TB at the Human-Elephant Interface

Review of interspecies transmission

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All case counts and rates for 1993–2003 have been revised based on updates received by CDC as of April 1, 2005.
Considerations about TB exposure
Probability of spread of TB

• Infectiousness of index patient
  – Colony count
  – Cavitary disease
  – Degree of cough

• Length of contact

• Closeness of contact

• Immune system of recipient
Microbiology

- “TB” denotes infection with organisms of *M tuberculosis* complex
  - *M tuberculosis*  *M africanum*
  - *M bovis*  *M microti*  *M canetti*

- Infection with other species
  - Non-tuberculous mycobacteriosis
Diagnosis of TB

- Evidence of active TB?
  - Evaluate symptoms
    - chronic cough, fever, weight loss, night sweats
  - Evaluate CXR
    - Cavitary disease, miliary disease
    - Non-specific infiltrate
  - If (+) -> 3 sputa for smear & culture
  - If NO -> place PPD
Pulmonary TB - apical
Miliary TB
Non-Pulmonary Syndromes

- Musculoskeletal
  - Large joints
  - Pott’s disease (spine)
- Liver
- Spleen
- Lymph nodes / Scrofula
- Adrenal (#1 cause of adrenal insuff worldwide)
- Genital (ovarian, uterine & epididymal)
- Kidney
- Brain abscess & meningitis
Vertebral TB

Pott’s Disease
TB lymphadenitis

*Scrofula*

- Adults – TB more common
- Children – *M avium* more common
Diagnosis of Latent TB Infection
Tuberculin Skin Testing

- Intradermal injection 5 TU PPD
- Measure *induration* not erythema
PPD Interpretation

• Immune suppressed ≥5 mm
• Health care workers ≥10 mm
• Outbreak investigation ≥10 mm
• No TB risk factors ≥15 mm
Gamma-Interferon

- QuantiFERON-TB Gold (US & Europe)
- T SPOT-TB test (Europe)

  - T-cell IFN-γ response
  - TB antigens: ESAT-6 & CFP-10
  - Good performance in high risk populations
  - Preferable for immunosuppressed pts

Whalen JAMA 2005, 293:2785 (editorial)
PPD & Risk for active infection

- ~5-10% in first 2 yrs after conversion
- 0.5% per yr afterwards
- Higher in age <5 yrs
- Increase in elderly (?)
- Increase with immune suppression
  - Cancer
  - Steroids
  - Cancer chemotherapy
TB as a Zoonosis
Index Herd: 1996-7

• Three elephant cases confirmed
• Two diagnosed post-mortem
• Public health evaluation of facility staff

*Michalak et al 1998; Emerg Inf Dis 4:283-7
Exposure risks for staff

- Staff quarters part of same bldg as animals
  - Separate ventilation systems (???)
  - Doors kept open between sections
  - Social events in barn
- Barn layout
  - Poor cross ventilation
  - Single 3’ ceiling fan
- Necropsy attendance
  - 1994 (& 1983?)
PPD test results

<table>
<thead>
<tr>
<th>Staff group</th>
<th>n</th>
<th>Initial (+)</th>
<th>Converted</th>
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<tbody>
<tr>
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<td>12</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Tiger</td>
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<td>4</td>
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- High number of baseline (+) tests
- Indeterminate date of exposure
- One elephant worker with (+) CXR
Index Herd - IS6110 typing

- Trainer (+) CXR
- Smear (-), culture (+)

<table>
<thead>
<tr>
<th>Lane</th>
<th>Specimen</th>
<th>Year</th>
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<td>1994</td>
</tr>
<tr>
<td>2</td>
<td>Elephant</td>
<td>1996</td>
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<tr>
<td>6</td>
<td>Human</td>
<td>1996</td>
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</tbody>
</table>
Index Herd - issues

• No baseline data
  – Unable to classify PPD(+) as recent vs old exposures

• Transmission direction
  – Considered elephant to human BUT
  – Cannot know for certain
  – Cannot know if other staff was index case
California Zoo 1997-2000

Oh et al
EID 2002, 8 (11) 1290-3
The Outbreak

• Index cases: 2 elephants
  – Elephant died of salmonellosis (Mar’97)
  – TB found on post-mortem
  – 2nd elephant with (+) trunk wash (Apr’97)

• Other cases
  – Rocky Mountain goats
    • 1 died of TB pneumonia
    • 2 with (+) skin tests & CXR; later (+) culture
  – 1 Black rhinoceros - with (+) culture
Molecular epidemiology

LA Zoo

Index Herd
Keepers & staff

• 336 of 1088 employees screened
  – 332 with known job category
    • 35% animal handlers or vets (2/3 Caucasian)
    • 7% groundskeepers (2/3 Hispanic)
  – 55 (18%) of 307 with (+) PPD
    • Males RR = 3.7
    • Groundskeeper RR = 2.6
    • Construction worker RR = 2.5
    • At elephant necropsy RR = 2.9
  – No positive cases in humans
Elephant Refuge

Murphree et al
EID 2011; 17 (3) 366-71
The Elephants

• Acquired 10 elephants
  – Two in 2004, eight in 2006
• Known exposed herd within past 10 yrs
• Original 2 eleph: history culture (+) TB
  – One died 2005
  – Other rx’d for TB for 1 yr then released from isolation
• 2009: 3rd elephant developed active TB
The staff

• Baseline
  – Known need for TB vigilance
  – Developed isolation policies
  – PPD testing on all staff

• PPD conversions
  – 9 / 46 skin test conversions

• Murphree for more details
Risks for PPD conversion

elephant refuge

• Significant risk factors
  – Quarantine area exposure 2009
  – Non or episodic usage of N95 masks

• Non-significant risks
  – Foreign born
  – Work in prisons, homeless shelter
  – Close contact with elephants
  – Work in barns during cleaning
Lessons & summary
Common themes

• Poor or no use of N95 masks
• Close quarters of elephants
• Aerosol generation during barn cleaning
• Only one facility with baseline PPD data
  – Does not allow discrimination of exposures
Lessons learned - I

• Need for baseline screening of staff
  – PPD testing
  – Exposure history to TB
  – Health history (risk for acquisition)

• Yearly PPD testing
  – PPD converters may signal risk to elephants OR from elephants
Lessons learned - II

• Policies & practices
  – Develop adequate isolation policies
    • N95 mask usage with known / suspect culture (+)
    • N95 fit testing & instruction in use
    • Strict quarantine for culture or suspect (+)
  – Assume high likelihood of reactivation *if*
    • RT increasing strength with (+) MAPIA
    • Symptoms of TB
Lessons learned - III

• Ascertain TB risks in elephants
  – Map prior exposures (15 years)
  – Determine treatment history
    • Effectiveness (levels)
    • Length
    • # drugs used
  – Maintain high degree of suspicion
    • High for known contact with culture (+)
    • Highest for any prior culture (+)
Public health & Elephant TB

• Careful outbreak evaluation
  – Determine real (vs perceived) risks to staff
  – Determine likely (vs perceived) risks to public

• Discussion of Public health issues and occupational risks and prevention strategies:
THINK TB
AFB smear

• Positive smear
  – Signifies > 1,000 cfu/ml of sample
  – Cannot discriminate TB from non-TB

• PCR detection
  – Specificity >95%
  – Sensitivity ~60% with smear (+)
AFB smear
TB transmission & pathogenesis

• Gastrointestinal
  – Bacterial travel to terminal ileum
  – Picked up in LN of Peyer’s patches
  – Granulomas form in local LN
  – Spread to peritoneum