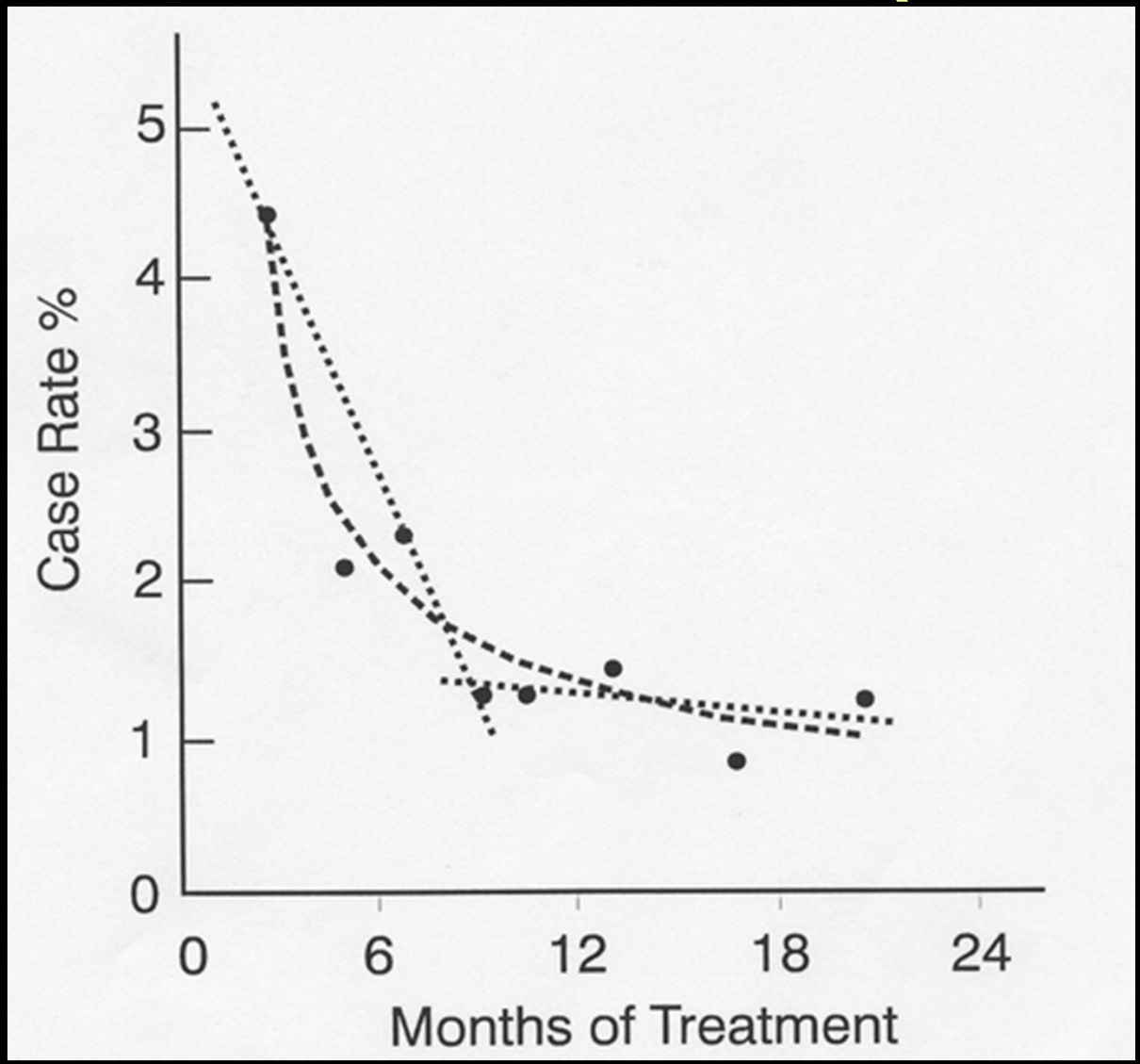
If > 2 month interruption, re-evaluate for active TB before restarting

*Recommended for children < 18 years

+Recommended for pregnant women.

ATS/CDC/IDSA 5/2000; Update 8/2003

TB Case Rates *vs.* No. of Months INH Treatment (Bethal Data)



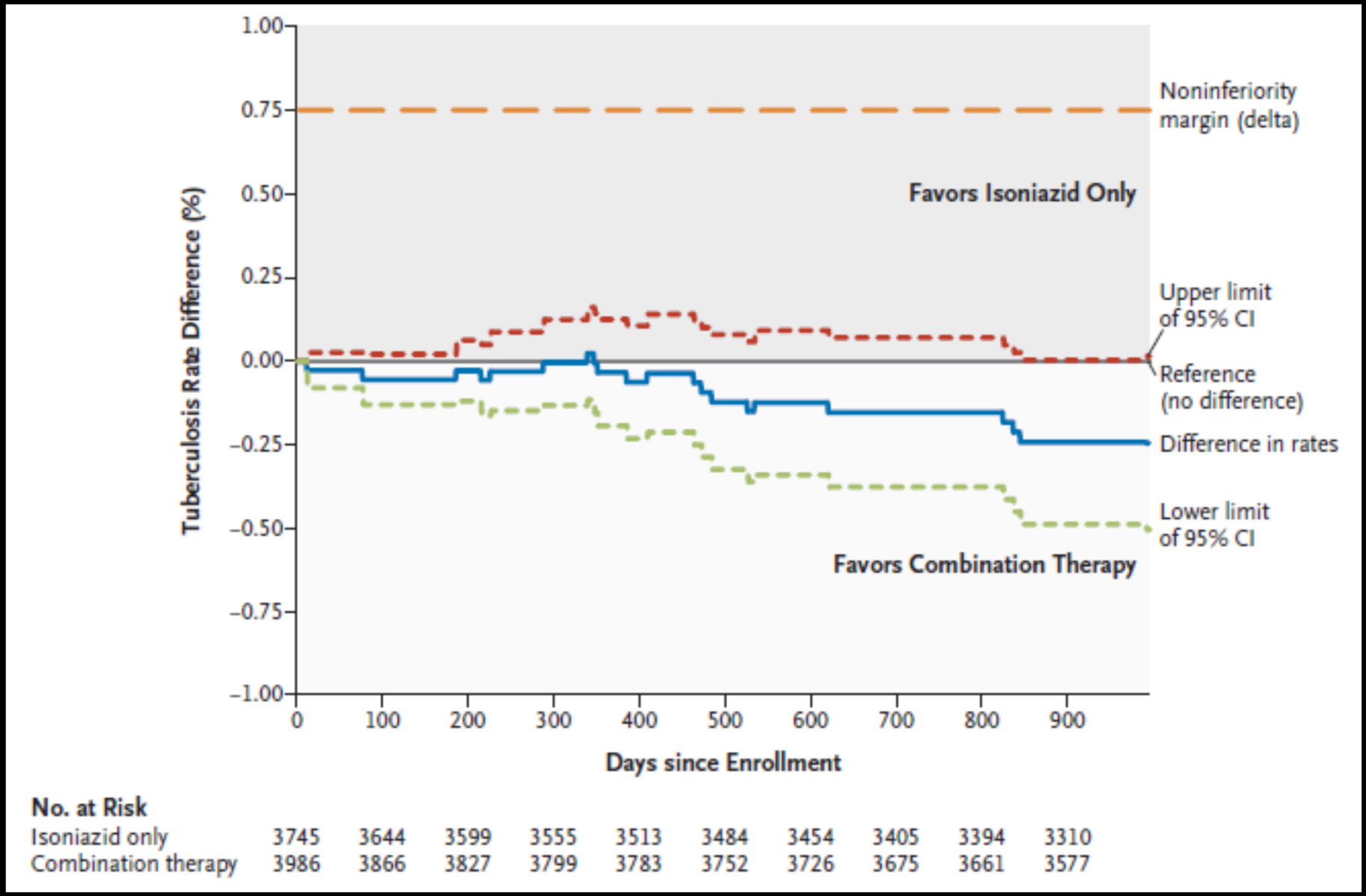
Comstock GW: *Int J Tuberc Lung Dis* 1999

Even Shorter Treatment = Reality…

- *New regimen*: INH 900 mg plus Rifapentine 900 mg weekly x 3 months (12 doses, DOT)
- Open Label, Randomized Noninferiority trial 2011
  - *New regimen* (DOT) vs INH x 9 mos (not DOT)
  - N ~ 8000 US & Canada x 33 mos (few HIV, children)
  - Target population: TST converters & +TST old healed TB chest x-ray
  - Result: *New Regimen* equivalent to 9 mos INH
    - Drug d/c d/t adverse events 4.9 vs 3.7%
    - Increased hypersensitivity (*New*) vs hepatotoxicity (INHx9)
    - Trend toward *New regimen* better than INHx9
      - *New Regimen* group: TB rate ~50% lower
      - Rx completion rate 82% *vs* 69%

Sterling TR et al. *NEJM* 2011;365:2155-66

New Regimen vs INHx9



No. at Risk

Isoniazid only	3745	3644	3599	3555	3513	3484	3454	3405	3394	3310
Combination therapy	3986	3866	3827	3799	3783	3752	3726	3675	3661	3577

Sterling TR et al. *NEJM* 2011;365:2155-66

Real World Recommendation

- *New Regimen* (DOT) does not replace INHx9, but equal option for Rx LTBI
- (Iowa) Dept Public Health provides INHx9 at no cost for anyone diagnosed w/ LTBI
- IDPH agrees *New Regimen* equivalent to INHx9
  - *New Regimen* costs **10x** the standard INHx9 regimen
  - IDPH able to cover high cost of *New Regimen* (not DOT)
  - Policy for your state?
- *New Regimen* not recommended for the following:
  - Child <2
  - HIV/AIDS taking HART
  - Pregnant women
  - Contacts of INH &/or Rif resistant TB

Real World Dosing

- **INH:** 900 mg max for those ≥ 60 kg or
  15 mg/kg rounded up to the nearest 100 mg
  Formulations: 300 & 100 mg tabs
- **Rifapentine:** 900 mg max for ≥ 50 kg
  10.0–14.0 kg 300 mg
  14.1–25.0 kg 450 mg
  25.1–32.0 kg 600 mg
  32.1–49.9 kg 750 mg
  Formulation: 150 mg tabs (others in development)
- INH-Rifapentine combo being developed

Rifamycins Better Than INH?

- INH monotherapy (6 or 9 mos) plagued by low completion rates, programmatic challenges & hepatotoxicity

From > 20 yrs of studies (~1500 trials), 53 RCTs LTBI Rx systematically selected & reviewed

- Each included relative efficacy & adverse events
- Applied Bayesian network meta-analysis
  [Allows comparison two distinct Rx regimens
  when no trials directly compare them]

Stagg et al. *Ann Int Med* 2014;161:419-26

LTBI Rx: Rifamycins Better Than INH?

Comparison to standard INH monotherapy:

- Rifampin x3-4 months ranked highly for both efficacy & hepatoxicity
- INH & Rifampin x3-4 months also ranked well
- INH & Rifabutin trended well but data NS
- Surprise: INH & Rifapentine not as well as above

Regimens containing rifamycins more effective alternative?

Stagg et al. *Ann Int Med* 2014;161:419-26

More Real Data Coming

- HALT trial: Evaluates Non-DOT Rifapentine vs INH monotherapy
- CDC trial: INH x 9 mos vs Rifampin x 4 mos

Treatment for S.B.

- INH daily x 9 months
- County public health department supervised treatment:
  - PHN performed Clinical Monitoring
  - 30 day supply aliquots of INH provided
  - Completed 9 months w/in 9 months

Summary Points

- Screen persons at high risk for TB (eg, foreign born)
- Seek to distinguish active vs. latent TB infection
- LTBI diagnosis reviewed
  - Decision to test = Decision to treat!
  - Highest risk subgroups identified
- Role for IGRA: QFT-Gold, T-Spot.*TB*
- LTBI treatment update
  - Can be shortened to 3 months (INH/rifapentine x 12 doses)
  - Data re-evaluation $\rightarrow$ Rifamycin better than INH?
- (Iowa) Department of Public Health provides TB Rx at no cost to patient

Monitoring on INH Treatment

- Educate the patient
  - Liver disease symptoms & signs
  - Stop meds until contact made with health care
- The critical element for preventing INH toxicity is Clinical monitoring…PHN
  - Absolutely necessary to do, absolutely necessary to do well & absolutely necessary to document well.
- LFTs (ALT, AST) at baseline in selected cases
  - Hx of liver disease, EtOH, pregnancy, HIV
  - Repeat monthly if abnormal at baseline, symptomatic, or pregnant
  - Stop meds:
    - Symptomatic, LFTs 3x upper limit of normal (ULN)
    - Asymptomatic, LFTs 5x

ATS/CDC/IDSA 5/2000

Clinical Monitoring

- Instruct patient to report following adverse drug reactions (ADRs):
  - Rash
  - Anorexia, nausea, vomiting, or pain in RUQ
  - Fatigue or weakness
  - Dark urine
  - Persistent numbness in hands or feet
- Monthly visits should include review of:
  - Rationale for treatment
  - Adherence to therapy
  - Symptoms consistent with ADR(s)
  - Plans to continue treatment

Liver Safety Issues for INH

- Deaths from INH hepatitis in 1960s
- 1971-72 PHS Study (14,000 pts)
  - 1% overall rate of INH related hepatitis
  - Age related increase
    - 0.3% (<35)
    - 2.3% (>50)
  - 4x increase a/w EtOH
  - 8 deaths due to INH hepatitis
- Review of PHS data (Comstock *JAMA* 1986)
  - 7/8 deaths occurred in Baltimore
  - Death certificate review: XS deaths due to cirrhosis in 1972
  - Unidentified co-factor related to cluster of cirrhosis cases ?
- Subsequent studies: risk is lower

Latest CDC Data on INH Liver Toxicity

- SAEs during LTBI Rx, 2004-2008
- 17 patients with SAEs, all hepatotoxicity
  - 2 children < 15 yrs of age; Adults median age 39
  - One patient HIV seropositive for Hep C, HIV
  - 5/17 liver transplant (one child), 5/17 died (one transplant)
- 10/17 patients with CDC on-site investigation
  - Prescribers followed ATS/CDC guidelines for Clinical Monitoring
  - Symptoms 1-7 months after INH started
  - Fatigue, nausea, abdominal pain in 7 patients who waited for jaundice to seek medical attention
  - 2 patients INH discontinued within 3 days of symptoms, 8 stopped at least one week after symptom onset; all after medical instruction
- Death & liver transplantation ~1/150,000 - 1/220,000
- SAEs idiosyncratic reaction, independent of dosing, possible anytime during treatment, can occur in children

MMWR 2010 59(08):224-229

Deaths from INH Hepatitis

- Rates in women increased
  - Pregnancy & immediate post-partum period (3 mos)

  (Snider DE et al: *ARRD* 1992; Franks et al: *Pub Health Rep* 1989)
- Concurrent acetaminophen questionable

(Murphy et al: *Ann Int Med* 1990; Burk et al: *Res Comm. Chem Path Pharm* 1990)
- INH death rate reduced by Clinical Monitoring
  - Stopping INH at symptom onset reduces deaths
    (Moulding TS, et al: *ARRD* 1989)
  - 7/8 liver transplants for INH hepatitis: Pts continued INH >10 d beyond symptom onset
    (CDC: *MMWR* 1993)

Safety Issues for INH:
Current Practice Outcomes

- Most PHD practice Clinical Monitoring vs. biochemical monitoring
- Clinical Monitoring:
  - Educate for Rx related ADRs & Reviews adherence
  - Stop INH if any question until consult with clinician
  - CDC: “Medical providers should emphasize to patients that INH treatment should be stopped immediately upon the earliest onset of symptoms (e.g. excess fatigue, nausea, vomiting, abdominal pain, or jaundice), even before a clinical evaluation has been conducted, and that initial symptoms might be subtle and might not include jaundice.”

Monitoring on Treatment

- Educate the patient
  - Liver disease symptoms & signs
  - Stop meds until contact made with health care
- Clinical monitoring monthly…PHN
- LFTs (ALT, AST) at baseline in selected cases
  - Hx of liver disease, EtOH, pregnancy, HIV
  - Repeat monthly if abnormal at baseline, symptomatic, or pregnant
  - Stop meds:
    - Symptomatic, LFTs 3x upper limits of normal (ULN)
    - Asymptomatic, LFTs 5x ULN

ATS/CDC/IDSA 5/2000

More Case Examples & Discussion

Factors Causing False-Negative TST

- Anergy = Weakened immune system ⇒ Inability to react to TST
  - Anergy testing utility in TST-negative persons not demonstrated in clinical trials
- New TB infection (eg, 2-10 weeks post exposure)
- Newborns
- Live virus vaccination (eg, measles, smallpox) suppresses TST response
- Overwhelming disease (eg, miliary TB)
- Poor TST administration technique

How Should Immunosuppressed Persons at Risk for TB Be Managed?

Empiric treatment for LTBI even when TST or IGRA neg on repeat testing 8-10 weeks after exposure

- Advanced HIV infected contacts
- Children < 5 years who are contacts
- Contacts with other causes of immunosuppresion
- Persons who are to receive treatment with TNF alpha antagonists

TNFα Antagonists

- Block TNFα activity which is required for granuloma formation & containment of *M tuberculosis*
- Used for RA, Crohn's disease, Psoriasis and a variety of other immune mediated diseases

  Remicaid (inflixamab)

  Embril (entanercept)

  Humira (adalimumab)

  Cimzia (certolizumab)

- Patients should be evaluated for LTBI w/ IGRA or TST
- Treatment of LTBI should be initiated prior to therapy

Questions Remain

- Unknown
  - Does treatment of LTBI need to be completed prior to use of TNF-α antagonist?
- Unknown
  - Does a person at risk of TB who is TST negative need to be treated?
    - Consider treatment of high risk TST negative patients
- No need to continue INH after completion of treatment for LTBI

Case 2

- 36-year-old Native American female
- History of diabetes
- 35 weeks pregnant
- TST = 18 mm of induration
- No symptoms of TB disease
- CXR, CBC, LFTs normal
- No known contact with TB patient

Case 2

Questions

1. What are this patient's risk factors for TB infection or disease?

2. What is the appropriate management for this patient?

Case 2

Discussion of risk factors

- Persons with diabetes mellitus are 2 to 4 times more likely to develop TB disease than those without diabetes
- Risk may be higher in insulin-dependent diabetics and those with poorly controlled diabetes

Case 2

Discussion of management

- Pregnancy has minimal influence on the pathogenesis of TB or the likelihood of LTBI progressing to disease
- Pregnant women should be targeted for TB testing only if they have specific risk factors for LTBI or progression to disease
- Some experts prefer to delay treatment until after the early postpartum period, unless the woman has recent TB infection or HIV infection

Case 3

- 41-year-old Hispanic male
- Moved to U.S. from Mexico 4 years ago
- Known contact of infectious TB case
- TST = 5 mm of induration
- 3 months later TST = 23 mm of induration
- No symptoms of TB disease
- Normal CXR, CBC, AST, and bilirubin

Case 3

Questions

1. What are the patient's risk factors for TB infection or disease?

2. Has the management of this patient to date been appropriate?

Case 3

Discussion of risk factors

- Patient is a contact of an infectious TB case
- Recent immigrant to the U.S. from a country with a high prevalence of TB. Such persons have increased rates of TB
- If the patient had not been a contact, the recent immigration (less than 4 years) would have made him a candidate for TB testing, but the 5-mm reaction would not be considered positive

Case 3

Discussion of management

- Should be treated for LTBI if TST reactions ≥ 10 mm of induration
- As a contact of an active TB case, 5 mm of induration is considered positive
- This patient should have been treated for LTBI immediately after the first TST

Case 4

- 56-year-old White male
- Works in a mycobacteriology lab
- TST result negative 1 year ago
- M. *marinum* infection in his hand 8 months ago
- TST result 5mm
- QFT-G test positive
- No symptoms of TB disease, CXR normal
- No known contact with a TB patient & no known spills or accidents in the lab