A compartmental model for the within-herd spread of M. bovis in Irish cattle herds

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A Compartmental Model for the Within-Herd Spread of *Mycobacterium bovis* in Irish Cattle Herds

J.M. Griffin and D.H. Williams

**Introduction**

Following the introduction of an eradication programme, the apparent prevalence of tuberculosis in cattle in Ireland fell from 17% in 1954 to less than 0.5% in 1965. Further progress has been prevented possibly due to transmission from wildlife, particularly the badger. The contribution of within-herd spread has not been quantified; it is believed to play an important role, despite the fact that all cattle are tuberculin-tested annually and reactor animals are removed on testing positive. This study seeks to make a quantitative estimate of the importance of within-herd transmission.

**Materials & Methods**

*Compartmental Model*

A compartmental model with compartments representing the *Mycobacterium bovis* disease status of individuals in a herd was developed. Each animal is considered as belonging to one of four possible states: susceptible state S; incubating states U (non-reactive to the tuberculin test) and R (reactive to the test) and infectious, state I. Following infection, when a susceptible animal moves from state S, it is then assumed to move sequentially through states U, R to I.

In modelling disease in an infected herd the number of animals in each of the four states at time t, S(t), U(t), R(t) and I(t), are regarded as continuous functions of time. The rate at which animals in a herd become infected is assumed to follow a Reed-Frost model, so that \(dS/dt = \ln(1 - \beta) S(t) I(t)\). Here \(\beta\) is the transmission coefficient and is defined as the proportion of the herd that will become infected each day as a result of each infectious animal. Transitions between the states U, R and I are specified by the mean time an animal would spend in the state and the following differential equations:

\[
\begin{align*}
\frac{dU}{dt} &= -\ln(1 - 1/\text{Days in U}) U(t) + \ln(1 - 1/\text{Days in R}) R(t) \\
\frac{dR}{dt} &= -\ln(1 - \beta) S(t) I(t) + \ln(1 - 1/\text{Days in U}) U(t) \\
\frac{dI}{dt} &= -\ln(1 - \text{Days in R}) R(t)
\end{align*}
\]

*Herd test data*

Boundary conditions for the equations representing a herd were based on herd test data. The current tuberculin-testing regime in Ireland involves an annual tuberculin test for all cattle herds. Any herd containing an animal that fails a tuberculin test is classified as ‘restricted’ and all remaining animals are tested at two-monthly intervals. The herd returns to a clear status only when it passes two successive tests. For the study twenty herds were randomly selected from all 402 herds that had one or more tuberculosis breakdowns between 1988 and 1996 in an area of County Kilkenny. A total of 35 breakdowns were recorded in the 20 herds during the study period.

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Boundary conditions
Herd test data were used to set the total number of animals in the herd at a time prior to each breakdown. The number of animals in U was increased (with S decreased) to obtain a good fit of the resulting solution to the observed data. This represented an initial external source of infection, assumed to occur at the mid-point between the last clear herd test and the breakdown herd test. Following each tuberculin test, the values of S(t), U(t), R(t) and I(t) were re-set to reflect the removal of test-positive animals. The number removed from each category was determined by a specificity parameter (for S) and sensitivity parameters for U (taken to be 0.1), R, and I. Sensitivity for R and I were assumed to be equal and were estimated to obtain a good fit. The value of S(t) was increased to maintain a constant herd size. The number of reactor animals which had tuberculous lesions at post-mortem examination was calculated as a fixed proportion of test-positive animals.

Model solution and parameter estimation
The solution to the differential equations with the specified boundary conditions, and parameter estimation using least squares and test data, were carried out using ModelMaker®. Parameters were assumed to have a common value for all herds, with the exception that the pre-breakdown adjusted number of animals in the state U was estimated for each breakdown. The estimation was repeated by removing potentially influential herds, by modelling these separately, and by altering the time of the external infection.

Results
In the model simulation using data from all study herds (Model 1), the total number of reactor animals was 254. Forty-nine (19%) of these had lesions at post-mortem examination. These values corresponded closely to the observed data where the number of reactors animals was 255 and the number of animals with lesions was 48. The optimised values for the shared parameters are shown in Table 1.

Herds 5 and 6 accounted for two thirds of the total error sum of squares. When Herd 5 was omitted the estimate of the transmission coefficient decreased to less than $10^{-16}$. A set of optimised parameter values was obtained by fitting a model for Herd 5 on its own. The optimised values for the shared parameters are shown in Table 1 (Model 2).

In Model 1, it was assumed that infection was introduced into the herd at the mid-point between the last clear test in the herd prior to the breakdown and the breakdown test. In Model 3 the date of introduction of infection was changed to the date of the last clear test prior to the breakdown, and optimised parameters are also shown in Table 1. The main impact of the earlier introduction of infection was a decrease in the number of days spent in the R state and in the transmission coefficient.
Table 1. Optimised values of the model parameters for all herds (Model 1), Herd 5 alone (Model 2) and for all herds when pre-breakdown infection is immediately after the last clear test (Model 3).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission coefficient</td>
<td>.00053</td>
<td>.0006</td>
<td>.0003</td>
</tr>
<tr>
<td>Days_in_U</td>
<td>23.42</td>
<td>34.30</td>
<td>31.34</td>
</tr>
<tr>
<td>Days_in_R</td>
<td>365.14</td>
<td>365.00</td>
<td>256.51</td>
</tr>
<tr>
<td>Se_RI</td>
<td>0.904</td>
<td>0.89</td>
<td>0.890</td>
</tr>
<tr>
<td>Sp</td>
<td>0.994</td>
<td>1</td>
<td>0.994</td>
</tr>
<tr>
<td>Lesion rate</td>
<td>0.287</td>
<td>0.41</td>
<td>0.290</td>
</tr>
<tr>
<td>No. (% of reactors due to external infection</td>
<td>92 (36%)</td>
<td>18 (32%)</td>
<td>43 (17%)</td>
</tr>
<tr>
<td>No. (% of reactors due to transmission</td>
<td>77 (30%)</td>
<td>39 (68%)</td>
<td>126 (50%)</td>
</tr>
<tr>
<td>No. (% of reactors false positives</td>
<td>85 (33%)</td>
<td>0</td>
<td>85 (33%)</td>
</tr>
</tbody>
</table>

Discussion

Estimated values of the transmission coefficient were broadly in line with the range of values obtained by other studies. (Stoneham and Johnson, 1987, Barlow et al., 1997, Kean et al., 1999). Their low values support the results of transmission trials that have been carried out in Ireland (O’Reilly and Costello, 1988, and Costello et al., 1998) which indicate that cattle do not readily infect other cattle.

Estimated values of the test specificity and sensitivity are also consistent with other studies (Costello et al., 1997). In Ireland, where all animals are tested on an annual basis, assuming no prevalence of M. bovis would provide a conservative estimate of test specificity of 0.995, consistent with the model estimate of 0.994, as this is based on a sample of herds at times when the herds were restricted.

The model fitting process showed evidence of within-herd transmission, but the evidence depended on including the data from Herd 5, which was unusual by comparison with the selected herds but not within the population. Herd 5 presented reactors in considerable numbers over three successive tests.

References

A simulation model for the spread of bovine tuberculosis within New Zealand cattle herds. Preventive Veterinary Medicine 32: 57-75.


