ADVANCES IN THE DIAGNOSIS, CONTROL AND ERADICATION OF
BOVINE TUBERCULOSIS (MYCOBACTERIUM BOVIS) IN DOMESTIC AND WILD ANIMALS

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Summary: This paper provides an update on recent advances in the diagnosis of bovine tuberculosis (TB), use of epidemiological tools, vaccination against TB and management of wild animal sources of infection. More sensitive and specific methods of diagnosis in the form of whole blood and serological tests, combined with more rapid means of identifying Mycobacterium bovis through liquid culture or polymerase chain reaction testing, will improve the effectiveness of TB diagnosis. A range of epidemiological analyses and DNA fingerprinting techniques, provide improved methods to target control efforts.

Low-dose BCG (bacille Calmette-Guérin) vaccine does provide protection for both cattle and farmed deer from challenge with M. bovis, and a test appears to be able to discriminate between vaccinated and infected animals. The outcome of future vaccine research will provide control options for countries that currently lack a compulsory TB control programme, or have wild animal reservoirs of infection.

Wild animal reservoirs of TB present an obstacle to eradication of the disease from cattle in some countries. Controlling TB in these countries is dependent on maintaining the wild animal TB reservoir population at low densities for extended periods. Cost or environmental concerns may preclude this option in some countries. Vaccination of the wild animal reservoir population is a future option for control.

1. INTRODUCTION

The infection caused by Mycobacterium bovis is an ancient insidious and chronic disease of cattle (44, 80). TB has also been identified in a wide range of mammals (44, 110), most of which appear to be spillover hosts (76). Mycobacterium bovis also causes clinical disease in humans indistinguishable from that caused by M. tuberculosis (44, 51), with which it is closely related. When TB is confined to cattle, diagnostic testing, slaughter of reactors and restricted movement from infected herds will eradicate the disease (9, 28, 89). It is, however, a long-term project requiring adequate funding, infrastructure, knowledge and above all, positive behaviour and motivation of all stakeholders involved (34, 78, 81). Possible consequences of failing to control TB in cattle include transmission of infection to humans, as well as other domestic and wild animal species. Wild animal maintenance (reservoir) hosts of TB (76) pose major impediments to controlling infection in cattle populations with which they interact (77, 87, 90, 111). Maintenance hosts may also act as sources of infection for other wild and domestic animals (19, 24, 65, 76).

Eighty-four (54%) of the 155 OIE Member Countries responded to a questionnaire requesting information on aspects of bovine TB. Of the respondents, 32% indicated they had either never had TB or had eradicated the disease, 33% had a compulsory national TB control programme in place, 16% indicated that they had a mixture of compulsory and voluntary control and the remaining 19% had no programme. Information from the survey was collated and some items are presented in Table 1.

The purpose of this paper is to update OIE Member Countries on recent advances in TB diagnosis, use of epidemiological tools, vaccination against TB and management of wild animal sources of infection.
2. TUBERCULOSIS IN CATTLE AND OTHER DOMESTIC ANIMALS

The clinical signs and pathology of bovine TB in cattle and other animals have been reviewed by a number of authors (9, 44, 96). Tuberculosis has also been found as an enzootic disease in other farmed livestock including deer and goats (66, 113). Other species such as pigs, sheep, dogs and cats are probably infected as spillover hosts (76). Thirty-four per cent of respondent countries indicated that they had identified TB in other domestic animals, including donkeys, water buffalo and camelds.

2.1. Infection and the immune response in cattle

Cattle become infected via the respiratory route (44, 76, 88). However, some authors (58, 85, 96) contend that infection via the oral route may also be important as M. bovis has been found to survive on pasture for between 4 and 70 days, depending on season, climatic conditions and site sampled (59, 85). The palatine tonsil is a possible common portal of entry for infection obtained via the nasal or oral routes (23, 66).

Under effective control programmes, clinical cases of TB are rare (88), and cattle-to-cattle spread of infection is uncommon, as infected animals are removed prior to becoming infectious (7, 76). Once an animal is infected with M. bovis, the rate of progress of infection is dependent on a number of factors including genotype, immune status and stress (46). Following exposure to M. bovis, two immunological pathways, Th1 and Th2, may be activated. If the Th1 response predominates, then protective immunity will be initiated and the host is more likely to contain the infection. If, however, the Th2 immune response predominates, then a more severe form of tuberculosis may occur (49, 118). To be successful, a vaccine needs to stimulate or enhance the protective immune response. Measuring these immune responses forms the basis of new in vitro diagnostic tests.

2.2. Diagnosis of tuberculosis

Most infected cattle mount a demonstrable cell-mediated immune response when infected with M. bovis (110). The intradermal tuberculin test measures this response and has formed the basis for eradication of bovine TB from a number of countries (34, 81, 96). The intradermal tuberculin test has also been used successfully in a range of other domestic animals (21, 53). In cattle, the test has a moderate to good sensitivity of 65-90%, and a relatively high specificity of 98-99% (45, 71, 118). Non specific reactivity to the intradermal tuberculin test and lack of sensitivity have caused problems in TB control programmes (56, 71, 118). A range of in vitro blood tests have been developed for the diagnosis of tuberculosis. As the cell-mediated response predominates, the most widely used blood tests measure T cell responses, rather than antibody responses.

a) Interferon gamma (IFN-γ) assay

IFN-γ is a cytokine that is released when sensitised lymphocytes are stimulated by antigens such as bovine purified protein derivative (PPD). The IFN-γ released is detected in an enzyme-linked immunosorbent assay (ELISA). The use and interpretation of the assay on cattle has been extensively reviewed (118, 119). In cattle, the IFN-γ assay has a reported sensitivity of 88-96.6%, and a specificity of 96.2-98% (72, 118, 119). The IFN-γ assay has been reported to detect infection in cattle earlier than the intradermal tuberculin test (40, 82). There is also a reported enhanced IFN-γ response to bovine PPD in infected cattle for a period of 7-60 days after tuberculin testing (39, 118, 119). The IFN-γ assay has been used as a diagnostic test on Asian and African buffalo (97), goats (40, 53) and a modified version is currently being evaluated on farmed deer (F. Griffin, pers. comm.). The IFN-γ assay has been approved as a primary diagnostic test for cattle in Australia (118) and is available as a commercial kit1.

A major disadvantage of skin testing is desensitisation for a period of 60 days (98). Thus, retesting with, for example, the comparative cervical test to investigate suspected non-specific reactivity has to be delayed. This delays the identification of infected herds and is an inconvenience for cattle owners. The enhanced IFN-γ response following tuberculin testing has been used in New Zealand as the basis of a short interval (10-30 days) retest following a positive intradermal test. This serial test was found to have a sensitivity of 88% and specificity of 93% and has been approved for use in this capacity (105). Field data collected over the past three years suggests that the IFN-γ assay has a significantly higher sensitivity than the comparative cervical test. Test procedures to take advantage of this have been introduced.

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1 The IFN-γ assay is packaged and sold as Bovigam™ by the Commonwealth Serum Laboratories Ltd., Victoria, Australia.
A further refinement to improve the specificity of this serial retest assay is being investigated. Replacing the bovine and avian PPDs in the IFN-γ assay with ESAT-6, a *M. bovis*-specific antigen, improves specificity, but with a slight drop in sensitivity (95). In future, a range of *M. bovis*-specific antigens may replace bovine PPD and improve both the sensitivity and specificity of the IFN-γ assay. Depending on cost, these same antigens may also replace the bovine PPD tuberculin used in the intradermal test, improving its specificity and sensitivity.

The use of the IFN-γ assay to enhance the identification of infected animals via parallel testing\(^2\) has also been investigated and approved for use in New Zealand (106). When used as a parallel test, the IFN-γ assay had a sensitivity of 90% (73).

The advantages of using the IFN-γ assay are: increased sensitivity; it represents a standardised approach to the test; it can be used as often as required, even after tuberculin testing; animals only need to be assembled and held once. The disadvantages of the IFN-γ assay are its relatively high cost and the need to transport blood samples to a laboratory for incubation within 30 hours of collection.

\(b\) Lymphocyte proliferation assay (LPA)

The LPA is another *in vitro* cell-mediated immunodiagnostic assay that has been used to diagnose TB in animals. It is a difficult assay to perform and has not found favour as a general diagnostic test for *M. bovis* in animals (118).

Nevertheless, a blood tuberculosis (BTB) test that combines an LPA with a serological ELISA has been developed (48). The combination of a cell-mediated test with an antigen detection test means that the BTB test has a wide diagnostic spectrum. The BTB test had a sensitivity of 95% and a specificity of 98% in farmed red deer (48). It has been approved as both a primary and ancillary serial test for diagnosis of TB in deer in New Zealand and the United States of America (USA), but is an expensive test to perform. A modified LPA has also been approved as an ancillary parallel test for cattle in New Zealand.

In New Zealand, both the modified LPA and the IFN-γ assay are routinely used as parallel tests to clear TB from chronically infected herds, or herds that have suffered large breakdowns (3).

\(c\) Serological tests

Serological tests such as the ELISA measure antibody titres to *M. bovis*. Most reports on ELISA indicate either a low sensitivity or specificity, that have precluded it being used as a primary diagnostic test for TB (118). However, intradermal tuberculin testing significantly enhances an infected animal’s response to the ELISA, relative to non-infected animals (54, 118).

In New Zealand, an ELISA has been approved for use on farmed deer following intradermal tuberculin testing, as a component of the serial BTB test, and on its own as an ancillary parallel test in infected deer herds (3). As an ancillary parallel assay, the combined sensitivity of the intradermal test and ELISA was 95% and had a specificity of 85% (47).

There are indications that the antibody isotype detected in the ELISA has an impact on sensitivity. The ratio of IgG\(_1\) response before and after intradermal tuberculin testing to a defined antigen (rMPB70) appeared to differentiate skin test reactors with lesions from those without (60).

\(d\) Culture of *M. bovis*

The gold standard for the diagnosis of tuberculosis in animals is the culture of *Mycobacterium bovis*. Problems with culture include the dangers to human health associated with handling zoonotic mycobacteria, and that it takes for up to 9 weeks for *M. bovis* to grow on solid media.

Recently, the BACTEC 460 TB system (Becton Dickinson), a radiometric liquid culturing system, was adapted for the isolation of *M. bovis*. The system isolates *M. bovis* in approximately half the time taken by conventional culture systems (G. de Lisle pers. comm.), yet it has the same sensitivity as solid culture media (120).

\(^2\) In parallel testing, cattle are tested with both the caudal fold and IFN-γ tests and animals positive to either test are declared reactors.
e) Polymerase chain reaction (PCR)

An alternative to culturing, is to use PCR to identify *M. bovis* in animal tissues, particularly those submitted from suspect lesions. Data indicate that the PCR has a sensitivity of 90% relative to culture and identified as positive, culture-negative samples that had large numbers of acid-fast organisms (AFOs) and macroscopic TB lesions (4, 115). Thus, the PCR may be correctly identifying as infected occasional samples containing non-viable *M. bovis*.

For tissues containing AFOs, the PCR provides a rapid and highly sensitive diagnostic test for detecting *M. bovis*. However, its sensitivity and technical complexity currently precludes it from replacing bacterial culture.

3. EPIDEMIOLOGICAL TOOLS

Controlling tuberculosis in cattle on a country wide or regional basis, is a long term and expensive project (34, 81, 96). Epidemiological tools provide the means to improve the cost-effectiveness of TB control programmes.

3.1. Database

The database forms the core of any large TB control programme. In its basic form it needs to securely maintain herd and animal testing information, as well as maintain control over reactor animals and infected herds. It should also provide reports on testing schedules, data for assessing disease progress and for evaluating epidemiological problems and associated risks. Ideally, the database should have a relational structure that will provide flexibility in storage of a wide range of information related to the herd or farm. This will enable expansion to accommodate new information, such as animal movements. It should also be compatible with databases containing spatial information such as property locations, or areas where wild animal populations are being controlled (103). The use of a data warehouse also makes it easier to extract data for epidemiological analysis from large relational databases (T. Ryan pers. comm.).

Sources of spatial data include satellite imagery for information on land cover, and Global Positioning Systems (GPS) for accurately recording locations of infected wild animals or infected herds (69).

3.2. Epidemiological analyses

Depending on the database structure, the information stored and the ability to link with other databases, a range of epidemiological analyses can be undertaken to investigate or assess risks associated with TB problems at a herd or regional level. They include a range of simple, but important animal and herd TB statistical analyses such as: prevalence rates; incidence rates; herd break down and clearance rates; relative risks; attributable risks, and herd transition matrixes. Rates can be compared between districts or regions to identify comparative progress or associations (27, 91), or for specific purposes such as identifying the impact of cattle movement on herd breakdown rates (22).

Identification of differences in rates, or relative risks may require further investigation and analyses. These could take the form of cross-sectional surveys to identify the prevalence of infection in wild animals (93), case-control studies to assess risk factors of herds or animals becoming infected (37, 50, 68, 69), and prospective studies to evaluate hypotheses (100).

Multivariate analytical techniques may also be used. These may include: survival analyses to investigate patterns of disease over time; multiple logistic regression analysis to investigate factors responsible for between herd spread, or to determine habitat factors that are associated with location of TB possum (*Trichosurus vulpecula*) clusters (69, 80); and cluster analysis to assess whether clusters of infected herds may signify infection in wildlife (69).

3.3. Modelling

Modelling uses known and best estimates of information to predict future events. Models can assist in providing a simple means of identifying the important factors in a TB control programme, and indicate areas for future research. Models have been used to investigate options for controlling spread of TB within and between herds (7, 8, 104, 114). They have also been used in New Zealand to investigate a range of control strategies, including culling, vaccination against TB and immunocontraception as a means of eradicating infection from possum populations (5, 6, 94, 101).
3.4. Decision support systems

Decision support systems make use of a suite of integrated tools, including models to assist administrators and farmers to make decisions on cost-effective TB control programmes. In New Zealand, a decision support system, EpiMAN-TB, is being developed that ‘comprises a relational database, map display and spatial analytical tools, simulation models of the spread of TB between possums at both farm and regional levels, and expert systems.’ (70). The decision support system is designed to improve the cost-effectiveness of possum control programmes.

3.5. Differentiating \textit{M. bovis} isolates

Determining the source of a newly identified TB infection in domestic or wild animals enables disease control managers to better target control efforts. DNA ‘fingerprinting’ is used to differentiate \textit{M. bovis} isolates by characterising DNA variations that occur on certain sites in the chromosome. Methods of differentiating \textit{M. bovis} isolates, together with their advantages and uses are discussed by various authors (29, 30, 31, 33, 35).

To varying degrees, these methods provide an objective means of differentiating \textit{M. bovis} isolates. This provides a practical means of identifying likely sources of infection identified in cattle and deer herds, as well as wild animals (10, 33, 35, 52, 116).

4. VACCINATION OF DOMESTIC ANIMALS

Reviews of vaccine trials conducted in the 1950s concluded that BCG (bacille Bilié de Calmette-Guérin) offered no sufficiently protective effect to cattle, and had not contributed to the control of bovine TB. As a consequence, in 1959 the World Health Organization recommended that vaccination of cattle cease (96). Due to the resurgence in human TB, and the problems being experienced in controlling TB in domestic animals, TB vaccination has re-emerged as an important research area.

For domestic animals, the major problem has been in producing a vaccine that consistently provides high efficacy against challenge and does not interfere with the interpretation of the intradermal tuberculin test. Factors that appear to influence the efficacy of vaccination with BCG in cattle include the size of the dose, the strain and viability of the BCG organism, method of presentation, host genotype, environmental stressors and pre-exposure to other mycobacteria (12, 57, 83). For protective immunity against tuberculosis it is vital that vaccination initiates the appropriate (Th1) immune response (11, 49). Vaccination with live mycobacteria has the advantage that they continue to produce a range of antigens that provide continued stimulation of the correct host immune response (83), whereas killed BCG in oil or killed \textit{Mycobacterium vaccae} did not protect cattle or deer (15, 49).

Recent trials indicate that vaccination of calves and red deer with either single or double low doses of BCG (15, 49), by a variety of routes, afforded good protection\(^3\) following challenge with \textit{M. bovis}.

One of the disadvantages of vaccinating cattle with BCG is that the cattle become tuberculin reactive for up to 18 months (14, 74). Possible solutions include using a recombinant BCG vaccine that induces a smaller intradermal reaction to tuberculin (108), or testing animals using the IFN-\(\gamma\) assay with the ESAT-6 antigen to differentiate between BCG vaccinated and infected cattle (17).

Other approaches to vaccination have concentrated on finding alternatives to BCG. Recent approaches include attenuation of \textit{M. bovis}, identification of the protective antigens for use in recombinant vaccines or expression in live attenuated bacteria and viruses, and investigation of DNA vaccines. In this regard, vaccination of calves and guinea-pigs with attenuated strains of \textit{M. bovis} afforded equivalent or greater protection against challenge with \textit{M. bovis} than BCG vaccinated animals (13, 36). \textit{Mycobacterium tuberculosis} DNA vaccines have enhanced the Th1 response in previously infected mice to help clear the infection, as well as providing protection against TB in healthy animals (63).

\(^3\) Protection includes protection against infection (no \textit{M. bovis} cultured) and disease (no gross lesions, but \textit{M. bovis} cultured), relative to unvaccinated animals.
5. SELECTION FOR GENETIC RESISTANCE IN DOMESTIC ANIMALS

An alternative approach to vaccination is to select for cattle that are genetically resistant to infection with *M. bovis* (83). Lines of cattle and sheep have been selected for resistance to a range of diseases (75) and selected lines of cattle have shown observable resistance *in vitro* to *Brucella abortus* (109).

Initial work indicates that there is a genetic basis to susceptibility and resistance to TB in deer (67). It has been noted though that susceptibility and resistance are both relative to the challenge level of infection. Thus resistant animals may still be susceptible if exposed to relatively high levels of infection (11). With rapid developments in molecular immunology and genetics, markers for detecting genetic resistance may in future assist in controlling bovine tuberculosis.

6. TUBERCULOSIS IN WILD ANIMALS

6.1. Epidemiology

TB has been identified in a wide range of wild animal species (76, 77, 96). Twenty-two per cent of countries surveyed indicated that they had identified TB in wild animals within the past 10 years. TB was reported as being found in wild deer, possums, pigs, goats, cattle, buffalo, ferrets, stoats, foxes, lions, cheetahs, kudu, baboons, other monkeys, hares, elk, hedgehogs, wallabies and seals. In the majority of instances, infection is not self-sustaining within the species and consequently they are described as spillover hosts (76).

In most cases, spillover hosts are predators or scavengers and once tuberculosis has been eliminated from the maintenance host (cattle), then infection disappears from the spillover host population (77). Spillover hosts are usually not involved in the spread of infection, but occasionally may act as a source of infection for other animals (77).

In rare instances, largely as a result of overlapping home ranges, high wild animal density, and presence of infected cattle or farmed deer, *M. bovis* is transmitted to a wild animal species where it becomes self-sustaining. These wild animal maintenance hosts may also act as a source of infection for other animals including cattle. Maintenance hosts include possums (*Trichosurus vulpecula*) in New Zealand (61, 77, 84); badgers (*Meles meles*) in the United Kingdom and the Republic of Ireland (26, 37, 43, 76); white-tailed deer (*Odocoileus virginianus*) in Michigan, USA (24); African buffalo in the Kruger National Park, South Africa (38), and in a number of other areas (76, 96). Wild animal maintenance hosts were identified in 11 (13%) countries surveyed. In these countries, eradication of TB from herds through a test and slaughter programme may be compromised by re-infection following contact with wild animal reservoirs of infection (28, 61).

Issues that appear critical to maintaining infection within a wild animal species include localised close contact of animals either at their den sites (77, 117) or, for ruminants, in their close feeding or grazing habits (24, 38). This facilitates horizontal aerosol spread. Pseudo-vertical spread of infection from mother to offspring appears to be an important route of infection for young animals (77, 85). Fighting, biting, grooming and mating may be important to varying degrees in maintaining infection in possum and badger populations (55, 77, 85). Spread of wild animal infection is facilitated by emigration of infected sub-adult, usually male, possums and badgers from their maternal range (76, 77).

Other wild animal species may become infected as a result of predation or scavenging. In a number of areas of New Zealand, high TB prevalence rates have been recorded in ferret (*Mustela furo*) populations (64, 99). In some areas, TB-infected ferrets are considered to be acting as a source of infection for cattle and deer (62, 99).

TB is spread to cattle and deer largely as a result of direct contact between a severely weakened and disorientated possum, ferret or badger in the terminal stages of TB (25, 37, 85, 92), and inquisitive, dominant cattle or deer (28, 92, 107). In contrast, some researchers believe that TB is spread from badgers to cattle through urine and faeces (37, 85), with badger latrines being more likely to be grazed by lower dominance cattle (58).

Feral deer in New Zealand are believe to become infected after direct contact with TB possums in the same manner as for cattle and farmed deer (65, 86). In contrast in Michigan, USA, supplemental feeding provides increased opportunities for contact and spread of infection within the wild deer population (24). Thus in these instances, wild deer appear to be acting as a maintenance host for TB.
6.2. Locating tuberculous wild animals

The presence of wild animal reservoirs of TB is traditionally detected through the persistent re-infection of cattle and farmed deer herds within a defined area. Cross-sectional wild animal surveys may then be undertaken to detect the source of the infection. In New Zealand, because TB possums are clustered spatially and temporally (77), infection may be difficult to detect in cross-sectional surveys. As a consequence, emphasis has shifted to surveying scavenger species such as ferrets and feral pigs as well as feral deer, depending on the habitat. As scavenger species all have large home-ranges that overlap with those of numerous possums, and once infected appear to live longer than TB possums, they provide a good indicator as to the presence or absence of infection.

7. CONTROLLING TUBERCULOSIS IN WILD ANIMAL POPULATIONS

7.1. Population control

A number of models have indicated that in the absence of immigration, TB can be eradicated from an infected possum population by maintaining it below a certain threshold density (5, 101).

Based on model predictions and historical findings, the New Zealand TB control programme has maintained low possum densities (<20% of pre-control levels) over approximately 3 million hectares at a cost of US $15 million per year. This has been pivotal in causing a 53% reduction in the number of infected cattle and deer herds since 1994 (2, 20, 28, 91). TB has also been eradicated from domestic and wild animal populations in six small areas (28).

Similar progress in reducing herd breakdowns and TB incidence rates in cattle has been observed following badger removal (27, 43). Lowering density also forms the basis of the management plan for control of tuberculosis in white-tailed deer in Michigan (24).

In New Zealand, the possum is an introduced species that threatens a number of indigenous flora and fauna populations. Controlling possums for TB and conservation purposes is expensive and biocontrol methods are therefore being investigated as a future means to achieve this (41, 42, 102).

In other countries, where the maintenance host may be an indigenous and protected species, such as the badger, large-scale culling programmes as practised in New Zealand may not be acceptable. Local badger control around infected herds, or the testing and removal of test positive badgers may provide temporary relief from infection for local herds, but will not eliminate the disease from the wild animal population (76).

7.2. Vaccination

An alternative to removal is vaccination of the maintenance host to protect it from TB. Vaccination does not need to prevent infection in the wild animal population at risk, but rather reduce transmission of M. bovis to cattle, deer and other wild animals (57, 77).

Vaccination of possums with BCG intranasally, subcutaneously, or via the duodenum all reduced the severity of tuberculosis in possums following challenge relative to unvaccinated or orally vaccinated possums (1, 16). Cost-effective means of delivering BCG to possums and assessing the length of time BCG induced protection lasts are currently being investigated (18). Thus vaccination potentially provides another tool for the programme for controlling TB in possum populations in New Zealand.

A TB vaccine may also provide an acceptable means of controlling TB in badger populations (32, 57, 85). As badgers regurgitate food for their cubs, this also provides a potential means of reducing pseudo-vertical transmission of infection (57).

7.3. Eradication of tuberculosis from the wild animal populations

It is important to be able to identify when tuberculosis has been eradicated from the wild animal populations. In New Zealand, for several years prior to declaring that TB has been eradicated from an area, ferrets, feral pigs and deer are surveyed as a means of detecting any residual wild animal infection.
8. CONCLUSION

In vitro diagnostic tests with increased sensitivity and specificity provide the means to rapidly eradicate infection from herds with minimal wastage of animals resulting from false-positive test results.

Relational databases together with a range of epidemiological tools can be used to identify associations between infected cattle populations, management techniques and local environmental and ecological factors. These provide the basis for sound epidemiological analysis of disease risk factors, which in turn allows for implementation of more precise and effective measures to contain, control and eradicate infection.

The range of new technologies enables managers to design TB control programmes to better target local conditions and improve both cost-effectiveness and farmer acceptability. These tools also provide for increasingly sophisticated risk management approaches to TB control, which are required where wildlife reservoirs of the bacillus compromise the effectiveness of traditional, technically simple programmes based on test and slaughter and livestock movement control.

Since the OIE International Animal Health Code recommendations for TB control were written, there have been major developments and advances in TB diagnostics and epidemiology, and it is likely that effective vaccines will soon be available for controlling TB in a range of animal species. Some of these new disease control tools will have applications for improved management of wildlife reservoirs of TB. It is therefore recommended that the current OIE International Animal Health Code be reviewed to take account of these findings and advances.

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