Tuberculosis

Bovine tuberculosis at the animal–human–ecosystem interface

Introduction

Bovine tuberculosis is a chronic disease of animals caused primarily by *Mycobacterium bovis* (*M. bovis*), a member of the *M. tuberculosis* complex. The disease is characterized by progressive development of specific granulomatous lesions or tubercles in lung tissue, lymph nodes or other organs. The incubation period ranges from months to years, but acute stages of the disease can develop during the course of infection, when lesions progress rapidly.

Bovine tuberculosis is an important disease in livestock and in a wide range of wild animal species worldwide. Bovine species, including bison and buffaloes, are particularly susceptible to the disease, but nearly all warm-blooded animals can be affected. *M. bovis* is also known to affect humans, causing a serious public health problem when it becomes endemic.

Similar to the human form of tuberculosis, bovine tuberculosis is commanding growing attention from the international community. This is because of the serious increase in the number of infected herds and the subsequent effect on animal production, combined with the significant impact of *M. bovis* infection on public health, and the permanent threat of infection from animal reservoirs. Despite the long history of disease recognition, the epidemiology of *M. bovis* is not well understood, especially in wildlife. In some developed countries, the disease has been eliminated from the livestock population, but in other countries wildlife species have been identified as reservoir hosts, representing a continuous threat and source of infection of cattle and making complete eradication difficult. In less developed countries, the disease is maintained in bovines and continues to cause significant losses in the cattle farming sector, with serious implications for public health, especially where there is no effective surveillance and control programmes are weak or non-existent. In response to the global importance of bovine tuberculosis for both animal and public health, the Food and Agriculture Organization of the United Nations (FAO) has recognized it as a priority infectious disease that should be controlled at the animal–human–ecosystem interface, through national and regional efforts.

This article does not aim to provide a comprehensive description of bovine tuberculosis, which can be found elsewhere (Michel, Müller and van Helden, 2010; Thoen et al., 2009), but rather to outline the main features of bovine tuberculosis in cattle and wildlife, the impact of the disease on public health, and perspectives on its control, with particular reference to the situation in developing countries.

Global distribution and socio-economic impact

The geographical distribution of bovine tuberculosis has changed drastically over recent decades. Prior to the introduction of control measures and milk pasteurization in developed countries, tuberculosis was widely distributed throughout the world. Eradica-
tion programmes based on surveillance and test-and-slaughter policies to clear herds of infected animals virtually eliminated tuberculosis from livestock in many developed countries. Today, many countries in Europe and North America, and Australia are free of the disease or close to its complete eradication in livestock. However, the maintenance of *M. bovis* infection in wildlife species has significantly compromised eradication efforts in countries such as Ireland, New Zealand, the United Kingdom of Great Britain and Northern Ireland and parts of the United States of America (Thoen et al., 2009).

In developing countries, data on the prevalence of bovine tuberculosis are minimal, and the information available may not represent the true epidemiological status of the disease. Although bovine tuberculosis is notifiable in many countries, it is often underreported, particularly in countries that lack effective disease surveillance and reporting systems. The insidious nature of the disease, which does not cause fulminating outbreaks with high mortality, is likely to decrease recognition and reporting, leading to a lack of measures for its control.

Despite disease underreporting in developing countries, however there is sufficient evidence to indicate not only that the prevalence of disease is higher in the developing nations, but also that in the absence of national control and eradication programmes, it is increasing worldwide, particularly in Africa, Asia and Latin America (Thoen et al., 2009). According to the World Animal Health Information Database (WAHID) of the World Organisation for Animal Health (OIE), 70 countries reported bovine tuberculosis cases in their cattle populations in 2010, and 49 countries in 2011 (Figure 1).

The economic impact of bovine tuberculosis on livestock production is extremely difficult to determine accurately. The disease decreases livestock productivity and may be economically devastating for the cattle industry, especially the dairy sector. Milk yields and draft power can be significantly reduced, with direct effects on the livelihoods of poor livestock holders. Most important is the impact of infection in humans – particularly women and children, who appear to be more susceptible to the disease – in countries with poor socio-economic conditions and weak veterinary and public health services. Although estimates of the costs associated with bovine tuberculosis and its

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**Figure 1:** Geographical distribution of bovine tuberculosis (BTB) for 2010 and 2011 based on OIE six monthly reports

Source: OIE WAHID adapted by FAO EMPRES-i.
control refer only to specific countries, all data suggest that worldwide economic losses due to the disease are significant. These losses include those related to animal production, markets and trade, as well as the costs of implementing surveillance and control programmes. Losses to tuberculosis are also extremely important when endangered wildlife species are involved.

Impact of *M. bovis* infection on human health

Bovine tuberculosis is a zoonotic disease that can have serious consequences for public health. Transmission of *M. bovis* from cattle to humans was once common in developed countries, but human infections have been virtually eliminated in countries with effective programmes for eradicating the disease in cattle, and high standards of food safety, particularly the pasteurization of milk. The incidence of human tuberculosis due to *M. bovis* varies considerably among countries, depending on the prevalence of the disease in cattle, socio-economic conditions, consumer habits, and food hygiene practices. In developed countries, *M. bovis* generally accounts for an insignificant share of total tuberculosis cases in humans. It causes less than 2 percent of all tuberculosis cases in the United States of America (CDC, 2011), and has been estimated to cause less than 1.5 percent of confirmed human cases in the United Kingdom of Great Britain and Northern Ireland (de la Rua-Domenech, 2006). In the Netherlands, *M. bovis* infection represented about 1.4 percent of all tuberculosis cases during 1993 to 2007 (Majoer *et al.*, 2011).

In developing countries, the occurrence of human tuberculosis due to *M. bovis* is difficult to determine accurately, and probably remains underreported owing to the diagnostic limitations of many laboratories in isolating the microorganism and distinguishing *M. bovis* from *M. tuberculosis*. Prevalence of the disease is likely to be higher in countries where *M. bovis* infection is endemic in cattle, and milk is not routinely pasteurized. Some reports have speculated that *M. bovis* accounts for 10 to 15 percent of human tuberculosis cases (Cosivi *et al.*, 1998), while other estimates range from 0.4 to 8 percent, demonstrating that *M. bovis* is an important factor in human tuberculosis (Grange, 2001). Consumption of untreated dairy products from infected cows is the usual mode of transmission of tuberculosis from animals to people. This mode is particularly dangerous for children, who appear to be most susceptible to the disease in rural areas. The infection can also occur through airborne transmission, especially where humans work in the immediate vicinity of infected cattle or carcasses and/or share premises with infected animals. People suffering from *M. bovis* tuberculosis can retransmit the infection to cattle, but this is not common. Mounting evidence supports the likelihood of human-to-human airborne transmission of *M. bovis* from patients with pulmonary disease, but the relative contribution of this mode to new infections in humans is unknown (LoBue, LeClair and Moser, 2004).

As is also true of *M. tuberculosis* infection, the risk of *M. bovis* infection in humans is likely to increase where HIV/AIDS prevalence is high, because immunosuppressed AIDS...
patients are susceptible. Cases of HIV-related human tuberculosis due to *M. bovis* have been reported in many developed countries (WHO, 1994). The potential impact of an AIDS pandemic or HIV infections in humans on the transmission of *M. bovis* to and among humans is of great concern and requires careful consideration wherever bovine tuberculosis is still a major problem (WHO, 1994; Grange, 2001).

**Tuberculosis in wildlife**

Bovine tuberculosis has emerged as an increasingly important disease of both captive and free-ranging wildlife populations. Tuberculosis in wildlife increases public health concerns and interferes with tuberculosis eradication programmes in cattle. *M. bovis* can infect a wide range of wild animals, which can act as either reservoir hosts, capable of maintaining and spreading the infection by intra-species transmission, or spill-over hosts, when infection is not maintained in the wildlife population. The range of wild animal hosts and reservoirs of infection varies among regions. The African buffalo (*Syncerus caffer*) is considered to be a maintenance host for *M. bovis* in South Africa’s Kruger National Park (Michel, Müller and van Helden, 2010), with infection spill-over to other wildlife species in the park (de Vos et al., 2001). Wapiti (*Cervus elaphus*) and bison (*Bison bison*) are considered wildlife reservoirs of *M. bovis* infection in Canada (Nishi, Shury and Elkin, 2006); the white-tailed deer population is the first acknowledged wildlife reservoir of bovine tuberculosis in the United States of America (de Lisle et al., 2002); European badger (*Meles meles*) populations are reservoir hosts in Ireland and the United Kingdom of Great Britain and Northern Ireland (Corner, 2006); and brushtail possums (*Trichosurus vulpecula*) are the primary wild maintenance hosts of bovine tuberculosis in New Zealand (Nugent, 2011). Tuberculosis in captive deer or wild cervids has been observed in many countries in Europe and North America. There is increasing evidence that wild boars (*Sus scrofa*), once thought to be spill-over hosts, are actually maintenance hosts of *M. bovis* for other wildlife and domestic animals in Europe (Parra et al., 2008). Wildlife may contaminate cattle by direct or indirect contact, and many questions remain regarding wild and *M. bovis* transmission at the livestock interface. Although direct transmission is probably rare, it may be possible when infected animals are at a late stage of the disease. Indirect transmission is more frequent through contamination of the environment, water and feed by excretions of wildlife.

**Options for control and eradication of bovine tuberculosis**

Control and eradication of bovine tuberculosis is a desirable objective both from an animal health perspective and because of the zoonotic implications of *M. bovis*. Control and eradication have been achieved in many countries through test-and-slaughter policy combined with abattoir surveillance.

**Surveillance of bovine tuberculosis, and testing tools**

The tuberculin skin test is the standard testing tool for detecting tuberculosis in live animals and is the primary cattle screening tool currently available. It is referred to
as a single intradermal test when bovine tuberculin is used alone, and an intradermal comparative test when both bovine and avian tuberculins are used. The latter can distinguish between infections with *M. bovis* and sensitization to other Mycobacteria species. The tuberculin skin test has been widely applied for screening in eradication campaigns, with successful results in many countries. Nevertheless, the test has limitations, including difficulties in interpreting results and imperfect test accuracy. This lack of performance, particularly when infected animals are not picked up, can impede progress in a herd sanitation programme using test and slaughter. Unnecessary elimination of false positive reactors may also have serious implications on cattle management. Additional limitations are related to the time, expense and stress of handling cattle multiple times. The test requires 72 hours between administration of the tuberculin and reading of the reaction, so cattle have to be handled twice.

Several other tests have been developed to improve diagnosis and screening of bovine tuberculosis. Among these is the interferon gamma assay, which detects the production of gamma interferon by the T lymphocytes in the blood. Studies on the specificity of this test have contributed to significant improvements in the detection of *M. bovis* in cattle and wildlife populations. However, the interferon gamma assay is not used routinely for diagnosis of bovine tuberculosis and appears to be impractical for use in developing countries, as it requires delivery of samples to the laboratory within a day, for processing using relatively sophisticated and expensive techniques (Michel, Müller and van Helden, 2010; de la Rua-Domenech, 2006).

Studies have compared the sensitivity and specificity of the tuberculin skin test and the interferon gamma assay (Whipple *et al.*, 1995; Wood *et al.*, 1991). These studies showed that for both tests results may differ depending on the conditions in which the test is performed, the reagents used, the chosen cut-off point for the stage of development of the infection, the immune status of the animal, etc.

Identification of bovine tuberculosis by meat inspection at slaughterhouses is another important surveillance instrument, although its sensitivity is rather low. Depending on the prevalence of the disease in the country, abattoir surveillance can be used as a cost-efficient method alone or combined with routine cattle testing. However, this assumes reliable inspection practices at slaughter, supported by an efficient animal identification system and adequate record-keeping at both the farmer and the slaughterhouse levels.

**Test and slaughter**

Most of the countries that have eradicated or markedly reduced the prevalence of bovine tuberculosis in cattle have done so through effective implementation of a test-and-slaughter policy. Herds are tested using the tuberculin skin test and reactors are immediately removed for slaughter. The herds are then retested after prescribed periods, until no further reactors are detected and there is no evidence of tubercules in reactors at slaughter.
The success of control programmes based on test-and-slaughter strategy depends on institutional and technical requirements, including:

- an efficient cattle identification system that allows effective trace-back to the herds of origin of tuberculous animals detected through slaughterhouse surveillance;
- a high standard of meat inspection practices, enabling effective surveillance for tuberculous lesions in animals passing through slaughterhouses;
- an animal health information system for recording relevant information, including epidemiological investigations, and data analysis to monitor progress and guide decision-making;
- a legal framework for enforcing control measures and compensating farmers for slaughter of tuberculin-positive reactors;
- full control of movement of cattle, including cross-border transhumance;
- political support, with the cooperation of stakeholder groups and public awareness, to ensure the success of the bovine tuberculosis control and eradication programme;
- public awareness campaigns and sensitization of farmers and the general public on bovine tuberculosis hazards and hygiene practices, and awareness of the objectives, benefits, challenges and other implications of surveillance and control;
- incentives for farmers to adhere to the eradication programme, such as guaranteed milk prices and favourable subsidies for disease-free herds;
- financial resources for adequate and speedy compensation of farmers for losses due to removal of infected animals;
- laboratory diagnostic capability for tuberculosis diagnosis based on the isolation and species identification of the bacterium from tuberculous lesions on organs.

Treatment and vaccination
The treatment of tuberculosis-affected livestock with medications has had limited success and is forbidden in most countries, particularly because of the potential for increasing the drug resistance of Mycobacteria. A few rare animal species in captivity have been treated with medications, but this is not really a viable option for a herd of free-ranging animals (Michel et al., 2006). At present, control or eradication by means of treatment is neither feasible nor permitted in most countries.

Currently, the only vaccine against M. bovis infection is bacille Calmette-Guerin (BCG), which is a live attenuated strain of M. bovis. Apart from the limited efficacy of BCG vaccine in cattle, it can also compromise the tuberculin skin testing of animals. BCG vaccination has been tested in wildlife through experimental and field trials with
promising results (Buddle et al., 2011). However, so far, no practical or effective vaccination approaches have been developed for any species. With advanced research on the genome sequences of *M. bovis* and the BCG vaccine, and the development of other types of vaccines such as subunit vaccines (in the form of desoxyribonucleic acid [DNA] vaccines) or adjuvated protein subunit vaccines, along with improved understanding of the protective immune response, it may become feasible to design and develop effective mycobacterial vaccines and vaccination strategies for preventing or controlling bovine tuberculosis in cattle or wildlife (Buddle et al., 2011).

**Limitations to bovine tuberculosis surveillance and control in developing countries**

In developing countries, bovine tuberculosis is still common, especially in the dairy sector. The upsurge in peri-urban dairy production, unregulated animal movement, lack of animal identification, lack of surveillance at slaughterhouses, and weak veterinary services all contribute significantly to the poor control of animal tuberculosis in these countries.

Although regular tuberculin skin testing and elimination of infected animals has been successful in eradicating or significantly reducing bovine tuberculosis from cattle herds in many developed countries, these control measures are not always affordable and may not be practical in many parts of the world. In some cases, the policy of test and slaughter is in place, but it is not always vigorously pursued, and positive reactor animals may not be effectively quarantined or culled. This is largely because of legal and economic constraints such as the high cost of sustainable testing and slaughter of infected animals, and the subsequent compensation to farmers. Results may therefore be the opposite of those intended, with the policy contributing to the spread of disease through the sale of reactors. It is likely that some countries need to adopt feasible strategies for progressive control of animal tuberculosis by introducing interim measures such as segregation and phased slaughter of reactors, while improving biosecurity on farms. Although this approach may reduce the economic loss for the farmer, its usefulness may be limited by the difficulty of managing the segregation of reactors.

Limited laboratory diagnostic capacity is one of the major constraints to bovine tuberculosis control programmes in many developing countries. Diagnosis of tuberculosis is usually limited to microscopic evaluation of the microorganism on smears, making it difficult to confirm infected cases and identify the strains of *Mycobacterium* involved.

Post-mortem inspection at slaughterhouses is a cost-efficient method for passive surveillance of bovine tuberculosis. However, the quality of detection of tuberculous lesions in slaughterhouses can vary within the same country, with implications for the effectiveness of surveillance. In addition, routine post-mortem surveillance may not be possible if slaughtering facilities are limited. For instance, in many African countries there are few abattoirs, and more than 50 percent of slaughters take place informally, with no meat inspection (Michel et al., 2004).
Lance data do exist, they are not always integrated into the national official notification system, and so are not used effectively.

Insufficient collaboration at the regional level, lack of quarantine and border security, and illegal movement across borders between neighbouring countries have also been identified as factors contributing to the persistence of bovine tuberculosis and undermining control efforts in several developing countries.

Rural communities in many developing countries are not aware of the risk factors associated with the transmission of bovine tuberculosis, and living conditions often promote the spread of *M. bovis* infection in humans. In these situations, the risk of zoonotic transmission should be addressed through education and prevention programmes to inform cattle owners about the risks of bovine tuberculosis and the necessity for pasteurizing milk and inspecting carcasses after slaughter.

**Conclusions**

Bovine tuberculosis remains of great concern worldwide. In developed countries, significant progress has been made in controlling and eradicating the disease in cattle, primarily via test-and-slaughter strategies, and in humans via improved hygiene practices for and pasteurization of milk. However, eradication programmes in some countries are constrained by the presence of endemic infection in wildlife reservoir hosts. Multisectoral research efforts seek to improve understanding of the role of wildlife host reservoirs in the dynamics of *M. bovis* infection in cattle and to develop sustainable control strategies using a variety of tools and measures targeting both cattle and wildlife. Many authors support the introduction of control options that include the development of appropriate vaccines and their deployment in vaccinating wildlife where test-and-slaughter programmes have failed. Improved testing tools and additional research on *M. bovis* are also needed.

In developing countries, the disease continues to cause significant losses in the cattle industry, with implications for food security and trade. In the absence of effective surveillance and control strategies, bovine tuberculosis continues to be a major public health problem, especially in countries where the prevalence of infection in cattle is high, consumption of raw milk products is common, and malnutrition and other immunosuppressive conditions exacerbate the danger of the infection. The impact of bovine tuberculosis on public health is likely to worsen given the potential increase in drug resistance of *M. bovis* in situations where human infections are not effectively treated. There are still critical gaps in understanding of disease patterns, the real extent of the disease in cattle and other animals, and the strains involved. Better surveillance of bovine tuberculosis is required in many countries, through improved post-mortem inspection, efficient tracing of infected animals to their herds of origin, regular tuberculin skin testing, and effective laboratory diagnostic support. There is also need for qualified veterinary staff at slaughterhouses to ensure adequate meat inspection practices and standards. Effective implementation of these activities would allow countries...
to generate quality data and acquire sufficient knowledge of the epidemiology of the disease for developing strategic, cost-efficient and effective control programmes. From successful experiences in many developed countries, it can be concluded that bovine tuberculosis can be controlled only when there is strong political and producer support, an appropriate legal framework to enforce control measures, and active participation of all concerned in finding practical and affordable control options that are suitable for each country and each epidemiological context. Eradication is a more difficult target and requires many factors to be in place, including the necessary financial resources.

Tuberculosis due to *M. bovis* has a complex epidemiological pattern, which includes the transmission of infection within and among humans, domestic animals and wildlife. Control and eradication of bovine tuberculosis provides an ideal platform for the One Health approach, which can be operationalized through adapted approaches for improving surveillance and meat inspection, promoting milk pasteurization at the community level, and strengthening intersectoral collaboration. FAO is working in this direction by developing and implementing a One Health approach for comprehensive and integrated control of animal diseases that have impacts on public health, food security and human livelihoods.

References


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