TUBERCULOSIS IN SOUTH AFRICAN WILDLIFE: WHY IS IT IMPORTANT?

Prof Michele A. Miller

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Prof Michele A. Miller
Department of Biomedical Sciences
Faculty of Medicine and Health Sciences
Stellenbosch University

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BIOGRAPHY

Professor Michele Miller grew up in Wisconsin, United States of America (USA) and completed her MS and PhD in Veterinary Sciences-Immunology degrees, and a Doctor of Veterinary Medicine degree, at the University of Wisconsin-Madison. She did her postdoctoral training at the San Diego Zoo, investigating immunology and diseases of wildlife. Michele then went on to work as a clinician in several large zoos in the USA, including being a veterinary manager at Disney's Animal Kingdom for 12 years. During this time, she also obtained a Master of Public Health (MPH) degree from the University of Florida-Gainesville. Michele's interest in veterinary research first brought her to South Africa in the early 2000s to collaborate on projects in the Kruger National Park. This led to additional partnerships with Professor Paul van Helden and his team. In 2014, Michele started her full-time position as the National Research Foundation South African Research Chair in Animal Tuberculosis at Stellenbosch University, while being based in the Kruger National Park. Along with Doctor Sven Parsons, they lead the Animal TB Research Group, which utilises a 'One Health' approach to investigating the diversity of mycobacterial infections and consequences of disease, especially in South African wildlife.

Michele is active in international conservation projects in Africa, Asia and Latin America. She is past president of the American Association of Zoo Veterinarians, current veterinary advisor for hippos, rhinoceros and elephants for the USA Association of Zoos and Aquariums, TB scientific advisory subcommittee member for the United States Animal Health Association and new Chair of the Wildlife TB Study Group in South Africa.

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INTRODUCTION

Tuberculosis (TB) is an ancient disease affecting both people and animals. Evidence of TB has been documented in bones from prehistoric mastodons (Johnson, 2006). The earliest records describing animal TB suggest that Indian (Asian) elephants were infected prior to 2 000 BC (Manchester, 1984). The spread of this species as far as modern-day Turkey may have led to the introduction of TB into species such as goats and cattle, which were domesticated between 8 000 and 7 700 BC in the Middle East. TB was present throughout Europe by Medieval times, and the disease in cattle appeared to be associated with the growing dairy industry by the 15th century. As European settlers migrated to South Africa, they brought their cattle and introduced bovine TB along with the animals. The first recorded case of TB in cattle in South Africa was in 1880. With ongoing importations of livestock from Europe (predominantly the United Kingdom [UK]), Australia and South America during the 19th and early 20th centuries, there were probably multiple introductions of this alien disease into the country. The advent of TB testing for imported cattle resulted in the destruction of infected imported cattle and recognition of the significance of the disease. In 1911, South Africa declared bovine TB as one of the first notifiable livestock diseases (DAFF, 2013).

TB IN SOUTH AFRICAN WILDLIFE

The first South African wildlife cases of bovine TB were reported in a greater kudu and a common duiker in the Eastern Cape in 1928 (Renwick et al., 2007). Due to the concern about animal and public health, the Bovine Tuberculosis Eradication Scheme for cattle was implemented in South Africa in 1969 (DAFF, 2013). Although not considered a significant issue at the time, sporadic cases of bovine TB continued to be found in wildlife, with the first case in the Kruger National Park identified in an impala in 1967. Despite the successful reduction in bovine TB in cattle in South Africa to a prevalence of 0.04% by the early 1990s, a new threat was recognised in wildlife with the report of the disease in African buffalo herds in the southern Kruger National Park in 1990 (DAFF, 2013; Renwick et al., 2007). Introduction of *Mycobacterium bovis*, the causative agent of bovine TB, was suspected to have occurred through transmission between infected domestic cattle living on the border of the park and buffalo (Michel et al., 2006). The spread of bovine TB to additional species was documented in the Kruger National Park from the early 1990s. These species included lions, cheetahs, greater kudu, baboons, leopards, warthogs and banded mongooses (De Vos et al, 2001; Renwick et al., 2007).

In Hluhluwe-iMfolozi Game Reserve in KwaZulu-Natal, a similar spread of the disease to wildlife was recorded. The first case of bovine TB was diagnosed in a black rhinoceros in 1970. Buffalo were found to be infected in 1986 with increased spread among herds (Michel et al., 2006). Lions, greater kudu and bushpigs have also been shown to be infected since the 1990s. Additional TB cases in wildlife have been diagnosed on private farms and game reserves in South Africa (LM deKlerk-Lorist, personal Communication April, 21, 2015).

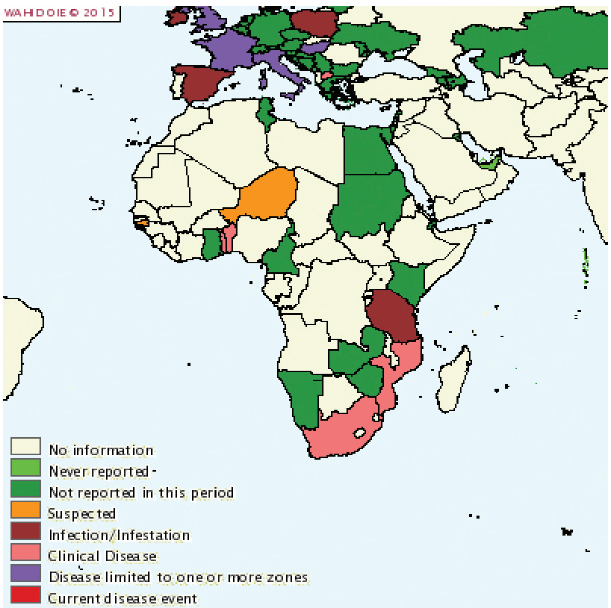

Figure 1: Bovine tuberculosis in wildlife reported to the Office International des Epizooties (OIE) January–June 2014

Although most cases of TB in wildlife are due to infection with *M. bovis*, there are a number of organisms in the *M. tuberculosis* complex that affect a wide range of hosts. *M. tuberculosis, M. africanum* and *M. canetti* primarily infect humans while other mycobacteria appear to be animal adapted (*M. mungi, M. surcattiae* and the dassie bacillus) (Alexander et al., 2010; Good and Duignan, 2011; Parsons et al., 2008, 2013). *M. bovis*, the cause of bovine TB, has a wide host range, including domestic livestock and wild mammals such as lions, European badgers, white-tailed deer and African buffalo (Fitzgerald and Kaneene, 2012).

IMPACT OF TB ON ANIMAL AND HUMAN HEALTH

Since TB is a chronic infection, it may take months to years for animals to show clinical signs of disease. Infected individuals may shed bacteria for long periods without apparent evidence of disease, resulting in transmission through direct contact or contamination of the environment. As the disease advances, animals may experience decreased milk production and fertility, loss of body condition and coughing or other respiratory signs, and may progress to death (or be at increased risk of predation) (DAFF, 2013; De Vos et al., 2001).

In addition to the direct impact on animal health and productivity, infected individuals present a risk of transmitting TB. Consumption of unpasteurised dairy products or infected animal products, exposure to contaminated environments (including pasture and water) or close prolonged contact can result in transmission to other animals as well as humans (Cosivi et al., 1998; Good and Duignan, 2011).

Figure 2: Potential exposure to bovine tuberculosis through unpasteurised milk
Source: (Rural Poverty Portal, n.d.).

Prior to implementation of disease control programmes, bovine TB was a significant global animal and public health threat. Establishment of TB control and eradication programmes in a number of developed countries in the early to mid-20th century resulted in substantial decreases in infection in both cattle and people (FAO, 2012). In the United States of America (USA), it was estimated that 20% of human TB cases were due to *M. bovis* prior to instituting pasteurisation and cattle testing. With the implementation of an eradication programme in the early 1900s, the USA has accomplished almost complete eradication of TB in cattle. However, the discovery of TB in wildlife species in the USA, the UK, South Africa, Australia, New Zealand, Spain and other countries has confounded the issue of animal TB control (Fitzgerald and Kaneene, 2012).

With the advent of control programmes, animal TB has become a primarily economic disease in developed countries (Cosivi et al., 1998; FAO, 2012). Losses associated with restriction in trade, restricted animal movement, decreased production, increased biosecurity costs and expenses associated with testing and restocking have been identified as major burdens for farmers and the wider agricultural industry (Ayele et al., 2004). In many developing countries, livestock are associated with social status and reflect personal wealth. The presence of TB can have serious implications for the livelihood and community standing of the family that owns infected animals. TB in wildlife has the potential to impact communities through spillback into livestock, infection from hunting or butchering game, decreased tourism and loss of income to wildlife industries (Bekker et al., 2012; Malama et al., 2013).

SIGNIFICANCE OF TB IN WILDLIFE

Rich biodiversity is one of South Africa's greatest heritages. The broad range of ecosystems supports a wide variety of wildlife species. However, since most mammals can be affected by mycobacterial infection, it is not surprising that at least 21 wildlife species in South Africa have been documented with TB (AL Michel, personal Communication March 2, 2015; Renwick et al., 2007). These include species such as leopards, cheetahs, wild dogs, large spotted genets, spotted hyenas, banded mongooses, Chacma baboons, honey badgers, impalas, common duikers, bushpigs, warthogs, bushbucks, eland, nyala, hartebeest, blue wildebeest, giraffes and black rhinoceros. Infections in these animals are considered to be a 'spillover' from other species. In contrast, there are species that are 'maintenance' hosts for TB, including *M. bovis* in African buffalo and possibly greater kudu and lions. Maintenance hosts are species in which the infection can persist without introduction from an external source. The presence of multiple susceptible hosts complicates the management and control of TB since the maintenance of infection will be affected by the interactions of different species, variable susceptibility, the influence of environmental factors (such as temperature, and feed and water availability) and the ability of the pathogen to persist in the host and environment (Renwick et al., 2007). With diminishing habitats, there are increased wildlife-livestock-human interfaces and a growing threat of infectious disease transmission.

Figure 3: Example of livestock-wildlife interface in South Africa

The emergence of TB in wildlife has created significant concern among conservationists, private game and cattle farmers, agriculture regulatory agencies and the public health sector. There are large knowledge gaps regarding the role of different species in perpetuating or amplifying the impact of this chronic pathogen. Although the incubation period of the disease is unknown, wild animals appear to be able to harbour mycobacteria for months to years. As infection progresses, there is evidence that TB may decrease reproductive and other fitness parameters; however, it may not significantly affect population numbers unless the animals experience other stressors such as drought or concurrent disease (Michel et al., 2006). This suggests that infected animals may remain in the population for extended periods, unlike in the case of acute diseases such as rabies or rinderpest, which result in rapid mortality. This confounds control measures for preventing introduction or decreasing transmission of disease, especially in complex ecosystems.

The direct effects of TB on wildlife have been documented. For example, buffalo herds with a higher prevalence of bovine TB had worse body condition and lost condition faster in the dry season than those with lower bovine TB prevalence (Caron et al., 2003). Although there was no observed impact on age structure in this study, the authors suggested that affected buffalo might be more susceptible to predation by lions. However, researchers found that chronic bovine TB in buffalo in Hluhluwe-iMfolozi Park was associated with decreased adult survival and a reduced population growth rate (Jolles et al., 2005). Since chronic infection does not result in large-scale mortality or rapid changes in population structure, the effects on resilience to disease and other stressors may not become apparent for years.

TB in some species may lead to high mortality and even to localised extinction of infected groups. This has been observed in banded mongooses in Botswana (caused by infection with *M. mungi*) and meerkats in the Kalahari (caused by *M. suricattae*) (Alexander et al., 2002, 2010; Drewe et al., 2009; Parsons et al., 2013). In addition to the direct impact on these populations in an ecosystem, these animals are important prey items for other species and their loss may influence predator populations.

The long-term consequences of wildlife TB in South Africa are unknown. A group of experts conducted a workshop in 2009 to model the impact of bovine TB on lion populations in the Kruger National Park. The simulations covering the next 50 years showed that bovine TB was likely to cause an overall decrease in the lion population (a 35–75% decline in the current population) before stabilising (Keet et al., 2009). Since the Kruger National Park is one of the remaining strongholds for lions in Southern Africa, this scenario suggests a serious threat to the survival of the species.

Figure 4: Mycobacterium bovis-infected lioness

In areas where there are TB maintenance hosts or the likelihood of repeated introductions, there is an ongoing risk of spillover to other species. As the prevalence of TB in reservoir hosts such as the African buffalo rises, there is an increasing threat of spillback into cattle at interfaces. Such an event has recently been documented in communal cattle in areas bordering the Kruger National Park (Musoke et al., 2015).

Wildlife TB can significantly impact conservation activities. The presence of TB may influence management decisions and resource allocation, which could have effects on other programmes. Control and management concerns may result in restrictions on the movement of animals, resulting in 'population islands', with subsequent influence on genetic diversity and resilience to disease, environmental changes and overall biodiversity (Michel et al., 2006).

Disease risks may alter public perception of wildlife based on threat of transmission to livestock, impact on livelihoods, including utilisation of wildlife, and potential to infect humans (Bekker et al., 2012; Carstensen et al., 2011). For example, detection of bovine TB in free-ranging white-tailed deer in Minnesota (USA) led to broad public support for aggressive management strategies that produced a rapid reduction in disease prevalence (Carstensen et al., 2011). In contrast, the lack of backing by farmers, hunters and the general public for these measures in Michigan (USA) resulted in ongoing outbreaks in both cattle and deer populations. In Southern Africa, since people and livestock may share land and water resources and people utilise wildlife for economic purposes, potential disease transmission could result in decreased tolerance in already limited habitats. In addition there is a threat to ecotourism, including hunting and game viewing (Renwick et al., 2007).

Wildlife TB has been identified by the Food and Agriculture Organization of the United Nations (FAO) as an "increasingly important disease" (FAO, 2012, p.5). It also states that "in response to the global importance of bovine tuberculosis for both animal and public health, the Food and Agriculture Organization of the United Nations (FAO) has recognized it as "a priority infectious disease that should be controlled at the animal-human-ecosystem interface, through national and regional efforts" (FAO, 2012, p. 2).

Increased awareness of TB in wildlife is the first step in addressing the ecological, conservation, socioeconomic and public health issues associated with this disease. Research is crucial to understanding the epidemiology, pathogenesis, risk factors associated with intra- and interspecies transmission and zoonotic potential. Some of the limitations for advancing comprehension of wildlife TB are the lack of resources to conduct studies, including lack of funding, a paucity of validated tests and constraints on accessing animals.

ADVANCES IN UNDERSTANDING WILDLIFE TB

Research programmes are continually being developed to investigate various aspects of TB in wildlife. One of the key areas is the exploration of the different hosts' immune responses and the development of diagnostic tests, especially for wildlife species. This is a main focus of the new National Research Foundation South African Research Chair in Animal TB and the Stellenbosch University Animal TB Research Group (http://www.sun.ac.za/english/faculty/healthsciences/Molecular_Biology_Human_Genetics/animaltb/Pages/default.aspx). Ongoing projects include identifying novel biomarkers of infection and disease, routes of transmission and effects of co-infections (for example feline immunodeficiency virus infection in lions), and developing and validating techniques for improved detection of mycobacterial organisms in species such as rhinoceros, African buffalo, lions, warthogs and greater kudu, among others.

Figure 5: Stellenbosch University Animal TB Research Group 2015

Application of knowledge gained through scientific investigations is essential to addressing the issues associated with wildlife TB. For example, a recent study has shown that a test and cull programme implemented for bovine TB in African buffalo in Hluluwe-iMfolozi Park has effectively reduced transmission in this population (Le Roex et al., 2015). Alternative approaches to disease control are also being investigated, such as the vaccination of Kalahari meerkats as a method of reducing transmission and development of disease (Drewe and Patterson, 2015).

Since TB research requires expertise and input from diverse fields, the Stellenbosch University Animal TB Research Group is actively collaborating with partners at the University of Pretoria, South African National Parks, KwaZulu-Natal Wildlife, the Department of Agriculture, Forestry and Fisheries as well as other local and regional stakeholders. International colleagues are also an essential part of current and future research, including scientists from the Royal Veterinary College in the UK, Colorado State University (USA) and other academic institutions across the globe. The goal is to contribute to greater knowledge that will inform strategies for the prevention and management of animal TB.

CONCLUSIONS

TB is a global threat to wildlife health. It directly impacts animal productivity and fitness and can lead to an increase in the rate of mortality. Wildlife TB also has significant socioeconomic, ecological and conservation consequences, especially for threatened and endangered species. Large knowledge gaps regarding the epidemiology, pathogenesis and risk factors associated with TB exist, particularly at wildlife-livestock-human interfaces. Research is crucial for informing strategies to prevent and manage this threat to wildlife.

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