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This book is dedicated to the memory of Charles Thoen, coeditor of this book who died unexpectedly before its publication. We will remember him for his enthusiasm, commitment, and the contributions that he made until his death to the knowledge base of bovine tuberculosis in all its forms.

Preface

Africa, considered to be the cradle of humankind, is a vast continent characterized by the richness of and variation in its ecosystems and human and animal populations. It faces major challenges as part of the developing world, and many of the countries on the continent are of the poorest on the globe. The lack of financial resources, inadequate medical and veterinary services, levels of poverty, underdevelopment, lack of service delivery, political instability, ethnic conflict, and serious diseases of humans and animals complicate these issues in most, if not all, of its countries.

This book deals specifically with tuberculosis of animals in Africa and its zoonotic implications for human populations in the various countries. It is known that human tuberculosis was rife in Egypt at the time of the Pharaohs, and it is thought that tuberculosis in cattle existed in North Africa since ancient times. At that time, and even now, nomadic human–animal population movements seem to facilitate the spread of the disease throughout various regions in Africa.

Tuberculosis is one of the major economically important global diseases of humans and animals. It is of as great importance in Africa as it is elsewhere and it is endemic in African countries that report their disease status to the WHO and the OIE. In many of the countries, confirmation of the causal agent and determination of species and strains are not practiced because of the lack of suitable laboratories and of inadequate financial, human, and material resources. In most of the African countries, available funds are allocated to dealing with more immediate devastating animal diseases such as rinderpest (now eradicated), CBPP, and foot-and-mouth disease. Bovine tuberculosis, however, remains important as it limits the ability of countries to participate in international trade in animals and animal products to countries that are free from the disease, or are in the process of eradicating it.

For many years, it has been assumed that colonization and the importation of foreign cattle resulted in the introduction and spread of bovine tuberculosis in Africa. However, recent research suggests that unique African strains of *Mycobacterium bovis* occur in Western and Eastern Africa, and it appears that the disease in cattle in Africa was present before the importation of bovine tuberculosis-infected foreign cattle from Europe and Australia. It does appear though that the introduction of the foreign strains of *M. bovis* contributed to the large diversity of *M. bovis* strains isolated from cattle across Africa.

Tuberculosis in animals is caused by a number of bacteria of the genus *Mycobacterium*. It is a chronic, contagious disease and, dependent on the mycobacterial species, has a wide host range and various routes of transmission.

The epidemiology of tuberculosis in animals is complex, and is even more so in Africa, given the extreme variation in ecosystems, poor border control, and farming practices that vary from extensive to intensive and, in many instances, the movement of livestock over vast distances because of nomadism and transhumance.

In parts of Africa, more recently, spread of *M. bovis* to wildlife has become common, and in some instances, wildlife species became maintenance hosts of the disease. In this respect, the role of lechwe (*Kobus leche*) in Zambia and that of African buffaloes (*Syncerus caffer*) in South Africa, Zimbabwe, Tanzania, and Uganda are good examples. This development has serious consequences for countries attempting control and eradication of the disease in domestic stock as it has been shown that when bovine tuberculosis occurs in a number of species in a complex ecological system, eradication by applying current control measures becomes impossible. Cross-border control of the movement of wildlife is even more difficult than that of livestock, and this movement may become a bone of contention in the development of the large number of trans-frontier parks that straddle the border of a number of southern African countries.

The increasing use of contemporary molecular techniques, such as VNTR, in African countries as presented in this book, provides greater insights not only into the status of bovine tuberculosis in African countries, but, moreover, the interrelatedness of outbreaks across international borders.

The information provided by current African research presented by the different contributors to the book and the reports of different African countries provide a better understanding of the epidemiology of *M. bovis, M. africanum*, and other closely related pathogenic mycobacteria in cattle, wildlife, and zoonotic tuberculosis in Africa. This improved understanding should be utilized by policy makers and animal and human health authorities to improve their decision-making and chances of success when attempting to control and eradicate the disease in their respective countries. It is also clear that future activities aiming to control and eliminate tuberculosis in animals and humans should employ interdisciplinary collaboration between medical and veterinary medical professionals as embodied by the philosophy of the "One Health" approach.

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Introduction

Nicolaas P. J. Kriek

1.1 Introduction

Africa is a vast continent, and it is the second largest on the planet. It is subdivided into 54 countries with a large diversity of ethnic groups and languages, an enormous livestock population, and a unique diversity of wildlife. Its human population in 2013 exceeded 1.1 billion; and it is expected to reach 2.5 billion by 2050, and 4.4 billion by 2100. The African countries have a tumultuous history, and currently they remain some of the least developed and poorest of all countries globally. The impact of incursions and colonization by other nations, and human migration shaped the current distribution of the main ethnic groups, and the contour and size of the individual countries that now exist in Africa.

Livestock numbers on the continent are large, and this form of agriculture is critical in sustaining many of the communities, of which in Western and Eastern Africa, large numbers live nomadic lives. Nomadic communities participate in one or other form of transhumance, characterized by the seasonal migration of people and their livestock across international boundaries, making disease control in livestock almost impossible. This diversity of people, livestock husbandry practices, and wildlife present major challenges to policy makers and regulatory authorities, including those managing and controlling diseases. Many of the epidemic diseases of humans and animals of global importance are prevalent on the continent and affect the wellbeing of humans and the distribution of its livestock and wildlife. A large number of these diseases are zoonoses, and livestock, but particularly wildlife, play a major role in sustaining these infections. The complexity of the demographics of Africa and the lack of technical personnel and financial resources have a profound effect on the ability of the continent to manage these important diseases.

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Tuberculosis is of major importance in livestock, wildlife, and humans and has a global distribution. With its many manifestations and numerous species susceptible to infection by the mycobacteria that cause the disease, it is endemic on the continent and is present in its humans, livestock, and wildlife. The content of this book deals with the various aspects of *Mycobacterium bovis* infection in Africa in livestock (cattle in particular), wildlife, and humans that are prone to contract this serious infection.

1.2 A Brief Overview of the Important Aspects

The chapters in this book deal with specific aspects of the disease caused by *M. bovis* in humans, livestock, and wildlife with the focus on Africa and the challenges associated with the detection, epidemiology, control, and eventual eradication of the disease from the continent. It also contains a number of country reports that focus on the specific situation in each of the countries. As only a few of the countries of Africa have the ability, and committed to report on the status of tuberculosis in their human and animal populations, these may be assumed to reflect the status in most, if not all, countries in the various regions of Africa: those on the Mediterranean rim, Western Africa, and the Sahel, and in Central, Eastern, and Southern Africa.

The second chapter provides a broad overview of the status of the disease and its control in Africa. Bovine TB (BTB) is globally a notifiable disease and is classified by the World Animal Health Organization (the OIE) as being of socioeconomic and of public health importance. It is now also classified as one of the important neglected zoonoses. Against this background and the known presence of the disease in humans and animals in Africa since antiquity, little is known about its current status even though the first diagnosis of BTB in livestock was made in South Africa in 1880 and in wildlife during the course of the 1920s, and it is now known to occur throughout the continent.

For long, it has been assumed that the European settlers introduced BTB into Africa during the time of colonization, but it subsequently transpired that there are a number of indigenous strains, the Af clonal complexes of *M. bovis*, causing BTB in Africa. Control of the disease is complicated by its characteristically slow, insidious spread in cattle herds and populations, the lack of specific clinical signs, and the difficulty of eradicating the disease from livestock even in the developed countries in the world. The limited knowledge about the disease by African farmers, consumers of products, veterinary authorities, and policy makers, and limited human and financial resources are the major reasons why little attention is still given to the control and eradication of the disease from African countries.

The complexity of the epidemiology of BTB is a major reason for the difficulties experienced in controlling it. Bovine TB is a multihost disease that also occurs in wildlife, some of which are maintenance hosts. Given the experience in some of the developed countries, such as the UK, New Zealand, and the USA, it appears to be impossible to eradicate the infection once one of the wildlife species in the same ecosystem becomes a maintenance host of the infection. Initially, BTB was considered to be a disease of intensively farmed cattle housed during winter, and that it would not be a problem in extensively farmed cattle. This still appears to be the situation in Africa where there remains a perception, shown since to be false, that local breeds were less susceptible to the infection, and that the extensive management systems practiced in many parts of the continent, will limit the extent of the disease, and thus its importance. Based on these assumptions, the lack of information about the distribution and extent of the infection in African livestock and wildlife, and the limited financial and human resources, policy makers and veterinary authorities mainly focus on the control of what they consider to be a more serious threat, the acute epidemic and endemic infectious diseases.

The marked increase in the size of the human population on the African continent and the rapid rate of urbanization are causing an increasing change in animal husbandry practices. To augment their income and to satisfy the burgeoning demand for milk of the expanding urban populations, there is now a trend to establish small-scale dairy farming in urban and periurban areas, and these practices result in a marked increase in the prevalence of BTB in many of those herds. As the disease remains uncontrolled in most of the countries on the continent, increasing numbers of people consume unprocessed, infected milk, given the ethnic cultural habit in many parts of Africa to consume raw, unprocessed, or soured milk, and meat.

Internationally, the control of BTB is increasingly complicated by the presence and persistence of the disease in free-ranging wildlife and its bidirectional spread at the wildlife–livestock interface. It is anticipated that Africa, with its rich diversity of wildlife species, will also be plagued by this problem. Examples of maintenance hosts that have already been identified in Africa include African (Cape) buffaloes (*Syncerus caffer*), greater kudus (*Tragelaphus strepsiceros*), and Kafue lechwe (*Kobus leche kafuensis*), and there may be others. The role of these maintenance hosts is largely poorly researched, and they may in future prove to be a major obstacle in controlling and eradicating BTB from Africa.

The most pressing problems in dealing with the issues are the lack of application, and the absence of statutory control policies including surveillance for the presence of BTB in most of the African countries. These events result in a lack of information required to develop sound control policies and programs. In most African countries, there is a total lack of information about the presence of the disease, its impact on the livestock sector, and its role in humans as a serious, but neglected, zoonosis.

It is critical for African countries to address the challenges and dangers of the presence of the disease, given the rapid expansion in the numbers of humans and animals on the continent that will enhance the impact of the disease, and if it remains uncontrolled, it may reach catastrophic proportions. Additionally, the presence of uncontrolled BTB across the continent will inevitably have a major negative impact on the international drive to eradicate TB in humans within the next few decades, irrespective of the specific cause and the presence of zoonotic TB.

Chapter 3, dealing in more detail with zoonotic TB caused by *M. bovis*, also emphasizes the lack of information about the prevalence of the disease in humans in Africa, primarily because of the lack of sufficient laboratory infrastructure and funding to distinguish between *M. tuberculosis* and *M. bovis* isolates. Humans contract the disease in different ways: by drinking unpasteurized milk, by inhaling infected droplets when in close contact with infected animals shedding mycobacteria, and by eating meat contaminated with *M. bovis*. The prevalence of zoonotic TB in Africa is unknown but it is known to be higher in countries in which the prevalence of the disease in cattle is high and in countries where BTB is common, and in which 10–15% of humans may suffer from zoonotic TB.

There is a general attitude, based on the universal lack of information about zoonotic TB and anecdotal evidence, that zoonotic TB in Africa is not a problem, and thus does not merit monitory expenditure to create the necessary diagnostic infrastructure. As a result, the role that it may play in the epidemic occurrence of TB in humans in Africa is largely ignored. This is against the background of the extent to which it occurred in some of the European countries before BTB was controlled in cattle and milk was pasteurized, where 50% of TB cases in children with lymphadenitis, and 65% of intestinal TB cases, were due to an *M. bovis* infection. Zoonotic TB is the main reason for introducing pasteurization of milk and for justifying the massive financial expenditure over many decades by developed countries to control BTB in their national cattle herds. Large sections of the African population do not have access to pasteurized milk and prefer to drink raw milk, or partially fermented milk. Ethnic practices also cause people to eat high-risk meat and meat products, and contrary to common belief, certain sectors of the nomadic people live in close association with their animals, thus enhancing the likelihood of contracting the disease caused by *M. bovis* by inhalation.

The likelihood that HIV-AIDS may enhance human infection with *M. bovis* in Africa has been raised as an additional reason why more attention should be given to this infection, but it appears, according to the limited available information, that this is not the case. One further important complication of not identifying *M. bovis* in human TB cases is the likelihood of the development of drug-resistant *M. bovis* strains as it is already resistant to rifampicin, one of the front-line drugs used for treatment of TB in humans. In this context, XDR *M. bovis* strains have been identified, and if they are to extend into Africa, their presence may develop into a health threat that would be most difficult to deal with.

The current *liaises faire* approach by policy makers and the human and veterinary regulatory authorities may yet prove to be a risky one, given the general lack of information about the disease. The occurrence of hotspots of *M. bovis* infection has been reported in Tanzania where, in areas, the prevalence of zoonotic TB in humans reached 10–38%. There may be many more such hotspots, and with the expected increase in the human population and urbanization, the general lack of control of the disease in cattle and the ignorance of farmers and consumers about the disease, zoonotic TB may have disastrous effects in times to come. As an example, an average herd prevalence of 10.5% and an in-herd BTB prevalence of up to 90% have been reported in intensive dairy farms in Ethiopia, and it is only reasonable to expect that this would eventually also be reflected in the number of zoonotic TB cases in those areas.

Chapter 4 deals with the control of the disease by applying the multidisciplinary approaches of One Health to facilitate the control and eradication of human TB, thus implying also the control and eradication of BTB. The complexity of BTB, because of the involvement of multiple susceptible species including humans, and the presence of wildlife maintenance hosts, makes it imperative that a broad multidisciplinary approach be adopted to engender some hope of success with the attempted control and eradication of both BTB and zoonotic TB in Africa. The WHO and other international agencies recently emphasized the importance of controlling BTB and of zoonotic TB in an attempt to eradicate human tuberculosis during the course of the next few decades. To do this, a number of issues will have to be addressed including determining the extent of BTB in Africa, the burden of the disease in the human population, the role of human-to-human transmission, and understanding the molecular epidemiology of the disease to allow the development of appropriate control strategies. The extent, cost to control, and complexity of the disease are such that to have any hope of successfully dealing with it will require a multidisciplinary approach. The One Health approach would enable authorities to focus on improved surveillance, the development of novel diagnostic methods, coordinated research, controlling the disease in targeted populations, and emphasizing food safety by raising the awareness of all stakeholders about the risks involved. It too will aid in developing effective policies and focusing on joint human and animal health interventions with committed funding by the respective governments and international donors. These activities require the development of a comprehensive plan for the continent, which can conceivably be coordinated by the AU, and aligning the activities to those included in the WHO roadmap for the eradication of zoonotic TB.

Although it has been known since the 1920s that various African wildlife species may contract BTB, for many years little attention has been given to the disease in wildlife in Africa. The occurrence of BTB in African wildlife and its impact on the epidemiology of the disease is dealt with in Chap. 5. Currently, at least, 29 different free-ranging wildlife species have been diagnosed with BTB. Few of them, such as African buffaloes, greater kudus, warthogs, and Kafue lechwe are maintenance hosts, sustaining the infection and transmitting the disease to cattle and other species at the interface. Most of the others are spillover hosts that may, or may not, play a role in transmitting the disease to other wildlife, livestock, and humans.

Globally, the role of wildlife as maintenance hosts of *M. bovis* infections, and their role in the epidemiology of the disease increasingly became apparent during the last few decades. This situation creates a major challenge for Africa against the background of the diversity of its wildlife and the extensive intermingling at the interface between wildlife, livestock, and humans in many parts of the continent. Bovine TB in wildlife may also impact negatively on the species infected, particularly those that are endangered and close to extinction, on conservation efforts, and on the income generated by the lucrative wildlife ranching enterprises in Southern Africa. Fundamentally, the only way in which the infection in wildlife could eventually be controlled would be by vaccination, but no effective vaccine has yet been developed. For African countries that want to attempt to control and eradicate

BTB, the extent of the infection and the epidemiology of the disease in wildlife will have to be determined, to allow the development of effective control programs that will have the potential to guide activities to eradicate the disease.

Wildlife, livestock, and humans are also infected by other species of the *Mycobacterium tuberculosis* complex (MTC) that evolved between 40,000 and 70,000 years ago from a common ancestral human pathogen of African origin. Many of these mycobacteria are host-specific but others cross species barriers. Some of the mycobacterial species are primarily found in Europe and Asia, but others, the African sublineage of the RD9-deleted clade, occur mostly in Africa. *Mycobacterium africanum*, a common cause of TB in humans in Western Africa, is rarely isolated from domesticated animals. The details of other wildlife-related species, including the chimpanzee bacillus, the dassie bacillus, *M. mungi*, *M. surricattae*, and *M. orygis*, are dealt with in Chap. 6. These organisms appear to be particularly host-specific and transmission to humans and livestock seems to be unlikely. However, being able to identify these mycobacteria may be important in the understanding of the epidemiology of TB in humans and animals, and the consequences of these infections for free-living wildlife and domesticated species. It is important, though, to keep in mind that the growth characteristics of these bacteria are poorly defined, that they are usually slow growers, and that they are difficult to culture. In addition, the genetic markers used to define lineages of the MTC may be ambiguous, and may result in the misclassification of some of the species in the MTC.

To adequately design control strategies for BTB, knowledge of its epidemiology that varies from country to country and even within countries is important. The data available for Africa are largely incomplete, fragmented, historical, often contradictory, and difficult to process. That which is known is collated in Chaps. 7 and 8, respectively, presenting the data based on the Epidemiologic Problem Oriented Approach (EPOA) and its molecular epidemiology. The lack of formal control measures for BTB, prevailing animal husbandry practices such as transhumance (leading to the uncontrolled movement of cattle and other livestock within and between countries), increasing urbanization and burgeoning smallholder dairy farming in urban and periurban areas, and the presence of the infection in a large number of wildlife species are distinctly different from the situation on other continents. Because of these differences, the epidemiology of BTB and zoonotic TB is anticipated to be different from those on other continents and unique for the African continent. Diagnosing the infection remains one of the most critical issues and is an additional complicating factor because of the lack of sensitivity and specificity of the various currently available diagnostic techniques.

The primary mode of transmission of the disease is dependent on the individual species, and often varies, depending on the local animal husbandry practices, within countries. In cattle, the main mode of transmission is by inhalation, but in certain settings, *per os* infection is important. Aerosol transmission is particularly important in cattle in a confined airspace and with crowding, but it also occurs when they are exposed to droplets of contaminated water, droplets expelled during eructation when grazing, and by inhaling contaminated dust particles. The presence of lesions in the palatine tonsils indicates that *per os* infection may be more important in cattle than previously anticipated. However, *per os* infection appears to play a lesser role in the transmission of the infection, as much higher doses than with aerosol transmission are required for cattle to contract the disease. This mode of infection, however, is more commonly seen in goats and camels. Few calves, unless fed pooled milk containing *M. bovis,* contract the disease by consuming infected milk because of the low occurrence of the infection in the udder of cattle. Predators, such as lions, too are prone to contract the disease *per os* while eating *M. bovis*-infected organs and tissues. Licking, grooming, and suckling also may result in *per os* transmission. Other forms of transmission, such as the percutaneous route, appear to be important in lions and in kudus.

Several host-specific risk factors play a role in cattle contracting the disease, and these are often related to specific management practices. Commonly, higher prevalences are encountered in urban and periurban smallholdings following uncontrolled movement of cattle between herds. But, contrary to the general expectation, in Africa, high prevalences can also be encountered in extensively managed cattle and other livestock because of the practice of housing them indoors at night in confined, roofed enclosures. Herd size, high animal densities, and the housing of cattle and other domesticated species are often proxies for the presence of and a high prevalence of the infection. Other herd-level risk factors in Africa include mixed rearing of domestic stock, such as goats, sheep, and camels, and intermingling with wildlife at the wildlife–livestock interface. Age is a risk factor and increasing numbers of infected animals are generally encountered with advancing age. This is particularly important in parts of Africa where cattle are kept for purposes other than the production of meat and milk; in those instances, the numbers of livestock owned are a sign of wealth, and they form part of a complex traditional social system. The role of gender as a predisposing factor varies according to management systems, and under specific circumstances, both cows and heifers, or oxen may present with higher prevalence rates. There were perceptions that breed may also play a role in susceptibility, and that African cattle breeds were more resistant to becoming infected with *M. bovis*, but ultimately it transpired that specific management practices were more important in determining the prevalence of the infection in the different breeds. Immune status may determine susceptibility to infection, and this too is an important risk factor in Africa, particularly in those animals owned by transhumant ethnic groups. Immunosuppression is a characteristic of animals kept under poor hygienic conditions, those subjected to climatic and feed stress, crowding and poor ventilation, and those with coinfections with pathogens that characteristically cause immunoincompetence.

Against the background of the very limited information about the extent and spread of BTB in Africa, it is clear that its distribution is not uniform. Its prevalence varies substantially between countries and also within countries where in certain regions the within-herd prevalence may be as high as 50%. This variation suggests the presence of hotspots of BTB within countries, and these may be the consequence of management practices, locality such as urban and periurban areas, and, in rural areas, factors such as communal water points and pastures and the aggregation of various herds during vaccination campaigns, at dip tanks, and at auction markets. Intermingling with wildlife maintenance hosts and contamination of the environment by feces or exudates following which mycobacteria may remain alive for varying periods of time that may be as long as 6 weeks during the winter, are additional sources of *M. bovis*.

The main epidemiological factors of importance in Africa determining persistence and spread of the infection include: the growing population and increasing demand for milk and meat, pastoral and transhumance husbandry practices, increasing herd sizes, confinement with high animal densities, and the practice of housing animals in homes during the night for security purposes. These practices are likely to persist indefinitely, and unless addressed, will serve to perpetuate the presence of BTB throughout Africa.

The use of molecular epidemiological techniques has become common practice in the developed countries to analyze outbreaks and the origin and spread of BTB. It is only recently that these techniques have been applied in some countries in Africa, but sufficient information has been generated to provide a broad understanding of the epidemiological dynamics of the disease on the continent. Using spoligotyping, deletion analysis, MIRU-VNTR, and RFLP as typing techniques, an evolving pattern of the distribution and movement of different *M. bovis* types could be determined.

A number of pivotal events that occurred over the last four millennia most likely determined the distribution of the various *M. bovis* types. The major events include, particularly, the occupation by the Romans and Arabs during earlier times, the migration of various ethnic groups within Africa, the more recent colonization by European countries, and the consequence of the devastating rinderpest epidemic that decimated cattle herds and caused a bottleneck in their numbers toward the end of the nineteenth century. Typing confirmed the presence of unique indigenous African strains of *M. bovis* that existed before colonization that has for long been assumed to introduce BTB into Africa. Based on archeological findings, it appears that *M. bovis* was already present in cattle and other livestock on the European continent about 4000 years ago and that it may thus also have been present in cattle in certain regions of Africa at that time. The distribution of these African strains was probably determined by the migration of ethnic groups in Africa, including the Bantu, from Western Africa, and the Luo, Mande, and Omoti people in Eastern Africa. Currently, there are two groups of *M. bovis* in Africa, those that are unique to the continent and those introduced by the settlers from the colonial countries. This latter group, having been introduced after the rinderpest epidemic, appears to be, with the exception of those in Western Africa, the major types of *M. bovis* in most of the African countries. In addition to the Af1, Af2, and the putative Af3 and five clonal complexes, a number of unique African spoligotypes also occur, for instance, in Chad, Tunisia, Ethiopia, Uganda, and Zambia to the south. Two complexes, Af1 and the putative AF5, occur in Western Africa particularly in Chad, Niger, and Cameroon, while most of the spoligotypes that occur in low frequency tend to be country-specific. The Af2 clonal complex is limited to the countries in eastern East Africa, as are some spoligotypes referred to as the "indigenous East African spoligotypes." The situation in Northern and South Africa is quite different, and in these regions, most of the spoligotypes belong to the Eur1 clonal complex, while in Madagascar all the isolates belong to the putative Af3 complex. Within this context, the dynamics and practices of livestock movements, the prevailing animal husbandry practices, and trade have had the biggest impact on the distribution of the various strains in the different African regions. Examples of these dynamics include the massive Sahel-Western African transhumant movement of humans and their livestock across international borders. These movements provide in-contact networks that promote the spread of the infection. In Eastern Africa, where the in-country profiles are more distinct, the effect of transhumance appears to be less, but it is, nonetheless, still apparent. Sudan appears to be the point of convergence of the two giant carousels of transhumant movement, and it may eventually play a pivotal role in the further dissemination of the various types of *M. bovis* in that part of Africa. In many of these countries, because of the changing dynamics in farming practices, and attempts to genetically improve the local breeds, there are also centrifugal and centripetal movements of cattle that, given the absence of any form of control of BTB, enhance the spread of the disease within these countries. Similar patterns of migration do not exist in Southern Africa, except for the localized migration in Zambia in the Kafue basin. In Southern Africa, as is the case in Zambia, and perhaps a developing trend in South Africa, the role of free-ranging wildlife in the epidemiology of the disease may become an important factor. Its role in the epidemiology of the disease in countries on the continent currently remains speculative because of the limited information about the disease dynamics in wildlife and their role in sustaining the infection in livestock. The extending wildlife–livestock interface, may yet, as in other countries, prove to complicate the control of BTB to the extent where it becomes impossible to control it. Application of molecular epidemiological techniques should equally address many of the questions about zoonotic TB, and the extent to which it occurs in those communities and groups of people at risk of contracting the infection.

A number of issues hamper progress in the management and control of zoonotic TB. In addition to the general assumption that it is not a problem in Africa, the lack of adequate disease control and eradication policies, the absence of continental reference databases and laboratory capacity for the isolation and genotyping of *M. bovis*, and the weak transdisciplinary and interlaboratory collaboration are major obstacles that will have to be overcome to get some degree of cooperation in regional and continental levels if the control of both BTB and zoonotic TB is to succeed in Africa.

Diagnosing BTB in live and dead animals is dealt with in Chap. 9. This is one of the most critical global impediments in the attempt to control BTB and zoonotic TB. The available tests and procedures all lack sensitivity and specificity, and are essentially herd, and not individual animal, tests. In spite of these deficiencies, some of the developed countries still managed to control and eliminate the disease from their cattle herds, albeit at a substantial cost, and over many years. In Africa, the lack of the technical capability and financial resources to use these tests commonly reduces the will of the politicians and regulatory authorities to control the disease.

As there is an international drive to eradicate human TB, by implication BTB and zoonotic TB must also be eradicated. Effectively eradicating the disease is dependent on the availability and use of detecting all the infected animals. In Africa, the lack of financial resources largely determines the diagnostic techniques that can be used, and meat inspection at slaughter remains the only affordable method by which the disease can be diagnosed and its spread and prevalence determined. Detecting BTB by meat inspection lacks sensitivity and specificity with the result that the information generated by its use is incomplete and unreliable. In many African countries, only a small percentage of carcasses for human consumption are processed, and most livestock are slaughtered informally and are not subjected to meat inspection. Using the data generated by the abattoirs largely becomes a process of counting numbers, without providing information that will augment the possibility of reducing the infection. There is a substantial variation in the epidemiology of BTB in individual countries and it is important that appropriate data are available to design effective control and eradication programs specifically for each individual country.

In addition to testing and applying the test-and-slaughter approach to deal with the disease, pasteurization of milk is the single most important intervention by which to reduce the prevalence of zoonotic TB. Although there is an increase in the provision of pasteurized milk, a large proportion of milk in Africa is still consumed raw, or after fermentation, particularly in rural areas where many ethnic groups are ill informed about the dangers associated with zoonotic TB and prefer raw instead of treated milk and meat. These practices remain a major risk, the extent of which is likely to increase with the increasing numbers of humans and cattle on the continent.

Tuberculosis is a disease without visible clinical signs, except for those in which it has reached an advanced stage. Even then, the signs are nonspecific and could be confused with those caused by a number of other diseases. This, too, is the situation in wildlife in which BTB may be asymptomatic, or cause nonspecific lesions that do not allow a definitive diagnosis. The intradermal skin tests (the single and comparative intradermal, and the caudal fold tests), and the INF-γ assay are the only ones approved by the OIE for use in cattle for diagnostic purposes. Although there is an increasing number of other tests, including serology, none of them has been validated and their interpretation remains uncertain, and many are less sensitive and specific than the skin tests. With the exception of African buffaloes for which the skin tests have been validated, the same situation prevails in wildlife.

In addition to being prohibitively expensive in Africa, the use of the skin tests in cattle and other livestock is also impaired by a number of other factors. One of the biggest problems in Africa is the lack of adequate road networks and other infrastructure to do the tests, and the reluctance of cattle owners to return their cattle to the testing site to evaluate the reaction. Further impediments include the limited availability of tuberculin, and the lack of trained human resources to do the tests. A number of other factors such as the impact of various types of stress and coinfection with diseases that cause immunosuppression and suppress the test reaction when doing the single intradermal test also play a role. Nonspecific reactions caused by infection with nontuberculous mycobacteria that cause nonspecific reactions in as many as 50% of animals tested in specific test cohorts are also major complicating factors in many parts of Africa.

Of all the available postmortal diagnostic techniques, meat inspection and necropsy remain the least expensive and, if correctly applied, one of the most specific and sensitive of the available diagnostic tests. For it to be used effectively, investigators must be adequately trained because of the extensive inter- and intraspecific variation in the macroscopical and histopathological appearance of the lesions and the difficulty of detecting them when only single lesions are present. In addition, the issue of no visible lesions and latent infections complicates the matter even further. Commonly when doing routine meat inspection in abattoirs about 50%, and in some reports, up to 90% of BTB cases are not detected. The meat inspection protocols in Africa are mostly insufficient for the purpose, and many of the meat inspectors are not well trained. If meat inspection is to be used as a diagnostic technique, the working conditions of meat inspectors will have to be improved and their workload reduced, the physical facilities in which they work will have to be improved, and quality control measures will have to be instituted.

The physical appearance of the lesions of BTB is not that typical. Hence, a final diagnosis cannot be made on visual inspection alone, and confirmation of the diagnosis should be made by histopathological examination, or preferably, by culture, which is considered the gold standard for diagnosing TB. The success of culturing is dependent on a number of factors including the way in which the specimens are collected, their storage and transport, and the media on which they are cultured. Culture in itself is only a means of isolating the bacteria, and they must be identified and typed using specific techniques. The commonly used molecular typing techniques in Africa include RFLP, spoligotyping, deletion analysis, and MVLA-VNTR, but their use is limited because of the cost, and the lack of trained human resources and adequate laboratory infrastructure. The interpretation of most of these tests also has to be adapted for specific countries because of the variation in the molecular biological characteristics of the strains circulating in each of them. Using combinations of tests is one way of solving this problem, but it is necessary to combine different tests for different countries, based on the variation, and the molecular characteristics of the *M. bovis* strains in each of them. Since most of the initial diagnoses are made during postmortal examination, confidently diagnosing BTB in African wildlife is even more challenging given the marked variation in the appearance of the lesions in the various species. This is an important issue because of the anticipated importance of wildlife in the epidemiology of the disease in many countries on the continent and the importance of determining their role in the epidemiology of the disease.

In Chap. 10, the available options for the control of BTB are dealt with. Because of the complexity of the disease, the lack of reliable diagnostic techniques, the absence of an effective vaccine, and the expected duration and cost of eradication programs, it is almost impossible for most of the African countries to attempt controlling the disease. The test-and-slaughter approach that has been applied by the developed countries is, however, currently the only available option, and poor countries will have no alternative when attempting to control BTB, but to apply the process in a selective way by focusing on hot spots of the infection, and those animals in areas that are of epidemiological significance. Testing alone is not the solution to the problem. To have any hope of success, surveillance to determine the extent and distribution of the infection, and to allow risk factor analysis, increasing the knowledge and attitude of farmers and policy makers, improving the competency of veterinary and abattoir officials, and improving movement restrictions and biosecurity measures should be addressed. Whether the African countries will be able to do this is a moot point, and without the support of international agencies and NGOs, it is unlikely that they will be close to attaining the international goal of eradicating both human tuberculosis, and by necessity, BTB because of its zoonotic potential.

Chapters 11–23 are reports of the situation in 13 of the 54 countries on the continent. In many of them, BTB is recognized as a major animal health problem. The variation in the status of the disease, its economic impact, the application (or lack) of control measures, and the zoonotic role of BTB is probably an adequate reflection of the situation in those countries that are not represented. These chapters provide a focused rendition of the situation that varies from a total lack of information, to the more sophisticated control programs applied by South Africa.

The information provided also emphasizes the marked differences in husbandry practices, ethnic traditions, and mostly the lack of control of the disease because of the lack of movement control within and across international borders. In addition, the lack of dealing with known BTB infections by not removing infected animals from the system and allowing free movement of them within countries and across international borders further complicate the process. These country reports also provide some insight into the ethnic practices that enhance the risk of contracting zoonotic TB and the general lack of knowledge about the disease, its dynamics, and the risk that it poses to human health.

If the content of this book manages to create awareness of an important neglected disease on the continent and to stimulate some form of activity to address the problems caused by *M. bovis* infections, it would contribute substantially to increasing the health and welfare of the humans and the health and productivity of the animal populations in Africa. We believe that this book provides useful information that will provide policy makers and regulatory authorities with a sound basis to enable them to make better-informed decisions about the importance of the disease and the need for its control and eventual eradication from the continent.

Chapter 2
The Current Status of Bovine Tuberculosis in Africa

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Tuberculosis in humans and animals is an ancient contagious disease, with a worldwide distribution. The cause of the disease in cattle, *Mycobacterium bovis*, has a wide host range that include domesticated animals, wildlife, and humans in which it has been categorized as a neglected zoonosis. The World Organization for Animal Health (OIE) considers it to be a notifiable disease because of its socioeconomic impact and public health importance. It is one of the most challenging endemic diseases to control and eradicate because of its complex epidemiology, insidious nature, and multiple wildlife maintenance hosts that can sustain the infection within ecosystems.

Before the detection of the presence of indigenous Af1 and Af2 strains of *M. bovis* that existed in Western and Eastern Africa before colonization, it was for long assumed that BTB was introduced by the settlers into the various African countries during the time of colonialism. During that time, it became a well-known livestock disease in many parts of Africa. Currently, the disease is present in many African countries but, due to the lack of financial and human resources, and the political will, only a few of them attempt to apply adequate control measures. As

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a consequence, the extent and the epidemiology of BTB in Africa are largely unknown, and the disease, with few exceptions, is mostly diagnosed during meat inspection in abattoirs and by the very limited use of routine tuberculin skin testing.

According to the OIE's WAHID, 24 of the member countries failed to provide any information about the presence of BTB in their country during the course of time, and it remains unknown whether the infection is present in them. Of the countries that include cases or outbreaks of BTB in their reports to the OIE, only 28 consider it as important enough to deal with as a notifiable disease in livestock, and only 4 list it as a notifiable disease in wildlife that now appear to play a pivotal role in the epidemiology of the disease in certain countries and should always be considered when attempting to control the disease in cattle.

Bovine TB in Africa is a regional threat, particularly at the human-livestock-wildlife interface. Few countries in Africa are currently conducting BTB eradication schemes, and those that do, most do not adhere to the OIE-based norms and standards for the successful control of the disease. The limited attention given to BTB and zoonotic TB in Africa against the background of its projected, almost unbridled increase in the numbers of its inhabitants has the potential for them in the future to become overwhelming animal and public health problems. These important but neglected diseases are likely to have a detrimental effect on the general population far in excess of what is currently perceived to be the case; this is because, by choice, the extent and the importance of a disease in livestock and humans that has been present from antiquity remain largely unknown and uncontrolled in Africa.

2.1 Background

Bovine tuberculosis (BTB), caused by *Mycobacterium bovis*, is a corrosive, insidious, debilitating, and contagious infectious disease of domesticated and wild animals and of humans. It has a worldwide distribution and is one of the most important illnesses of cattle. It spreads extensively within animal populations before clinical signs and the effects of the disease become visible.

The World Organization for Animal Health (OIE) lists BTB as a notifiable disease as it considers it to be of socioeconomic or public health importance within countries, with a negative impact on the international trade of animals and animal products and hence local livelihoods (Benkirane 1998; Skuce and Neill 2004). Because of its spread to wildlife and the establishment of wildlife maintenance hosts, BTB has the potential to affect the well-being of wildlife populations and the sustainability of ecosystems (Renwick et al. 2006). Countries with a thriving cattle industry apply regulations that control the trade of animals and their products to protect the national herd from the introduction of BTB, its spread to wildlife, to limit the risk of zoonotic human infection, and to prevent reintroduction of the disease following its eradication (Cousins 2001).

The disease in the various species is characterized by the development of tuberculous granulomas in the lungs, lymph nodes, intestines, liver, kidneys, and other organs, thereby affecting their health that eventually has a detrimental effect on their productivity. Presentation of the disease is variable: clinical signs are absent in the early stages, whereas animals with advanced disease present with non-specific signs such as weakness, anorexia, emaciation, and coughing. The characteristics of the disease and its manifestation are species-dependent and are usually determined by the route by which the animals are infected. There is a marked variation in organ tropism between species, the distribution of the lesions throughout the body, and the physical appearance of lesions between and, often, within species.

Mycobacterium bovis, the etiological agent of BTB, is a member of the *Mycobacterium tuberculosis* complex (MTC) (Skuce et al. 2012). Contrary to *M. tuberculosis*, it has an exceptionally wide mammalian host range (domesticated animals, wildlife, and humans), and it also has the ability to persist in the environment, the time of its survival being dependent on local climatic and environmental conditions (O'Reilly and Daborn 1995). It is important too as a significant public health threat as the infection causes zoonotic TB in humans following their close contact with infected animals or after consuming *M. bovis*-containing raw milk and milk products (Cosivi et al. 1998). Based on experience gained to date in countries actively attempting to eradicate the disease, it is clear that BTB is one of the most challenging endemic diseases to deal with, because of its complex epidemiology, the insidious nature of the disease, and the multiple hosts that sustain the infection within ecosystems. It is generally considered to be one of the neglected zoonotic diseases, and it is increasingly attracting the attention of the international community because of its quest to eradicate human tuberculosis in the foreseeable future.

2.2 Historical Perspectives

Bovine TB is a worldwide animal health problem, and the infection was most likely disseminated with the movement of people as they migrated, taking their livestock with them, and settled on the various continents and islands across the globe (Smith 2012). In the 1800s and early1900s, BTB caused considerable losses in the cattle industry (Martin 1994), and with the development of an intensive livestock industry in Europe and America in the early part of the twentieth century, the disease was recognized as a significant problem when intensive cattle farming was practiced. At that time, BTB was considered characteristically to be a disease of housed animals, and it was virtually unknown in extensive, rural farming systems in which the opportunity for droplet transmission was remote.

Because BTB, associated with intensified cattle production in the post-industrial revolution era, was a threat to animal and human health, several countries (led by the USA) attempted its eradication by:

1. Implementing BTB control programs for cattle
2. Improving milk hygiene and implementing pasteurization of milk for human consumption