

## Bovine Tuberculosis Summary

### Introduction

1. This note provides a brief summary of an analysis undertaken by a DISCONTTOOLS group of experts on Bovine Tuberculosis. They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details can be downloaded from the web site at <http://www.discontools.eu/> by selecting Disease Database, then the specific disease and highlighting the variables of interest. This is completed by selecting “create a report” which can then be downloaded as either a PDF or Excel spread sheet

### Disease profile

2. Bovine tuberculosis (BTB) caused by mainly by *Mycobacterium bovis* but also increasingly by *M. tuberculosis*, affects cattle, other domesticated animals and certain wildlife species. Other species of the *M. tuberculosis* complex previously considered to be *M. bovis* include *Mycobacterium caprae* and *Mycobacterium pinnipedii*. These species are also known to be zoonotic. While *M. bovis* causes zoonotic TB in humans, the majority of TB cases in humans are caused by *M. tuberculosis*.
3. Cattle are considered the primary target for BTB, species such as goats are also highly susceptible and can maintain infection in the absence of cattle. Wildlife can act as maintenance hosts or reservoirs and represent a serious problem in several countries. Among wildlife species that act as maintenance hosts are brush-tailed opossums in New Zealand, badgers in the UK and Ireland and kudu and African buffalo in southern Africa.
4. The main routes of transmission vary greatly between species. In cattle, *M. bovis* is believed to be transmitted between animals usually by the respiratory route during. In infected cattle, bacteria can be shed in respiratory secretions, faeces and milk and to a lesser extent in urine, vaginal secretions or semen. Ingestion appears to be the primary route of transmission for carnivores. *M. bovis* can infect humans primarily by the ingestion of unpasteurized dairy products but also by aerosols and through breaks in the skin.
5. Disease progression and mortality rates vary greatly in different species. In cattle, BTB is usually a slowly progressive condition with no obvious signs of disease in the early stages. In the later stages, symptoms include emaciation, fever, weakness, lack of appetite and respiratory distress. Infections can remain persistent for years. In countries with eradication programs, most infected cattle are identified early and overt clinical symptoms are uncommon.

### Risk

6. Human disease caused by *M. bovis* is rare in countries with successful BTB control and eradication programs, established meat inspection procedures and milk pasteurisation. Where BTB is poorly controlled in livestock and consumption of raw milk or unpasteurised dairy products is frequent, BTB may represent a human health risk. Control and eradication programs are based on test-and-slaughter procedures in cattle. These measures can be very expensive and consequently are seldom used in developing countries. Reservoirs of infection in wildlife render complete eradication difficult in several countries.
7. In countries without disease control, cattle-to-cattle transmission rate can be high, particularly when animals are kept intensively. There is a high risk of farm to farm and transboundary spread of infection through the movement of infected cattle. Pre-movement testing reduces this risk but testing may not detect all infected animals.



## Diagnostics

8. The predominant method for diagnosis of BTB in live cattle is the tuberculin skin test, consisting of an intradermal injection of a purified protein derivatives from a culture of *M. bovis* (*bovine PPD*), or, alternatively to increase specificity, the comparison of reactions induced after injection of bovine and avian PPD (the latter produced from a culture of *M. avium*). IFN- $\gamma$  release assays (IGRAs) have also been developed and are being increasingly applied. When used in combination with skin tests, overall sensitivity is increased.
9. Tuberculins are largely undefined and difficult to produce and standardise (e.g. BCL3 facilities are required, including animal facilities to perform guinea pig potency assays). Therefore, the development of defined skin test reagents based on specific *M. bovis* antigens would be beneficial to overcome these limitations of tuberculin.
10. Several serodiagnostic tests have been developed or are presently being developed but generally lack sensitivity compared to IGRA and skin test, but have been usefully applied in some wildlife and domestic animal species (e.g. deer or South American Camelids).
11. Better tests that are rapid, specific and simple are needed for live animals, particularly for cattle in developing countries, and for wildlife species.

## Vaccines

12. At present the only potentially available vaccine is BCG, which is a live attenuated strain of *M. bovis* used for humans since the 1920s. Studies with BCG showed variable efficacy in cattle at population and individual animal levels. Although BCG prevented can prevent the development of pathology/bacillary persistence in a proportion of animals, as in humans, in most studies, BCG vaccination did not prevent infection but reduced the number and severity of pathology and thus likely reduced transmission. The use of BCG will however compromise specificities of tuberculin-based tests and the development of DIVA tests for cattle is essential. The commercial potential for effective vaccines is high in some countries where BTB remains a problem, in particular UK and Ireland.
13. Improved vaccines for cattle are under active development based on genetically modified BCG or *M. bovis*, DNA, protein or virally vectored subunits, used stand-alone or in conjunction with BCG. Non-sensitising vaccines would overcome the problem of skin test sensitisation associated with BCG-based strategies.
14. BCG vaccines may reduce *M. bovis* in wildlife reservoirs and an injectable vaccine has been licensed for use in badgers in UK. The further development of delivery systems for the application of vaccines in wildlife is needed.

## Pharmaceuticals

15. Antimicrobial treatment is not applicable for BTB control in livestock.

## Knowledge

16. Further investigations into the host pathogen interactions and the immune response would provide valuable information of use in the development of new vaccines and better diagnostic tools. A better understanding of the epidemiology of *M. bovis* infections in cattle and cattle herds would enable strategies to be developed for the use of new vaccines when available. The role of environmental persistence of *M. bovis* in the epidemiology and transmission of BTB to cattle needs further investigation.
17. Knowledge is lacking concerning the occurrence and epidemiology of BTB in developing countries. Even though the prevalence of BTB in cattle is widely known in most European countries, information is lacking on infection by *M. bovis*, *M. caprae*, *M. pinnipedii* and even *M. tuberculosis* in other animal species. Similarly the pathogenesis, morbidity and clinical signs associated with disease in other animal species are not well described. Further studies on different wildlife species are needed in developed and developing countries in order to develop effective diagnostic tests and vaccination control approaches.



## Conclusions

18. Control programs have eliminated or nearly eliminated this disease from domesticated animals in many developed countries although complete eradication is exceedingly difficult to achieve particularly if a wildlife reservoir is present. BTB represents an important human health risk particularly in developing countries where control is absent or poor.
19. Aspects of the epidemiology, pathogenesis, host pathogen interactions and immune response require further study in order to develop improved diagnostic tests and vaccines.