EPIDEMIOLOGY OF TUBERCULOSIS IN ELEPHANTS, 1994-2011, UNITED STATES

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Overview

- Methods
  - Case Definition
- Demographic information
- Apparent Prevalence
- Mortality
- Diagnostic Testing
- Conclusions
- Analysis Strengths and Limitations
- Recommendations
Methods

- APHIS database for elephants
  - Population: elephants currently monitored for TB and elephants ever confirmed infected with TB
  - Sex
  - Species
  - Living/Died
  - Trunk wash (TW)
  - Serology - Pretreatment
    - ElephantTB Stat-Pak®, multi-antigen print immunoassay (MAPIA)
    - Official tests except 4 for which no official tests available
  - Bacteriology/culture

- Case definition for a TB infected elephant
  - Isolation of *Mycobacterium tuberculosis* or *M. bovis* by culture from bodily secretions/excretions or tissue samples
Demographic Information

- Information for 480 elephants
- 405 (84.5%) female
  - 75 (15.6%) male
- 274 (57.1%) Asian elephants
  - 206 (42.9%) African elephants
51/480 (10.6%) elephants confirmed with *M. TB* or *M. bovis*
- 43/405 (10.6%) female
- 8/75 (10.6%) male
1-8 new cases per year
- Median = 3.0
- Mean = 3.2
3/480 (0.6%) new TB cases annually
TB 5.7X more frequent in Asian than African elephants

<table>
<thead>
<tr>
<th>Species</th>
<th>M TB Positive</th>
<th>Total Elephants</th>
<th>Percent Infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>6</td>
<td>206</td>
<td>2.9%</td>
</tr>
<tr>
<td>Asian</td>
<td>45</td>
<td>274</td>
<td>16.4%</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td>480</td>
<td>10.6%</td>
</tr>
</tbody>
</table>
n = 51 elephants, including one elephant with *M. bovis* in 2000
Putting Prevalence into Perspective

- There were 4.2 new TB cases per 100,000 people in 2008 in the United States*
- At 3.0 new cases per an estimated 450 living elephants, if there were 100,000 elephants, that would equate to approximately
  - 677 cases/100,000 elephants/year
- New TB cases are being detected in US elephants at 161X higher rate than in the US human population
  - 677/4.2 = 161

*Centers for Disease Control and Prevention, Morbidity and Mortality Weekly Report, March 20, 2009; 58(10):249-253
- Of the 51 confirmed TB cases
  - 33 (64.7%) have died
- Of these
  - 6/6 African elephants died
  - 27/45 Asian elephants died
- TB and other disease conditions found at necropsy
- Not a true case mortality rate
- Further evaluation of comorbidities, age and treatment needed

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<tr>
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<th>Died</th>
<th>Total Infected</th>
<th>Percent Died</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>6</td>
<td>6</td>
<td>100.0%</td>
</tr>
<tr>
<td>Asian</td>
<td>27</td>
<td>45</td>
<td>60.0%</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>51</td>
<td>64.7%</td>
</tr>
</tbody>
</table>
Mortality by Sex, 1994-2011

- Of the 51 confirmed TB cases
- 72.1% of females have died
- 25.0% of males have died
- Mortality in females with TB 2.9X higher than in males with TB

<table>
<thead>
<tr>
<th>Sex</th>
<th>Died</th>
<th>Total Infected</th>
<th>Percent Died</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>31</td>
<td>43</td>
<td>72.1%</td>
</tr>
<tr>
<td>Male</td>
<td>2</td>
<td>8</td>
<td>25.0%</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>51</td>
<td>64.7%</td>
</tr>
</tbody>
</table>
Diagnostic Testing - Sensitivity

Confirmed Infected Elephants
Trunk wash
- Material collected then cultured
- Isolation of mycobacterium confirms infection by gold standard

ElephantTB Stat-Pak® – initial serology test
- Evaluates for presence of antibodies to *M TB* bacteria

Multi-antigen print immunoassay – follow-up to Stat-Pak®
- Evaluates for presence of antibodies to a larger number of *M TB* antigens than Stat-Pak®
# Pretreatment Sensitivity: Trunk Wash, Stat-Pak and MAPIA

<table>
<thead>
<tr>
<th>Test</th>
<th>TW Positive or SP Reactive (%)</th>
<th>TW Negative or SP Nonreactive (%)</th>
<th>Confirmed Infected Elephants*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trunk Wash (TW)</td>
<td>30 (62.5)</td>
<td>18 (37.5)</td>
<td>48</td>
</tr>
<tr>
<td>Stat-Pak (SP)</td>
<td>19 (100.0)</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>Stat-Pak / MAPIA</td>
<td>18 (100.0)</td>
<td>0</td>
<td>18**</td>
</tr>
</tbody>
</table>

*51 elephants met the case definition - *M TB* or *M. bovis* isolated from bodily secretions / excretions or tissue samples. Of the 51 elephants meeting the case definition, 48 have been tested by trunk wash, 19 by Stat-Pak® and 18 by multi-antigen print immunoassay (MAPIA)

**MAPIA pending for one case
Concordance*: Trunk Wash and Stat-Pak

<table>
<thead>
<tr>
<th>Test</th>
<th>Trunk Wash Positive</th>
<th>Trunk Wash Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stat-Pak Reactive</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>Stat-Pak Nonreactive</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Of 51 elephants that met the case definition of *M* TB or *M. bovis* isolated from bodily secretions / excretions or tissue samples; 19 have been tested by both trunk wash and Stat-Pak®.
Diagnostic Testing

Elephants not culture positive for *M TB* or *M. bovis*
### Trunk Wash Negative: Stat-Pak and MAPIA Results

<table>
<thead>
<tr>
<th>Test</th>
<th>SP Reactive or MAPIA pos (%)</th>
<th>SP Nonreactive or SP NR and MAPIA neg (%)</th>
<th>Total Elephants Not Culture Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stat-Pak</td>
<td>77 (20.4)</td>
<td>300 (79.6)</td>
<td>377*</td>
</tr>
<tr>
<td>Stat-Pak / MAPIA**</td>
<td>24 (6.4)</td>
<td>351** (93.6)</td>
<td>375</td>
</tr>
</tbody>
</table>

*Of 429 elephants, 52 not tested by Stat-Pak®

**MAPIA results for 77 Stat-Pak reactive samples, 51 were negative. Results excluded for two with suspect results.
In confirmed infected elephants
- Trunk wash testing detected TB in 30/48
  - 37.5% false negative
- Stat-Pak only, positive results in 19/19
  - No false negatives

The balance of the elephant population = 429
- Trunk wash negative (~412), or not tested yet (17)
- Stat-Pak®/MAPIA, evidence of antibodies to \( M \ TB \) in 24 elephants
- Potential for false positives exists
- MAPIA may be reducing change of false positives?
Conclusions

- Overall apparent prevalence 10.6%, 1994-2011
  - Annually 1-8 new cases detected thru surveillance
    - Median 3.0 new cases per year
  - TB transmission continuing to occur vs recrudescence in historically exposed individuals
- Females and males equally affected
- Overall mortality 64.7%; higher in female elephants, African elephants
  - >80% of US herd is female
- Asian elephants 5.7X more likely to be infected with $M$ TB than African elephants
In confirmed infected elephants, trunk wash (TW) testing has substantial number of false negative results, compared to serology

- 37.5% vs 0%, TW vs Stat-Pak (SP)
- TW detects localized shedding
- SP/MAPIA detects systemic antibody production

Serologic testing provides evidence of *M* *TB* infection in TW negative elephants
Analysis Strengths and Limitations

- **Strengths**
  - Information on entire population
    - Superior to sampling portion of population

- **Limitations**
  - Age, comorbidities, treatment, exposure - not included in analysis
    - Important in evaluating prevalence, mortality
  - Limited information for TW negative elephants
  - Small number of infected African elephants
Recommendations

- Surveillance testing critically important
  - To enhance case detection and implement mitigations to decrease transmission risks
  - Follow-up testing of Stat-Pak reactive and MAPIA positive elephants

- Develop database standards of information collected for TB infected and TW negative animals
  - Plan for additional analyses

- Epidemiologic studies needed to determine specific risk factors for transmission

- Follow guidelines to decrease animal to animal and animal to human transmission risk
Thank you

TB lesioned lung tissue from Stat-Pak®, MAPIA+ elephant