POTENTIAL PATHWAYS FOR *MYCOBACTERIUM BOVIS* ZOONOTIC TRANSMISSION TO HUMANS

by

LAUREN ENGLAND

B.S., Kansas State University, 2008

A report submitted in partial fulfillment of the requirements for the degree

MASTER OF PUBLIC HEALTH

Diagnostic Medicine/Pathobiology

College of Veterinary Medicine

KANSAS STATE UNIVERSITY

Manhattan, Kansas

2012

Approved by:

Dr. Robert Larson

Abstract

Veterinary Services, a branch of Animal Plant Health Inspections Services, has the responsibility to protect our nation's animals and animal products through disease control and eradication programs, surveillance and monitoring. During the course of my experience working with Veterinary Services, I learned about program diseases and the different ways veterinary medical field officers and epidemiologists work together to control, monitor and survey these diseases. Veterinary Services has been working to eliminate bovine tuberculosis in the United States since the early 1900's. The Bovine Tuberculosis Eradication Program has been largely successful but tuberculosis keeps resurfacing in pockets around the U.S. leading to the conclusion that there must be a wildlife reservoir. *Mycobacterium bovis* is the cause of bovine tuberculosis and is considered a zoonotic pathogen. *M. bovis* has been reported to infect a wide range of host species including cattle, goats, sheep, pigs, cats, dogs, bison, badgers, possums, antelopes, elephants, seals, and humans(1). Through my experiences working with Veterinary Services, I was able to learn about the bovine tuberculosis eradication program and to explore different avenues in which *M. bovis* could be transmitted to humans. My report discusses the potential pathways for *M. bovis* zoonotic transmission to humans and my experiences working with Veterinary Services.

Table of Contents

List of Figures

Abbreviations

APHIS- Animal and Plant Health Inspection Services

BAI- Bureau of Animal Industry

BCG- Bacille Calmette-Guerin

CCT- Comparative Cervical Test

CFT- Caudal Fold Test

ELISA- Enzyme-linked Immunosorbent Assay

FY- Fiscal Year

HEPA- High-efficiency Particulate Air

HIV- Human Immunodeficiency Virus

M.bovis- *Mycobacterium bovis*

NAHMS- National Animal Health Monitoring Systems

NVSL- National Veterinary Services Laboratory

TB- Tuberculosis

US- Unites States

USDA- United States Department of Agriculture

VS- Veterinary Services

Preface

My Experiences with Veterinary Services

For my field experience, I worked with Animal Plant Health Inspection Services (APHIS), Veterinary Services (VS) as a veterinary student trainee. The scope of my work was focused on learning about animal diseases that APHIS is working to manage and the steps being taken to prevent, control, and eliminate these diseases. I spent the summer assisting Veterinary Medical Officers and Veterinary Services Staff as they worked in the field throughout Kansas. I also worked with State Animal Health and Public Health officials and gained an understanding and appreciation of the roles and relationships between state and federal regulatory agencies and how they work together with industry partners, private veterinary practitioners and producers to control and/or eradicate various program and regulatory diseases, as well as potentially zoonotic diseases. In the field, I worked with National Animal Health Monitoring System (NAHMS) which conduct surveys and field studies to collect data on animal health and management in livestock species. This summer, NAHMS was focused on the sheep industry and we collected biological samples including fecal samples to test for enteric pathogens and parasites, and blood samples to test for Q fever and Ovine Progressive Pneumonia. The participating producers also filled out a questionnaire on their management practices. The collected information will be compiled, analyzed, and used to set policy, settle trade issues, assess the need for additional research and answer producer and consumer questions regarding the industry.

While working in the Topeka office of Veterinary Services, I learned about the import and export services offered by VS. Veterinary Services play an important role in safeguarding the health of our nation's agricultural products by inspecting animal product facilities. Veterinary Services is also in charge of import and export requirements for animals, animal products and biologics.

Alongside Veterinary Medical Field Officers, I helped inspect quarantine and holding facilities for exporting cattle to Russia. Russia requires an extensive amount of tests and vaccinations. I learned that planning and timing is essential to coordinating these export activities. I also helped to inspect facilities that export animal products to other countries.

Also, during my field experience, I spent a week at the National Veterinary Services Lab (NVSL) in Ames, Iowa. NVSL is committed to safeguarding human and animal health by providing accurate laboratory support and diagnostics. While at NVSL, I observed the preparation techniques for different reagents used in diagnostic testing. Additionally, I observed diagnostic tests and research projects aimed to improve diagnostic testing. I also spent a week at the Western Regional Office of Veterinary Services where I learned about the development of protocol for regulatory programs and about the development and implementation of emergency preparedness programs that target outbreaks in diseases of importance including foreign animal diseases and zoonotic diseases.

Introduction

Mycobacterium bovis is the cause of bovine tuberculosis and is known to infect humans and a host of other wildlife and domesticated species (1). Humans typically become infected with *M. bovis* through inhalation of aerosols or the consumption of unpasteurized infected dairy products. When humans are infected via the aerosolized route, they develop pulmonary tuberculosis characterized by granulomatous lesions in the lungs and adjacent lymph nodes. When humans are infected by consuming contaminated dairy products, they develop lesions in the tonsil and intestinal mucosa (1). The disease is chronic, progressive, and debilitating because Mycobacterium species are slow growing (2). Human *M. bovis* infections leading to pulmonary tuberculosis are indistinguishable radiologically, clinically, and pathologically from *Mycobacterium tuberculosis* infections (2). This warrants the need for genotyping strains of Mycobacterium to determine the true prevalence of *M. bovis* in human tuberculosis infections. It is believed that due to lack of isolating and identifying strains of TB in human hospitals, the actual number of human *M. bovis* infections may be underestimated (3).

Since 1917, Veterinary Services has been working to eliminate bovine tuberculosis in the United States through the Bovine Tuberculosis Eradication Program (4). The eradication program has proven to be hugely successful and has reduced the prevalence of bovine tuberculosis in cattle from 5% in 1917 to .0001% today (5).

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 (5). In 1865, veterinarians believed that bovine tuberculosis was a highly contagious disease and that humans could be infected from consuming undercooked meat or unpasteurized milk from tuberculosis infected cattle (5). Despite these claims, Robert Koch announced that the bovine and human strain of tuberculosis were identical and tuberculosis infected cattle posed little risk to humans and no precautions needed to be taken regarding milk or meat consumption from infected cattle. While this did hinder public health advancements, Koch also contributed to detection of tuberculosis by developing the first tuberculin in 1882 (6). Koch promoted his tuberculin as both a preventative and treatment for tuberculosis. It was quickly discredited as both a preventative and treatment, however, it was observed that animals injected with tuberculin developed systemic reactions including hyperthermia. After the discovery, tuberculin was adopted as a test for detection of tuberculosis in cattle (6).

In the early 1900's, meat inspection was conducted by the Bureau of Animal Industry (BAI). The BAI instructed inspectors to condemn animals and carcasses showing signs of acute disease, high fevers, or any animal suspected of having diseases that could endanger public health. These guidelines only applied to meat being shipped interstate or internationally (5). States set guidelines for their own meat inspection and there was large variability between states. In 1906, the Federal Meat Inspection Act was passed and enforced that all cattle infected with tuberculosis be condemned. In reality, carcasses were condemned based on severity of the disease. Localized diseased lesions were trimmed off the carcasses and passed, while carcasses with disseminated disease were condemned. The continued condemning of carcasses infected with tuberculosis created the need to establish an indemnity fund to compensate producers and an eradication program to decrease the prevalence of the disease (5).

In 1917, the Tuberculosis Eradication Division established the first Uniform Methods and Rules for the Bovine Tuberculosis Eradication Program. The program aims to mitigate disease introduction in the U.S., control and manage any outbreaks, and conduct active surveillance (4).

As part of an active bovine tuberculosis surveillance program, APHIS Food Safety and Inspection Services Veterinarians work in slaughter facilities and other inspected facilities and are in charge of submitting thoracic granulomas for inspection (7). Meat inspection by FSIS veterinarians is a key method of tuberculosis surveillance in cattle. The veterinarians are trained in detection of granulomatous lesions (Figure 3) and they are required to submit a set number of tissue samples for testing to NVSL (8).

The primary screening test for detecting tuberculosis in live cattle is the caudal fold tuberculin test. The bovine tuberculosis testing procedure begins with the caudal fold tuberculin test (CFT). Purified protein derivative tuberculin is injected intra-dermally in the caudal tail fold. The same veterinarian who performed the test returns in seventy-two hours to check the site for any reaction including swelling, redness, or hardness (9). If the cow reacts to the tuberculin, the cow is labeled as suspect and the whole herd is quarantined and the reactor cow undergoes further testing. The next test in the procedure is the comparative cervical test (CCT) and it is only done on animals that react to the CFT. The CCT must be done within ten days of the CFT test (9). Cervical skin thickness is measured using special calipers and the skin is shaved in two sites. One site is injected with avian tuberculin and the other site is injected with bovine tuberculin. The same veterinarian who performed the test returns in seventy-two hours and the calipers are used to measure for differences between the two injection sites to determine to which strain the immune system is reacting (9). The cow is then assigned to one of the three classifications, negative, suspect or reactor. If the cow is suspect, the owner can decide between euthanasia or further testing in sixty days (9). During the sixty days, the herd is quarantined. If the cow is a reactor, the cow is removed from the farm and undergoes further testing and necropsy (9).

Indemnity for infected cattle is contingent on the availability of federal funds and based on the fair market value of the animal.

Worldwide tuberculosis is the second greatest killer of humans due to a single infectious agent. Tuberculosis is a leading killer of HIV infected humans causing 25% of all HIV related deaths (10). In the United States, the prevalence of human tuberculosis is 4.8 per 100,000 population (10). In African and Asian countries, 80% of the population will test positive with tuberculin tests (10). Most of these are latent infections with only a small percentage developing full clinical disease. Multidrug-resistant strains of tuberculosis have been documented in almost every country with tuberculosis. The growing resistance to treatments is believed to be caused by mismanagement of tuberculosis treatments. The World Health Organization has ‘A Stop TB Strategy’ in place to reduce the global disease burden of TB by 2015 (10). Most human tuberculosis infections are due to the causative agent *Mycobacterium tuberculosis* with only a small percentage of human tuberculosis infections caused by *Mycobacterium bovis*. With the Bovine Tuberculosis Eradication Program, the United States is doing its part to ensure that bovine tuberculosis in the U.S. is not contributing to the global tuberculosis crisis.

Chapter 1

Zoological Animals

Humans have reportedly been infected with *M. bovis* from elephants, tigers, seals, and rhinoceros (11). The risk for human exposure is higher from zoo animals such as seals and elephants that interact regularly with handlers and trainers. These animals could also be a source of infection for other susceptible species including other zoo animals and surrounding wildlife.

Tuberculosis infections in captive elephants have been well documented worldwide. *Mycobacterium tuberculosis* is the most commonly cultured organism from these infections however*; Mycobacterium bovis* has also been cultured (12). Tuberculosis is spread from elephants to humans through the aerosol route via the elephant's trunk, which makes elephant handlers the most at risk for zoonotic transmission of *M. bovis. M. bovis* has also been documented to settle in dust and dirt and therefore, any workers who enter into the elephant sanctuaries could potentially be at risk (13).

Recommendations

These recommendations are from the Center for Disease Control and Prevention (16), USDA APHIS Import Requirements (14) and the European Association of Zoos and Aquaria Transmissible Disease Handbook (15). I compiled the recommendations and put them in order of importance.

1. Require tuberculosis screening tests during annual exams to help diagnose early infections (14). Species that should undergo annual testing include bovids, primates, sea lions, camelids, elephants, cervids and rhinoceros. Since false negatives are common in

early infections, new arrivals to the zoo should be tuberculosis tested and quarantined for a least sixty days and then retested at the end of the sixty days (5). Bovids, primates, sea lions and camelids should be skin tested, elephants should be ELISA tested, cervids should be tested using the comparative cervical test and rhinoceros' should be tested using the caudal fold skin test (15). Early detection of tuberculosis infected animals will help prevent further exposure to healthy animals and humans (14).

2. Require yearly tuberculosis skin testing of handlers and workers to increase detection of TB (11).
3. Increase education about the potential risks and hazards associated with working in close contact with zoo animals (16). Of particular importance are zoo animal handlers and veterinarians and workers who have indirect contact with the zoo animals such as staff who clean cages, handle soiled laundry, and dispose of contaminated scalpel blades, necropsy knives and needles (17). Workers who are in contact with infected animals should use respiratory (N95) HEPA filtered masks during all direct or indirect contact with infected animals, such as cage cleaning, medication administration, feeding, and watering (17). Increased education and requiring proper protective equipment will reduce the risk of transmitting tuberculosis (17).
4. Require adherence to strict infection control methods during animal necropsies and medical procedures (18). Respiratory protection and protective gloves should always be used during animal necropsies. If the animal is suspected or known to have tuberculosis Veterinary Services should be contacted and further precautions need to be taken such as approved, pre-fitted particulate filter respirators (17).

5. Encourage workers and visitors to wash hands to reduce the risk of disease transmission (16). Hand washing signs should be posted at all exits from animal areas and in all restrooms. Proper hand washing instructions are: wet hands with running water; place soap in palms; rub together to make a lather; scrub hands vigorously for 20 seconds; rinse soap off hands. If possible, turn off the faucet by using a disposable paper towel. Dry hands with a disposable paper towel. Liquid hand soap is preferred over alcohol based instant hand sanitizers (19).
6. Prohibit food in animal areas and include transition areas between animal areas and non-animal areas (16).
7. Vaccinate workers at the highest risk of exposure with the BCG vaccine. However, the effectiveness of the Bacille Calmette-Guerin (BCG) vaccine against tuberculosis is unpredictable and the vaccine induces tuberculin sensitivity. The vaccine is not currently being used in the United States (1).

Chapter 2

Cattle of Mexican Origin Including Rodeo Stock

"During FY 2006, over one million bovine were imported from Mexico. In a previous audit, USDA reported that 75 percent of the bovine infected with TB found in the United States were imported from Mexico (20). USDA also previously reported that bovine imported from Mexico typically spent up to 14 months at United States farms before going to slaughter, with each Mexican-origin bovine infected with *Mycobacterium bovis* potentially spreading the disease during that time (20)." The prevalence of human tuberculosis infections in Mexico is 18 per 100,000 population which is higher than in the U.S. (21). Furthermore, the communities in the U.S. that border Mexico have a higher incidence of cattle TB than the rest of the nation (Figure 1 and 2).

Many factors contribute to the high rate of human tuberculosis infections in Mexico including limited access to healthcare, low socioeconomic status, and a lack of education about the transmission of TB (21). Bovine tuberculosis is endemic in Mexico especially in Mexican dairy cattle (3). While the overall incidence of *Mycobacterium bovis* in Mexico varies by region, the northernmost regions have a lower incidence of TB than the southernmost regions (22). This is largely due to the collaboration of Northern Mexico states and the U.S. to lower the incidence of tuberculosis.

To mitigate the risk of infection by imported dairy cattle, the U.S. has banned the importation of Holstein cattle (23). The USDA also has import protocols for the importation of all Mexican cattle into the U.S. The regulations require that all animals in the shipment have been tested and/or certified for tuberculosis according to the requirements for the type of cattle and the TB status of the state or zone of origin (23). The protocols also require proper identification of the animal and herd of origin in order to facilitate trace backs (23). The United States also aids Mexico with their efforts to eliminate tuberculosis by developing TB programs in the northern states of Mexico closest to the U.S. border. While these efforts have helped to decrease the risk of TB infected cattle imported from Mexico, TB positive cattle are still being identified and U.S. feeder cattle in close proximity to Mexican feeder cattle are considered the highest at risk for developing *M. bovis* infection. Rodeo and roping cattle imported from Mexico pose a similar risk (24).

The primary screening test for detecting tuberculosis in cattle is the caudal fold tuberculin test. The CFT has a sensitivity of 81.9% and specificity of 96.3% (25). However, newly infected cattle generally do not react to the intradermal injection of tuberculin (26). But by requiring that the entire herd be tested, there is a greater probability of correctly classifying herd-status because increasing the number of cattle being tested in a herd increases the herd sensitivity. However, there are issues with the caudal fold tuberculin test, none of the tests currently available for the ante-mortem diagnosis of bovine TB allow a perfectly accurate determination of the *M. bovis* infection status of cattle (26). There are many factors that could result in false negative test results including improper handling and administration of tuberculin and early tuberculosis infections that have yet to trigger an immune response. Cross reactions from other strains and species of Mycobacterium could result in false positive test results (26). It is impossible to be sure that the tuberculosis screening tests accurately identify the disease status of the cattle and because of the risk of false-negative test results, *M. bovis* infected Mexican cattle could potentially be imported and become a source of exposure to U.S. cattle, wildlife, and humans.

Recommendations

These recommendations are from the USDA APHIS: A New Approach for Managing Bovine Tuberculosis: Veterinary Service Proposed Action Plan (4). I compiled the recommendations and put them in order of importance.

1. Ban importation of Mexican cattle into the U.S. This would eliminate the risk of spreading bovine tuberculosis from Mexican cattle to American cattle. However, this could bring about further political and trade issues which are beyond the scope of this paper.
2. Promote accurate animal identification of all cattle to facilitate trace back during outbreak investigations. Rapid trace back to the animal of origin with testing and quarantining of exposed herds would decrease the number of cattle and other animals exposed to bovine tuberculosis (4).
3. Require rodeo cattle to have annual TB testing for interstate movement to rodeo events (4).
4. Require that certain classes of cattle be sent directly to slaughter or to designated quarantine feed yards immediately following importation and not allowed to mix with other cattle at feed yards (4). This would ensure that high risk cattle do not spread tuberculosis to healthy herds (4).
5. Require risk evaluations, herd plans, or additional testing for herds exposed to imported animals (4).
6. Increase sampling rates at processing plants for imported higher risk cattle (4).

Chapter 3

Cervids

Cervid production has become an increasingly popular industry in the U.S. with captive deer and elk herds located all across the nation. Bovine tuberculosis in cervids did not become a significant issue in the U.S. until 1991 when an outbreak *of M. bovis* in Canada was traced back to an elk herd in the U.S. (7). Following the outbreak, the USDA VS began including cervids in the Bovine Tuberculosis Eradication Program. Overtime, the USDA VS developed Uniform Methods and Rules for the cervid tuberculosis eradication program (7).

Wild cervids are known to carry *M. bovis* and pose a serious risk to livestock and captive deer and elk herds (7). Sharing of fence lines with wildlife as well as feeding and concentrating wild deer and elk increase the risk of spreading tuberculosis to livestock and other wildlife. The white-tailed deer populations in parts of Michigan are known to be endemic with TB and the disease has been spread to coyotes, red foxes, raccoons, black bears and bobcats in the surrounding areas (7, 28). 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 (29). Veterinarians, epidemiologists and wild life specialists believe that the high population density of deer combined with the practice of baiting and feeding, predisposed Michigan to this outbreak (29). Veterinary Services has collaborated with the Michigan Department of Agriculture and Department of Natural Resources to create an intensive surveillance and control program for certain areas of Michigan (7). They have prohibited the supplemental feeding and baiting of the white-tailed deer and have reduced the density of the deer population (28). The main risk of zoonotic transmission of tuberculosis is to occupational workers that come in close contact to cervids such as cattle and cervid herd owners, hunters, and veterinarians (7).

Recommendations

These recommendations are from the USDA APHIS: A New Approach for Managing Bovine Tuberculosis: Veterinary Service Proposed Action Plan (4), the Michigan Department of Natural Resources (33) and the Bovine Tuberculosis in Michigan Wildlife and Livestock Database (32). I compiled the recommendations and put them in order of importance.

1. Target testing of cattle, domestic bison, and captive cervid herds in wildlife endemic areas and increased surveillance in wildlife to ensure rapid disease detection and prevent further spread. This will enhance the overall efficiency and effectiveness of the surveillance system (4).
2. Encourage hunting of deer in tuberculosis endemic areas to depopulate the deer population (29). White tailed deer are the maintenance host and primary reservoir for bovine tuberculosis in the U.S. Reducing the deer population to biological carrying capacity will reduce the density and number of deer that can carry and spread tuberculosis (29).
3. Encourage hunters to take precautions when killing and dressing deer and elk in tuberculosis endemic areas (7). Safe handling and processing practices include not handling or consuming wildlife that act sick or appear abnormal, wearing heavy rubber or latex gloves while handling and processing deer and elk carcasses, thoroughly cleaning and sanitizing tools and work areas, and disposing of carcasses in landfills or by normal

garbage pick-up (30). Safe handling, proper protective equipment and proper disposal of cervid carcasses will reduce the risk of spreading tuberculosis (30).

4. Double fencing and fences that are at least 7 feet tall should be considered in endemic areas to prevent nose to nose contact between wildlife and livestock (29).
5. Routine cleaning of feed bins and water troughs on cervid and cattle farms to prevent contaminated feed and water transmission of TB (29).
6. Prevent sharing of feed and water troughs between cattle and deer (29).
7. Store livestock feed out of reach of wildlife to prevent feed transmission of tuberculosis (29).
8. Integrate tuberculosis testing with existing surveillance for other diseases of hunter-killed cervids like chronic wasting disease (4).
9. Support research to develop vaccines and bait delivery strategies to reduce the prevalence of TB in wildlife (4).

Chapter 4

Non-Cervid Wildlife

M. bovis is known to infect a wide range of host species including wildlife and domestic species. While many species can be infected with *M. bovis*, the typical distribution and number of lesions help determine the species' ability to excrete the bacilli and act as a reservoir host (31). In the U.S., the primary wildlife reservoir for *M. bovis* is the white-tailed deer, however in other countries the reservoirs are other wildlife species. In Britain and Ireland, the wildlife reservoir is the badger, and in New Zealand, reservoirs are the ferret and opossum (31).

On the Hawaiian island of Molokai, the reservoir host for bovine tuberculosis is feral swine (32). Depopulation of the feral swine population is used to manage TB in Hawaii (32). Focal depopulation was introduced to the U.S. in the early 1960's when M. bovis was discovered in feral swine in California (7). In Michigan, hunters are encouraged to hunt and kill feral swine as part of an aggressive control plan aimed at controlling the growing number of feral swine (33). Testing of sentinel species has also been used to monitor bovine tuberculosis. Sentinel species are species that mirror TB levels in deer and have moderate home range sizes so they are within the area where they contracted the tuberculosis infection. Sentinel species used to monitor bovine tuberculosis include coyotes and feral swine (29).

Recommendations

These recommendations are from the Michigan Department of Natural Resources (33) and the Bovine Tuberculosis in Michigan Wildlife and Livestock Database (32). I compiled the recommendations and put them in order of importance.

1. Reduce the population density of known reservoir hosts (34). Reducing the population of feral swine to biological carrying capacity will reduce the density and number of swine that can carry and spread tuberculosis (29).
2. Continue testing in sentinel species, coyotes and feral swine, to ensure that tuberculosis does not become endemic in any other wildlife (29).
3. Increase public understanding and acceptance of the importance of depopulating reservoir species. Public approval and tolerance of aggressive control measures will help ensure compliance in managing tuberculosis (34).

Chapter 5

Unpasteurized Dairy Products

Historically, consumption of unpasteurized dairy products from infected cows was the main source of infection of *M. bovis* to humans. In developing countries, where pasteurization is not practiced, the incidence of tuberculosis from this route is still a serious public health issue (35). Routine pasteurization has eliminated the risk of most human infections from contaminated dairy products in developed countries (27). Recently, there have been outbreaks of *M. bovis* from contaminated unpasteurized cheese products in New York City and California (36,37). Epidemiologic investigations have traced the origin of the infections back to soft fresh cheese from Mexico. One study was undertaken to determine the prevalence of *M. bovis* in fresh cheeses originating in Mexico and entering the U.S. (37). The study sampled 203 cheese samples confiscated by United States Customs and Border Protection in San Diego, California. The cheese samples had all been purchased in Mexico and were being imported into the U.S. through noncommercial channels (37). The study found that 10 cheese samples were positive for Mycobacterium and one sample was identified as *M. bovis* (37). This study proves that *M. bovis* can be recovered from fresh cheese and therefore, human infections can still occur via consumption of unpasteurized dairy products (37).

Recommendations

These recommendations are from the article, 'Recovery of *Mycobacterium bovis* from soft fresh cheeses originating in Mexico," found in the journal Applied and Environmental Microbiology 2007 (37). I compiled the recommendations and put them in order of importance.

1. Prohibit selling of raw, unpasteurized milk and dairy products and discourage ‘black market’ selling of raw milk and dairy products through public education (37). 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. The campaign for raw milk pushes for a return to small scale, pasture raised dairy herds with minimal processing (38). These claims are not based on scientific fact; however, the benefits of pasteurization have been well documented.
2. Disseminate education about the importance of pasteurization of all dairy products including soft fresh cheeses (37).

Conclusion

Bovine tuberculosis has proven to be a serious disease with human health, animal health and trade implications. 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 (5). While significant progress has been made to eradicate the disease, complete eradication is still out of reach. It will take the combined effort of federal, state and wildlife officials to continue with the eradication efforts (21).

References

1. L.M. O'Reilly, C.J. Daborn. The epidemiology of *Mycobacterium bovis* infections in animals and man: a review. Tubercle and Lung Disease 1995. 76 Supplement 1, 1-46.

2. D. Neil Wedlock, Margot A. Skinner, Geoffrey W. de Lisle, Bryce M. Buddle. Control of *Mycobacterium bovis* infections and the risk to human populations. Microbes and Infection 4 2002. 471-480.

3. Milián-Suazo F, Pérez-Guerrero L, Arriaga-Díaz C, Escartín-Chávez M. Molecular epidemiology of human cases of tuberculosis by Mycobacterium bovis in Mexico. Prev Vet Med. 2010 Oct 1;97(1):37-44.

4. United States Department of Agriculture Animal and Plant Health Inspection Service Veterinary Services. A New Approach for Managing Bovine Tuberculosis: Veterinary Services' Proposed Action Plan. July 2009 P 1-12.

5. Mitchell V. Palmer and W. Ray Waters, "Bovine Tuberculosis and the Establishment of an Eradication Program in the United States: Role of Veterinarians," Veterinary Medicine International, vol. 2011, Article ID 816345, 12 pages, 2011. doi:10.4061/2011/816345

6. Alan L. Olmstead and Paul W. Rhode, "An Impossible Undertaking: The Eradication of Bovine Tuberculosis in the U.S."

7. International Office of Epizootics. J.S. VanTiem. The public health risks of Cervid production in the United States of America. 1997 Aug 16 (2), 564-570.

8. U.S. Department of Agriculture Office of Inspector General, Midwest Region. Audit Report: Animal and Plant Health Inspection Service's Control Over the Bovine Tuberculosis Eradication Program. September 2006. Report No. 50601-0009-Ch.

9. UC Davis. Bovine testing procedures for tuberculosis. www.vetmed.ucdavis.edu/vetext/INF-DA/TestingforTB.pdf

10. World Health Organization. Tuberculosis. WHO 2012. http://www.who.int/topics/tuberculosis/en/

11. Kathleen Michalak, Connie Austin. Sandy Diesel, J. Maichle Bacon, Phil Zimmerman, and Joel N. Maslow. *Mycobacterium tuberculosis* infection as a Zoonotic Disease: Transmission between Humans and Elephants. Emerg Infect Dis. 1998 Apr-June.

12. T. Angkawanish, W. Wajjwalku, A. Sirimalaisuwan, S. Mahasawangkul,T. Kaewsakhorn, K. Boonsri, V. P. Rutten. *Mycobacterium tuberculosis* infection of Domesticated Asian Elephants in Thailand. Emerg Infect Dis 2010 Dec;16(12):1949-51.

13. Murphree R, Warkentin JV, Dunn JR, Schaffner W, Jones TF. Elephant-to-human transmission of tuberculosis, 2009. Emerg Infect Dis 2011 Mar. http://www.cdc.gov/EID/content/17/3/366.htm

14. Kansas Department of Agriculture, Division of Animal Health. Import Requirements.

15. Transmissible Diseases Handbook. Tuberculosis in Zoo Species: Diagnostic Update and Management Issues. European Association of Zoos and Aquaria Working Group Members.

16. Center for Disease Control and Prevention. Compendium of Measures to Prevent Disease Associated with Animals in Public Settings, 2011. National Association of State Public Health Veterinarians, Inc. (NASPHV) Recommendations and Reports. May 6, 2011 / 60(RR04);1-24.

17. The National Tuberculosis Working Group for Zoo and Wildlife Species. Guidelines for the Control of Tuberculosis in Elephants. October 29, 2008.

18. Oh P, Granich R, Scott J, Sun B, Joseph M, Stringfield C, et al. Human exposure following Mycobacterium tuberculosis infection of multiple animal species in a metropolitan zoo. Emerg Infect Dis 2002 Nov. 8.

19. Center for Disease and Control. MMWR. Hand washing recommendations to reduce transmission from animals in public settings. July 6, 2007 / 56(RR05);16-17.

20. U.S. Department of Agriculture Office of Inspector General, Midwest Region. Audit Report USDA's Control Over the Importation and Movement of Live Animals Report. March 2008. Report No. 50601-0012-Ch.

21. Center for Disease Control and Prevention. Preventing and Controlling Tuberculosis Along the U.S.-Mexico Border. Mark N. Lobato, M.D., J. Peter Cegielski, M.D. M.P.H. Division of Tuberculosis Elimination National Center for HIV, STD, and TB Prevention. 2001 Jan. 50(RR1);1-2.

22. United States Department of Agriculture, Animal and Plant Health Inspection Services, Animal and Animal Product Import requirements. http://www.aphis.usda.gov/import_export/animals/cattle_import.shtml

23. Protocol for the import of steers and spayed heifers cattle and bison (feeders) from Mexico. USDA, APHIS, VS, National Center for Import and Export April, 2009.

24. Texas Animal Health Commission. Resolution regarding tuberculosis test requirements for cattle imported from Mexico. July 2003.

25. M.L. Monaghan, M.L. Doherty, J.D. Collins, J.F. Kazda, P.J. Quinn. The Tuberculin Test. Veterinary Microbiology Volume 40 Issues 1-2. May 1994 pgs. 111-124.

26. R. de la Rua-Domenech, A.T. Goodchild, H.M. Vordermeier, R.G. Hewinson, K.H. Christiansen, R.S. Clifton-Hadley. Ante mortem diagnosis of tuberculosis in cattle: A

review of the tuberculin tests, γ-interferon assay and other ancillary diagnostic techniques. Res Vet Sci. 2006 Oct;81(2):190-210.

27. J. M. Grange. *Mycobacterium bovis* infection in human beings. Tuberculosis 2001. 81(1/2). 71-77.

28. World Organization of Animal Health. OIE Press Release: Update on wildlife diseases. http://www.oie.int/en/for-the-media/press-releases/detail/article/update-on-wildlife-diseases/

29. S. M. Schmitt, D. J. O'brien, S. D. Fitzgerald, C. S. Brunning-Fann. Bovine Tuberculosis in Michigan Wildlife and Livestock. Wildlife Disease and Zoonotics. Michigan Bovine Tuberculosis Bibliography and Database. University of Nebraska - Lincoln 2002.

30. Michigan Department of Natural Resources. Precautions When Handling and Processing Deer and Other Wild Game. http://www.michigan.gov/dnr/0,1607,7-153-10363_10856_10905-47502--,00.html

31. C. S. Bruning-Fann, S. M. Schmitt, S. D. Fitzgerald, J. S. Fierke, P. D. Friedrich, J. B. Kaneene, K. A. Clarke, K. L. Butler, J. B. Payeur, D. L. Whipple, T. M. Cooley, J. M. Miller, D. P. Muzo. Bovine tuberculosis in free-ranging carnivores from Michigan. Journal of Wildlife Diseases, 37(1), 2001, pp. 58–64.

32. Stephanie Bany, Jerome Freier. Use of GIS to Evaluate Livestock-Wildlife Interactions Relative to Tuberculosis Spread on Molokai Island, Hawaii. Wildlife Disease and Zoonotics. Michigan Bovine Tuberculosis Bibliography and Database. University of Nebraska – Lincoln. 2000.

33. Michigan Department of Natural Resources. Summary of Wild Swine Eradication Planning.

http://www.michigan.gov/dnr/0,4570,7-153-10370_12145_55230-252371--,00.html

34. Michelle Carstensen, Daniel J. O'Brien, Stephen M. Schmitt. Public acceptance as a determinant of management strategies for bovine tuberculosis in free-ranging U.S. wildlife. Veterinary Microbiology 151 (2011) 200-204.

35. O. Cosivi, J.M. Grange, C.J. Daborn, M.C. Raviglione, T. Fujikura, D. Cousins, R.A. Robinson, H.F.A.K. Huchzermeyer, I. de Kantor, and F.-X. Meslin. Zoonotic Tuberculosis due to *Mycobacterium bovis* in Developing Countries. Emerging Infectious Diseases. 1998 January-March Vol. 4, No. 1: 59-70.

36. Center for Disease Control and Prevention. A Winters, C. Driver, M. Macaraig, SS. Munsiff, C. Pichardo, J, Driscoll, M. Salfinger, B. Kreiswirth, J. Jereb, P LoBue, M. Lynch. Human tuberculosis caused by *Mycobacterium bovis.* CDC June 2005. 54(24);605-608.

37. N. Beth Harris, J. Payeur, D. Bravo, R. Osorio, T. Stuber, D. Farrell, D. Paulson, S. Treviso, A. Mikolon, A. Rodriguex-Lainz, S. Cernek-Hoskins, R. Rast, M. Ginsberg, H Kinde. Recovery of Mycobacterium bovis from soft fresh cheese originating in Mexico. Applied and Environmental Microbiology. Feb 2007. p.1025-1028.

38. A campaign for real milk. Jan 2000. http://www.realmilk.com/

Figure 1. U.S. – Mexico Border States

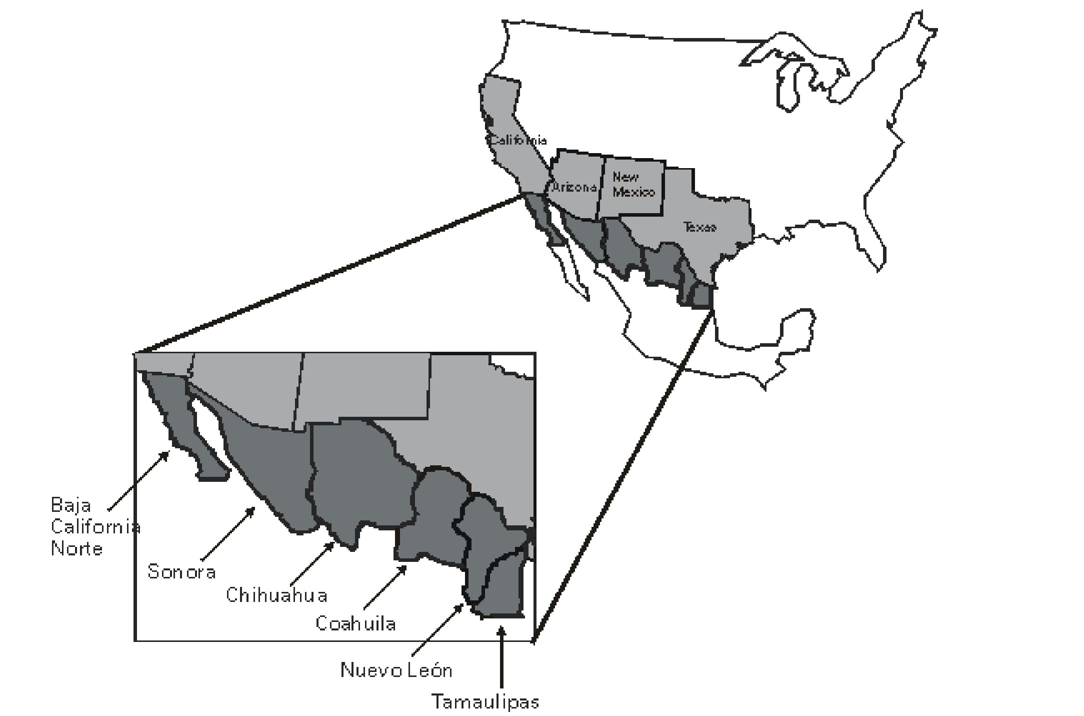
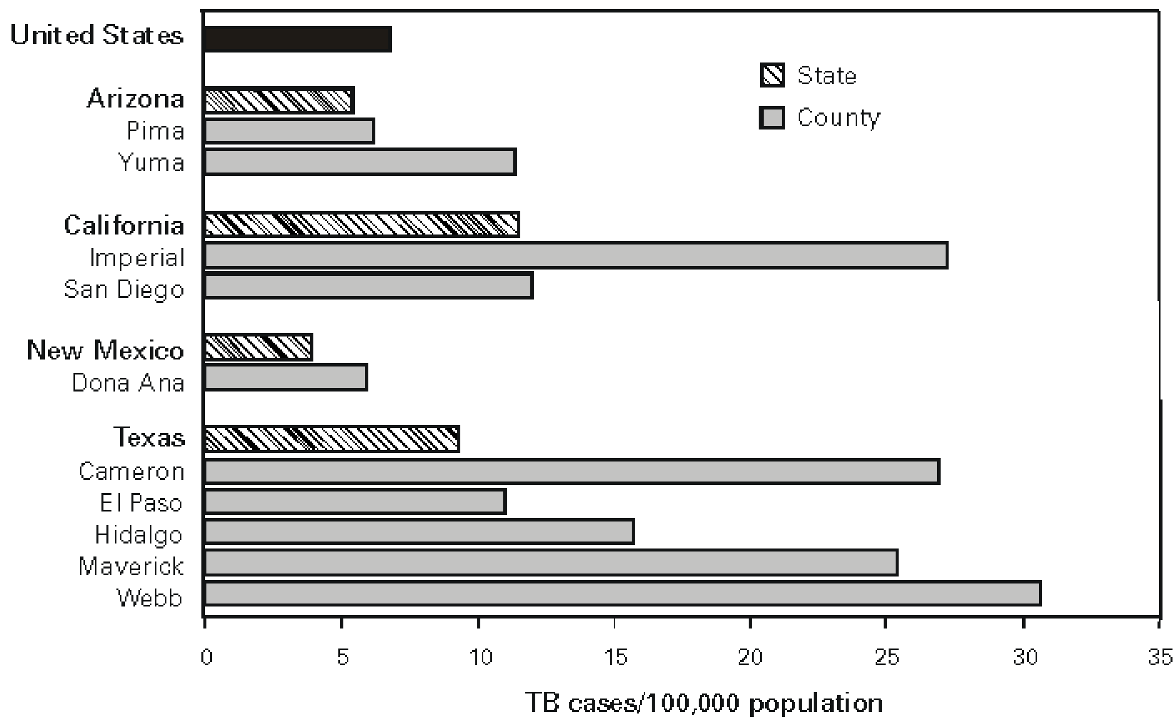


FIGURE 2. Tuberculosis (TB) rates in U.S. states and counties* bordering Mexico, 1998



* Only border counties with ≥10TB cases/100.000 were included.

Figure 3.Tuberculosis infected, granulomatous lymph node