

Simulation model of paratuberculosis control in a dairy herd

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ABSTRACT

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A simple simulation model of the control of paratuberculosis in a dairy herd was developed using a spreadsheet program. Reed–Frost methods were used to calculate new infections. Age-specific culling rates for infected animals (indexed to the annual herd replacement rate) were used as Markov chain transition probabilities for calculating culling probabilities. The predictive value model was used as the means of determining the probability that diagnostic tests would correctly identify infected animals for culling. This deterministic probability model was validated with previously published data from a 5 year field study on the control of paratuberculosis in an 80 cow dairy herd. Sensitivity analysis of the model variables was performed. Calf-management techniques that reduce the number of effective cow–calf contacts (k_3) decreased the prevalence of paratuberculosis in a herd at a rate in direct relation to the value of k_3 . Test-and-cull control measures also decreased the prevalence of disease in the herd; test sensitivity was the sole determinant of the effectiveness of this control strategy. Use of both calf-management and test-and-cull methods provided the quickest means of controlling paratuberculosis (which is consistent with reports in the literature). The model provides a simple method of predicting the rate at which paratuberculosis can be controlled or eliminated from a dairy herd and has the potential of being used for the economic evaluation of control programs. Because of the model's flexibility, it can be used to examine a variety of strategies for specific herds.

INTRODUCTION

Walker et al. (1988a, b) were the first to attempt the development of a model of paratuberculosis (Johne's disease) infection in a dairy herd. In an effort to develop a simpler model of paratuberculosis and to define factors that are most critical to the spread of the disease in a dairy herd, we developed

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the epidemiological model of paratuberculosis described previously (Collins and Morgan, 1991a).

The purpose of the present study was to refine the model to allow simulation of intervention strategies to control the spread of the disease. These strategies were diagnostic testing of adults and culling of test-positive animals, and/or calf-management techniques that minimize the exposure of calves to *Mycobacterium paratuberculosis* or enhance calf resistance to infection (i.e. vaccination). Validation and sensitivity analysis of the resultant model were carried out.

METHODS

Model description

An epidemiologic model of bovine paratuberculosis was described previously (Collins and Morgan, 1991a). This model accounted for the transmission of disease from cows to calves, the risk of disease introduction to a herd by the purchase of infected cattle and attrition (using age-specific culling rates) of infected cattle from the herd. The model was dynamic and output was illustrated by plotting the dependent variable (disease true prevalence) against time at 1 year intervals.

Variables input at the initial stage of the epidemiological model were as follows.

H herd size, i.e. adults in the milking herd, assumed to be all animals 2 or more years old.

Br birth rate in the herd (annual per capita basis).

R replacement rate (annual basis for adult milking cows).

n_0 number of infected cows at $t=0$ (considered as 2 year olds).

n_2 number of heifer replacements purchased per year.

p_2 risk of paratuberculosis in purchased replacement cattle.

k_1 number of effective cow-calf contacts per year prior to change in calf management practices.

Variables added to these for the control model were as follows.

k_3 number of effective cow-calf contacts per year as a result of change in management. This variable can be 'switched on' by switch no. 2.

Se diagnostic-test sensitivity.

Sp diagnostic-test specificity.

S1 switch no. 1. True prevalence (*TP*) at which the test-and-cull procedure was invoked.

S2 switch no. 2. True prevalence at which k_3 was invoked to reflect a change in management affecting effective cow-calf contacts per year (usually the same value as switch no. 1, but distinguished to allow each control method to be used separately).

Modification of the epidemiological model to study the impact of control procedures on the infection rate in a herd required the incorporation of parameters describing the accuracy of the diagnostic test used and a means of changing the number of effective cow-calf contacts per year resulting from improved hygiene or vaccination (k_3). Positive and negative predictive values were calculated to determine the probability of a correct diagnosis. Specific calculations are outlined below.

The predictive value of a positive test (PVP) and the predictive value of a negative test (PVN) were calculated as described previously (Vecchio, 1966; Dierksheide, 1987)

$$PVP = \frac{TP \times Se}{TP \times Se + (1 - TP)(1 - Sp)}$$

$$PVN = \frac{Sp(1 - TP)}{Sp(1 - TP) + TP(1 - Se)}$$

where TP is recalculated at each time interval of the model.

True prevalence was distinguished from apparent prevalence (AP) — the rate of positive test results in a population. Apparent prevalence was calculated from true prevalence by alteration of the equation of Marchevsky (1974) using the selected diagnostic-test sensitivity and specificity

$$AP = TP(Sp + Se - 1) - Sp + 1$$

The number of animals that were true positive (TPOS), false positive (FPOS), true negative (TNEG) or false negative (FNEG) was calculated as follows

$$TPOS = AP \times H \times PVP$$

$$FPOS = AP \times H - TPOS$$

$$TNEG = [H - (AP \times H)] \times PVN$$

$$FNEG = [H - (AP \times H)] - TNEG$$

By initiating the model with one infected cow in a herd and letting the disease spread through the herd prior to initiating control efforts, infected animals were distributed among all age groups. If no test-and-cull procedure was invoked, culling of infected adults was based on the age-specific cull rates described in the epidemiological model (Collins and Morgan, 1991a). When switched on, diagnostic testing was applied to all adults (aged 2 years or older) at the beginning of each year.

The number of infected animals culled (due both to test results and to usual culling) from each age class was calculated by multiplying the number of infected animals in each age class by the proportion of infected cattle correctly identified by the diagnostic test (Se), then adding (to the product of that

calculation) the age-specific culling rate applied to the remainder of the animals. The next year's true prevalence (TP_{t+1}) was the sum of the remaining (undetected, uncultured) infected cattle in all age classes plus infected replacements added to the herd (raised on the farm or purchased), divided by the herd size.

Like the epidemiological model described previously (Collins and Morgan, 1991a), the paratuberculosis control model was created using Lotus 1-2-3^R (Lotus Development Corp.) running under DOS 3.3 on a microcomputer with 640 kilobytes (K) of memory. When calculations were carried out for a 50 year period, the program occupied 270 K of memory.

Model validation

Age-specific culling rates in the model were validated previously (Collins and Morgan, 1991a). The paratuberculosis control model was validated by comparing the output of the model with data from a field study of a 5 year effort to control paratuberculosis in a dairy herd using test-and-cull procedures together with calf management by isolation (Ringdal, 1965). Parameters (such as herd size and diagnostic test accuracy) from the field study were used as the respective model variables. Other variables such as k_3 (effective contact rate resulting from the calf isolation procedure) were estimated to provide the best fit of model output to the observed data.

Sensitivity analysis

Standard methods for sensitivity analysis of model variables were used (Martin et al., 1987). Variables in the model not examined previously (Collins and Morgan, 1991a) were tested by changing each over a range of reasonable values and comparing the effects on the control of paratuberculosis, with the results expressed graphically by plotting true prevalence against time. Specific variables examined were Se , Sp , effective cow-calf contacts per year after institution of a control program (k_3), the prevalence of disease in the herd when the control program was initiated (SI) and whether the herd was open or closed. In addition, differences in paratuberculosis control were tested when using a test-and-cull program alone versus other management practices alone, or both combined.

RESULTS

Model validation

The study of Ringdal (1965) was the only published data describing a long-term effort to control Johne's disease in a heavily infected herd by test-and-

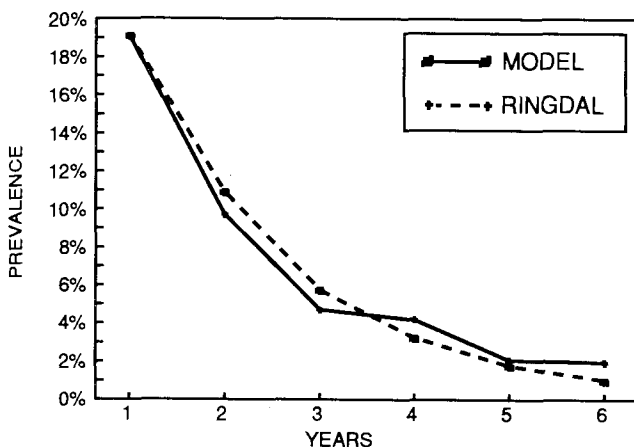


Fig. 1. Model validation. Comparison of the predicted rate of elimination of paratuberculosis from a dairy herd by the model data from a 5 year study on paratuberculosis control (Ringdal, 1965).

cull and calf-management procedures. The herd of Jersey cattle in the study had an average adult population over the study period of 77 cows. Ringdal used fecal culture as the basis for diagnosis, but supplemented it with the complement fixation (CF) test for antibodies to *M. paratuberculosis* (Jensen, 1956). Testing was carried out annually. All fecal culture-positive cows were culled immediately and CF-positive cows were culled as soon as convenient. Calves were isolated from the adult cattle. Adults culled from the herd were necropsied and thoroughly examined for paratuberculosis. The sensitivities of fecal culture and the CF test in the herd were 56% and 52%, respectively. In combination, the tests were 71% sensitive. Because the isolation of *M. paratuberculosis* from feces is considered definitive for the diagnosis of paratuberculosis, and because fecal culture was the primary test used for the selection of cows for culling, a test specificity of 99.9% was used in the model. Variables used to give the best fit of the model to observed data were $Br=0.95$ calves per cow year⁻¹, $R=0.21$ replacements per cow year⁻¹, $k_1=2.1$ and $k_3=0.8$. It was assumed that no outside purchase of cattle occurred. At every year of the study, the predicted prevalence of paratuberculosis in the herd closely matched that observed by Ringdal (Fig. 1).

Sensitivity analysis of model variables

Each variable was changed individually. Unless otherwise stated, all other model variables were as follows: $H=100$; $Br=0.95$; $R=0.25$; $n_0=1$; $n_2=0$; $p_2=0.05$; $k_1=2.0$; $Se=0.70$; $Sp=0.99$; $SI=0.10$; $S2=0.10$.

Diagnostic-test sensitivity and specificity

Test sensitivity was related directly to the rate of control of paratuberculosis by a test-and-cull program (Fig. 2). Only tests with a sensitivity higher than 70% would reduce the prevalence of paratuberculosis to less than 1% in less than 10 years. Test specificity had no effect on the prevalence of paratuberculosis in a test-and-cull program.

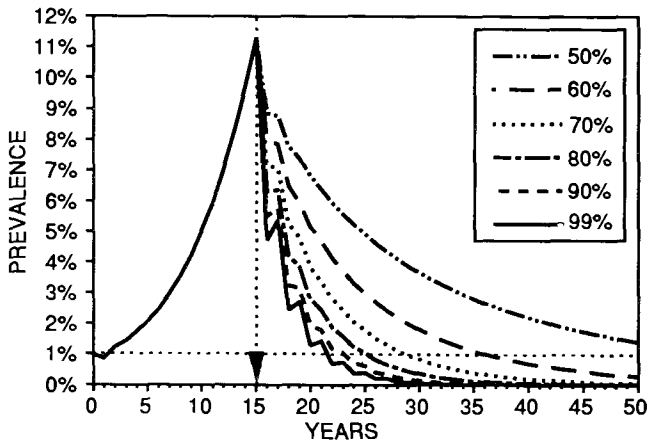


Fig. 2. Effect of diagnostic-test sensitivity on the rate of elimination of paratuberculosis from a dairy herd. The arrow indicates the beginning of the test-and-cull program.

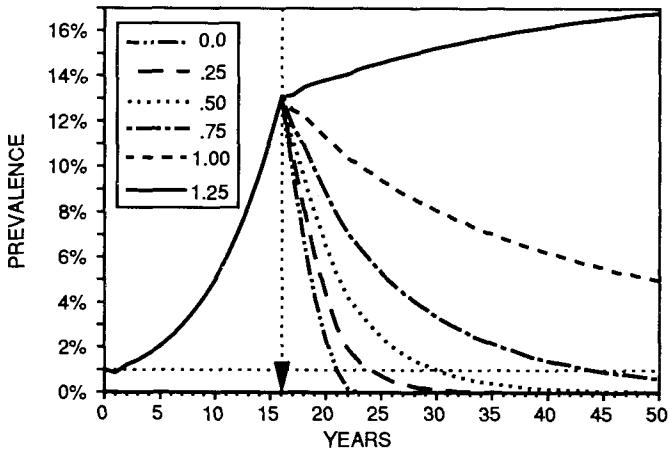


Fig. 3. Effect of changes in effective cow-calf contact (k_3) on a paratuberculosis control program. The arrow indicates the beginning of management changes (improved hygiene) to decrease the transmission of *M. paratuberculosis* to calves.

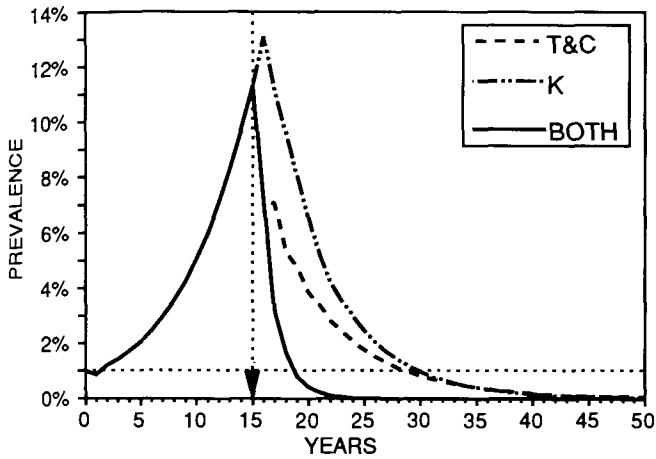


Fig. 4. Effect of a test-and-cull (T&C) paratuberculosis control program using a diagnostic test with $Se = 70\%$ and $Sp = 99\%$, a calf-management program (decrease effective cow-calf contacts, k_3 , to 0.5), or both on the rate of paratuberculosis elimination from a dairy herd. The arrow indicates the beginning of control programs.

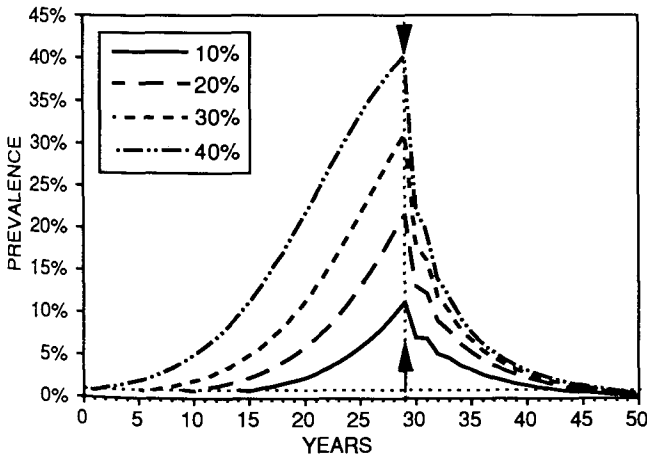


Fig. 5. Effect of the paratuberculosis prevalence at which a test-and-cull program for paratuberculosis is initiated on the rate of elimination of the disease from a dairy herd.

Effective contact rate (k_3)

Control of paratuberculosis by changing the number of effective cow-calf contacts per year had a dramatic effect on paratuberculosis prevalence (Fig. 3). Decline in paratuberculosis prevalence began when k_3 was reduced below

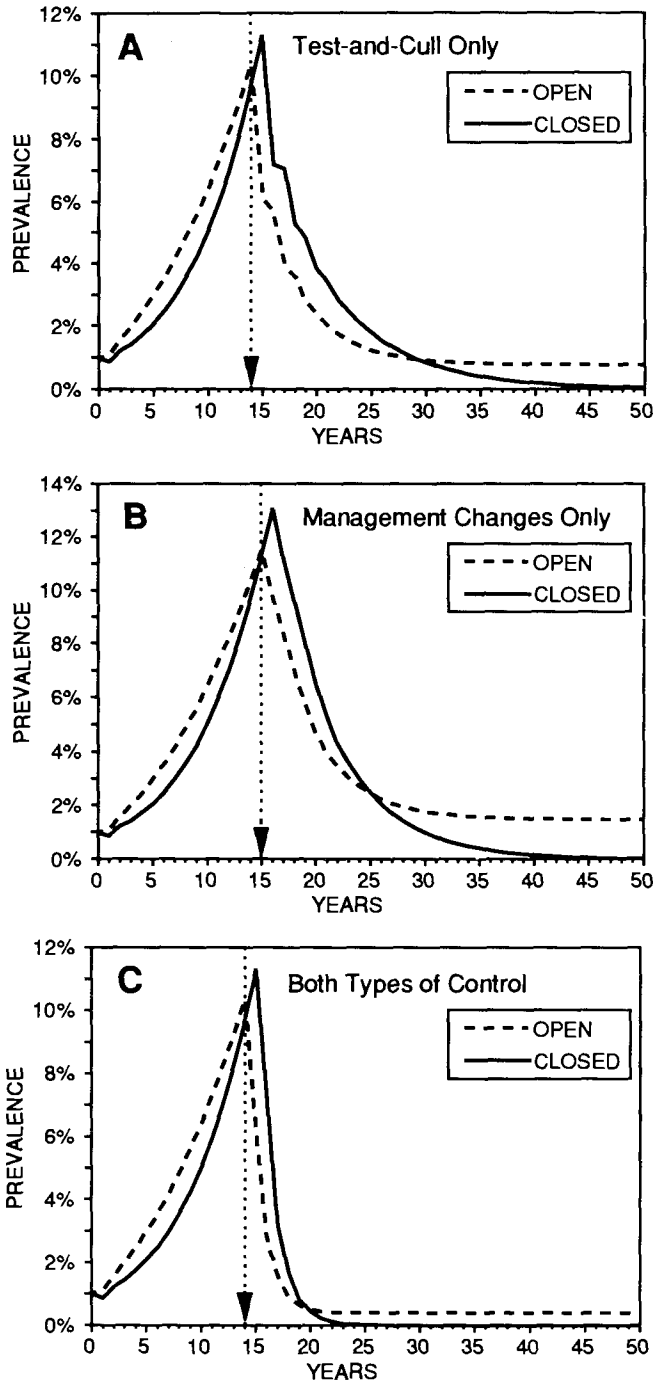


Fig. 6. Comparison of paratuberculosis control in open and closed herds (after paratuberculosis prevalence reached 10% (arrow)) by three techniques: (A) test-and-cull program only using a test of $Se=70\%$ and $Sp=99\%$; (B) calf management only with effective cow-calf contacts (k_3) reduced to 0.5; (C) both of the above procedures used together.

1.25. Reduction of the prevalence to 1% was achieved in 15 years when $k_3=0.5$ and in 10 years when $k_3=0.25$. However, even if all transmission of paratuberculosis to calves was halted ($k_3=0$), it took 7 years to eliminate the disease from the herd through normal culling.

Effect of using both test-and-cull procedures and management changes to control paratuberculosis

Figure 4 compares model outputs for control programs using (1) test-and-cull methods only ($Se=70\%$ and $Sp=99\%$), or (2) management methods that achieve a reduction in effective cow-calf contacts per year to 0.5, or (3) both test-and-cull and calf-management techniques. The test-and-cull program was faster than the management technique at reducing the infection rate in herds (although all prevalences eventually became equally low). The use of both methods simultaneously achieved the fastest control of paratuberculosis.

Paratuberculosis prevalence at which a test-and-cull control program is started; switch level (S1)

Paratuberculosis control by test-and-cull, using a diagnostic test with a sensitivity of 70% and a specificity of 99%, was modeled using each of four prevalence levels (10, 20, 30 and 40%), as the point at which the control program was invoked. The curves were then juxtaposed by shifting each curve to line up the start of the control program (Fig. 5). Prevalences fell most rapidly with the high-prevalence switches. After 7 years, the switch levels modeled had prevalences within a few percent of each other.

Open compared with closed herds

The control of paratuberculosis in open herds (buying 5 of the 25 annually required replacements) versus closed herds is shown in Fig. 6. Prior to control, open herds reached a prevalence of 10% sooner than closed herds. During the initial years of the control program, the prevalence in open herds declined faster than in closed herds. Eventually, however, open herds stabilized at a low paratuberculosis prevalence, while closed herds reached a prevalence of zero.

DISCUSSION

Model variables selected to provide the best fit of model output to field data were well within the range of expected values for dairy herds. Comparison of additional field studies would be desirable, but to the best of our knowledge none have been reported. With the data available, therefore, we conclude that the model satisfies one test for validity and apparently mimics reality.

The model was consistent with observations on paratuberculosis control made by other investigators. Specifically, the control of paratuberculosis in a dairy herd requires many years (Ringdal, 1965; Julian, 1975; Moyle, 1975). Management techniques that diminish the transmission of *M. paratuberculosis* from cows to calves can control the disease (Doyle, 1956; Larsen, 1972; Julian, 1975; Moyle, 1975; McCaughan, 1989). Diagnostic testing of whole herds and culling of all test-positive animals can control paratuberculosis effectively (Larsen, 1972; Julian, 1975; Moyle, 1975; Collins and McLaughlin, 1989). The use of both test-and-cull and calf-management techniques will be most effective. The model we described also produced results that compare favorably with those produced by the investigators using the model by Walker et al. (1988), although comparison of two models is not suggested as a means of model validation (data not shown).

The effective contact number (before or after institution of control measures) is a parameter that encompasses direct cow-calf transmission (congenitally, via shedding in milk, or via ingestion of contaminated maternal feces) and indirect transmission (by fecal contamination of the environment). The model assumes that no adult transmission of disease occurs. In the absence of calf management to control paratuberculosis transmission, the number of effective contacts per year is thought to be approximately 2.0–3.0. This is because this range of values for k_1 resulted in 40% of raised heifers being infected when the disease reached prevalences in excess of 20%—consistent with Ringdal (1965).

The model was sensitive to k_3 (the number of effective cow-calf contacts per year after institution of calf-management procedures to control the disease). Realistic values for k_3 are hard to estimate. Fitting the model to field data suggested that the calf-isolation procedures practiced on the Jersey farm studied by Ringdal resulted in a decrease in effective cow-calf contacts to $k_3=0.8$. No details were described in the field study about how rigorous the calf isolation was. If we assume that calves were removed promptly from their dam after birth to a separate facility (essentially eliminating the possibility of direct *M. paratuberculosis* transmission to calves by ingestion of contaminated milk or feces), then the infections that occurred in replacement animals must have been due to either congenital infection, fecal contamination of calf-rearing areas, transmission between calves, or adult transmission of infec-

tion—all of which occur experimentally, but have been thought to play minor roles under natural conditions (Doyle, 1956; Julian, 1975; Gilmour, 1976; Chiodini et al., 1984). This illustrated how fitting of the model output to data from field investigations of paratuberculosis control on farms could be a means of quantitating the relative benefits of different techniques for interrupting transmission of the disease. Because k_3 encompasses host, pathogen and environmental factors (Abbey, 1952), changes in k_3 can be used to model vaccination strategies as well as hygiene practices.

The model was also sensitive to diagnostic-test sensitivity, but was totally insensitive to diagnostic-test specificity. Economic considerations aside (Collins and Morgan, 1991b), the model indicated that the 'best test' to use in a paratuberculosis control program is the one that is most sensitive. While less specific tests will not alter the rate of disease control, they will cause a greater frequency of false-positive test results and thus more culling of non-infected animals. Since in most instances diagnostic-test sensitivity is balanced against test specificity, final determination of the optimal test for use in a paratuberculosis control program will require the incorporation of economic considerations, including the cost of the test itself.

It is essential for comparing diagnostic tests that test sensitivities have been calculated using the same 'gold standard' of disease definition (Sackett et al., 1985). Generally, paratuberculosis test sensitivity values reported in the literature conform to the definition: percentage of test-positive animals among those found infected by histopathology at slaughter or by isolation of *M. paratuberculosis* from tissues at slaughter or from feces ante mortem. It is also possible, however, to use only fecal culture as the basis for paratuberculosis diagnosis. This could be very important if further research shows that a significant percentage of exposed animals become infected and develop an immune response, but do not progress to excreting *M. paratuberculosis* in their feces — as has been suggested (Chiodini et al., 1984). If not all infected animals are infectious, then the former definition of test sensitivity may not be appropriate for modeling purposes. Defining diagnostic-test sensitivity based on infectious (*M. paratuberculosis* present in feces) instead of infected animals would change test sensitivity markedly and would yield different results for diagnostic-test comparisons.

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