Latent Tuberculosis Infection: Update on Diagnosis & Treatment

Dane County’s TB Summit 2012
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Denver Metro Tuberculosis Control Program
Denver Public Health Department
Objectives

1. Define LTBI and the role of LTBI treatment in the US TB elimination goal
2. Describe the barriers to expanded targeted testing and treatment of LTBI
3. Describe the challenges of diagnosing LTBI and use of IGRAs
4. Describe the short-course regimens for LTBI treatment
LTBI: Cell-mediated immunity to TB proteins associated with risk for TB (Puerto Rico BCG Trial, 1949-1951)

- 82,269 children age 1-19 yrs with ≥ 6 mm PPD
- 1,400 TB cases in 19 yrs: 90 per 10^5 / year
  - > 16 mm: 160 per 10^5 / year
  - 11-15 mm: 98 per 10^5 / year
  - 6-10 mm: 46 per 10^5 per year
- Those > 15 mm PPD: 5% active TB in 19 yrs.
- Peak rates ages < 4 yr. and 19 yrs

TB Rate by Age in PPD+ Puerto Rican Children

Figure 1. Incidence of tuberculosis among initial reactors to tuberculin, by age when tuberculosis was first diagnosed.
LTBI: Cell-mediated immunity to TB proteins associated with risk for TB but reduced by INH treatment for 52 vs 24 or 12 weeks

Table 6. Efficacy of various durations of isoniazid therapy compared with placebo for "completer-compliers"

<table>
<thead>
<tr>
<th>Regimen</th>
<th>No. of participants</th>
<th>No. of cases</th>
<th>Incidence</th>
<th>Percentage reduction</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>5616</td>
<td>83</td>
<td>15.0</td>
<td>0</td>
<td>13.6</td>
</tr>
<tr>
<td>12-I</td>
<td>6039</td>
<td>61</td>
<td>10.4</td>
<td>31</td>
<td>9.4</td>
</tr>
<tr>
<td>24-I</td>
<td>5437</td>
<td>25</td>
<td>4.7</td>
<td>69</td>
<td>4.3</td>
</tr>
<tr>
<td>52-I</td>
<td>4543</td>
<td>5</td>
<td>1.1</td>
<td>93</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*Culture-positive tuberculosis per 1000 persons at risk.

Fig. 2. Annual incidence of culture-positive tuberculosis: "completer-compliers", by regimen.

IUAT trial of 28,000 with ≥ 5 mm TST & fibrotic lesions, Bull WHO 1982
TB Case No. 1

• Call received at Denver TB Control from hospital physician: AFB growing on sputum collected 17 days earlier at DHMC – patient in home hospice for progressive pulmonary fibrosis (8 day adm.)
• Patient located, home hospice nurse called – patient had expired that morning
• M. tuberculosis, susceptible to 1st-line drugs identified smear-neg. sputum & tracheal aspirate
• Contact investigation: 4 of 8 adults, with LTBI, 6 children not infected
Previous medical history:

• 1997 first seen in CHS as 62 y.o. Mexican-born woman with prior CVA, hypertension & lung fibrosis

• Followed at FQHC, Pulm & Rheum Clinics through 2010

• No recorded TST

March 2006 earliest image
Follow-up X-rays

May 2008

December 2010: TB r/o with (-)TST & AFB smears
Further progression

Admission

D/C: 10 days before death
TB Case No. 1: Potentially preventable case & death

- Birth in Mexico & parenchymal fibrotic lesions – candidate for evaluation for inactive TB & treatment
- TB excluded due to negative TST and negative smear - < 50% of pulmonary TB smear + so empirical treatment may have been effective
- Would knowledge of LTBI on admission altered treatment?
Case 2: US-born 2 yr old male child: Preventable TB?

- Mother hospitalized with recurrent pneumonia
  - Cavitary nodules on CT
  - Sputum AFB 2+
- Child asymptomatic
  - TST 12 mm
  - Congenital urinary tract abnormalities, corrected
  - INH, rifampin, EMB, PZA started
Case 3: Mother with hemoptysis - CT PE
Case 3: 31 yr old Mexican-born mother with multiple bouts of pneumonia for past 2 yrs

1st Adm.
- TST 24 mm 5 yr ago antepartum at MCPN – referred to DPH
- Normal X-ray, no return to TB Clinic for INH after 5th child
- Two admissions for pneumonia 2 yrs prior – TST negative
- Improved, not resolved with levofloxacin, then ciprofloxacin
- Tx with TMP/SMX & clarithromycin 1 yr prior by primary care
Discussion for Cases 1 - 3

- Patients in primary and specialty care miss opportunities for TB prevention
- US-born children with foreign-born parents are at increased risk for acquiring TB from family members
- Timely diagnosis of important but relatively rare events are challenging - delays in diagnosis & treatment of TB lead to ongoing transmission
- Preventable TB cases continue to occur due to failures to diagnose & treat latent TB infection in populations at increased risk for TB
TB Elimination

Definition: one reported case of active disease due to *Mycobacterium tuberculosis* (TB) per million population/yr

- U.S. Advisory Council for the Elimination of Tuberculosis in the United States (ACET)
  - Established in 1987
  - Goal set in 1989 for year 2010

- WHO Stop TB Partnership
  - Goal set in 2005/2006 for 2050
Critical Barrier to TB Elimination: Prevalence of LTBI & Associated TB Case Rates
(Data from 1999-2000 & 2000)
Bennett 2007, CDC 2000
Latent TB Infection

**Figure 1.** Lifetime Risk of Active Tuberculosis among Persons with a Non-conversion Positive Tuberculin Skin Test.

Risks were calculated with the assumption of a decrease in risk of 10 percent per decade.

Horsburgh, NEJM 2004 350; 20: 2060-7
Targeted testing & LTBI treatment in U.S.: limited use, poor completion

- TB Epidemiologic Studies Consortium (TBESC) survey estimates for 2002*
  - 291-433,000 started treatment
  - 95% in public health, corrections, refugee clinics, shelters – few in pediatrics, private
  - 17% with LTBI declined to start treatment
  - 53% who started treatment failed to complete

*Sterling AJRCCM 2006, Horsburgh Chest 2010
Will it be possible to engage all U.S. medical care providers, professional organizations, community organizations in TB prevention?

- IGRAs recommended for BCG vaccinated patients – cost & logistics being addressed
- Shorter regimens for LTBI are being used:
  - Rifampin 4 months  
    – H Young CID 2009, others
  - INH+rifapentine once-wk for 3 months
- Developing guidelines & record systems for risk assessment, testing & treatment

New diagnostic tools at last: Interferon-gamma Release Assays

- Blood test for detecting TB infection
- Requires only 1 visit to get a result
- Less subject to reader bias and error
- More specific with less cross-reaction with non-tuberculosis mycobacterium and BCG than the TST

Lancet 2000;356:1099-104
Commercially Available IGRAs

QuantiFERON® - TB Gold
One blood test, One clear answer

A 21st Century Solution for Latent TB Detection
Assessment of IGRA (Quantiferon-TB Gold) vs Tuberculin Skin Testing during TB Screening of U.S. visa applicants in Vietnam

Randall Reves, MD, MSc, Denver Public Health Department for the TB Epidemiologic Studies Consortium (CDC Div. of TB Elimination) and the Div. of Global Migration and Quarantine, the Methodist Hospital Research Institute (Houston), Cho Ray Hospital Visa Medical Department, FIND
Background for Vietnam 2009 (WHO)

- Population 88 million
- Est. TB cases 180,000, rate 200 per $10^5$, prevalence 0.33%
- VN origin for 584 (4.5%) of US TB cases in 2008
- Each year > 25,000 applicants for permanent US residency screened for TB in Vietnam using CDC Technical Instructions
  - 80% at Cho Ray Hospital Visa Unit, Ho Chi Minh City, remainder at IOM in HCMC
  - 2007 TB TI initiated in HCMC in 2/08
  - Previous collaboration with CDC on culture study
Evaluation of QuantiFERON-TB Gold in tube (QFT) & TST during TB screening of U.S. visa applicants in Vietnam

• Compare sensitivity – case detection of culture-confirmed pulmonary TB in adults during screening
  – Inference: sensitivity of TST/IGRA as 1st step in case detection during status change exams – TST first, CXR only if ≥ 5 mm
  – Inference: sensitivity during targeted testing (e.g. students)

• Estimate “specificity” for LTBI
  – Compare age-specific prevalence (cumulative incidence)
  – Are we “comfortable” with fewer IGRA LTBI diagnoses?
QFT and TST Results: 1,501 participants

<table>
<thead>
<tr>
<th>Test result</th>
<th>TB-CXR Culture (+)</th>
<th>TB-CXR Culture (-)</th>
<th>Normal CXR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n)</td>
<td>% (n)</td>
<td>% (n)</td>
</tr>
<tr>
<td><strong>TST category</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 10 mm</td>
<td>81.1 (107)</td>
<td>61.5 (531)</td>
<td>47.9 (242)</td>
</tr>
<tr>
<td>≥ 5 mm</td>
<td>89.4 (118)</td>
<td>79.4 (686)</td>
<td>70.3 (355)</td>
</tr>
<tr>
<td>&lt; 5 mm</td>
<td>10.6 (14)</td>
<td>20.6 (178)</td>
<td>28.1 (139)</td>
</tr>
<tr>
<td><strong>QFT category</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>positive</td>
<td>87.1 (114)</td>
<td>67.4 (582)</td>
<td>32.5 (164)</td>
</tr>
<tr>
<td>negative</td>
<td>12.1 (17)</td>
<td>32.3 (279)</td>
<td>66.9 (338)</td>
</tr>
<tr>
<td>indeterminate</td>
<td>0.8 (1)</td>
<td>0.4 (3)</td>
<td>0.6 (3)</td>
</tr>
<tr>
<td><strong>Total number</strong></td>
<td>132</td>
<td>864</td>
<td>505</td>
</tr>
</tbody>
</table>
Age-specific TST & QFT results: conclusions

- **TX-CXR:** Declining % TST+ & QFT+ follows decreasing TB frequency with age: suggests declining specificity of TB-CXR
- **Normal X-ray:** Increasing prevalence TST+ & QFT+ with age but lower frequency for QFT suggests better specificity for LTBI

![Graph showing test-positive proportion in participants by age and CXR](image)
Conclusions

• Specificity of QFT appears better than TST based on age-specific TB prevalence with normal CXR
• LTBI over diagnosed with TST: Prevalence may be one-third lower using QFT than TST-10 mm (32% vs 48%) - implications for LTBI treatment
• Limitations: only 26 children 2-14 years enrolled
  – Problem: 16.5% of applicants, few TB cases, many Class B2 LTBI referrals to US health departments
  – Performance of QFT in children currently was studied in Mexico, the Philippines and Vietnam (TBESC TO 31)
• Successful collaboration with Panel Physician site at Cho Ray Ray Hospital using largely existing screening exam database
Study Team

Cho Ray Hospital, Vietnam
  Duong Thi Cam Nhung, Hoang Hoa Hai, Tran Thi Thanh Nga, Le Thien Huong Loan, Nguyen Huu Phuoc, the Visa Medical Department and the Laboratory

TMHRI, Texas – epidemiological & laboratory expertise
  Ed Graviss, Ngan Ha, Duc Nguyen, Hung Luu, Yen Pham

Denver Health, Colorado
  Kirsten Wall – Study Coordinator
  Matt Parker – data analysis

Centers for Disease Control, Georgia
  DGMQ: John Painter, Susan Maloney
  DTBE: Lilia Manangan, Denise Garrett

FIND, Switzerland
  Rick O’Brien, Madhukar Pai
Evaluation of Interferon-\(\gamma\) Release Assays in the Diagnosis of Latent TB Infection in U.S. Healthcare Workers:
on TBESC Task Order 18

Some near-final results
On behalf of the CDC TB Epidemiological Studies Consortium & the TO 18 Protocol Team
Design and Population

• Longitudinal study
  – HCWs undergoing routine LTBI testing
  – TST- positive HCW recruited to participate

• 4 sites: Denver, Houston, Baltimore, NYC

• Inclusion:
  – ≥18 yrs; informed consent; undergoing routine screening

• Exclusion:
  – Current or prior active TB; TST within 6 months prior to enrollment

• Target sample size 2500 with baseline tests
Testing Methods

• TST Mantoux with Tubersol
  – Administered, interpreted by study-trained personnel
• QuantiFERON®-TB Gold In-Tube (“QFT”)
  – Cellestis, Inc: package insert
  – Performed, interpreted by trained technologists
• T-SPOT®.TB (“T-SPOT”)
  – Oxford Immunotec, Ltd: package insert
  – Performed, interpreted by trained technologists

• Test kits purchased from the companies
• No financial support or donations from companies
• Technical representatives from each company assisted in training study laboratory technologists
Baseline positive TST, QFT, T-Spot for 2418 HCW: 5.2%, 4.9%, 6.0%: combinations for 2246 with all valid results

<table>
<thead>
<tr>
<th>TST</th>
<th>QFT</th>
<th>T-SPOT</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>33</td>
<td>1.5%</td>
</tr>
<tr>
<td>Pos</td>
<td>Neg</td>
<td>Neg</td>
<td>80*</td>
<td>3.6%</td>
</tr>
<tr>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td>25</td>
<td>1.1%</td>
</tr>
<tr>
<td>Neg</td>
<td>Pos</td>
<td>Neg</td>
<td>47</td>
<td>2.1%</td>
</tr>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>Pos</td>
<td>85</td>
<td>3.8%</td>
</tr>
<tr>
<td>Pos</td>
<td>Pos</td>
<td>Neg</td>
<td>7</td>
<td>0.3%</td>
</tr>
<tr>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
<td>1</td>
<td>0.04%</td>
</tr>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>1968</td>
<td>87.6%</td>
</tr>
</tbody>
</table>

*Associated with foreign-birth and BCG vaccination
Cumulative conversion rates with 6, 12 & 18 month repeats

<table>
<thead>
<tr>
<th></th>
<th>Conversion</th>
<th>Reversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST</td>
<td>21 / 2418 (0.9%)</td>
<td>n/a</td>
</tr>
<tr>
<td>QFT</td>
<td>138 / 2263 (6.1)</td>
<td>81 / 106 (76%)</td>
</tr>
<tr>
<td>T-SPOT</td>
<td>177 / 2137 (8.3)</td>
<td>91 / 118 (77%)</td>
</tr>
</tbody>
</table>

Conversion = (-) baseline (+) 6, 12 or 18 month
Reversion = (+) at 6 or 12, (-) next 6 month test
Conclusions:

In this study of 2500 HCW in 4 US institutions

- Risk for TB infection appears quite low - TST conversion 0.9%
- IGRAs identify false-positive TST in FB HCW
- Similar to other studies, conversions with both IGRA are over 6-fold higher with over 75% of conversions negative in 6 months
- Major strength of study – use of both IGRA & TST provides data to suggest that false-positives explain many of TST and IGRA results - as expected in testing low-risk populations
- Immediate retesting might be a strategy to identify false-positive test results - J Gray,
Thanks to

- CDC: Paul Weinfurter, Denise Garrett, Grace Thiongo
- Denver: **Charles Daley**, Robert Belknap, Matt Parker, Randall Reves, Kirsten Wall
- Houston: Ed Graviss, Larry Teeter
- Baltimore: Wendy Cronin, Elizabeth Munk, Jonathan Golub
- NYC: Daniel Brodie, Joyce Thomas, Yael Hirsch-Moverman
Retesting strategy for QFT+ HIV-infected patients at low-risk for TB exposure

Table 2. Results of Repeated Positive QuantiFERON-TB Gold In-Tube Assays by Tuberculosis Exposure Risk and HIV Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total No.</th>
<th>QFT 2</th>
<th>Odds of Reversion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Negative, No (%)</td>
<td>Positive, No. (%)</td>
</tr>
<tr>
<td>All patients</td>
<td>49</td>
<td>35 (71.4%)</td>
<td>12 (24.5%)</td>
</tr>
<tr>
<td>No tuberculosis risk</td>
<td>41</td>
<td>33 (80.5%)</td>
<td>6 (14.6%)</td>
</tr>
<tr>
<td>From high-tuberculosis-incidence country²</td>
<td>8</td>
<td>33 (80.5%)</td>
<td>6 (14.6%)</td>
</tr>
<tr>
<td>CD4 cell count &lt;200 cells/mm³</td>
<td>2</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>CD4 count &gt;200 cells/mm³</td>
<td>47</td>
<td>35 (74.5%)</td>
<td>10 (21.3%)</td>
</tr>
<tr>
<td>On ART</td>
<td>43</td>
<td>31 (72.5%)</td>
<td>11 (25.6%)</td>
</tr>
<tr>
<td>HIV RNA &lt;48 copies/mL</td>
<td>35</td>
<td>27 (77.1%)</td>
<td>7 (20%)</td>
</tr>
</tbody>
</table>

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; QFT, QuantiFERON-TB Gold In-Tube assay.

² Defined as a country with >20/100 000 tuberculosis cases per year.

J Gray, CID 2011
IGRA:

- Promising technology
- Convenient, more lab expense $30-$100
- Improved specificity in lower-risk BCG vaccinated populations
- Specificity not as high as 2-step TST in HCW – retesting and other strategies to be evaluated
Other cytokines: greater separation of IP-10 for TB cases vs controls
New LTBI treatment tools: What do we want to know about short-course regimens, compared to INH?

- Effectiveness
  - Efficacy
  - Acceptability/Tolerability
  - Completion rate
- Safety
- Cost
- Cost-effectiveness
What we know out INH (Gold std)

73,375 patients, HIV-negative

- 11 RCT ‘62-94 with 2-yr f/u (over 100,000 in published studies, 44 studies excluded)
- Effectiveness 60% (56% vs 62%, 6 vs 12 mo.)
- Reduced TB morbidity, not total mortality
- INH hepatitis: 1:200 or 0.5%
- Fatal hepatitis: 1:7,000 or 0.00014%

Note: Improved survival in HIV+ (Wilkinson, 1998)
Short-course options

• 4R: 4-mo. rifampin
• 3HR: 3-mo. isoniazid+rifampin
• 2RZ: 2-mo. rifampin/PZA – EXCLUDED

• 3HP: 3-mo. (12-dose) INH + rifapentine
RCT of toxicity study of 9H vs 4R
(Menzies D, Ann Intern Med 2008)

Figure 2. Interval from randomization to dropout or treatment completion.

All patients included.
RCT toxicity study of 4R vs 9H: Canada, Saudia Arabia, Brazil, Gr 3-4 AE  
(Menzies D, Ann Intern Med 2008)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>All AE % (n)</th>
<th>Hepatic % (n)</th>
<th>Hematol % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4R (n=418)</td>
<td>1.7 (7)</td>
<td>0.7 (3)</td>
<td>0.5 (2)</td>
</tr>
<tr>
<td>9H (n=422)</td>
<td>4.0 (17)</td>
<td>3.8 (16)</td>
<td>0.2 (1)</td>
</tr>
</tbody>
</table>
Meta analysis of 3HR vs 6/9H
(Ena, CID 2005)

• Five RCT selected
  – 3 HIV(+): 1,390 in Spain, Uganda
  – 2 HIV(-)/NT: 536 in Hong Kong, Spain
• Efficacy: 4.2 vs 4.1% developed TB
• Tx-limiting toxicity: 4.9 vs 4.1%
• Hepatotoxicity (limited data): 1-6% vs 5-18%
Why use 3-4 HR vs 4R?

- Toxicity likely increased adding INH
- Cost increase with combination caps
- Example: 4HR for asymptomatic, culture-negative patients with stable X-rays: e.g., 57 y.o. VN man in US 28 yrs, brief hemoptysis, levofloxacin 7 days
57 y.o. man with 6 neg sputum AFB, treated 4 => 6 HR . . then reported as clinical TB
3HP (12 dose DOT) vs 9 mo. INH self-administered

- TB rate 7/3986 (0.19%) vs 15/3745 (0.43%) (NS)
- Completions 82% vs 69% (p < 0.001)
- Discontinuation (AE) 4.9% vs 3.7% (p < 0.0009)
- Hepatotoxicity 0.4% vs 2.7% (p < 0.001)

Sterling T, TBTC Study 26 NEJM 2011
INH 9 months vs 3 HP
## Summary Efficacy & Completion
(adapted from Landry J, Menzies D, 2008)

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Efficacy</th>
<th>Mean compl.</th>
</tr>
</thead>
<tbody>
<tr>
<td>9H</td>
<td>90-92</td>
<td>53</td>
</tr>
<tr>
<td>6H</td>
<td>41-76</td>
<td>49-79</td>
</tr>
<tr>
<td>4R</td>
<td>Unknown</td>
<td>72</td>
</tr>
<tr>
<td>3HR</td>
<td>37-96</td>
<td>62-91</td>
</tr>
<tr>
<td>2RZ</td>
<td>84-99</td>
<td>56-70</td>
</tr>
<tr>
<td>3HP</td>
<td>As good as 9H!</td>
<td>High with DOT</td>
</tr>
</tbody>
</table>
Cost effectiveness: 9H, 4R, 3H
Holland, AJRCCM 2009

- TB contacts age 39 yrs
- Assumption of 93% efficacy made for full completion of each regimen
- Assumptions made regarding adverse events for newer regimens
- Untreated: 64 cases/1000 contacts
- Lifetime total cost/untreated contact: $1527
- Finding: 4R dominated & was cost-saving
## Cost effectiveness: 9H, 4R, 3HP

Holland, AJRCCM 2009

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Total treatment $</th>
<th>Ave. lifetime$/cont*</th>
<th>Incremental $/contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>9H</td>
<td>237</td>
<td>680</td>
<td>-848</td>
</tr>
<tr>
<td>9H DOT</td>
<td>1841</td>
<td>2002</td>
<td>+475</td>
</tr>
<tr>
<td>4R</td>
<td>212</td>
<td>495</td>
<td>-1032</td>
</tr>
<tr>
<td>3HP DOT</td>
<td>503</td>
<td>776</td>
<td>-751</td>
</tr>
</tbody>
</table>

*Average lifetime cost per untreated contact = $1527
Implementation issues

• Current formulation: Nine pills once weekly
  – INH 300mg (3)
  – rifapentine 150 mg (6) without pyridoxine
• Availability was limited initially
• Cost considering DOT higher than 4 R
• DOT will probably not be the only mode
  – Precautions for overdose – especially with language barriers common in high-risk populations
  – Monitoring approaches to be developed, evaluated
  – Clinical research by TBTC being planned
2RZ: Lessons not to be forgotten

- Approval basis 3 RCT
  - All developing country, HIV+ with 18-19% mortality rate
  - Total 2RZ treated 791, 380, 360

- CDC-funded Ph 4 study (n=1,211); Lobato 2005
  - Jail inmates (844), homeless (367)
  - Completion rates: 48%, 44%
  - Severe hepatoxicity in 15 (1.3%), 1 fatal

- Expanded surveillance (n=8087), McElroy 2005
  - Deaths – 0.9 per 1,000 (n=7)
  - Hospitalizations – 2.8 per 1,000 (n=30)

- Lessons: LTBI regimens require large studies
  - Prevent TB with 4,000 per arm – appears a safe as 9 INH
  - Phase 4 monitoring will still need to be done
Too many rifampin drug-drug interactions (184) to remember.
Conclusion

• 3HP, 12-dose DOT regimen
  – Results of TBTC study exciting!
  – Well tolerated DOT in > 4,000 subjects
  – Efficacy given DOT “as good as” 9H self-administered

• How do we go forward now?
  – Public health settings
  – Primary care, private practice settings
Another Tool: The Online TST/QFT Interpreter

The Online TST/QFT Interpreter

Version 2.0

The following tool estimates the risk of active tuberculosis for an individual with a tuberculin skin test reaction of 5mm, based on their clinical profile. It is intended for adults tested with standard tuberculin (5 TU PPD, or 2 TU RT-23). For more details about the algorithm used, go to the About page. The current version of the algorithm contains modifications of the original version, which was described in a paper by Menzes, et al. (2000). For further information see references, or contact dick.menzes@unil.ch.

Please select the best response for each field:

- **TST Size:**
  - Select...

- **QFT Result:**
  - Select...

- **Age:**
  - Select...

- **Age at immigration (if person immigrated to a low TB incidence country):**
  - Select...

- **Country of birth:**
  - Select...

- **BCG status:**
  - Select...

- **Contact with active TB:**
  - Select...

**Results**

Once you have completed the form, click on "Submit" and your results will show up in this space.

For inquiries, and suggestions please contact dick.menzes@unil.ch.
Brief Reports

Using Computerized Clinical Decision Support for Latent Tuberculosis Infection Screening

Andy W. Steele, MD, MPH, Sheri Eisert, PhD, Art Davidson, MD, MPH, Taylor Sandison, MD, Pat Lyons, Nedra Garrett, Patricia Gabow, MD, Eduardo Ortiz, MD, MPH

Results: Among 4135 patients registering during the post-intervention phase, 73% had at least one CDC-defined risk factor, and 610 met the alert criteria (birth in a high-risk TB country and aged <40 years) for potential screening for LTBI. Adherence with the LTBI screening guideline improved significantly from 8.9% at baseline to 25.2% during the study phase (183% increase, \( p < 0.001 \)).

Conclusions: This study demonstrated that computerized, clinical decision support using alerts and guided web-based documentation increased screening of high-risk patients for LTBI. This type of technology could lead to an improvement in LTBI screening in the United States and also holds promise for improved care for other preventive and chronic conditions. (Am J Prev Med 2005;28(3):281–284) © 2005 American Journal of Preventive Medicine
<table>
<thead>
<tr>
<th>Year</th>
<th>No.</th>
<th>Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>14,068</td>
<td>4.8</td>
</tr>
<tr>
<td>2006</td>
<td>13,732</td>
<td>4.6</td>
</tr>
<tr>
<td>2007</td>
<td>13,286</td>
<td>4.4</td>
</tr>
<tr>
<td>2008</td>
<td>12,905</td>
<td>4.2</td>
</tr>
<tr>
<td>2009</td>
<td>11,537</td>
<td>3.8</td>
</tr>
<tr>
<td>2010</td>
<td>11,182</td>
<td>3.6</td>
</tr>
</tbody>
</table>

*Cases per 100,000. Updated as of July 21, 2011
## Progress toward TB elimination

(1.0 case per million/yr)

<table>
<thead>
<tr>
<th>Area (data yr)</th>
<th>Cases</th>
<th>Population (millions)</th>
<th>Rate per million</th>
<th>Year goal*</th>
</tr>
</thead>
<tbody>
<tr>
<td>World (2009)</td>
<td>8,800,000</td>
<td>6,869</td>
<td>1,280</td>
<td>2050</td>
</tr>
</tbody>
</table>

*US, CDC1989; WHO, 2010; Raviglioni, Lancet 2006
TB elimination faces major challenges

- Neither the US or global TB elimination plans are likely to meet the goals of TB elimination
- National and global TB are interconnected
- Funding for more rapid development and implementation of new tools for diagnosis, treatment and prevention will be critical
- Medical providers plus public health providers play key roles in timely diagnosis
- Targeted testing & treatment for LTBI will need to be embraced by primary care providers – implementation & evaluation of new tools will be critical to success (now in US, later globally once TB incidence falls)