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A Simulation Model for Tuberculosis in Cattle in Ireland

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Introduction

Traditionally, information on the epidemiology of animal diseases has been obtained by laboratory experiments or field studies. These can be time consuming and costly, however. Bovine tuberculosis is a particularly difficult disease to study under laboratory conditions because it has a long and variable incubation period and the onset of the clinical phase of the disease is often prolonged. Apart from ethical and human health considerations, it is often impractical to infect a large number of animals to observe the progress of the disease under experimental conditions.

An alternative approach to laboratory experiments and field studies is to use a mathematical model to replicate as closely as possible the behaviour of an infection as it passes through a population of animals. Models can be used to describe and predict the dynamics and outcomes of a variety of ecological processes, including the transmission of infectious disease. Epidemic models have been used to investigate the role of disease in population processes, in order to compare disease management strategies and to assess risk of disease transmission within and among species (Anderson and May, 1979; Anderson, 1982; Barlow, 1996; Heesterbeek and Roberts, 1995). Simulation models are built using combinations of arithmetic and logical processes. Each individual animal in a herd or a group of herds can be tracked over a period. The animal can be exposed to infectious individuals and other experiences. Outputs relating to herd dynamics and disease incidence can be obtained.

There is a need to quantify the relative importance of all routes of infection into herds, thereby enabling the most appropriate and cost effective measures to be implemented. The goal of this study was to develop a simulation model that would enable us to have a better understanding of the epidemiology of tuberculosis in cattle.

Methods

The simulation model was developed to provide an understanding of the epidemiology of tuberculosis in cattle and to provide support for policy makers involved in the compulsory bovine tuberculosis eradication programme in Ireland. It is a stochastic discrete-entity model. It is designed to simulate the tuberculosis profile of a cattle herd over a ten-year period. C++ programming using the Microsoft Visual C++[®] software package is used to specify the model, simulate data, and estimate the parameters. The model consists of two main components - one that allows the transition of animals between states, and the other that simulates tuberculin testing. Following infection, it is assumed that bovine tuberculosis in an animal develops sequentially through states U (unreactive to the tuberculin test and non-infectious), R (reactive to the test and non-infectious), and I (reactive to the test and infectious) and that these states are mutually exclusive. The rate at which animals in a herd become infected with *Mycobacterium bovis* from infectious cattle directly is assumed to follow a Reed-Frost model.

The main parameters of interest are the transmission coefficient, the interval between exposure to infection from an external source, the number of animals that are infected during such an event, the number of days spent in the different states, and the sensitivity and

specificity of the tuberculin test. The contribution of false positive animals to the total reactor population is also estimated. The relative importance of within-herd spread of infection compared to transmission from an external source is evaluated.

The parameters are estimated by fitting the model data to tuberculin test field data from cattle herds distributed throughout Ireland. A tabu search based method as implemented by OptQuest Callable Library[®] (OptTek Systems, Inc., Boulder, Colorado, USA) commercial software programme is used to optimise the values of these parameters. The values of a number of eight key output variables, such as the number of reactors disclosed in a herd and the number of new breakdowns disclosed in a ten-year period, are combined in a specially designed objective function to produce one single measure of fit between the field data and the model data. The commercial software package, Design-Expert[®] (Stat-Ease, Inc. Minneapolis, Minnesota, USA) is used to carry out a sensitivity analysis of the model parameters. It is also used to obtain optimised values for the model parameters, using a metamodelling approach. A scenario analysis is carried out to evaluate different possible strategies for controlling the disease.

Conclusions

The main findings are as follows:

- In the sensitivity analysis, the parameters controlling the specificity of the tuberculin test are highly influential, especially given the very narrow range between the lower and upper bounds. In contrast, the parameters controlling the sensitivity of the test have little impact on the output variables. Other highly influential parameters are:
 - The mean interval between exposure to an external source
 - The probability that an exposure to an external source results in a small number of animals becoming infected
- In the final optimised model, false positives contribute about 35% of all reactors.
- The optimised value for the mean interval between the exposure of a herd to an external source of *M. bovis* is 5.7 years. Despite this relatively long interval, transmission from an external source is the main source of infection and accounts for approximately 60% of reactors in the final model.
- It is not possible to find a unique optimised value for the transmission coefficient by fitting the model data to the field data. Based on the values of the transmission coefficient available from the scientific literature, within-herd transmission accounts for only about 3% of reactors in the final model.
- Less than 10% of the infected animals that were declared reactors at tuberculin tests are in the infectious state.
- An increase in the screening test interval from 12 to 18 months results in little change in the total number of reactors disclosed in a herd over a ten-year period.
- The results suggest that the extensive use of supplementary tests, such as the interferon- γ test, would be of little benefit. However, supplementary tests may be useful in particular well-defined situations.
- The use of an APT (number of reactor animals per thousand tests) as the sole measure of prevalence of tuberculosis can be misleading.

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