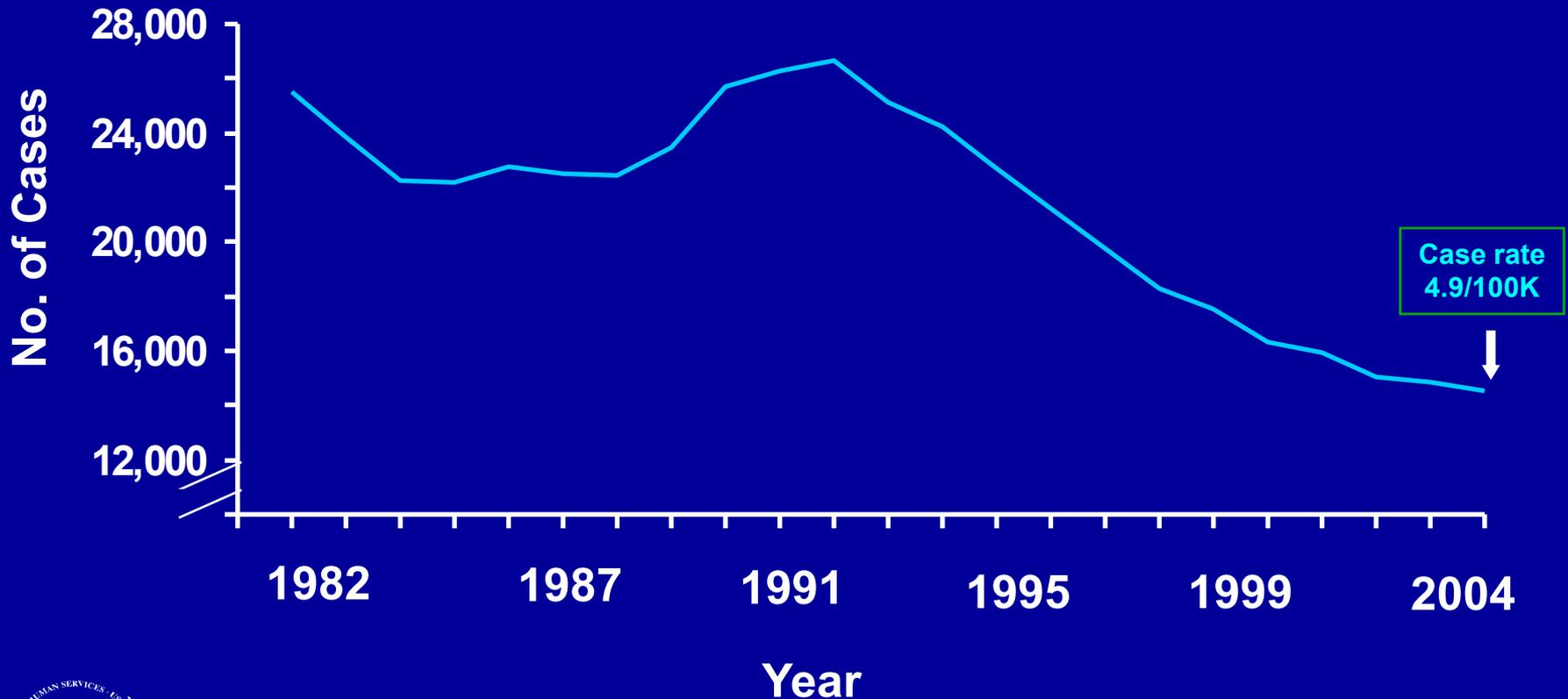


TB at the Human-Elephant Interface

Review of interspecies
transmission

Joel Maslow MD PhD MBA
Associate Dean for Research
University of Pennsylvania

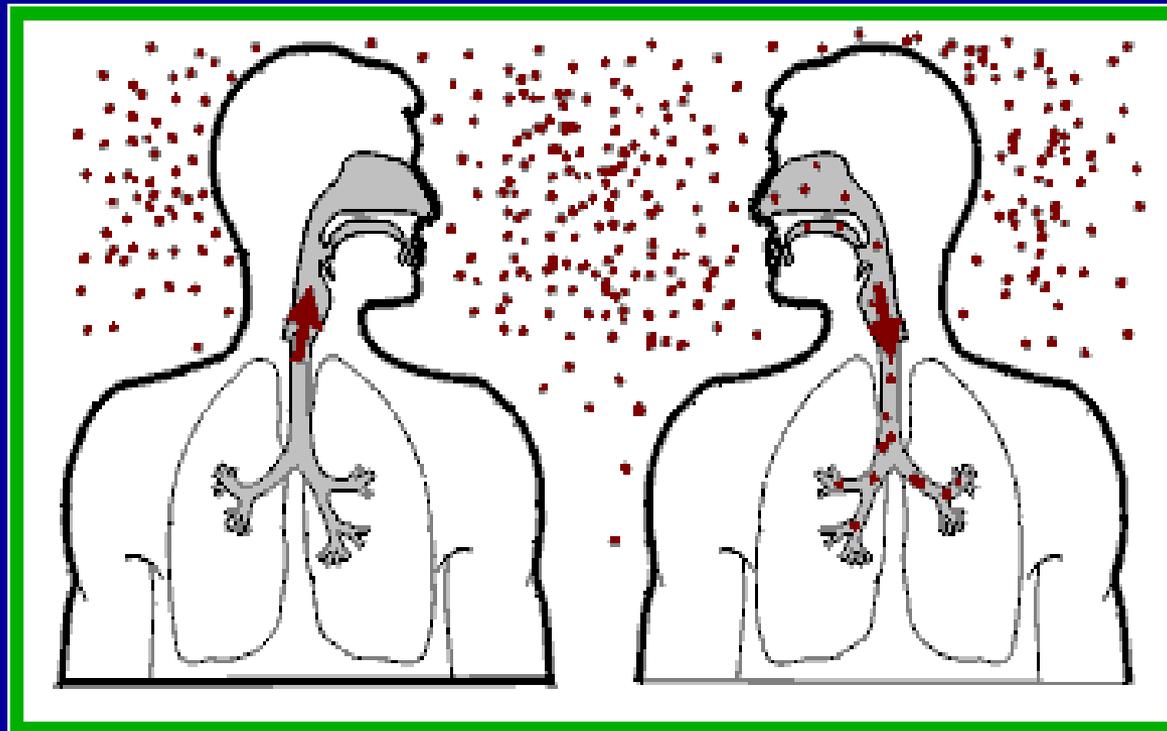
Reported TB Cases United States, 1982–2004



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
 - Cavitory disease
 - Degree of cough
- Length of contact
- Closeness of contact
- Immune system of recipient

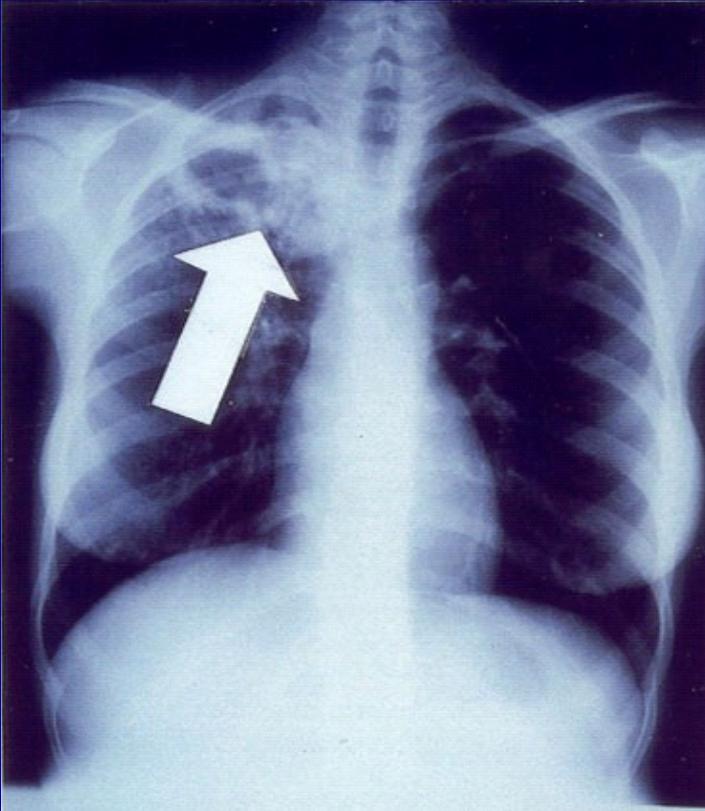
Microbiology

- “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
 - Cavitory disease, miliary disease
 - Non-specific infiltrate
 - If (+) -> 3 sputa for smear & culture
 - If NO -> place PPD

Pulmonary TB - apical



Miliary TB

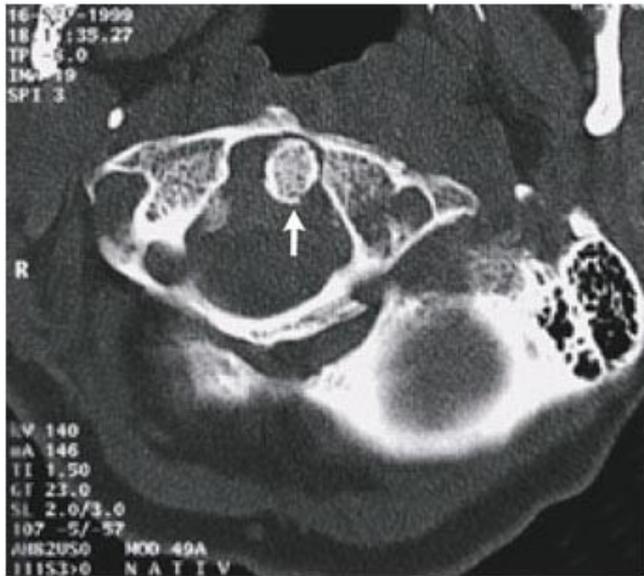


Non-Pulmonary Syndromes

- 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



A



B

TB lymphadenitis

Scrofula

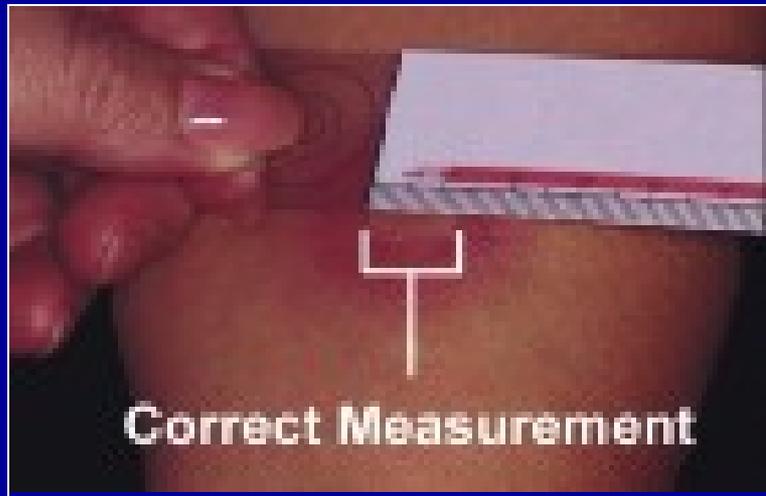
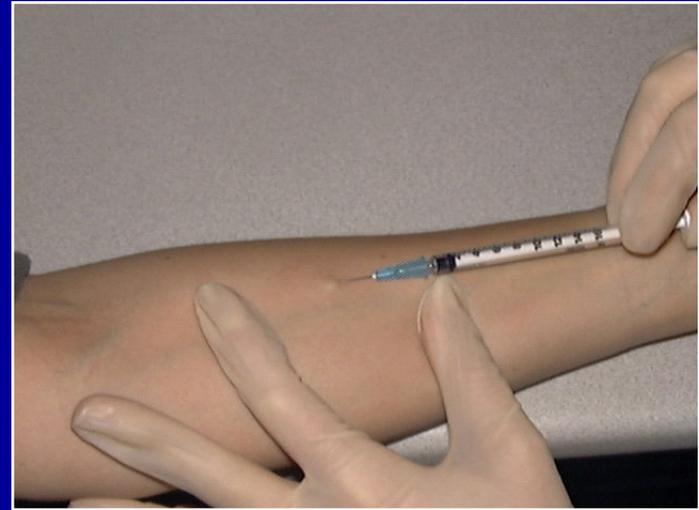


- Adults – TB more common
- Children – *M avium* more common

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

Pai et al JAMA 2005, 293:2746 Kang et al JAMA 2005, 293:2756
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

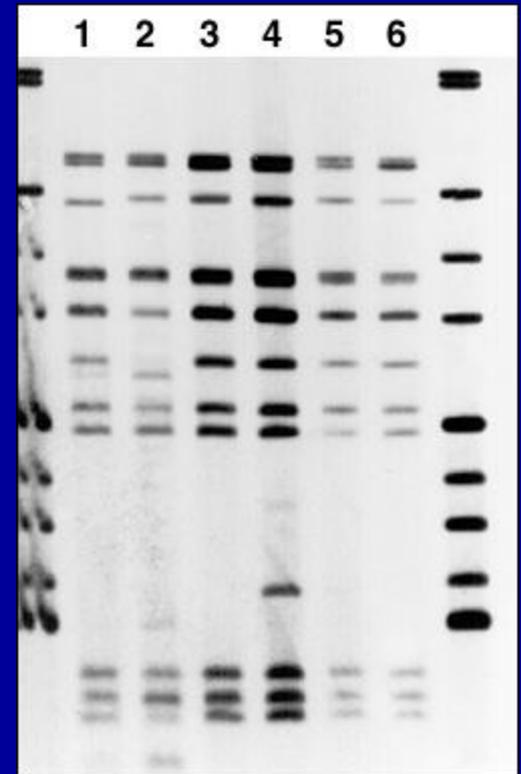
<u>Staff group</u>	<u><i>n</i></u>	<u>Initial (+)</u>	<u>Converted</u>
Elephant	12	5	2
Tiger	10	4	1

- High number of baseline (+) tests
- Indeterminate date of exposure
- One elephant worker with (+) CXR

Index Herd - IS6110 typing

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

Lane	Specimen	Year
1	Elephant	1994
2	Elephant	1996
3	Elephant	1996
4	Elephant	1996
5	Elephant	1996
6	Human	1996



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

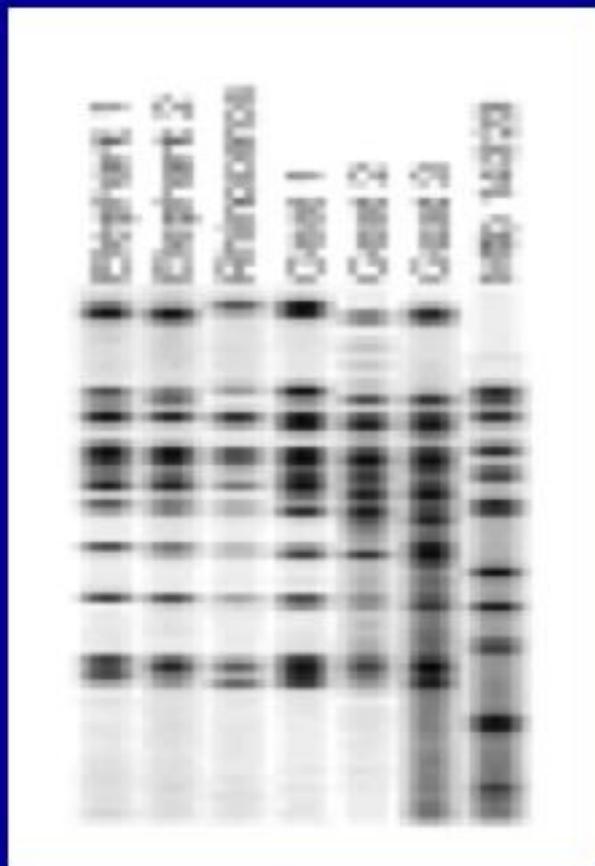
Oh et al

EID 2002, 8 (11) 1290-3

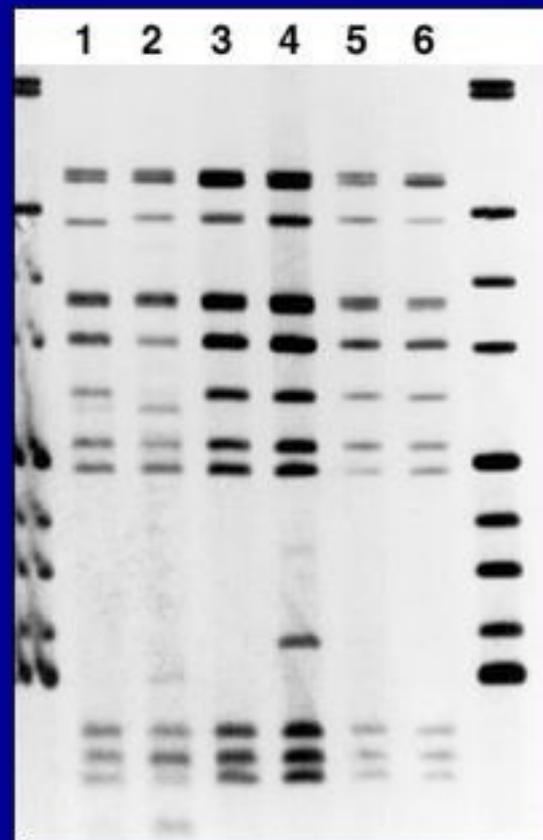
The Outbreak

- 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

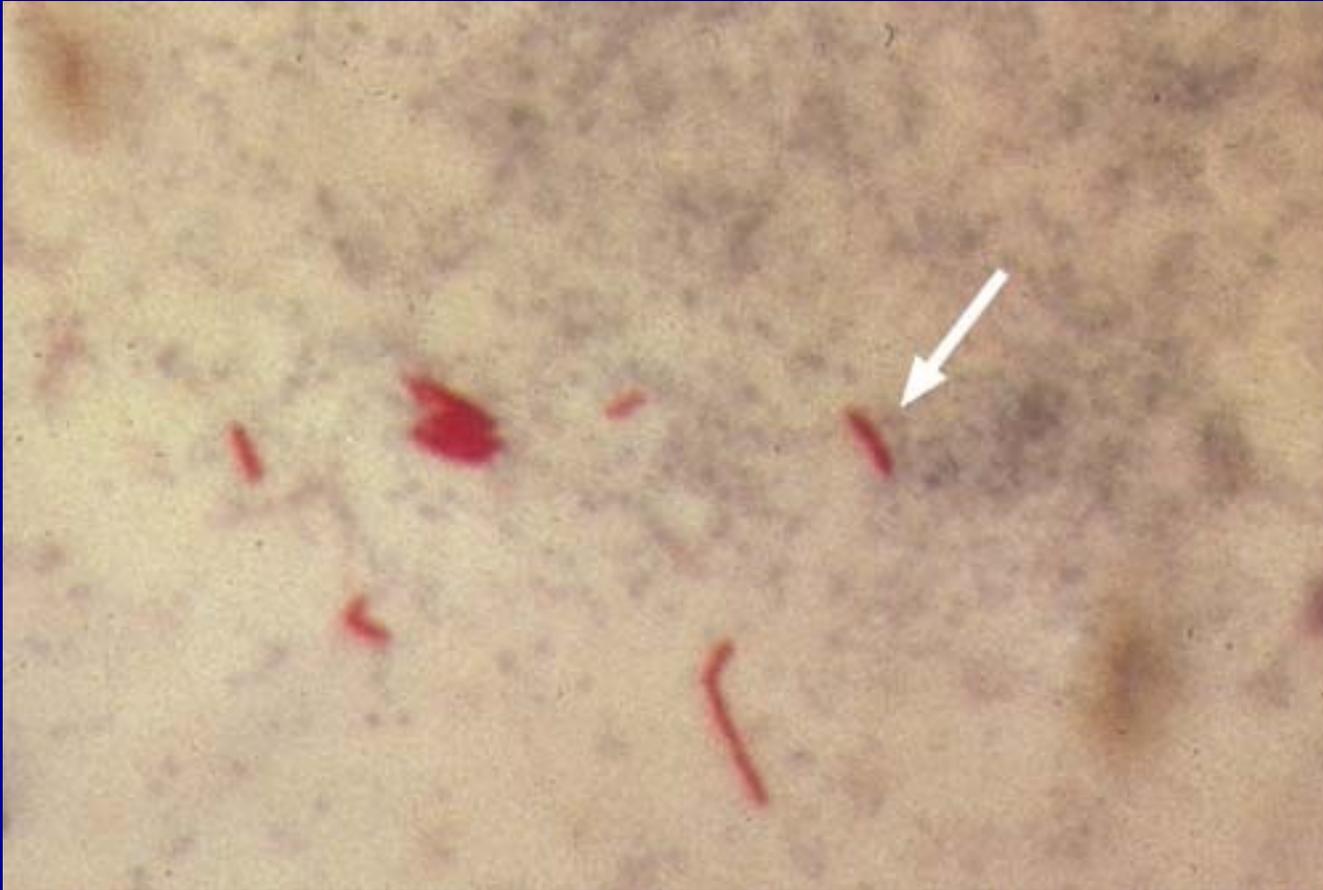
- Careful outbreak evaluation
 - Determine real (vs perceived) risks to staff
 - Determine likely (vs perceived) risks to public
- Discussion of Public health issues and occupational risks and prevention strategies:
 - Ryan “Tuberculosis in Circus Elephants” So. Cal Vet Med Assoc 1997 (Jan) 8-9
 - Davis M “Mycobacterium tuberculosis risk for elephant handlers and veterinarians” Appl Occup Environ Hyg 2001; 16 (3): 350-3

THINK TB

AFB smear

- Positive smear
 - Signifies $> 1,000$ cfu/ml of sample
 - Cannot discriminate TB from non-TB
- PCR detection
 - Specificity $>95\%$
 - Sensitivity $\sim 60\%$ 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