Tuberculosis in the 21st Century

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In my opinion, the recent media coverage of the case of drug resistant tuberculosis involving international travel was:

A. Balanced
B. Overblown
C. Confusing
D. None of the above
In the World

• One out of every three persons has been infected with tuberculosis. . . .

• Our story begins . . . .
Reported TB Cases by Race/Ethnicity*
United States, 2005

Hispanic or Latino (29%)
Black or African-American (28%)
Asian (23%)
White (18%)
American Indian or Alaska Native (1%)
Native Hawaiian or Other Pacific Islander (<1%)

*All races are non-Hispanic. Persons reporting two or more races accounted for less than 1% of all cases.
TB Case Rates* by Age Group
United States, 1993–2005

*Updated as of March 29, 2006.
Estimated HIV Coinfection in Persons Reported with TB: United States, 1993–2004*

*Updated as of March 29, 2006.

Note: Minimum estimates based on reported HIV-positive status among all TB cases in the age group.
Reporting of HIV Test Results in Persons with TB by Age Group: United States, 1993–2004*

*Updated as of March 29, 2006.

Note: Includes TB patients with positive, negative, or indeterminate HIV test results and persons from California reported with AIDS. (HIV test results are not reported from California)
Adult TB Cases* by Homeless Status*
1994-2001

* Adult TB case = TB in person aged ≥18 years
* Homeless within year prior to TB diagnosis
Adult TB Cases* by Correctional Facility Status,* 1993-2001

* Adult TB case = TB in person aged ≥18 years old
* Resident of correctional facility at the time of TB diagnosis
Selected Risk Factors: Ten-Year Period, WA 1993-2005

Unemployed, Homeless, Alcohol, Previous Diagnosis

% of Cases

Place
TB Case Rates*: United States, 2005

*Cases per 100,000.

- ≤ 3.5 (year 2000 target)
- 3.6–4.8
- > 4.8 (national average)
TB Low-Incidence States,* 1990–2000

* ≤3.5 TB cases per 100,000 population (Year 2000 target)
Countries of Birth of Foreign-born Persons Reported with TB: US, 2005

- Mexico (25%)
- Philippines (11%)
- Vietnam (8%)
- India (7%)
- China (5%)
- Haiti (3%)
- Guatemala (3%)
- Other Countries (38%)

*Updated as of March 29, 2006.
Proportion of Foreign-born Cases:
WA, 1996-2006
Drug Resistance
Drug Resistance Definitions

• Primary drug resistance
  ▪ Applies to previously untreated patients who are found to have drug-resistant organisms, presumably because they have been infected from an outside source of resistant Mycobacterium tuberculosis.

• Acquired drug resistance
  ▪ Applies to patients who initially have drug-susceptible bacteria that become drug-resistant due to inadequate, inappropriate, or irregular treatment or, more importantly, because of non-adherence in drug taking.
Multidrug-Resistant Tuberculosis (MDR)

- Resistance to at least two of the best anti-TB drugs, isoniazid and rifampicin.
- These drugs are considered first line agents.
Extensively Drug Resistant TB (XDR TB)

• This is a rare type of multidrug-resistant tuberculosis.

• It is resistant to almost all drugs used to treat TB, including all first line agents and the best second-line agents: fluoroquinololones and at least one of three injectable agents (amikacin, kanamycin, or capreomycin).

• There have been only 49 cases in the US since 1993.

*Updated as of March 29, 2006.

Note: Based on initial isolates from persons with no prior history of TB.
Primary Anti-TB Drug Resistance:
WA, 1996-2006

Note: Based on initial isolates from persons with no prior history of TB. MDR TB defined as resistance to at least isoniazid and rifampin.
Primary MDR TB: US, 1993–2005*

*Updated as of March 29, 2006.

Note: Based on initial isolates from persons with no prior history of TB. MDR TB defined as resistance to at least isoniazid and rifampin.
Primary MDR TB: WA, 1996-2006

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New Diagnostics

- Quantiferon
- MTD testing
- Universal genotyping
Commonly Asked TST Questions (1 of 2)

• How do you know and ensure that the medical community using the TST is properly trained?
• Can you place a TST on a Thursday and read on a Monday?
• Who needs a two-step test and why?
• What is the boosted response?
Commonly Asked TST Questions (2 of 2)

• What if the longitudinal reading of the TST is 12mm and the horizontal (official reading) is 8mm? Is that considered positive?

• Can I accept a negative reading if the patient said there was absolutely no reaction and there is no reaction on day four after the test?

• We switched products from tubersol to aplisol, and I noticed more “positives.” We retested with tubersol, and all were negative. Which test do I believe?
The Answer

• Quantiferon
  ▪ Blood-based testing method
MTD

- Mycobacterium Tuberculosis Direct Test (MTD)
- Nucleic acid amplification
- Sensitivity 85.7%–97.8%
- Criteria for use:
  - Smear-positive cases
  - Highly suspicious cases
  - If it will change treatment
Universal Genotyping

• All TB cultures from WA state now sent to CDC for genotyping “fingerprinting”

• Spoligotyping

• MIRU pattern

• Goal is to detect clusters
Homeless TB Cases in King County by Treatment Start Date

- Non-outbreak RFLP
- Outbreak RFLP
- No known epi link (RFLP pending)
- Second RFLP cluster
- Epi-link (RFLP pending)
- Clinical case

No. Cases

Treatment Start Date

- Jan
- Mar
- May
- Jul
- Sep
- Nov
- Jan
- Mar
- May
- Jul
- Sept
- Nov
- Jan
- Mar
- May
- July
- Sept
- 2002
- 2003
- 2004
Treatment

• DOT (consistency is key)
  ▪ Latent TB infection nine months
  ▪ Pulmonary six months
  ▪ Meningitis 12 months
  ▪ Adenopathy six months
  ▪ Bone/Joint 12 months

• Monthly weight check
Treatment Evaluation

- HIV screen
- Hep B and C (if risk factors)
- AST
- ALT
- Bilirubin
- A.Phos.
- Creatinine
- Platelets
- Vision testing (if Ethambutol used > 2 mo.)
Ongoing Diagnostic Monitoring

• Monthly sputum collection (until two negative smears).
• Look for smear positive cases after initial two months of therapy.
• Liver function tests if abnormalities on screening or risk factors for hepatitis.
DOT or Not to DOT

• Strongly recommended.

• Patient centered approach is more successful.
  - Social service support
  - Treatment incentives and enablers
  - Housing assistance
  - Substance abuse treatment
TB Case #1: “Doc, can he fly home?”

• 17-year-old male exchange student from Azerbaijan.
• BCG at birth.
• One month of cough, hemoptysis, weight loss, and acute chest pain.
• He presents to your office. . .now what do you do?
Feedback Poll

What is your first step?

A. Place a PPD and order a chest radiograph
B. Place this patient in an N-95 mask
C. Start four drug therapy
D. All of the above
Results

- PPD 19 mm
- Cavitary right upper lobe on radiograph
- AFB smears all negative
The Rest of the Story

• Sputum MTD was positive
• Repeat of the AFB at state lab was positive
• INH, Rifampin, PZA and Ethambutol started
• Patient instructed not to fly home
• Held from last two days of high school
• Contact investigation begun
• Host family asks to have him removed from home.
Further Dilemmas

• Where can he go?
• When can he fly home?
• How certain are you that this is not XDR?
Feedback Poll

Can he fly home?

A. Yes

B. No
Contact Dr. Lindquist

You can call Dr. Lindquist with your TB-related questions at:

360-337-5237
206-718-2664

Or contact him by e-mail at:

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