

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

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April 5-6, 2011

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

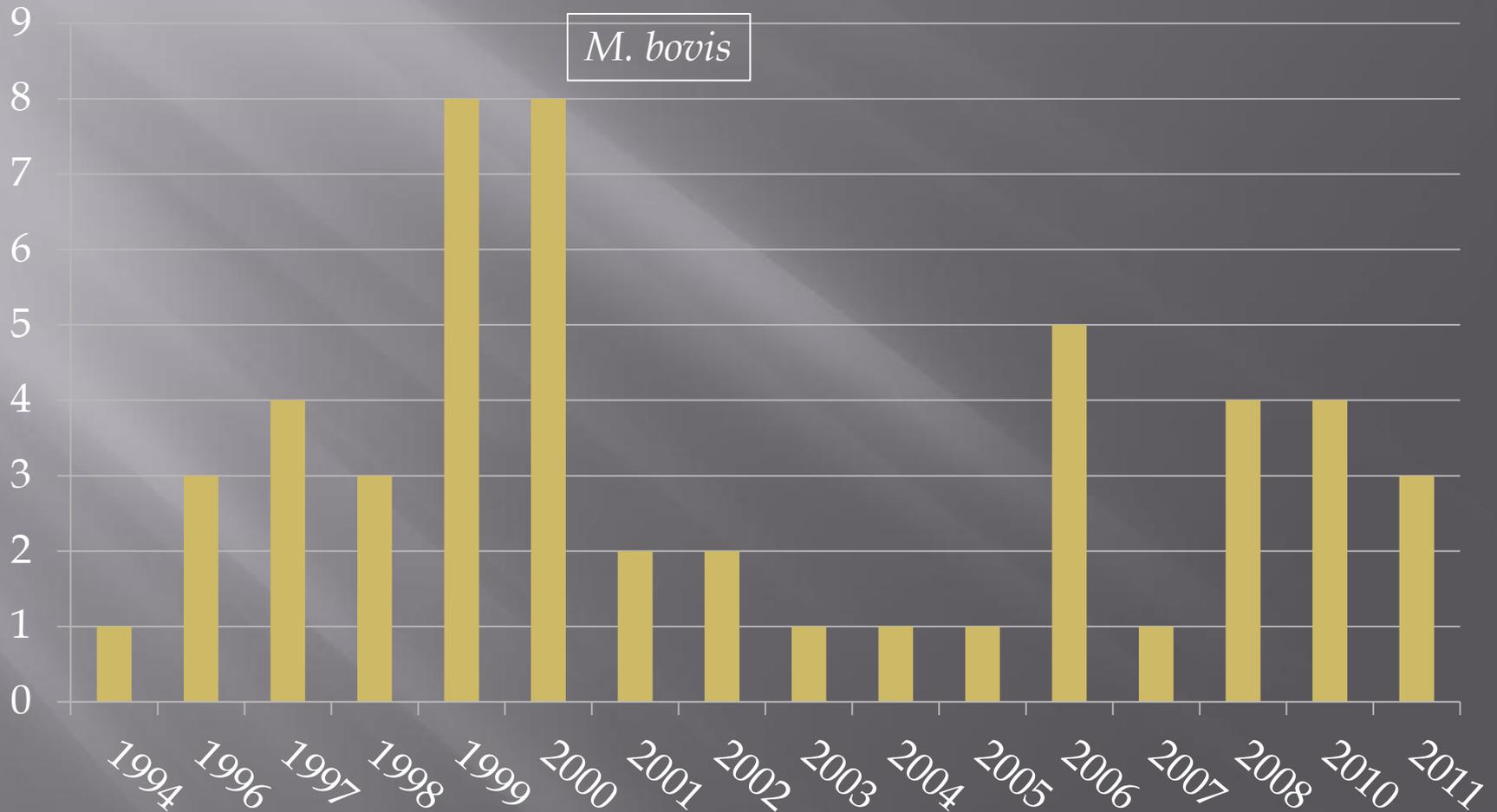
- ▣ Information for 480 elephants
- ▣ 405 (84.5%) female
 - 75 (15.6%) male
- ▣ 274 (57.1%) Asian elephants
 - 206 (42.9%) African elephants

Apparent Prevalence, 1994-2011

- ▣ 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

Species	M TB Positive	Total Elephants	Percent Infected
African	6	206	2.9%
Asian	45	274	16.4%
Total	51	480	10.6%

Year of Diagnosis, 1994-2011



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

Mortality by Species, 1994-2011

- ▣ 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

Species	Died	Total Infected	Percent Died
African	6	6	100.0%
Asian	27	45	60.0%
Total	33	51	64.7%

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

Sex	Died	Total Infected	Percent Died
Female	31	43	72.1%
Male	2	8	25.0%
Total	33	51	64.7%

Diagnostic Testing - Sensitivity

Confirmed Infected Elephants

Diagnostic Testing Options

- ▣ 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

Test	TW Positive or SP Reactive (%)	TW Negative or SP Nonreactive (%)	Confirmed Infected Elephants*
Trunk Wash (TW)	30 (62.5)	18 (37.5)	48
Stat-Pak (SP)	19 (100.0)	0	19
Stat-Pak / MAPIA	18 (100.0)	0	18**

*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

Test	Trunk Wash Positive	Trunk Wash Negative
Stat-Pak Reactive	18	1
Stat-Pak Nonreactive	0	0

*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

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

*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.

Diagnostic Testing: Summary

- ▣ 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

Conclusions con't

- ▣ 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**

