Tuberculosis in humans and cattle in Ethiopia: Implications for public health

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Aim

- Tuberculosis
  
  - How can we apply advances in molecular biology to inform disease control?
Historical overview

- Robert Koch, 1882
  - *Mycobacterium tuberculosis*

- Ireland
  - Geary (1930)
  - Seminal review of TB death rates
2008 Deaths: 1.8 million; New cases: 9.4 million
Leading killer of people with HIV
Extrapulmonary TB

Main sites of Extra pulmonary tuberculosis

Central nervous system
- Meningitis

Lymphatics
- Scrofula (of the neck)

Pleura
- Tuberculosis pleurisy

Disseminated
- Miliary tuberculosis

Bones and joints of spine
- Pott's disease

Genito-urinary
- Urogenital tuberculosis
Drug treatment

• Limited drugs for treatment
• Prolonged drug course
  – 6 months, 3 drugs
• Emergence of drug resistance
  – Multi- and Extensively drug resistant (MDR-, XDR-TB)
• Directly Observed Therapy, Short course (DOTS)
Vaccine

- Bacille Calmette et Guérin (BCG)
- Most widely used vaccine in the world
- Protection against pulmonary TB: 0-80%
Ethiopia

- Pop 83 million
- High TB burden
  - 378 new cases/100,000
- 36% extrapulmonary TB
- eTB: Kenya: 17%; Nigeria: 5%; South Africa: 16%
- Why is extrapulmonary TB so high in Ethiopia?
  - HIV co-infection?
Bovine Tuberculosis

• Lung disease
  – caused by *Mycobacterium bovis*

• Infects a range of domestic animals, wildlife and man
  – Transmission to man through drinking infected milk, eating infected raw meat
  – *M. bovis usually linked to extrapulmonary disease*

• Developed countries: disease controlled to protect public health
  – Identify and slaughter infected cattle; compensate farmers
    • Rep. Ireland: €35 million
    • UK £100 million
Ethiopia and bovine TB

• Ethiopia
  – Largest cattle population in Africa

• Move to import “exotic” cattle breeds
  – Improved productivity
  – >Susceptibility to bTB

• Impact on human health?
  – Unpasteurised milk, raw meat
  – Urban areas: 82% of the milk is supplied unpasteurised to consumers

• What is the burden of zoonotic transmission?
• Burden of *M. bovis* infection is unknown
  – Inform public health
• Requires accurate diagnosis
  – Culture
  – Strain differentiation
• Current methods
  – Minimal culture
  – Old biochemical tests
  – Simple molecular test to tell the difference between *M. tuberculosis* and *M. bovis*
• Some data to suggest that ~18% of eTB in Ethiopia due to *M. bovis*
The *M. tuberculosis* complex
M. tuberculosis complex genomics

- Genome: all the DNA in an organism
- *M. tuberculosis* and *M. bovis* highly genetically related
Deleted regions from *M. bovis*

- Comparative genomics
- Identified DNA regions that were
  - deleted from *M. bovis*
  - but present in *M. tuberculosis*
- Regions of difference (RD loci)
- So given an isolate from a TB patient, can now easily tell if it is *M. tuberculosis*, or *M. bovis*. 
Loss of DNA through evolution...

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<thead>
<tr>
<th>Hosts</th>
<th>Human</th>
<th>Human?</th>
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<th>Antelope</th>
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An evolutionary aside...
“For instance, measles and tuberculosis arose from diseases of cattle…”

The research approach

• Determine the extent of bovine TB
  – “Skin-testing” cattle

• Isolate bacteria causing TB in cattle
  – Culture bacteria from lesions identified in cattle carcasses in abattoirs

• Isolate bacteria causing TB in humans
  – Fine needle aspirates from neck lymph nodes from patients with suspected TB lymphadenitis

• Molecular methods
  – What are the strains causing eTB in humans?
  – Same as those causing bTB in cattle?
Abattoirs: Stefan Berg/AHRI
FNAs of patients: Abraham Asseffa
Bovine TB in Ethiopia

• Prevalence survey
  – Extensively raised: 3% of animals have bTB
    • Zebu
  – Intensively raised: 13.5% (some dairy farms ~50%)
    • “Exotics”

• Abattoir samples
  – 32,800 cattle examined
  – ~4% lesions, with 11% of these lesions positive for mycobacteria
  – 50% of culture positives were *M. bovis*
  – ~6% *M. tuberculosis* (!)
Host preference

Diagram showing the evolutionary relationships among different species, with labels for each species at the bottom: Human, Human?, Human?, Antelope, Seal, Vole, Goat, Cow. The diagram includes illustrations of these species.
M. tuberculosis transmission to cattle?
M. tuberculosis transmission to cattle?

Gobena Ameni
Addis Ababa University
Results: FNA samples

- Prior data had suggested ~18% of eTB cases due to *M. bovis*
- *But...*
- Human FNAs
  - >1000 samples; 33% culture positive
  - no *M. bovis*; all *M. tuberculosis*
- Unexpected
  - Humans can be infected with *M. bovis*
Cause of eTB in Ethiopia?

• HIV co-infection?
• Reporting bias?
• New type of *M. tuberculosis*?
  – Molecular characterisation
  – Predilection for extrapulmonary sites?
Economic impact

- Prevalence of bovine TB is relatively low
  - High in dairy farms
    - Vaccination of elite dairy herds?
  - Pasteurisation
    - 82% of the milk is supplied unpasteurised to consumers

- Evidence for transmission of bovine TB to humans lacking

- Public health standpoint, no economic justification for control of bTB
• Human TB
  – High rates of extrapulmonary TB not caused by *M. bovis*

• Bovine TB
  – Greatest impact in intensive farms

• Transmission of human TB to cattle
  – Mode of transmission?
  – Reservoir of human infection?

• Economic impact
Acknowledgements

“Bovine Tuberculosis in the Developing World”

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