This is to certify that the
dissertation entitled

THE HUMAN HEALTH ASPECTS OF THE
MYCOBACTERIUM BOVIS (BOVINE TUBERCULOSIS)
OUTBREAK IN MICHIGAN

presented by

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has been accepted towards fulfillment
of the requirements for the

DOCTORAL degree in LARGE ANIMAL CLINICAL SCIENCES

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2/29/08
Date

THE HUMAN HEALTH ASPECTS OF THE *MYCOBACTERIUM BOVIS* (BOVINE TUBERCULOSIS) OUTBREAK IN MICHIGAN

By

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A DISSERTATION

Submitted to
Michigan State University
In partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Large Animal Clinical Sciences

2008

ABSTRACT

THE HUMAN HEALTH ASPECTS OF THE *MYCOBACTERIUM BOVIS* (BOVINE TB) OUTBREAK IN MICHIGAN

By

Melinda Jean Wilkins

The current outbreak of *Mycobacterium bovis* (bovine TB) in the white-tailed deer *(Odocoileus virginianus)* and cattle populations of the northeastern portion of the lower peninsula of Michigan offers a unique research opportunity to explore the health impact of the outbreak on human health. Five independent research projects were conducted, each focusing on a different aspect of how humans interact with deer and cattle, potential exposure via pets, and examination of evidence of subclinical infection in an analysis of TB skin test data from the affected counties.

The first project was a survey of deer hunters in both the bovine TB endemic and non-endemic areas. The study determined that less than half were practicing basic health precautions, such as wearing gloves, when handing potentially infected deer carcasses.

The second project summarized the human cases of *M. bovis* infection reported in Michigan from 1997 - 2007. Two of these patients were infected with the same genetic strain of *M. bovis* circulating in the deer and cattle populations of Michigan, and both had had exposure to deer in the endemic area.

The third project examined the role that domestic pets on infected cattle farms might play in the transmission of *M. bovis* to both humans and non-infected livestock. This study concludes that in Michigan, pets would expectedly play a minimal role in disease transmission on the farm. This conclusion is based on a variety of factors, but

mainly due to a lack of evidence of infection in the pets, probably because the affected cattle herds are detected in the early stages of infection.

The fourth project focused on the human "costs" of the disease control efforts in cattle by measuring the incidence density of human injuries acquired while TB testing livestock in 2001. Most of the injuries were found to be preventable, and recommendations were made to decrease injuries in the future.

The fifth project used risk factor exposure data for both *M. tuberculosis* and for *M. bovis* paired with tuberculosis skin test (TDT) results from 12 local health departments to determine if evidence is suggestive of the presence of subclinical tuberculosis infections in persons with exposure risks. Being foreign born or a venison processor were found to be significant risk factors for having a positive TST. This data intimates that venison processors should be added to the list of groups targeted for public health prevention messages for *M. bovis*.

These projects together elucidate distinct human health risks associated with the Bovine TB outbreak in Michigan, and suggest that hunters, venison processors, veterinarians, and owners of infected herds should receive targeted risk prevention messages tailored to their specific routes of exposure to *M. bovis*. Surveillance efforts to detect human cases of *M. bovis* should continue with thorough investigations to determine likely sources of exposure, as *M. bovis* will likely remain endemic in this part of Michigan for the foreseeable future.

This work is dedicated to my family, especially my partner, parents and siblings who were continuous in their support and encouragement. I also dedicate this to my children, in hopes that they will find passion and joy in the educational process and enjoy both learning and teaching as much as I have.

ACKNOWLEDGEMENTS

I would like to take this opportunity to acknowledge the contribution of the many individuals who made the completion of this work possible. Without your selfless contributions of time and knowledge this work would never have been completed. First and foremost, I acknowledge the unending patience and support of Dr. Paul Bartlett, my major professor. Dr. Bartlett's quiet and unhurried leadership made it possible for me to complete this Ph.D. on a timetable compatible with the rest of my life and my many competing priorities. I also acknowledge my other committee members, Drs. Matthew Boulton, John Kaneene, Barbara Robinson-Dunn, Theresa Bernardo, and Ronald Erskine. Together they have all unselfishly contributed time, knowledge and expertise to my work, allowing me to mature as a researcher and an individual. I am honored to have benefited from such a collective pool of wisdom. Dr. Corinne Miller also deserves special mention for her role as a committee member (2001-2004) and her willingness to serve as my external examiner.

I would like to thank Sarah Trembley, Jennifer Sexsmith, Chrysin Wood, Drs. Kimberly Signs and Shelley Stoneciper for their help with on-farm data collection, and Jennifer Dewitt and Melissa Gallego for help with data entry. A special thanks to Dr. Kathy Schwarts and her staff at the Alpena Animal Hospital, and USDA Veterinary Services and Wildlife Services for support with the pet study. I also thank the staff of Health District #2, Health District #4, and

Northwest Michigan Community Health Agency for their participation in the tuberculosis skin testing project.

I am grateful for the financial support I received from Dr. Bartlett for assistance with tuition and student support, from the College of Veterinary Medicine for the Dissertation Completion Fellowship, and especially for the cooperative agreement support from USDA, APHIS. Without such support, this project would not have been possible. I also would like to acknowledge the scheduling flexibility offered by my supervisors at Michigan Department of Community Health throughout this project period.

Finally, I would like to acknowledge my family's contribution to this work. They all contributed in so many large and small ways, past and present. I hope that all who offered support and assistance at any point along the way will know that I am truly grateful for you, and grateful for this wonderful opportunity to learn and grow. I hope to make you proud, and I will take every opportunity to assist the next generation of students and lovers of learning.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

SETTING

Mycobacterium bovis (bovine TB) is an organism of great historical importance in the United States. Due to its high prevalence in the nation's cattle population, and the transmission of the organism to humans via milk, it was a fairly common human pathogen from its first recognition as a disease causing agent in 1882 (Koch, 1882) until the 1920's when it was a major impetus for the milk pasteurization laws. After pasteurization of milk became commonplace, the human disease burden due to *M. bovis* infection was substantially reduced (Grange, 1994). However, control of the disease in cattle proved more difficult, and the prevalence in cattle remaining high until 1918, when the Animal Industries Board (the precursor to United States Department of Agriculture) initiated a national eradication campaign (Frey, 1995). Michigan gained (Bovine) Tuberculosis Free status in 1979. *M. bovis*, in both cattle and humans, remained quiescent for 20 years (Free ranging white-tailed deer, website).

In 1994, a white-tailed deer in Alpena County, Michigan was killed by a physician who noticed tan nodules in the chest cavity. Suspecting, tuberculosis, the animal was presented for testing (Free ranging white-tailed deer, website); *M. bovis* was diagnosed. Animals from two captive cervidae herds within the immediate area of the positive deer were tested, but no additional infected cervidae were found. In spring 1995, all livestock (70 herds) within a 5 mile radius of the positive deer were tested, but no infected herds were found. In 1995, 18 deer (of 403 tested) were found to be infected with *M. bovis;* in 1996, 56 positive deer were found (of 4966 tested); in 1997, 73 positive deer were found (of 3720 tested). In 1998, an Alpena County beef herd was found to be infected. By the end of 1998, two more cattle herds were found to be infected, both in neighboring Alcona County, Michigan (Summary of gross and histologic examination, website).

In October of 2001, Senate Bill 1339 required the testing of all dairy herds and other herds in the 'high risk" areas to be completed within 12 months, and testing of all cattle in non-high risk areas to be completed within three years. To meet the immediate and large-scale demands for TB testing livestock, a cadre of private veterinarians was recruited to conduct TB-herd testing and a high number of injuries to veterinarians were anecdotally being reported to regulatory officials. Surveillance for *M. bovis* in the deer population was primarily based on visual inspection, by Michigan Department of Natural Resources check station personnel, of hunter-killed deer, and was geographically focused in the counties in the northeast portion of the lower peninsula of Michigan.

By October, 2007, a total of 42 Michigan cattle herds have been diagnosed with Bovine TB. Michigan lost its Federal TB Free Accreditation Status in 2000. Five hundred and sixty-eight deer have been have been found infected (out of 153,740 tested) and the disease now maintains itself in the wild deer population and is considered endemic in the northeastern portion of the lower peninsula of Michigan.

In addition to deer and cattle, numerous other species have been found positive for bovine TB, including; coyotes, raccoons, black bear, bobcat, red fox and opossum. (Summary of Michigan wildlife bovine tuberculosis surveillance, website). These species are believed to be "dead-end", or spill-over hosts and not contributory to the maintenance of the disease (Bruning-Fann, 2001). However, disease in these species leads to the potential exposure to the organism by trappers and taxidermists.

Efforts to control the disease in the deer population have led to feeding and baiting bans in affected counties. These bans, designed to reduce the congregation of deer, have led to a decreased number of hunters frequenting these areas which in turn has resulted in a substantial loss of income to hunting-related industries (deer crops, hotels, restaurants, etc.). In addition, the testing requirements and loss of trade revenue has placed a considerable burden on Michigan's cattle and dairy industries.

Including 2007, the total amount of resources dedicated to control the disease in Michigan now exceeds $90 million with the state government contributing $70 million, and the federal government contributing $23 million, over the previous 12-13 years. The majority of funding was dedicated to the control of disease in cattle (M. Ankney, Bovine TB Program Coordinator, personal communication, Nov 9, 2007).

PURPOSE STATEMENT

Since the discovery of *M. bovis* in Michigan's cattle and free-ranging white-tailed deer, much attention, research and funding has focused on *M. bovis* control and surveillance efforts, prevalence estimation, testing and diagnostic methodology. Relatively little attention has focused on the role of *M. bovis* as a zoonotic disease. The purpose of this dissertation is to explore the human health effects of the bovine TB outbreak on Michigan residents, and includes both zoonotic and non-zoonotic affects on the public's health.

That *Mycobacterium bovis* is a zoonotic agent is not in question, nor is the susceptibility of all warm-blooded animals to infection (de Lisle 2001; 2002). However, the role of *M. bovis* as a zoonotic agent in the current outbreak setting, and the actual risk of transmission to humans, has not been established. Historically, exposure to *M. bovis* in the U.S. was via the gastrointestinal route (consumption of raw milk), via the inhalation of aerosols from cattle with pulmonary infection, or by the cutaneous route (prosectors and butchers) following exposure to infected carcasses. With *M. bovis* infection endemic in the white-tailed deer population in Northeast Michigan, new routes of exposure required assessment. With the re-emergence of bovine TB in cattle, traditional or historical routes of exposure need to be re-visited and the lingering question about the potential role of pets as reservoirs of infection for cattle or humans necessitated examination in the current Michigan setting. In addition, exploring the rate of veterinarian injury and the risk factors contributing to injuries will offer insight into the "human costs" of large scale animal disease control efforts. Below, the research questions and a short summary of findings are presented for each of the five projects included in the dissertation.

Research questions and summary of findings

Project 1 - *Mycobacterium bovis* (bovine TB) exposure as a recreational risk for hunters: results of the Michigan hunter survey – 2001.

Because *M. bovis* (bovine TB) is endemic in the white-tailed deer population of northeastern Michigan, hunters may be exposed to *M .bovis* via cutaneous inoculation while field dressing deer or by ingestion of undercooked venison. Michigan hunters have heretofore received inconsistent messages about their risk of acquiring tuberculosis from recreational exposure to deer. The most common health advice offered has been to wear gloves while field dressing deer and to thoroughly cook venison meat products. The objective of this study is to collect data to quantify the usage of these self-protective activities and to characterize hunters practicing these activities. This data was collected by surveying 1,833 hunters who had successfully harvested deer in or near Michigan's Bovine TB endemic area in 2000. The survey participation rate was 78%. Most hunters (89%) reported field dressing deer, 43% of whom wore gloves. Most hunters (95%) reported eating venison; 55% of whom reported their venison was always cooked thoroughly. Several hunter characteristics including older age, female gender, higher awareness level, and area of residence, were significantly associated with the practice of these self-protective activities. The survey results suggest that hunters should receive consistent advice encouraging the use of gloves while field dressing deer and the thorough cooking of venison products before consumption.

Project 2 - Human *Mycobacterium bovis* infection associated with the Bovine TB outbreak in Michigan, 1994 – 2007.

In the period between 1994 and October of 2007, *M. bovis* was found in 42 cattle herds and 568 wild deer in Michigan. Based on genotyping analyses, the strain of *M. bovis* circulating in Michigan's deer and cattle remained genetically stable over this duration. Although *M. bovis* is a zoonotic pathogen, this outbreak strain was not detected in a human until 2002, with the occurrence of a human pulmonary isolate. In 2004, cutaneous disease caused by *M. bovis* was documented in a hunter. This report summarizes the epidemiologic and molecular investigation of these two human cases who shared the deer/cattle outbreak strain of *M. bovis*. The results of this investigation confirm recreational exposure to infected deer in Michigan as a potential, albeit low, risk for acquisition of *M. bovis* infection in humans.

Project 3 - Absence of *Mycobacterium bovis* infection in dogs and cats residing on infected cattle farms – Michigan, 2002.

A cross-sectional field study was performed to evaluate dogs and cats living on farms with *M. bovis* (bovine TB) infected cattle. Our purpose was to determine pet infection status and assess their risk to farm families and/or tuberculosis-free livestock. Nine farms participated in the study. Data and specimens were collected from eighteen cats and five dogs from nine farms. ELISA testing for *M. bovis* and *M. avium* was conducted. Fifty-one biological samples were cultured; all were negative for *M. bovis*, although other *Mycobacterium* species were recovered. No radiographic, serologic or skin test evidence of mycobacterial infection was found. These negative results may be due to the low level of bovine TB infection in the cattle and the infrequent exposure of pets to cattle residing on the same farm. We found no evidence that pets residing on bovine TB-infected Michigan cattle farms pose a risk to humans or bovine TB-free livestock, however precautionary advice was provided.

Project 4 – Veterinarian injuries associated with Bovine TB testing livestock in Michigan, 2001.

Determining the injury rate for working with cattle is difficult since a wide range of persons perform a diverse assortment of procedures on cattle in highly variable circumstances. There is also generally a lack of denominator data regarding the number of cattle receiving each type of procedure. Testing all the cattle in an entire state with a uniform procedure for each animal afforded an opportunity to relate human injury data to a known number of animals handled while carrying out a standardized procedure. The objective of this study was to capture the type and incidence density of injuries associated with TB-testing a large number of cattle, bison and goatherds, and to delineate the various factors contributing to the risk of injury. Additionally, two known mortality events associated with bovine TB testing in Michigan are summarized. A survey was mailed to all veterinarians (N=259) who had completed at least five official bovine TB herd tests in Michigan in 2001. Collected data regarded basic demographics and health status, work experience, veterinary specialty, and practice information. Veterinarians were requested to complete a separate injury questionnaire for each injury received while TB testing livestock in 2001. Risk ratios were calculated, based on the incidence density of injuries per 10,000 animals tested, to compare the characteristics of the injured veterinarians to the non-injured veterinarians. Accurate addresses were found for 247 eligible veterinarians, 175 of whom returned the survey for a participation rate of 71% (175/247). Thirty-five veterinarians reported a total of 53 injuries (10 major, 12 minor and 31 self-treated). Individual veterinary characteristics and the type, cause and location of each injury are described. The overall incidence density of injuries was 1.9 per 10,000 animals tested. Female gender (RR=3.26), having less than 10 years of practice (RR=1.81), being employed by the government (RR=4.54), smoking (RR=5.97) and working 50 hours or less (RR=1.87) were found to be significantly associated with a higher rate of injury per 10,000 animals tested. The human "costs" in terms of injuries, must be considered when decisions are made to initiate large-scale livestock disease control programs, although these costs are more difficult to measure than the financial costs of a budgeted control program. Effort and resources must be allocated to reduce the number and frequency of preventable injuries, and to monitor the public health impact of ongoing disease control efforts.

Project 5 - A comparison of risk factors for exposure to *Mycobacterium tuberculosis* and *Mycobacterium bovis* in northern Michigan.

First recognized in white-tailed deer in 1994, *Mycobacterium bovis* has since been found in several cattle herds and is now considered endemic in the deer population of the northeastern part of the lower peninsula of Michigan. Numerous additional species are also infected, such as coyotes, raccoons, black bear, red fox, bobcats and opossum. Because of the occurrence in wildlife and re-occurrence in cattle, persons in the affected area deemed to be at an elevated risk of exposure include: hunters, trappers, taxidermists, venison processors, beef or dairy producers and farm/livestock workers. The health departments covering 12 counties in the northeastern part of the lower peninsula of Michigan participated in this study. A survey was administered which included a list of *M. bovis*-specific exposure risk factors and a list of *M. tuberculosis*-specific exposure risk factors. Each health department was asked to complete and attach the survey to each tuberculosis skin test (TST) reporting form, and send the de-identified form to the Michigan Department of Community Health. To measure the associations between each risk factor and TST results, either a relative risk with 95% confidence intervals was used, or the Fisher's exact test when cell size was ≤ 5, as appropriate. Overall, there were 29 positive TST reactors, out of 1268 TST records submitted for a positivity rate of 2.29%

(29/1268). Being a venison processor was associated with a positive TST reaction (p=0.047) and well as being foreign born (p=0.019). This finding suggests that venison processors may benefit from targeted public health prevention messages to reduce likelihood of exposure to *M. bovis*.

IMPORTANCE OF FINDINGS

The finding of this dissertation indicates that there are sub-populations of people that may be at an elevated risk for infection with the outbreak strain of *M. bovis* in Michigan. Additionally, personnel involved in the massive cattle testing programs are at risk of physical injuries associated with TB testing livestock. These five projects are independent from each other, but each addresses a different aspect of the overall question, "What are the human health effects of the bovine TB outbreak in Michigan?"

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CHAPTER 1

LITERATURE REVIEW

Because the topic area of "*Mycobacterium bovis*" is so expansive, with a history dating back to the domestication of cattle (4000-8000 BC), and a host range that includes all warm-blooded animals, it is necessary to clearly delineate what will be covered, and more importantly, what will not be covered in this literature review. Topics to be covered include a brief history of the organism and a history of the disease status in cattle and wildlife leading to a description of the setting in which the current Michigan outbreak is occurring. Human infection with *M. bovis* will be described in terms of clinical manifestations (pulmonary, alimentary, and cutaneous), pathogenesis, latency, immune response and detection using the tuberculosis skin test. Routes of exposure for humans, as well as populations at risk of exposure will be covered. The role of dogs and cats in the transmission of *M. bovis* and a summary of injuries associated with large animal veterinary work will be covered as well. Topics that are outside the scope of this dissertation, and therefore will not be covered by this literature review, include: vaccine development in humans or animals, diagnostic techniques in humans (other than TST) and animals, the microbiological or molecular characteristics of *M. bovis*, the role of co-infection with HIV, and the animal disease control efforts in livestock or wildlife populations.

MICHIGAN OUTBREAK SETTING - OUTBREAK HISTORY IN DEER, CATTLE, AND OTHER SPECIES

Although an association between a wasting disease in cattle and consumption in humans had been suspected for many centuries, it was Robert Koch, who in 1882, discovered the tubercle bacillus (Koch, 1882). Koch first believed that bovine and human tuberculosis were caused by the same organism and named cattle as a source of infection for humans. Koch later changed his opinion following research by Smith (Smith, 1898) showing small but constant differences between bacilli of human and bovine origin. Koch considered humans to be immune or only very slightly susceptible to tuberculosis of bovine origin, and that control measures (in cattle) were unnecessary (British Congress on Tuberculosis, 1901). Several groups of researchers were skeptical of this conclusion and began a period of intensive research lasting form 1901 to 1911. The most notable of these research groups was the British Royal Commission on Tuberculosis which clearly established the risk of bovine tuberculosis to human health and confirmed that milk was the principle route of exposure to humans (Frances, 1959). The history of *M. bovis* is well summarized by Grange and Yates (1994), and Grange (1995).

It was in 1917 that the United States Board of Animal Industries, officially began the effort to eradicate tuberculosis in cattle. The disease was causing more losses than all other livestock diseases combined. In humans, tuberculosis was also the number one cause of incapacity and death, with many of these cases due to drinking raw milk from tuberculous cows (Frey, 1995). In the first year of the program, 4.9% of the cattle were reactors to the tuberculin skin test; in 1930 the percentage had dropped to 1.8%, and in 1940 to 0.5% (Frey, 1995). From 1959 to 1987, the reactor rate dropped from 0.2 to 0.01% (USDA, 1990). In the 1990's, on the verge of eradicating the disease at the national level, several new herds were detected in a handful of states (Frey, 1995). An assessment was completed in which several new factors contributing to the persistence of *M. bovis* in the cattle population were identified including: reliance on testing and slaughter surveillance, the enzootic milkshed region of El Paso, TX, importation of infected steers from Mexico, the finding of *M. bovis* in exotic hoofstock in zoos, gameparks, auctions and other facilities and the presence of disease in camelidae (Bleem, 1993).

In 1994, in Alpena County, Michigan, a white-tailed deer (*Odocoileus virginianus*) was killed. The hunter, who noticed tan nodules in the chest cavity, suspected tuberculosis, and presented the carcass for testing; *M. bovis* was diagnosed (Payeur, 2002). Animals from two captive cervidae herds within the immediate area of the positive deer were tested, but no additional infected cervidae were found. In the spring of 1995, all livestock (70 herds) within a 5 mile radius of the positive deer were tested, but no infected herds were found. In 1995, 18 deer (of 403 tested) were found to be infected with *M. bovis;* in 1996, 56 positive deer were found (of 4966 tested); in 1997, 73 positive deer were found (of 3720 tested). In 1998, an Alpena County beef herd was found to be infected. By the end of 1998, two more cattle herds were found to be infected, both in Alcona County, Michigan (Free ranging white-tailed deer, website).

Twenty years after obtaining the bovine TB Accredited-free status from the US Department of Agriculture in 1979, Michigan lost that designation to become a Non-Modified Accredited state on June 22, 2000, joining Texas as the only other US state that did not have a Free status for bovine TB.

As of October, 2007, a total of 42 Michigan cattle herds were diagnosed with bovine TB. Five hundred sixty-eight deer were found infected (out of 153,740 tested) and the disease now maintains itself in the wild deer population and is considered endemic in the northeastern portion of the lower peninsula of Michigan. The disease pathology and transmission in deer in has been well described by Towar (1965) and more recently by Schmitt (1997), Palmer (1999; 2000), and O'Brien (2001). The epidemiology of the current outbreak in Michigan deer has likewise been well described (Schmitt, 1997; 2002; O'Brien, 2002).

In addition to deer and cattle, numerous other species have been found positive including: coyotes, raccoons, blackbear, bobcat, red fox and opossum (Summary of Michigan wildlife bovine tuberculosis surveillance, website). These species are felt to be incidental, or spill-over hosts and not significant in the maintenance of the disease in the wild (Bruning-Fann, 1998, 2001a).

A large amount of information can be found on the Emerging Infectious Disease website (http://www.michigan.gov/emergingdiseases), under the heading of Bovine Tuberculosis. Two chronologies are posted: "A Chronology of bovine TB in Michigan since 1975", and "History of Legislation and Regulation for bovine TB eradication in Michigan's wildlife". In addition, two databases are maintained with current information about new cases of bovine TB in both cattle and wildlife: "Summary for Michigan Wildlife Bovine Tuberculosis Surveillance" and "Summary of gross and histologic examination and mycobacterial culture of tuberculosis cases in cattle and captive deer in Michigan 1996 – 2007".

HUMAN INFECTION WITH *M. BOVIS*

General characteristics of *M. bovis* as an organism

Mycobacteriae are aerobic, non-spore forming, nonmotile, slightly curved or straight rods. They have thick cell walls containing mycolic acids with free lipids making them acid-fast stainers (gram positive) (Pfyffer, 2003). All *Mycobacterium* are able to survive for weeks to months on inanimate objects if protected from sunlight, but are easily killed by UV light and heat. They are more resistant to acids, alkalis, and some chemical disinfectants than are most other non-spore-forming bacteria (Pfyffer, 2003). *M. bovis* is a member of the *M. tuberculosis* complex, a complex related by a >99.9% DNA-DNA homology (Gordon, 2001) sharing the characteristic of being human pathogens, some more significant than others. They are all obligate pathogens with their major ecological niche being the tissues of warm-blooded animals (Pfyffer, 2003).

Immune response

Even after over a century of study, very little is known about the virulence factors of *M. tuberculosis* and *M. bovis* or how the protective immune response is triggered within the infected host (Collins, 1994). Initial response to infection is by the unactivated macrophage, in which the organism replicates without restriction until the macrophage bursts. Lymphocytes, specifically sensitized T lymphocytes, cause the release of gamma interferon. The liberation of gamma interferon causes the activation of the macrophages (Todar, 2007). The immunologically activated macrophage induces a bacteriostasis, which is usually sufficient to protect the host, but will not entirely eliminate the infection, so that reactivation can occur whenever the cellular defenses are depleted (Collins, 1994). Acquired immunity following mycobacterial infection usually develops within 4-6 weeks and is associated temporally with the onset of delayed hypersensitivity to mycobacterial antigens such as purified protein derivative (PPD). Acquired resistance is mediated by T lymphocytes. Antimycobacterial antibodies, though present in many patients, do not play a protective role in tuberculosis because infection with mycobacteria is intracellular, and if extracellular, it is resistant to complement killing due to the high lipid concentration in its cell wall (Todar, 2007; McMurry, 2007).

Tuberculosis skin test (TST)

The most common way to measure the prevalence of latent tuberculosis in a population or an individual, is the use of a tuberculosis skin test (TST), most commonly the Mantoux test. The Mantoux technique consists of an intradermal injection of 0.1 ml of tuberculin purified protein derivative (PPD) (also known as 5 tuberculin units). Interpretation of the Mantoux TST is based on the size (in mm) of induration measured at 48-72 hours post intradermal injection. The PPD reaction is based on the delayed-type hypersensitivity reaction of a patient previously infected with mycobacteria, with the positive reaction correlated histologically to the presence of mononuclear cells at the site of injection (Huebner, 1993). Classification of the TST reaction is based on epidemiological data, categories of potential risk factors for exposure to *M. tuberculosis,* with cut-off points for positive reactions of 5mm, 10 mm or 15 mm, depending on the risk factors of exposure. For a person with no known risk factors for exposure to tuberculosis, an induration of greater than 15 mm would be required to have their reaction classified as positive (CDC, 2005a). A TST will induce a positive reaction to infection with *M. tuberculosis* or mycobacteriae other than tuberculosis (MOTT) (including *M. bovis*), although generally speaking, a tuberculin reaction caused by infection with MOTT tends to be smaller than those elicited by infection with *M. tuberculosis* (Dasco, 1990).

There is variability in the administration of the test, interpretation of the test and among individual immune reactions to the test. There is little agreement on the sensitivity and specificity of the procedure, multiple factors (both host and administrator) lead to problems with false positive and false negative reactions (Huebner, 1993), and the TST does not differentiate between infection with *M. tuberculosis* and *M. bovis* (Dasco, 1990). However, despite the variability and caveats associated with Mantoux testing, the PPD has enormous clinical utility to detect latent tuberculosis infection in populations considered to be at high risk for exposure and infection (Dasco, 1990).

The interpretation of the TST is based strictly on exposure to, and infection with, *M. tuberculosis*. Infection with *M. bovis* would be expected to elicit a smaller reaction than one caused by infection with *M. tuberculosis* because PPD is a mixture of antigens derived from *M. tuberculosis* (Dasco, 1990). Individuals with *M. bovis* exposure risk factors would only be considered positive if their TST induration were 15 mm or greater, thus many latent cases of *M. bovis* infection may be missed using the current TST interpretation guidelines (CDC, 2005b).

Pathogenesis and clinical manifestations in humans

The pathogenesis of mycobacteria depends on the site of infection. In pulmonary tuberculosis, tuberculous mycobacteria enter the alveoli by airborne transmission of droplet nuclei containing viable, virulent organisms. A portion of the infectious innoculum resists destruction by the alveolar macrophages and persists, eventually multiplying and killing the macrophage (McMurray, 2007). The accumulating mycobacteria stimulate an inflammatory focus which matures into a granulomatous lesion characterized by a mononuclear cell infiltrate surrounding a core of degenerating epithelioid and multinucleated giant (Langhans) cells, eventually forming the primary lesion or tubercle. The tubercle may become enveloped by fibroblasts and its center often progresses to caseous necrosis. Liquification of the caseous material and erosion of the tubercle into an airway may result in cavitation and the release of massive numbers of bacilli into the sputum. In a resistant host, the tubercle eventually becomes calcified and the infection latent (McMurray, 2007).

Early in infection, mycobacteria may be spread directly into circulation by erosion of the tubercle into a pulmonary vessel, or indirectly through the lymphatics to the hilar or mediastinal lymph nodes, and then via the thoracic duct, into the circulation. Erosion of the arterial blood vessels resulting in the escape of blood into the air passages and the coughing of sputum stained with bright red arterial blood (hemoptysis) is a common feature of advanced, post-primary pulmonary disease in humans (O'Reilly, 1995). Other organs may become seeded via the extrapulmonary hematogenous dissemination of the organism (McMurray, 2007).

When exposure is by ingestion, the pathogenesis is similar, with the principle site of involvement being the mesenteric lymph nodes with subsequent dissemination. Tonsils may also be the port of entry for infection (Kakekhel, 1989). This alimentary route of infection leads to extra-pulmonary forms of tuberculosis, where infection can become established in the cervix, and less frequently in the axillary lymph nodes leading to chronic skin tuberculosis (Moda, 1996). In countries where tuberculosis in cattle is common, cervical lymphadenitis is the predominant clinical presentation in children while pulmonary tuberculosis, and to a lesser degree, extrapulmonary forms, are found in adults (O'Reilly, 1995). In Canada, prior to the national bovine TB eradication campaign, *M. bovis* accounted for 50 to 70% of cervical and 80% of abdominal tuberculosis. Mortality rates were estimated to be between 10 and 30% primarily attributed to secondary hematogenous spread (Panesar, 2002). In San Diego, California, USA, Danker, (1993) reviewed 25 pediatric cases of *M. bovis* occurring from 1979 to 1992; 44% presented with cervical adenitis, 28% had abdominal manifestations and only 12% had pulmonary symptoms.

The last presentation of tuberculosis to be discussed is cutaneous. Cuntaneous tuberculosis takes several different forms and clinical manifestations comprise a considerable number of skin changes. Tappeiner and Wolfe (1993) use a classification that distinguishes between exogenous infection and endogenous spread of *M. tuberculosis/bovis.* Once in the host's tissues, the mycobacteria multiply intracellularly and the infection is characterized by the appearance of polymorphonuclear leukocytes, and influx of mononuclear cells, and by the later development of epithelioid cells and necrosis. The development of a certain type of skin tuberculosis depends on the causative organism, the general condition and reactivity of the host, and the mode of introduction of the bacteria into the skin. Cutaneous *M. bovis* and *M. tuberculosis* manifestations are identical (Tappeiner, 1993). Exogenous infection can be classified as primary inoculation tuberculosis (or tuberculous chancre), which is infection of the nonimmune host, and tuberculosis verrucosa cutis (or warty tuberculosis), which is infection of the immune host. Endogenous spread of existing infection can be classified as lupus vulgaris, scrofuloderma, metastatic tuberculosis abscess, acute military tuberculosis or orificial tuberculosis. Each form is well described by Tappeiner (1993).

Primary inoculation tuberculosis results from inoculation of mycobacteria into the skin or less frequently into the mucosa. Some form of injury is mandatory as tubercle bacillus cannot penetrate the normal intact skin barrier (Sehgal, 1990). Tuberculosis of exogenous source is the most likely manifestation for persons who are exposed to carcasses of *M. bovis* infected animals (farmers, butchers and knackers), with inoculation through wounds or existing abrasions. Clinically, a papule develops into a ragged, painless ulcer which may be accompanied by regional lymphadenopathy (Kakakhel, 1989). Lesions usually heal but may progress to lupus vulgaris, scrofuloderma or rarely, to military tuberculosis (Miller, 1955). In sensitized individuals, tuberculosis verrucosa cutis (warty tuberculosis) starts as small, solitary, firm, symptomless reddish-brown or purple indurated warty papule with an inflammatory halo. The papule gradually extends to become a plaque that eventually results in atrophic scars. Regional lymphadenitis is rare (Kakakhel, 1989).

Reactivation of old primary foci of infection with consequent clinical disease may be triggered by immunodepression resulting from old age, co-morbidities, poor nutrition and stressful life events (Tinker, 1959; Sauret, 1992). The most common sites of secondary extra pulmonary involvement include the genitourinary tract, bones and joints, and the central nervous system, and in adults often represent a reactivation of the disease at the primary site(s) of childhood exposure (Gobels, 2000).

Before efforts to control *M. bovis* in cattle were initiated, contaminated milk was the principle vector for the transmission of the disease to humans and the majority of the lesions were extrapulmonary (Grange, 1995). Human pulmonary cases were considered rare and were more prevalent in rural vs. urban areas (due to aerosol exposure to infected cattle). After elimination of contaminated milk as a vector, the distribution of the anatomical sites of disease changed considerably with the lung becoming the predominant site, genitourinary disease becoming more prevalent, while lupus vulgaris became rare (Grange, 1995). In the 1960's with the control of the disease in the cattle population of developed countries, the extra pulmonary presentations (due to reactivation of latent infection) again became predominant and remain so today.

There are conflicting opinions in the literature regarding the severity of human infection with *M. bovis*. Hedvall (1942) is often cited for claiming that in humans, cases of pulmonary disease due to *M. bovis* and *M. tuberculosis* are indistinguishable, clinically, radiologically, and pathologically. However, more recent work suggests the pathogenicity of *M. bovis* may be less than that of *M. tuberculosis* (Enarson, 1995). Work in both Denmark (Magnus, 1966a, 1966b, 1966c) and Sweden (Sjogren, 1974) suggests that the relative risk of developing active tuberculosis, following infection with *M. bovis*, was less than that following infection with *M. tuberculosis*.

Human exposure to *M. bovis* and populations at risk of infection

Humans can be exposed to *M. bovis* from infected domesticated livestock. Although found in a wide range of wild and domesticated mammals (deLisle 2001; 2002) cattle remain the primary reservoir species for *M. bovis* and thus the main source of human infection. Of the domesticated animals, cattle, farmed buffalo and goats are considered reservoir hosts of *M. bovis*, while pigs, cats, dogs, horses and sheep are considered spillover, or "dead end" hosts. Infection of humans from cattle can occur via inhalation of aerosols, direct contact with the animal (Baldwin, 1967), indirectly in an abattoir setting (Robinson, 1988; Georghiou, 1989; Cousins, 1999), through the consumption of infected milk or dairy products (Robert, 1999; O'Reilly, 1995; CDC 2005c), or by handling infected carcasses (Tappiener, 1993). A case of tuberculous chancre in a 14 year old, subsequent to being gored by a bull, was described by Ara (2000).

Scientific literature describing the role of domestic pets in the transmission of *M. bovis* on the farm (livestock to pet, pet to livestock) is fairly limited and quite dated. While uncommon in both dogs and cats, historic data suggests that dogs were more likely to be infected with *M. tuberculosis* following exposure to infected humans, while cats were more likely infected with *M. bovis* with exposure assumed to be related to the consumption of contaminated animal products (Birn, 1965). Historically, farm cats and dogs were at very high risk of acquiring *M. bovis* from infected cattle; 4 of 9 dogs and 24 of 52 cats were affected after exposure to positive cattle in a Pennsylvania study (Snider, 1971a). It is therefore feasible that pets could play a role in the maintenance of *M. bovis* on a farm (Greene, 1998), however, literature describing pet transmission to cattle is hypothetical (McLaughlin, 1974) or limited to references from eastern Europe in the 1950's and 60's (Schliesser, 1957; Beinhauer, 1958; Milbrant, 1960; Pavlas, 1965).

Literature describing the role of pets in transmission of *M. bovis* to humans is also very limited, although transmission would again be biologically plausible. Early necropsy studies (1930-1965) revealed a tuberculosis prevalence ranging from 2.0 to 13% in cats and 0.4% to 2.0% in dogs (Snider, 1971b). There is no evidence that dogs and cats have transmitted *M. bovis* infection to humans; only one inconclusive cat-to-human reference was found (Isaac, 1983).

In Michigan, wild carnivores and omnivores are considered dead-end hosts for *M. bovis*. These animals are most typically exposed to infection via the consumption of infected deer carcasses, thus resulting in a gastrointestinal clinical presentation with limited potential for transmission to people or other animals (Bruning-Fann, 1998; 2001). Humans have been infected by handling ill elk and infected elk carcasses in Canada (Fanning, 1991; Nation, 1999). In the US, one case is reported describing a hunter infecting himself with a contaminated hunting knife while field dressing infected deer in Michigan (Wilkins, 2008). In two zoos, humans have been infected by inhaling aerosols generated while cleaning the pens of an *M. bovis* infected rhinoceroses (Dalovisio,1992; Stetter, 1995). Seals have also been blamed for the aerosol transmission of *M. bovis* to human trainers (Thompson, 1993).

Until recently, human-to-human transmission was considered almost irrelevant due to the preponderance of extrapulmonary infection with only anecdotal reports in the literature (Griffith, 1937; Ruys, 1939; Hedvall, 1942; Sigurdsson, 1945; Wigel, 1972) and lack of molecular subtyping techniques has made proof of such transmission difficult (Grange, 1994). Nosocomial outbreaks of *M. bovis* infection among HIV infected patients, in Madrid, Spain from 1993-1998 are well described by Guerrero (1997), Samper (1997) and Rivero (2001). The disease was spread via aerosol transmission. More recently, a family cluster of *M. bovis* cases in San Diego California, was identified that suggested human-to-human transmission (LoBue, 2004). In 2007, a cluster of six cases of *M. bovis* was identified in young adults in the United Kingdom, only one of whom had zoonotic links to cattle or had consumed unpasteurized dairy products. One patient died, and four had risk factors predisposing them to tuberculosis disease. This was the first time in decades that human-to human transmission was documented in the United Kingdom (Evans, 2007).

Although *M. bovis* can survive for long periods outside an animal host, there are no records of human infection by *M. bovis* coming from a direct environmental source (Biet, 2005).

Populations at risk of exposure

Various persons are considered at risk of exposure to and infection with *M. bovis* based on their occupation. Workers in the livestock industry, abattoir or rendering plant workers, veterinarians and animal handlers are at greatest risk of infection with *M. bovis* (Collins, 1983; Liss, 1994; McKenna, 1996; Cousins, 1999) primarily via aerosol transmission. In the past, primary inoculation tuberculosis caused by *M. bovis* was known as "butcher's wart" and was considered an occupational disease of butchers, farmers and knackers (handlers of poor quality or deceased livestock) (Tappiener, 1993).

M. bovis has recently become established and endemic in the white-tailed deer population in the northeastern portion of the lower peninsula of Michigan, with the subsequent spill over into additional wildlife species. The outbreak situation has created additional categories of persons at potential risk of exposure to *M. bovis* including hunters, trappers, and taxidermists, guides, wildlife conservation officers, venison consumers and wildlife rehabilitators. Laboratory, veterinary and other regulatory personnel examining deer carcasses as part of routine surveillance procedures may be exposed to *M. bovis* through direct contact with infected tissues and aerosolized particles (Wilkins, 2003; 2008; USDA, 1996). During an outbreak in Canada involving elk, 8 of 30 of the veterinarians exposed to *M. bovis* infected herds were TST positive compared to 1 of 20 veterinarians not exposed (Fanning, 1991).

INJURIES ASSOCIATED WITH VETERINARY PRACTICE

Veterinary practitioners are often classified as having a primary employment focus in companion animal practice, large animal practice or a combination of both. Regardless of their concentration, veterinary practice presents occupational hazards from physical, biological and chemical agents (Jeyaretnam, 2000). An occupational hazard survey found needle punctures, kicks and crush or handling injuries as the leading cause of injury to veterinarians in large animal practices (Poole, 1999) while cat bites, dog bites and needle punctures topped the list in companion animal practices (Poole, 1998). A survey of AVMA members in Minnesota and Wisconsin found hands, shoulder/arm, leg, head, back and feet to be the most frequently injured anatomic structures (Landercasper, 1988). Occupational injuries of zoo veterinarians have also been specifically studied (Hill, 1998), as well as practice hazards unique to pregnant veterinarians (Moore, 1993). In a large Minnesota study of all licensed veterinarians, factors found to increase the risk of veterinary injury included smoking, lack of sleep, lifting heavy patients, inexperience, and lack of availability of assistants. In contrast, participation in aerobic activities, increasing age and male gender were found to decrease the risk of injury (Gabel, 2002).

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CHAPTER 2

MYCOBACTERIUM BOVIS (BOVINE TB) EXPOSURE AS A RECREATIONAL RISK FOR HUNTERS: RESULTS OF THE MICHIGAN HUNTER SURVEY—2001.

ABSTRACT

Tuberculosis caused by *Mycobacterium bovis* (Bovine TB) is endemic in the white-tailed deer population of northeastern Michigan. Hunters may be exposed to *Mycobacterium bovis* via cutaneous inoculation while field dressing deer or by ingestion of undercooked venison. Michigan hunters have received inconsistent messages about their risk of acquiring tuberculosis from recreational exposure to deer. The most common health advice offered has been to wear gloves while field dressing deer and to thoroughly cook venison products. Data were collected to quantify these self-protective activities and to characterize hunters practicing these activities. In 2001, we surveyed 1,833 hunters who had successfully harvested deer in or near Michigan's Bovine TB endemic area in 2000. The survey response rate was 78%. Most hunters (89%) reported field dressing deer, 43% of whom wore gloves. Most hunters (95%) reported eating venison; 55% of whom reported their venison was always cooked thoroughly. Several hunter characteristics including older age, female gender, higher awareness level, and area of residence, were significantly associated with the practice of these self-protective activities. The survey results suggest hunters should receive consistent advice encouraging glove use while field dressing deer and the thorough cooking of venison products before consumption.

INTRODUCTION

Although cattle are the historical reservoir species for *Mycobacterium bovis* (Bovine TB) in the United States, tuberculosis caused by *M. bovis* has become endemic in the wild white-tailed deer population in the northern lower peninsula of Michigan (Schmitt, 1997). Identified initially in a young cow and a hunter-killed white-tailed deer in 1994, the distribution within various animal populations has been explored by several state and federal agencies. Prior to the October 2001 mailing date of this survey, 371 infected cervidae, carnivores or omnivores had been found in 12 of Michigan's 83 counties: 342 wild white-tailed deer, one elk, 13 coyotes, four black bear, four bobcats, two opossum, two raccoons, two red fox and one domestic cat (Michigan Department of Natural Resources, 2001). Most of the infected wildlife and all of the infected farms (including one captive white-tailed deer farm, 16 beef herds and two dairy herds) were found within a five county area where the disease is considered endemic (United States Department of Agriculture, 2001). The "endemic" area includes, Alcona, Alpena, Montmorency, Presque Isle, and Oscoda counties.

Infected cattle have been a source of infection for humans, via direct inhalation of the organism and ingestion of unpasteurized dairy products from infected herds (Grange, 1994; Wigle, 1972). Abattoir workers have been infected during the processing of cattle (Robinson, 1988; Cousins, 1999; Georghiou, 1989). Recently, cervidae have been documented as the source of *M. bovis* infection for humans; infection resulted from exposure to live elk and the processing of cervidae carcasses (Fanning, 1991).

Mycobacterium bovis in Michigan humans

Although *M. bovis* is a well-recognized zoonotic agent, available evidence has shown no change in the incidence of *M. bovis* infections in Michigan's human residents since the outbreak in deer was recognized. Since 1995, the expected incidence rate of *M. bovis* infection in Michigan residents is approximately one new case per year with a range of 0-2 cases; the number of humans diagnosed with tuberculosis in Michigan has ranged from 287 to 443 per year with <0.5% of these cases attributed to infection with *M. bovis* (Michigan Department of Community Health, 2002). At the time of the survey, none of the human cases of *M. bovis* in Michigan were related to the current outbreak of Bovine TB in Michigan's deer and cattle, based on epidemiologic case-investigations and pulse-field gel electrophoresis (PFGE) analysis of *M. bovis* isolates from humans and deer completed by the Michigan Department of Community Health Laboratory (Michigan Department of Community Health, 2002, unpublished data).

Mycobacterium bovis in Michigan deer

For deer, the most probable routes of exposure to *M. bovis* are via inhalation or ingestion, with the organism initially colonizing the tonsils before spreading to the cranial lymph nodes and thoracic tissue (Schmitt, 1997; Palmer, 1999; 2000; O'Reilly, 1995). The pulmonary form of infection is the most contagious to other mammals via coughing and aerosolization of the organism (Sigurdsson, 1945). Likewise, for mammals, exposure to *M. bovis* via inhalation is more likely to lead to infection than exposure via the gastrointestinal or cutaneous route (Whiting, 1994). Based on the 2000 deer harvest survey data, an apparent prevalence estimate of 0.82% was generated for the five-county endemic area (O'Brien, 2002).

While it is unlikely that hunters would be exposed to aerosolized droplets from infected deer, they often have close contact with the deer carcass during field dressing, raising the possibility of cutaneous exposure. Primary inoculation tuberculosis (tuberculous chancre, cutaneous primary complex) is very rare in developed countries due to control efforts in cattle and humans (Kakakhel, 1989). In the past, primary inoculation tuberculosis caused by *M. bovis* was known as "butcher's wart" and was considered an occupational disease of butchers, farmers and knackers (handlers of poor quality or deceased livestock) (Tappeiner, 1993). Cutaneous exposure to *M. bovis* during field dressing may occur when hunters cut themselves while field dressing or when hunters field dress with an unprotected, open wound or abrasion on their hands or forearms. Injury is required for infection, as tubercle bacillus cannot penetrate normal intact skin (Kakakhel 1989; Sehgal, 1990). Field dressing a deer entails the removal of all organs from the abdominal and chest cavity.

Hunters are also likely to consume venison products; therefore, exposure to *M. bovis* via the ingestion of undercooked, infected meat is a possibility. The infection of humans via the consumption of infected meat has not been documented in scientific literature. The severity of *M. bovis* infection in humans is similar to infection with *M. tuberculosis;* both are highly dependent on the site of infection and immune status of the individual (Cousins, 1999).

Bovine TB and health in the media

Literature in the form of brochures, newsletters, press releases, and internet web pages, has been distributed by state and federal agencies, Michigan State University, and local health departments. From 1998 through 2000, the Michigan Press Reading Service collected over 3000 newspaper articles with keywords "Bovine TB" (Table 2.1). Ten percent of the articles state that humans are susceptible to *M. bovis* infection. Of the articles noting the zoonotic potential of *M. bovis*, an average of 66% say the risk to humans is none, negligible, or low, and offer no further advice on avoiding exposure to the organism. The remaining articles do offer advice on avoiding exposure to the organism that includes cooking venison thoroughly until the meat is no longer pink and the juices run clear and wearing rubber or latex gloves while field dressing deer.

Table 2.1 : Summary of the public health content of newspaper articles containing keywords "Bovine TB" collected by Michigan Press Reading Service, 1998-2000.

	1998 No. (%)	**1999** No. (%)	**2000** No. (%)
Total articles referencing "Bovine TB" in Michigan Press	790	1410	843
No. articles noting human susceptibility to Bovine TB	79 (10.0)	119 (8.4)	104 (12.3)
Statements made or advice offered			
No or negligible risk - no advice	44 (55.7)	25 (21.0)	39 (37.5)
Low or small risk - no advice	20 (25.3)	56 (47.1)	14 (13.5)
Cook meat thoroughly (low risk)	11 (13.9)	27 (21.0)	14 (13.4)
Cook meat thoroughly (low risk), skin test	0	0	7 (6.7)
Cook meat thoroughly and wear gloves	2 (2.6)	8 (6.7)	5 (4.8)

Table 2.1 (cont'd)

Wash hands and wear gloves	1 (1.3)	1 (0.8)	1 (1.0)
Have a TB skin test if concerned	1 (1.3)	2 (1.7)	24 (23.1)
Total	79 (100.1)	119 (100)	104 (100)

In Michigan, no evidence of transmission from deer to humans had been found at the time of the survey, therefore the human health risk was considered only hypothetical despite thousands of human-deer interactions in the outbreak area. Consequently, a concerted effort was made by all involved regulatory agencies to present the risk of human acquisition of *M. bovis* via recreational exposure as small, for two principle reasons. First, controlling the Bovine TB outbreak in deer necessitates reducing the number of deer in affected areas, a process that requires active hunter participation. Second, the local economies of these sparsely populated areas are highly dependent on the seasonal income provided by hunters.

Because information on the prevalence of preventive behavior by hunters was lacking, the Michigan Departments of Community Health (MDCH) and Natural Resources (MDNR) conducted the Michigan Hunter Health Survey (MHHS). It's primary purpose was to estimate the percentage of hunters taking measures to reduce their exposure to *M. bovis* and to determine which hunter characteristics are associated with the practice of these self-protective measures. A secondary objective was to collect information on the types of meat products made from venison, hunter perceptions of the risks posed by Bovine TB, and appropriate venues for disseminating future public health information.

METHODS

Target population

The population target for this survey was hunters who successfully harvested at least one deer during the 2000 hunting season in one of 11 counties in the northcentral and northeastern portion of lower peninsula of Michigan as shown in the lower portion of Figure 2.1. The sample frame consisted of hunters who responded to the MDNR's 2000 Deer Harvest Survey (Frawley, 2000), which received surveys from 36,021 respondents statewide who successfully took at least one deer during the 2000 hunting seasons.

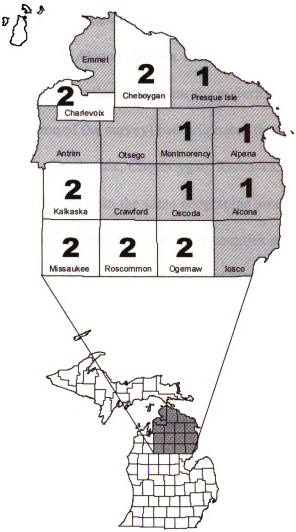

Figure 2.1 : Location of Stratum 1 counties (bovine TB found in animals) are indicated by the "1" and Stratum 2 counties (no bovine TB found in animals) are indicated by the "2" within the state of Michigan. The shading counties within the enlarged area indicate counties in which bovine TB positive deer had been found, at the time of the survey.

Michigan Hunter Health Survey

The sample for the 2001 MHHS included all 1833 hunters who responded to the 2000 Michigan Deer Harvest Survey and harvested deer in the eleven counties of interest. Stratum 1 counties, Alcona, Alpena, Presque Isle, Montmorency and Oscoda, are contiguous and were selected because the majority of positive deer and all the positive farms (at the time of the survey) had originated from these counties. Stratum 2 consisted of six counties, Charlevoix, Cheyboygan, Kalkaska, Missaukee, Ogemaw, and Roscommon, chosen from the same geographic area as Stratum 1 counties, but no TB positive animals had been found in these counties at the time of the survey (Figure 2.1, enlarged portion) (Michigan Department of Natural Resources, 2001).

Questionnaires were sent to 884 to hunters harvesting in Stratum 1, and 949 to hunters harvesting in Stratum 2. The first mailing occurred in mid-October and the second in early November 2001. For hunters failing to return the questionnaire, two follow-up phone calls were made with administration of the questionnaire over the phone when possible.

In addition to the variables listed in Table 2.2, the hunter's date of birth was collected as well as whether they had ever had a TB skin test. The experience variable measured the number of seasons hunted and was calculated using the hunter's current age minus age started hunting and multiplied by frequency of hunting variable. For example, a 40 year old who started hunting at age 14 and reported hunting every other year {[(40 – 14) x 0.5] = 13} is Experience Level 3 (10-19 seasons). Figure 2.2 defines areas of hunter residence and the number of respondents from each area.

Table 2.2 : Michigan Hunter Health Survey responses, total and per strata.

Variable	Responses Total No. (%)	Responses Strata 1* No. (%)	Responses Strata 2† No. (%)
Total	**1420**	**697 (49.1)**	**723 (50.9)**
Gender			
Male	1322 (93.1)	657 (94.3)	665 (92.0)
Female	98 (6.9)	40 (5.7)	58 (8.0)
Age category			
14-19	81 (5.7)	43 (6.2)	38 (5.3)
20-29	108 (7.6)	56 (8.0)	52 (7.2)
30-39	273 (19.2)	124 (17.8)	149 (20.6)
40-49	404 (28.5)	204 (29.3)	200 (27.7)
50-59	290 (20.4)	131 (18.8)	159 (22.0)
60+	264 (18.6)	139 (19.9)	125 (17.3)
Hunting frequency			
Every year	938 (66.4)	459 (66.0)	479 (66.8)
Almost every year	412 (29.2)	210 (30.2)	202 (28.2)
Every other year	20 (1.4)	7 (1.0)	13 (1.8)
Every 3-5 yrs	26 (1.8)	12 (1.7)	14 (2.0)
Every 6-10 yrs	4 (0.3)	1 (0.1)	3 (0.4)
Over 10 years between	12 (0.8)	6 (0.9)	6 (0.8)
Age first started hunting			
4-14	726 (52.5)	360 (53.4)	366 (52.1)
15-17	295 (21.4)	147 (21.8)	148 (21.0)

Table 2.2 (cont'd)

18-24	211 (16.0)	101 (15.0)	110 (15.6)
25+	145 (10.1)	66 (9.8)	79 (11.2)
Experience level			
1 (1-3 seasons)	95 (6.9)	42 (6.3)	53 (7.6)
2 (4-9 seasons)	105 (7.7)	51 (7.6)	54 (7.7)
3 (10-19 seasons)	246 (18.0)	118 (17.6)	128 (18.3)
4 (20-29 seasons)	399 (29.1)	195 (29.1)	204 (29.2)
5 (30-39 seasons)	300 (21.9)	148 (22.1)	152 (21.8)
6 (40+ seasons)	224 (16.4)	117 (17.4)	107 (15.3)
Field dress own deer			
Yes	1256 (88.7)	618 (89.0)	638 (88.4)
No. deer field dressed			
1	589 (51.9)	289 (51.6)	300 (51.5)
2	354 (31.2)	168 (30.0)	186 (32.0)
3-4	148 (13.0)	74 (13.2)	74 (12.7)
5-9	33 (2.9)	18 (3.2)	15 (2.6)
10+	18 (1.0)	11 (2.0)	7 (1.2)
Wear gloves field dressing			
Yes	541 (43.2)	275 (44.7)	266 (42.3)
Cut self field-dressing			
Yes	60 (4.9)	30 (5.0)	30 (4.8)
Eat any venison			
Yes	1362 (96.6)	665 (96.4)	697 (97.3)

Table 2.2 (cont'd)

Eat smoked venison			
Yes	466 (34.8)	235 (35.9)	231 (33.8)
Eat venison jerky			
Yes	694 (51.2)	324 (48.9)	370 (53.3)
Eat venison sausage			
Yes	774 (54.5)	386 (58.4)	388 (56.0)
Cooked thoroughly			
Never	25 (1.8)	13 (2.0)	12 (1.7)
Sometimes	190 (14.0)	88 (13.3)	102 (14.7)
Usually	402 (29.7)	205 (31.0)	197 (28.4)
Always	738 (54.5)	355 (53.7)	383 (55.2)
Bovine TB Awareness			
Not aware of problem	6 (0.4)	1 (0.1)	5 (0.7)
Somewhat informed	238 (17.0)	76 (11.1)	162 (22.7)
Informed	757 (54.1)	374 (54.5)	383 (53.6)
Very informed	399 (28.5)	235 (34.3)	164 (23.0)
Threat to hunters in general			
Not aware of problem	11 (0.8)	3 (0.4)	8 (1.1)
No threat	466 (33.4)	265 (38.9)	201 (28.2)
Small threat	661 (47.4)	307 (45.1)	354 (49.6)
Medium threat	212 (15.2)	87 (12.8)	125 (17.5)
Big threat	45 (3.2)	19 (2.8)	26 (3.6)

Table 2.2 (cont'd)

Risk to personal health			
Not aware of problem	6 (0.4)	2 (0.3)	4 (0.6)
No risk	746 (53.3)	383 (55.7)	363 (51.0)
Small risk	550 (39.3)	262 (38.1)	288 (40.4)
Medium risk	85 (6.1)	35 (5.1)	50 (7.0)
Big risk	12 (0.9)	5 (0.7)	7 (1.0)
Discussed with health professional			
Yes	135 (9.6)	79 (11.5)	56 (7.8)
Skin tested due to BTB concern			
Yes	19 (1.4)	13 (2.0)	6 (0.9)
Preferred source BTB health info‡			
Hunting Assoc. Newsletters	331 (23.3)	163 (23.4)	168 (23.2)
DNR Hunting/Trapping Guide	866 (61.0)	412 (59.1)	454 (62.8)
Hunting/Sports Magazines	560 (39.4)	273 (39.2)	287 (39.7)
Hunting/Sports TV programs	589 (41.5)	279 (40.0)	310 (42.9)
DNR Web page	365 (25.7)	174 (25.0)	191 (26.4)
Bovine TB Web page	208 (14.6)	106 (15.2)	102 (14.1)

*Alpena, Alcona, Presque Isle, Montmorency, Oscoda.

†Charlevoix, Cheboygan, Kalkaska, Missaukee, Ogemaw, Roscommon.

‡More than one answer possible, percentages do not equal 100.

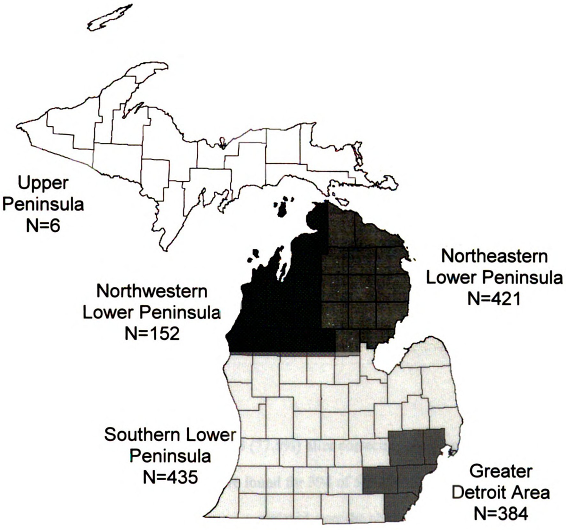

Figure 2.2 : Map of Michigan showing geographic areas of residence and the number of survey respondents residing in each area.

ANALYSIS

Associations between both glove use or thoroughness of cooking and hunter characteristics were assessed using relative risks for binomial variables and the Mantel-Haenszel Chi square test for trend for ordinal variables. A linear test for trend compared increasing age, experience, levels of awareness, perception of risk to personal health and perception of threat to hunters in general with the likelihood of wearing gloves and with thoroughness of cooking. The cooking variable was categorized as "always" cook thoroughly versus "other" (never, sometimes, and usually cook thoroughly) for analyses. Glove use, thoroughness of cooking, awareness level, risk perception and threat perception of Stratum 1 and Stratum 2 hunters were compared. Resulting p-values of ≤ 0.05 were considered significant. Data were analyzed using SPSS Version 10.0 software (SPSS Inc., Chicago, IL).

RESULTS

Survey response

The response rate was 1420/1808 (77.5%) after correcting for 25 undeliverable mailing addresses. Phone numbers were found for 394 of 516 (76%) non-responding hunters. An additional 44 surveys were completed over the phone. There was no significant difference in response rate by gender ($p<0.14$) or Stratum 1 verses Stratum 2 ($p<0.17$). The average age of responders was significantly greater than non-responders (46.1 years verses 39.5 years, $p<0.001$). Hunters residing in the southern lower peninsula and Detroit area had a significantly higher response rate than hunters residing in the northern lower peninsula (80.8% versus 71.3%, $p<0.01$). The responses to survey questions are summarized in Table 2.2.

Glove use

Eighty nine percent of hunters field dressed their own deer in 2000. Of these, 43.2% reported wearing gloves while doing so. Characteristics of hunters and the relative risk of wearing gloves are found in Table 2.3. Tests for trend showed a significant, positive linear trend between increasing awareness level ($p<0.03$), increasing perception of threat ($p<0.03$), and increasing perception of risk ($p<0.05$) with the use of gloves while field dressing.

Table 2.3 : Characteristics of hunters associated with their likelihood of wearing gloves while field dressing during the 2000 hunting season.

Binomial Variables	**Relative Risk**	**95% Confidence Level**
Gender Female vs. male	1.28	0.99 – 1.66
Hunting location Stratum 1 vs. 2	1.06	0.93 – 1.20
Area of residence Southern LP/Detroit vs. Northeast/Northwest LP	**1.38**	**1.19 – 1.59**
Discussed TB Health concerns with health professional	1.04	0.84 – 1.27
Ordinal Variables	χ^2 test statistic*	p-value for trend†
Increasing levels of awareness about Bovine TB	**4.54**	**0.03**

Table 2.3 (cont'd)

Increasing perception of Bovine TB threat to hunters in general	**4.99**	**0.03**
Increasing perception of Bovine TB risk to personal health	**3.91**	0.05
Increasing age categories	1.07	0.30
Increasing level of experience	1.42	0.23

* Tested using Mantel-Haenszel test for trend.

† Results in bold indicate statistical significance at the $\alpha \leq 0.05$ level.

Thoroughness of cooking

Fifty-five percent of hunters reported consuming venison always cooked until it is no longer pink and the juices run clear. Characteristics of hunters and the relative risk of consuming venison always cooked thoroughly are found in Table 2.4. Tests for trend showed a significant positive linear trend only between increasing age and thoroughness of cooking ($p<0.01$).

Table 2.4 : Characteristics of hunters associated with their likelihood of reporting consuming venison from the 2001 hunting season as always cooked thoroughly.

Binomial Variables	Relative Risk	95% Confidence Level
Gender Female vs. male	**1.30**	**1.12 – 1.50**
Hunting location Stratum 1 vs. 2	0.97	0.88 – 1.07

Table 2.4 (cont'd)

Area of residence Northeast/Northwest LP vs. Southern LP/Detroit	**1.20**	**1.09 – 1.32**
Discussed TB Health concerns with health professional	0.98	0.83 – 1.16

Ordinal Variables	χ^2 test statistic*	p-value for trend†
Increasing levels of awareness about Bovine TB	2.76	0.10
Increasing perception of Bovine TB threat to hunters in general	0.03	0.89
Increasing perception of Bovine TB risk to personal health	0.13	0.72
Increasing age categories	**8.37**	**<0.01**
Increasing level of experience	2.01	0.16

*Tested using Mantel-Haenszel test for trend.

† Results in bold indicate statistical significance at the $\alpha \leq 0.05$ level.

Location of hunter harvest

Survey results also indicated hunters harvesting deer in Stratum 1 were significantly more likely to report being informed or well informed about the TB problem than hunters hunting in Stratum 2 ($p<0.01$). Stratum 1 hunters were also significantly more likely to consider the public health threat of Bovine TB to be small to none ($p<0.01$).

DISCUSSION

Glove use

Our results indicate that nearly nine out of 10 (89%) respondents field dressed their own deer with fewer than half (43%) wearing gloves while doing so. Approximately 30,730 deer were harvested within the five county endemic area (Stratum 1) in 2000 (Frawley B, MDNR, personal communication). As the apparent prevalence of infected deer for this area is 0.82%, approximately 252 positive deer were harvested. Our survey results indicate that 55.3% of Stratum 1 hunters did not wear gloves while field dressing. Therefore we estimate up to 139 (252 x .553) Stratum 1 hunters may have field dressed positive deer without wearing gloves. Of potentially more concern are the 5.0% or 12 to 13 hunters (252 x 0.05) who reported cutting themselves enough to bleed while field dressing these positive deer.

Although latex or heavy rubber gloves may not protect against a cut during the field dressing process, gloves may lessen the severity of the cut, protect pre-existing wounds from exposure to the organism, and decrease surface contamination of the hands while handling internal organs. The average period of time between field dressing and hand washing was 98 minutes, allowing many opportunities for hand-to-mouth contact to occur.

Statewide, as hunter's level of Bovine TB awareness increased, so did the likelihood of wearing gloves while field dressing. Likewise, as the perception of threat to hunters and risk to personal health increased, so did the likelihood of wearing gloves while field dressing.

Gastrointestinal exposure

The probability of finding *M. bovis* in the muscle tissue of bovines and cervids with disseminated disease is poorly defined. In a 1999 study, 45% of TB positive Michigan deer bore *M. bovis* lesions outside of the cranial area (O'Brien, 2001). Research on the dissemination of the organism and lesions in deer and cattle has focused almost exclusively on tissue samples taken from the lymphatic and pulmonary systems, liver, kidney and spleen. Only one recent study on the experimental transmission of *M. bovis* in deer reported the presence of *M. bovis* in intercostals and diaphragm muscle samples, but the study did not examine muscle tissues generally consumed by hunters (Palmer, 2001). The acquisition of *M. bovis* from the ingestion of infected meat has not been documented in humans. However, infection following the consumption of infected bovine or cervid carcasses has been reported in other mammalian species including domestic and wild felids such as lions and bobcats, coyotes, raccoons, red fox, and black bear (Isaac, 1983; Keet, 2000; Bruning-Fann, 2001). Humans generally avoid consuming the pulmonary and lymphatic tissue most likely to harbor the organism and usually cook meat before consuming it, further reducing the risk of ingesting large numbers of organisms.

Venison processed in a licensed food establishment or processed for retail sale is regulated by Michigan Department of Agriculture (MDA). MDA estimates less than 20% of all Michigan hunter-harvested venison is processed under state regulation (MDA, Food and Dairy Division, 1998). The remainder is processed for home consumption by unregulated and seasonal processors. Venison is often further processed into jerky and sausage without regulatory oversight, making the inclusion of lymphatic tissue into sausage mixtures or the surface contamination of steaks or roasts more likely. Smoking of sausage and drying of jerky usually requires a long heating time at low temperature and is often completed by unregulated processors or within the home. Outbreaks of human disease caused by *E. coli, Salmonella*, and *Trichinella* have been linked to the consumption of sausage and jerky made from beef or wild game (CDC, 1995a; 1995b; 1995c, 1996).

Because venison is very lean, it can become tough when thoroughly cooked, consequently, there may be a tendency toward undercooking. It is difficult to assess the risk of acquiring *M. bovis* through consumption of undercooked venison. For solid pieces of meat, the risk would likely be from surface contamination occurring during gutting or processing. *M. bovis* survived in wieners kept at 50°C (122°F) for 90 minutes but was killed at a temperature of 60°C (140°F), held for six minutes (Merkal, 1980). Most hunters are probably not at risk from consuming steaks, roasts or pan-fried sausages. However, the hunting community needs education on the proper time and temperature requirements for preparing smoked venison, venison sausages and venison jerky. Proper knife sanitation, meat handling and adequate cooking temperatures will substantially reduce the risk of human illness. State-wide, hunters with a high level of awareness about Bovine TB, and hunters who perceived *M. bovis* to be a public health threat or personal health risk were more likely to report always cooking venison thoroughly, although the trends were nonlinear.

Hunting location and hunter residence

Hunting in Stratum 1 versus Stratum 2 counties had no effect on the hunter's decision to wear gloves nor the likelihood of always cooking venison thoroughly. In contrast, the hunter's area of residence did impact their decision to wear gloves, with hunters living in the northern lower peninsula counties being significantly less likely to wear gloves but significantly more likely to always cook venison thoroughly than hunters living in the southern lower peninsula and Detroit area. These strong associations are likely due to cultural and hunting practice differences between the northern resident hunters who hunt "locally" versus southern resident hunters who drive up for a long weekend. Hunting is a way of life for many northern Michigan residents; many hunt and consume a wide variety of wild game species. Perhaps in the northern counties, the practice of thoroughly cooking game meat is simply ingrained in the population, just as the practice of wearing gloves is not.

Compared with Stratum 2, Stratum 1 hunters considered themselves better informed and also considered Bovine TB to be less of a threat to hunters in general and less of a threat to their personal risk. This suggests an inverse relationship between level of Bovine TB awareness and concern about the public health implications of Bovine TB in the highest risk counties. Perhaps the efforts of the regulatory agencies to reassure Stratum 1 hunters that their health risks are small have given Stratum 1 hunters a sense of complacency. Message fatigue is another possibility, as much of the media focus has been on the endemically infected counties of Stratum 1.

Almost 10% of the hunters surveyed reported consulting with health professional about the possibility of catching Bovine TB, suggesting concern within this community. However, consultation with a health professional did not increase the probability these hunters would choose to wear gloves or report consuming venison always cooked thoroughly. This indicates needed improvement in regulatory agencies educating the medical community, and the medical community educating hunters. This finding may be a result of the conflicting public health messages conveyed to the public since the outbreak began.

This survey has several limitations. Recall error may be a factor as hunters were asked to recall events 10 to 12 months distant. Nonresponse bias is another possible limitation as responders were significantly older and more likely to reside in the southern part of Michigan than nonresponders. The 2000 Michigan Deer Harvest Survey was not evaluated for the presence of bias. Any nonresponse bias present in 2000 Michigan Deer Harvest Survey would carry over to the MHHS as the latter study population was selected from the former. Finally, data detailing when and why hunters adopted the self-protective measures of interest were not collected. Therefore the impact of public health outreach efforts on hunter behavior cannot be evaluated.

CONCLUSION

The mixed results of this survey may reflect confusion from inconsistent public health messages regarding risk of exposure and acquisition of Bovine TB. The best approach to reduce the risk of transmission to hunters and venison consumers is to prevent exposure. A simple and consistent public health message encouraging glove use while field dressing deer and the thorough cooking of all venison products is needed. This public health message should target several audiences including: hunters, taxidermists, venison processors, venison consumers, medical personnel and the regulatory/advisory community.

Hunters may be more receptive to public health advice in the future because of the discovery, in February 2002, of a human case of *M. bovis*. This case is genetically and epidemiologically linked to the same strain of *M. bovis* currently circulating in deer and cattle, suggesting the zoonotic risk of transmission is no longer only hypothetical (Michigan Department of Community Health, 2002). Also, the discovery of Chronic Wasting Disease (CWD), a transmissible spongiform encephalopathy, in the free-ranging deer of Wisconsin has raised concerns of Michigan hunters. Although evidence to date does not indicate that CWD is a zoonotic agent, hunters will be looking to state agencies for information and recommendations. This period of heightened awareness should be utilized wisely to promote a simple and consistent public health message.

Specific recommendations should be provided to hunters regarding the best practices for field dressing deer, aging and processing venison, and cooking venison and other wild game. Based on survey results, the MDNR's Annual Hunting and Trapping Guide would be the best venue for distributing public health information to hunters. Efforts are underway to expand the hunter health section of this popular publication. The challenge will be to raise hunter awareness enough to persuade them to adopt basic exposure prevention, without unduly inflating perceptions of risk and so dissuading them from hunting in the areas where hunting is beneficial to the local economies and critical for disease control and eradication efforts.

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CHAPTER 3

HUMAN *MYCOBACTERIUM BOVIS* INFECTION ASSOCIATED WITH THE BOVINE TB OUTBREAK IN MICHIGAN, 1994-2007

ABSTRACT

Mycobacterium bovis or bovine TB, is endemic in the white-tailed deer population of the northeastern counties of Michigan's lower peninsula. Between 1994 and February, 2007, *M. bovis* was found in 41 cattle herds and 561 wild deer in Michigan. Based on genotyping analyses, the strain of *M. bovis* circulating in Michigan's deer and cattle has remained consistent for the duration of the outbreak. Although *M. bovis* is a zoonotic pathogen, this outbreak strain was not detected in a human until 2002, with the occurrence of a human pulmonary isolate. In 2004 cutaneous disease was documented in a hunter. This report summarizes the epidemiologic and molecular investigation of these two human cases who share the deer/cattle outbreak strain of *M. bovis*. The results of this investigation confirm recreational exposure to infected deer in Michigan as a potential, albeit low, risk for acquisition of *M. bovis* infection in humans.

INTRODUCTION

Historically, *M. bovis* infection in humans has been associated with the consumption of unpasteurized milk and dairy products (Enarson, 1995; Wigle, 1972) and this remains the most important route of exposure in developing countries as well as US populations exposed to unpasteurized dairy products imported from countries where *M. bovis* remains prevalent (Dankner, 1993; CDC, 2005). Before the US began pasteurization of milk and implementation of a national control program in cattle, *M. bovis* reportedly accounted for 6%-30% of human tuberculosis cases (McKenna, 1995). Exposure through dairy products was virtually eliminated in Michigan following implementation of statewide milk pasteurization regulations mandated in 1948 (Michigan Compiled Law, Act 291 No. 288.131, 1947). Cutaneous infection with *Mycobacterium* species also became very rare in the US following the reduction of infection in both humans and cattle (Tappeiner, 1993).

M. bovis infection in humans is of particular concern to both public health and animal health officials in Michigan due to the endemic nature of *M. bovis* in the state's wild white-tailed deer population, and the subsequent discovery of infection in 41 Michigan cattle herds (Michigan Bovine Tuberculosis Eradication Project Activities Report and Conference Proceedings, 2005). The presence of *M. bovis* infection in deer presents several new possible occupational and recreational routes of exposure for hunters, trappers, taxidermists, venison processors and venison consumers (Wilkins, 2003). To increase hunter awareness, the Michigan Department of Natural Resources has included bovine tuberculosis (TB) information in their annual Hunting and Trapping Guide since 1996 (MDNR, 2006; D. O'Brien, personal communication; Michigan Department of Natural Resources, 2007).

Although *M. bovis* is a well-recognized zoonotic agent, available evidence indicates no increase in the incidence of *M. bovis* infections in Michigan residents since the current outbreak began in 1994 (unpublished data, Michigan Department of Community Health [MDCH], 2007). Since 1995, the incidence rate of *M. bovis* infection in Michigan residents has been approximately one new case per year (with a range of 0-3 cases), for a total of 13 cases. Less than 0.5% of all human cases of tuberculosis in Michigan can be attributed to *M. bovis* infection. No genetic or epidemiologic link to the circulating deer/cattle outbreak strain circulating in northeastern Michigan has been identified among 11 of the human *M. bovis* cases identified in Michigan residents from 1995 through March of 2007. These findings were based on restriction fragment length polymorphism (RFLP) analysis, spoligotyping or mycobacterial interspersed repeat units (MIRU) typing (unpublished data, MDCH, 2007). Of these 11 cases, eight occurred in recent immigrants; seven were from Mexico and one from Bosnia. The remaining three cases were US-born, instate residents, diagnosed at ages 74, 75, and 79 years; two of whom reported a history of raw milk consumption in their youth. Table 3.1 shows the diversity of spoligotyping and MIRU typing results from nine available human specimens, unrelated to the deer/cattle outbreak. All genotyping of isolates mentioned in this report was performed at the MDCH, Bureau of Laboratories, Lansing, MI, using RFLP, spoligotyping and MIRU guidelines currently recommended by Centers for Disease Control and Prevention (CDC) (Yang, 1998; Cowen 2002; 2004; Kwara, 2003). Spoligotyping results were compared to the International *M. bovis* Spoligotyping Database (closed database, internet).

Table 3.1 : Non-epidemiologically linked human *M. bovis* spoligotyping and MIRU typing results, Michigan, USA.

Country of Birth	Site	Year Collected	International Spoligotype*	MIRU type†	Spoligotypes
USA	Cervical LN	1997	SB1210	Not available	□■□■□□■■□□□□■■■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
USA	Spine	1997	SB0131	Not available	■■□■□■■■□■□■■■■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Mexico	Abd Abscess	1998	SB0140	232224152322	■■□■■□■□□□□□■■■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Mexico	Sputum	1998	SB1210	Not available	□■□■□□■■□□□□■■■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Bosnia	Cervical LN	2000	SB1215	232314353312	■■□■■■■□□□□□■□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Mexico	Sputum	2003	SB0121	232314223322	■■□■■■■■□■■■■■■□■■■■□■■■■■■■■■■■■■■■■■□□□□□
USA	Cervical LN	2003	SB0121	232324252322	■■□■■■■■□■■■■■■□■■■■□■■■■■■■■■■■■■■■■■□□□□□
Mexico	Cervical LN	2005	SB1216	232124233222	□□□■■■■■□■□■■■■□■■■■■■■■■■■□□□■■■■■■■■□□□□□
Mexico	Cervical LN	2007	SB0140	231224243322	■■□■■□■□□□□□■■■□■■■■■■■■■■■■■■■■■■■■■■□□□□□

* International Spoligotype Database; available from http://www.mbovis.org

† Mycobacterial interspersed repeat units (MIRU) type described by Cowen, 2002.

The remaining two human cases of *M. bovis* occurred in US-born, Michigan residents with epidemiologic and molecular links to the outbreak strain of *M. bovis* circulating in the deer and cattle of northern Michigan. The first case was diagnosed in 2002; the second case was diagnosed in 2004. These two human cases are the focus of this report.

CASE 1, 2002

Clinical History

In January 2002, a male aged 74 years sought medical care for malaise, weakness, anorexia, and fever of 38.9°C of one week duration. His past medical history was significant for ischemic bowel disease, cerebral and peripheral vascular disease, partial gastrectomy for peptic ulcer disease, and left upper pulmonary lobectomy for squamous cell carcinoma (December 1999). He was placed on gatifloxacin for a possible urinary tract infection but returned one week later with no improvement and with additional complaints of abdominal pain, nausea, and weight loss of 5 kg. He was maintained on antibiotics and returned on February 1st when he was hospitalized with persistent fever, non-productive cough and a chest radiograph revealing post-obstructive infiltrate involving multiple segments of the left upper lobe. The infiltrate was felt to be consistent with necrotizing pneumonia. A tuberculosis skin test (TST) was negative and a sputum smear was negative for acid-fast bacteria (AFB) (*Mycobacterium*). He was started on piperacillin/tazobactam, and azithromycin. After five days of therapy the patient had not improved clinically; chest radiograph revealed an increasing left side infiltrate and diagnostic bronchoscopy was performed. This specimen yielded an AFB positive smear. The patient was diagnosed with presumptive pulmonary tuberculosis and started on four-drug therapy with isoniazid, rifampin, pyrazinamide, and ethambutol. The patient deteriorated clinically over the ensuing ten days, developing a right pneumothorax and hypoxic bowel disease secondary to mesenteric thrombosis. Subsequently, he underwent bowel resection; his post-operative outcome was complicated by septic shock, adult respiratory distress syndrome and multi-organ failure. He expired on day 16 of his hospitalization.

Laboratory confirmation of tuberculosis, speciation, and antimycobacterial susceptibility testing were pending at the time of his death. Autopsy findings were limited to the thoracic cavity. The cut surface of the left lung revealed diffuse areas of parenchymal coagulative necrosis with a tan-gray-yellow friable appearance occupying 85% of the cut surface; only 25% normal-appearing lung tissue was present. There was no coagulative necrosis noted grossly in the right lung. The histopathologic findings from the autopsy report indicated numerous intracellular and extracellular *Mycobacterium* with a beaded appearance which raised the possibility of atypical *Mycobacterium avium* infection. No evidence of residual squamous cell carcinoma was found. The final culture results from the bronchial specimen were reported by MDCH, Bureau of Laboratories, Lansing, MI, as *Mycobacterium bovis* on April 11, 2002. Genotyping (RFLP) analysis revealed the *M. bovis* isolated from Case 1 shared the RFLP pattern of the predominant deer/cattle strain endemic in northeastern Michigan. Further testing of this isolate revealed spoligotyping and MIRU results matching the patterns of the circulating deer/cattle strain (Table 3.2).

Table 3.2 : Epidemiologically linked *M. bovis* spoligotyping and MIRU typing results, Michigan, USA.

Species	Year Collected	International Spoligotype*	MIRU type†	Spoligotypes
Deer 1	1997	SB0145	Not available	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Bovine 1	1998	SB0145	Not available	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Bovine 2	1999	SB0145	232224253322	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Bovine 3	1999	SB0145	232224253322	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Bovine 4	2002	SB0145	232224253322	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Human Case 1	2002	SB0145	232224253322	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Deer 2	2003	SB0145	232224253322	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Human Case 2	2004	SB0145	232224253322	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□
Deer 3‡	2004	SB0145	232224253322	■■□■□□□□□□□□□□■□■■■■■■■■■■■■■■■■■■■■■■□□□□□

* International Spoligotype Database; available from http://www.mbovis.org

† Mycobacterial interspersed repeat units (MIRU) type described by Cowen, 2002.

‡Deer shot by Case 2.

Contact Investigation

Three close personal contacts of the patient and 133 potentially exposed hospital staff were tested either immediately following Case 1's presumptive TB diagnosis, and again at 10 weeks post-exposure, or only at 10 weeks post-exposure. All personal contacts and hospital staff had non-reactive tuberculosis skin tests and no person-to-person transmission was detected.

Exposure History

In his youth, Case 1 resided in southeastern Michigan on a farm in an area geographically distant from that presently endemic for bovine TB. His current (second) wife reported he drank unpasteurized milk as a youth but that he had not done so for several decades. He was married previously and his first wife was reportedly diagnosed with tuberculosis following their divorce over 40 years before but this could not be substantiated. He was not known to have any other exposure to an active TB case. Case 1 moved to the edge of Deer Management Unit (DMU) 452 in 1994. DMU 452 has been, and continues to be, the focal area for the bovine TB outbreak in white-tailed deer. There, he and his second wife ran a business with a buck pole on the property where hunters displayed deer they had harvested. He and his wife fed deer on the property, a common local practice, but stopped when feeding was banned in 1999 (O'Brien, 2006). Although at one time he was an avid hunter, he had not hunted in at least ten years nor was he known to have consumed venison over that period of time. However, in 2000 he helped his brother and a friend of his brother's hang and transport a harvested deer that had been shot on his property. This friend was subsequently TST positive at 20 mm induration, although chest radiograph was negative, and he was placed on isoniazid for treatment of latent (therefore noninfectious) TB infection. A review of this individual's history revealed he had been exposed to an uncle with active TB many years previously. No laboratory samples were available from either the friend or his uncle for culture, speciation or RFLP analysis.

Discussion – Case 1

This patient had several potential routes of exposure to *M. bovis*, including the consumption of raw milk as a youth, exposure to an unconfirmed case of active TB in his ex-wife over four decades earlier, hunting of white-tailed deer and consumption of venison although not in the ten years before his death, handling a deer carcass from the DMU 452 vicinity in 2000 and recreational feeding of white-tailed deer. The patient's earliest possible exposures occurred during the initial years of TB control in Michigan's human and livestock populations. The state's cattle population was not certified by USDA as free of bovine TB until 1979. The address for the farm on which Case 1 resided was not available, so the historical herd health records could not be retrieved, if they still exist. Similarly, searching his ex-wife's medical records would likely prove fruitless as no laboratory culture would be available for DNA analysis and no differential tests were available at that time. Lacking records or cultures, the probability of these two potential routes of exposure cannot be further elucidated.

This patient was in poor health at the time of his death and suffered from both acute and chronic illnesses. His poor health would have rendered him more susceptible to infection with *M. bovis*, and more likely to progress from latent infection to clinical disease. The pathology results from his lung resection in December, 1999 provided no evidence of tuberculosis infection so infection was likely acquired subsequently. His chest radiograph during final hospitalization and autopsy results showed severe pulmonary involvement. The autopsy did not include abdominal findings and it is unknown whether *M. bovis* was present in his mesenteric lymph nodes, which could suggest exposure through consumption of infected milk or meat.

Case 1's RFLP, spoligotyping and MIRU results matched that of the circulating deer/cattle strain suggesting exposure to infected cattle or deer. The lack of recent exposure to cattle suggests deer to be the more likely source of his infection. Information about the patient's exposure history was collected by proxy from the patient's surviving spouse and, therefore, relevant exposure details may have been missed. It is unlikely that a conclusive route of exposure can be determined for this patient although one may be reasonably inferred from the available clinical and epidemiological evidence.

CASE 2, 2004

Clinical history

Case 2 occurred in a 29 year old, previously healthy male with no significant past medical history. On October 1, 2004, he shot a white-tailed deer in Alcona County, Michigan, where *M. bovis* is endemic in the deer population. While field dressing the animal, he sustained a small puncture wound to the base of his left index finger with a hunting knife. He also noted tan nodules in the chest cavity classically associated with *M. bovis*. Approximately 18 days post-injury, his left index finger became inflamed and painful. He sought medical treatment from his family physician, who placed him on oral antibacterial therapy (cephalexin). Based on his exposure to a deer, a tuberculin skin test was administered and was read as negative. After approximately 10 days of antibacterial therapy, the wound had not improved and the patient reported the abrupt onset of increased pain and decreased mobility of the finger. He was referred to an orthopedic specialist who diagnosed infectious tenosynovitis of the flexor tendon of the left index finger. He was hospitalized and treated with intraveneous antibiotics (cephazolin). The infected finger was incised and drained, and a wound culture was sent to the laboratory. This specimen was received by MDCH on November 1, 2004. Microscopic examination of this specimen did not reveal the presence of acid-fast bacilli. He was discharged after a two-day hospitalization on cephalexin. He was readmitted to the hospital 12 days later with subcutaneous infection at the initial puncture site, which did not appear to involve the flexor tendon. The wound was again incised and drained, and he was treated with intraveneous ampicillin/sulbactam for four days, and discharged on amoxicillin/clavulanate. On November 23, 2004, a slide made of growth from the broth culture medium was positive for acid-fast bacilli. Genetic probe results confirmed *Mycobacterium tuberculosis* complex on November 24, 2004, and the submitting hospital was notified. Case 2 was started that same day on the standard four-drug therapy for *Mycobacterium tuberculosis* (isoniazid, pyrazinamide, ethambutol, and rifampin). By December 7, 2004, the culture was reported as resistant to pyrazinamide at 100mcg/ml, suggesting *M. bovis.* At this point, pyrazinamide was dropped from the treatment regimen. *M. bovis* was confirmed on December 21, 2004, based on susceptibility to thiophen-2-carboxylic acid hydrazide (TCH) and detection of pyrazinamidase activity.

A second skin test placed on January 7, 2005 (14 weeks post exposure) by the local health department, was positive with a 6mm induration. Case 2 remained on antibiotic therapy for nine months with no further complications involving his finger.

Contact Investigation

Tuberculosis skin testing results performed on Case 2's immediate family members were negative at 14 weeks post exposure (wife and child) and 27 weeks post exposure (2nd test for child only), indicating no person-to-person transmission had occurred.

Exposure History

At the time Case 2 field dressed the white-tailed deer, he immediately noted the classic tan nodules in the chest cavity associated with bovine TB. Because he was in an area he knew to be endemic for *M. bovis* transmission, he assumed the deer to be unhealthy and promptly buried it. After undergoing treatment for his infected finger in early December, he led Michigan Department of Natural Resources staff back to the site of the buried carcass. The carcass was retrieved and the chest cavity was determined to be heavily lesioned (Figure 3.1). Although the carcass had been buried for over nine weeks, samples from the chest cavity were submitted to the MDCH laboratory for culture. After numerous attempts using alternative decontamination techniques, a viable culture was obtained on January 10, 2005, with pure growth on February, 28, 2005. Spoligotyping and MIRU results of the isolate taken from the recovered deer carcass were identical to the patterns of the strain recovered from the Case 2's finger. In addition, these patterns were identical to the *M. bovis* strain circulating in the deer and cattle in northeastern Michigan as shown in Table 3.2.

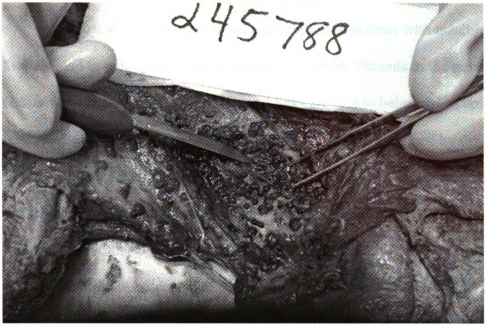

Figure 3.1 : Photo of the chest cavity of the deer shot by Case 2, retrieved after being buried for 9 weeks, displaying the classical nodular lesions of *M. bovis* infection in deer. Photo: JS Fierke, DJ O'Brien, SM Schmitt Wildlife Disease Laboratory, Michigan Department of Natural Resources.

Discussion – Case 2

The investigation of Case 2 provided strong evidence of transmission of *M. bovis* infection from an infected deer to a human via percutaneous inoculation with a contaminated hunting knife. The patient's history of a hunting exposure was essential to proper diagnosis and treatment of this very rare form of tuberculosis.

CONCLUSION

Because these two persons were infected with isolates with matching genotypes, they are said to belong to the same genotyping cluster. Patients in the same genotyping cluster who share known epidemiological links are said to belong to an epidemiologically confirmed genotyping cluster as determined by protocols described by the National TB Controllers Association and the CDC (CDC, 2004). Although the epidemiologic evidence presented for Case 1 is not irrefutable, it is the opinion of the authors that both cases are part of a cluster that is epidemiologically as well as genotypically confirmed.

The initial tuberculosis skin test was negative in both of these cases. For Case 1, the test was negative most likely due to cutaneous anergy. For Case 2, the skin test was administered too soon following exposure. He was tested prior to the 8-10 week period required for his immune system to mount a detectable response. His second skin test was appropriately interpreted as positive at 6 mm induration by staff from the local public health department. However, a 6 mm induration would traditionally be classified as negative based on his lack of standard risk factors used by CDC (CDC, 2006). In both cases, initial negative skin test results made diagnosis problematic for the physicians involved with healthcare.

Based on a 2001 survey of 1,833 hunters who had successfully harvested deer in or near Michigan's bovine TB endemic area, it was determined that 89% of hunters field dressed their own deer, and only 43% of them wore gloves when doing so (Wilkins, 2003). Based on the 2001 prevalence estimate in the deer population and the survey results, up to 139 hunters in the endemic counties may have field dressed positive deer without wearing gloves and up to 12 hunters would cut themselves while field dressing these positive deer (Wilkins, 2003). However, this is the only case that has come to the attention of public health officials. Since the time of the survey, the apparent prevalence of *M. bovis* infection in the white tailed deer population has been declining (Michigan Bovine Tuberculosis Eradication Project Activities Report and Conference Proceedings, 2005) in the affected counties, but more counties now report positive deer. Cutaneous or percutaneous exposure to *M. bovis,* while field dressing infected deer, continues to be a potential risk for Michigan hunters.

The confirmation of a hunter acquiring cutaneous *M. bovis* from an infected deer supports the need for public health precautions for deer hunters. First, hunters should wear heavy latex or rubber gloves while field dressing deer. Although latex or heavy rubber gloves may not protect against a cut during the field-dressing process, gloves may lessen the severity of the cut as well as protect pre-existing wounds from exposure to the organism. Secondly, prior hunter education was critical in the second case, because the hunter recognized the deer as infected, and specifically mentioned his exposure each time he sought medical treatment. Thirdly, efforts to raise the index of suspicion of the medical community regarding cutaneous and other occupational or recreational exposures to bovine tuberculosis continues to be important, so that appropriate diagnoses can be made. Finally, in both cases, the initial negative tuberculin skin test complicated the diagnostic efforts. It is an ongoing challenge to ensure that both public and private providers appropriately apply and interpret the tuberculin skin test.

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CHAPTER 4

ABSENCE OF *MYCOBACTERIUM BOVIS* INFECTION IN DOGS AND CATS RESIDING ON INFECTED CATTLE FARMS -- MICHIGAN, 2002

ABSTRACT

A cross-sectional field study was performed to evaluate dogs and cats living on farms with *Mycobacterium bovis* (bovine TB) infected cattle. Our purpose was to determine pet infection status and assess their risk to farm families and/or tuberculosis-free livestock. Nine farms participated in the study. Data and specimens were collected from eighteen cats and five dogs from nine farms. ELISA testing for *M. bovis* and *M. avium* was conducted. Fifty-one biologic samples were cultured; all were negative for *M. bovis*, although other *Mycobacterium* species were recovered. No radiographic, serologic or skin test evidence of mycobacterial infection was found. These negative results may be due to the low level of bovine TB infection in the cattle and their infrequent exposure to pets residing on the same farm. We found no evidence that pets residing on bovine TB-infected Michigan cattle farms pose a risk to humans or bovine TB-free livestock, however precautionary advice was provided.

INTRODUCTION

Causing disease in a wide range of mammals, *M. bovis* has the broadest host range of the members of the *M. tuberculosis* complex (O' Reilly, 1995) and is well established as a zoonotic disease. Historically, milk-borne transmission has been responsible for most human *M. bovis* infections. In developed countries, this route of transmission was virtually eliminated following the widespread adoption of pasteurized milk. *M. bovis* has recently become established in the wild white-tailed deer population of the northeast portion of Michigan's lower peninsula. Identified in 1994 in a hunter-harvested white-tailed deer, *Mycobacterium bovis* has been found in 449 deer (out of 105,885 tested) through 2002. From 1996-2002, several additional species have been tested and found positive for *M. bovis* infection in Michigan including: coyotes (19), raccoons (8), black bear (7), bobcat (4), red fox (3), opossum (2) and elk (2) and one semi-feral domestic cat (Summary of Michigan Wildlife Bovine Tuberculosis Surveillance, 2007; Kaneene, 2002). At the time of this study (August 2202), 23 infected cattle herds had been found (Summary of gross and histologic examination and mycobacterial culture of tuberculosis cases in cattle and captive deer in Michigan 1996 – 2007, database on the Internet). The wide diversity of infected species suggests several potential new routes of transmission for *M. bovis* from animals to humans.

Pet to Cattle, Cattle to Pet

Scientific literature describing the role of domestic pets in the transmission of *M. bovis* on the farm (livestock to pet, pet to livestock) is fairly limited and quite dated. While uncommon in both dogs and cats, historic data suggests that dogs were more likely to be infected with *M. tuberculosis* following exposure to infected humans, while cats were more likely infected with *M. bovis* with exposure assumed to be related to the consumption of contaminated animal products (Birn, 1965). Historically, farm cats and dogs were at very high risk of acquiring *M. bovis* from infected cattle; 4 of 9 dogs and 24 of 52 cats were affected after exposure to positive cattle in a Pennsylvania study (Snider, 1971). It is therefore feasible that pets could play a role in the maintenance of M. *bovis* on a farm (Greene, 1998), however, literature describing pet transmission to cattle is hypothetical (McLaughlin, 1974) or limited to references from Eastern Europe in the 1950's and 60's (Beinhauer, 1958; Milbrant, 1960; Pavlas, 1965; Schliesser, 1965).

Transmission from pets to humans

Literature describing the role of pets in transmission of *M. bovis* to humans is also very limited, although transmission would again be biologically plausible. Early necropsy studies (1930-1965) revealed a tuberculosis prevalence ranging from 2.0 to 13% in cats and 0.4% to 2.0% in dogs (Snider, 1971). There is no evidence that dogs and cats have transmitted *M. bovis* infection to humans; only one inconclusive cat-to-human reference was found (Isaac, 1983). In Michigan, wild carnivores and omnivores are considered dead-end hosts for *M. bovis*. These animals are most typically exposed to infection via the consumption of infected deer carcasses, thus resulting in a gastrointestinal clinical presentation with limited potential for transmission to people or other animals (Bruning-Fann, 2001).

Clinical presentation

Clinical findings in dogs infected with *Mycobacterium tuberculosis* include: anorexia, loss of body weight, lethargy, vomiting and leukocytosis; radiography revealed pleural and pericardial effusion, ascites, and hepatomegaly (Si-kwang, 1980). In cats, the most common clinical sign associated with *M. bovis* infection was a moist skin lesion (de Lisle, 1990). Additional clinical signs included lymphadenopathy (primarily the head and mesenteric lymph nodes) and liver, spleen and lung lesions in generalized cases (deLisle, 1990; Kaneene, 2004). It is also notable that in the Pennsylvania study, tuberculosis infection frequently occurred without apparent clinical signs in the pets (Snider, 1971).

Pets and the Control of bovine TB

The regulatory response following the detection of *M. bovis* infection in a herd of cattle is to place the farm under quarantine. The herd is then either scheduled for depopulation, or placed on a rigorous testing schedule to remove TB responders from the herd (USDA, 1989). Federal recommendations include removing other susceptible livestock and pets from the farm during the cattle depopulation phase (Clifford, 2006). However, regulatory officials in Michigan have not included pets in their depopulation efforts.

This study assesses the potential role that dogs and cats may play in the transmission of *M. bovis* to livestock and humans, and evaluates their possible role in the epidemiology of the current Michigan outbreak. To accomplish this objective, we evaluated the exposure and bovine TB-infection status of the dogs and cats living on farms where cattle had recently been diagnosed with *M. bovis*. Pet owners on these farms were also offered advice on how to prevent pet exposure to *M. bovis* and how to minimize human exposure to potentially infected dogs and cats.

METHODS

Farm enrollment

From October, 1997 until August, 2002, 23 Michigan cattle farms were found to be infected with *M. bovis* and were placed on a control program by the Michigan Department of Agriculture. Our study took place in June and August 2002 and attempted to include all recently or currently infected farms. All farms were located in the northern portion of the lower peninsula of Michigan. Repeated attempts were made to contact the owners of all 23 farms to invite participation in the study. Phone calls were attempted initially, followed by several on-farm visits if phone contact was not successful.

Pet enrollment

A pet was considered eligible for inclusion in the study if it was >6 month of age and resided on the farm when infected cattle were present. All cats including "barn", "feral," and "indoor only" cats were eligible for the study. Written informed consent was obtained from the pet owner for each specific pet and each clinical procedure. History information obtained regarding each pet included age, gender, physical description, range (cats - indoor only, indoor/outdoor, outdoor only; dogs – tied, loose, able to wander off the farm), diet, raw milk exposure, time living on farm, exposure to cattle (share barn), vaccination status and medical history. Live traps were used if necessary for outside cats. If the owner desired, the pets were spayed or neutered as well. The pets were returned to the farm within two days. If the owner did not wish to have the dog or cat returned to the farm, consent for euthanasia was obtained.

Clinical exam and specimen collection

The clinical exam and sample collection took place at a local veterinary clinic. Procedures were performed by a single veterinarian to ensure consistency. Sedation was used at the clinician's discretion. For both cats and dogs, the protocol included a physical exam, radiographs of the chest and abdomen, fine-needle aspirate of any enlarged superficial lymph nodes, the collection of rectal and oral swabs and a 5ml blood sample. For cats, a combined FeLV and FIV ELISA test was done. Remaining serum was frozen and sent to Dr. C. Thoen's Laboratory at the College of Veterinary Medicine, Iowa State University, Ames, Iowa, USA for comparative ELISA (*M. bovis* and *M. avium*) (Thoen, 1980) testing. For dogs, 0.1 ml of 250 TU PPD was placed intradermally in the inner surface of the pinna, with interpretation of the skin test made by the researcher within 48-72 hours (Greene, 1998). If the owner consented to euthanasia of unwanted feral animals, the above protocol was followed with the exception of the collection of the fine needle aspirate and the fecal and oral swabs. The animals were euthanized at the clinic and transported on ice the next day to the Michigan State University, Diagnostic Center for Population and Animal Health, East Lansing, MI.

Necropsy protocol

Necropsies were performed the day following euthanasia. The necropsy included gross examination of all tissues, and the collection of the following tissue pools for mycobacterial culture: cranial (parotid, submandibular & retropharyngeal) and thoracic (mediastinal and tracheo-bronchial) lymph nodes and lungs, abdominal lymph nodes (mesenteric & ileo-cecal), abdominal viscera (spleen, liver, kidney), small and large intestine. The following tissues were fixed in formalin and examined histologically:

brain, cranial lymph nodes, tonsil, trachea, lung, thoracic lymph nodes, heart, spleen, kidney, liver, pancreas, adrenal gland, abdominal lymph nodes, small and large intestine. Ziehl-Neelsen acid fast staining was applied only to slides exhibiting lesions suggestive of mycobacteriosis on the histological exam.

Radiological exam

The radiographs were examined by a veterinary radiologist, Radiology Department at the Michigan State University, College of Veterinary Medicine, for evidence of mycobacterial infection. The radiologist was given only the animal's age and study identification number. The lung fields were to be examined for evidence of mycobacterial infection, and the thorax and abdomen were examined for signs of lymphadenopathy.

Microbiology and strain typing

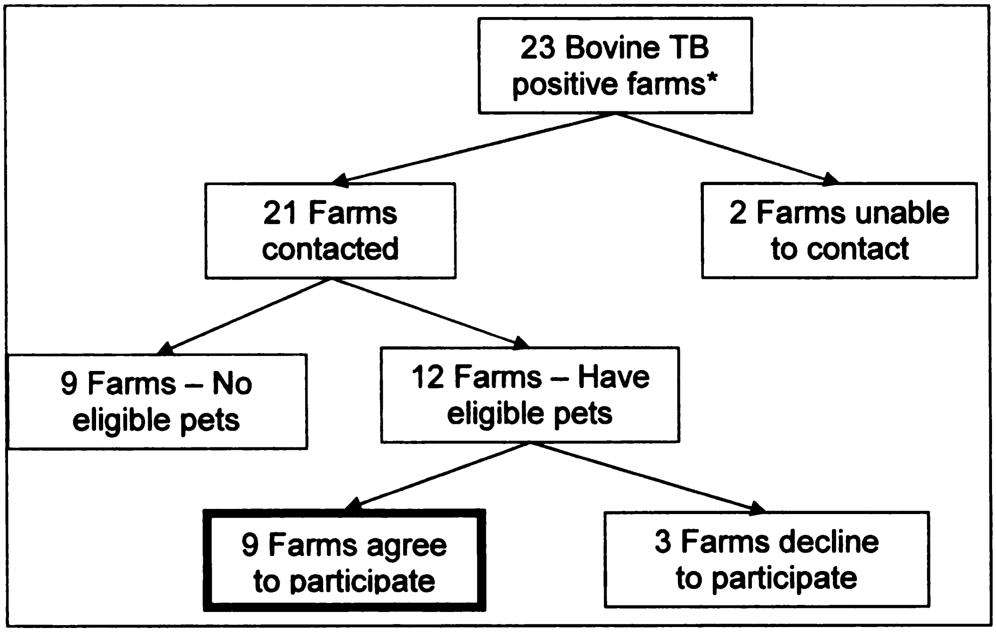
Mycobacterial culture and identification was performed at the Michigan Department of Community Health, Bureau of Laboratories, Lansing, MI. Recommended procedures were followed for specimen digestion, concentration and examination (Kent, 1985). Sediment of concentrated specimens was examined microscopically for acid-fast bacilli. Sediment of the specimens was then re-suspended by the addition of 1.5 mL of PBS solution, and aliquots were inoculated onto a slant that contained Lowenstein-Jensen medium (Lowenstein-Jensen BB20909, Becton-Dickinson, Sparks, MD), onto a slant that contained a Middlebrook-based medium (Middlebrook 7H11S, Becton-Dickinson, Sparks, MD) and into a vial that contained broth for microbial culture (Bactec 12B broth vial, Becton-Dickinson, Sparks, MD). Media were examined for growth at least weekly for 8 weeks. Acid-fast bacteria were tested by use of a genetic probe (Accuprobe, Gen-Probe, San Diego, CA) (Reisner, 1994) to determine whether the bacteria were members of the *M. tuberculosis* complex. Biochemical testing and high performance liquid chromatography were used to differentiate *M. bovis* from other members of the *M. tuberculosis* complex and to speciate other mycobacteria (Kent, 1985; Butler, 1991; Metchock, 1995).

Determination of exposure period

We estimated the minimum period during which the dog or cat could have been exposed to infected cattle as the difference between the first date when the cattle on the farm tested positive for bovine TB using the caudal fold skin test results and the date when the infected cattle were depopulated or the farm was placed on a herd testing and removal plan. Next, the age of the pet at the time of study enrollment was used to determine the number of months during which the pet and the infected cattle both resided on the farm. This estimate is considered the minimum exposure duration, because the cattle may have been positive for months to years prior to being tested and found to be positive for bovine TB. The exposure period became progressively shorter as the bovine TB eradication efforts in Michigan became more efficient at early detection.

RESULTS

Twenty-three farms had been identified as Bovine TB positive by August 2002. After numerous attempts to contact each farm owner, 21 (91%) farm owners were successfully contacted and invited to participate in the study. Nine (43%) of the 21 contacted farmers had no dogs or cats eligible for inclusion. Twelve (57%) had eligible pets, of which nine (75%) agreed to participate (Figure 4.1). Eighteen cats and five dogs were enrolled from these nine farms (7 beef, 2 dairy). Characteristics including age, gender, diet, housing and exposure for enrolled dogs and cats are summarized in Table 4.1.



*Number of positive farms as of 8 August 2002

Figure 4.1 : Flow diagram to show how participating farms were selected

Table 4.1 : Summarized characteristics of study participants by species.

Characteristic	Cats (N=18)	Dogs (N=5)
Gender	11 Male (61%)	2 Male (40%)
Average age (yrs)	4.1 (range 1.0-12.5)	6.1 (range 2.0–11.5)
Routinely fed	Yes n=15 (83%)	Yes n=5 (100%)
Fed raw milk	Yes n=5 (28%)	Yes n=0 (0%)

Table 4.1 (cont'd)

Outdoor only	Yes n=12 (67%)	Yes n=4 (80%)
Known or likely to have shared barn with infected cattle	Yes n=18 (100%)	Yes n=0 (0%)
Average exposure period* (mos)	2.3 (range 1.0 -7.0)	4.0 (range 2.0-8.0)

*Calculated as the minimum possible exposure period

Cats

Only four cats (22%) had ever been vaccinated (for any disease) and only one cat was current on its vaccines. All cats were FIV negative; two (11%) cats were FeLV positive. The two FeLV positive cats were euthanized and a full necropsy performed. The 18 cats suffered from the expected range of barn cat ailments: earmites/otitis externa 5 (28%), bloated abdomen 3 (17%), missing hair/poor haircoat/scabby skin 3 (17%), tracheitis 2 (11%), enlarged submandibular lymph nodes 2 (11%), conjunctivitis 2 (11%), runny eyes, poor teeth, congestion of the lungs, and diarrhea (1 each). Sixteen oral swabs and 16 fecal swabs were submitted for mycobacterial culture (two per live cat). In addition, eight pooled organ samples were submitted for culture (four per each of the two euthanized cats). All culture results were negative for *M. bovis*; one fecal culture was positive for *M. avium* complex. Radiographs of the heart and lungs were found to be unremarkable for all 18 cats; no signs of lymphadenopathy in the abdomen or thorax were noted. Gross pathological and histological examination of the two euthanized cats revealed no evidence of mycobacterial infection. Three cats tested positive for *M. avium* at the 1:160 dilution, two of these cats also tested positive for *M. bovis* but at less than the 1:160 dilution and were assumed to be cross-reacting with *M. avium.*

Dogs

All dogs were allowed to run loose on the farm and presumably had substantial contact with the cattle. No dogs showed noticeable or measurable TB skin test response at 48 – 72 hours. An oral swab and a fecal swab from each of the five dogs were submitted for mycobacterial culture (two per dog). All culture results were negative for *M. bovis*. Two fecal cultures were positive for *Mycobacterium* species (Group IV unclassified). Radiographs of the heart and lungs were found to be unremarkable for all five dogs, comments include: mild right loss of cranial waist (n=1) and widened mediastinum due to fat, loss of cranial cardiac waist, mild right heart enlargement (n=1). No signs of lymphadenopathy in the abdomen or thorax were noted. We detected negative responses on the ELISA test for all five dogs for the *M. bovis* and *M. avium* PPD antigens.

DISCUSSION

The herds on the participating farms had a low prevalence of cattle infected with *M. bovis*. Only 14 of the 869 (1.6%) cattle tested were either suspect or positive using the comparative cervical test. Following necropsy of all comparative cervical suspect and reactor cattle, an average of less than one gross lesion per bovine (11/14) was found in the cattle on the participating farms, indicating the absence of advanced, heavily diseased cattle with the potential to shed high numbers of infectious organisms. The low prevalence of infection in the herd and low severity/early progression of infection in individual animals may explain the apparent lack of transmission to the dogs and cats.

During the course of the outbreak in Michigan, the control and eradication efforts by state and federal agriculture officials intensified. Positive farms were quickly identified by contact tracing or by area testing, and the time between diagnosis and depopulation was shortened. Thus, the period of time during which pets were exposed to infected cattle became progressively shorter. The detection and control efforts also decreased the likelihood of infected cattle progressing to a clinical stage of disease where *M. bovis* would be transmitted via shedding into the milk.

The historic method of infection for cats with bovine TB has been through the consumption of infected raw milk. Five of the study cats came from the two dairy farms. Although these five cats (28% of 18) did routinely consume raw milk, it is highly unlikely that any of the milk cows had infection that had progressed to the point of shedding *M. bovis* in their milk. Only one animal was found positive by comparative cervical testing per dairy farm and only one gross lesion was detected in each of these positive cows. Furthermore, none of the positive cows had lesions in the supra-mammary lymph nodes, further reducing the likelihood of shedding of organisms into the milk. All of our study cats were likely to have slept in the barn with the infected cattle. However, because the cattle were not heavily infected, exposure via aerosolized droplets was unlikely.

Wild carnivores have acquired *M. bovis* infection in Michigan (Bruning-Fann, 2001) presenting as gastrointestinal infection presumably as the result of consuming gut piles left from hunted infected deer, or by scavenging or hunting infected animals. In our study population, all five dogs were routinely fed by their owners, decreasing the likelihood that they would consume deer gut piles. According to the owners, the dogs were routinely allowed to run loose on the farm, but did not often leave the farm premise, so exposure to gut piles would expectedly have been rare. The study dogs did not sleep in the barns with the infected cattle so aerosol transmission is also unlikely.

Transmission of *Mycobacterium* species from an infected dog has never been documented. Carnivores are most likely to be infected via consumption of infected milk or meat and present with gastrointestinal infection. Thus cats and dogs are generally felt to be less likely to transmit the disease unless the disease progresses to a systemic infection due to suppression of the immune system. Four out of five of our study dogs were strictly outdoor dogs and all were in fair to good health, making them a very low risk for clinical disease and shedding, even if they had become infected.

Cats pose a higher transmission risk to both humans and cattle than dogs for several reasons: they have a closer relationship with both cattle (sharing the barn, consuming raw milk) and with humans (more likely to be indoor/outdoor and sleep in same bed as humans), they have recently been proven scavengers (Ragg, 1995) and they are susceptible to common viruses, feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV), which specifically compromise their immune system. An immunocompromised cat is more susceptible to infection in general, and a correlation between FIV, *M. bovis* infection and clinical disease has been recently hypothesized (Moines, 2000). Thus, cats infected with FeLV or FIV and exposed to *M. bovis* could pose a much higher risk to human owners (and cattle) than an immuno-competent cat, as the disease is more likely to progress clinically, increasing the likelihood of transmission to others.

Diagnosis of *M. bovis* in live dogs or cats is very difficult, and our study protocol included all non-invasive procedures available at the time. Only two cats were offered for post-mortem exam; both were positive for FeLV, perhaps making them the best candidates for *M. bovis* isolation if it were present.

CONCLUSION

In the final analysis, no evidence was found to indicate the transmission of *M. bovis* from infected cattle to farm dogs or cats. The likelihood of dog and cat infection was judged to be minimal due to a low risk of cattle exposure, a low expected exposure dosage and a relatively short duration of exposure to the infected cattle. In Michigan, even if a farm dog or cat were to become infected, its potential to transmit infection to humans or cattle is estimated to be very low.

Recommendations

Despite the low risk of infection of pets and transmission from pets, the following prevention recommendations were made to pet owners on the farms infected with bovine TB:

- Do not feed pets raw milk.
- Keep house cats strictly in the house and barn cats out of the house.
- If barn cats are allowed into the house, keep them away from your face, especially if they are ill.

- Do not allow dogs to roam freely.
- Keep pets healthy (fed and vaccinated) because an ill or weak animal is more susceptible to infection with Bovine TB and more likely to progress to clinical disease if infected.

In addition, each farm owner is strongly encouraged to have family and employees skin tested for possible *Mycobacterium tuberculosis* complex exposure on an annual basis.

Regulatory veterinarians should carefully assess the health status of pets on infected cattle farms and seriously consider following the federal recommendations to depopulate pets that have been heavily exposed to infected cattle. Cattle owners should clearly understand that pets do pose a health threat, albeit remote, to their family and to TB free livestock purchased to re-populate the farm. Because skin testing in both dogs and cats is unreliable, and infected pets may be asymptomatic, the development and use of reliable ante-mortem tests should be considered as an in-vivo testing alternative for domestic pets on *M. bovis* infected farms. In fact, a study by several of the authors is currently under way evaluating several different ante-mortem assays for bovine tuberculosis detection in cats.

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CHAPTER 5

VETERINARIAN INJURIES ASSOCIATED WITH BOVINE TB TESTING LIVESTOCK IN MICHIGAN, 2001.

ABSTRACT

Determining the injury rate for working with cattle is difficult since a wide range of persons perform a diverse assortment of procedures on cattle in highly variable circumstances. There is also generally a lack of denominator data regarding the number of cattle receiving each type of procedure. Testing all the cattle in an entire state with a uniform procedure for each animal affords an opportunity to relate human injury data to a known number of animals handled while carrying out a standardized procedure. The objective of the current study is to capture the type and incidence density of injuries associated with TB-testing a large number of cattle herds, and to delineate the various factors contributing to the risk of injury. Additionally, the two known mortality events associated with bovine TB testing in Michigan will be summarized. A survey was mailed to all veterinarians (N=259) who had completed at least five official bovine TB herd tests in Michigan in 2001. Collected data regarded basic demographics and health status, work experience, veterinary specialty, and practice information. Each veterinarian was also requested to complete a separate injury questionnaire for each injury received while TB testing livestock in 2001. Risk ratios were calculated, based on the incidence density of injuries per 10,000 animals tested, to compare the characteristics of the injured veterinarians to the non-injured veterinarians. Accurate addresses were found for 247 eligible veterinarians, 175 of whom returned the survey for a participation rate of 71% (175/247). Thirty-six veterinarians reported a total of 53 injuries (10 major, 12 minor and

31 self-treated). Individual veterinary characteristics and the type, cause and location of each injury are described. The overall incidence density of injuries was 1.9 per 10,000 animals tested. Female gender (RR=3.26), having less than 10 years of practice (RR=1.81), being employed by the government (RR=4.54), smoking (RR=5.97) and working 50 hours or less (RR=1.87) were found to be significantly associated with a higher rate of injury per 10,000 animals tested. The human "costs" in terms of injuries, must be considered when decisions are made to initiate large-scale livestock disease control programs, although these costs are more difficult to measure than the financial costs of a budgeted control program. Effort and resources must be allocated to reduce the number and frequency of preventable injuries, and to monitor the public health impact of ongoing disease control efforts.

INTRODUCTION

Twenty years after obtaining the bovine TB (bTB) Accredited-free status from the US Department of Agriculture in 1979, Michigan lost that designation to become a Non-Modified Accredited state on June 22, 2000 joining Texas as the only other US state that did not have Free status for bTB. Michigan's loss of Free status for bTB was due to the recent confirmation of *Mycobacterium bovis* (i.e. bovine TB) infection in seven cattle herds in the northeastern portion of the lower peninsula of Michigan. To remain in compliance with the federal Pasteurized Milk Ordinance and the Michigan Grade A Milk Law of 2001 (Act 266 of 2001) all dairy herds in the state (~3000 herds, ~300,000 milk cows) were required by the Michigan Department of Agriculture (MDA) to be TB tested within 12 months. In addition, all beef cattle (~10,000 herds, ~700,000 cattle), bison and goat herds in the state were required to be tested by the end of 2003 (2000; 2004). To meet this large scale and immediate demand for TB testing, the MDA hired federally-accredited private veterinarians on a fee-basis to supplement the existing state and federal veterinary field staff. The fee-basis veterinarians were hired without selection for their current practice focus. The purpose of this study is to capture the type and frequency of injuries in veterinarians associated with TB testing a large number of cattle, bison and goat herds, to delineate the various factors contributing to the risk of injury, and to summarize two known mortality events associated with bTB testing in Michigan.

Veterinary practitioners are often classified as having a primary employment focus in companion animal practice, large animal practice or a combination of both. Regardless of their concentration, veterinary practice presents occupational hazards from physical, biological and chemical agents (Jeyaretnam and Jones, 2000). An occupational hazard survey found needle punctures, kicks and crush or handling injuries as the leading cause of injury to veterinarians in large animal practices (Poole et al., 1999) while cat bites, dog bites and needle punctures topped the list in companion animal practices (Poole et al., 1998). A survey of AVMA members in Minnesota and Wisconsin found hands, shoulder/arm, legs, head, back and feet to be the most frequently injured anatomic structures (Landercasper et al., 1988). Occupational injuries of zoo veterinarians have also been specifically studied (Hill et al., 1998), as well as practice hazards unique to pregnant veterinarians (Moore et al., 1993). In a large Minnesota study of all licensed veterinarians, factors found to increase the risk of veterinary injury included smoking, lack of sleep, lifting heavy patients, inexperience, and lack of availability of assistants. In contrast, participation in aerobic activities, increasing age and male gender were found to decrease the risk of injury (Gabel et al., 2002).

Unlike prior veterinary injury research focusing on practice specialty or demographic characteristics such as age and gender, this study investigates injuries associated with one particular task, the TB-testing of livestock. This study is part of a larger effort to assess the human health risks associated with the current bovine TB outbreak in Michigan (Wilkins et al., 2003, 2008).

METHODS

Animal testing

At the time of the study, cattle, bison and goats were screened for TB using the caudal fold test (CFT) with intradermal placement of *M. bovis* antigen under the tail head. A CFT is considered positive at 72 hours when skin thickness of the injection site is measured at 4 mm or more. If positive, a comparative cervical test (CCT) was performed by a state or federally employed veterinarian (hereafter referred to as "regulatory" veterinarians), placing separate intradermal injections of *M. bovis* and *M. avium* 12.5 cm apart on the neck. A CCT was considered positive if the skin thickness at the *M. bovis* injection site is 4 mm greater than the *M. avium* site (Clifford, 2006).

To properly place and interpret both the CCT and the CFT test, the animal must be adequately restrained, often requiring the use of veterinarian-supplied heavy equipment such as portable chutes and panels. For an official test (CFT or CCT) each animal must be handled twice, separated by 72 hours. For this study, an animal "tested" means the animal was handled twice, and refers to both caudal fold and comparative cervical tests. The term "herd test" is non-specific and may correctly refer to the testing of a single animal or alternatively may refer to the testing of hundreds of animals comprising an entire herd.

Study population

The study population included all veterinarians who had completed at least five official TB herd tests in Michigan in 2001. The list of official herd tests was obtained from U.S. Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services - Michigan. The mailing addresses for all veterinarians licensed in Michigan were purchased from the Bureau of Health Professions, Michigan Department of Community Health. The lists were combined to create a mailing list for 259 eligible veterinarians, who collectively performed 9,326 herd tests.

Data collection

The first survey instrument was mailed in September 2002. It was resent to non-responders, with a new cover letter, three weeks later. Available addresses were inaccurate for 12 veterinarians, so 247 received the survey. Of these, 175 veterinarians returned the survey for a participation rate of 71% (175/247).

The survey was pilot-tested on 7 veterinarians to ensure the clarity of each question and the availability of adequately descriptive answer options. The survey questions were primarily close-ended or short fill-in-the-blanks. There was one open-ended question to allow the veterinarian the option to "in your own words, describe the circumstances leading to the injury and the injury itself". The survey took between 5 and 25 minutes to complete, depending on the number of injuries reported.

The following information was collected for each injury: severity, month of occurrence, when in the course of the farm visit the injury occurred, availability of assistants, location on body, type and cause of the injury, type of animal or equipment involved, contributing factors (animal behavior, facilities, weather, assistants, personal issues, whether the current injury was a re-aggravation of a prior injury, as well as the preventability of the injury. Microsoft Excel and SPSS 12.0 (Chicago, IL) were used to manage the data.

Classification of Injury

Veterinarians were asked to categorize their injuries as major, minor and self-treated. Major injuries were defined as injuries that required immediate treatment (hospitalization, outpatient visit to an emergency room or urgent care center) within 4 hours of incident and/or resulted in over 16 hours of lost work time. Minor injuries were defined as requiring non-immediate treatment for the injury from a physician or human health professional within seven days of the incident and/or 4-16 hours of lost work time. The self-treated category included treatment provided to themselves or received from their veterinary staff and resulted in <4 hours lost work time. Because the veterinarians had such a propensity to self-treat -- even severe injuries (Landercasper et al., 1988), their reluctance to seek human medical advice, and to continue working while injured (indicated by our data), the injury categories were collapsed for the final analysis, making our final definition consistent with prior work (Landercasper et al., 1988).

ANALYSIS

Because the number of herds and number of animals tested did not follow a normal distribution, the Mann-Whitney U test was used to compare responding veterinarians to non-responders on the basis of the median number of herd tests completed, and the median number of animals tested. The injury details and veterinarian characteristics are reported by both number and percent. Because several veterinarians reported more than one injury and because each veterinarian did not test the same number of animals, incidence density (number of injuries per animal tested) was the most appropriate epidemiologic measure to describe our results. To compare the characteristics of the injured veterinarians to the non-injured veterinarians, a risk ratio was calculated based on the incidence density of injuries per 10,000 animals tested, using Epi Info 6.04b (Centers for Disease Control and Prevention, Atlanta, GA). Factors found to be significantly contributing to the risk of injury in the incident density analysis were included in a bivariate analysis using χ^2 testing to further examine inter-relationships between risk factors. Additionally, a portion of these risk factors were examined to determine their direct relationship with the likelihood of injury (as a binomial outcome), as opposed to their contribution to the *rate* of injury (incidence density analysis).

RESULTS

Responders vs. Non-responders

Responding veterinarians tested a median number of 28 herds (5^{th} percentile = 5; 95^{th} percentile = 84.4) compared to 20.5 herds (5^{th} percentile = 5; 95^{th} percentile = 66.7) for non-responding vets; the difference was not found to be significant (p = 0.197 using Mann-Whitney U test). Responding veterinarians tested a median of 1055 animals (5^{th} percentile = 32.7 ; 95 percentile = 4769.3) compared to 1006 (5^{th} percentile = 28.5; 95 percentile = 3608.8) for nonresponders; the difference was not found to be significant (p=0.434, by Mann-Whitney U test). No additional variables were available for comparison.

Summary of Injuries

Thirty-six veterinarians reported a total of 53 injuries (10 major, 12 minor and 31 self-treated). Sixty-one percent of the injuries were caused by direct contact with animals; the remaining 39% were caused by equipment use or failure. Only 13.3% of the injuries were a re-aggravation of prior injuries, and the veterinarians thought 81.1% of the injuries could have been prevented. During the course of the farm visit, the majority (75%) of the injuries occurred when placing or reading the TB test or ear tagging the animal, followed by preparing for/ setting up equipment for TB testing (15.4%) and finally, disassembling or cleaning TB equipment (5.8%). Hands (28.6%), legs (21.4%), thorax/ribs (15.7%) and arm/shoulder (12.9%) were the most common location of the injury on the body followed by the head (5.7%), back, foot, abdomen/internal organs (4.3% each), nose and neck (1.4% each) with many veterinarians listing more than one location for a single injury (n = 70). Strains/sprains (30.2%) and abrasion/contusion (30.2%) were the most common types of injury reported, followed by open wound/laceration (15.1%), fracture (11.3%), allergy/irritant (5.7%), spinal cord injury, internal injury, and "other" described as a hematoma behind the kneecap (1.9% each). The injuries were most directly caused from being kicked (17.9%) or crushed/pinned by animal (17.9%), pushed/head butted by animal (14.3%), or pinched/crushed by equipment (10.7%) (Table 5.1). To capture the factors contributing to the injury, veterinarians were encouraged to indicate as many contributory factors as needed to describe the incident (n = 104). The main animal behavior factors include unusually aggressive (7.7%) or unusually frightened behavior (7.7%) on the part of the animal. Facility-related factors include inadequate animal restraint (10.6 %) or inappropriate workspace (7.7%). The main weather-related factors include rain (4.8%), and cold temperature (4.8%). The main assistant-related factors include too few (9.6%) or inexperienced (8.7%) help. Personal issues include feeling rushed or in a hurry (7.7%) or overly tired (2.9%) (Table 5.2). The primary animals (n=38) involved with the injury include: beef cow (42.1%), dairy cow (29.0%), beef other (7.9%), beef bull, dairy other (5.3% each), and dairy bull, bison bull, bison cow, and goat (2.6% each).

Table 5.1 : Cause of injury while TB testing livestock in Michigan, 2001.

	N	%
Kicked	10	17.9
Crushed/pinned by animal	10	17.9
Pushed/headbutted	8	14.3
Pinched/crushed by equipment	6	10.7
Needle stick	4	7.1
Lifting/moving equipment	4	7.1
Slip/trip/fall	4	7.1
Lifting/pushing animal	3	5.4
Allergic/irritant*	3	5.4
Repetitive motion	3	5.4

Table 5.1 (cont'd)

Motor vehicle accident	1	1.8
Total	56	

*self injected tuberculin (n=2) hornets (n=1)

Table 5.2 : Factors contributing to risk of injury while TB testing livestock in Michigan, 2001.

	N	%
Animal Behavior		
Unusually aggressive	8	7.7
Unusually frightened	8	7.7
Extremely unpredictable	5	4.8
Unusually protective	1	1.0
Facilities		
Inadequate animal restraint	11	10.6
Table 5.2 (cont'd)		
Inappropriate work space	8	7.7
Poor flooring	6	5.8
Poor lighting	3	2.9
Assistants*		
Too few	10	9.6
Inexperienced	9	8.7
Poor animal handling skills	4	3.8
Unhelpful (poor attitude)	2	1.9
Too many	0	0.0

Table 5.2 (cont'd)

Weather		
Rain	5	4.8
Cold temperature	5	4.8
Hot temperature	3	2.9
Snow	2	1.9
Ice	1	1.0
Personal Issues		
In hurry/felt rushed	8	7.7
Overly tired	3	2.9
Inexperienced	1	1.0
Poor physical condition	1	1.0
Lacked adequate training	0	0.0
Total	104	

*Includes help provided by testing veterinarian and help provided by producer.

Characteristics of Veterinarians

The characteristics of the study population (n = 175) detailed in Table 5.3 include: gender, age, practice type, years of practice, number of hours spent in vehicle each week, number of days worked per week, number of hours worked per week, number of hours of sleep per night, percentage of time spent on-call, self-assessment of health, number of times they exercised per month (defined as brisk aerobic activity lasting 20 minutes or more), tobacco smoking, tobacco chewing, seatbelt use, body mass index (BMI) and percentage of time doing TB work.

Table 5.3 : Characteristics of Study Population – Michigan veterinarians testing five or more livestock herds for TB in 2001.

Characteristic	N	%
Gender	n=75	
Male	141	80.6
Female	34	19.4
Age	n=168	
26-35	27	16.1
36-45	53	31.5
46-55	60	35.7
56-65	22	13.1
>65	6	3.6

Table 5.3 (cont'd)

Practice type	n=175	
Private	160	91.4
Government	14	8.0
Other	1	0.6
Years of Practice	n=175	
<5	21	12.0
5-9	18	10.3
10-19	51	29.1
20-29	48	27.4
30-39	30	17.1
>39	7	4.0
Hours in vehicle/wk	n=175	
0-4	34	19.4
5-9	20	11.4
10-14	45	25.7
15-19	34	19.4
20-24	30	17.1
>24	12	6.9
Days worked per week	n=175	
0-3	1	0.6
4-5	57	32.6
6	99	56.6
7	18	10.3
Hours worked per week	n=175	
0-29	8	4.6
30-49	32	18.3
50-59	58	33.1
60-69	51	29.1
>69	26	14.9

Table 5.3 (cont'd)

Hours sleep per night	n=172	
5	7	4.1
6	32	18.6
7	85	49.4
8	42	24.4
>8	6	3.5
%Time on-Call	n=174	
0-4	34	19.5
5-9	18	10.3
10-19	43	24.7
20-49	42	24.7
50-99	24	13.8
100	12	6.9
Self health assessment	n=169	
Poor	0	0.0
Fair	7	4.1
Good	87	51.5
Excellent	75	44.4
No. times exercise/mo	n=175	
0	48	27.4
1-10	70	40.0
11-20	39	22.3
>20	18	10.3
Smoke	n=175	
No	166	94.9
Yes	9	5.1

Table 5.3 (cont'd)

Chew tobacco	n=175	
No	168	96.0
Yes	7	4.0
Body Mass Index	n=174	
Underweight <18.5	1	0.6
Normal 18.5-24.9	58	33.3
Overweight 25-29.9	77	44.3
Obese >29.9	38	21.8
Seatbelt use while working	n=175	
Always	130	74.3
Usually	33	18.9
Sometimes	5	2.9
Rarely	4	2.3
Never	3	1.7
% Time doing TB work	n=175	
<5%	40	22.9
5-9%	50	28.6
10-19%	40	22.9
20-39%	25	14.3
40-99%	12	6.9
100%	8	4.6

Incidence Density

Overall, 1.9 veterinary injuries were found per each 10,000 animals tested, or 9.3 injuries per 1000 herds tested. To compare the rate of injury between different groups of veterinarians, the incidence density was used to generate a rate ratio (relative risk).

The veterinarians were compared using several different grouping variables including gender, years of practice (<10 years vs. 10 or more years), practice type (private vs. regulatory), hours of work per week (50 or less vs. >50), percentage of time spent doing companion animal work (> 50% vs. 50% or less), percentage of time spent on-call (20% or more vs. <20%), working with assistants (always and usually vs. sometimes, rarely and never), hours of sleep per night (<8 vs. 8 or more), tobacco smoking (users vs. non users) and chewing habits (users vs. non users), seatbelt use (always and usually vs. sometimes, rarely and never), BMI category (obese and overweight vs. normal and underweight) and number of herds tested (<30 vs. 30 or more). Female gender (RR=3.26), having less than 10 years of practice (RR=1.81), being a regulatory veterinarian (RR=4.54), being a smoker (RR=5.97) and working 50 hours or less (RR=1.87) were found to be significantly associated with a higher rate of injury per animal tested. All variables and 95% confidence intervals are shown in Table 5.4. No factors were found to be significantly protective.

Table 5.4 : Veterinary characteristics and associated rate ratios of risk of injury per animal tested (incidence density) by veterinarians TB testing livestock in Michigan, 2001.

Characteristic	N*	# Injuries *	# Animals Tested	Injury Rate/ 10,000 Animals	Rate Ratio	95% Confidence Intervals
All Veterinarians	172	52	269,765	1.93		
Gender						
Female	31	17	34,993	4.86	3.26	**1.83 – 5.82**
Male	141	35	234,772	1.49		

Table 5.4 (cont'd)

Years of Practice						
<10 Years	39	19	65,107	2.918	1.81	**1.03 – 3.18**
10 or greater	136	33	204,658	1.612		
Practice Type						
Regulatory	11	12	17,080	7.026	4.54	**2.38 – 8.68**
Private	160	39	252,235	1.546		
Hours of Work/wk						
50 or less	73	25	89,371	2.80	1.87	**1.08 – 3.22**
> 50	99	27	180,394	1.50		
%Time Spent SA						
>50%	68	8	47,820	1.67	1.10	0.51 – 2.40
50% or less	92	31	204,415	1.52		
% Time on Call						
20% or more	79	30	120,211	2.50	1.68	0.97 – 2.91
<20%	92	22	147,849	1.49		
Work With Assistants						
Always/Usually	91	29	144,888	2.00	1.22	0.71 – 2.09
Sometimes/Rarely/ Never	80	23	122,113	1.88		
Hours Sleep/Night						
<8	123	37	202,981	1.82	0.793	0.44 – 1.45
8 or greater	48	15	65,274	2.30		

*Excluded three veterinarians for whom number of animals tested was missing (one of whom reported an injury).

Bivariate Analysis of Risk Factors

Bivariate analysis of the factors found significant in the incidence density analysis was conducted using χ^2 analysis. Four of the variables (gender, number of hours worked per week, type of practice, and years of practice) were compared to each other, to examine between-risk factor associations (Table 5.5). There was a strong association between the type of practice and hours worked with private practitioners much more likely to work 50 hours or more (61.5%) compared to regulatory veterinarians (7%) (OR = 20.76;CI = 2.72 – 890.81). Another significant association was found between gender and practice type, with a higher percentage of females (57%) in regulatory positions compared to private practice (16%) (OR 6.92; 95% CI 1.90 – 26.00). The association between practice type and years of practice was also found to be significant with a higher percentage of regulatory veterinarians (50%) having less than 10 years of practice experience compared to private practitioners (20%) (OR=4.03; 95% CI 1.11-14.41). Finally, having less than 10 years of practice was significantly associated with the female gender (OR= 3.85; 95% CI 1.93 – 11.18). Gender and number of hours worked per week, and years of experience and number of hours worked per week were not found to be associated.

Table 5.5 : Bivariate analysis of risk factors found to be significant in the incidence density analysis.

Variables			Odds Ratio*	95% Confidence Interval
Practice type by hours worked per week				
	<50 hrs	50 or more hrs		
Government	13	1	**20.76**	**(2.94 – 890.81)†**
Private	62	99		
Practice type by gender				
	Female	Male		
Gov/Regulatory	8	6	**6.92**	**(1.90 – 26.00)†**
Private	26	135		
Practice type by years of practice				
	<10 yrs	10 or more yrs		
Gov/Regulatory	7	7	**4.03**	**(1.11 – 14.41)†**
Private	32	129		
Years of practice by gender				
	Female	Male		
<10 yrs	15	24	**3.85**	**(1.93 – 11.18)**
10 or more yrs	19	141		

Table 5.5 (cont'd)

Hours worked per week by gender

	Female	Male		
<50 Hrs	18	57	1.66	(0.73 – 3.76)
50 or more hrs	16	84		

Hours worked per week by years of practice

	<10 Yrs	10 or more Yrs		
<50 Hrs	18	57	1.19	(0.55 – 2.58)
50 or more hrs	21	79		

*Mantel-Haenszel odds ratio.

† Exact confidence limits used when expected cell size <5.

Stratified Analysis

The final step in the analysis included using χ^2 analysis to examine the relationship between injury (injured yes or no) and gender, stratified by practice type, and the relationship between injury and practice type, stratified by gender. For gender and injury, the crude odds ratio was 2.66 (95% CI 1.07 – 6.58) with women more likely to be injured than men. But, once stratified by stratified by practice type, the odds ratios differed; for private practice OR = 2.87 (CI = 1.02 – 8.01), for regulatory practice OR = 1.6 (CI = 0.15 – 17.02) with women still more likely to be injured, but the association by strata was barely, or no longer statistically significant. The adjusted odds ratio was 2.54 (95% CI 1.01 – 6.53). For practice type and injury, the crude odds ratio was 3.28 (95% CI 0.86 – 11.61) with regulatory veterinarians at higher risk of injury than private practitioners. Stratified by gender, the odds ratios differed; for female regulatory veterinarians the OR = 1.13 (95% CI 0.14 – 7.50), for males regulatory veterinarians the OR = 5.43 (95% CI = 0.67 – 42.59), neither was statistically significant. Because gender is an effect modifier, an adjusted odds ratio was not reported.

A closer look at the gender variable using χ^2 analysis revealed that females were no more likely than males to report major injuries (odds ratio 1.04, p=0.96), but they were more likely to report minor (OR 4.10, p=0.01) and self-treated injuries (OR 2.38, p=0.05).

Mortality

Two mortality events associated with the current TB testing efforts in Michigan occurred. Although not captured by the survey, they bear mentioning as they contribute tremendously to the human cost of the control program. In September, 2000, a 60 year old, male cattle producer was attacked and killed by a Holstein bull as he was separating animals during the course of a routine TB herd test on his farm (Mcclellan, 2000). In September, 2006, a 27 year old female USDA-employed animal health technician was killed in a motor vehicle collision on her way to an early morning TB testing appointment (Judge, personal communication).

DISCUSSION

Large-scale animal disease control and management efforts are necessary and difficult tasks assigned to the U.S. Department of Agriculture and state Departments of Agriculture. The solvency of many agribusinesses depends on the ability to export livestock and livestock products. To maintain or expand export markets, the US must obtain and maintain certain prevalence levels for diseases of international significance, such as bTB. The "costs" for the needed disease control programs are often measured in program expenses (state and/or federal appropriations) or in terms of markets lost or restricted. Prior to 1997, the Michigan Department of Agriculture's bTB eradication efforts were supported by existing departmental resources. From 1997 to January 2001, nearly $29 million in State resources had been newly appropriated; an additional $6 million in federal funds was made available in fiscal year 2000-2001, specifically for the control of bTB in Michigan (Thiel, 2001). A team from Michigan State University estimated the total economic costs of bovine TB to the Michigan livestock industry to be $21.1 million in fiscal year 2000-2001 and then decrease to $17 million in FY 2009-10 (Wolf and Ferris, 2000). Among these large dollar amounts and the inevitable political wrangling, the human cost in terms of injury and death of program-related personnel, can be easily lost.

The direct public health impact of the current bovine TB outbreak in Michigan as previously described (Wilkins et al., 2008) is perceived to have been minimal, with only two outbreak-associated human cases reported. However, the public health impact of a disease includes not only the direct effects of the disease itself but also the health costs associated with the control of the disease. For example, although foot and mouth disease is not a zoonotic, the 2001 outbreak in Great Britain "is considered a human tragedy, not just an animal one" (Mort et al., 2005) and has been blamed, by the media, for several suicides (Champion, 2001; Dennis, 2001; Smith, 2001; Williams, 2001). In the case of bovine TB, the true public health impact of the disease must include the health impact of the control efforts. In this case, the decision to TB test the entire cattle population of

Michigan not only generated a direct economic cost, but also had negative health effects on both veterinary staff and cattle producers. A simplistic comparison of morbidity and mortality events suggests that the control of the disease has had a greater negative impact on human health than did the disease itself (only two human cases). However, it must be remembered that, unlike injuries, bovine TB is a transmissible disease. Left uncontrolled in livestock, the number of human cases could escalate. The direct impact on human health of handling and testing large numbers of cattle is one of the costs that must be considered.

This study's estimate of 1.9 veterinary injuries per each 10,000 animals tested, should be useful to regulatory veterinarians when estimating the total impact of future disease control programs for bTB and perhaps for other diseases that require a similar type of individual animal restraint and handling.

The very high risk ratio for injuries among regulatory vs. private veterinarians is not a surprising finding. Private veterinarians were paid $40.00 per herd visit and $8.00 per head, so private practitioners had a clear financial incentive to test the larger herds. In Michigan, larger herds tend to be dairy herds, which generally have cattle that are more used to being handled and are housed in better working facilities. The smaller herds, primarily beef, were generally left for the regulatory veterinarians. Because of their natural temperament, dairy cows are less dangerous to handle and test than are beef cows and more restraining equipment is generally needed, and less is usually available, to handle beef animals. In addition, only regulatory veterinarians can place a comparative cervical test, which requires firmly restraining the animal's head in order to access the neck.

The bivariate analysis revealed strong associations between several of the factors found to be contributing to the risk of injury in the incidence density analysis. These associations are not surprising. That few regulatory veterinarians work over 50 hours per week is not unexpected, since a 40 hour work week is the standard for government practice. A 40 hour work week likely explains the strong female presence in the regulatory work force, as these positions may offer women the better possibility of a reasonable work/home-life balance than full-time private practice. During the initiation of the state-wide testing effort, both USDA and MDA were hiring veterinarians. These positions would be quite appealing to new graduates (with reasonable hours, good benefits), explaining the high proportion of regulatory veterinarians with less than 10 years experience. Recent hiring would also contribute to the high percentage of female veterinarians, since the classes graduating from Michigan State University, College of Veterinary Medicine have been predominantly female for the last 20 years.

Female gender was significantly associated with an increased *rate* of injury in the incidence density analysis. The association remains significant in the comparison between gender and injury after controlling for the confounder of practice type (adjusted OR = 2.54; CI 1.01 – 6.53), but only barely reaching statistical significance. Further, the association between regulatory practice and injury remained elevated only for males, upon stratification by gender, suggesting gender is an effect modifier in the relationship between practice type and likelihood of sustaining an injury.

Our study included only veterinarians who tested five or more herds in 2001, therefore excluding veterinarians with the least experience with TB-testing. Recall bias may be a factor as the survey instrument was mailed in September of 2002, asking about injuries occurring in 2001. Most major or minor injuries are memorable, but some of the more minor injuries may have been forgotten. Any recall bias, would expectedly have caused a bias toward the underreporting of the self-treated injuries. However, a reporting bias may have occurred in that veterinarians with injuries to report may have been more interested in the study and therefore more likely to return their questionnaire than those who did not have injuries. Lastly, this study was limited to veterinarians and did not include animal health technicians or other farm assistants. Although assistants do not place or read TB tests, they are often responsible for moving the animals and setting up the testing area, which may make them as likely as the veterinarian to be injured. Injuries to non-veterinarians were excluded to better enable determination of an accurate incidence density based upon a definable numerator (injuries) per 10,000 animals tested.

CONCLUSION

The study population reported that 81% of these injuries could have been prevented, generally by slowing down enough to 1) calmly move animals instead of rushing them, 2) properly restrain animals (especially using chutes instead of milking parlors for dairy cattle and restraining even "tame" animals 3) properly maintaining equipment 4) clearing work area of obstacles such as shovels and manure. The U.S.D.A. and state Departments of Agriculture can better control the execution of on-farm testing by developing on-farm standard operating procedures (SOPs) for animal handling/restraint and require their own staff and fee-basis veterinarians to attend annual training and review the SOPs regularly. In addition, regulatory employers should allow herd tests to be scheduled with enough time to focus appropriately on safety and shift the emphasis from herd tests completed, to herd tests completed safely. Ongoing training and monitoring of the safety and health of regulatory staff should be extended to privately employed fee-basis veterinarians as well. This study determined the rate of injuries that can be expected while TB testing livestock per animal tested and per herds tested. Although the relationships are complicated, gender to some degree, and practice type, to a greater degree, are the main risk factors leading to an elevated rate of injury and an elevated likelihood of injury in this setting.

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CHAPTER 6

A COMPARISON OF RISK FACTORS FOR HUMAN EXPOSURE TO *M. TUBERCULOSIS* AND *M. BOVIS* IN NORTHERN MICHIGAN.

ABSTRACT

First recognized in white-tailed deer in 1994, *Mycobacterium bovis* has since been found in 42 Michigan cattle herds and is now considered endemic in the wild white-tailed deer population of the northeastern part of the lower peninsula of Michigan. Numerous additional species have been found infected including: coyotes, raccoons, black bear, red fox, and opossum. Because of the occurrence in wildlife and re-occurrence in cattle, a list of *M. bovis*-specific risk factors for exposure was developed for residents of the geographically affected area. The list includes being hunters, trappers, taxidermists, venison processors, beef /dairy producers or a farm/livestock worker. The health departments covering 12 counties in the northeastern part of the lower peninsula of Michigan participated in this study. A survey was developed which included the list of *M. bovis*-specific exposure risk factors and a list of *M. tuberculosis*-specific exposure risk factors (from CDC). The health departments were asked to complete and attach the survey to each tuberculosis skin test (TST) reporting form, then send the de-identified form to the Michigan Department of Community Health. To measure the associations between each risk factor and the TST results, a relative risk with 95% confidence intervals, or a Fisher's exact test was used. Overall, there were 29 positive TST tests, of 1268 TST records submitted, for a positivity rate of 2.29% (29/1268). Two risk factors were found to be significantly associated with a positive TST, being a venison processor

RR=2.49; p=0.047) and being foreign born (RR=9.36; p=0.019). The positive association found for being foreign born was expected, but the association between having a positive TST and being a venison processor suggests that this population may benefit from increased surveillance efforts and targeted public health prevention messages to raise awareness about the risk of *M. bovis* exposure.

INTRODUCTION

First recognized in a white-tailed deer in 1994, *M. bovis* (bovine TB) has been found in 42 cattle herds and is now considered endemic in the deer population of the northeastern part of the lower peninsula of Michigan. Several other wildlife species (coyotes n=19, raccoons n=8, black bear n=7, bobcat n=4, red fox n=3 and opossum n=2 (Summary of Michigan wildlife bovine tuberculosis surveillance, internet) have also been found infected with the deer/cattle outbreak strain of *M. bovis*. Due to the presence of infected wildlife and cattle in this area, persons with exposure to these animals may be at higher risk of exposure to *M. bovis,* a zoonotic organism with one of the broadest host ranges of all known pathogens (O'Reilly, 1995).

The authors developed a list of Michigan-specific risk factors for residents which includes being a: hunter, trapper, taxidermist, venison processor, beef or dairy producer or farm/livestock worker. According to CDC, persons at higher risk for exposure to or infection with *M. tuberculosis* include: close contacts of persons known or suspected to have TB, foreign-born persons from areas that have a high TB prevalence, residents and employees of high-risk congregate settings, some medically underserved, low-income populations as defined locally, high-risk racial or ethnic minority populations, defined locally as having an increased prevalence of TB, infants, children, and adolescents exposed to adults in high-risk categories, persons who inject illicit drugs; any other locally identified high-risk substance users, health care workers who serve high-risk clients (CDC, 2005).

Data available to the Michigan Department of Community Health (MDCH) does not indicate an increase in the number of human cases of *M. bovis* in Michigan, since 1994 (MDCH unpublished data). When humans are exposed to *M. tuberculosis*, 30-40% of exposed close contacts become infected. If they do not progress to clinical disease, they are considered to have latent TB infection (LTBI) (CDC, 2005). Approximately 5-10% of latently infected individuals will develop active TB disease at some point in their life, with the highest risk within the first two years of infection (CDC, 2005). In humans, disease caused by *M. tuberculosis* is usually a pulmonary presentation, and transmission is usually human-to-human via aerosol droplets. Data about the infection rate for persons exposed to *M. bovis* are not available, but would likely be less because *M. bovis* infection in the US is more likely caused by ingestion of raw dairy products which leads to a gastrointestinal presentation, with human-to-human transmission rare. That said, once an individual is infected with *M. bovis*, the likelihood of progression from latent infection to clinical disease would be similar to that of *M. tuberculosis*.

The most common way to measure the prevalence of LTBI in a population is the use of the Mantoux tuberculosis skin test (TST). A TST will react positively to infection with *M. tuberculosis* or *Mycobacterium* other than tuberculosis (MOTT) (including *M. bovis*). Generally speaking, a tuberculin reaction caused by infection with MOTT tends to be smaller than those elicited by infection with *M. tuberculosis* (Dasco, 1990).

Our objective was to determine if evidence existed to indicate the presence of latent human infections with *M. bovis*. Our plan was to look at TST results in a region of Michigan where *M. bovis* is endemic in the deer population and *M. tb* risk factors are low. If skin tests results were found to be associated with exposure to the known animal reservoirs of *M. bovis*, this would suggest that latent or undiagnosed *M. bovis* infections might be occurring in the Michigan human population.

METHODS

The health departments covering 12 counties in the northeastern part of the lower peninsula of Michigan were asked to participate in this study. A survey was developed and printed on a sticker which was attached to each TST skin test reporting form. Survey questions included a list of exposure risk factors for both *M. bovis* and *M. tuberculosis*. Health department were asked to complete and attach the survey to each TST skin test reporting form. Once the TST was interpreted and the survey completed, the report was de-identified and mailed to MDCH. The 12 counties were in three different local health jurisdictions, District Health Department No. 2 (Alcona, Iosco, Ogemaw, Oscoda counties), District Health Department # 4 (Alpena, Cheboygan, Montmorency, Presque Isle counties), and Northwest Michigan Community Health Agency (Antrim, Charlevoix, Emmet, Otsego counties). The population of this area is approximately 256,548 (2000 Census) and the largest population center is Alpena (population 10,364). The study began October 1, 2001 and continued through December, 2003. Each county began participation at slightly different times, and continued participation for various lengths of time. To better ensure comparability, and to avoid counting individuals more than once, no more than 12 consecutive months of data was used from each county. The time period for collection ranged from 9 to 12 months per county.

To measure the associations between each risk factor and TST results, the relative risk with 95% confidence intervals, or Fisher exact test (when an expected cell size < 5), was used to measure the strength and statistical significance of the association (EpiInfo 6.04, CDC, Atlanta).

TST Interpretation

Interpretation of the Mantoux TST is based on the size (in mm) of induration measured at 48-72 hours post intradermal injection of 0.1 mm of tuberculin purified protein derivative (PPD). Classification of the TST reaction is based on categories of potential risk factors for exposure to *M. tuberculosis* (CDC, 2005) with cut-offs of 5mm, 10 mm and 15 mm used, depending on the risk factors of exposure. Although the TST report usually included the measurement of induration for reactive TSTs, the researchers did not have sufficient information to categorize each reactor. Therefore, the interpretation (positive or negative) rendered by the public health nurse completing the report was used in this study.

RESULTS

The number of completed TST records submitted to MDCH with the number of months of participation for each local health jurisdiction is included in Table 6.1. Overall, there were 29 positive TST reactors out of 1268 TST records, for a positivity rate of 2.29% (29/1268).

Table 6.1 : The time period of participation and number of completed TST records received from each local health jurisdiction.

Local Health Jurisdiction	Number of Months of Participation	No. Completed TB Skin Test Reports Submitted	No. of Positive TB skin Tests	% Positive TB Skin Tests
Health District # 2	12.0	250	6	2.4
Health District # 4	10.7	541	8	1.5
NW Michigan Community Health Agency	10.8	477	15	3.1
Total		1268	29	2.3

For Health District # 4, risk factor data for exposure to *M. tuberculosis* was missing from 130 records and risk factor data for exposure to *M. bovis* was missing from 34 records. These records were excluded from the risk factor analysis. Relative risk results for each exposure risk factor are found in Table 6.2.

Table 6.2 : Comparison of tuberculosis skin test results by *M. bovis* and *M. tuberculosis* exposure risk factors using relative risk analysis.

	No. Positive TST Results	No. Negative TST Results	Relative Risk (with 95% CI)	F. E. pvalue
Risk Factors for *M. Bovis*				
Hunter				
Yes	9	288	1.43	
No	20	925	(0.66-3.11)	
Trapper				
Yes	0	18	N/A	
No	29	1195		
Taxidermist				
Yes	0	2	N/A	
No	29	1211		
Venison Processor				
Yes	5	91	2.49	**0.047***
No	24	1122		
Beef or Dairy Producer				
Yes	2	29	2.89	0.128*
No	27	1884		
Farm/Livestock Worker				
Yes	2	35	2.41	0.161*
No	27	1178		
Risk Factors for *M. tuberculosis*				
Contact with known or suspected case				
Yes	0	42	N/A	N/A
No	29	1075		

Table 6.2 (cont'd)

Live or work in a congregate setting				
Yes	11	295	1.66	
No	18	814	(0.73 – 3.48)	
Health care worker				
Yes	2	200	0.343	0.064*
No	27	909		
Foreign born				
Yes	2†	7	9.358	**0.019***
No	27	1110		

*Fisher's exact p-value used because of small cell size

†Both from Taiwan

DISCUSSION

The overall rate of TST positivity for this study was 2.3%, lower than the 3.3% to 5.2% rate expected based on an estimate of 9.6 – 14.9 million persons residing in the US with latent tuberculosis infection (Bennett, 2003) divided by the estimated US population of 285,125,973 (July 2002, US Census data http://www.census.gov/popest/states/tables/NST-EST2006-01.xls). This area of Michigan is very homogenous with little racial or ethnic diversity. African Americans make up a small percentage the population in these 12 northern counties, 0.3 - 0.7% compared to 14.3% for the state of Michigan as a whole, and 12.3% for the US. Likewise, persons of Latino or Hispanic origin comprise only 0.6-1.4% of the 12 county population, versus 3.8% of Michigan's population and 14.4% of the US population. Foreign-born persons are underrepresented with 1.2 - 1.7% of the 12 county population compared to 5.3% for Michigan, and 11.1% of the US (US Census Bureau, 2005). This area was chosen because of the presence of *M. bovis* in the deer and cattle population, but also because it lacks several of the exposure risk factors for *M. tuberculosis* (such as high rates of illicit drug use, foreign born persons, persons known or suspected to have TB, and high-risk racial or ethnic minority populations) that drive the TST rates in more diverse and urban settings.

We do know that hunters are being exposed to *M. bovis* by handling infected deer carcasses. Based on a 2001 survey of 1,833 hunters who had successfully harvested deer in or near Michigan's endemic area, it was determined that 89% of hunters field dressed their own deer, and only 43% of them wore gloves when doing so. Based on the 2001 prevalence estimate in the deer population and the survey results, up to 139 hunters in the endemic counties may have field dressed positive deer without wearing gloves and up to 12 hunters would cut themselves while field dressing these positive deer (Wilkins, 2003). Another recent paper (Wilkins, 2008) reported two human cases of *M. bovis* with molecular and epidemiologic links to the outbreak in deer and cattle, with one hunter infected after cutting himself as he opened the chest cavity of an infected deer. Abattoir workers have been infected during the processing of cattle (Robinson, 1988; Cousins, 1999; Georghiou, 1989), and cervidae have been documented as the source of *M. bovis* infection for humans with infection resulting from exposure to live elk and the processing of cervidae carcasses (Fanning, 1991). Cutaneous infections can resolve without treatment, but the infected individuals would respond positively to a TST.

Our study results showed an expected association between TST positivity and being foreign born (and likely exposed, vaccinated with BCG, or both) (RR=9.36;

p=0.019). However, the statistically significant association between being a venison processor (RR= 2.49, p=0.047) and TST positivity is new, but perhaps not unexpected. In addition, the risk was found to be elevated if the individual was a beef or dairy producer (RR= 2.89; p=0.128), or a livestock worker (RR=2.41; p=0.161) although these finding were not statistically significant. Four of the five TST positive venison processors were also hunters, as was one of the two beef or dairy producers and one of the two farm/livestock workers, so their exposure, if it was to *M. bovis*, could have been recreationally associated with hunting.

Primary inoculation tuberculosis is rare in developed countries where tuberculosis has been largely controlled in cattle populations. However, before state and federal efforts to control the disease in cattle, it was much more prevalent and known as "butcher's wart" (Kakakhel, 1989). Venison processed in a licensed food establishment or processed for retail sale is regulated by the Michigan Department of Agriculture (MDA). According to the MDA, less than 20% of all Michigan hunter-harvested venison is processed under state regulation (MDA, Food and Dairy Division, 1989).

These findings suggest that venison processors and anyone working with cattle in the endemic area may benefit from targeted public health prevention messages to reduce likelihood of exposure. Persons in these (potential) risk categories should also be encouraged to receive an annual TST to enable the earliest possible detection of infection. Latent infection with *M. tuberculosis* is 90% curable, that is, the likelihood of progressing from latent infection to clinical disease decreased from 10% to 1% following treatment (Centers for Disease Control and Prevention, 2000). It would be reasonable to assume the cure rate for latent *M. bovis* infection would be similar.

There are several limitations in this study, the first being the TST itself. There is variability in the administration of the test, interpretation of the test and among individual immune reactions to the test. There are problems with false positive and false negative reactions, and it does not differentiate between infection with *M. tuberculosis* and *M. bovis*. This study focused on TSTs conducted by local health departments and did not include TSTs performed in the private setting. Our study results represent approximately 25% of the TB testing occurring in this area on an annual basis (unpublished data, M. Gallego, Michigan State University, 2007), thus limiting our ability to generalize the results. The relatively small number of positive results (n=29) makes it difficult to accurately measure associations.

Also of concern is that the interpretation of the TST is based strictly on exposure to, and infection with, *M. tuberculosis*. Infection with *M. bovis* (MOTT) would be expected to elicit a smaller reaction than one caused by infection with *M. tuberculosis* because PPD is mixture of antigens derived from *M. tuberculosis* (Dasco, 1990). An individual with only *M. bovis* exposure risk factors would only be considered positive if their TST induration were 15 mm or greater, thus many latent cases of *M. bovis* infection may be missed using the current CDC TST interpretation guidelines. In fact, the only reported case of cutaneous tuberculosis caused by *M. bovis* related to the current outbreak had an initial negative TST followed by a 6mm reaction 14 weeks post exposure (MDCH unpublished data).

CONCLUSION

It is safe to say that basic public health advice including the use of gloves when field-dressing deer and the thorough cooking of venison, should continue to be offered to all residents of the *M. bovis* endemic area, with an extra effort to reach hunters and venison processors. In addition, people exposed to deer or cattle should be advised to receive annual TSTs. Targeted surveillance of venison processors should be considered, using the TST and the newly available Quantiferon-gold blood (to help distinguish between latent infection with *M. tuberculosis* vs. other mycobacteriae) to better delineate the unique risk factors for exposure in this population of Michigan. In addition, MDCH (in conjunction with the Centers for Disease Control and Prevention) should strongly consider adding *M. bovis*-specific risk factors to the TST interpretation guidelines for areas in which *M. bovis* is present in animal populations.

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CONCLUSION

The purpose of this dissertation is to clarify the human health effects of the bovine TB outbreak on Michigan residents. Each of five projects addressed an area of risk to human health and used methodologies best suited to address that particular issue. The studies characterized the risks in greater detail than what was previously available. As with most field research, each study suffered from limitations typically encountered when working in the "real" world. Several new hypotheses were generated, ideas for further studies proposed and public health prevention recommendations produced.

The Hunter Health Survey (Chapter 2) characterized the self-protective behaviors practiced by 1,833 hunters in the northeastern corner of the Michigan's lower peninsula. Because hunters could be exposed to *M. bovis* via the cutaneous or the gastrointestinal routes, the survey focused on hand washing and glove use practices, as well as cooking and venison consumption practices. The likelihood of foodborne exposure to *M. bovis* was found to be remote. However, exposure via the cutaneous route was found to be not only possible, but expected at the rate of 12-13 cases per year. This conclusion was supported by the documentation of the first cutaneous infection in a Michigan hunter in 2004. Based on the findings of this study, the Michigan Department of Natural Resources Annual Hunting and Trapping Guide now encourages hunters to wear gloves when dressing venison and to cook all game meat thoroughly.

Michigan residents diagnosed with *M. bovis* infection from 1994-2007 are described in the second project (Chapter 3). Two of these patients were infected with the genetically identical strain of *M. bovis* circulating in the deer and cattle populations involved in the current outbreak in Michigan. The exposure history and clinical course of these two patients are described in detail. The 2004 patient diagnosed with cutaneous *M. bovis* infection was indisputably infected via exposure to an infected deer, with the deer's lesion and the hunter's wound yielding isolates with matching genotypic patterns. The patient diagnosed in 2002 yielded the same strain of *M. bovis*, from a pulmonary sample, which genotypically matched the endemic strain in both deer and cattle in Michigan. *M. bovis* was identified *post mortem* on this patient, who had a number of potential routes of exposure to *M. bovis*, including hunting, residence on the edge of the epicenter of the outbreak (Deer Management Unit 452), drinking raw milk in the 1930's and close contact with a family member with TB (60 yrs prior). Although his route of exposure will never be definitively explained, the fact that his isolate matched the pattern of the outbreak strain provides strong epidemiologic evidence of a recent exposure to an infected animal (most likely deer) in Michigan. That his exposure history yielded no "smoking gun" raises the possibility that additional and/or unexplored routes of exposure may exist.

The pet study (Chapter 4) evaluated 23 dogs and cats residing on farms with *M. bovis* infected cattle. For 21 of the pets, only non-invasive methods were used to assess their health and TB infection status. Two cats underwent full necropsy. All results were negative for evidence of *M. bovis* infection. Three cats tested positive for *M. avium* at the 1:160 dilution, of which two also tested positive for *M. bovis* at less than the 1:160 dilution. These results were therefore interpreted to be cross-reactions with *M. avium*. In addition, three rectal swabs from these animals yielded positive cultures for *M. avium* or *Mycobacterium* species (Group IV unclassified), suggesting that the non-invasive protocol would likely have produced positive results if *M. bovis* was actively being shed in feces at the time of the study. These negative findings were not surprising, given that the average number of months these pets were exposed to infected cattle was only 2.3 months for cats and 4 months for dogs. In addition, the cattle herds in Michigan were not heavily infected (few lesions per cow and a small number of cows per herd), the herds were diagnosed very quickly, depopulation also took place quickly, and only two of the farms were dairies, where raw milk was fed to pets. In Michigan, under the current intensive bovine TB testing protocols for cattle, pets do not appear to play any role in perpetuating *M. bovis* infection on cattle farms, nor do they appear to pose significant risk to their owners. However, the fact that a semi-feral cat living in the endemic area was diagnosed with advanced *M. bovis* disease in 2000 reminds us that cats certainly have the potential to pose an exposure risk to the humans with whom they interact. In light of MDA's decisions to not depopulate domestic pets on infected farms along with the removal of cattle, a list of recommendations for farm owners with pets was generated to keep the risk to a minimum.

Fifty-three injuries were reported among 175 veterinarians TB testing livestock in 2002 (Chapter 5). Veterinarians reported that animal behavior, poor working facilities, weather, lack of availability and inexperience of assistants and personal issues all contributed to the risk of injury. Over 80% of these injuries were reported to have been preventable by slowing down enough to calmly move animals instead of rushing them, properly restraining animals, properly maintaining equipment and clearing the work area of obstacles. The estimated rate of injury (1.9/10,000 animals tested) should be useful to regulatory agencies planning any large scale animal disease control efforts that require individual animal restraint. Two human deaths associated with the bovine TB control effort in Michigan are also described. This project was important to elucidate the "human costs" of animal disease control efforts, an issue easily overshadowed by financial and political costs.

Exposure to risk factors for both *M. tuberculosis* and *M. bovis* were collected for 1,268 persons receiving tuberculosis skin test (TST) in the 12 counties of northern Michigan. The TB skin test (TST) project (Chapter 6) yielded a background positivity rate of 2.3% for the participating counties, which is well below the national estimate of 5-10%. This low rate is expected, as the national TB rates are driven by two high-risk populations, neither of whom are highly represented in the counties of northeastern Michigan; homeless persons (with a history of injection drug use and or alcohol abuse) and foreign born persons, primarily from Asia. Being foreign born and being a venison processor were the two exposure risk factors proving to be a significantly associated with a positive TST reaction. These results indicate that venison processors may be at elevated risk of exposure to *M. bovis*, and would therefore benefit from targeted *M. bovis* prevention information. Although the TST is a crude measure, which includes reactions to both *M. tuberculosis* and *M. bovis* exposure, it none-the-less provides a starting point for monitoring long-term trends in this rural, relatively homogenous population of Michigan.

Based on the work presented in this dissertation, recommendations were generated to decrease the risk of exposure to *M. bovis*, and to reduce injuries associated with the bovine TB control efforts in Michigan. Several of these recommendations have already been adopted by appropriate regulatory agencies.

- Develop educational materials specific for venison processors.

- Develop educational material targeting hunters.
- Develop educational materials for physicians regarding the clinical presentation of cutaneous *M. bovis* infections so that early and accurate diagnoses can be made.
- Continue to offer training to health care professionals on the proper administration and interpretation of the TST .
- Owners of cattle infected with bovine TB should be counseled by both human and animal health officials that *M. bovis* is a zoonotic organism and that precautions can be taken to avoid infection.
- Initial two-step tuberculosis skin tests, followed by an annual skin test should be recommended for all veterinarians, livestock owners whose cattle have tested positive, hunters, taxidermists and trappers.
- The USDA and The Michigan Department of Agriculture should develop on-farm standard operating procedures for animal handling/restraint with a focus on the safety of the animal handlers.

The strength of these studies is their timeliness, as the questions about human health risks only become more pressing as the bovine TB outbreak in Michigan continues. A similar outbreak in Minnesota was detected in 2005. Each study had its own limitations, which are addressed in detail within each chapter. The shortcoming present in almost all studies was small sample size, which affected the study regarding bovine TB farms with pets, TST positive reactors, injuries and human cases of *M. bovis* infection. Another limitation common to several studies is the ability to generalize the results beyond the geographic area currently experiencing the *M. bovis* outbreak in wildlife and cattle in Michigan.

Several scientific advances could dramatically alter the quality of data available for assessing human health risk from *M. bovis,* including the availability of better *in vivo* tests for *M. bovis* in pets (under development), and the increased use of the interferon-gamma test (QuantiFERON-TB Gold®) to detect *M. tuberculosis* in humans, which could help research efforts if used in series with the TST. Changes in the pattern of disease in both cattle and wildlife, or changes in disease control efforts, would also change the routes and frequency of human exposure to *M. bovis.* Public health prevention messages should be developed, delivered, and then their impact should be measured as a continuation of the work presented in this dissertation.

APPENDICES

APPENDIX A

DEER HUNTER HEALTH SURVEY

M-222
99999-1422

MICHIGAN DEPARTMENT OF NATURAL RESOURCES, WILDLIFE DIVISION
PO BOX 30030 LANSING MI 48909-7530

DEER HUNTER HEALTH SURVEY

This information is requested under authority of Part 435, 1994 PA 451, M.C.L. 324.43539.

Attn. Wildlife Surveys: 99999-1422

99999-1422-011022-5

MELINDA WILKINS
2111 HOLLY WAY
LANSING MI 48910

Please fill in the blank, or mark the box next to your answer for each question.

1. **How old were you when you started hunting deer?** _______ years old

2. **Since your first deer hunt, how often have you hunted deer?**
   - 1 ☐ Every year 2 ☐ Almost every year 3 ☐ Every other year
   - 4 ☐ Every 3 to 5 years 5 ☐ Every 6 to 10 years 6 ☐ More than 10 years between hunts

3. **Last year (in 2000), did you field dress a deer?** 1 ☐ Yes 2 ☐ No *(If "No", skip to #4)*
   - A. How many deer did you field dress last year? _______ deer
   - B. Did you wear rubber or latex gloves when field-dressing deer last year? 1 ☐ Yes 2 ☐ No 3 ☐ Unsure
   - C. Did you cut yourself (enough to draw blood) while field dressing deer last year? 1 ☐ Yes 2 ☐ No 3 ☐ Unsure
   - D. How many hours passed between field dressing deer and washing your hands last year? _______ hours

4. ***Did the person who field dressed your deer in 2000 wear rubber or latex gloves while field dressing?*** *(Skip this question if you field dressed your own deer last year)* 1 ☐ Yes 2 ☐ No 3 ☐ Unsure

5. **Did you eat any venison from deer killed in 2000?** 1 ☐ Yes 2 ☐ No *(If "No", skip to # 6)*
   - A. Did you eat any smoked venison made from deer killed last year? 1 ☐ Yes 2 ☐ No 3 ☐ Unsure
   - B. Did you eat venison jerky made from deer killed last year? 1 ☐ Yes 2 ☐ No 3 ☐ Unsure
   - C. Did you eat venison sausage made from deer killed last year? 1 ☐ Yes 2 ☐ No 3 ☐ Unsure
   - D. Was the venison from last year's deer cooked until it was no longer pink and the juices ran clear?
     - 1 ☐ Never 2 ☐ Sometimes 3 ☐ Usually 4 ☐ Always

PR2057-5 (Rev. 09/27/2001)

Questions continue on reverse side.

6. How well informed are you about the Bovine TB problem in white-tailed deer in northeastern Michigan?

1 ☐ Was not aware of a problem

2 ☐ Somewhat informed (aware of the problem)

3 ☐ Informed (understand the scope of the problem, types of animals involved, efforts to control outbreak)

4 ☐ Very informed (avidly follow the issue and keep up-to-date on new findings and control efforts)

7. For deer hunters in general, do you think the Bovine TB problem in Michigan's white-tailed deer is a public health threat?

1 ☐ No threat 2 ☐ Small threat 3 ☐ Medium threat 4 ☐ Big threat 5 ☐ Was not aware of a problem

8. Do you feel that your personal health is at risk because of the Bovine TB problem in white-tailed deer in northeastern Michigan?

1 ☐ No risk 2 ☐ Small risk 3 ☐ Medium risk 4 ☐ Big risk 5 ☐ Was not aware of a problem

9. Have you ever discussed the possibility of catching Bovine TB with a health professional? 1 ☐ Yes 2 ☐ No

10. Have you ever had a TB skin test? 1 ☐ Yes 2 ☐ No 3 ☐ Unsure

A. Have you ever been tested <u>because</u> of your health concerns about catching Bovine TB? 1 ☐ Yes 2 ☐ No

11. From where would you like to receive information about personal health considerations related to Bovine TB? *(Check as many as apply)*

1 ☐ I do not wish to receive health information

2 ☐ Hunting association newsletters

3 ☐ DNR's Hunting and Trapping Guide

4 ☐ Hunting/Outdoor sports magazines

5 ☐ DNR's web page

6 ☐ Hunting/ Outdoor sports TV programs

7 ☐ Bovine TB web page

8 ☐ Other sources – Please list:

____

____

____

Please place the completed survey in the postage-paid return envelope and drop it in the mail. Thank you for your help!

APPENDIX B

INJURY SURVEY TOOLS

VETERINARY INJURY SURVEY – BASIC INFORMATION SHEET
(One per vet whether or not you were injured in 2001)
(Reformatted for Dissertation)

Please fill in the blank, or mark the box next to your answer for each question.

General Information

1. **Year of Birth __ __ __ __** 2. **Gender** ☐ Male ☐ Female
3. **Year of graduation from Veterinary School _______.**
4. **No. of years "working with or handling" large animals (including equine) prior to vet school** ___yrs
5. **How many years have you been practicing veterinary medicine?** ___yrs

Work Information for 2001 Only (Approximates are fine)

6. **In what type of practice were you primarily employed during 2001?**
   - ☐ Private clinical practice
   - ☐ Government/Regulatory
   - ☐ College/University
   - ☐ Other (please specify) ______________________________
7. **How many hours per week did you spend in a work related vehicle (driving or riding)?** ____hrs
8. **How many days per week did you usually work?** ____days
9. **How many hours per week did you usually work?** ____hrs
10. **How many hours of sleep did you get per night during your average work week?** ____hrs
11. **What percentage of your work time was spent on emergencies coverage (being on call)?** ____%
12. **What percentage of your work time was spent doing TB-related work?** ____%

Health Information for 2001

13. **How many times/month did you participate in aerobic activity lasting 20 min or more?** ____/mo (examples - jogging, brisk walking, playing sports, working out, aerobics, swimming, biking)
14. **What was your body weight and height in 2001?**
    ____(lbs) ___ft ___in
15. **How would you rate your overall health in 2001?**
    ☐ Excellent ☐ Good ☐ Fair ☐ Poor
16. **When working, how often do you wear your seatbelt?**
    ☐ Always ☐ Usually ☐ Sometimes ☐ Rarely ☐ Never
17. **Did you regularly smoke?** ☐ Yes ☐ No **or regularly chew tobacco?** ☐ Yes ☐ No

Practice Information for 2001

18. **Please indicate the percentage of time you spent working on each species (totaling 100%).**

____ Beef	____ Captive cervidae	____ Dogs and cats
____ Dairy	____ Swine	____ Avian, reptiles, pocket pets
____ Equine	____ Small ruminants	____ Wildlife (excluding captive cervidae)

____ Other ____

19. **When TB testing livestock or cervidae, how often did you have technical or lay personnel available to assist you?**

□ Always □ Usually □ Sometimes □ Rarely □ Never

20. **When TB testing livestock or cervidae in 2001, how often did you provide the restraint equipment (chute, gates or panels)?**

□ Always □ Usually □ Sometimes □ Rarely □ Never

Injuries in 2001

The definition of **INJURY** is: --"an acute traumatic event occurring as a result of TB testing activities either on a client's or employers premises, or during TB work-related driving activities that resulted in:

- Restriction of normal activities for at least four hours; **and/or**
- Loss of consciousness, loss of awareness or amnesia for any length of time; **and/or**
- The use of medical assistance (includes, suturing, antibiotics, splinting, x-rays, surgery, and physical therapy whether obtained from others or yourself).

This definition includes injuries associated with any TB-related work activities such as interacting with animals, clients or staff, preparing for TB test administration or reading, administering or reading TB skin tests, clean-up and disassembly of testing equipment, administrative functions, and travel as part of your TB-related work. Both intentional and unintentional events (animal-inflicted or self-inflicted) are included in this definition.
It includes but is not limited to such injuries as:

- Bites, laceration, fractures, sprains, strains, skin punctures;
- Allergic reactions, including asthma and dermatitis;
- Ergonomic and repetitive motion injuries

20. **Did you sustain at least one injury associated with TB testing livestock or captive cervidae in Michigan during calendar year 2001 according to the definition given above?**

□ Yes - Please complete one or more of the attached sheets, starting with Injury Data Collection Sheet No. 1 for your most severe injury. Please return this page and the data collection sheets in the postage paid envelope provided.

□ No - Please return this page in the self-addressed postage paid envelope provided.

Drawing
By completing and returning this page of the survey, you will be entered into the drawing for a Michigan State University, College of Veterinary Medicine sweatshirt. If you answered yes to Question No. 20 above, please fill out the appropriate number of Injury Data Collection Sheets and return these as well.

If you win one of the five sweatshirts, what size would you prefer? Adult sizes: □ Small □ Medium □ Large □ X Large □ XX Large

Thank you so much for your cooperation!

Injury Data Collection Sheet No. 1
(For your most severe injury in 2001)

Please fill out both sides for each injury sustained while TB testing livestock or cervidae in 2001. "TB testing" includes placing the skin test (caudal fold, single cervical, or comparative cervical) and reading the test as well as any blood collection for TB testing. If you sustained more than 4 injuries in 2001, please complete the data collection sheets for your four most severe injuries, starting with Sheet No. 1 for the most severe injury.

1. **Month in which injury occurred** _____________, 2001

2. **Severity of Injury**
   - ☐ Major - required immediate treatment (hospitalization, outpatient visit to emergency room urgent care center, within 4 hours of incident)
   - ☐ Minor - required non-immediate treatment for the injury from physician or human health professional within 7 days following the injury
   - ☐ Self treated - please specify treatment (such as simple first aid, antibiotics, suturing, reduction of fracture) by self or veterinary staff ________________________

   ____

3. **Number of days (or hours) of work time lost because of this injury**
   ____ days **or** ____hours

4. **When in the course of the farm visit, did the injury take place? (Please check only one)**
   - ☐ Traveling to a TB testing (or reading) appointment
   - ☐ While preparing for or setting up equipment for TB testing (or reading)
   - ☐ While placing (or reading) TB tests
   - ☐ While disassembling or cleaning TB testing equipment
   - ☐ Filling out TB test charts (on farm or in vehicle)
   - ☐ Traveling from a TB testing (or reading) appointment
   - ☐ Other – please comment ____

5. **Were other people working with you at the time of the injury?**

a. Veterinarians, besides yourself?	☐ No ☐ Yes -- **If yes, how many?** ____
b. Animal health technicians or your own hired help?	☐ No ☐ Yes -- **If yes, how many?** ___
c. Animal owner	☐ No ☐ Yes
d. Laborers provided by herd owner (family members, farm help, neighbors)	☐ No ☐ Yes -- **If yes, how many?** ___

6. Location of Injury on Body (please indicate primary site with a "1" and secondary sites with "2's")	**7. Type of Injury** (please check the best answer)	**8. Cause of Injury** (please check the best answer)
□ Eyes	□ Fracture	□ Needle stick
□ Nose	□ Traumatic head injury	□ Lifting or pushing animal
□ Teeth	□ Spinal cord injury	□ Kicked by animal
□ Head (other)	□ Dislocation	□ Bitten by animal
□ Neck	□ Strain/sprain	□ Pushed/headbutted animal
□ Arm/shoulder	□ Internal injury	□ Fallen on by animal
□ Hand	□ Open wound/laceration	□ Crushed/pinned by animal
□ Leg	□ Abrasion/contusion	□ Lifting or moving equipment
□ Foot	□ Burn	□ Pinched/crushed by equipment
□ Back	□ Toxic exposure	□ Motor vehicle accident
□Thorax including ribs	□ Allergy/Irritant	□ Allergic to/Irritated by:
□ Abdomen/internal organs	□ Slip/trip/fall	____________________
□ Genitalia	□ Other _____________	□ Other _____________
□ Other________________		

9. **Was the injury caused by direct contact with an animal?** □Yes□ No **(If "no" skip to #11)**

10. **What kind of animal was involved?**

Dairy	□ Cow	□ Bull	□ Other	□ Don't know or remember
Beef	□ Cow	□ Bull	□ Other	□ Don't know or remember
Bison	□ Cow	□ Bull	□ Other	□ Don't know or remember
Elk	□ Cow	□ Bull	□ Other	□ Don't know or remember
Deer	□ Doe	□ Buck	□ Other	□ Don't know or remember
Small Ruminants		□ Goat	□ Sheep	

Other ____

11. **Was the injury caused by equipment (use or failure)?** □Yes □ No **(If "no" skip to #13)**

12. **Please briefly describe the type of equipment involved and what happened to cause the injury.**

____

____

13. **In your opinion which of the following factors contributed to your injury? (Mark as many factors as apply to this incident)**

Animal Behavior
- □ Unusually aggressive
- □ Unusually frightened
- □ Extremely unpredictable
- □ Unusually protective

Facilities
- □ Poor flooring
- □ Poor lighting
- □ Inadequate animal restraint
- □ Inappropriate work space (cramped, couldn't reach animal)

Weather
- □ Rain
- □ Snow
- □ Ice
- □ Cold Temp
- □ Hot Temp

Vet Techs or Hired Help
- □ Too few
- □ Too many
- □ Inexperienced
- □ Unhelpful (poor attitude)
- □ Poor animal handling skills (spooked/rushed the animals)

Farm Help
- □ Too little
- □ Too much
- □ Inexperienced
- □ Unhelpful (poor attitude)
- □ Poor animal handling skills (spooked/rushed the animals)

Personal Issues
- □ Overly tired
- □ Inexperienced
- □ You were in a hurry or felt rushed
- □ You lacked adequate training
- □ Your poor physical condition

Other factors contributing to the injury incident________________________________

14. **Was this the re-aggravation of a previous injury?** □ No □ Yes

15. **In your opinion, could this injury have been prevented?** □ No □ Yes
    If yes, how?

____

____

16. Optional – **In your own words, briefly describe the circumstances leading to the injury and the injury itself:**

____

____

____

Thank You!