Potential Pathways for *Mycobacterium bovis* Zoonotic Transmission to Humans

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Outline

- Field experience with Veterinary Services
- *Mycobacterium bovis* pathogenesis
- History of tuberculosis in the U.S.
- Bovine tuberculosis testing procedures
- 5 ways humans can potentially be exposed to tuberculosis

1. Zoological Animals
2. Cattle of Mexican origin
3. Cervids
4. Non-cervid wildlife
5. Unpasteurized dairy products

Role of APHIS Veterinary Services

- Veterinary Biologics
  - Assure that animal vaccines and biologics are safe, pure, potent, and effective
  - Regulate licensing and production of veterinary vaccines and biologics
  - Inspect and monitor the production of veterinary biologics
- Disease control and eradication
  - Program and monitored diseases
  - Quarantine infected or possibly exposed animals
  - Testing and examination to detect infection
  - Cleaning and disinfection of infected premises

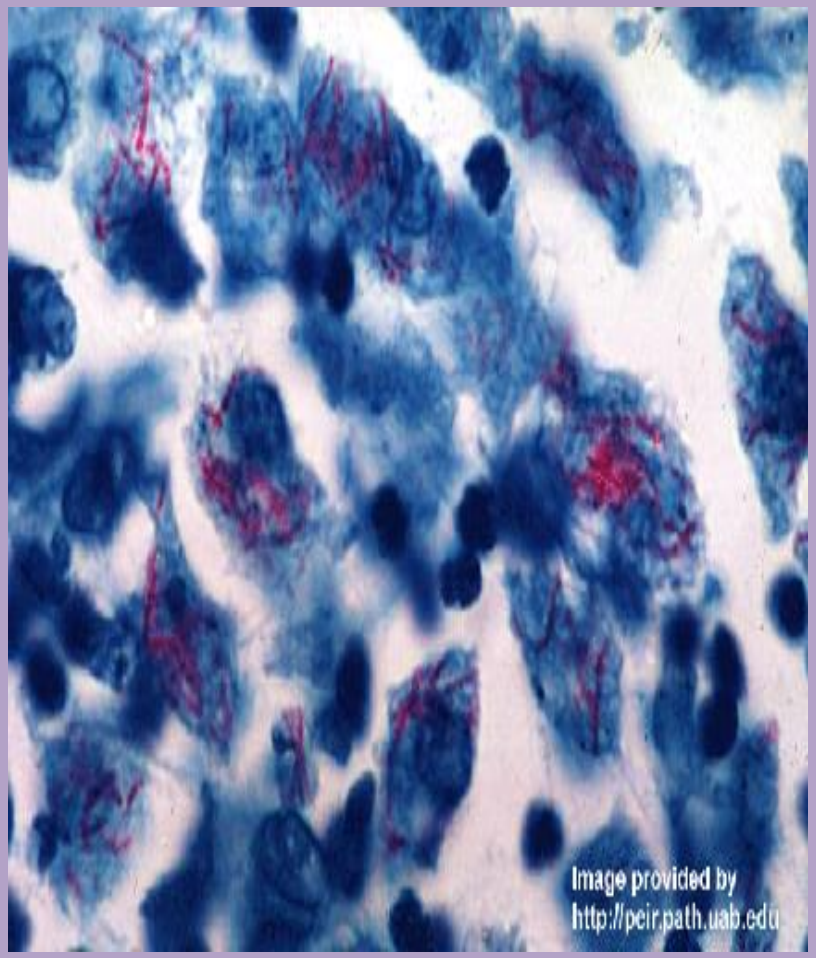
My field experience with Veterinary Services

- NAHMS- conduct surveys and field studies to collect data on animal health and management in livestock species
- NVSL- National Veterinary Services Lab in Ames, IA
- Import and Export
- Field Veterinary Medical Officers
- Brucellosis Laboratory

Mycobacterium bovis

- Reported to infect a wide range of host species including cattle, goats, sheep, pigs, cats, dogs, cervids, bison, badgers, possums, antelopes, elephants, seals, and humans
- Humans typically get infected via inhalation of aerosols or the consumption of unpasteurized infected dairy products
- Characterized by granulomatous lesions in the lungs and adjacent lymph nodes

Mycobacterium bovis



- Gram +
- Acid fast stain
- Rod shaped
- Grow very slowly
- Granulomas

Pathogenesis

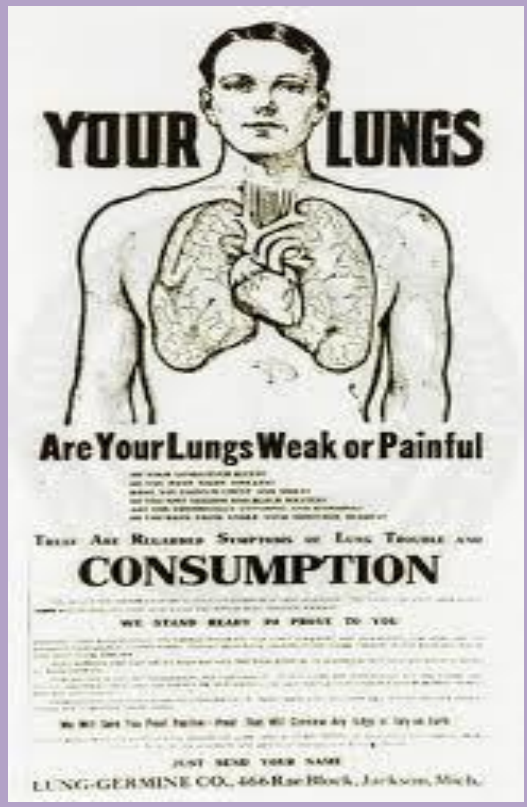
- Intracellular survival
- Humoral and CMI immunity
- CMI leads to granuloma formation
- Infection via aerosol transmission leads to the development of pulmonary TB and lesions in the lungs and adjacent lymph nodes
- Infection via oral transmission, consuming contaminated dairy products or meat, leads to the development of lesions in the tonsil and intestinal mucosa

Human TB

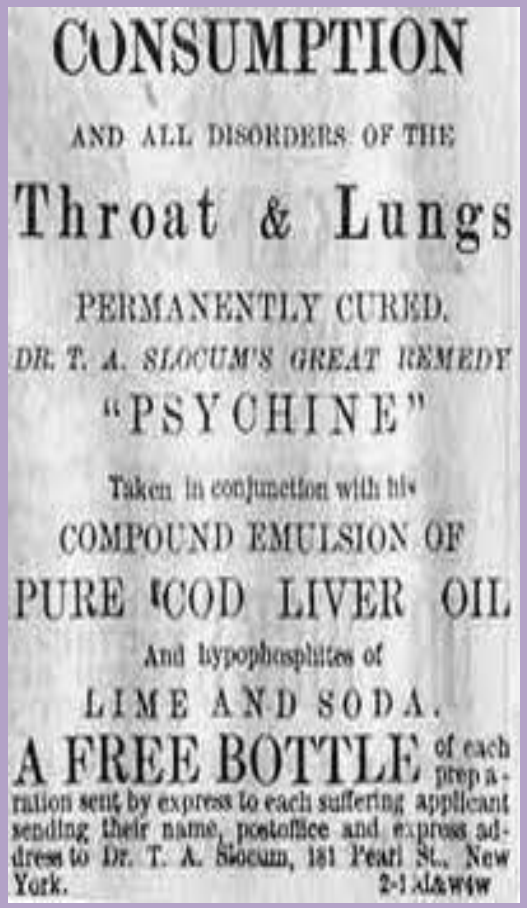
- In African and Asian countries, 80% of the population will test positive with tuberculin tests. Most of these are latent infections with only a small percentage developing full clinical disease
- In the U.S., 5-10% of the population will test positive for TB(5)
- Human *M. bovis* infections leading to pulmonary tuberculosis are indistinguishable radiologically, clinically, and pathologically from *M. tuberculosis* infections
- Warrants the need for genotyping in hospitals

History of Tuberculosis

- At the turn of the 20th century, tuberculosis was the leading cause of death in the United States with an estimated 10% of the human tuberculosis cases caused by bovine tuberculosis(1)
- In children, it was estimated that closer to 25% of tuberculosis cases were caused by bovine tuberculosis (1)
- In 1917, the prevalence of TB in cattle was 5% (1)
- Historically, TB was called ‘Consumption’ because the disease was said to consume a person from the inside out



TB in the 1800's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- Tuberculosis was contracted by consuming raw or undercooked contaminated meat and unpasteurized milk
- Robert Koch developed tuberculin in 1882. Nobel prize winning discovery(2)
- The interpretation of the tuberculin test was based on multiple temperature readings over a 24 hour period

TB in the early 1900's

- In 1908, Charles Mantoux developed the intradermal tuberculin test and it became the official method (1)
- In 1917, the Tuberculosis Eradication Division established the first UM&R for the Bovine Tuberculosis Eradication Program (1)
- The UM&R also established the guidelines for the herd accreditation and the first tuberculosis free herd was established 6 months later (1)
- Eventually the program was expanded to include bison in 1987 and cervidae in 1993 (3)

Early Meat Inspection

- In the early 1900's, meat inspection was conducted by the Bureau of Animal Industry (1)
- Animals and carcasses showing signs of acute disease, high fevers, or any animal suspected of having diseases that could endanger public health were condemned
- Only applied to meat being shipped interstate or internationally
- States set their own laws and there was large variability between states

1906 Federal Meat Inspection Act

- Enforced that all cattle infected with tuberculosis be condemned
- In reality, localized diseased lesions were trimmed off the carcasses and passed, while carcasses with disseminated disease were condemned
- The condemning of TB diseased animals created a need to establish an indemnity fund to compensate producers and an eradication program to decrease the prevalence TB

Bovine TB Eradication Program

- In 1917, the Tuberculosis Eradication Division established the first UM&R for the Bovine Tuberculosis Eradication Program (1)
- In the early years of the TB eradication program, the plan utilized whole herd testing and slaughter
- By 1965, the prevalence of TB was less than .1% and the direction of the program was changed to slaughter surveillance instead of whole-herd testing (3)
- Slaughter surveillance is still the method used today

Bovine TB Eradication Program

- Surveillance program
- Meat inspection is the key method of *M. bovis* surveillance
- FSIS veterinarians work in slaughter facilities and other inspected facilities and are in charge of submitting thoracic granulomas for inspection
- Required to submit a set number of tissue samples for testing to NVSL

Slaughter Surveillance

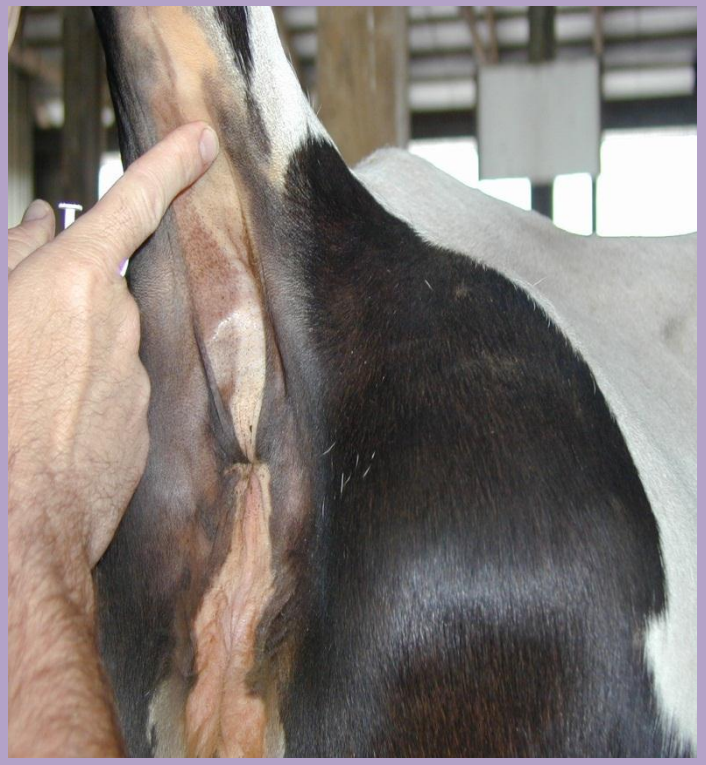
- When a positive animal is identified on histopathology, the cow is traced back to its herd of origin and an epidemiological evaluation is conducted with intradermal testing of the herd of origin and any other cattle that might have been exposed

Tuberculosis Testing

- The primary screening test for detecting tuberculosis in cattle is the caudal fold tuberculin test
- Newly infected cattle do not react to the intradermal injection of tuberculin
- The caudal fold tuberculin test has high specificity for Mycobacterium and a lower sensitivity
  - Higher number of false negatives

Bovine TB Testing Procedures

- Caudal fold tuberculin test (CFT)
  - First screening test in the TB testing process
  - PPD is injected under the tail
  - The site of injection is checked 72 hours later for any changes
  - If the animal is a reactor they undergo further testing (6)



Bovine TB Testing Procedures

- Comparative cervical test (CCT)
  - Only done on animals that respond to the CFT
  - 2 injection sites
  - The sites of injection are checked 72 hours later for changes using calipers to determine which strain the immune system is responding
  - Classified as negative, suspect, or reactor (6)

Zoological Animals

- *M. bovis* infects a wide range of host species including cattle, cervids, bison, badgers, possums, antelopes, elephants, seals, and humans
- The risk for human exposure is higher from zoo animals such as seals and elephants that interact regularly with handlers and trainers
- Tuberculosis infections in captive elephants have been well documented worldwide
- Spread from elephants to humans through the aerosol route via the elephant's trunk and documented to settle in dust and dirt

Recommendations for Prevention

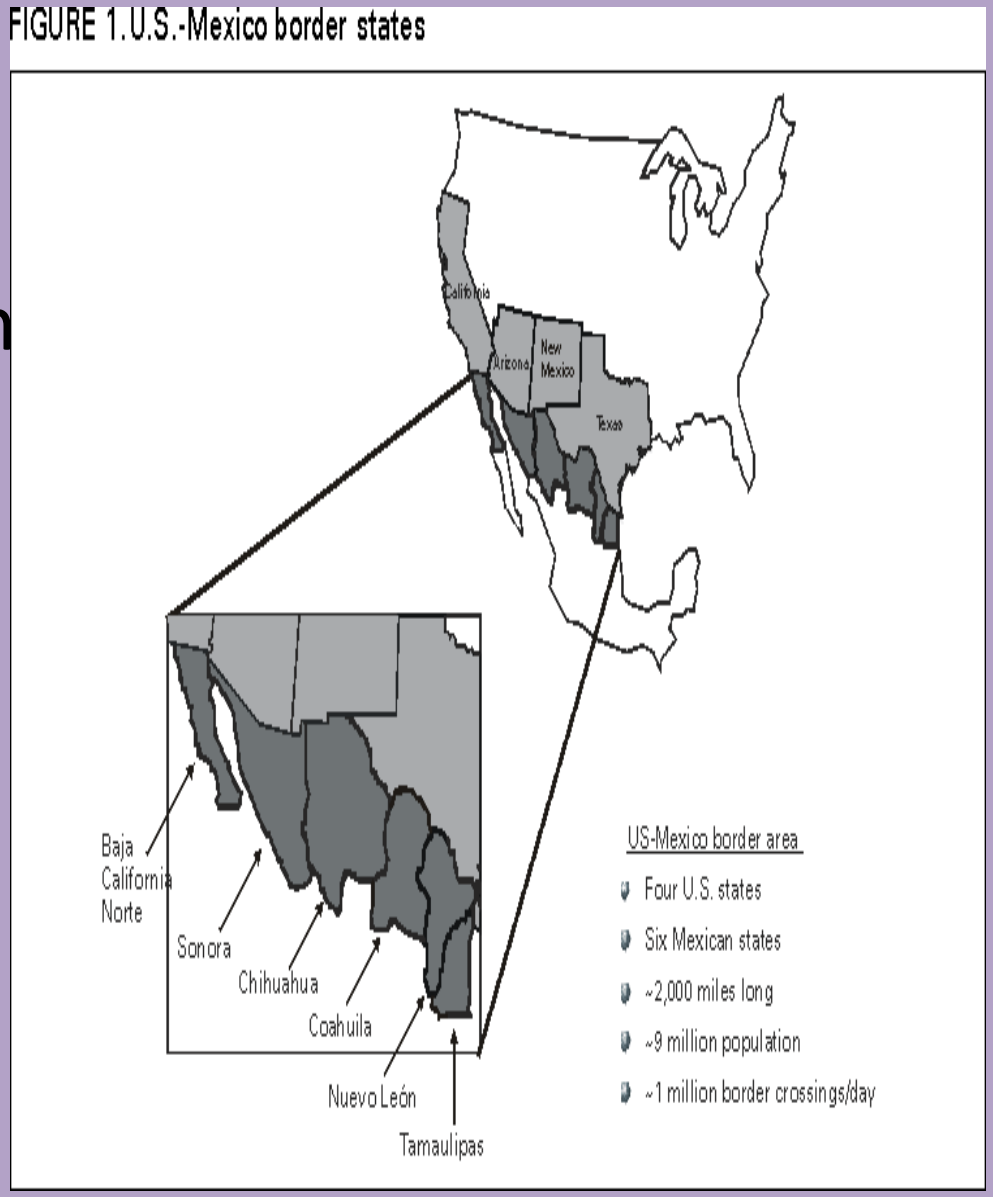
1. Require tuberculosis screening tests during annual exams for animals highest at risk. Species that should undergo annual testing include bovids, primates, sea lions, camelids, elephants, cervids and rhinoceros
2. Require regular tuberculosis skin testing of handlers and workers to increase detection of TB
3. Increase education about the potential risks and hazards associated with working in close contact with zoo animals

Recommendations

4. Require adherence to strict infection control methods during animal necropsies and medical procedures
5. Encourage workers and visitors to wash hands to reduce the risk of disease transmission
6. Prohibit food in animal areas and include transition areas between animal areas and non-animal areas

Cattle of Mexican Origin

- The number of tuberculosis infections in Mexico is higher than in the U.S.
- Cattle imported from Mexico typically spent up to 14 months at U.S. farms before going to slaughter



Cattle of Mexican Origin

- Bovine tuberculosis is endemic in Mexico especially in Mexican dairy cattle
- The northernmost regions of Mexico have a lower incidence of TB than the southernmost regions
- The U.S. aids Mexico with their efforts to eliminate tuberculosis by developing TB programs in the northern states of Mexico closest to the U.S. border

USDA Import Protocols

- USDA has banned the importation of Holstein cattle from Mexico
- Import protocols for the importation of all Mexican cattle into the US
  - All cattle be tested for TB
  - Proper identification

Recommendations

1. Ban importation of Mexican cattle into the U.S.
2. Promote accurate animal identification of all cattle
3. Continue R&D of more sensitive screening tests
4. Require rodeo cattle to have annual TB testing for interstate movement to rodeo events

Recommendations

5. Require that certain classes of cattle be sent directly to slaughter following importation
6. Require additional testing at ports for higher risk cattle
7. Require risk evaluations, herd plans, or additional testing for herds exposed to imported animals
8. Increase sampling rates at processing plants for imported higher risk cattle

Cervids

- Cervid production has become an increasingly popular industry in the U.S. with captive deer and elk herds located all across the nation
- In 1991, an outbreak *of M. bovis* in Canada was traced back to an elk herd in the U.S. (8)
- Following the outbreak, the USDA VS developed Uniform Methods and Rules for the cervid eradication of tuberculosis

Cervids

- The white tailed deer populations in parts of Michigan are known to be endemic with TB
- The high population of deer combined with the practice of baiting and feeding, predisposed Michigan to the outbreak
- Prohibited the supplemental feeding and baiting of the white tailed deer and have reduced the density of the deer population by hunting

Cervids

- White tailed deer is the reservoir host in the U.S.
- The situation is unique in that reports of self-sustaining *M. bovis* infection in a wild, free-ranging cervid population in North America had not been previously reported
- The main risk of zoonotic transmission of TB is to occupational workers that come in close contact to cervids such as cattle and cervid herd owners, hunters, and veterinarians

Recommendations

1. Target testing of cattle, domestic bison, and captive cervid herds in wildlife endemic areas and increased surveillance
2. Encourage hunting of deer in tuberculosis endemic areas to depopulate the deer population
3. Encourage hunters to take precautions when killing and dressing deer and elk in tuberculosis endemic areas

Recommendations

4. Double fencing should be considered in TB endemic areas
5. Routine cleaning of feed bins and water troughs on cervid and cattle farms
6. Prevent sharing of feed and water troughs between cattle and deer
7. Store livestock feed out of reach of wildlife
8. Integrate tuberculosis testing with existing surveillance for other diseases of hunter-killed cervids like chronic wasting disease
9. Support research to develop vaccines and bait delivery strategies to reduce the prevalence of TB in wildlife

Non-Cervid Wildlife

- *M. bovis* is known to infect a wide range of host species
- The distribution and number of lesions helps determine a species ability to excrete the bacteria and act as a reservoir host
- U.S. wildlife reservoir is the white-tailed deer
- Different wildlife reservoirs in other countries

Non-Cervid Wildlife

- On the Hawaiian island of Molokai, the reservoir host for bovine tuberculosis is feral swine
- Depopulation of the feral swine population is used to manage TB in Hawaii
- In Michigan, hunters are encouraged to hunt feral swine

Recommendations

1. Reduce the population density of known sentinel species
2. Continue testing in sentinel species to ensure that tuberculosis does not become endemic in any other wildlife
3. Increase public understanding and acceptance of the importance of depopulating sentinel species

Unpasteurized Dairy Products

- Historically, consumption of unpasteurized dairy products from infected cows was the main source of infection for humans
- In developing countries, where pasteurization is not practiced, the incidence of tuberculosis from this route is still a serious public health issue
- Routine pasteurization has eliminated the risk of most human infections from contaminated dairy products in developed countries

Unpasteurized Dairy Products

- Recently, there have been outbreaks of *M. bovis* from contaminated unpasteurized cheese products in NYC and CA
- The origins have been traced back to soft fresh cheese from Mexico
- One study sampled 203 cheese samples being imported through non commercial channels and found:
  - 10 samples contaminated with *M. tuberculosis (7)*
  - 1 sample contaminated with *M. bovis (7)*

Recommendations

1. Prohibit selling of raw, unpasteurized milk and dairy products and discourage ‘black market’ selling of raw milk and dairy products
2. Disseminate education about the importance of pasteurization of all dairy products including soft fresh cheeses

Raw Milk Movement

- The raw milk movement has been growing in popularity across the U.S.
- Advocates for consuming unpasteurized milk claim that pasteurized milk causes everything from cancer to heart disease
- They also claim that pasteurized milk destroys enzymes, denatures milk proteins, and promotes the growth of pathogens

Conclusion

- Bovine TB is a serious disease with human health, animal health and trade implications
- Worldwide, human TB is still very prevalent and is one of the leading causes of death in HIV/AIDS patients
- In the U.S., through the collaboration of veterinarians, livestock producers, and health officials the prevalence of bovine tuberculosis in cattle has been reduced from 5% in 1917 to .0001% today (1)
- The presence of wildlife reservoirs has kept complete eradication just out of reach but with the continued effort of federal, state and wildlife officials bovine tuberculosis should continue to remain under control

Images

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