Zoonotic Tuberculosis at the Human-Livestock-Wildlife Interface

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Outline

• Background
• Rationale
  ▫ Systematic Literature Review
  ▫ Preliminary Field Data
• Conclusion/Implications
Tuberculosis in Humans

- TB in humans is primarily caused by *Mycobacterium tuberculosis* (*M. tb*)
- TB is an infectious-contagious disease and represents one of the leading causes of death from an infectious disease worldwide.
  - 8.7 million new cases of TB in 2011
  - 1.4 million deaths in 2011 (WHO Annual TB report, 2011)
    - (3,833 deaths/day)
Mycobacterium bovis (M. bovis)

- The main host of *M. bovis* is cattle

- 128 out of 155 countries reported the presence of *M. bovis* infection and/or clinical disease in their cattle population between 2005 and 2008 (Michel et al, 2010)

- Most warm-blooded vertebrates can be infected, including humans
Transmission & Pathology of *M. bovis* in Humans (Zoonotic TB)

- Orally (unpasteurized dairy products) or through inhalation
  (Michel *et al.*, 2010)

- Patients with extra-pulmonary disease had increased odds of having *M. bovis* vs. *M. tb*  (Hlavsa *et al.*, 2008)

- *M. bovis* can be an important etiological agent for extra pulmonary TB, especially in HIV-infected patients.  (Cicero *et al.*, 2009)
**M. bovis** Resistant to PZA

- *M. bovis* is naturally resistant to pyrazinamide (PZA), a critical component to effective short course TB treatment.
  - Thus, patients with undiagnosed *M. bovis* are being treated sub-optimally.
Challenges of Zoonotic TB

- Conditions in the developing world: (Cosivi et al., 1998; Thoen et al., 2006).
  - Higher prevalence of bovine TB in livestock
  - Lack of milk pasteurization
  - Human immunodeficiency virus (HIV)
  - Close interaction between humans, livestock, and wildlife species
Challenges of Zoonotic TB

- **1.4%** is the generally perceived estimate for the proportion of human TB cases infected with *M. bovis*.
  - Lack of targeted surveillance

- Scientific evidence indicates that the true risk of human TB caused by *M. bovis* is under investigated/under estimated/under reported.

Research questions

1) What is the range of risk estimates of *M. bovis* infection (zoonotic TB) among humans diagnosed with TB?

- The **risk** of zoonotic TB was defined as the proportion of human TB patients infected with *M. bovis*.

2) What are the key study design characteristics that may contribute to the heterogeneity between different studies when estimating the risk of zoonotic TB?
Key Study Characteristics

- Inclusion/Exclusion Conditions
  - Culture Positive
  - Skin test Positive
  - Urban vs. Rural
  - Child vs. Adult

- Demographic Characteristics
  - Culture Media Used
  - Molecular Techniques

- Diagnostic & Differentiation Protocols
  - Extra-pulmonary Sources
  - Pulmonary Sources

- Samples Collected
Range of risk estimates of *M. bovis* infection

- There is a large variation (a range of 0-45%) in the risk estimates of *M. bovis* infection in human TB patients.
- 16 of the studies (26%) reported a >10% risk of *M. bovis*. 
Results

Distribution of key study characteristics

- **53%** of studies used culture positive TB patients as patient inclusion criteria.
- **32%** of the studies evaluated extra-pulmonary samples.
- **48%** of the studies used Stonebrink as a culture medium for the growth of *Mycobacterium tuberculosis complex* species.
- **8%** evaluated the risk of zoonotic TB specifically in children specifically in children.
- **11%** evaluated the risk of zoonotic TB among TB patients from rural areas.
Preliminary Field Data - Zambia

• Recent retrospective study analyzed sputum samples from 917 patients assumed to be infected with *M. tb*
  • 8 patients with *M. bovis*, all of whom were cattle farmers.

• Currently have ongoing study looking at the rural Namwala district of Zambia
  • Sample includes 45 human patients diagnosed with TB
  • 15 (33%) have been initially classified as infected with *M. bovis* based on culture morphology (cultured on Stonebrink medium)
    • 13 of these patients indicated that they consume raw milk
  • Currently, strain typing is pending to confirm *M. bovis*
One Health Collaboration - Kenya

- Collaborating with physicians in Kenya that noticed monoresistance to pyrazinamide (PZA) among TB patients in rural areas.
  - 2012: 6% of *M. tb* complex isolates were monoresistant to PZA

- Role of socio-cultural practices & the true risk of *M. bovis* infection in these rural communities of Kenya.

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Conclusions

- There is considerable variation in the risk estimates reported for *M. bovis* infection among human TB patients (range 0-45%).

- Key study characteristics differ considerably, which can have an effect on the risk estimates reported by different studies.
  - Rural communities are underrepresented in the current literature.
  - A considerable amount (>50%) of studies did not use the recommended culture medium to grow *M. bovis*, nor were extra-pulmonary samples evaluated.
Implications

• Epidemiology, pathology, and treatment challenges associated with *M. bovis* infection among humans are significant.

• Studies are needed to assess the risk of zoonotic TB among populations in regions where socio-cultural and economic factors increase the risk posed by this zoonosis.
  - Patient enrollment, sampling procedures, and laboratory protocols need to be carefully considered.
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Questions?

“Looks like it's back to the horse burgers.”

http://www.shelbourn.com/gazette/gazette-2013.05.09g.jpg

http://img.metro.co.uk/i/pix/2011/09/00/article-126366866678-0DCB345A00000578-16043_4f909.jpg
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