Chapter 19
Tuberculosis: A Transboundary Animal Disease in Sahel Africa and Its Connected Regions

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Abstract Tuberculosis is one of the transboundary animal diseases that can spread extremely rapidly, irrespective of national or international borders. Tuberculosis is a zoonotic disease and a poverty-related disease that affects both humans and animals, and it is caused by members of the *Mycobacterium tuberculosis* complex (MTC). Globally, tuberculosis (TB) is a major public health problem with about 9 million people around the world effected by tuberculosis (TB), of which nearly 2 million people died with or from the disease. Tuberculosis is a major cause of death due to infectious diseases, competing with the human immunodeficiency virus (HIV). The burden of tuberculosis in Sahelian Africa has increased tremendously as a result of continuing poverty, political instability, and threat by violence, and these have impeded greatly the progress in implementing effective TB control measures. The majority of the people in the Sahelian region are by tradition and culture semi-nomads and are into farming and raising livestock in a system of transhumance as a way of utilizing the Sahel and sustaining themselves; hence there is that close contact between humans and their animals which translates to a high likelihood of zoonotic transmission between animal and humans. *Mycobacterium tuberculosis* affects humans mainly, while *Mycobacterium bovis* affects a wide range of host species including humans and wild and domestic animals, for example, camel and cattle. This chapter reviews tuberculosis in cattle and other domestic animals like sheep and goats in the Sahel Africa and its connected regions while drivers, history, epidemiology, clinical signs, diagnosis, and modes of transmission were reviewed and methods for the prevention and control of tuberculosis in cattle and other domestic animals like goats and sheep were highlighted.

Keywords Tuberculosis · Transboundary · Zoonosis · Sahel Africa

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History of Tuberculosis

Before recorded history, tuberculosis and other species of mycobacteria have been in existence (James 1999). Mycobacteria belongs to the genus of Actinobacteria under the family Mycobacteriaceae (Ryan and Ray 2004). The Actinobacteria genus includes pathogens known to cause serious diseases in vertebrate animals, including tuberculosis and leprosy (McMurray 1996). However, the Latin prefix "myco" means both fungus and wax, which is the "waxy" compounds in the cell wall (McMurray 1996). This attribute makes *Mycobacterium* acid-fast in nature (Bhamidi 2009).

Tuberculosis in cattle and other domestic animals like goats and sheep is caused by *Mycobacterium tuberculosis* complex (MTC), specifically *M. bovis* and *M. caprae* species (Pavlik et al. 2002; Prodinger et al. 2002; Erler et al. 2004). Tuberculosis is characterized by an accelerating development of specific granulomatous lesions of tubercles in affected tissues like the spleen, lymph nodes, and lungs (Omer et al. 1995). Mycobacterium also affects cattle, birds, frogs, fish, small reptiles, and frogs. There has been a risk of transmission of *Mycobacterium bovis* from animals to humans through the ingestion of milk and dairy products by humans (McMurray 1996). However, due to eradication of infected cattle and pasteurization of milk bovine tuberculosis is rarely found in the USA and sub-Saharan Africa. Mycobacterium is easily destroyed by sunlight and ultraviolet irradiation but can survive in the dust and air for weeks and months (McMurray 1996).

During the eighteenth century, many researchers assumed that the days of tuberculosis as a threat to the US population had passed and an incidence of 20,000 new cases per year was slowly declining, even though tuberculosis was still the leading infectious cause of death globally (McMurray 1996); however, the situation in the nineteenth century changed dramatically. After the nineteenth century, the incidence of tuberculosis slightly increased and kept increasing primarily due to the acquired immunodeficiency syndrome (AIDS) epidemic according to Control of Communicable Diseases and Prevention (2007). At the same time, multiple drug resistance strains of *M. tuberculosis* were on the increase.

Geographical Distribution and Economic/Public Health Importance

Bovine tuberculosis (BTB) is one of the transboundary diseases and an infectious disease caused by *Mycobacterium bovis* a member of the *Mycobacterium tuberculosis* complex (MTC) (Ameen et al. 2008). *Mycobacterium tuberculosis* complex species that affect cattle primarily are the *Mycobacterium bovis* and *Mycobacterium caprae* but also affect goats, camels, horses, pigs, dogs, and cats among other animals including human beings (Erler et al. 2004; Prodinger et al. 2002; Thoen and Steel 2009). In the Sahel Africa, tuberculosis in goats and sheep is primarily caused by *M. caprae* species which has a serious socioeconomic impact as

comparable as *M. bovis* and poses a public health threat to the livelihoods of livestock farmers. Tuberculosis in animals can lead to reduction in the quality and quantity of meat, milk and diary products, livestock products like hides, skins, and fibers, and animal power for transport and traction.

According to Corbett et al. (2003), worldwide, tuberculosis caused about 2 million deaths and about 9 million new cases had been reported annually, with the sub-Saharan Africa having the highest annual risk of infection with TB, probably due to upsurge of HIV/AIDS pandemic, globalization, land encroachment, and climate change. Globally, *M. bovis* accounts for 3.1% of all human TB cases (Ameen et al. 2008). The global TB burden as a result of *M. bovis* and *M. caprae* in Sahelian Africa is not known. This may be due to the fact that human TB due to *M. bovis* and *M. caprae* cannot be differentiated from that due to *M. tuberculosis* with respect to clinical signs and symptoms and pathological and radiological features (Ameen et al. 2008).

Tuberculosis as reported by Thoen and Steel (2009) contributes largely to the cause of human morbidity and mortality in many developing countries including sub-Saharan Africa. Human tuberculosis (HTB) is caused by *Mycobacterium tuberculosis* but in some cases caused by *M. bovis* from ingestion of contaminated milk. In developed countries, before the advent of control and elimination of bovine tuberculosis (BTB) in which one of the strategy for control was the introduction of milk pasteurization, zoonotic infection with *M. bovis* was a major cause of HTB (Cosivi et al. 1998). In geographic regions where tuberculosis is prevalent in animals, human tuberculosis cases due to *M. bovis* and *M. caprae* occurred (Thoen and Steel 2009) resulting from the ingestion of contaminated unpasteurized milk, raw meat, or improperly cooked meat and also by inhaling cough spray from infected livestock (Ayele et al. 2004).

Tuberculosis (TB) in animals is regarded as a poverty-related zoonosis with little or no attention given to it (WHO 2006). TB in animals has a serious economic impact on livestock, thereby reducing quality and productivity in livestock (Müller et al. 2008). In addition, it can persist in wildlife reservoirs and thus affect the complete ecosystem (Müller et al. 2008). As reported by WHO (2006, 2008), TB is still prevalent in the developed countries; however, it is commonly found prevalent in developing countries, with insufficient financial and human resources to control the disease (Zinsstag et al. 2006).

Tuberculosis in animals is still widespread in the Sahel Africa and its connected regions. The Sahel region of Africa is greatly involved in animal production with countries like Mali, Mauritania, Somalia, Ethiopia, Pakistan, Nigeria, Kenya, Niger, Egypt, and the United Arab Emirates being among the main cattle producing countries and also with published reports documenting the presence of tuberculosis (Müller et al. 2008; Anita 2014). In the Sahel Africa, TB caused by *M. bovis* and *M. caprae* species in humans seems to be especially prevalent among the pastoralists (Cadmus et al. 2006), who herd their cattle across the borders of the country. Pastoralists use milk which they do not usually boil from their cattle for food. TB in humans as a result of *M. bovis* and *M. caprae* species is becoming a serious public health issue in developing countries like Sahel Africa as humans and animals share

the same micro-environment and dwelling premises especially in rural areas. The close contacts between humans and animals are increasing everyday globally due to increase in population density and growth especially in low-income developing countries where livestock production is their mainstay and offers a pathway out of poverty (WHO 2006).

In areas without infectious wildlife, nomadic movement which involves the movement of cattle, goat, and sheep from one route to another route remains a possible means for transmission of tuberculosis (WHO 2006). Factors that influence the routes by which cattle, sheep, and goats become infected include age, environment, and local farming practices. Infection via the alimentary (ingestion) route can also be seen in young calves ingesting milk from tuberculosis dams, although mesenteric (intestinal) lesions are relatively rare in countries with advanced control programs (Pavlik et al. 2002). Factors that influence direct transmission via the respiratory route include high stocking density and substantial cattle, sheep, and goat movement. However, zoonotic diseases affect livestock and humans with significant adverse effects on animal productivity and the health of the population especially among the poor and who are more vulnerable to the diseases (Pavlik et al. 2002). According to Corbett et al. (2003), emerging or reemerging animal and human TB caused by pathogenic bacteria of the family of *Mycobacterium tuberculosis* complex is becoming widely spread and affects the livestock industries and human health in the Sahelian African countries (Ayele et al. 2004).

Tuberculosis in cattle, sheep, and goats affects their health, reduces profitability, impacts negatively on international trade, and can alter genetic improvement toward desirable traits in animals (Boland et al. 2010). It also has a negative impact on the welfare of families who are into farming. Transmission from animals to humans and humans to animals still occurs and is considered a public health risk and of high concern, despite control measures and policies instituted by the government which includes herd testing, pasteurization, effective meat inspection, health surveillance, and BCG vaccination (Moda et al. 1996; Smith et al. 2004). Although there is the risk of transmission from humans to animals, some more recent opinion considers this risk to be negligible (Torgerson and Torgerson 2010). Hence, TB control is currently more focused on the implications of international trade. Despite the efforts made toward the eradication of TB through sustained and costly implementation of various control and eradication programs beginning from the nineteenth century, TB has not been eradicated in the Sahelian Africa and its connected regions.

Epidemiology

Tuberculosis caused by *Mycobacterium species* has a worldwide distribution (OIE 2007). In several countries, TB remains a major and costly infectious disease of cattle and other domesticated and wild animal populations which include badgers, possums, deer, goats, sheep, camelids, etc. (Pollock and Neill 2002; Carslake et al. 2011). According to OIE (2011) and Cousins and Roberts (2001), TB in cattle,

sheep, and goats is of socioeconomic or public health importance in developing countries and of significance to the international trade of animals and animal products.

A key to understanding bovine TB epidemiology can be seen in the relationship between infection and disease (TB) and the relationship between disease and transmission. Biological, social, and environmental factors are known to influence both transmission and susceptibility of the host (WHO 2014).

Zoonotic tuberculosis is the result of TB infection among domestic species. These domestic animals that play a significant role in the epidemiology of zoonotic tuberculosis include goats, sheep, pigs, farmed deer, and camel, while cases in horses, cats, and dogs are rare (Anita 2014). The occurrence and the distribution of *Mycobacterium* infection in cattle and sheep from a global point of view is low but varies greatly in the husbandry system of the Sahelian African countries. TB infection in animals like goats can be the result of co-grazing with cattle herds infected by TB (Anita 2014).

In pastoralist communities of the Sahelian Africa and its connected regions, animals like camels provide meat and milk and serve as draft power for transportation of goods especially for long-distance journey. The constant close connection between pastoralists and their animals promotes the bidirectional transmission of tuberculosis from animals to humans. The existence of TB and how widespread and significant TB is in camel population is still largely unknown; however, research has shown its presence in the United Arab Emirates, Egypt, Mauritania, Somalia, Pakistan, and Niger as reported by Anita (2014).

Zoonotic TB is the result of the adaptability of Mycobacterium species in different hosts (Radostitis et al. 2000). Zoonotic TB Infection due to *M. bovis* was once a major problem in developed countries, but following the implementation of eradication programs and policies such as test-and-slaughter policy and milk pasteurization, the incidence drastically reduced (Cousins and Roberts 2001). Despite these efforts, surveillance and control activities for bovine tuberculosis are often inadequate and unavailable. Approximately 85% of the cattle population and 82% of the human population of the Sahelian Africa are in regions where surveillance and control activities for bovine tuberculosis are either inadequate or unavailable, thereby making the burden and the epidemiologic and public health impact of the infection among animals and humans greatly unknown (Cosivi et al. 1998). With the emergence and reemergence of drug-resistant strains of *Mycobacterium* species and the rise in TB and HIV/AIDS co-infection, assessing the burden of this disease and its current situation in Africa are further complicated (WHO 2011).

Transmission

M. bovis and *M. caprae* can be transmitted by the inhalation of aerosols, by ingestion of any animal product infected with the disease, or through breaks in the skin. However, the routes of transmission vary between species. Cattle, goats, and sheep

serve as reservoirs for tuberculosis. In the absence of main maintenance hosts, populations of spillover hosts do not harbor *Mycobacterium* indefinitely, but may transmit the infection between their members (or to other species) for a time. However, due to high population density, some spillover hosts can become reservoirs for TB (Etter et al. 2006).

Cattle excretes *M. bovis* and *M. caprae* in milk, respiratory secretions, feces, and sometimes in the urine, vaginal secretions, or semen. A larger number of organisms may be shed in the late stages of infection. According to Menzies and Neill (2000), carriers include asymptomatic and anergic carriers. In most cases, *M. bovis* and *M. caprae* are transmitted between cattle via aerosols as a result of close contact among cattle. Animals like sheep and goats become infected when they ingest the organism, as seen in calves that nurse from infected cows. It is important to note that not all infected cows transmit the disease to their young calves (Menzies and Neill 2000). Transmission of any of the *Mycobacterium* species can be either direct through close association between animals and humans or indirect from exposure to viable bacteria in a contaminated environment like pasture, feed, and housing. Movement of cattle, sheep, and goats during co-grazing can facilitate most transmission in areas without infectious wildlife (Barlow et al. 1997). Risk factors like age, environment, and practice of local farming are likely to influence the routes by which cattle, sheep, and goats become infected. Other factors that promote direct transmission via the respiratory route include natural cattle, sheep, and goat behavior and high stocking density.

Clinical Signs

In animals like cattle, sheep, and goats, granulomatous lesions are seen mainly in the lungs, lymph nodes, and spleen (Anita 2014). Often affected animals may remain for so many years without showing any clinical signs. However, some of the classical signs include difficulty in breathing, persistent and painful cough which may develop during chronic stage accompanied by hyperpnea and dyspnea, and drastic change in the animal's body condition, and the animal gradually emaciates with dull and sunken eyeballs (Anita 2014) (Plate 19.1).

Diagnosis

Diagnosis of TB in live cattle in the field involves the use of tuberculin skin test especially among herds of cattle. The tuberculin skin test is conducted by injecting tuberculin intradermally into the cattle. A positive is shown by a delayed swelling around the site of injection and this is otherwise known as hypersensitivity reaction. Bovine tuberculin can be used alone when performing the tuberculin skin test or a comparative test can be employed to distinguish reactions to *M. bovis* from other

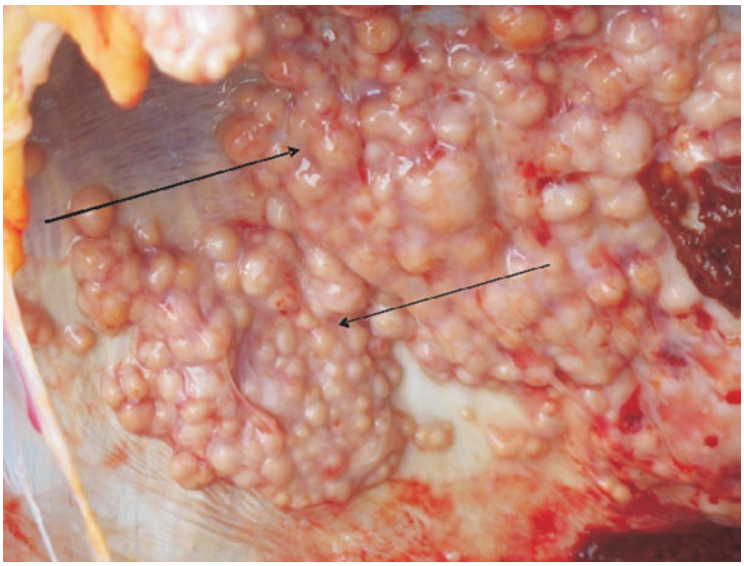

Plate 19.1 Picture showing small discreet grayish nodules (arrows) indicative of tubercle lesions in the lungs of a cow

environmental *Mycobacterium* species (Cousins and Florisson 2005). The use of tuberculin skin test for detection of TB infection is constrained by test sensitivity. A reduction in testing frequency results in increased prevalence and a reduced ability to detect disease. To compound this, a substantial proportion of cattle, sheep, and goats were never tested for TB (Mitchell et al. 2005), and there is also a period of reduced reactivity in infected animals following an initial tuberculin test, the precise duration of which has not been determined.

Laboratory Tests

However, a presumptive diagnosis of TB is done using the acid-fast bacilli (AFB) test whereby direct smears from clinical samples or tissues may be stained with immunoperoxidase technique, Zeihl-Neelson stain, or a fluorescent acid-fast stain (Cousins and Florisson 2005).

For confirmation of TB infection in animals and the differentiation of the causative agent Mycobacterium species, culture test is conducted and usually done by the isolation of *M. bovis* and *M. caprae* on selective media such as Lowenstein-Jensen medium and incubated for a period of 8 weeks (Ochei and Kolhatker 2008). The cultural characteristics of the organism isolated can be confirmed with biochemical tests or the use of polymerase chain reaction (PCR) assay which is quicker but very expensive.

Other molecular techniques that have been applied for TB detection include (a) genetic fingerprinting techniques, for example, spoligotyping; (b) lymphocyte proliferation and gamma interferon assays (a blood test that measures cellular immunity); (c) enzyme-linked immunosorbent assays (ELISA) which measure antibody titers to *M. bovis* and *M. caprae*; and (d) GeneXpert MTB which is a cartridge-based automated diagnostic test that can identify *Mycobacterium tuberculosis* (MTB) complex including *M. bovis* and *M. caprae* and resistance to rifampicin (RIF). With additional financial support provided by the US National Institute of Health (NIH) and OIE (2011), the GeneXpert MTB technique was jointly developed by the laboratory of Professor David Alland at the University of Medicine and Dentistry of New Jersey (UMDNJ) (WHO 2013) in collaboration with the Foundation for Innovative New Diagnostic.

According to the World Health Organization (WHO 2010), the GeneXpert MTB/RIF was endorsed for use in TB endemic countries as categorized by WHO, and its major milestones for global TB diagnosis were also declared after an 18 months rigorous assessment of its effectiveness in TB, MCR-TB, and TB/HIV co-infection on the field (Small and Pai 2010). The GeneXpert test has the propensity to revolutionize TB diagnosis (Van Rie et al. 2010). Deoxyribonucleic acid (DNA) sequences specific for *M. bovis* and *M. caprae* and rifampicin resistance can be detected by the GeneXpert/RIF using polymerase chain reaction technique and relies on the Cepheid GeneXpert system, a platform used for rapid and simple nucleic acid amplification tests (NAAT) (Van Rie et al. 2010). This is achieved by the purification and concentration of the isolate genomic materials or testing of lymph nodes and other tissues from the captured bacteria by sonication and subsequently amplifying the genomic DNA by PCR. Molecular beacons in a real-time format using fluorescent probes were used to identify all the clinically relevant rifampicin resistance-inducing mutations in the RNA polymerase beta (rpo ß) gene in the *M. bovis* and *M. caprae* genome. Xpert TB replaced smear microscopy with a pooled sensitivity of 88% and specificity of 98%. However, sensitivity was only 67% and specificity 98%, when Xpert TB was employed for use as an add-on in cases of negative smear microscopy (Steingart 2013).

Another important molecular technique is the loop-mediated isothermal amplification (LAMP) which is known as a single-tube technique for the amplification of deoxyribonucleic acid (Mori et al. 2001). LAMP is a very cheap isothermal which eradicates the need for expensive thermocyclers used in conventional polymerase chain reaction and can serve as an alternative technique in the future for detection of certain diseases. LAMP technique can be combined with a reverse transcription step to allow for the detection of ribonucleic acid (RNA). LAMP can be used as a simple screening technique on the field or can be used by clinicians at the point of care (Sen and Ashbolt 2010). According to MaCarthur George (2009), in low- and middle-income countries, LAMP may be useful for infectious diseases diagnosis. Major advantages of LAMP include: (1) it is a relatively new DNA amplification technique, (2) simple to use, and (3) relatively inexpensive. In LAMP method, either two or three sets of primers or a polymerase with high strand displacement activity plus a replication activity are used to amplify the target sequence at a constant temperature

of 60–65 °C. Four different primers are employed to identify six different regions on the target gene, and this increases the specificity of LAMP. However, as a result of the specific nature of the action of these primers, the quantity of DNA produced in LAMP is substantially higher than the amplification produced by PCR. Research has shown that LAMP is widely being used for detecting infectious diseases such as tuberculosis (Geojith et al. 2011). However, in developing countries, the use of LAMP technique for the detection of other common pathogens is yet to be extensively validated (Small and Pai 2010).

Spoligotyping is a new method developed recently and used for the detection and typing of *M. bovis* and *M. caprae* bacteria simultaneously (Andrea et al. 2005). This method involves the amplification of a highly polymorphic direct repeat locus in the *M. bovis* and *M. caprae* genome by polymerase chain reaction (PCR). Results can be obtained from a *M. bovis* and *M. caprae* culture within 1 day. Features of spoligotyping include: (1) it is very rapid, (2) it can detect causative bacteria, and (3) it provides epidemiologic information on strain identities (Andrea et al. 2005). Spoligotyping is very useful in the surveillance of tuberculosis transmission and in interventions to prevent further spread of this disease especially when implemented in a clinic setting.

Latent Infection

In human TB epidemiology, the concept of "latent" infection is well supported and is defined as where the pathogen resides long term in the host which may or may not be detectable (Manabe and Bishai 2000). However, where infection is relatively common, productive (transmitting) infection is rare. Latent TB is currently regarded as a spectrum of pathogen burden and host immune control (Sridhar et al. 2011), and it is seen to occur when the pathogen is forced into a state of allegedly nonreplicating persistence by a host response (Palmer and Water 2006). However, current researches suggest that these interactions between the pathogen and the host response are largely pathogen driven (Bold and Ernst 2009; Ehlers 2010; Sasindran and Torrelles 2011).

As reported by Brites and Gagneux (2011), the ability of pathogens to establish latent infections enhances the transmission of TB. This ability may have evolved as a means of adaptation for persistence when population densities were low. Prolonged latency period as a result of reactivation may provide an opportunity for these pathogens to overtake an entire generation to access new vulnerable. *M. tuberculosis* has an enduring phenotypic feature, which could allow it to resist the antibacterial resistance of the host and to adapt to long-term survival within the host (Keren et al. 2011) and possibly even the environment. Though the extent of latency and reactivation applicable to cattle and other animal populations is not yet known (Van Rhijn et al. 2008), the process of latency and reactivation has been reported to operate in cattle and possibly other animal populations (Pollock and Neill 2002). The significance of a latent infection is that it can, under normal conditions, reactivate to full-blown TB. The physical nature of the animal during latency determines what strategies

to be employed such as post-exposure vaccination and what more effective method to be employed for diagnosis in order to detect the disease at the latent phase. For instance, the disease may not be detectable by current diagnostics methods, if it is truly dormant and hidden from the immune system.

Based on analysis of the size and distribution of lesions in cattle, Fritsche et al. (2004) suggests that disease exacerbation could occur following periods of lesion dormancy, though relatively poor test sensitivity might explain such observations. The concept of latency in cattle can be further illustrated, when cattle with no physical lesions shown on any of the affected organs are positive for TB using IFN test (Neill et al. 1994; Monaghan et al. 1994) or culture test (Cassidy et al. 1999).

Prevention and Control/Adopted Surveillance and Control Strategies

One of the control strategies for the control of tuberculosis in cattle, sheep, and goats and other infected wildlife is the test-and-slaughter or test-and-segregation method (OIE 2007). Other control measures include quarantining of infected herds and sanitation and disinfection. To eliminate cattle that may shed the organism thereby increasing the risk of transmission among herds, affected herds are re-tested periodically by employing the use of tuberculin skin test, otherwise known as the Mantoux test. It is recommended by OIE (2007) that infected herds should be quarantined and animals that have been in contact with reactors should also be traced.

Test-and-slaughter technique is the best method to eradicate tuberculosis from domesticated animals (OIE 2007), though with very negative economic impact. Sanitation and disinfection is another method of prevention that involves the use of 5% phenol iodine solutions with a high concentration of available iodine, glutaraldehyde, and formaldehyde. The use of 1% sodium hypochlorite with a long contact time is also effective in an environment with low concentration of organic material (Cousins and Roberts 2001). Moist heat of 121 °C (250 °F) for a minimum of 15 min has been employed for destroying *M. bovis* in animal products (Cousins and Roberts 2001).

Another method that has shown to produce positive result toward the eradication of TB is culling to reduce the population density thereby decreasing transmission, though the occurrence of *Mycobacterium species* in wildlife reservoir hosts impedes these eradication efforts. Effects of culling include increase in the scattering of the remaining animals and restrictions of supplemental feeding areas (Lees 2004). To mitigate against the effect of culling, fencing around the hay storage areas can prevent access to wildlife. In addition, the interactions between wildlife and domesticated animals can be reduced by implementing biosecurity measures on farms (Cousins and Roberts 2001).

Adequate control measures in order to reduce the incidence in animals and humans should be adopted. The measures may include:

1. Intensified public education for the awareness about the public health implication of zoonotic TB.
2. Active surveillance for TB in goats, cattle, sheep, and other domestic animals at international borders should be instituted.
3. Test-and-slaughter policy should be adopted in order to improve animal and human health.
4. Government should enforce the policy of compulsory tuberculin skin testing of dairy animals such as cattle, twice a year, and destruction of all dairy animals positive for tuberculin skin test and secreting acid-fast bacilli, with full compensation to the owners.

Conclusion

In conclusion, the pastoralist nature of the people of the Sahelian Africa and its connected regions contributes significantly to the transmission of tuberculosis within this region and across borders. Reducing tuberculosis in the Sahelian region requires a long-term TB control and public health strategy which requires enormous capital in terms of finance and manpower.

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