Human Tuberculosis Caused by *Mycobacterium bovis*:
Identification, US and Global Epidemiology, and Transmission

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**M. tuberculosis Complex**

- *M. tuberculosis*
- *M. bovis*
  - BCG strains (attenuated *M. bovis* developed for vaccine)
- *M. africanum*
- *M. microti*
- *M. canetti*
- *M. caprae*
- *M. pinnipedii*
- *M. mungi*

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Which Organisms Are the Most Important Causes of Human TB?

- Developed countries (e.g., USA), estimates
  - *M. tuberculosis*: 98% of cases
  - *M. bovis*: 1.5% of cases
  - Others: very rare
  - Some geographic variation, e.g., San Diego
- Developing countries
  - Unknown, but *M. bovis* likely to account for higher percentage of disease where organism is enzootic in cattle and pasteurization is not widely used (e.g., parts of Africa)
Clinical and Radiographic Manifestations of Tuberculosis Caused by *M. bovis*

- *M. tuberculosis* disease and *M. bovis* disease in humans are clinically and radiographically indistinguishable
- Differentiation depends upon laboratory isolation and identification
- BCG dissemination results from vaccination or treatment for bladder cancer

Distinguishing Microbiological Characteristics of *M. bovis*: Culture

- Grows better on pyruvate containing media
- Less cord formation
- (Almost) universally resistant to PZA
- TCH* sensitive
- Niacin test negative
- Nitrate test negative

*thiphen-2-carboxylic acid hydrazide

Distinguishing Microbiological Characteristics of *M. bovis*: Genetic

- *pncA* mutation consistent with PZA resistance
- Spoligotyping and MIRU/VNTR (standard genotyping done for US isolates)
  - Different spacers and repeated sequences than *M. tuberculosis*
- Gene deletion analysis
  - *M. bovis* has lost certain genes
- Whole genome sequencing
- Genetic methods are best for identifying BCG
Susceptible Species

- Cattle
- Humans and non-human primates
- Goats, sheep, cats, dogs, pigs, buffalo, badgers, possums, deer, elk, bison, horses, foxes, hares, ferrets, antelope, camels, llamas, alpacas

History 1

- 1882: Koch’s discovery of tubercle bacillus
- 1898: Theobald Smith identifies differences between tuberculosis species infecting cattle (M. bovis) and humans (M. tuberculosis)

History 2

- 1901-1911: A British Royal Commission conducts extensive research
- Demonstrates cow’s milk infected with M. bovis caused extrapulmonary TB in people
- Increased risk of cervical lymphadenitis in children who drank cow’s milk
History 3

- 1908 first compulsory pasteurization law
- 1917 US State-Federal bovine TB eradication program
- Whole herd testing & culling of reactors
- Prior to pasteurization – estimated 10-30% of human TB cases due to *M. bovis*

Current Disease Burden and Epidemiology

*M. bovis* in Cattle Today

Cow (*Bos taurus*)
M. bovis: Africa and Latin America

M. bovis: Asia

Cattle in United States (2013)

• 48 states are TB free (eradicated)
• Exceptions are Michigan and California
  – MI: wildlife reservoir (deer)
  – CA?
M. bovis: Africa and Latin America

M. bovis: Asia
What is the actual worldwide human burden of *M. bovis*?

- Unknown
- Poor countries, which are high burden for TB, rely on AFB smear – do not perform cultures
- Many industrialized countries generally do not identify organism beyond *M. tuberculosis* complex
  - Increasing use of genotyping has changed this

Risk of Human Disease in North America

- In US and Canada, disease is rare due to pasteurization and eradication programs in cattle
  - *M. bovis* probably accounts for less than 1% of human TB cases
    - Higher in some areas: San Diego
- Mexico
  - One report found 17% of cattle in meat processing plants were infected with *M. bovis*
  - Up to 30% of milk is not pasteurized
  - Percent of human TB cases due to *M. bovis* is unknown, but likely higher than for US and Canada

Human *Mycobacterium bovis* Tuberculosis United States, 1995–2005

- 1.7% of TB cases with genotyping results
- 89% Hispanic
- 62% born in Mexico
- 19% age < 15 y.o. (compared with 2% for *M. tuberculosis*)
- 65% extrapulmonary disease site
- 26% HIV infected


<table>
<thead>
<tr>
<th>Year</th>
<th>Total Genotyped Cases</th>
<th><strong>Total</strong></th>
<th>Mycobacterium bovis cases</th>
<th><strong>U.S.-born</strong></th>
<th><strong>Foreign-born</strong></th>
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<tbody>
<tr>
<td></td>
<td>No.</td>
<td>No.² (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
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<td>100 (1.3)</td>
<td>33 (33.0)</td>
<td>67 (67.0)</td>
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<td>90 (74.4)</td>
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</table>
Transmission

- Foodborne: ingestion of contaminated unpasteurized dairy products
- Airborne: same as for *M. tuberculosis*
- Direct inoculation (cutaneous)
  - Butcher’s wart
  - Hunters

Foodborne Transmission in the United States
Real (Baja) California Cheese

• Fresh cheese (e.g., queso fresco) made in Mexico often from unpasteurized milk
• Not the type commercially available in United States; imported by individuals for their own consumption
• Bypasses FDA/USDA regulation and inspection

Discount Price: $7.56
every day
Volume price: $6.81
w/ $100.00 purchase
Wholesale price: $6.05
w/ $300.00 purchase

Queso Fresco

One of the most favorite Mexican cheeses, Queso Fresco is a fresh cheese of various sizes and shapes made from 100% cow's milk. The cheese has a grainy feel and very mild, fresh acidity. Queso Fresco is used for grilling and baking and it can also be used in salads. It softens but does not melt when heated.
Real (Baja) California Cheese

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Cycle of *Mycobacterium bovis* transmission between cattle and humans. The thickness of the arrows suggests probability. Adapted from Collins and Grange (1987).

But it can be more complicated…