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Computer simulation of Johne's disease in New Zealand dairy cattle

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ABSTRACT

Control options for Johne's disease (JD) are explored by computer simulation because intervention trials under field conditions would be too costly. The purpose of this review is to describe a simulation model developed in The Netherlands and adapted to dairy herds in Pennsylvania (USA). The paper consequently derives what information is required for the adaptation to New Zealand dairy herds and explains the methods by which that information is currently collected. The model 'JohneSSim' simulates the within herd development of JD based on time related changes. Time intervals are six months. JD is transmitted vertically through the placenta or from dam to calf around calving through direct contact, colostrum, rest milk or bulk milk, infected pasture, or through contact with adult replacement stock from other herds. Control options include test-and-cull, measures to prevent the infection of calves, vaccination, and grouping of animals by age. The simulation suggested that, in The Netherlands as well as in Pennsylvania, progressively improving calf-hygiene with little reliance on test-and-culling would decrease the prevalence considerably and was economically feasible (average benefit-costs-ratio excluding extra labor = 1.58). Test-and-cull was not economical even if a test with 80% sensitivity was available. Contract heifer rearing, colostrum management, and seasonal calving appear to be risk factors for transmission that have specific relevance for New Zealand dairy herds.

Keywords: Johne's disease; control; transmission; simulation; New Zealand situation.

INTRODUCTION

The investigation of control options for JD in field trials is extremely costly and time consuming because of its insidious nature and poor accuracy of diagnostic tests. Therefore, computer simulation of disease occurrence over time and associated economic effects is an attractive alternative.

A stochastic simulation model (JohneSSim) was developed by Groenendaal *et al.*, (2001). This model incorporated variations in risk according to age, herd infection status and specific calf-hygiene management systems. The input data were based on field studies and expert opinions. Predictions from this model have substantially influenced the Dutch national control program for paratuberculosis (Benedictus *et al.*, 1999). The management advice giving the highest benefit in terms of prevalence reduction and economic efficiency is currently subject to a long-term intervention trial involving 500 dairy farms in the Netherlands (Van Weering, personal communication). The simulation model has since been adapted to conditions that prevail in dairy herds in Pennsylvania (US) by Groenendaal and Galligan (1999).

The authors of this paper are currently investigating risk factors for Johne's disease in 427 New Zealand dairy herds and the dynamics of within-herd transmission in 5 infected herds. One objective of these studies is adaptation of the Dutch model to New Zealand conditions. The purpose of this paper is to describe the model and its outcome in The Netherlands and in Pennsylvania (USA). We also summarize the results obtained from the New Zealand studies so far.

DESIGN OF THE SIMULATION MODEL 'JOHNESSIM'

Because of the slow spread of Johne's disease and the long time intervals between infection and shedding and clinical Johne's disease, 'JohneSSim' uses time-steps of six months. The model simulates the course of Johne's Disease within a typical herd over a default period of twenty years to provide insight in the potential changes of the slow progression of disease. The model is dynamic (time is included as a variable) and uses the Monte Carlo method to predict an outcome distribution rather than a mean value (stochastic model). Simulations are carried out repeatedly to provide insight in the range of possible outcomes. JohneSSim simulates (a) herd dynamics, (b) disease dynamics, (c) control of the disease and (d) economic consequences at herd level. Details of infection routes and model parameters are described below.

Herd dynamics

Model parameters responsible for changes in herd composition are calving pattern, voluntary and involuntary culling and morbidity. Heifers calve at a default age of two years and the calving interval is set to twelve months. Calving can be seasonal (calving once a year) or non-seasonal (calving once in either of two 6-months intervals). Voluntary and involuntary culling occur twice each year (default = 30% per year). Herd size is maintained constant by setting annual culling and replacement rates equal.

Disease transmission

At any point in time, animals are in one of six states of infection. Cows are either non-infected (up to 1 year old and susceptible or older and non-susceptible) or infected (latent, low, high, or clinical infection). Infections occur either intra-uterine or before 12 months of age. The probability of infection via all routes, other than by vertical transmission, is influenced by farm management parameters. Intra-uterine transmission of Johne's disease depends on the infection status of the dam and varies from

0% for latent and low level infectious dams to 50% for clinically infected dams. Infection through contact around birth depends on (a) the state of infectiousness of the dam and (b) the states of infectiousness of other cows in the herd. The status of the other cows influences contamination of the calving area and the probability of pseudo-vertical transmission through exposure related to calving hygiene at and around birth. The model assumes that 30% of the low level infectious cows and all of the high level infectious and clinical cows shed *M. paratuberculosis* in colostrum. Two possible transmission routes via colostrum are considered; (i) from the dam to its offspring, and (ii) from cows to calves other than its own dam when mixed or pooled colostrum is fed. Feeding milk replacer prevents infection through colostrum. The infection probability for transmission via mixed (pooled) colostrum (ii) depends on the number of cows in the herd with colostrum (N), on the number of cows with infectious colostrum (n), on the dilution ratio, i.e. the of number of calves that get colostrum from one cow (a), and on the number of fully susceptible calves at the age of 0-6 months (b). The model assumes the following formula (I) to calculate the infection probability for transmission of infection to calves via colostrum (Groenendaal and Galligan, 1999):

$$P_{\text{calf infection through colostrum}} = a/(b * N) * [1 - (1 - a/b)^n]$$
I

Where
a = Number of calves that get colostrum from one cow
b = Number of calves at the age of 0-6 months
N = Number of cows in the herd that give colostrum
n = Number of high level infectious or clinical cows with infectious colostrum

Calves can also be infected by ingestion of infectious milk. The model considers three types of milk: bulk milk, rest milk (i.e. waste milk and milk from treated cows), and milk replacer. When bulk milk is deemed infectious (due to one or more highly infectious shedders) the model assumes that 20% of the highly infectious or clinical cows are shedding large amounts of *M. paratuberculosis* in milk. The probability for a calf becoming infected through infectious milk is assumed 95%. Feeding infectious rest milk to calves poses a higher risk of transmission than bulk milk because fewer cows contribute rest milk, hence the dilution ratio is smaller. The formula shown above applies here as well: the probability of infection via drinking rest milk depends on the number of cows with rest milk (N), the number of cows with infectious rest milk (n), the total number of calves between age of 0-6 months and the number of calves that get rest milk of one cow (a).

Infection from faecal contamination of the environment, especially through spreading of manure on pasture, is simulated by a stochastic Reed Frost process. The probability of infection in a calf via this means depends on the number of infectious cows and the number of effective contacts (*k* in formula II below). Effective contact rate describes the infectivity of the causative agent and the intimacy of contact between infectious and susceptible individuals depending on the level of hygiene at calving and calf rearing (Collins and Morgan, 1991 and 1992). Depending on management practices, *k* can vary between 0 (no contacts) and the number of adult cows (each calf has an effective contact with each adult cow). Reaching a zero level is unlikely. On an average Pennsylvanian farm without any control measures the number of effective contacts *k* were estimated to range from 2.5 to 5 per six month period (Groenendaal and Galligan, 1999). The Reed-Frost formula (II) is:

$$P_{\text{calf infection through faecal contamination}} = 1 - (1 - k * S / N)^I \quad [II]$$

Where
k = number of effective contacts (between calves and cows older than 2 years)
S = susceptibility (100% or 32 % for 0-6 months and 7-12 months, respectively)
N = number of cows older than two years;
I = number of low or high level infectious or clinical cows.

Johne's disease is introduced to a herd when infected bulls, cows and heifers are purchased or leased. The probability of introducing an infected animal depends on (a), the number of animals purchased and (b), the prevalence of disease in the population from which cows were procured. A 20% probability of buying at least one infected cow or heifer each year was estimated for Pennsylvania while it was assumed that farms buy a few animals every year. Based on apparent prevalence data for Pennsylvanian dairy farms and test sensitivity and specificity, an increase of one percent in true prevalence was assumed every year in the absence of disease control. If a control program was in place, the true prevalence was assumed to decrease by one percent annually.

Simulation
Monte Carlo simulations often make use of a triangular distribution when knowledge of the 'true' distribution is not known or when there is insufficient information to derive parameters for more complex distributions. The triangular distribution is useful if accurate information is not available. Only three, relatively intuitive parameters are required to define the distribution, minimum, most likely and maximum. However, the ease of describing the triangular distribution comes at a cost due to the crude nature of the distribution and its apparently non-biological triangular shape.

Economic consequences of Johne's disease
Economic consequences can be divided into two categories, (a) losses due to Johne's disease, and (b) costs of Johne's disease control. Economic losses are due to reduced milk-production, reduced slaughter value, premature culling, diagnosis and treatment costs, and impaired fertility. A major loss is due to decreased milk production estimated to range from 2.2% to 25% of the production of non-infected herd mates (Buergelt and Duncan, 1978; Benedictus *et al.*, 1987). The greatest loss is from premature culling and its impact on lost future milk production (Benedictus *et al.*, 1987). The JohneSSim model differentially allocates production losses according

to the infection status of infected animals. Assumed losses range from 5% for lowly infectious animals to 20% for clinically diseased animals (Groenendaal and Galligan., 1999). Other losses may be due to animals exhibiting clinical signs of Johne's disease or reduced milk production being culled prematurely, before reaching their optimum age of replacement. Such cows never realize their lifetime production potential. The model estimates this missed future income as the Retention Pay-off (RPO) value (Dijkhuizen and Morris, 1997). The RPO is defined as the value of production up to the optimum lifetime that is foregone due to premature culling.

Factors not taken into account by the simulation model include reduced fertility, potential loss of consumers confidence in milk infected with *M. paratuberculosis* and possible effects on export markets.

Simulation of control options

Simulated measures to control or prevent infection of calves were divided into (a) 'test-and-cull', i.e. removal of test positive cows, (b) measures to prevent the infection of calves by improvement of 'calf hygiene', (c) vaccination and (d) grouping of animals. Test-and-cull in the JohneSSim model can be specified by parameters for test sensitivity and specificity, minimum and maximum age of testing, frequency and interval of repeated testing and number of cows tested. Different consequences of the test results can be simulated e.g. culling after a positive test or confirmation with another test (animal level) or changing from a suspected to an unsuspected herd when all tests are negative (herd level).

Improved 'calf hygiene' practices reduce or eliminate certain spread parameters or infection routes in the simulation. In its current version, the model assumes vaccination to only increase the age at becoming infectious. In principle however, other vaccine characteristics such as inducing a certain degree of immunity or reducing the infectiousness or production losses of an infected cow can be modeled as well (Groenendaal *et al.*, 2001).

RESEARCH TO SIMULATE JOHNE'S DISEASE IN NEW ZEALAND DAIRY HERDS

A research project was initiated by Meat New Zealand, the New Zealand Dairy Board and Massey University in 1999. Its objectives were to investigate associations between environmental and farm management factors and infection/disease patterns of Johne's disease in cattle herds in three major regions in the North Island of NZ and to evaluate the impact of clinical and sub-clinical disease on production in infected animals. An important stated outcome was the development of a simulation model for the evaluation of a range of control options. Herd level risk factors were investigated through a case control study of 427 dairy herds and herd infection dynamics through a still underway 3-year longitudinal study of the disease in five herds(n = 5).

Case-control study

A questionnaire based case-control study was carried out to identify factors associated with the occurrence of clinical cases of Johne's disease in New Zealand dairy herds. In 1999, twelve co-operating veterinary practices in three major dairy cattle regions in the North Island of New Zealand, the Waikato, Taranaki and Wellington-Manuwatu-Wanganui regions, were contacted to identify farmers with reasonably long established dairy herds (> 3-5 years), in each of the following categories:

Category 1 Control herds
No history of clinical Johne's disease;
Category 2 Case herds
Low level of infection (average annual incidence 1997-99 up to 0.3 cases per cow year);
Category 3 Case herds
High level of infection (average annual incidence 1997-99 higher than 0.3 cases per cow year).

Questionnaires designed to collect data on herd demography and farm management practices with putative associations with occurrence of JD were posted to 664 farmers, of whom 438 (66%) responded. Eleven questionnaires were discarded due to faulty data, resulting in data for 427 farmers. There were 226 farms in Category 1, 99 in the Category 2 and 102 in Category 3. Farmers were asked to provide the numbers of cows that were culled due to Johne's disease in each of the 3 previous years. Associations between management factors and levels of disease were explored by multinomial logistic regression. The likelihood of Johne's disease increased in herds with a large proportion of pure Jersey or Friesian-Jersey cross-bred cows. It was positively associated with the number of purchased bulls and the number of herds of which bulls were purchased. Such herds also purchased more female replacement stock than herds that rarely purchased bulls. The risk of Johne's disease also increased with herd size and tended to decrease as the age at which calves got in regular contact with adult cattle increased beyond 12 months.

Longitudinal study

The information from this study provides an understanding of the dynamics of within-herd disease transmission, age at infection, seasonal effects and the age when cows become infectious or shedders. Since August 1999, five seasonal-calving dairy herds in the Manawatu region are followed for 3 seasons. The herds were enrolled because they had a history of clinical Johne's disease and were located close to Palmerston North. Blood, faeces and milk is sampled in early lactation (October) and again in late lactation (April). To date, approximately 1300 cows have been sampled repeatedly. One herd dropped was excluded from follow-up after it had no positive results after thee blood tests and two faeces culture tests. **Figures 1** and **2** illustrate the temporal prevalence of serological and culture test positive cows. Culture results appeared to be consistently higher in October, but serum antibody prevalence did not vary with season.

Because of the poor operating characteristics of diagnostic tests, repeated tests of the same cows are

FIGURE 1. Percent cows that were <u>culture positive</u> in the longitudinal study
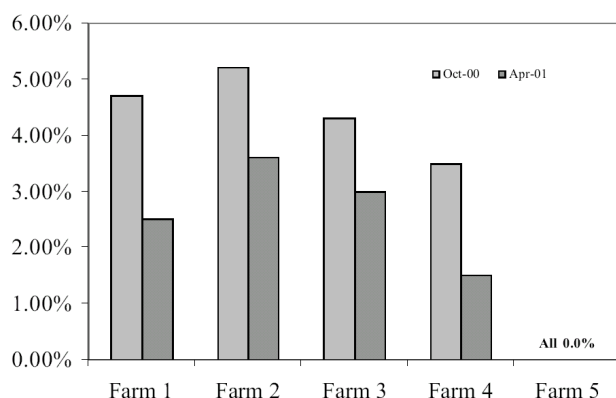
interpreted in parallel to improve the overall sensitivity (i.e. if any one of two or several tests is positive then the animal is regarded as infected). All cows are tested serologically and faeces is cultured from a cohort of up to 200 cows in each herd. Faeces samples are cultured for four months on a Herrold's egg yolk medium. The sensitivity of this test is approximately 20-60%, hence it is higher than that of the ELISA; its specificity is regarded 100%. However, faecal culture is prone to fungal contamination during the long culture period and about 10-20% of all samples may give inconclusive results.

Sera are tested using an Enzyme-linked immunosorbent assay (ELISA) with an approximate sensitivity of 10-50% depending on the infection status of the animal, and high specificity (>95%). Its high specificity was demonstrated by the excluded herd. Its 100 cows were tested three times at six months intervals and did not return any positive results.

Test results for each individual cow are combined with cow, production and fertility data provided by the Livestock Improvement Corporation (LIC) of the New Zealand Dairy Board. The data include birthyear, breed, calving dates, culling date and test day information on milk production and solids and somatic cell counts recorded four times per lactation.

Information from other studies

During the course of the project it became evident that more precise information about some influential

FIGURE 2. Percent cows that were <u>ELISA positive</u> in the longitudinal study
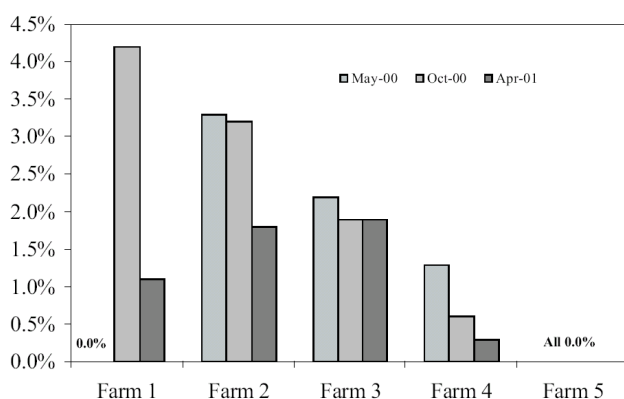
practices was needed for the simulation of Johne's disease in New Zealand dairy herds. Therefore, further information about calf feeding and management and disposal of slurry is currently being collected.

DISCUSSION

This discussion has two sections. The first section briefly describes the results of the Dutch model simulation study. The second section sets out the adaptations that will be required for the model to reflect New Zealand conditions.

Results of the Dutch simulation study

The study was performed in two stages, the first stage from May 1998 to January 1999 and the second from January to April 2000. Positive ELISA blood tests were followed up with a faecal culture test and if both tests were positive, the cow was culled.

The control measures that were simulated in the first stage of the study focused mainly on test-and-cull strategies for suspect herds in conjunction with a monitoring program to declare herds as 'currently free from Johne's disease'. The JohneSSim model predicted that eradication with sole reliance on 'test-and-cull' strategies was not possible within 20 years. In the absence of control the within-herd prevalence increased gradually. Annual ELISA blood testing with confirmation of infection by faecal culture and culling if both tests were positive resulted in a slower increase, but an increase nevertheless. The prevalence tended to decrease when the test-and-cull strategy was combined with improved calf management. However, none of these control options was economically effective. Simulation of a strategy with an 'ideal test' (80% overall-sensitivity) indicated that the prevalence would reduce at a significantly faster rate. However, that strategy was economically not attractive because of the high number of test-positive (young) and low level infectious animals that had to be culled.

In the second stage of the Dutch study the focus changed to greater reliance on calf-hygiene management because the simulation suggested that these were more effective in reducing prevalence. According to the simulation model, adoption of a progressing management improvement plan with little reliance on test-and-cull decreased the prevalence considerably (Groenendaal *et al.*, 2001). This program was economically more attractive than previous plans (average benefit-costs-ratio excluding extra labor = 1.58).

Model adjustment for dairy herds in New Zealand

Transmission mechanism parameters will need to be re-calibrated to suit local dairy production systems for application of the model in New Zealand. The 1999 case-control study, the 2000-03 longitudinal study, other ongoing investigations and expert opinion will contribute information to make these adjustments.

Prevalence information of low and high level infectious and clinical cows is required for all routes of infection. The case control study collected clinical case prevalence data, risk factors of herd management, and information on the frequency of those risk factors in New

Zealand dairy herds. The ongoing longitudinal study is providing information about within-herd infection dynamics and the economic effects of the disease.

Frequency distributions for management factors that are relevant to disease transmission are shown in **Table 1**. These data will aid in estimating infection probabilities of calves at various stages. Among farmers included in the case-control study (n = 427), 96% regularly fed colostrum to calves while 82% fed rest milk to calves. More detailed information about these management practices, and in particular about pooling of these milks is currently being collected in separate studies.

Features of New Zealand's pasture-based and largely seasonal dairy production systems of special reference to Johne's disease include the temporal distribution of large amounts of colostrum produced in the spring, direct and indirect pasture contamination and an almost permanent reliance on pasture from weaning on.

TABLE 1: Distribution of farming practices with relevance to transmission of Johne's Disease among 427 farms of the case-control study (1999)

The places cows are calved (n = 433):	
- in the paddocks with the rest of the dry herd	28.8 %
- in a springing group	77.9 %
- on a feed pad or an other grazing-off area	8.4 %
Time calves are aloud to stay with the dam after birth:	
- 12 hours or less	32.7 %
- 12 to 24 hours	7.3 %
- 24 hours or more	10.0%
Type of rearing facilities used on the farm:	
- shed with no separation into pens	8.9 %
- separate pens for groups of calves in a shed	83.0 %
- individual rearing crates	1.8 %
- outside with shelter	32.8 %
Calves younger than 4 months mixed with older cattle	8.0 %
Calves aged between 0-6 months in regular contact with older cattle	35.5 %
Calves aged between 7-12 months in regular contact with older cattle	11.9 %
Calves under 4 months of age run with adult cows in the hospital paddock:	
- never	60.9 %
- occasionally	29.5 %
- frequently	5.3 %
Slurry is sprayed on to pasture grazed by cows	61.4 %
Calves are grazed upon pasture sprayed with slurry	23.1 %
Cattle is send off the farm to graze	
- never	20.3 %
- occasionally	19.8 %
- regularly	59.9 %
Cattle from other farms is grazed on the farm	
- never	86.8 %
- occasionally	11.1 %
- regularly	2.1 %

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