Definitions

• CDC = U.S. Centers for Disease Control and Prevention
• TB = Tuberculosis
• IGRA = Interferon gamma release assay (“TB blood test”)
• TST = Tuberculin skin test, Mantoux, PPD
• LTBI = Latent TB infection
• LPH = Local public health agency
• MDH = Minnesota Department of Health
After this presentation, participants will be able to:

1. Understand the social context of tuberculosis and the role of public health in its prevention and control.

2. Describe key trends in the epidemiology of tuberculosis among immigrants to the U.S. and MN/ND.

3. Name the difference between immigrant and non-immigrant U.S. visas and be able to identify specific types of each.
After this presentation, participants will be able to:

4. Compare the purposes of the overseas U.S. Immigration Medical Exam versus a standard domestic TB screening.

5. Name 2 steps all health care providers can take to help eliminate TB in our communities.

6. Identify 2 challenges to successful TB outcomes in immigrant populations and describe how they may be overcome.
TB Basics: Pathogenesis and Transmission
Pathogenesis and Transmission

• TB is caused by a bacteria called *Mycobacterium tuberculosis* (MTB)

• TB spreads from person-to-person by tiny “droplet nuclei” suspended in the air after someone with infectious TB coughs, sings, talks, sneezes, etc.

• Most people with TB do not know how or when they became infected.
## Latent TB Infection & Active TB Disease

<table>
<thead>
<tr>
<th>Phase 1: Latent TB Infection</th>
<th>Phase 2: Active TB Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>A small number of TB germs are “asleep” in their body. This phase can last for a very long time.</td>
<td>A large number of TB germs are “awake” and spreading. Can be in the lungs or in other parts of the body.</td>
</tr>
<tr>
<td>No symptoms. TST or IGRA is positive. Chest x-ray is negative (normal or abnormal but not active TB disease.)</td>
<td>Symptoms may be present. 75-90% have positive TST. May have an abnormal chest x-ray.</td>
</tr>
<tr>
<td>Not infectious – non-reportable to MDH, reportable to NDDoH</td>
<td>May be infectious – mandatory reportable disease to MDH or NDDoH</td>
</tr>
<tr>
<td>Treated by taking 1-2 drugs for 3 - 9 months. **Rule out of active disease prior to treatment.</td>
<td>Treated by taking 3 - 4 drugs for 6 – 12 months. **Up to 2 years if MDR.</td>
</tr>
</tbody>
</table>
True or False: If I have a brief encounter with someone who has infectious TB (example: 30 minutes spent in same room without PPE), my chances of getting it are pretty high (> 50%).

Answer: FALSE
Transmission

Close exposure to someone with infectious TB

- 60-70% Uninfected
- 30-40% Infected

90% Latent TB Infection

- 50% within 1-2 years
- 50% > 2 years

10% Active TB

Persons with both HIV and LTBI have a 10% annual risk of developing active TB
TB Basics: Social Determinants
“[Tuberculosis] is a social disease...its understanding demands that the impact of social and economic factors on the individual be considered as much as the mechanisms by which tubercle bacilli cause damage to the human body.”

Dr. René Dubos (1901–1982)
Tuberculosis thrives in conditions of:

- Poorly ventilated or overcrowded living or working environments (including homeless shelters, prisons, and substandard housing)
- Poor health infrastructure
- Malnutrition or under-nutrition
- Drug and/or alcohol abuse
Increased Likelihood of Exposure to Persons with TB Disease

Persons at risk for acquiring TB include:

• Immigrants from TB-endemic regions of the world.

• Close contacts to person with infectious TB

• Residents and employees of high-risk congregate settings (e.g., correctional facilities, homeless shelters, health care facilities)

• Persons who abuse alcohol or drugs

Increased Risk for Progression to TB Disease

Persons at risk for progression to disease once infected include:

• HIV-infected persons
• Those with a history of prior, untreated TB or fibrotic lesions on chest radiograph
• Children ≤ 5 years with a positive TST
• Underweight or malnourished persons
• Those on TNF-α antagonists for treatment of rheumatoid arthritis or Crohn’s disease
• Those with certain medical conditions such as: Silicosis, Diabetes mellitus, Chronic renal failure or on hemodialysis, Solid organ transplantation (e.g., heart, kidney), Carcinoma of head or neck, Gastric bypass

Epidemiology of TB
Always remember:

Statistics are people with the tears washed away.

- A wise person
The Global Context of TB

2015 World Health Organization Global Statistics

• Estimated that 1/3rd of the world’s population has LTBI
• 10.4 million people with TB disease
  • Including 1 million children
  • Estimated 480,000 people with MDR-TB
• Only about 60% had access to quality TB care
• 1.8 million people died from TB
• 9th leading cause of death worldwide – kills more people than HIV
True or False:

Due to increasing immigration, the total number of active TB cases in the United States has increased over the past 10 years.

Answer: FALSE
TB in the United States

United States TB Cases & Rates, 1953-2011

Data source: cdc.gov/tb
Number of TB Cases Among U.S.-Born versus Non U.S.-Born Persons, United States, 1993–2015*

Data source: cdc.gov/tb

* As of June 9, 2016.
TB Case Rates Among U.S.-Born versus Non U.S.-Born Persons, United States, 1993–2015*

Data source: cdc.gov/tb

* As of June 9, 2016.
In 2015, the most common country of birth of non U.S-born persons who were diagnosed with active TB in the United States was:

A. India
B. Mexico
C. Somalia
D. Iraq
Countries of Birth Among Non U.S.-Born Persons Reported with TB, United States, 2015*

* As of June 9, 2016.

Data source: cdc.gov/tb
### Tuberculosis Morbidity and Mortality, Minnesota, 2012-2016

<table>
<thead>
<tr>
<th>Year</th>
<th>No. Cases (Rate)*</th>
<th>No. Deaths** (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>162 (3.0)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>2013</td>
<td>151 (2.8)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>2014</td>
<td>147 (2.7)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>2015</td>
<td>150 (2.7)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>2016</td>
<td>168 (3.1)</td>
<td>7 (4%)</td>
</tr>
</tbody>
</table>

* Cases per 100,000 population. Rates calculated using state population estimates from the U.S. Census Bureau.

**Represents only deaths due to TB disease or TB drug-induced toxicity
Active TB cases and incidence rate in North Dakota, 2012-2016

Source: NDDoH Division of Disease Control
Percentage of Non U.S.-Born Tuberculosis Cases, United States and Minnesota, 2007-2016

Ave: 82%

Ave: 63%
Number of active TB cases by place of birth, North Dakota, 2012-2016

Source: NDDoH Division of Disease Control
Tuberculosis Disease: Minnesota, 2012–2016

Hennepin: 303
Ramsey: 173
Suburban metro: 112
Greater MN: 190

Total: 778
TB in North Dakota

Tuberculosis Disease: North Dakota, 2012–2016

Source: NDDoH Division of Disease Control
True or False: In Minnesota, non U.S.-born patients with TB disease are more likely to have an extra-pulmonary site of TB than U.S.-born patients with TB disease.

Answer: TRUE
Tuberculosis Cases by Site of Disease and Place of Birth, Minnesota, 2011-2015

* Includes cases with or without concurrent pulmonary disease

* Pulmonary only  Extrapulmonary*

* * Includes cases with or without concurrent pulmonary disease
Tuberculosis Cases by Risk Category* and Place of Birth, Minnesota, 2011-2015

- Recent contact: 6% (All), 4% (USB), 2% (Non-USB)
- Other medical condition**: 20% (All), 21% (USB), 20% (Non-USB)
- Substance abuse†: 3% (All), 5.5% (USB), 3% (Non-USB)
- Healthcare worker: 7% (All), 8% (USB), 7% (Non-USB)
- HIV-infected: 4% (All), 1.5% (USB), 4% (Non-USB)
- Homeless: 6% (All), 2% (USB), 6% (Non-USB)
- Long-term care resident: 2% (All), 2% (USB), 0.3% (Non-USB)
- Incarcerated: 1.5% (All), 0.8% (USB), 0.7% (Non-USB)

* Risk categories are not mutually exclusive
** Conditions or therapies † † risk for progression to active TB disease, not HIV
† Alcohol abuse and/or illicit drug use
Non U.S.-Born Tuberculosis Cases by Country of Birth, Minnesota, 2011-2015

- Somalia: 28%
- Ethiopia: 13%
- Laos: 8%
- Viet Nam: 6%
- Mexico: 5%
- India: 5%
- Kenya: 4%
- Other: 31%

N = 612

- Refugee: 48%
- Immigrant: 29%
- Other*: 19%
- Unknown: 4%

* “Other” includes visitors, tourists, students, those arriving on employment visas

N = 612
Non U.S.-Born Tuberculosis Cases by Interval Between Arrival in U.S. and Diagnosis of Tuberculosis, Minnesota, 2011-2015

- <1 year: 18%
- 1-2 years: 15%
- 3-5 years: 16%
- 6-9 years: 15%
- 10+ years: 36%
- Unknown: <1%

N = 612
Basic elements of a TB Program:

1. Active TB disease
2. Contact investigation
3. Targeted testing and treatment of LTBI
4. Infection control measures in high-risk settings
Tuberculosis Cases by Method of Case Identification, Minnesota, 2012-2016

- TB symptoms: 81%
- Other: 19%

- TB contact investigations: 4%
- Incidental chest x-ray: 2%
- Other targeted testing: 3%
- Refugee health exam (domestic): 3%
- Overseas TB class follow-up: 3%
- Incidental lab result: 1%
- Other*: 3%

* “Other” includes: other immigration exam – 1% and employment screening (including health care worker screening) – 1.5%

N = 778
CDC Division of TB Elimination (DTBE) strategic plan goals:

• Domestic: eliminate TB in the U.S. (case rate of < 1/1,000,000)
• Global: contribute to reductions in global incidence and mortality by 50% each (compared to 1990)

**DTBE Priorities:**

1. Prevent new cases of infection and disease with *Mycobacterium tuberculosis*.
   - Find and cure all persons with TB.
2. Reduce TB in foreign-born persons residing in, or traveling to the United States.
3. Reduce TB in U.S. racial/ethnic minority populations and measure/address social determinants of health.
4. Reduce impact of multidrug- and extensively drug-resistant TB in the United States and globe.
5. Reduce HIV-associated TB in the United States and globe.
The U.S. Immigration System and Medical Exam
True or False:

People from all TB endemic countries must receive TB screening before they are allowed to come to the U.S.

Answer: FALSE
The U.S. Immigration System

Based on U.S. Department of Homeland Security Definitions
2015 Non-citizen Admissions to the U.S.

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immigrants</td>
<td>1,051,031</td>
</tr>
<tr>
<td>New Arrivals</td>
<td>508,716</td>
</tr>
<tr>
<td>Adjustment of status</td>
<td>542,315</td>
</tr>
<tr>
<td>Refugees/Asylees</td>
<td>77,036</td>
</tr>
<tr>
<td>Nonimmigrants/Temporary visa</td>
<td>181 million...</td>
</tr>
<tr>
<td>Pleasure</td>
<td>61,017,237</td>
</tr>
<tr>
<td>Business</td>
<td>8,008,659</td>
</tr>
<tr>
<td>Workers and families</td>
<td>3,722,543</td>
</tr>
<tr>
<td>Students</td>
<td>1,990,661</td>
</tr>
</tbody>
</table>
All persons applying for *immigrant* visas MUST have a medical exam done overseas as part of their application process. This includes:

1. Lawful permanent residents (LPR) “green card”:
   - Relatives of U.S. citizens or LPRs
   - Fiancées
   - Adoptees
   - Employees and investors
   - Special immigrant visas
   - Diversity program
All persons applying for *immigrant* visas MUST have a medical exam done overseas as part of their application process. This includes:

2. Lawful temporary residents (LTR) – Must adjust their status to LPR after one year.
   - Refugees
   - Asylees
   - Parolees
The U.S. Immigration System

Persons who wish to enter the U.S. temporarily apply for *non-immigrant* visas and do not need a medical exam. This includes:

- Students
- Tourists
- Temporary employment
- Business visitors
- Diplomats, athletes, entertainers
Medical Examination for Entry into the U.S.

*Pre-Immigration or Overseas Exam*

**Purpose:** To screen for certain medical conditions relevant to U.S. law

- Required for entry into the U.S. as an immigrant
- Administered by Panel Physicians (training and guidelines provided by CDC)
- NOT a comprehensive medical exam; expires in 3-6 months
### Excludable conditions

<table>
<thead>
<tr>
<th>Communicable diseases of public health significance</th>
<th>Physical and mental disorders with associated harmful behaviors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Infectious TB</td>
<td>• Psychoactive substance abuse and dependence</td>
</tr>
<tr>
<td>• Syphilis</td>
<td>• Other physical or mental abnormalities, disorders or disabilities</td>
</tr>
<tr>
<td>• Gonorrhea</td>
<td></td>
</tr>
<tr>
<td>• Hansen’s disease (leprosy)</td>
<td></td>
</tr>
</tbody>
</table>

**Removed from list:**

- HIV (2010)
- Chancroid
- Granuloma inguinale
- Lymphogranuloma venereum (2016)

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*Note: every immigrant regardless of their arrival category must have this screening in order to come to the USA.*
The U.S. Immigration Medical Exam

Tuberculosis Screening and Treatment Technical Instructions (TIs) using Cultures and Directly Observed Therapy (DOT) for Panel Physicians (‘07 TB TIs)

- Revised in 2007 from 1991 TB TIs
  - Global implementation – all countries as of October 1, 2013
  - DTBE & DGMQ involvement
  - Small update in 2009
The U.S. Immigration Medical Exam

‘07 TB TIs Components

• Medical history
• Physical examination
• TST (for ages 2-14) or IGRA*
• CXR (for ages ≥15 and those younger with + TST/IGRA)
• If abnormal CXR:
  • Sputum smears & cultures
  • Drug susceptibility testing on positive cultures
  • Treatment for active disease
  • Identify contacts to cases of TB disease

*Does not apply in countries where TB incidence rate is <20 cases per 100,000 population.
TB Classifications – 2007 TIs

No Class – All TB testing performed was negative or normal.

Class A TB – active TB disease, sputum smear and/or culture positive; requires a waiver (i.e., on treatment and smear negative prior to travel).

Class B1 TB, Pulmonary – CXR abnormal suggestive of TB with negative sputum smears and cultures; includes previously treated TB.

Class B1 TB, Extrapulmonary – evidence of extrapulmonary TB

Class B2 TB – LTBI (TST > 10 mm or IGRA +) and normal CXR

Class B3 TB – recent contact of a known infectious TB case
Post-immigration (domestic) follow-up

- Electronic notification system for all refugee and TB Class arrivals
- Provides overseas exam information for arrivals
- Database for outcomes of TB Class arrivals
- Enables jurisdictions to transfer records to other jurisdictions
- ALL states participating, some counties and clinic-level users
- Housed at CDC – DGMQ
Why is this domestic screening of immigrants important?

The overseas exam only clears the person for travel to the U.S. It rules out active, pulmonary, infectious TB at time of exam. It is *not* meant to be diagnostic of other TB conditions.

What is the purpose of a domestic TB evaluation?

To evaluate the person for active pulmonary TB, extrapulmonary TB, and LTBI, and to treat these conditions, if found.
(Potential) Opportunities for TB screening for non-U.S. born persons:

- Overseas Exam (not comprehensive)
- Domestic Refugee Health Assessment
- Domestic TB Class Follow-up
- Adjustment of Status
- Primary care
Roles – How can you help?

Winner of the "Not My Job" Award - ADOT
Litchfield Park, AZ 85
• 73 year old male, born in Laos
• Been in the U.S. for over 10 years
• Hx +TST and LTBI treatment with INH through public health
<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/2011</td>
<td>Pre-operative CXR: Consolidation in LUL. Unrelated surgery, incidental finding</td>
</tr>
<tr>
<td>7/2011</td>
<td>SOB. Chest CT: Left lung opacity c/w dense pneumonia. Treated with?</td>
</tr>
<tr>
<td>6/2013</td>
<td>Seen for cough: Dx bronchitis, given macrolide</td>
</tr>
<tr>
<td>10/2013</td>
<td>CXR for shortness of breath: Infiltrate in LLL and LUL</td>
</tr>
<tr>
<td>1/2015</td>
<td>Clinic visit for cough, SOB, night sweats, wt loss:</td>
</tr>
</tbody>
</table>

“C/O chronic cough and wheezing over past 6 months ... SOB climbing 12 steps ... no fever, night sweats, weight loss ... on bronchodilators with some benefit ... foreman of gravel company in Laos for 3 years in early 2000s.” P.E.: soft expiratory wheezing throughout all lung fields. CXR and CT ordered. Referral to Pulmonology: didn’t go.
2/2015  

Chest CT: Decreased size of opacity, but now cavitary

2/12/15: Chest CT. Indication: cough shortness of breath, abnormal CXR. Comparison: CXRs from 10/2/13 and 6/10/11 and chest CT from 7/23/2011 – Outpatient

‘Opacity in the medial aspect of the left lung has been present since at least 6/10/11 and has decreased in size. Much of the process has undergone central cavitation with associated volume loss in the left hemithorax... scattered nodular pulmonary opacities peripheral to the opacity at the left hilum have decreased in size, number and extent... wall thickening and luminal narrowing in the left upper and lower lobar bronchi... single right hilar lymph node is enlarged, but stable.’

Conclusion: “opacity in the medial aspect of the left lung has decreased in size and extent and undergone cavitation... though nonspecific, the chronicity, regression and cavitation favor sequelae of prior infection, including tuberculosis. No findings specific for active infection.”
6/2016  Presents to the ER

“presents with worsening chronic cough and hemoptysis . . . patient reports an intermittent chronic cough, but state this dramatically worsened approximately 2 days ago . . . 150 ml of blood”.

• Patient interviewed about ‘chronic cough’
  • He sought care repeatedly, at 3 different clinics due to continuing symptoms
  • Went to a healer but realized that was not helping
  • Went back to a provider
Finally! Sputum were collected and sent for AFB smear, PCR, and culture.

- **Diagnosis: Active Tuberculosis**

- **Given social history (lived in a refugee camp known to have had drug resistant TB) and prior LTBI tx – MDH sent specimen to CDC for molecular drug resistance testing**

- **Final results: Resistant to isoniazid, rifampin, (and ethambutol): MDR TB!**

- **Infectious period: 3/10/2011 - 6/10/2016.....5 years!**

- **Index to an outbreak of 11 cases of MDR TB and counting.**
The most important thing you can do:
Remember, approx. 80% of MN patients with active TB are diagnosed only after seeking care for symptoms.

- Keep TB in your differential if the patient has *any* risk
  - Even if the patient reports previous negative testing
  - Even if the patient reports previous LTBI treatment

- Avoid prescribing fluoroquinolones as broad-spectrum antibiotics if TB is a possibility
  - They are 2\textsuperscript{nd} line TB drugs and can make diagnosis more difficult
Health Care Clinic and Hospital Providers

The 2nd most important thing you can do:
Screen those at-risk for TB!

• Refer probable active disease patients to Infectious Disease and county public health for follow-up *mandatory report to state health dept

• Provide patient with education materials regarding their diagnosis.

• Prescribe treatment

• Monitor treatment - LTBI via clinic, if not referred to county public health

• Provide proof of treatment completion
Local Public Health

- Coordinate screening new arrivals and high-risk patients
  - Public health nurses often wear many disease “hats”
- Case manage probable and confirmed active disease patients
- Provide Direct Observed Therapy (DOT)
  - Active TB disease cases
  - High-risk LTBI, i.e. HIV, children ≤ 5 years
- Monitor patient treatment response; side effects, and adherence
- Conduct contact investigations
Community Organizations

• Provide reliable information and educational materials to communities affected by TB
• Assist in connecting people with health care and other available resources
• Advocate and spread the word – TB is still an issue in the U.S.
• But also...Fight the stigma!
Clinical Considerations

Estimated incidence of MDR/RR-TB in 2015, for countries with at least 1000 incident cases

* MDR = multidrug-resistant; RR = rifampicin-resistant
MDR/RR-TB = RR-TB cases including MDR-TB cases
IGRA use in persons born in TB endemic countries:

Preferred due to better specificity than the TST
• Specific to *Mycobacterium tuberculosis*
• Does not detect BCG

Important for persons born outside the U.S.
• May have been exposed to non-TB mycobacteria
• Many come from countries where BCG vaccination is common

Not recommended for children under 5 years old.

*If possible, ditch the TST!*
Social Considerations

Barriers to Successful Screening and Treatment

• Stigma of TB
• Lack of insurance or payment source
• One of many health or life issues
Social Considerations

Barriers to Successful Screening and Treatment

• Beliefs of origin of disease/preventative care
• Culture and trust of the health care system
• Transportation
• Language barrier
Resources and References
References and Resources


Ending Neglect: The Elimination of Tuberculosis in the United States (2000):

CDC Division of Tuberculosis Elimination Strategic Plan:
https://www.cdc.gov/tb/about/strategicplan.pdf

TB Technical Instructions for Panel Physicians: Implications for U.S. Practitioners
• 2012 webinar by the New Jersey Medical School/Rutgers Global TB Institute
http://globaltb.njms.rutgers.edu/educationalmaterials/audioarchives.html

CDC Division of Global Migration and Quarantine (DGMQ):
http://www.cdc.gov/ncezid/dgmq/

CDC’s Tuberculosis Screening and Treatment Technical Instructions (TB TIs) Using Cultures and Directly Observed Therapy (DOT) for Panel Physicians: http://www.cdc.gov/immigrantrefugeehealth/exams/ti/panel/tuberculosis-panel-technical-instructions.html

MDH TB Program Website: http://www.health.state.mn.us/tb
• Including patient education fact sheets in 17 different languages

CDC’s Updated Guidelines for Using IGRAs to Detect MTB infection – United States, 2010: http://www.cdc.gov/mmwr/PDF/rr/rr5905.pdf
“Every person with TB has the right to be treated for his or her disease. TB can be cured. This scourge can be defeated. So let us stop denying them this basic human right.”

– Archbishop Desmond Tutu,
Madrid, Sept 15th, 1999
Thank you!

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