Committee for Agriculture and Rural Development

Review of Bovine Tuberculosis

Written Evidence from the Agri-Food & Biosciences Institute (AFBI)

BACKGROUND TO BOVINE TB (bTB) WORK AT AFBI

1. AFBI's work on bTB includes a range of statutory and analytical testing for DARD, as well as a significant programme of research supported by DARD and other research funders.

Statutory and analytical work

2. The statutory and analytical work on bTB undertaken at AFBI is in direct support of the NI control program, and as required by European legislation. This work includes confirmation of bovine TB using a combination of histology, culture and molecular confirmation; performance of supplementary (blood) testing using interferon gamma (IFNG) assays; high resolution strain typing of TB isolates; and the laboratory examination of road kill badgers. DNA forensic typing of cattle by AFBI is also used by DARD to investigate potential cases of cattle identity fraud. All statutory tests are performed to EU and international methodology and to the ISO/IEC 17025(2000) accreditation quality standard.

AFBI bTB Research

3. AFBI has an international reputation for its research work on bTB, with key staff active in collaborative, international research networks. In total, AFBI staff have published or co-authored approximately 140 refereed scientific papers on bovine TB, as well as numerous non-refereed papers, scientific conference talks and technology transfer events. The work includes applied and basic research, reflecting the mix of DARD and externally-funded work.

4. The organisation has secured substantial external (non-DARD) funding for research in TB in a competitive, international field. The majority of these external projects are undertaken in collaboration with world-leading institutes across the UK, Ireland, and elsewhere, and allows NI to benefit from the latest international research findings. Recent external

funders include the EU, Defra, the Biotechnology and Biological Sciences Research Council (BBSRC), and Science Foundation Ireland.

5. Core DARD research funding in key areas such as TB molecular biology and immunology has been, and remains, critical to both this research effort and the statutory testing programme, and is necessary to maintain the capacity and expertise needed to undertake high quality internationally competitive research.

INTRODUCTION TO BOVINE TB

6. Bovine TB, which is caused by the bacterium *Mycobacterium bovis,* is generally recognised as the most difficult endemic animal disease problem in the UK and Ireland.

7. BTB is primarily a chronic respiratory disease of cattle, which in the advanced stage, is associated with loss of productivity. The causal organism presents a potential risk to human health, although such infections are now rare in developed countries due principally to the introduction of milk pasteurisation. Control of the disease is required under European legislation.

BOVINE TB TRANSMISSION

8. The epidemiology of bovine TB is complex, with current evidence indicating both cattle and wildlife sources of infection. The relative importance of these two sources is not known and importantly will vary across regions and over time, with factors such as the adequacy of cattle control measures, the infection pressure in wildlife populations and the degree of interaction between cattle and wildlife species being relevant.

Cattle-to-cattle transmission

9. BTB is primarily a respiratory (lung) disease of cattle and prior to the introduction of test and slaughter programmes, cattle-to-cattle transmission would have overwhelmingly predominated.

10. The predominant mechanism of cattle-to-cattle transmission is via aerosol involving close contact between animals. Indirect transmission

via faeces and contaminated objects is thought to be much less important, but cannot be discounted. Milk-borne infection (e.g. from cow to calf) can also occur on occasions.

11. Recent evidence, including collaborative work undertaken by AFBI and the Roslin Institute (University of Edinburgh), indicates that cattle vary in their genetic susceptibility to infection, raising the prospect of breeding animals with increased resistance to bTB. Variability in the susceptibility and infectiousness of individual animals due to non-genetic effects, such as inter-current disease and physiological status, are also likely.

Wildlife-to-cattle transmission

12. Wildlife reservoirs of bTB infection are recognised in a number of countries, including possums in New Zealand, white tailed deer in Michigan USA and wild boar on the Iberian peninsula. A wildlife source was first suspected in GB due to persistent foci of bTB infection in SW England and infected badgers were detected in Gloucestershire in 1971. Reports of infected badgers followed from the RoI and from 'Road Traffic Accident' surveys in NI.

13. Although bTB infection has been recorded in a range of both domestic and wildlife species, only badgers and possibly deer in some localised areas, are thought to be significant in the UK and Ireland. The evidence implicating badgers in the epidemiology of bTB includes the recorded occurrence of the infection in badgers; spatial similarities in the strain types infecting badgers and cattle; and the results of badger removal trials which have either increased or decreased the incidence of TB in cattle.

14. Badger to cattle transmission is thought to occur either directly via aerosol transmission when there is close contact between the species or indirectly via contaminated urine or faeces. Current evidence would tend to favour direct aerosol transmission though this is not conclusive. There is also published evidence from GB indicating cattle-to-badger transmission.

BTB CONTROL: CATTLE TESTING

15. Control of bTB was first initiated due to the human health risk with voluntary test and slaughter schemes introduced in the UK in the 1930s and later followed by compulsory schemes. Prior to the introduction of control schemes, infection in cattle was widespread with some estimates indicting 20-40% of cattle to be infected.

16. The aim of test and slaughter programmes is to detect and remove infected cattle as early as possible and thereby minimise the likelihood of further cattle to cattle spread. Importantly the effectiveness of these programmes depends on the accuracy of the tests used, as well as the nature of infectious contacts between animals.

17. Skin testing remains the standard test used in bTB control schemes worldwide, albeit in slightly different formats. The UK and Ireland use the single comparative intradermal tuberculin test (SCITT). This test has a very high specificity (~99.9%) meaning that there are relatively few false positive reactions. Estimates of sensitivity, which is a measure of how good the test is at detecting infected animals, are however variable (~55-90%). Recent estimates tend towards the lower end of this range and test sensitivity could probably be best described as moderate. Overall sensitivity of the SCITT at a herd level is however higher particularly with regular testing and when used with greater frequency in breakdown herds.

18. Efforts to develop alternative blood based tests have been hampered by the complex nature of the disease. The most common alternative test in use, including at AFBI, is the interferon gamma (IFNG) assay. This test has a higher sensitivity, but in its current format is more costly than the SCITT test and has a lower specificity (higher numbers of false positives), which limits its application to high risk situations.

19. There is evidence to indicate that bTB test sensitivity may be reduced by other diseases including Johne's disease and fluke infestation. This evidence includes work by AFBI in collaboration with University College Dublin, which has demonstrated experimentally that co-infection with the common parasite liver fluke reduces the immune response to bTB, as measured by both the skin and IFNG tests.

BIOSECURITY

20. Fundamentally BTB is an infectious disease (albeit that this appears variable) and biosecurity measures to limit transmission are a necessary part of control.

Measures to minimize cattle to cattle transmission

21. A broad range of measures have been proposed to prevent cattle to cattle transmission, based on minimising the likelihood of both direct and indirect transmission. These include cessation or limiting cattle purchases; pre- and / or post-movement testing; preventing close contact between neighbouring herds; biosecurity awareness;cattle and effluent management; and avoiding sharing equipment, etc.

Measures to prevent wildlife to cattle transmission

22. Measures to prevent wildlife to cattle transmission are more uncertain due to the more limited evidence base. For convenience these measures can be divided into measures at housing and at pasture. Measures at housing include preventing direct badger-cattle transmission by preventing badger incursions into farm buildings and preventing direct/indirect transmission by stopping badger access to feed and silage stores. Measures at pasture are aimed mainly at stopping indirect contact and include raising feed and water troughs, fencing off access to badger setts and alterations to grazing patterns.

DEALING WITH TB IN WILDLIFE

23. Dealing with TB in wildlife, and in badgers in particular, presents fundamental difficulties and can have unintended consequences. Direct intervention options are either badger culling or vaccination.

Badger culling

24. The results of badger culling interventions and trials are complex, and we have included only salient points here. In GB a series of badger culling approaches were undertaken during the 1970s, 80s and 90s with few conclusive outcomes. The Krebs review (1997) led to establishment of the Randomised Badger Culling Trial (RBCT) which compared proactive (area based) and reactive culling (in response to individual farm

breakdowns) to areas where no culling took place. In brief, proactive culling in the trial was associated with a modest beneficial effect (decrease in bTB) within the cull area but an initial detrimental effect (rise in bTB) in the 2km surrounding area (attributed by the authors to the so-called perturbation effect). Preliminary results from the reactive culling element showed a detrimental effect in the prevalence of bTB in local herds, and this part of the trial was stopped early. Results from the 'Four Area Trial' and the earlier East Offaly project in Ireland have shown beneficial effects from an area based culling approach.

25. The potential benefits of area-based culling do however need to be balanced against the ecological impact and the significant economic cost. Extrapolation of trial results to other areas with differing parameters such as badger densities, cattle density, husbandry and testing regimes, also requires a significant caution. Culling of small targeted areas will also have very limited impact on overall regional or national bTB levels.

Badger Vaccination

26. Currently there is one licensed vaccine (BCG), but notably this is an injectable vaccine and requires badgers to be caught (cage trapping) with all of the associated costs. Experimental and field data have shown the vaccine to give reasonable protection, but large field trials to demonstrate the impact on cattle bTB levels have not been undertaken. Further work on oral delivery vaccines is on-going in both GB and Ireland.

OVERVIEW OF AFBI TB RESEARCH

27. Due to the complex nature of bTB including the organism itself, the response of cattle to infection, the limitations of currently available diagnostic tests and vaccines, and major gaps in our knowledge of interactions between wildlife and cattle, disease eradication can only be based on increased emphasis on research.

Molecular and strain typing research

28. AFBI scientists have been at the forefront of developing strain typing methods for *M. bovis*, including the identification of genetic markers that are used internationally. These rapid and high-resolution techniques are applied routinely in NI as an aid to identifying sources of infection and for surveillance purposes (e.g. to track emerging strains). This surveillance has shown marked geographical clustering of strains, suggesting that the epidemic tends to be driven by local transmission events.

29. Importantly the integration of strain typing information with cattle movement and test data has started to answer fundamental questions about bovine TB epidemiology, including issues such as: is there strain variation in virulence?; are there strains which evade current skin tests?; how do cattle and wildlife strains compare?; what is the role of cattle movement?; how do NI strains compare to strains in GB, Ireland and beyond?

30. The work on strain typing has also led to other significant areas of investigation. Examples include the work on genetic susceptibility referred to earlier. A further recent pilot study with the University of Glasgow is using whole genome sequence methods to compare cattle and badger isolates at the highest level of detail possible and to model transmission events

Immunology research

31. Understanding the cattle immune response to infection is crucial to understanding bTB and to developing improved diagnostics and vaccines. Bovine TB immunological R&D at AFBI has included: understanding the early immune response; disease transmission between cattle; developing new diagnostics reagents; trialling novel vaccine candidates; and characterising the effects of co-infection on disease development and diagnosis.

32. Some examples of early work include the characterisation of the cells involved in the early immune response. Work in collaboration with other groups demonstrated the potential of a unique antigen, ESAT6, which is highly specific to TB and now used in the IFNG test. Central to this work has been the development of bovine models of infection that closely mimic natural infection using high containment facilities. AFBI's infection model is used widely in international collaborative research projects.

33. Bovine and human TB have many striking similarities. The expertise established at AFBI has attracted collaborative research from experts in human TB, leading to the sharing of diagnostic reagents and opportunities to evaluate potential new vaccines. Recently AFBI secured EU funding to develop a ferret infection model (to mimic badger infection). Work using this model has started to evaluate a novel vaccine candidate, which may offer advantages over the current TB vaccine (BCG) in conferring protection in animals that are already infected.

Epidemiology and Ecology R&D

34. Routine data collation and the majority of epidemiological research on bTB in Northern Ireland has to date been undertaken in-house by DARD's Veterinary Service. AFBI has however been recently funded by DARD to undertake three projects including: the TB Biosecurity Study, an analysis of IFNG testing and an ecological project on cattle-wildlife interactions. These projects are on-going at present.

FUTURE TB RESEARCH NEEDS

35. While significant bTB R&D has been undertaken both in NI and elsewhere, the challenges of bTB control are immense, with a multiplicity of factors driving both short and long-term disease trends.

36. Research in a number of areas is needed to address this challenge. In relation to cattle some examples include work to better understand: cattle to cattle transmission and the circumstances in which it most occurs; the impact of genetic and non-genetic effects on susceptibility; the effect of intercurrent diseases, including their impact on skin and other tests; improved bTB diagnostic tests including further development of IFNG and other assays; improved understanding of the general and molecular epidemiology of the disease.

37. In relation to wildlife, there is the need to better understand badger-cattle interactions and how best to minimise contact between these species. Work in relation to vaccine efficacy, improved vaccines and vaccine-delivery mechanisms are also long-term requirements.

38. In 2010, DARD commissioned AFBI to undertake four reviews of the scientific literature on cattle and wildlife bTB issues to help inform DARD considerations of future R&D needs. These reviews are available on the DARD website.

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