TOWARDS ERADICATION OF BOVINE TUBERCULOSIS IN IRELAND:

A CRITICAL REVIEW OF PROGRESS

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SUMMARY

There has been a national bovine tuberculosis eradication programme in Ireland since 1954. Initial progress was rapid, but has subsequently stalled despite the implementation of each of the accepted elements of disease control. Based on results from the East Offaly and four area projects, there is now conclusive evidence that wildlife (specifically transmission of infection badgers to cattle) are a key constraint to disease eradication in Ireland, with cattle-to-cattle transmission of relatively lesser importance. Ireland is currently implementing a comprehensive strategy to address this constraint, whilst maintaining existing measures to control cattle-to-cattle transmission. In the short-term, a national programme of wildlife control has been implemented in areas of high disease prevalence. In the longer term, Ireland is committed to the development of an effective badger vaccine and the implementation of a strategic programme of badger vaccination.

AN OVERVIEW OF THE ERADICATION PROGRAMME

Initial progress

There has been a national bovine tuberculosis eradication programme in Ireland since 1954. During the initial stages of this programme, progress was rapid leading to a considerable reduction in the prevalence of the disease by the mid 1960s. At this point, however, progress stalled (Sheehy & Christiansen, 1991), although disease prevalence has subsequently remained low (Figure 1). From the mid 1960s to the late 1980s, national attention focused on issues relating to quality control and biosecurity, and testing standards were subject to intense scrutiny. During this period, pre-movement testing was made mandatory, animal identification and the ability to trace animals was improved, strategic disease control measures were introduced in areas of high prevalence, and data analysis was enhanced following the advent of computerisation.

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The establishment of ERAD

In 1988, a major initiative was undertaken with the launch of ERAD (the Eradication of Animal Diseases Board), a new executive agency to oversee the management of the eradication programme. Over the following four years, an exhaustive programme of tuberculin testing (44 million tests on the 7 million cattle in the national herd over 4 years) was implemented, together with an extensive range of new and improved support measures. These measures included the refinement of a programme management system, a reactor collection service and improved compensation/hardship grants; random sample testing of herds by government veterinarians; the establishment of a specialised epidemiological research and tuberculosis investigation unit together with supporting laboratory services; continuation of a pre-movement test; improved control of dealers; depopulation of problem herds; improved cattle tags and checking of cattle at factories and marts; extended restriction and de-restrictions; the establishment of local ERAD committees and a TB farm advisory service; the development and implementation of a farmer awareness campaign, covering a range of issues including disease-proof fencing and cleansing and disinfection; improved post-mortem procedures during factory surveillance; establishment of badger research and control services; improved control of slurry/factory waste; control of calf movements; attention to the cleaning of trucks of the reactor collection service; and improved District Veterinary Office (DVO) procedures (Downey, 1990,
However, despite these intensive measures, and a substantial investment of financial and human resources, no substantive progress was observed.

To the present day

Following this period and to the present day, Ireland continues to implement a comprehensive disease control programme. As part of the ERAD legacy, a detailed research programme was initiated to identify and address constraints to disease eradication in Ireland. There has also been significant epidemiological input into policy formulation.

CATTLE-TO-CATTLE TRANSMISSION

The importance of cattle-to-cattle transmission has been reviewed by Griffin and Dolan (1995), based on information from experimental and observational studies. There is evidence of bacterial excretion from some infected animals (Pollock & Neill, 2002), and transmission of infection has been demonstrated under experimental conditions (Griffin & Dolan, 1995). However, based on evidence from the field, cattle-to-cattle transmission (measured indirectly using incidence of disease – but not necessarily infection – among in-contact animals) may be relatively uncommon under Irish conditions. Although brought-in animals have been identified as an important cause of herd breakdowns, there is generally little evidence of transmission from each primary case (Flanagan et al., 1998; Griffin, 1991). Similarly, substantial breakdowns are not common, despite very close contact during winter housing. Nonetheless, it is frequently difficult to determine the specific cause of herd breakdowns, and therefore the relative importance of cattle-to-cattle transmission and other sources of infection. This is particularly problematic in situations where higher rates of within-herd prevalence are found, and it is often difficult to distinguish between lateral spread and a common source, such as wildlife (Griffin, 1992). For this reason, a weighting system is now used to enable field staff to rate the relative importance of a series of infection sources (O’Keeffe & Higgins, 2003). Given this background and in order to quantify the relative importance of cattle-to-cattle transmission under Irish field conditions, it is essential to first understand the importance of transmission of infection from wildlife.

THE IMPORTANCE OF WILDLIFE

Building evidence

Ongoing disease problems, despite comprehensive eradication programmes to prevent cattle-to-cattle transmission, have been experiences in a number of countries, notably New Zealand, the United Kingdom and, more recently, the state of Michigan in the USA. In each of these countries, the existence of a wildlife reservoir of *Mycobacterium bovis*, the causal agent of tuberculosis in cattle, has impeded, or has been perceived to impede, eradication of this zoonotic disease (Krebs et al., 1997; Morris & Pfeiffer, 1995; O’Brien et al., 2002).

In Ireland, evidence has been building of the potential role of badgers (*Meles meles*) in bovine tuberculosis, including recognition that badgers are highly susceptible to *M. bovis* infection (Gormley & Costello, 2003), with tuberculosis being endemic within the badger population in Ireland (O’Boyle et al., 2003). Indeed, a prevalence approaching 50% was identified in a recent
M. bovis infection in Irish badgers was first reported in 1975 (Noonan et al., 1975). Further, there has been a range of observational epidemiological evidence linking badgers and tuberculosis in cattle, including: (1) an association between the risk of herd breakdown and distance to badger setts in co. Offaly, with risk increasing in association with the number of infected badgers that were captured in the nearest infected sett (Martin et al., 1997). However, results from later work, using data from co. Kilkenny, were less certain, using detailed methods to quantify badger exposure, including the period of time that cows had access to housing and to specific farm fragments (during grazing) (Olea-Popelka et al., unpublished); (2) the identification of identical strains of M. bovis in local cattle and badger populations (Costello et al., 1999); and (3) ongoing disease problems, despite intensive disease control efforts in Ireland aimed at early detection and prevention of cattle-to-cattle transmission.

Definitive evidence

The above-mentioned information, on its own, is not sufficient to prove disease causation. In particular, it provides little direct evidence in support of a temporal relationship (providing evidence for transmission of M. bovis from badgers to cattle). To illustrate, it is possible to have coincident disease (with identical strains) in local badgers and cattle but without badgers being the source of infection. This could occur, for example, if cattle were to infect badgers (and not vice-versa). Given this context, a field trial offers the best opportunity to critically assess the impact of badger removal on the control of tuberculosis in cattle herds in Ireland. Therefore, the East Offaly and four area projects have been studies of major national importance. Each has sought to provide conclusive evidence of the contribution, or otherwise, of badgers in bovine tuberculosis.

The East Offaly project was conducted during 1989 to 1995, with badgers being proactively removed under licence from a central inner Project area (528 km²) and outer Buffer zone (210 km²), but not from the surrounding Control Area (1456 km²). These areas, which were centred in county Offaly, were similar in terms of cattle husbandry, land-type and land-use, badger densities at project start, and tuberculin testing regimes (both in terms of frequency and interpretation). A total of 1,264 badgers (an average of 0.34 badgers/km²/year; with 12% disease prevalence based on lesion detection at post-mortem) were removed from the Project area during the 7-year study period, with a removal intensity during the first 2 years of the study (when 71.0% of badgers were captured, Dolan et al., 1994) of 0.85 badgers/km²/year. Based on multivariable analyses, there was a significantly lower proportion of new confirmed tuberculous herd restrictions among cattle in the Project Area as compared the Control Area (Ó'Máirtín et al., 1998a; Ó'Máirtín et al., 1998b). According to Eves (1999), the most striking change was the absence of large outbreaks of disease in cattle in the Project Area in later years of the project. This effect has continued to the present day, with the rate of herd restrictions within the Project Area generally remaining at approximately one-third of the national average (Bob Hammond, personal communication). Although concern has been raised concerning the use of ‘doughnut-type’ design and the potential for continuing migration of badgers from the Control to the Project control area (Phillips et al., 2003), this will have had the effect of making it harder to detect a treatment effect, if one was present.

The four area project has sought to build on the East Offaly project, and to determine the effect of badger removal at a number of sites representing a wider range of farming environments. The study was conducted from September 1997 to August 2002 in matched removal and reference areas (average area of 245.1 km²) in counties Cork, Donegal, Kilkenny
and Monaghan. Badger removal was intensive and proactive throughout the study period in the removal areas (removal intensity of 0.57 badgers/km²/year during the first 2 years of the study), but reactive (in response to major tuberculosis outbreaks in cattle) in the reference areas (removal intensity during equivalent period of 0.07 badgers/km²/year). During the study period and after accounting for all key confounders, there was a significant difference between the removal and reference areas in all four counties in both the probability of, and the time to, a confirmed herd restriction due to tuberculosis. To illustrate, in the final year of the study the odds of a confirmed herd restriction in the removal (as compared to the reference areas) were 0.25 in Cork, 0.04 in Donegal, 0.26 in Kilkenny and 0.43 in Monaghan, and the hazard ratios (removal over reference) ranged from 0.4 to 0.04 (a 60–96% decrease in the rate at which herds were becoming the subject of a confirmed restriction) (Griffin et al., in press). Some concerns have been raised regarding the validity of this study (Donnelly et al., 2003), however, these have proved unfounded following critical evaluation (Griffin et al., in press).

**CURRENT UNDERSTANDING OF DISEASE EPIDEMIOLOGY IN IRELAND**

The key role of badgers, within a context

The East Offaly and four area projects have provided compelling evidence of the key role of badgers as an infection source for cattle herds in cattle. However, it is critical that these studies are considered within a clearly-defined context. The Irish bovine tuberculosis eradication programme is comprehensive, incorporating each of the accepted elements of disease control, including mandatory annual tuberculin testing of all animals in the national herd and early, ongoing removal of infected animals. It has long-been suspected that another source of the bovine tubercle bacillus is involved, given the lack of national progress towards eradication despite these efforts. These suspicions have now been confirmed, with the results from these two studies clearly highlighting wildlife (and specifically transmission of infection from badgers to cattle) as a key constraint to disease eradication in Ireland. These findings are of national importance and provide compelling evidence of the linkage between proactive badger removal and tuberculosis in Irish cattle. Note that this linkage (and the consequent impact of proactive badger removal) would not have been evident if the national control programme were less effective. To illustrate, if cattle-to-cattle transmission were still common, differences in disease incidence between the removal and reference areas would not have been as marked.

The relative importance of cattle-to-cattle and badger-to-cattle transmission

On the basis of these studies, cattle-to-cattle transmission is believed to be of relatively less importance than badger-to-cattle transmission in Ireland. Although we are not yet able to quantify the relative importance of these routes of transmission (this is currently under investigation; Paul White, personal communications), there is a range of evidence to support this view. Firstly, there has been a lack of progress since the 1960s, and particularly during the ERAD era, despite the implementation of control measures that are known to eliminate cattle-to-cattle transmission. In the absence of wildlife reservoirs, these measures proved effective in the eradication of disease from Australia (Neumann, 1999). Also, the results from the east Offaly and four area projects clearly demonstrate a substantial – and significant – reduction in tuberculosis in cattle herds following proactive badger removal (Griffin et al., in press; Ó Máirtín et al., 1998a; Ó Máirtín et al., 1998b). Further work is currently underway to determine the source of infection in the removal area breakdowns. Based on preliminary
information, at least some of the breakdowns in the removal area can be attributed to effects outside the removal area, including the purchase of infected cattle from outside the removal areas and ongoing badger activity at the periphery of these areas (Barrett & More, unpublished). In Ireland, there is also a substantial disparity between disease prevalence in badgers and cattle. In a recent survey of captured badgers, using improved post-mortem technique and laboratory support, the prevalence of infection approached 50% (L. Corner, personal communications). In contrast, the apparent incidence of infection in cattle during 2002 was 0.4% (29,162 bovine reactors, from a population of approximately 7 million cattle)(Anon., 2003). Finally, as a result of mandatory annual testing and early and ongoing removal of infected animals (Good et al., 2003), there is limited opportunity for Irish cattle to become infectious (that is, capable of transmitting infection) prior to detection. This view is supported by field evidence, where singleton reactor breakdowns (that is, breakdowns involving only a single reactor) accounted for between 38.3 and 44.4% of all breakdowns each year during 1987-1997 in Ireland (O'Keeffe & Crowley, 1995), despite very close contact between animals throughout winter housing. It is important to emphasise that disease transmission is affected by the number of contacts per unit time, the transmission potential per contact and the duration of infectiousness (Halloran, 1998). Therefore, there are a range of factors that will influence the relative importance of cattle-to-cattle and badger-to-cattle transmission, including the property of the particular infectious agent, and significant host and environmental factors (including efficiency and frequency of testing, and methods of management, including stocking density) (Baldock, 1997). Therefore, although these conclusions are relevant to the Irish situation, they should be extrapolated to other regions with care.

The mechanism of badger-to-cattle transmission

Although the importance of badgers in the epidemiology of bovine tuberculosis in Ireland is now clear, the mechanism of badger-to-cattle transmission remains uncertain. Based on the pathological evidence (Costello et al., 1998; O'Boyle, 1999, 2000, 2002; O'Boyle et al., 2003; O'Keeffe et al., 1996), lesions in infected Irish badgers are most-common in the thoracic cavity (bronchial and mediastinal lymph nodes and lung tissue) and head region (pharyngeal, parotid and submandibular lymph nodes), confirming the respiratory route as an important route of exit (O'Boyle, 2002). In cattle, the aerogenous route, rather than ingestion, is believed to be the main route of entry (Phillips et al., 2003), noting that infection with M. bovis can be established in cattle following the inhalation of one or a small number of tubercle bacilli in an aerosol droplet (Pollock and Neill, 2002). Consequently, transmission of infection may be most efficient when cattle and infected badgers are sharing the same airspace. There is evidence of badgers frequenting housing, with farmers being unaware of their presence (Cheeseman and Mallinson, 1981). Although attention to this point has particularly focused on the terminally-ill badger (Phillips et al., 2003), infected but apparently healthy badgers may also be infectious and a risk to cattle, albeit at a lower level (L. Corner, unpublished). Our understanding of the interface between cattle and badgers is complicated by results of several recent Irish studies. Although cattle and badgers tended to have similar M. bovis strains within broad geographic areas, badger strains were not strongly clustered within an area, leading the authors to speculate about the dynamic nature of badger movements (Olea-Popelka et al., in press; Olea-Popelka et al., submitted).
In order to eradicate tuberculosis from the Irish cattle population, Ireland will need to sustainably control tuberculosis in badgers, with which cattle may come in contact (Gormley & Collins, 2000). However, this presents significant challenges for scientists and policy-makers (Gormley & Costello, 2003), including the international legal protection, and national status, afforded to badgers; the potential for increases in badger numbers, as a consequence of agricultural intensification and increase in productive pastures; the close physical proximity of badgers and cattle, given the preference for Irish badgers to locate setts in hedgerows (Hammond et al., 2001); and the high prevalence of infection among Irish badgers (L. Corner, unpublished). Ireland is currently implementing a comprehensive strategy to address these challenges, whilst maintaining existing measures to control cattle-to-cattle transmission. In the short-term, the Department of Agriculture and Food is implementing a national programme of wildlife control when and where wildlife are implicated in on-farm breakdowns of bovine tuberculosis (O’Keeffe et al., 2002). These activities are focused in areas of high disease prevalence. In these areas, badger removal will form the basis of temporary disease control (by minimising contact between cattle and infected badgers), and will also provide potential locations for vaccination trials and (later) usage (O’Keeffe et al., 2002). In the longer-term, Ireland is committed to the development of an effective badger vaccine and the implementation of a strategic programme of badger vaccination, with the aim to reduce *M. bovis* transmission between infected badgers and susceptible cattle (Gormley & Costello, 2003). The feasibility of such an approach was first considered in 1994, with input from scientists from Ireland and Northern Ireland (Ellis et al., 1994). Current work is focusing on the use of a live vaccine based on *M. bovis* BCG (L. Corner, unpublished) which might persist in the host and continuously prime the protective cellular immune response (Gormley & Costello, 2003). Results from early experimental studies have been promising (L. Corner, unpublished).

In association with these efforts, epidemiological research is being conducted by, or in partnership with, the Centre for Veterinary Epidemiology and Risk Analysis in a number of complementary areas. With respect to the national control programme, there is ongoing database development, as well as investigations concerning the benefit-cost of a targeted pre-movement test and the efficiency of factory surveillance. More generally, work has commenced on breakdowns instigated by a factory lesion detection, on aspects of badger ecology in Ireland (including diet, reproduction and overall population size), and on work to support vaccine development (including bait-uptake and disease transmission studies).

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