Mycobacterium bovis infection and control in domestic livestock

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Summary

Bovine tuberculosis, caused by Mycobacterium bovis, is a well-known zoonotic disease which affects cattle world-wide. The public health risk has been alleviated in many countries by the introduction of pasteurisation, but the disease continues to cause production losses when poorly controlled. The Office International des Epizooties classifies bovine tuberculosis as a List B disease, a disease which is considered to be of socio-economic or public health importance within countries and of significance to the international trade of animals and animal products. Consequently, most developed nations have embarked on campaigns to eradicate M. bovis from the cattle population or at least to control the spread of infection. The success of these eradication and control programmes has been mixed. Mycobacterium bovis infects other animal species, both domesticated and wild, and this range of hosts may complicate attempts to control or eradicate the disease in cattle.

Keywords

Bovine tuberculosis – Cattle – Control – Domestic animals – Mycobacterium bovis.

Introduction

Bovine tuberculosis – the nature of the disease

Bovine tuberculosis is a disease characterised by the progressive development of characteristic granulomas, or tubercles, in the lungs, lymph nodes, and/or other organs, which affects the health of the individual animal and has a detrimental effect on animal production (32). The disease is infectious and can spread within a herd before any signs of disease are obvious. Infection may be localised with no obvious clinical symptoms or may cause chronic debilitating disease. In some cases, the infection lies dormant for many years, spreading only when the animal is subjected to additional stresses such as overstocking or drought, or if the immune system deteriorates in old age. Mycobacterium bovis has been detected in cattle in almost every country of the world (78). Control of bovine tuberculosis, like control of human tuberculosis, relies on early diagnosis, removal of infected animals and tracing and containment of contact exposed cases.

The primary mode of spread of bovine tuberculosis between herds is by the introduction of infected animals into non-infected herds. Evidence exists for nose-to-nose transmission (25, 59, 60), which could play a role in transmission between neighbouring properties. The most important factors determining the occurrence and spread of tuberculosis within a herd of cattle are the number of infected individuals, the number of young stock exposed to these infected animals, and the measures taken to prevent spread. The mode of transmission in cattle is principally horizontal, but not all infected animals transmit the disease. However, most cattle suffering from pulmonary tuberculosis and tuberculous mastitis are infectious, and in some infected individuals, urine, vaginal secretions, semen or faeces may also contain tubercle bacilli and act as a means of disease transmission between animals.

Mycobacterium bovis infection is spread to cattle primarily through the inhalation of infectious aerosols, either from a coughing or sneezing animal with open tuberculosis or from infected dust particles. Given the predominance of aerosol transmission, infection is spread more rapidly in intensive animal husbandry situations than in extensive or rangeland conditions such as those existing in many parts of northern Australia and in South Africa (75). Aerosol transmission is effective only over short distances (1 m to 2 m) and hence cattle density is a significant factor in the rate of transmission. Consequently, on dairy farms with a high density of cattle, or
in production systems which house animals together for extended periods, the transmission rate between susceptible animals may be very high. In stables and barns used to house tuberculous cattle, infected droplets and particles may be constantly present in the air, presenting a hazard to susceptible animals and farm workers.

Although cattle densities in northern Australia are generally very low, opportunities for transmission were created when cattle densities increased around the few available watering holes in central and Western Australia and the Barkly Tablelands in the Northern Territory where neither natural surface water nor troughs are available. By contrast, in the extreme north of the Northern Territory, where surface water is ample, a favourable environment for transmission amongst cattle and buffalo is created when animals are forced onto small islands formed by flooding during the wet season (26). Disease also appears to spread more rapidly in locations where animals are kept in crowded conditions, such as zoos, where stress may adversely affect the ability of the host to withstand infection (77).

Spread of tuberculosis by ingestion of infectious material has also been reported, whether by drinking infected milk or ingesting contaminated pastures or feed (60, 67). Cutaneous, congenital and genital infections have been recorded but are considered rare (48, 67). Iatrogenic transmission to the mammary gland has resulted from contaminated intramammary infusions (60). In practice, infection is acquired almost exclusively by the inhalation of infected droplets. Alimentary infection may be primary, as occurs in calves drinking the milk of cows with tuberculous mastitis, or may be secondary from swallowing mycobacteria-laden exudate from the lungs. Tonsillar infection with secondary involvement of regional lymph nodes may result from the ingestion of bacilli in the food.

The period of infectiousness can be lengthy if disease is left uncontrolled; an excreting carrier may transmit the infection for months or even years. Large numbers of tubercle bacilli may be excreted in the milk of cows with tuberculous mastitis; the number of viable bacilli in the milk of a cow may be sufficient to contaminate the milk of as many as 100 uninfected cows when such milk is pooled for transportation. Separated, skimmed milk, purchased by farmers from milk-processing factories to feed calves, has been known to contribute to the spread of M. bovis in this way.

**Maintenance host versus spill-over (end) host**

Domestic (and non-domestic) animals may be considered as either 'maintenance' or 'spill-over' hosts for M. bovis. If a species is a maintenance host, infection can be maintained within that population and passed on to subsequent generations of that species, as well as to other susceptible hosts. In contrast, spill-over or end hosts may be very susceptible to infection with M. bovis (and develop substantial disease), but removal of the source of infection results in a reduction in the prevalence of disease, and therefore infection is not sustained within the animal population concerned. Cattle are the original and most well-known reservoir or maintenance host for M. bovis and buffalo are also accepted as maintenance hosts. In Australia, deoxyribonucleic acid (DNA) typing has provided evidence that many infected buffalo harbour a strain of M. bovis that can be differentiated from that found in cattle (D.V. Cousins, unpublished data), supporting the suggestion that buffalo are maintenance hosts for M. bovis. One of the greatest threats to any control programme is infection in a wild (or feral) maintenance host that cannot be controlled. Examples of this are the badger (Meles meles) in the British Isles and the Australian brushtail possum (Trichosurus vulpecula) in New Zealand.

Spill-over hosts become infected when the challenge level is relatively high. In comparison to maintenance hosts, spill-over hosts appear to be more commonly infected by routes other than the respiratory route. Pigs are generally considered to be spill-over hosts. When husbandry practices were altered in the early 1920s, to remove infected milk and offal from the diet of pigs, the prevalence of M. bovis infection declined rapidly. This effect also has been reported in feral pigs in northern Australia (20, 50). Cats, dogs, horses and sheep are also considered to be spill-over hosts. Disease control programmes obviously focus on controlling infection in maintenance hosts, but consideration of other susceptible animals is also important to avoid any risk to the success of the programme or to public health. Goats may be considered to be maintenance or spill-over hosts, depending on the type and location of the enterprise. In Spain, goats are known to maintain infection and some evidence exists of transmission of infection to humans (40).

**Definition of 'domestic animals'**

For the purpose of this chapter, the term 'domestic animals' covers the following: bovines (including cattle and farmed or domesticated buffalo), goats, pigs, sheep, horses, camelids (camels, alpacas and llamas), dogs and cats. A discussion of M. bovis infection in wild and feral species is given later in this book by de Lisle et al. (30).

**Reasons for eradication or control (public health, productivity and trade)**

The three principal reasons for the eradication of tuberculosis from cattle populations are as follows:

a) the risk of infection to the human population

b) losses in productivity of infected animals

c) the risk that trade restrictions might be imposed by countries which are well-advanced in the eradication progress.

In cases where bovine tuberculosis was established in dairy cattle, the disease posed a serious public health risk, especially for children, through the ingestion of tuberculous milk (56, 72). In the United States of America (USA), the costs of bovine...
tuberculosis to the community in terms of human health have been estimated to be between US$30 and US$300 million per year (69). More recent economic assessments suggest that in Argentina, the annual loss due to bovine tuberculosis is approximately US$63 million (22). Similarly, the socio-economic impact of bovine tuberculosis on agricultural and human health sectors in Turkey was estimated to be between US$15 and US$59 million annually (6).

Mycobacterium bovis was established as an important zoonosis in the early 1900s, when the percentage of cases of tuberculosis caused by M. bovis totalled 5%–30% in Great Britain (71) and 6%–30% in the USA (45). By 1937, bovine tuberculosis accounted for up to 25% of all human tuberculosis and 2%–5% of pulmonary tuberculosis in the British Isles (37), with children most commonly affected. Before the implementation of eradication schemes, the frequency of bovine pulmonary tuberculosis in humans was demonstrated to be directly related to the prevalence of bovine tuberculosis in cattle (37, 41). The threat to public health has been largely alleviated in most countries by the introduction of pasteurisation, in some cases aided by the vaccination of infants with the attenuated strain of M. bovis bacillus Calmette-Guérin (BCG).

Clearly, one of the principal reasons for control of tuberculosis in recent times is to supply a 'clean' product to the international market place. The requirement of the international community for countries to provide scientific evidence of disease status is likely to provide additional pressure for progress in disease eradication and control programmes, and for continued disease surveillance. Thus, the desire for disease freedom for trade purposes, coupled with an economic need to maximise productivity continue to be the primary driving forces for eradication.

Domestic animals affected by Mycobacterium bovis

Cattle and domesticated or farmed buffalo

Mycobacterium bovis is the primary cause of tuberculosis in cattle and swamp or Asiatic water buffalo (Bubalus bubalis). All species of cattle are affected, although Bos indicus (large horned cattle with a hump such as zebu and Brahman) may be more resistant to the disease than Bos taurus (small horned cattle without a hump, e.g. European breeds) (65). Mycobacterium bovis causes tuberculosis in cattle in almost every country of the world (64). Infection has been reported in 69% of countries in the tropics and in 80% of countries in Africa. Tuberculosis is considered to be one of the most important diseases of cattle in the People's Republic of China, despite the absence of official prevalence figures. Mycobacterium bovis causes a spectrum of disease in cattle, ranging from generalised tuberculosis that affects almost every organ of the body, to cases in which the organism infects a single lymph node, causing a single tubercle which may or may not cause further disease.

Water buffalo in northern Australia were originally imported from Indonesia, but were probably infected by the first dairy cattle brought to the Northern Territory in the 1920s. Domestic buffalo in India are known to be infected with M. bovis. The overall prevalence of infection in buffalo was almost three times that in cattle when testing was conducted in four states of India (46). The first isolation of M. bovis from water buffalo in the Indochina region was performed in two emaciated swamp buffalo that died in north-eastern Thailand in 1992 (43). In a follow-up study of diseased animals in Thailand, the most common lesions in buffalo were caseous granulomas in the thoracic lymph nodes; localised and generalised infections were found depending on the progression of the disease (44). Tuberculosis has also been confirmed in buffalo in Egypt (58). Farmed water buffalo in Egypt were infected at almost three times the rate of cattle (33). Pigs

Pigs are susceptible to M. bovis infection and M. bovis was a common cause of tuberculosis in pigs in the early to mid-1900s. Disease levels in pigs usually reflect those in cattle, and prevalences in the order of 20% have been recorded in some pig populations. The oral route is the most important route of infection in domestic pigs, most frequently caused by feeding milk, milk products or offal from infected cows. Generalised infection was common, but following the implementation of measures to reduce tuberculosis in dairy cattle, the incidence of tuberculosis in pigs has declined; for example, in Australia, incidence was reduced from 17% in 1913 to 0.84% in 1928 (26). In the USA, the rate of tuberculous lesions due to M. bovis in slaughtered pigs declined from 15.2% in 1924 to 1.09% in 1970 (1). Tuberculosis in domestic pigs is now rare in countries that have successfully implemented tuberculosis control programmes, although 3.8% of tissues from suspect tuberculous pigs in New Zealand between 1987 and 1993 were found to be infected with M. bovis (28). Tuberculosis is not considered to be particularly contagious amongst domestic pigs or to spread easily from pigs to other animals. In most cases, the disease is self-limiting and no control measures are required.

Goats

Mycobacterium bovis has been known to cause tuberculosis in goats, although the importance of the disease varies depending on the country and the type of enterprise in question. In most cases, infection occurs as a direct result of contact with infected cattle. Infection in several herds of goats in India between 1941 and 1942 was associated with common grazing of goats and heavily-infected cattle (46). In one case where common grazing had occurred for four years, 24.7% of 417 goats gave a positive result to the tuberculin test and 90% of these had tuberculous lesions. In Australia, where
goats are rarely kept with cattle, a single case of M. bovis infection in a goat has been reported (24). In this case, goats were grazing with infected cattle (with a prevalence of 35%) at abnormally high stocking rates. Although the goats appeared malnourished, infection was only detected in a single animal after skin testing and subsequent culture of reactor lymph nodes. No lesions were detected at necropsy of the reactor goats, suggesting that the goats were not as susceptible to the infection as the cattle. A low prevalence of tuberculosis in goats has also been reported in Taipei China (49).

Tuberculosis in goats appears to be widespread in Mediterranean countries and is a serious disease (39). While mixed farming of cattle and goats is not common practice in these countries, common grazing areas sometimes provide close contact. In Spain, tuberculosis in goats is a comparatively common occurrence. Recent reports have suggested that the histopathological responses to infection in goats and cattle may be different. The caprine lesions, although more severe than bovine lesions, appeared to contain fewer organisms; this was attributed to a difference in either the immune response of the host or the strains infecting cattle and goats (38). Until recently, tuberculosis in goats in Spain was considered to be due to M. bovis. However, strain differences were detected in the isolates from goats and sheep using DNA fingerprinting techniques (3, 39). The zoonotic aspects of this strain have been confirmed by evidence of transmission to humans (40) and a recent study suggests that the organism responsible for tuberculosis in goats in Spain is a variant of M. bovis (61). This strain has genetic and phenotypic differences from classical M. bovis and has been named M. tuberculosis subsp. caprae (4). This strain has been detected in both goats and sheep in Spain, but not in cattle. The subspecies M. caprae has probably evolved in goats and is now maintained in that host in Spain.

**Farmed or domesticated camels (camels, alpacas and llamas)**

Tuberculosis was known to occur in dromedary camels (Camelus dromedarius) in Egypt in the early 1900s. Between 1910 and 1916, 2.9% of camels slaughtered in Cairo were tuberculous and the bovine strain was implicated. Camels in Egypt were often kept in close association with cattle and the route of infection was usually the respiratory tract (51). The lungs and bronchial lymph nodes were always affected and lesions were restricted to these organs in 60% of cases. Generalised tuberculosis, with numerous lesions in the principal organs and carcass lymph nodes, was observed in 7% of cases. In 1983, tuberculosis was diagnosed in two of nineteen bactrian camels (Camelus bactrianus) in the USA (9); pulmonary infection due to M. bovis has also been reported in camels in Mauritania (10).

Alpacas (Lama pacos) are known to be susceptible to M. bovis infection (2, 31), although reports of infection in their natural habitat in South America are few. Recently, a case was diagnosed in an alpaca in New Zealand (G.W. de Lisle, personal communication). *Mycobacterium* bovis infection has been reported in llamas (Lama glama) in zoological collections in the USA (84) and in a small herd of llamas in the United Kingdom (UK), where infection was linked to cattle and badger populations in the surrounding area (5). *Mycobacterium* bovis was isolated from lung and lymph nodes of two llamas, one of which had ‘cluster of grapes’ lesions scattered over the parietal pleura, lungs and pericardial sac. The authors concluded that tuberculosis should be considered in the differential diagnosis in cases of illthrift with or without obvious respiratory signs. Most of the reports of tuberculosis in llamas and alpacas are associated with groups of animals in zoological collections, suggesting that exposure in a confined area and the stress of an artificial environment may lead to increased disease transmission in these species.

**Horses**

*Mycobacterium* bovis infection in horses is uncommon; when disease occurs, the primary lesions are found in the abdomen, suggesting ingestion as the cause of infection (82). The incidence of tuberculosis in horses is very low in countries with a national programme to eradicate tuberculosis. Information from experimental infection suggests the horse is relatively resistant to infection with *M. bovis* (34). The course of disease appears to be chronic, with the first symptoms being loss of body condition, despite normal appetite. Lesions are often found in the mesenteric lymph node and liver and lung lesions are normally present.

**Sheep**

Tuberculosis caused by *M. bovis* is rare in sheep, mainly because of the nature of sheep husbandry and the fact that sheep are rarely exposed to infectious material (34). The relatively high incidence of tuberculosis (0.14%-0.22%) in sheep killed in abattoirs in Germany between 1904 and 1918, compared with only eight confirmed cases in Great Britain between 1900 to 1980, adds weight to the theory of husbandry playing an important role, since the sheep in Germany were housed. Although Chauvass considered that sheep were relatively immune to experimental infection with *M. bovis* (13), several authors consider sheep to be highly susceptible to infection (34, 82). Prevalence of up to 18% has been observed in New Zealand where sheep were grazing heavily contaminated pastures (27). The distribution of lesions in this case suggested that ingestion was the cause of infection in 51% of animals and inhalation in 48%. Cordes et al. tested 281 sheep in an infected flock of 19,000, and found thirty-two animals to be skin test positive (17). Thirty-two of forty-three animals with gross lesions were smear positive or culture positive for *M. bovis*. Gross lesions were generally large and numerous, but varied from being extensive to few. Histopathology revealed that in most cases only a few acid-fast organisms were present. Cordes et al. reviewed the literature on susceptibility of sheep to infection with *M. bovis* and considered these animals to be fairly susceptible to infection with *M. bovis* via the oral route (17).
Dogs
Although experimental studies have revealed that dogs are equally susceptible to M. bovis and M. tuberculosis infection (52), summaries of bacteriological studies have indicated that tuberculosis in dogs is more frequently caused by M. tuberculosis. In a study detailing 592 cases of tuberculosis in dogs up to 1951, M. tuberculosis caused more than twice as many cases as M. bovis (14). An extensive review by Snider reported tuberculous lesions in 0.1%-6.7% of dogs subjected to necropsy between 1930 and 1970 (74). Pulmonary tuberculosis is more likely to occur in the dog than the cat, and disseminated disease can occur in both species.

Cats
Cats are considered to be more susceptible to M. bovis than to M. tuberculosis (11, 12, 74) and infection generally results from exposure to infectious material from tuberculous cattle. In a review of published papers in 1945, 96% of cases (n = 147) were due to M. bovis and the remainder to M. tuberculosis (80). Infection with M. bovis in cats was quite common in Europe before bovine tuberculosis was effectively controlled; Snider reported tuberculous lesions in 2%-13% of cats subjected to necropsy between 1930 and 1970 (74). Tuberculous lesions were seen most frequently in the alimentary tract and mesenteric lymph nodes, indicating that infection was most likely to be acquired by ingestion of infected unpasteurised cows milk.

Non-healing skin lesions similar to those of cat leprosy, but caused by M. bovis have been reported in New Zealand. In a study of fifty-seven M. bovis-infected cats between 1974 and 1986, 56% had skin lesions (29). Although the skin lesions could have occurred as a result of bite or scratch wounds inflicted by infected possums or cats, this could not be substantiated. Lesions in the head and mesenteric lymph nodes in 11% of the cats suggested infection occurred as a result of cats eating tuberculous feral animals or licking skin lesions rather than as a result of drinking infected milk. The majority of the infected cats were from rural or suburban areas where M. bovis was also present in feral and wild animals. Despite the large number of acid-fast organisms in some of the skin lesions, no evidence was found of spread of infection to any of the owners. Restriction endonuclease typing identified a cluster of twelve cats possessing the same type. The cats were assumed to have been infected from a single point source (29). Tuberculosis caused by M. bovis has been reported to be associated with feline immunodeficiency virus (55).

In a study of twenty-seven cases of tuberculosis in cats in Spain from 1984 to 1994, a cause was determined in eighteen of the cases and 61.2% of these were due to M. bovis (62). Tuberculous lesions were observed in the abdominal cavity (22.3%), thoracic cavity (22.2%), or in both locations (55.5%). Lungs and mediastinal lymph nodes were always affected and most cases had miliary tuberculosis.

Disease control
The economic impacts of endemic diseases and disease control programmes have been reviewed by Tidsell et al. (79). Decisions relating to control of endemic disease are normally made by the government and the producer (the latter represented by an official body). To enable an informed decision to be made, information is required on the level of disease present, the level of control to be adopted, the extent of involvement needed, and methods of funding animal health programmes (particularly the distribution of costs between taxpayers and the livestock industry). However, because of the complex relationships between animal health, production impacts, market access and non-production benefits of livestock, economic assessments may be secondary to political imperatives. A cost-benefit analysis applied to the brucellosis and tuberculosis eradication campaign in Australia in 1987 aimed to ‘examine what the future extent of the programme should be and the allocation of assistance to producers’. An epidemiological model was used to simulate costs of control and an econometric model of the beef industry in Australia was employed to estimate the benefits of different control procedures (76). Retention of access to the international market was acknowledged as the principal benefit of the programme, although the benefits of free animal movement within Australia once eradication had been achieved and the reduced risk to human health were recognised (76). Risk analysis is increasingly used to ensure that programmes remain focused and relevant.

Whole herd test and slaughter programmes
Whole herd test and slaughter programmes have been used world-wide for the control of bovine tuberculosis as well as other diseases such as brucellosis and contagious bovine pleuropneumonia. A number of versions of the tuberculin test have been applied, but most programmes now use a purified protein derivative from culture of M. bovis (PPD-B). Normally, 0.1 ml of tuberculin is injected intradermally and the site of injection is examined 72 h later for swelling or increased skin thickness as a measure of a cellular immune response to the PPD-B antigens. The frequency of testing is defined by the programme rules. The sensitivity of the tuberculin test varies and was reported by Monaghan et al. to be in the range of 77%-95% (mean 86%) (54). More recent reports suggest that the sensitivity of the comparative tuberculin test may be in the region of 90% in Ireland (23). Environmental mycobacteria are known to complicate the interpretation of the tuberculin test in countries such as the UK and the Republic of Ireland, and a comparative tuberculin test using PPD-B and a PPD derived from culture of M. avium (PPD-A) is used to overcome this problem. As the tuberculin test lacks sensitivity, multiple tests must be performed in herds at prescribed time intervals to increase the confidence of detecting all infected animals.
In Australia, the apparent low sensitivity of the tuberculin test (between 65.6% [83] and 72% [35]), especially under extensive farming conditions, was recognised as a significant problem. Given this low sensitivity, repeat herd testing was required to increase confidence in a decision to remove quarantine and movement restrictions after apparently successful eradication. The agreed tuberculin testing schedule in Australia (standard definitions and rules [SDRs]) consisted of four whole-herd tests with no disease detected by these tests (Table I). The tests had to be completed in a minimum of twenty-four months to attain a 'confirmed free' (CF) status. A herd was required to successfully undergo this series of tests before being released from quarantine. In 1993, a fifth confirmatory test was introduced for herds that had been previously infected, in recognition of the potentially very long incubation period for this disease. This test became known as the 'monitor test' or 'eight year test' (CF3 in Table I).

Under the system presented in Table I, herds were able to maintain a disease-free status by two means, namely: testing or monitoring. If a herd with no history of tuberculosis had no detectable disease when tested for the first time, the herd was classified as 'tested negative' (TN). A herd could maintain a TN status or progress to CF status, the highest disease-free status possible, by periodic testing. Alternatively, if 10%-30% of the cattle in a herd were sent for slaughter over three years with no tuberculosis detected, the herd achieved the status of 'monitored negative' (MN).

As bovine tuberculosis is progressively eradicated from a country, the number of non-specific reactors (in terms of percentage of reactors showing no gross lesions at necropsy) increases. Thorough examination of the carcass is necessary to detect the very small lesions that may be present in skin test reactors as disease prevalence declines. In addition, as the number of infected animals declines, confirmation of diagnosis by laboratory means becomes increasingly important to determine whether reactors identified by a positive tuberculin test are non-specific reactors or animals with non-visible lesions infected with M. bovis.

**Whole herd tests in extensive farming conditions**

In extensive farming situations such as those common in the north of Australia, different strategies have had to be developed to ensure a whole herd test (47, 68). Some unique systems were developed to assist mustering of all cattle over vast areas. Trap yards were developed whereby cattle were enticed into a yard by water or feed, and once inside were held for further testing or sale for slaughter. Helicopters were increasingly used to assist horseback riders with mustering cattle into yards for testing. If a stock muster was not complete, any infected animal(s) left behind remained a source of infection for animals released after a clean herd test. Because of the difficulties of obtaining complete musters in inhospitable country, paddock checks with subsequent remustering or destruction of any unmustered cattle or buffalo in the more difficult areas were implemented. In the latter stages of the campaign, individual or small groups of cattle that could not be mustered were destroyed by aerial shooting from helicopters during inspections performed at specified intervals after mustering. Shooters were trained in the safe handling of rifles and accurate shooting techniques to ensure that animals were humanely destroyed.

**Abattoir surveillance methods**

Monitoring for lesions consistent with tuberculosis by post-mortem examination of cattle carcasses at abattoirs is a critical element of tuberculosis eradication. However, meat inspection procedures are estimated to detect only 50% of cattle with tuberculous lesions, compared with a detailed necropsy procedure that included slicing lymph nodes in a laboratory at 2 mm intervals and visual examination of the cut surfaces (85%) (21). Effective monitoring requires meat inspectors to show diligence, be well-trained, examine the correct tissues and submit granulomas for laboratory examination which should use histopathology and/or

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**Table I**

**Bovine tuberculosis herd classification scheme used in Australia**

<table>
<thead>
<tr>
<th>Herd status</th>
<th>Definition</th>
</tr>
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<tbody>
<tr>
<td>Suspect (SU)</td>
<td>A herd in which surveillance information suggests that the herd may be infected, but further evidence is necessary to classify the herd as infected or otherwise</td>
</tr>
<tr>
<td>Infected (IN)</td>
<td>A herd in which tuberculosis has been confirmed by laboratory diagnosis</td>
</tr>
<tr>
<td>Restricted (RD)</td>
<td>A previously infected herd that has had a negative herd test at least 30 days after a previous test and removal of reactors</td>
</tr>
<tr>
<td>Provisionally clear (PC)</td>
<td>A previously infected herd that has had two consecutive negative tests at an interval of not less than 6 months</td>
</tr>
<tr>
<td>Confirmed free (CF)</td>
<td>A previously PC, TN or MN herd that has had a least one further negative test (i.e. the third test) without evidence of tuberculosis at an interval of not less than 6 months after achieving that status</td>
</tr>
<tr>
<td>Confirmed free one (CF1)</td>
<td>When the herd was previously classified as IN this may be referred to as CF1 status</td>
</tr>
<tr>
<td>Confirmed free two (CF2)</td>
<td>A herd that has had one further test (i.e. the fourth test) at least 12 months after the test to achieve CF1 status</td>
</tr>
<tr>
<td>Confirmed free three (CF3)</td>
<td>A herd that has had a test in accordance with the requirements for the surveillance test, 8 years after the last known tuberculosis or all exposed stock have been sent for slaughter</td>
</tr>
<tr>
<td>Tested negative (TN)</td>
<td>A herd not previously classified as infected that has had at least one negative test without evidence of tuberculosis</td>
</tr>
<tr>
<td>Monitored negative (MN)</td>
<td>A herd in which adequate surveillance information indicates that the herd is free of tuberculosis, but a negative test has not been performed</td>
</tr>
</tbody>
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microbiological methods to detect \( M. \) bovis infection. Diagnosis based on gross appearance seems to be unreliable. In a small abattoir survey in New Zealand, only approximately 50% of tuberculous granulomas were accurately diagnosed on gross inspection, and a significant number of actinobacillosis lesions were misdiagnosed as tuberculosis (66).

**Importance of animal identification and tracing for abattoir surveillance and movement control**

A system of animal identification is an essential means of animal traceback. The identification system should be permanent, easy to apply, inexpensive, legible and capable of identifying individual animals within herds in a specified area or region of the country. An animal movement monitoring system should also be installed to provide information regarding movement of animals between herds through sale or exchange of livestock. The use of self-adhesive plastic or vinyl tags applied to the tail indicating details of the ownership and property or premise of origin of each animal was successful in Australia. The importance of animal identification as a means of tracing animal movements cannot be underestimated. Without an animal identification scheme, new cases of tuberculosis detected by abattoir inspection cannot be traced to the property of origin, with the result that infected premises remain undetected.

**Treatment of bovine tuberculosis**

In certain circumstances, some countries may consider treatment of infected animals with isoniazid (INH) (e.g. for extremely valuable animals). However, as INH is not a guaranteed cure (a 78% bacteriological cure rate is possible [42]), this cannot be regarded as a means of eradicating disease. Treatment regimes require daily dosing for up to two or three months, and hence INH is rarely seen as a practical alternative to stamping-out methods.

**Factors affecting the success of an eradication programme**

For eradication or control programmes to be successful, a number of factors need to be considered. Many of the following are considered to have contributed to the success of the campaign to eradicate tuberculosis in Australia. Many of these will apply to other national programmes.

a) A simple and clear campaign goal

In Australia, the goal was the elimination of \( M. \) bovis from all cattle and buffalo herds. Although at one stage a goal of biological freedom was considered, the global mobility of travellers potentially infected with \( M. \) bovis and the fact that \( M. \) bovis may reactivate in the elderly meant that this goal would be impossible to achieve. Some countries opt for a control programme and others aim for eradication. In some developing countries, bovine tuberculosis is a low priority in terms of animal diseases, and management of the disease is minimal.

b) A national approach and industry involvement

Although states or provinces may administer control programmes within their jurisdictions, a national approach to eradication was considered essential to achieve eradication throughout the country. Initially in Australia, each state was responsible for the programme in that state, but in 1966, a national approach was recognised as essential to avoid a loss of export markets, the consequent economic and social disruption to dairy and beef producers, and the resulting costs to the community. In 1966, the Commonwealth, State and Territory Ministers for Agriculture recommended that action be initiated nationally to eradicate both brucellosis and tuberculosis as soon as feasible, and this recommendation was subsequently adopted by the Commonwealth, State and Territory Governments. The National Brucellosis and Tuberculosis Eradication Campaign (BTEC) commenced in Australia in 1970. In this way, all states and territories were involved and had ownership of the campaign. The national approach to the campaign was driven by a committed cattle industry and supportive governments. The commitment of industry to the programme was paramount, and was seen as a key component of success in Australia. The cattle industry played a vital role in both financial and programme management aspects of BTEC.

c) The importance of standardisation

Standardisation of the management and implementation of the eradication programme across the country was seen as essential to the success of the programme, and engendered confidence in decision-making. Having defined herd status and area status, each with different levels of associated risk of disease, mutual recognition of these criteria by all state and territory authorities was necessary to promote confidence in the information received about herds and areas, and to assess the risk of the movement of cattle. This mutual recognition of the level of risk was principally achieved through the establishment and recognition of standardised procedures. The SDRs for the campaign in Australia were first documented in 1975 and played a major role in the ultimate success of the campaign. The SDRs set the minimum standards acceptable to all states and territories for the running of the campaign. These were regularly reviewed and updated as the campaign progressed. The SDRs describe the requirements for both herd and area status. Area status was based on factors including the prevalence of the disease and degree of control. Progression in status provided increasing confidence that the disease had been eliminated. Similarly, quality control of all aspects of the diagnosis of tuberculosis and standardisation of the diagnostic procedures were essential components of the campaign. The standardised laboratory techniques (Australian standard diagnostic techniques [ASDTs]), which detail minimum diagnostic standards for laboratory tests for the diagnosis of tuberculosis, were first prepared in 1989 (18) and were updated as new techniques and new requirements for the campaign were identified (19, 70).
d) Political will and funding
Political stability is important for any disease control programme. A change in government or change in political focus can cause major disruption to a programme. An eradication or control programme needs adequate funds to progress. In some countries, funding is entirely provided by government. This poses difficulties when such funding competes against other government budget items such as health, education, policing and the other myriad activities that are competing for diminishing government funds. In addition, if industry is not involved in the management and funding, then producers may not be committed to the campaign. In Australia, the BTEC was a collaborative effort funded by the State and Territory Governments, the Commonwealth Government and, from 1973, the cattle industry of the country. The industry contributed through levies, initially on exports, then on slaughter and live cattle exports, and during the latter stages of the campaign, on cattle transactions. Slaughter levies started in 1976 at AUS$1.00 per head and transaction levies started in 1991 at AUS$2.10 per head. By the close of the eradication campaign in 1997, the transaction levy had decreased to AUS$0.17 per head. The cattle industry had ownership of the programme through involvement in funding and management.

e) Constant review of strategies and progress
In any eradication or control programme, a continual assessment of progress and goals is necessary. A financial imperative exists to ensure that the funds invested are appropriately spent and achieving the required progress. Risk analysis can be applied to ensure that the programme is focused.

f) Strong and enforceable laws to support the campaign
Legislation may be required to ensure that the programme proceeds effectively. Legislative changes may be necessary to provide industry funding and to ensure that quarantine and movement restrictions can be enforced. A key element for the success of any control programme is uniform law and effective co-operation between cattle producers and agencies involved in implementing the programme.

g) Compensation paid to owners of animals required to be slaughtered
Co-operation with owners is facilitated by paid compensation. The need to slaughter reactors, and when required, depopulate animals, will be best supported by owners when compensation can be provided for animals that are removed from the property. This enables owners of infected properties to continue raising livestock, or to change emphasis, thereby minimising the risk to the livelihood of these livestock farmers.

h) A high level of competence at all levels
Control of bovine tuberculosis relies on a high level of competence at all levels, including farmers, stock inspectors, veterinarians and campaign managers. Continued education can be achieved through regular workshops, seminars, field exercises and training sessions provided by specialists. The importance of working as a team to solve problems and understand the contributions of other professionals and team members cannot be underestimated. Public relations and educational aspects of tuberculosis control are an important consideration in developed and developing nations. An increased level of understanding about tuberculosis, the importance of the campaign and the benefits of a successful campaign is invaluable. This can be achieved through open communication using a variety of communication methods, including written, verbal and electronic means.

i) Support provided by a national laboratory diagnostic service
Diagnosis of bovine tuberculosis relies increasingly on laboratory support, preferably provided by a well-organised and integrated national laboratory diagnostic service. Laboratories involved in the programme must be dependable and have proven capabilities. Microbiological diagnosis of mycobacterial disease requires specialist skills and facilities in addition to strict adherence to safety issues. A country-wide tuberculosis control programme assumes the existence and availability of a national reference laboratory with substantial expertise available for consultation, training, provision of quality control programmes and follow-up services. A national reference laboratory may also provide specialist services such as rapid DNA-based testing and identification services and DNA fingerprinting for epidemiological investigations.

j) An active and appropriate research programme
Gaps in knowledge of the disease can be filled by a creative and well-organised research programme funded by governments and the livestock industry. Research on the effectiveness of different types and doses of tuberculin, survival of the organism in particular environments, the involvement of other mycobacteria in tuberculin reactions, together with studies on the impact of feral animals on the success of the programme, and the search for improved diagnostic tests, have all contributed to a greater understanding of M. bovis infection in various environments, improved diagnosis and have led to an enhanced ability to manage the eradication campaign. Different epidemiological situations will necessitate research which focuses on different aspects of the disease process. For example, in countries with a feral animal reservoir problem, research will need to address the impact and control of such wild animal hosts.

Measuring the progress of tuberculosis eradication
The progress of tuberculosis eradication in developed countries can be measured according to three criteria (15), as follows:

a) the past and current extent of tuberculosis within national cattle herds
b) the nature of any recognised impediments to the successful conclusion of the eradication campaign

c) the current real or perceived risks of reinfection of 'clean' herds.

Consideration of these three criteria allows most countries undergoing eradication to be classified as belonging to one of five groups, as detailed below.

Group 1
Eradication is achievable, identified impediments to success are surmountable and the risk of reinfection is minimal.

Group 2
Eradication is achieved or achievable, but impediments to success are recognised and represent a real or perceived continuing risk of infection.

Group 3
Significant advances have been made towards eradication, but complete eradication has been impeded by one or more factors which constitute a real and continuing risk of infection.

Group 4
Significant progress has been achieved in controlling tuberculosis in cattle, but the programme has stalled principally because of endemic disease occurring in a wildlife reservoir.

Group 5
Progress has been hindered by both an endemic wildlife problem and significant problems with reinfection of clean herds by cattle-to-cattle spread of the infection.

Current situation
Table II summarises various national eradication programmes categorised by progress, impediments to completion and risk of reinfection (as proposed by Clifton-Hadley and Wilesmith [15]). Australia, which exceeds the standards set by the Office International des Epizooties (OIE) to achieve official tuberculosis-free status, is an example of a Group 1 programme.

More recent evidence suggests that the tuberculosis situation in Great Britain has worsened and that Great Britain is now more likely to belong in Group 5, along with Northern Ireland and the Republic of Ireland. The USA may move up into Group 2 if the large milking herds in Texas, a long-term reservoir of M. bovis infection, are to be depopulated, as has been reported.

Declaration of a country as ‘tuberculosis-free’
According to the OIE (63), to qualify as officially free from bovine tuberculosis, a country or part of a country needs to satisfy the following requirements:

a) bovine tuberculosis is notifiable in the country
b) 99.8% of the herds in the considered geographical area have been officially free from bovine tuberculosis for at least the past three years as disclosed by periodic testing of all cattle in the area to determine the absence of bovine tuberculosis (periodic testing of all cattle is not required in an area where a surveillance programme as described in paragraph d) below reveals that at least 99.9% of the cattle have been in herds officially free from tuberculosis for at least six years)
c) cattle introduced into a country or zone officially free from bovine tuberculosis must be accompanied by a certificate from an official veterinarian attesting that they come from a herd of cattle officially free from bovine tuberculosis or from a country or zone officially free from bovine tuberculosis
d) a country or zone officially free from bovine tuberculosis must have a Veterinary Administration which should be able to trace and test the herd of origin of any reactor to a tuberculin test disclosed after removal from the considered territory. Also animals which disclosed gross pathological lesions of tuberculosis in an abattoir or elsewhere. In addition, such a country or zone must have in place a surveillance programme to ensure the discovery of bovine tuberculosis

Table II
Progress in eradication of bovine tuberculosis in developed countries
Group 2 has been subdivided to highlight countries in which recent infection in farmed deer has been perceived as a threat to control in the national cattle herd (Group 2a)

<table>
<thead>
<tr>
<th>Group</th>
<th>Control/eradication progress</th>
<th>Impediments to completion</th>
<th>Risk of reinfection</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>Australia</td>
</tr>
<tr>
<td>2a</td>
<td>+++</td>
<td>-</td>
<td>+</td>
<td>Canada, Denmark, Sweden</td>
</tr>
<tr>
<td>2b</td>
<td>+++</td>
<td>-</td>
<td>+</td>
<td>Austria, Belgium, Finland, France, Germany, Iceland, Italy, Japan, Luxembourg, Norway, Portugal, Spain, Switzerland, The Netherlands</td>
</tr>
<tr>
<td>3</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>Hungary, United States of America</td>
</tr>
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<td>4</td>
<td>+</td>
<td>+++</td>
<td>++</td>
<td>Great Britain, New Zealand</td>
</tr>
<tr>
<td>5</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>Northern Ireland, Republic of Ireland</td>
</tr>
</tbody>
</table>

* +++ degree of relative progress, number of impediments/risk
  ** minimal or low risk
Source: Clifton-Hadley and Wilesmith [15]
should the disease be present in the country or zone, through slaughter monitoring and/or tuberculin testing.

The declaration of tuberculosis-free status by Australia goes beyond the OIE definition. The declaration is based on the fact that the entire country has been an 'impending free' area for five years. 'Impending free' means that no herds were known to be infected at the time of the declaration (in 1992), an approved monitoring and granuloma submission programme was in place, no herds were classified as infected (IN) or restricted (RD; one clear test) at the time of declaration, and eradication of any new cases of tuberculosis could be performed within twenty-four months. 'Free area status' also required an approved monitoring and granuloma submission programme, and the national veterinary committee had to be satisfied that tuberculosis had been eradicated, no herds were classified as IN, RD or provisionally clear (PC; two clear tests) at the time of declaration, and movement controls were in place for cattle from herds that had tuberculosis and had achieved CF1 status.

Many developed nations are currently grappling with the questions of 'when is free really free' (i.e. when does a 'classification' of free indicate true freedom or complete eradication?) and what level of surveillance is required. As bovine tuberculosis is a chronic disease that can lie dormant for many years, it is difficult to pinpoint when infection is actually eliminated from the entire animal (cattle) population. The OIE definition of freedom from tuberculosis does not require absolute freedom from infection, and as long as the OIE guidelines mentioned previously are adhered to, the country or area does not lose its 'free status' if occasional cases of tuberculosis are detected. However, although countries can be considered free (or virtually free) of bovine tuberculosis (and other diseases such as foot and mouth disease), the World Trade Agreement continues to require these countries to prove the absence of disease by providing documentation of surveillance methods and testing performed. As yet, no agreement has been reached regarding an acceptable level or duration of surveillance.

Sweden declared freedom from tuberculosis in 1958, after a comprehensive test and slaughter programme which lasted for forty years (81). Sporadic cases only have been reported since that time, the last reported in 1978. However, M. bovis infection was reintroduced in fallow deer in 1987 and programmes now focus on control of the disease in deer populations. Tuberculin testing for bovine tuberculosis was halted in 1970 and meat inspection remained as the main surveillance tool. A similar situation exists in Denmark where the last case of tuberculosis in cattle was recorded in 1998, although bovine tuberculosis is also present in farmed deer in Denmark. Switzerland has successfully eradicated tuberculosis from the cattle population, quoting the last case in 1991. Australia is the only major exporter of beef and beef products to be free of brucellosis, tuberculosis and foot and mouth disease. Both the USA and Canada now accept the tuberculosis-free status of Australia, but some countries in the Middle East and Asia are still hesitant to accept this status, as evidenced by the requests for tests on live cattle exported to these countries.

Control of bovine tuberculosis in developing countries

A distinct difference in attitude to eradication or control of bovine tuberculosis exists between the developed and developing nations. Eradication and control programmes are expensive to run and require an organised and consistent approach as outlined in detail above. The needs of countries also differ. For countries that are major exporters of meat and milk products, the benefits to trade or perceived threats to trade are major incentives to continue or progress with a campaign to eradicate zoonotic diseases such as bovine tuberculosis and brucellosis. In contrast, control of bovine tuberculosis is rarely high on the political agenda of governments of developing nations, many of which have higher priorities in terms of animal or public health. Human tuberculosis occurs in epidemic proportions in many developing nations worldwide, and when combined with the spread of human immunodeficiency virus (HIV) infection, this represents a serious ongoing threat to whole populations in these countries (57). The world-wide incidence of cases of tuberculosis attributable to HIV was estimated to increase more than three-fold, to 1.4 million (14% of the total cases) by 2000 (22). Approximately 40% of cases are expected to occur in South-East Asia and 40% in sub-Saharan Africa.

Information regarding the levels of bovine tuberculosis is scarce in developing nations. A review of the status of bovine tuberculosis in Africa, Asia and Latin America by Cosivi suggested that the prevalence data available in many countries was insufficient and that less than half the countries applied control measures for bovine tuberculosis based on a test and slaughter policy and disease notification (22). More than 94% of the population of the world live in countries in which control of bovine tuberculosis in cattle and buffalo is either limited or completely absent. The contribution of M. bovis to the prevalence of human tuberculosis is unknown in many of these countries, but the lack of control measures brought about by financial constraints, lack of trained personnel and lack of political will (or stability) mean that bovine tuberculosis (and zoonotic tuberculosis) will continue to endure as long as poverty and malnutrition exist (53). Where circumstances prevent the use of a test and slaughter programme, alternative strategies need to be considered. Programmes based on slaughterhouse surveillance and traceback of tuberculous animals to herds of origin may be more appropriate. Measures to prevent spread of infection should be of paramount importance, and can be achieved with trained public health personnel, public education and proper hygienic practices. Segregation and elimination of infected animals should be encouraged, as should promotion of heat treatment of milk (pasteurisation programmes) and neonatal BCG vaccination to control tuberculosis in the community.
The role of vaccination in control of bovine tuberculosis

Vaccination has not generally been seriously considered in test and slaughter programmes because of cross-reaction with the tuberculin test used for disease diagnosis. However, a vaccine could potentially be administered, either to wildlife in areas in which an infected feral animal reservoir compromises the effectiveness of test and slaughter elimination programmes, or to domestic animals in developing nations that cannot afford a test and slaughter strategy. The attenuated M. bovis strain BCG has been used for human vaccination in the past with variable efficiency (16) and M. vaccae has also been heralded as a potential candidate. Both of these vaccines have also been evaluated for use in cattle (7, 8). Recent research on potential candidate vaccines, the development of large animal models in deer (36) and cattle, together with new delivery systems for wildlife, hold great promise for more effective vaccines against animal and human tuberculosis (73).

Conclusion

Bovine tuberculosis remains as one of the most important animal diseases affecting international trade. Although cattle are the primary host for M. bovis infection, the organism has one of the widest host ranges of any infectious agent, including many other domestic animals, wildlife species and humans. The reasons given for the control of bovine tuberculosis – public health, loss in production and/or trade issues – continue to apply, despite the fact that the importance of each factor may differ depending on whether a developed or developing nation is under consideration. It has long been recognised that bovine tuberculosis can be eliminated from a country or region by implementation of a whole herd test and slaughter programme, provided that no other host reservoir of infection exists. This approach has worked well for some countries. In special environments, the development of innovative methods may be necessary to obtain full musters so that complete herd tests can be achieved. However, control programmes in developed countries are increasingly being complicated by infection of feral animal hosts that are abundant or protected, and subject to difficulties or restrictions in terms of biological control. Importation of infected hosts other than cattle (usually deer) has restricted progress or retarded control programmes for bovine tuberculosis in some countries. Developing nations continue to lack the resources and/or political stability to sustain conventional control programmes and rely on education and public health measures to reduce the risk to public health. Research aimed at developing a suitable vaccine and delivery system may be the only practical means of disease control in these circumstances.

L'infection due à Mycobacterium bovis chez les animaux domestiques et sa prophylaxie

D.V. Cousins

Résumé

La tuberculose bovine, due à Mycobacterium bovis, est une zoonose bien connue qui sévit dans le monde entier. L'introduction de la pasteurisation a permis, dans de nombreux pays, de réduire les risques pour la santé publique, mais, en l'absence d'une bonne prophylaxie, la maladie continue de provoquer des pertes dans les élevages. L'Office international des épizooties classe la tuberculose bovine parmi les maladies de la Liste B, en raison des graves problèmes socio-économiques et de santé publique qu'elle pose aux pays affectés et de son impact sur les échanges internationaux d'animaux et de produits d'origine animale. La plupart des pays industrialisés ont donc lancé des campagnes pour éradiquer M. bovis du cheptel bovin ou, tout au moins, pour éviter sa propagation.
Ces programmes d'éradication et de prophylaxie ont rencontré des succès divers. Outre les bovins, *Mycobacterium bovis* infecte d'autres espèces animales, domestiques et sauvages, et la diversité de ces hôtes rend plus complexes les plans de prévention ou d'éradication de la maladie chez les bovins.

**Mots-clés**

Infección por *Mycobacterium bovis* y control del patógeno en el ganado

D.V. Cousins

**Resumen**
La tuberculosis bovina, causada por *Mycobacterium bovis*, es una enfermedad zoonótica bien conocida que afecta al ganado vacuno del mundo entero. Aunque la pasteurización ha servido en muchos países para reducir los riesgos de salud pública ligados a la enfermedad, ésta sigue causando pérdidas productivas cuando no se aplican estrictas medidas de control. La tuberculosis bovina figura entre las enfermedades de la Lista B de la Oficina Internacional de Epizootias, lo que quiere decir que está considerada una enfermedad importante por sus repercusiones socioeconómicas o de salud pública dentro de los países y también por su incidencia en el comercio internacional de animales o productos de origen animal. De ahí que en la mayoría de los países industrializados se hayan emprendido campañas destinadas a erradicar *M. bovis* de la cabaña vacuna o cuanto menos a controlar la propagación de la infección. Esos programas de control y erradicación se han saldado con éxito parcial. *Mycobacterium bovis* infecta a otras especies animales domésticas y salvajes, y tal variedad de huéspedes puede complicar los intentos de controlar o erradicar la enfermedad en el ganado vacuno.

**Palabras clave**
Animales domésticos – Bovinos – Control – Mycobacterium bovis – Tuberculosis bovina.

References


