Does *Mycobacterium bovis* contribute to the case load of human tuberculosis in Namibia?

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Abstract

Namibia has one of the highest infection rates of human tuberculosis (TB) in the world. The causative agent is generally asserted to be *Mycobacterium tuberculosis*. Renewed concerns have been raised globally in the last decades regarding the emergence of *Mycobacterium bovis* as a contributor to human TB. The pathogen is harbored by a number of mammalian animal species and, hence has a high zoonotic potential. Numerous investigations in recent years show evidence of the spread of *M. bovis* from the wildlife-livestock interface to humans in southern African countries. Rural communities in these regions are most at risk since livestock can easily be infected. Namibia is considered to be free of bovine TB in cattle because no cases have been reported since 1995. However the disease may be under-diagnosed in single cases especially in remote areas because of the slow and chronic course. Weakened animals might be slaughtered privately, with contaminated meat and raw milk from infected cows or goats being consumed. The aim of this review is to discuss the complex issues of diagnosis and epidemiology, and to highlight the importance of the differentiation of mycobacteria species in the medical laboratory for the outcome of patient treatment. *M. bovis* is clinically indistinguishable from human TB, possesses intrinsic resistance to at least one of the four first-line anti TB drugs, and shows a tendency to develop multidrug resistance. It poses a high risk predominantly for immuno-compromised individuals, as HIV-patients for example. Since Namibia has both - a high case load of HIV and TB - the occurrence and risk of zoonotic *M. bovis* in southern Africa should be discussed.

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1 Introduction

Namibia has one of the highest infection rates of human tuberculosis (TB) in the world, the high case load being attributed mainly to co-infection with Human Immuno-deficiency Virus (HIV) (WHO Report 2012; National Guidelines for the Management of Tuberculosis, 2012). Much is being done at the level of implementation, monitoring and evaluation of TB and leprosy control programs, and particularly on the programmatic management of drug-resistant tuberculosis (Ministry of Health and Social Services Annual Report 2012/2013). It is stated in the National Guidelines that TB in Namibia is almost always caused by *Mycobacterium tuberculosis* (Mtb) and rarely by other mycobacteria. However, this is a statement that needs to be elucidated since the conventional diagnostic methods, such as chest X-ray and sputum smear microscopy, cannot distinguish between different species of mycobacteria, and the clinical picture is indistinguishable from other forms of TB.

The genus *Mycobacterium* not only encompasses the causative pathogens of the human disease complexes tuberculosis and leprosy, but comprises numerous, ubiquitous, saprophytic species that are widespread in nature including several pathogenic species affecting animals as well as humans.

Mycobacterium bovis is the causative agent of bovine tuberculosis (bTB) in livestock, wild ruminants, such as bison, buffaloes or kudus, wild and/or domestic carnivores, and birds. Almost all warm-blooded animals can be affected. With some other mycobacteria species, this microorganism belongs to the *Mycobacterium tuberculosis* complex (MTBC). Bovine TB is known as a zoonotic disease, since the microbial organism spreads readily from animals, animal products and excretions to humans. BTB is a notifiable disease in most countries with slaughter policies and eradication programs (Cosivi et al. 1998). Some authors consider bovine TB as a relevant zoonotic human pathogen that aggravates the burden of HIV/AIDS and TB infection in Africa in addition to malnutrition (Ayele et al. 2004).

It might become of concern in the future to establish an accurate diagnosis, because global trends suggest a reoccurrence even in the industrialized countries, not only of TB, but also of human tuberculosis caused by *Mycobacterium bovis*. This brought *M. bovis* back into the focus of the stakeholders of public health, medical doctors, veterinarians and scientists because of the high zoonotic potential of the infection. Epidemiologic investigations revealed

that TB due to *M. bovis* mainly occurs in immigrants from the third world, either as silent or reactivated infection (Rivero et al. 2001; Mignard et al. 2006; Majoor et al. 2011).

It is not only the problem of the developed countries to deal with this issue, but this also raises the question of the contribution of *M. bovis* to the TB case load in Namibia. Due to its route of infection, this pathogen tends to cause extrapulmonary tuberculosis in the human patient. This term refers to a spread of tuberculous infection to sites outside the lungs, e.g., lymph nodes, pleura, brain, kidneys, or bones (McGraw-Hill Concise Dictionary of Modern Medicine, 2002).

The WHO reported 11, 145 TB case notifications in 2012 for Namibia, with 2, 063 cases of extrapulmonary TB (WHO Report 2012). Since an exact diagnosis of the causative agent could not always be performed, the role of *M. bovis* in the human TB case load remains an open question.

Numerous epidemiologic studies have been done in the last decades regarding the incidence of *M. bovis* in animals worldwide and in regard to the African continent, mainly the Sub Saharan region (Michel, A. 2002; Michel et al. 2006; Munyeme et al. 2008; Katale et al. 2012; Palmer et al. 2012; de Garine et al. 2013;).

Renewed concerns were upraised as a large proportion of the population lives in rural areas at the animal-human interface, and a spillover of infection from reservoir wildlife-hosts to domestic animals or even humans always constitutes a risk. The opposite route of infection poses a risk as well, because humans with *M. bovis* TB can also infect domestic animals or pets.

Abundant literature exists discussing the epizoonotic matter, the options for proper diagnosis and identification of the infectious agent, prevention, and treatment. No definitive solution is in sight so far, but initiatives need to be taken. The aim of this review is to highlight the situation in Namibia and propose initiatives.

2   Methods

To conduct this exploratory literature review, a number of online research engines were used including: Pubmed, Science Direct, and Google Scholar. Initially these web sites were searched for publications between May 2014 and January 2015. However the range of the search was extended back to 1983 when it became evident that despite comprehensive eradication programs bovine tuberculosis has re-emerged in the developed world in addition to spreading in developing countries, and has therefore been brought into the focus of public health. Since the existing literature spans a vast range of research relating to bovine tuber-

culosis, specific search terms were used to limit the yield in order to meet the intention of the review. Search terms used were: *Mycobacterium bovis*, bovine tuberculosis, zoonoses, Africa, Namibia. Limitations were then specified, for example, "in cattle". Articles or links from journals, magazines and periodicals of relevance were located; additionally, pieces of writing identified from the reference lists of relevant articles were included. Websites of several organizations were visited, such as 'World Organization for Animal Health' and 'World Health Organization'. Personal communication was sought with the Namibian State Veterinary Office, the Veterinary Council, the Central Veterinary Laboratory, and medical doctors from the TB ward of Katutura Hospital, Windhoek.

3   Epizoonotic situation in Sub Saharan Africa

In a report presented at a session of the World Organization of Animal Health (O.I.E.) at Paris 1983, Kleeberg, from the Tuberculosis Research Centre South Africa, described the global situation of human tuberculosis caused by *M. bovis* (Kleeberg 1984).The author concluded that human TB caused by *M. bovis* was less common than *M. tuberculosis* infection, but was still important. Although the incidence in the developed countries has been greatly reduced, wild animals such as badgers in Great Britain, opossums in New Zealand and kudus in South Africa could play an important role as spillover hosts of *M. bovis* and infect cattle herds. The function of primates and zoo animals as reservoir hosts was also underlined. The report did not loose of relevance since its publication.

In 1998, another article was issued from international authors working partly or the WHO and, partly for universities such as the Onderstepoort Veterinary Institute in South Africa (Cosivi et al. 1998). This paper discussed the importance of zoonotic tuberculosis due to *M. bovis* in developing countries, and stated that of 55 African countries only seven applied disease control measures as part of a test-and-slaughter policy and considered bovine TB as a notifiable disease. The authors found that approximately 85% of the cattle and 82% of the human population of Africa lived in areas where bovine TB was either partly controlled or not controlled at all. A review of zoonotic tuberculosis literature published between 1954 and 1970 in various countries around the world lead the authors to the estimation that approximately 3.1% of human TB cases were due to *M. bovis*. It was estimated that up to 10% of sputum isolates from patients in African countries could be positive for *M. bovis*. This evaluation was made even though *M. bovis* infection is known to more often cause extrapulmonary tuberculosis in man (Cosivi et al. 1998; Michel et al. 2009).

All authors agree that most likely these numbers do not mirror the real rate of *M. bovis* infection, since an exact diagnosis of the causative agent cannot be made in most cases of TB due to financial restrictions. Epidemiology and risk factors are summarized as follows:

the widespread distribution of *M. bovis* in the wild animal population, transmission being facilitated when wild and domesticated animals share water sources, pasture or territory, and the introduction of more exotic dairy breeds of cattle which are more susceptible for the infectious agent (Cosivi et al. 1998; Proano-Perez et al. 2009; Vordermeier et al. 2012); where maintenance hosts are present endemically in the wild, infection from these carriers to domestic animals is difficult to avoid; furthermore the consumption of unpasteurized milk, milk products and undercooked tuberculous meat are bad husbandry practices that increase the risk of infection.

The disease has an exceptionally wide mammalian host range, the bacterium being a robust pathogen that may survive in the environment, buildings, transport vehicles, pasture, and cow feces for several months, and in the soil for up to two years (Ayele et al. 2004).This may imply a contamination of the pasture and produce, and generally represents a potential source of infection for humans and animals.

As many cattle (and also small livestock) with bovine TB appear clinically healthy, the disease may stay undiscovered until progressive emaciation and weakness attract attention. In larger herds, the death of an infected animal might even pass unregistered or at least not raise suspicion. It may also happen that such an animal is slaughtered at home in order to utilize the meat as long as the animal is in slightly good shape. Some authors attest that the conditions for *M. bovis* transmission still exist unchanged in developing countries, and these populations even have a greater vulnerability due to poverty, HIV, and reduced access to health care (Michel et al. 2009). Consequently, the WHO, in conjunction with Food and Agriculture Organization of the United Nations and O.I.E. (Organisation Internationale des Epizooties, World Organization for Animal Health) has classified bovine tuberculosis as a neglected zoonosis in line with anthrax, brucellosis, echinococcosis, cysticercosis, rabies and trypanosomosis with special reference to developing countries (WHO Report 2006; Hortez et al. 2009).

4   The human-livestock-wildlife interface, a multi-species host-pathogen system?

The occurrence of bovine tuberculosis in wildlife in southern Africa became evident in the 1990s, when the bacterium was first isolated in buffalo in Krueger National Park (KNP) in Tanzania. The evidence suggested that buffalo herds contracted the disease by grazing with infected cattle in the same area (Renwick et al. 2007). The same authors stated that the more recent detection of other animal maintenance hosts would indicate the existence of bTB in Africa as a multi-host pathogen within a multi-species system. This means that the dynamics of infection differ largely from single-host systems, where the density of a

host population needs to exceed a threshold for the disease to invade and persist in the population. In multi-host system, there it is a threshold community configuration, where a lower population density may be replaced by a higher interaction rate between the different species, which results in the amplification of the spread of infection. These conditions occur all over Sub Saharan Africa, as the geographical situation favors the movement of animals through the savannahs.

A review from 2013 assessed the main risk factors of bTB spillover at the wildlife-livestock-human interface outside of KNP in Sub Saharan Africa (de Garine et al. 2013). *M. bovis* could be isolated from 17 wild mammal species, and although only four were suspected to play a role as maintenance host, the zoonotic risk was emphasized by the authors. A cross-sectional study carried out in 2008 in Zambia (Munyeme et al. 2008) revealed a high presence of bTB in the livestock-wildlife interface of certain regions of the country. This was considered to be a serious public health concern, since the communities live in close contact with their animals and are likely to consume untreated milk.

The generally accepted assumption that tuberculosis in humans results from a single infection with a single *M. tuberculosis* strain was challenged in 2004. A South African study showed that patients with active tuberculosis can have different strains in the same sputum specimen. Concerns were raised that a superinfection by *M. bovis* in human TB patients could play a potential role in regions where bTB is endemic (Warren et al. 2004; Michel et al. 2006).

The four most important African wildlife species susceptible to bTB mentioned in the research papers were African buffalo, greater kudu, Chacma baboon and carnivores (lion, cheetah, leopard). All four groups do also live in Namibia.

5   Situation in Namibia

In Namibia, the Animal Health Act from 2011 provides for the prevention, detection and control of animal disease (Animal Health Act 2011). Appendices containing the notifiable animal diseases are issued in this context. Regulations are promulgated in terms of the Act relating to the control of bovine tuberculosis. These order that compulsory testing of cattle must be performed in a bovine tuberculosis eradication area, which means that endemic bTB must be diagnosed in certain regions.

BTB is a notifiable disease, if suspected it must be reported to the Directorate of Veterinary Services. This will largely depend on the knowledge and responsibility of the animal owner/keeper who evaluates the health state of the animals. BTB is often clinically silent for long periods of time until emaciation, cough and general weakness occur. Illness can

easily be misjudged, with a diseased animal being slaughtered at home and consumed. In slaughter houses samples are only taken in cases of suspected bTB or evident signs such as enlarged cervical (or other) lymph nodes. A strict slaughter policy does not exist in the sense of an eradication program. It all depends on the alertness of the people involved if they become aware of signs of a *M. bovis*-infected animal.

Namibia is considered to be free of bovine tuberculosis, with the last occurrence in cattle since 1995 being reported in 2004, as indicated by 'screening' (Renwick et al. 2007). 'Screening' refers to a discovery test method that aims to detect healthy animals within a herd or a flock, which signifies a negative test result. The diagnostic test method commonly used is the delayed-type hypersensitivity intradermal skin test. The predictive value of a negative test and the prevalence of infection are inversely related (Adams 2001).

It remains a matter of speculation if, in the meantime, no cases of bTB occurred in the livestock or were simply never suspected or noticed, and verified using confirmation test methods. However the interpretation of those findings might depend on the focus of the observers. Two publications are to be mentioned which do not stress bTB in particular and focus more generally on zoonoses, but nevertheless come to a similar conclusion:

Kudakwashe and co-authors examined the prevalence of zoonotic infections reported in Namibia between 1990 and 2009 with regard to their potential impact on the growing wildlife industry (Kudakwashe et al. 2012). They confirmed a wide spectrum of zoonotic diseases in both livestock and wildlife species, with anthrax and rabies being most represented. The species distribution of zoonotic infection in Namibia during this time was published in the Annual disease report 2011 by the Directorate of Veterinary Services, and showed little evidence for bTB. For cattle, goat and suricate (indigenous mongoose), under two animals of each species were reported to be affected; only poultry were recorded with two or slightly more cases. The evaluation methods or criteria of the record however were not discussed (Directorate of Veterinary Services 2011).

The authors stated that the economic impact and the extent to which zoonoses contribute to human illnesses and death in the Namibian population were unknown, as these infections are likely to be considerably under-diagnosed. Another study was conducted in 2012 on behalf of the Meat Board, Namibia in order to examine the risk of animal disease hazards associated with import of animals and animal products (Thomson and Venter 2012).

This risk analysis concluded that the major animal disease threats to Namibia's livestock industries are posed by the illegal entry of live animals that are either smuggled across the country's borders or stray across the fencing system that protects Namibia's export zone against incursions from the north and north-east. The transboundary animal diseases (TADs) mentioned to cause the greatest danger to Namibia were: Foot and Mouth disease, Contagious Bovine Pleuropneumonia, Peste des Petits Ruminants, and Contagious Caprine

Pleuropneumonia.

It is evident that bTB is not part of the TADs as formulated in this study. This does not necessarily contradict the previously discussed findings, since the focus of the Meat Board study is clearly on the most frequent infectious diseases spread through food (food-borne diseases) and contact with diseased food-delivering animals. The diseases listed above are relatively easily to diagnose, and the classical signs appear early in the course of infection, which facilitates reporting to the Directorate of Veterinary Services or respective control entities. Conversely, bTB might only be diagnosed in vivo at a very late stage of infection, when the animal in question shows emaciation, weakness and/or respiratory distress. Such an animal is unlikely to be driven to market. However, this study sheds light on the different ways domestic and wild animals may cross borders, as for instance, by migrating to grazing places in times of drought, scarcity of food, or on wildlife escape-routes. Although not yet established statistically, bTB carriers could still cross/have crossed borders and spread the infection.

In Namibia, the animal health surveillance of livestock is carried out by the veterinary department of the Ministry of Agriculture, Water and Forestry. Control activities at the farm level are performed by teams of animal health technicians (AHTs) and official (State) veterinarians, who operate from a network of 17 State Veterinary Offices distributed throughout the country. This stands against the roughly 2.4 million heads of cattle countrywide to be screened, plus 2.6 million sheep, 2 million goats and 50.000 pigs, almost all of which are kept extensively on pastures/fields. The AHTs visit all registered livestock owners annually for an animal survey, control of obligatory vaccinations, conditions of environment and examination of physical appearance of the animals. It is evident that within the frame of this large program not all relevant epidemiological issues can be approached or solved (Thiermann and Hutter 2007).

As a member of World Trade Organization (WTO) and O.I.E., Namibia is bound to the provisions made by these cooperatives. In this context an evaluation of Namibian Veterinary Services was carried out in 2007 with the objective of identifying both strengths and gaps in their capabilities using the criteria set out in the O.I.E. Terrestrial Animal Health Code (2007).

The original idea of asking the O.I.E. for this evaluation came from Namibia's Agricultural Union. The strengths identified on the personnel level were high qualification, commitment and organizational skills, whereas a weakness was the lack of sufficient veterinary professionals and understaffed teams, with most of the field work being done by trained AHTs and not by veterinarians. No involvement of veterinarians or trained personnel in municipal and local nonexport abattoirs was seen in this study, and these can most likely be points of occurrence of emerging diseases. The study further reported that no ante-mortem and post-mortem inspection by veterinarians in local and municipal abattoirs were performed,

and the inspection in these abattoirs was only a meat hygiene inspection, with no animal health controls (Thiermann and Hutter 2007). The evaluation concluded, that active or passive surveillance programs exist for all of these diseases, but not all of them have effective control programs implemented.

Under 'detailed findings during visit', it was explicitly stated that: 'Tuberculosis in animals is not found in Namibia - all imported bovine receive intradermal test'. As a matter of fact there were no outbreaks of bovine tuberculosis in Namibia in the last decades, but this does not mean that undiagnosed and unreported cases of bTB did not occur. Due to the lack of the establishment of an exact diagnosis in animal and human patients, a number of unreported cases still occur, and hence pose a potential zoonotic risk.

6   Issues of Diagnosis

The diagnosis of tuberculosis in the human patient is routinely achieved by a combination of chest X-rays, the intradermal skin test (to detect cases of latent TB), and a sputum smear. Standard bacteriological procedures are well-described, and the staining of sputum, with acid-fast Ziehl-Neelsen or auramine stains followed by microscopy, can be performed immediately. Culturing of the microorganism on special media and identification of the different species of the MTCB by colony morphology and a panel of biochemical tests require several weeks, a biosafety level three laboratory, trained personnel and thorough practice. Decontamination procedure for specimen handling and incubation conditions must be observed. The basic laboratory tools of acid-fast staining and microscopy are not suited to distinguish between the numerous species of mycobacteria; not even the non-tuberculous environmental mycobacteria can be discriminated. An accurate diagnosis of *M. bovis* infection in the human patient cannot be established by the use of only basic laboratory methods, neither by the clinical examination or radiography. Research is ongoing for alternative methods that are rapid, cheap and easy to perform, in order to overcome the principal obstacles to improving in vivo and in vitro diagnosis of mycobacteria species (Adams 2001; Ayele et al. 2004;).

The most commonly used techniques are antibody-based, cell-mediated immunity-based, and molecular diagnostics. Molecular biology techniques based on genetic analysis have been proven to be the most successful in the differentiation of mycobacteria species and strains in isolates, for example nucleic acid recognistion methods. Genes coding for the MTCB-specific proteins are used, with insertion sequences targeted by polymerase chain reaction (PCR) or DNA probes. This way a variety of DNA-fingerprinting techniques has been developed to distinguish the MTCB isolates for epidemiological purposes. These methods cannot only distinguish between different species of mycobacteria but can also single out different strains

of *M. bovis* or *M. tuberculosis*. The most widely used method is spoligotyping (from 'spacer oligotyping'), which allows the differentiation of strains inside each species belonging to the MTCB, including *M. bovis* (O.I.E. Terrestrial Manual 2009).

The implicit drawbacks of this methodology are the high costs of technology and equipment, the need for thoroughly trained technicians and the reliability of material supply. Despite this, a widespread application of molecular typing in developing countries would clearly enhance the epidemiological surveillance of the disease.

7   TB-Diagnosis in Namibia

The Namibia Health Facility Census 2009 (Namibia Health Facility Census 2009) describes the situation for TB patients in Namibia as follows: "Most (87%) facilities provide tuberculosis (TB) diagnosis, treatment, and/or follow-up services. TB services are available in 96% of health centres, 88% of clinics, 80% of hospitals, and 56% of sick bays. Facilities in Caprivi and Oshana are most likely to offer TB services. Eighty-two percent of facilities offer any TB diagnostic services. Health centres (91%) are most likely to have TB diagnostic services. MoHSS (88%) and Mission/NGO facilities (89%) are more likely to offer TB diagnostic services than private (43%) or MoD/Police facilities (62%). Three-quarters (77%) of facilities report diagnosing TB using sputum microscopy, the recommended diagnostic procedure. However, less than half (48%) of those that reported using the sputum test had all the items needed for conducting TB sputum tests available on the day of the survey. Three-quarters (75%) of sick bays had all items needed to conduct the TB sputum test compared to less than half of hospitals, health centres and clinics."

It might be concluded that, at least in 2009, only half of the health facilities in the country were adequately equipped for the conduction of TB sputum tests, which is a comparatively simple and basic diagnostic screening tool. This method is also only suited to detect pulmonary tuberculosis and not the extra-pulmonary manifestations which also play a role in TB case load. Furthermore, a differentiation between *M. tuberculosis* and *M. bovis* cannot be made using this test. One of the implications of *M. bovis* infection is the intrinsic resistance of this species to pyrazinamide, one of the four first-line TB antibiotic drugs, and the prognosis is often poor. Multidrug-resistant strains of *M. bovis* have been detected in the USA and Spain in the last decades, particularly in HIV patients (Bouvet et al. 1993; Rivero et al. 2001; Katale et al. 2012).

In the TB ward of Katutura Hospital, Windhoek, a more precise diagnose can be established by means of GenXpert, a computerized method detecting DNA sequences for *M. tuberculosis* and rifampicin resistance by PCR. It is based on nucleic acid amplification tests

as described above. The system purifies and concentrates the bacilli from sputum samples and isolates genomic material from the bacteria. The process also identifies all clinically relevant rifampicin resistance genes, and results are obtained within 90 minutes. The test poses minimal biohazard risk and needs relatively little training to operate. The test limitations are that other members of MTBC, resistance to other antibiotic drugs, and extrapulmonary disease cannot be identified (GeneXpert 2014; Gene Xpert (Cepheid) 2014).

8   Animal testing

In vivo diagnosis of bovine tuberculosis in animals is mainly based on the intradermal skin reaction test carried out with purified protein derivative (PPD) from *M. bovis* culture. For details of this method, please refer to the following literature (Adams 2001; OIE Terrestrial Manual 2009; Michel et al. 2009; Strain et al. 2011). Sensitivity and specificity of this test method may vary depending on the timing of application, immune status of the animal, purity of PPD preparation, method of injection, exposure to field strains, immunosuppression post partum, and inter-observability in judging the DTH reaction. Molecular techniques are also being developed to facilitate animal testing, but in the meantime the use of direct smear microscopy of tissue material and bacteriologic culture are still regarded as the gold standard for TB diagnosis, although in practice are only feasible post mortem.

9   Conclusion

The emergence of bTB in developed countries, in addition to it being a multi-species host-pathogen at the animal-human interface in southern Africa, has led to an increased awareness worldwide of this disease and the potential zoonotic risk. Namibia, being chiefly an agricultural country and situated in the South West of the African continent, has one of the highest infection rates of human tuberculosis in the world, which may raise the question of the contribution of *M. bovis* to the TB case load. It was revealed that statistics and stakeholders of the Namibian Public Health Sector minimize the occurrence of bTB in livestock or wildlife, which may not reflect the epidemiological reality. Undiagnosed, and therefore, unreported cases of bTB are likely to occur in animals, particularly in remote rural areas close to the wildlife-interface, and represent a zoonotic hazard for the community. BTB shows a tendency to rather cause extrapulmonary tuberculosis in man, which makes a diagnosis more difficult or complex.

Clinical and laboratory diagnosis needs expertise and sophisticated equipment, particularly when it comes to the differentiation of species and strains of the MTBC. The classical

way of dealing with zoonoses would commonly be to start from the animal health aspect by involving the State Veterinary Offices. As these entities are chronically understaffed and in charge of the recording, testing for and limiting of other notifiable diseases mainly affecting meat producing animals and the export sector, no resources will be available. So it may become a task for UNAM and related stakeholders to describe some pertaining research questions, as for instance, to investigate the prevalence of bTB in a small sample of cattle in a defined rural area, e.g. in a wildlife-livestock-human interface in the northern parts of the country. Another option may be to test a patient cohort positive for TB also for the presence of *M. bovis*, which implies cooperation with laboratories outside the country. Likewise a resistance to conventional antibiotic drugs could be assessed in this context.

Beside this another approach is thinkable. Instead of trying to test huge numbers of animals, the inverse road can be taken - from a sample survey of diseased patients to the suspected source of infection:

1. A thorough anamnesis must be established for a patient suspected to have TB, the most costly aspect possibly being a translator and the acquisition of detailed knowledge by the investigator;

2. Questions to be asked will deal with the patient's background, living conditions, and occupation (including any contact to animals); this way a rough screening for zoonotic potential can be achieved;

3. Simultaneously a laboratory diagnosis for both *M. tuberculosis* and *M. bovis* should be established; it would be recommended to purchase suitable equipment for PCR-based molecular typing of mycobacterial species;

4. In cases of positive results for *M. bovis*, trace back the patient's background and inform the state veterinarian;

5. Find the potential animal source, and take relevant measures, to limit the source of infection (= targeted action);

6. Test contact persons specifically for *M. bovis*;

This could allow for the establishment of an exact diagnosis for the human patient as well as the ability to trace the animal source of infection for the case and possibly others. The advantage for the human patient lays in the early discovery of a disease with a poor prognosis in late discovery, the avoidance of unnecessary treatment with first-line drugs to which *M. bovis* is intrinsically resistant, and development of an effective treatment regimen.

Theoretically the relevant information is in place, however, the limitations of this review are the absence of recent data gained by own field studies in Namibia, or thorough cohort

survey carried out in the hospital settings. Online research did gather relevant data showing the increasing significance of the spillover of *M. bovis* from the wildlife-human interface in southern Africa and the imminent difficulties of the accurate identification of the causative agent. Practical work needs now to be done to get reliable data about the current situation in Namibia, in order to evaluate the epidemiological status in regard of this zoonosis.

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