Bovine Tuberculosis - Towards a Science Based Control Strategy

J. Bourne – Chairman, Independent Scientific Group:
C.A. Donnelly, D.R. Cox, G. Gettinby, J.P. McInerney, W.I. Morrison, R. Woodroffe.

In order that future TB control policies can be science based, Defra on ISG advice has put in place a comprehensive programme of research to better understand the epidemiology of TB in both cattle and badgers.[1,2,3] This research is now providing a flow of valuable data on a range of topics, extending beyond the trial on culling badgers that was originally proposed in the Krebs report.[4] Emerging data, as yet incomplete, will allow secure scientific conclusions to be drawn.[5]

The Randomised Badger Culling Trial (RBCT)

The RBCT design which has been described in detail[1-3] involves three experimental regimes – proactive culling, localised reactive culling and no badger culling, the latter providing a survey only control. The objective of proactive culling is to reduce badger densities to low levels across entire areas, and this is maintained by further regular culls. Reactive culling, by contrast, initiated in response to confirmed cattle TB breakdowns, focused on home ranges of badgers as a one off operation. Both culling methods were subject to badger welfare concerns.[5,7,8] The principal question addressed by the RBCT is "what contribution can proactive culling and reactive culling make to controlling cattle TB".

The trial was designed to provide reliable estimates of the effects of culling on TB breakdowns by the time 50 triplet years have been accumulated and, in addition, a range of epidemiological and other data to provide a better understanding of the disease in both cattle and badgers. Analysis of herd breakdown data, the measure of the impact of badger culling on the disease in cattle, is carried out by two members of the ISG, audited by an Independent external statistical auditor, at six monthly intervals.

Thus far the results from the proactive treatment remain inconclusive, the results of reactive culling, however, based on data up to August 2003, and a further analysis to August 2004, provided convincing evidence that reactive culling of badgers does not offer a beneficial effect large enough to make it useful as a potential policy option and that there is substantial, but not overwhelming, evidence of an adverse effect of the reactive strategy[6]. This component of the trial has been stopped.

The proactive treatment continues and 50 triplet years, which marks the predicted end of the trial, will be reached in early 2006.

Badger Welfare

Since the inception of the trial, the ISG has been committed to testing the effectiveness of badger culling policies that would constitute practicable policy options if they were found to be effective. It was considered that if culling strategies

had very serious impacts on conservation and animal welfare they would not be sustainable in the long term – not least because they would be rejected by the public, including landowners in trial areas. Two aspects of badger culling had major implications for badger welfare, the method of catching badgers – cage trapping, and the timing of culling in relation to badger breeding season and the avoidance of the starvation and death underground of dependant cubs whose dams had been killed.

A detailed analysis of cage trapping data evaluating the injuries sustained by badgers captured in cage traps and the effectiveness of a closed season on avoiding the death of badger cubs from starvation have been recently published.[7,8]

In summary while cage trapping may have consequences for badger welfare other than physical injuries (particularly stress) trial data demonstrate that most badgers (88%) confined to traps have no detectable injuries as a result of being confined in the trap and of those injured 74% record only minor skin abrasions. A minority (1.7%) experienced tooth damage likely to have involved serious (albeit short term) suffering. Modification to cage traps – smooth coating of wire mesh, and modified door mechanisms – have reduced abrasion and other injuries further.

In order to minimise leaving unweaned cubs to starve when their mothers are culled a closed season for culling was instituted during February, March and April based on the best available data on the timing of badger reproduction to cover the lactating period. In contrast to predictions from welfare groups that large numbers of cubs (upward of 2000) would die underground as a result of trial operations, data suggests that the number is less than 20 cubs per annum. Thus although the adoption of a closed season has some practical disadvantages, by limiting the time for badger culling and lengthening the response time for a reactive cull, it shows clear welfare benefits.

Risk Factors - TB99 Epidemiological Survey

Many risk factors in relation to environment and cattle husbandry practices have anecdotally been suggested as predisposing farms to TB breakdowns. Because of the large number of factors[3] these are not easily amenable to experimental investigation but useful information can be gained from the TB99 epidemiological case-control study which compares data from breakdown farms to non-breakdown farms in trial areas. This approach allows investigation into the wide range of factors such as herd size, land cover, soil type, grazing systems, housing, movement of cattle etc which are potentially associated with an increased, or a decreased, risk of TB in cattle.

An initial analysis of trial data from a clearly defined data set up to 2001 has been carried out and recently published.[9] Of the large number of factors screened for association with a herd TB breakdown those factors associated with an increased risk were found to be moving cattle on to farms from markets or farm sales, operating the farm over several premises, use of covered yard housing and the use of other undefined housing types. In contrast those factors found to be associated with a decreased risk of a herd breakdown were spreading of artificial fertilisers and farmyard manure.

In view of the approach, and the limited data analysis undertaken, the risk factors identified are cautiously regarded as being associated with TB herd breakdowns, and not proof of causation. The results have provided a focus and helped to inform farm practice. Further case-control analyses of post FMD TB99 data are ongoing, and in the light of the experience and findings from TB99 the modified, shorter Case Control Study form (CCS2005) has been designed for the further evaluation of herd breakdown risk factors. This new form was implemented in January 2005 and is being used to collect more information not only within the RBCT trial areas but elsewhere in England and Wales.

Other Trial Related Research

In addition to addressing the effects of two culling approaches on the incidence of cattle TB herd breakdowns, the RBCT provides valuable baseline epidemiological data. This includes the prevalence of TB in badgers, its relationship to social group size and structure and, importantly, the spatial relationship between TB infected badgers and cattle herd breakdowns. These data are currently being analysed and along with other trial related research on matters such as the impact of badger removal on other wildlife and badger density estimations will ultimately contribute to a cost-benefit analysis that will be considered by Defra when determining future policy options.

Disease Diagnosis

A critical requirement of a disease control programme is accurate and sensitive diagnosis. The tuberculin skin test coupled to restrictions of movement of animals from breakdown farms have contributed to the successful control of TB in many countries, and in parts of GB. However the use of these control procedures have not prevented the spread of the disease across wide areas of GB in the past two decades.

The tuberculin skin test was developed as a herd test, and in

initial TB control programmes it worked successfully to identify and eliminate infected herds or groups of animals within a herd. This type of herd application is now relatively rare and the test is used almost exclusively to identify individual infected animals. This application has exposed the limitations of the test, whose reported sensitivity for identifying individual infected animals is variable, and may be as low as 65% to 70%.[2,3,5,10]

These recognised shortcomings have encouraged the development of alternative in-vitro tests and in particular the IFN test. This is a laboratory-based test which involves the culture of whole blood with *M. bovis* antigen and measurement of interferon (IFN) production by responding T-lymphocytes.[11,12] This test has been used strategically in a number of international TB control programmes to complement the tuberculin test to identify a higher proportion of TB infected cattle in a herd.[11]

Refinements to the IFN test have been made,[13,14] further research is ongoing, and the point has been reached when the IFN test must be considered as an important component of a TB control strategy. This necessitates that the test be properly validated in the field in GB to determine its strategic value in a range of potential future control policy options.[5]

Cattle Tracing and Molecular Epidemiology

A significant recent research development has been provided by the opportunity to link cattle movement and molecular epidemiological data. Strains of *M. bovis* with a distinct genotype can now be identified and linked to specific geographical areas of the country.[15] In the wake of FMD following the destocking of affected farms, both within and outside trial areas, an opportunity was taken to undertake a detailed epidemiological study on all of these restocked farms in trial areas and those farms outside trial areas that subsequently suffered a TB herd breakdown. This study, although still in its early stages has demonstrated new breakdowns occurring in previously relatively TB free regions of the country, which can be linked by genotyping back to specific *M. bovis* strains in other distant regions of the country. Their demonstration in new regions is consistent with the movement of undiagnosed but TB infected cattle. The past belief, that the source of infection for these new breakdowns is diseased badgers moving over long distances, is highly unlikely since both behavioural and genetic evidence indicate that badgers tend not to make long range movements.

It is particularly worrying that Defra report that 60% of herd breakdowns in Cumbria, post FMD, are ascribed to cattle movement.[5] Initial analyses of cattle tracing data is also demonstrating the extremely large number of local cattle movements in high cattle density and high TB disease risk areas which further highlights the danger posed by the movement of infected undiagnosed cattle.[16]

Vaccines

Vaccines have the potential for disease management and might be seen to offer the ultimate approach to disease control. However, this potential element of a TB control policy can only be regarded as a long-term, uncertain option, and would need to be complemented by other control measures.

A recently published vaccine scoping study[17] has reported on the feasibility for pursuing a TB vaccination strategy. This study advised that there was currently no suitable vaccine available that could be considered for use in cattle although the potential for neonatal vaccination should be explored experimentally using the human vaccine, BCG (Bacillus Calmette and Guerin).

BCG might also be considered for use in badgers although there is only limited experimental information on its protective efficacy in badgers and further detailed consideration needs to be given to the design and scale of a field trial to demonstrate its impact on the target species, cattle. Such a trial would have to be on the scale and time frame of the RBCT, and would necessitate the development of a non-parenteral vaccine, possibly an oral vaccine. It would also need to be guided by the outcome of the RBCT, since wide scale culling of badgers could be expected to have a greater impact on cattle TB than vaccination of badgers. The suggestion of an initial "small scale" trial to demonstrate the impact of parenterally vaccinating badgers with BCG, on the disease level in badgers would necessarily involve the capture and culling of a large number of badgers and would need to surmount considerable logistical difficulties if reliable data are to be gained.[5]

The ROI Four Areas Trial

The recent publication of the Republic of Ireland Four Areas badger removal trial[18] has given rise to considerable interest and raised questions on its value to policy development in this country. The ISG commentary to Ministers on this study recognised the strong evidence provided that badgers have a role in propagating TB in cattle, confirming earlier field assessments made in GB.[4] However the most that could be concluded from the ROI data was that virtual elimination of badgers over a substantial area, and maintained over time, is likely to have a beneficial effect on the incidence of TB in cattle. Quantitative assessment of the benefit accruing in the ROI study is made difficult in that the impact of culling varies in the four counties studied and the impact of, albeit limited, culling in the reference areas is unclear. However the qualitative assessment of the range of reduced incidence of cattle TB that is claimed to have been achieved (50% to 75%), by virtual badger elimination, is likely.

The ROI study usefully adds to the data-base on badger culling and may ultimately help interpret findings of the RBCT. However because of almost complete co-operation with culling from

landowners, seemingly low badger density, different capture methods and reduced welfare constraints, and cattle movement practices and testing procedures in Ireland, it makes it difficult to predict the impact of the same policy, even if exactly implemented in GB.

The results from the ROI study we believe provide no information relevant to the explanation of (or evaluation of) the lack of benefits (and potential risks) of reactive badger culling and have little value for predicting the conclusions to be expected from the proactive versus survey-only comparison in the RBCT or on policy options up to now considered feasible in GB.

Preliminary Interpretation of Research findings

Research findings support the view that TB in cattle and badgers is interlinked involving cross species and within species transmission of infection. The quantitative significance of the various components of this interplay to disease development and its maintenance in either species is unknown. However the disease in each species appears to have its own dynamic. The relevance of this is that a trial of any badger culling strategy (short of complete and sustained elimination) can only provide a measure of the impact of that particular culling strategy on the incidence of TB in cattle and not the quantitative contribution of infected badgers to cattle TB. A further practical relevance is that if the disease was eliminated from badgers, by the elimination of badgers or the use of a highly effective vaccine, a residual disease problem in cattle would remain to be addressed.

The recognised limitations of the tuberculin test to identify all infected animals in a herd, the movement of diseased cattle between herds and the seemingly limited on-farm application of accepted precautions for infectious disease control, clearly highlight the necessary focus for an improved cattle based control of this disease.

The vexed question "what to do about wildlife?" in GB remains unanswered. A number of precautionary husbandry measures have been proposed to reduce cattle/ badger contact, although these have no strong scientific basis, they can be conceived to be sensible precautions that can be applied in many instances. Culling badgers may be seen as an option but data from historical localised badger removal operations and from the reactive component of the RBCT, indicate that localised culling of badgers will have no substantive impact on the disease in cattle. Conversely virtual elimination of badgers over a large area can be expected to do so. Whether more limited sustainable culling over a large area, as conducted in the proactive component of the RBCT, will have an impact on the disease in cattle that is considered to be useful remains to be seen.

[1] F.J.Bourne, C.A.Donnelly, D.R.Cox, G.Gettinby, J.P.McInerney, W.I.Morrrison and R.Woodroffe. Towards a sustainable policy to control TB in cattle – a scientific initiative. First report of the Independent Scientific Group on Cattle TB. 1998, PB3881, MAFF (London)

[2] F.J.Bourne, C.A.Donnelly, D.R.Cox, G.Gettinby, J.P.McInerney, W.I.Morrrison and R.Woodroffe. An epidemiological investigation into bovine tuberculosis. Second Report of the Independent Scientific Group on Cattle TB. 2000, PB4870, MAFF, (London)

[3] F.J.Bourne, C.A.Donnelly, D.R.Cox, G.Gettinby, J.P.McInerney, W.I.Morrrison and R.Woodroffe. An epidemiological Investigation into bovine tuberculosis. Third Report of the Independent Scientific Group on Cattle TB.2001, PB 5801, Defra (London).

[4] J.R.Krebs, R.Anderson, T,CluttonBrock, W.I.Morrison, D.B.Young, C.A.Donnelly, S.Frost, and R.Woodroffe. Bovine tuberculosis in cattle and badgers - An independent scientific review. PB3423, 1997 MAFF (London)

[5] F.J.Bourne, C.A.Donnelly, D.R.Cox, G.Gettinby, J.P.McInerney, W.I.Morrrison and R.Woodroffe. An Epidemiological Investigation into Bovine Tuberculosis - Towards a Science Based Control Strategy. Fourth Report of the Independent Scientific Group on Cattle TB. 2005, PB 10138, Defra (London)

[6] C.A.Donnelly, R.Woodroffe, D.R.Cox, F.J. Bourne, G.Gettinby, A.M.Le Fevre, J.P.McInerney, and W.I.Morrison. Impact of localised badger culling on tuberculosis incidence in British cattle, Nature, 2003, 426, 834-837.

[7] R.Woodroffe, F.J. Bourne, D.R. Cox, C.A. Donnelly, G. Gettinby, J.P.McInerney and W.I. Morrison. Welfare of badgers (Meles meles) subjected to culling: patterns of trap-related injury, Animal Welfare 2005, 14:11-17.

[8] R.Woodroffe, F.J. Bourne, C.L. Cheeseman, D.R. Cox, C.A. Donnelly, G. Gettinby, J.P.McInerney and W.I. Morrison. Welfare of badgers (Meles meles) subjected to culling: development and evaluation of a closed season, Animal Welfare 2005, 14: 19-25.

[9] W.T. Johnston, G. Gettinby, D.R. Cox, C.A. Donnelly, J. Bourne, R. Clifton-Hadley, A.M. Le Fevre, J.P. McInerney, A. Mitchell, W.I. Morrison and R. Woodroffe, Biology Letters doi:10.1098/rsbl.2004.0249 (published online)

[10] W.I. Morrison, F.J.Bourne, D.R.Cox, C.A.Donnelly, G.Gettinby, J.P.McInerney,and R.Woodroffe. Pathogenesis and diagnosis of infections with Mycobacterium bovisin cattle.The Veterinary Record 236-242, February 26th 2000.

[11] P.R.Wood, L.Corner, J.S.Rothel, C.Baldock, S.L.Jones, D.B.Cousins, B.S.McCormick, B.R.Francis, J.Creeper, and N.E.Tweedle. Field comparison of the interferon- gamma assay and the intradermal tuberculin test for the diagnosis of bovine tuberculosis.Australian Veterinary Journal,1991,68,286-290.

[12] P.R.Wood, L.Corner, J.S.Rothel, J.L.Ripper, T.Fifis, B.S.McCormick, B.R.Francis, L.Melville, K.Small, K.De Witte, J.Tolson, T.J. Ryan, G.W.de Lisle, J.C.Cox and S.L.Jones.A field evaluation of serological and cellular diagnostic tests for bovine tuberculosis.Veterinary Microbiology,1992,31,71-79.

[13] B.M.Buddle, A.R.McCarthy, T.J.Ryan, J.M.Pollock, H.M.Vordermeier, R.G.Hewinson, P.Anderson and G.W.deLisle. Use of mycobacterial peptides and recombinant proteins for the diagnosis of bovine tuberculosis in skin test-positive cattle.2003. Veterinary Record, 153, 615-620

[14] H.M. Vordermeier, A. Whelan, P.J.Cockle, L.Farant, N.Palmer and R.G.Hewinson. Use of synthetic peptides derived from the antigens ESAT-6 and CFP-10 for differential diagnosis of bovine tuberculosis in catttle.2001. Clin Diagn Lab Immunol 8, 571.

[15] N.Smith, J.Dale, J. Inwald, S.Palmer, S.V.Gordon,R.G.Hewinson and J.Maynard-Smith. Population structure of Mycobacterium bovis in Great Britain: clonal expansion 2003. Proc Natl Acad sci USA

[16] A.Mitchell, D. Bourn, J.Mawdsley, W.Wint, R. Clifton–Hadley and M. Gilbert. Characteristics of cattle movements in Britain - an analysis of records from the cattle Tracing System. 2005- in preparation.

[17] Independent Scientific group on cattle TB Vaccine Scoping Sub Committee. Development of vaccines for bovine tuberculosis. 2003, PB9102, Defra (London)

[18] J.M.Griffin, D.H.Williams, G.E.Kelly, T.A.Clegg, I.O'Boyle, J.D.Collins and S.J.More. The impact of badger removal on the control of tuberculosis in cattle herds in Ireland. 2005, Prev Vet Medicine.