

Epidemiology of tuberculosis among the foreign-born in the United States

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Overview

- The problem
- Methods of approach; strengths & weaknesses
 - Surveillance data
 - Molecular epidemiology
- Where do we go from here?

WHO: 1/3 of the world has latent tuberculosis infection (LTBI)

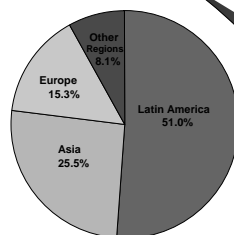


TB cases worldwide
From Frieden et al. Lancet 2003

WHO high-burden TB countries, 2004 (>80% of global TB)

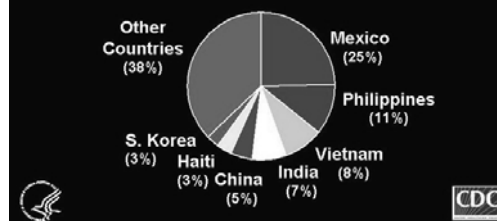
- | | |
|----------------------------|----------------------|
| ● Afghanistan | ● Myanmar |
| ● Bangladesh | ● Nigeria |
| ● Brazil | ● Pakistan |
| ● Cambodia | ● Philippines |
| ● China | ● Russian Federation |
| ● Democratic Rep. of Congo | ● South Africa |
| ● Ethiopia | ● Thailand |
| ● India | ● Uganda |
| ● Indonesia | ● Tanzania |
| ● Kenya | ● Viet Nam |
| ● Mozambique | ● Zimbabwe |

Percent Distribution of Foreign Born in the U.S. by World Region of Birth: 2000



The foreign born represent 10.4 % of the U.S. population, and 28.4 million people.

Countries of Birth for Foreign-born Persons Reported with TB United States, 2002



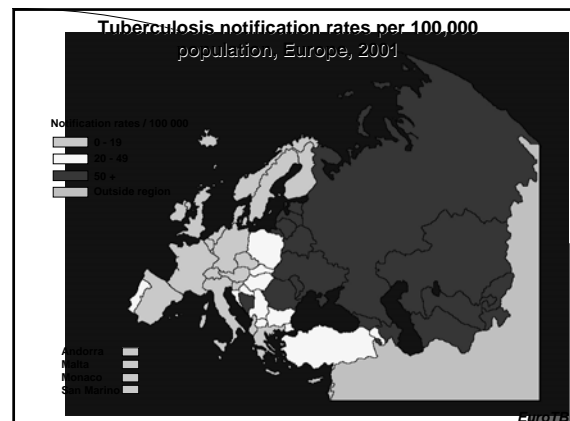


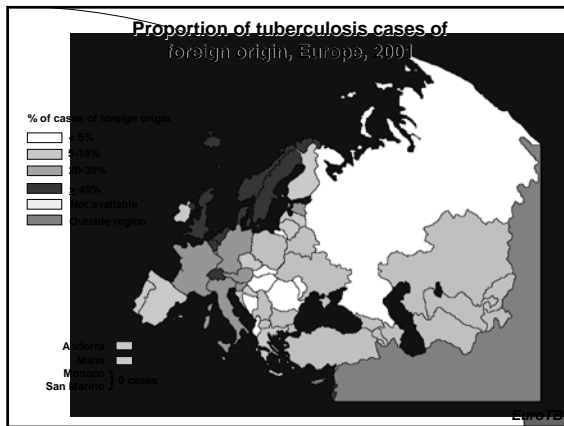
We are not alone

- What is happening in US has happened/is happening elsewhere:
- When did foreign-born TB cases exceed 50% of reported cases in other countries?
 - France: 1985
 - Canada: 1990
 - Netherlands: 1996
 - US: 2003

TB in established market countries

- US, Canada, Western Europe, Israel, Australia, New Zealand, Japan
- Comparisons can be difficult
 - Various definitions of foreign-birth: country of birth, country of citizenship, ethnicity
 - Country of origin may be missing by design (illegal to collect)





Israel: dramatic changes in a low prevalence country

- 1989-95: Population grew by 1 Million
 - 2002 Population = 6.1 Million
 - Europe/America-born 32.1%, Africa-born 14.6%, Asia-born 12.6% (2002) (from CIA Factbook)
- 4-fold increase in TB 1989-91 (Chemtob, 2002 & 2003)
 - FB TB 80-85% of all TB
 - former Soviet Union (>25% of cases in 1996): 38-172 per 100K
 - Ethiopia (54% of cases in 1991): 500-3000 per 100K

Surveillance Studies

What can we learn from them?

CDC studies of registry data (1)

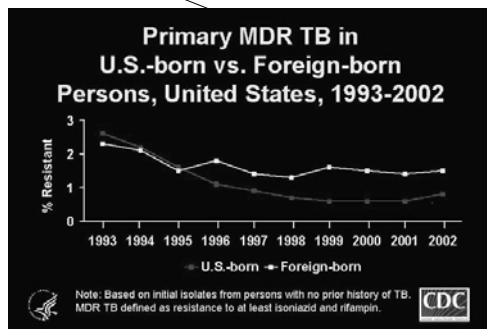
- McKenna MT, McCray E, Onorato I. The epidemiology of TB among foreign-born persons in the US, 1986-1993. (NEJM 1995).
 - 55% of cases diagnosed < 5 yrs; 30% < 1 yr post-arrival
 - More cases in younger immigrants than older immigrants, but lower case rate: cohort effect?
 - Largest relative difference between US-born and FB TB rates is among aged <15 yrs
 - → substantial recent transmission around time of immigration (pre and post)

CDC studies of registry data (2)

- Zuber PT, McKenna MT, et al. Long-term risk of tuberculosis among foreign-born persons in the United States. (JAMA 1997)
 - Long term residents arriving aged > 5 yrs have TB rate 2-6 times the rate of those who arrived before their 5th birthday → Imported TB responsible for most FB TB
 - Selective screening needs to be adapted to local circumstances – places of origin, SES, migration patterns

Drug resistance and the foreign-born TB case

- More complicated and expensive to treat
- Association with time in US
 - Greater rate among recent arrivals
 - TB acquired in country of origin?
- Rx for LTBI among FB needed, esp. those from high prevalence countries, but may be ineffective if there is resistance



CDC studies of registry data (3)

- Talbot EA, Moore M, et al. TB among foreign-born persons in the US, 1993-98. (JAMA 2000)
 - CA, NY, TX, FL, NJ, IL = 73.4% of FB TB
 - Most common birth countries vary by state:
 - TX, CA, IL: Mexico; FL: Haiti; NJ: India; NY: China, Dominican Republic, Haiti
 - 10% have known HIV infection
 - less likely to be paired with TB as HIV infection is excludable condition for entry to US
 - More than half of FB HIV/TB is in CA or NY
 - Mostly among persons from Haiti or Mexico

CDC studies of registry data (3, continued)

- Diagnosis of pulmonary TB in FB more likely by clinical criteria than in US-born: 14.3% vs. 10.9%
 - FB more likely than US-born to be smear-negative
 - 47.3% vs. 36.7%
 - And more likely to be culture-negative
 - 17.4 vs. 12.2%
 - High index of suspicion for TB among FB when chest radiograph is abnormal OR
 - Incomplete treatment prior to immigration?

CDC studies of registry data (3, continued)

- TB control activities targeting prompt identification of TB and completion of therapy *will not* reduce TB among the FB
- Geographic variation of TB requires locally tailored approaches
 - Areas with recent (case identification) vs. remote arrivals (screen for LTBI)
 - Areas of high isoniazid resistance may require alternative LTBI treatment regimens

Surveillance cannot tell us (1)

- Are persons with active disease entering the US?
 - Screening of immigrants – does it work?
 - Contribution of non-screened foreign-born
 - Temporary workers
 - International students
 - Undocumented
- Is current transmission taking place in the US?
 - Within foreign-born communities
 - From/to the foreign-born to/from the US-born

Surveillance cannot tell us (2)

- Among FB persons with latent TB infection (LTBI), who are high risk groups, i.e., likely to develop active TB?
- Who will accept treatment for LTBI? Who will complete treatment?

Surveillance cannot tell us (3)

- How a patient's lack of understanding of TB, cultural misunderstandings, economic barriers, lack of acculturation, etc. can contribute to delays in diagnosis
- How the health care system and health care providers can contribute to delays in diagnosis

Are persons with active disease entering the US?

Screening of immigrants as a TB control activity

- Who is screened?
 - Screened persons are those applying for permanent residence (overseas or in US) or refugee status
 - Immigration & Control Act of 1986: undocumented regularize status
- Classifications
 - Active, smear positive TB cases – excludable condition
 - B notifications – reports sent to local health departments (HDS), immigrants told to report to HDS
 - B1 chest radiograph suggesting active TB but negative sputum
 - B2 chest radiograph compatible with inactive TB

Some follow-up studies of B notifications (1)

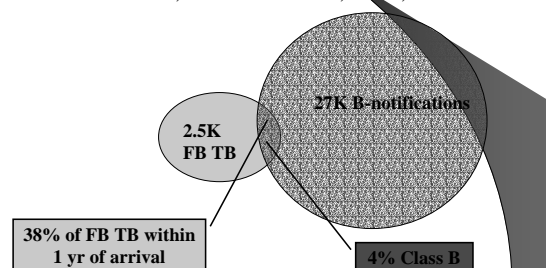
- DeRiemer K, Chin DP, et al. 1998
 - 893 immigrants & refugees with San Francisco as intended destination and a referral for further medical evaluation
 - 84% sought further medical evaluation
 - 7% had active TB: Class B-1 predictor of TB: 3.5 OR

Studies of follow-up (2)

- Zuber PL, Knowles LS et al. 1996
 - Los Angeles County registry matched against tracking system for immigrants & refugees with suspected TB
 - Tracking system contained
 - 5% of Mexican and Central American cases
 - 48% of NE Asian cases (Chinese, Korea, etc.)
 - 67% of SE Asian cases (Viet Nam, Thailand, etc.)

Studies of follow-up (3)

- Sciortino S, Mohle-Boetani, et al., 1999



Sciortino S, Mohle-Boetani, et al. 1999 (continued)

- But B notifications did not identify 87% of the smear-positive adult TB cases!

Screening of international students - NO

- 500,000 + international students in the US in 2000-2001.
 - Top 5 countries: India, China, Korea, Japan, Taiwan (Institute of International Education)
- CDC (Hennessey KA, 1998): screening for LTBI among college students is inconsistent and problematic
- Texas (Weis SE, 2001), Ohio (Nelson ME, 1995): TB among non-screened visitors is substantial

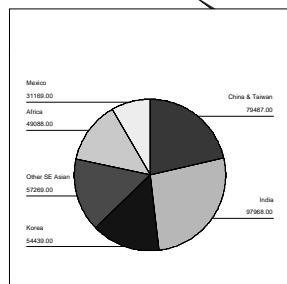
Screening of temporary workers - NO

- MMWR 45(47):1032-6, 1996.
 - 181 FB Hispanic TB patients in eight US counties in AZ, NM, TX, CA bordering Mexico, 1995.
 - 169 interviewed for the study, visa status not collected
 - 82% returned at least once to their country of origin
 - 35% returned at least monthly in the year preceding diagnosis
- Migrant workers
 - Difficulties in treating mobile populations
 - Migrant Clinicians Network www.migrantclinician.org
 - Restricted circuit, point-to-point, nomadic

H-1B visa category

- For professionals working in specialty occupations; limited to 65,000 annually
- Created by Immigration Act of 1990
 - Pre-1990: Abnormal x-rays plus negative sputum required waivers to enter country
 - Post-1990: Liberalization: to discourage sub-optimal overseas treatment
- Incidence of TB? Unknown.

Census 2000 estimates of temporary workers by selected countries of origin



Is current transmission taking place in the US?

- Within foreign-born communities
- From/to the foreign-born to/from the US-born

Molecular epidemiology (1)

- Identical fingerprints thought to represent recently transmitted disease (Alland et al. Bronx, NY & Small et al. San Francisco, NEJM 1994)
- US-born more likely than FB to have clustered (identical) IS6110 fingerprints
- Lack of fingerprint clustering among FB means reactivation, yet surveillance studies point to recently acquired disease!
 - Catchment area: FB from particular country/region in US. What about the those remaining back home?

Molecular epidemiology (2)

- Secondary typing methods
 - reduce extent of clustering (Burman WJ, 1997)
 - → reduce the proportion of TB due to “recent infection”
 - Validation: using epidemiologic links
 - Links found for
 - 11% of patients with discordant fingerprints
 - 78% of patient isolates that matched by both IS6110 and pTBN12

Molecular epidemiology (3)

- BUT there is clustering among FB TB
 - El Sahly et al., 2001: 30% of FB TB in Houston
 - Ellis BA et al., 2002: 35% of FB TB
 - AR, MD, MS, MI, NJ, Dallas plus 3 Counties in TX; and 6 Counties in CA
- Recent transmission?
- Limited genetic diversity in the country of origin (founder effect)?

Molecular epidemiology (4)

- Is transmission from the foreign-born to non-foreign-born occurring?
 - San Francisco: In 8 of 9 clusters that included both US & Mexican-born, index case was US-born (Jasmer RM et al., 1997)
 - Netherlands: RFLP shows transmission within FB communities and from FB to Dutch (Borgdorff et al., 1998)

Among FB persons with LTBI, who are high risk groups?

- Especially high-risk: children, health care personnel, the HIV infected, people with other co-morbidities (diabetes), smokers (?)
- Who will accept treatment for LTBI? Who will complete treatment?

“Foreign-born” children

- Higher prevalence of LTBI among children with FB parents, visitors from abroad, travel abroad (Lobato M et al., 1998)
- Source cases: < 50% of children have one
 - Harder to identify for FB children
 - However, of children with potential source cases, >50% of the source cases are FB (Sun SJ et al., 2002)

Occupational health

- FB health care personnel
 - hard to interpret annual TST: BCG? LTBI acquired in country of origin?
- FB TB patients more likely to be working than US-born TB patients
 - Implications for workplace contact investigations
 - Kim DY, Ridzon R, et al., 2002: DE poultry workers, work-related cluster ruled out using spoligotyping
 - Undocumented workers in particular industries

Where does surveillance go from here?

- RVCT Revision Working Group
 - projected roll-out 2006
 - Last revision 1992
- TB Epidemiologic Studies Consortium, Task 9
 - **“Enhanced surveillance to identify missed opportunities for prevention of tuberculosis in the foreign-born”**
 - pilot study beginning April 2004

Where does molecular epidemiology go from here?

- Many secondary typing methods available
 - Spoligotyping, others
- Approaches to quantify the extent to which fingerprints do not match
 - Genetic distance: expected waiting time for the steps required to diverge from a hypothetical common ancestor
 - Dice coefficient: measure of similarity
- Is an identical fingerprint necessary to conclude that there is a recent chain of transmission?