Using a Model of Magnesium Dynamics in Cows to Predict the Risk of Tetany in Dairy Herds

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Abstract: The onset of tetany, when dairy cattle have insufficient magnesium, has a huge impact both economically and on animal welfare. To aid our understanding of the factors that determine magnesium status in dairy cattle, we have adapted and improved a model of magnesium dynamics in sheep. As it stands, this model is of little practical use to a dairy farmer who is primarily concerned with the status of the herd and the risk that animals will contract tetany. In this paper we describe how we have attempted to use the model to give the dairy farmer more useful information. Our approach is to calibrate the model using easily-obtained measurements such as urine and milk magnesium fluxes and then use Monte Carlo simulations in which model parameters are varied randomly according to their statistical distributions. The result of each simulation is classified as the likelihood of tetany occurring based on the value of the simulated magnesium concentration in cerebrospinal fluid. With sufficient simulations we can estimate the risk of tetany for the herd as a whole. A sensitivity measure was used to determine the extent to which each parameter contributes to tetany and hence the importance of knowing its distribution more accurately. Initial results show that our approach has potential. However, the process whereby we use measurements of urinary magnesium flux to calibrate some of the model parameters needs to be improved and a comparison of the calculated risk with actual field data needs to be carried out.

Keywords: *Magnesium model; Tetany risk in dairy herds; Monte Carlo simulation;*

1. INTRODUCTION

The onset of tetany, when dairy cattle have insufficient magnesium, has a major impact both economically and on animal welfare (Feyter et al. 1986). Because the time between the onset of the symptoms of tetany and death is only a few hours, a farmer needs to be able to assess whether animals in a herd are at risk of succumbing to the disease *before* any symptoms are apparent. Although a great deal of experimental work has been done to elucidate the factors which cause tetany, the farmer still does not have the tools to provide a useful assessment of the risk that animals in the herd will contract the disease.

We have modified a model of magnesium dynamics in sheep (Robson et al., 1997) so that it represents magnesium dynamics in lactating dairy cows. In this paper we show how we are attempting to use this modified model to provide useful risk information for the farmer.

2. THE APPROACH

There is no single experiment that records all the information necessary to construct a model such as the one we have developed. Rather, the process of building a typical biological model involves gathering together information from a wide range of experimental studies and, after careful investigation and analysis, using it to construct the model equations and determine parameter values. Validation is carried out both for individual parts of the model and hopefully for the model as a whole. The experimental studies used to build the model are likely to come from various breeds of animal and may even come from different species. A model of magnesium dynamics in dairy cattle developed using this process may well exhibit behaviour consistent with the species as a whole but is unlikely to be able to represent exactly the behaviour of an individual animal. The modeller hopes that the equations in the model are correct and that reasonable variation in model parameters is sufficient to explain the differences between animals.

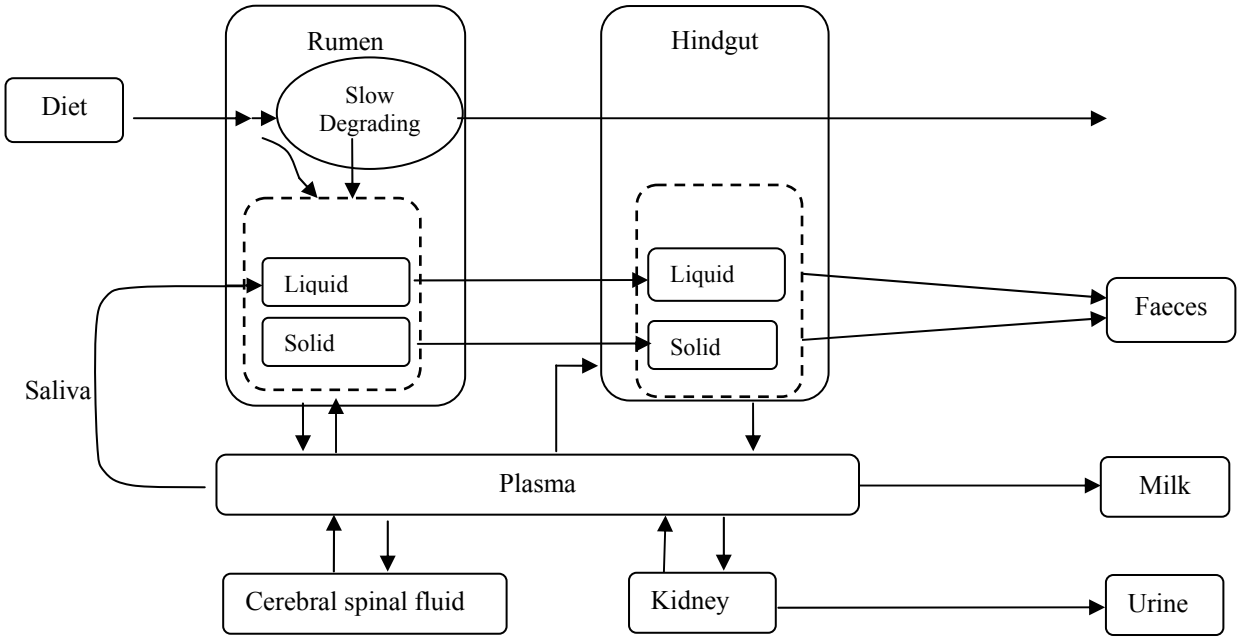

Figure 1. Schematic diagram of the model of magnesium dynamics in dairy cows. The arrows indicate magnesium fluxes. Full details of the model equations are available from the authors

In a particular herd, parameters will vary between animals, so that some will be more likely to contract tetany than others. If we have a disease criterion expressed in terms of one of the model's state variables, we can carry out Monte Carlo simulations to assess the risk that animals in a herd will contract the disease. Parameter values are selected randomly from their distributions; for each simulation we can determine whether that "animal" will contract the disease by comparing its state variable value with the disease criterion. If the number of diseased animals is N_d and the total number of simulations is N, then provided N is sufficiently large, the risk of disease is calculated as:

$$R_d = \frac{N_d}{N} \qquad (1)$$

There are some issues that need to be addressed when taking this approach:

1. There are a large number of parameters in the model some of which may have only a small effect on whether the animal contracts the disease. It would be sensible to carry out a sensitivity analysis and identify the parameters that most affect risk so that further effort can be put into improving knowledge of their distributions rather than those of parameters that have little effect.
2. The value of R_d from (1) would be for the species as a whole as determined by the overall model and would not give a farmer any useful information about the risk for a particular herd. The model needs to be calibrated to the particular herd under study.

The sections that follow describe the model of magnesium dynamics in cattle and how we have dealt with the issues above as we have attempted to use the model to estimate the risk of tetany in dairy herds.

3. THE MODEL

A schematic diagram of the model is shown in Figure 1. The modifications of the previous model pertaining to sheep (Robson et al. 1997) are mainly in the areas of lactation, hindgut secretion and absorption, urinary magnesium loss, saliva flow into the rumen and the transfer of magnesium to the cerebral spinal fluid that is its site of action as far as tetany is concerned. The model is expressed as a set of ordinary differential equations. Distributions for model parameters were taken from published data where this was available or else they were set following discussion with relevant scientists. Very little experimental work is available in relation to the hindgut absorption and secretion of magnesium so there is significant uncertainty in relation to those

parameters. Full details of the model equations and parameters are available from the authors.

Each simulation run on which this work is based was for a period of 10 days. Feeding periods were programmed to occur following normally observed patterns. Values used in the risk calculation were taken just before the commencement of the final feeding period, when they would be at their most critical.

4. RISK CRITERION

Authors such as Allsop & Pauli (1975) and Meyer & Scholz (1972) have shown that tetany occurs when the concentration of magnesium in the cerebral spinal fluid (M_{CSF}) falls below about 0.6 mmol/L. Accordingly, a simulated animal was consider to have contracted tetany when

$$M_{CSF} <= 0.6 \text{ mmol/L}. \qquad (2)$$

Calculation of risk using equations (1) and (2) gives an assessment of the risk if the herd continues to be subject to the same environmental conditions. But a farmer would also want to know what the risk would be if the situation was perturbed, perhaps due to bad weather causing a feeding period to be missed or if an increase in milk production was imposed.

5. SENSITIVITY ANALYSIS

To identify the parameters that predominantly influence the risk of disease, Monte Carlo simulations were carried out allowing all parameters to vary according to their distributions. The result of each simulation was classified as having contracted tetany (T) or not as determined by equation (2). For the ith parameter, the mean X_T^i and standard deviation ε_T^i of values for which tetany occurred were calculated and compared to the mean X^i and standard deviation ε^i for all values for that parameter used in the Monte Carlo simulations. The comparison was done using a t-test. Parameters not showing a significant difference between the two categories after 20,000 simulations were not varied in subsequent analyses. The sensitive parameters are listed in Table 1.

6. MODEL CALIBRATION

To make the risk assessment as specific as possible to the herd under study, we would like to be able to obtain information about the distribution of every model parameter in relation to that herd. That is clearly impractical. There are a few herd-specific measures available and we must use this information as best we can.

Table 1. Parameters in the model of magnesium in dairy cows that predominantly influence the risk of tetany.

Parameter Symbol	Description
C_D	Concentration of magnesium in the diet
S_{HG}	Hindgut absorption constant
C_K	Concentration of potassium in the rumen

6.1. Milk Production

Daily milk production for the herd as a whole is routinely measured as part of normal herd monitoring. This provides an estimate of the mean of the milk production parameter. The milk production of individual animals is measured as part of a herd test 2 or 3 times per season, providing an estimate of the standard deviation of the daily milk production for the herd. The mean of the distribution (assumed to be Normal) is adjusted according to the herd's daily production data. The magnesium concentration in the milk of each animal is relatively stable (Thielen, 2000) but there is significant variation between animals (McCoy, et al., 2001). This information is also potentially available from the herd test.

6.2. Urinary Magnesium

Kits are available for routine estimation of the daily flux of urinary magnesium (M_u) of individual animals. This provides an estimate of the mean and standard deviation of M_u for the herd. However, M_u is a model output, not a parameter. Therefore, to use these measurements to improve our knowledge of the distributions of model parameters, we need to carry out some sort of fitting process. As shown in Figure 2, distributions for the parameters $\{P_i, i \ni 1..N\}$ will produce a distribution for M_u as a result of the Monte Carlo simulations. The challenge then is to adjust the distribution of each parameter P_i until the simulated and measured distributions for M_u match.

In this initial study, we have taken the following simple manual approach to this fitting problem:

1. Rank the three parameters that predominantly determinine tetany (Table 1) in the order in which they are likely to be most strongly related to M_u. The ranking was done by inspection of the model equations. This resulted in a ranked set of parameters $\{P_i, i \ni 1..3\}$

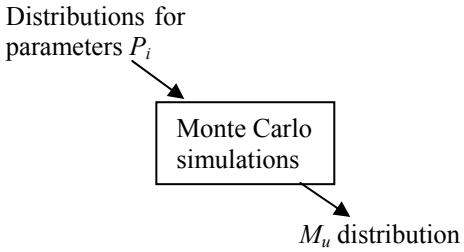

Figure 2. The relationship between the distributions of model parameters P_i and the distribution of urinary magnesium flux M_u

2. With the mean of each P_i initially at its standard value and the standard deviations of P_i set to zero, iteratively adjust the mean of each parameter in turn to give the best fit between the means of the measured and simulated M_u values. The iterative adjustments were constrained to prevent parameter means going outside predetermined physiologically reasonable ranges.
3. Using the mean parameter values resulting from step 2, iteratively adjust the standard deviation for each parameter in turn until the best fit between the measured and simulated standard deviations for M_u is obtained. The iterative adjustments were constrained to prevent the standard deviations from being greater than 30% of their respective means values.
4. Refine the mean values of the parameter distributions previously determined as the means and standard deviations are not independent in their effect on the calculated M_u.

With this simple approach to refining the parameter distributions, no real meaning can be assigned to the values that result. The ranking of the parameters as set out in step 1 of the process described above prevents that. Also, because the parameters were adjusted one at a time and in sequence, any covariation that might exist between model parameters is prevented from having an effect. However, our objective is to calibrate the model to the measured M_u data only so that we can calculate the risk of tetany in the herd. To assess whether our approach to finding the parameter distributions impacts the risk calculation, we changed the rank of the three parameters in step one and repeated the process.

7. RESULTS

As an initial assessment of this approach to determining the risk of tetany in a dairy herd, we applied it to a fictitious case as specified in Table 2.

Table 2. Specifications for the fictitious herd used to assess this approach to estimating risk. These distributions are consistent with a normal healthy herd.

Distribution of milk production	Normal with mean 18.5 L/day and standard deviation 2 L/day
Distribution of urine magnesium flux (M_u)	Normal with mean 1.0 gm/day and standard deviation 0.5 gm/day
Mean milk magnesium concentration	85 mg/L

7.1. Model Calibration

As explained previously, the distribution of daily milk production could be directly assigned to the distribution of the relevant model parameter.

The results of fitting the distributions of the three model parameters to the distribution of urine magnesium flux are given in Table 3.

Table 3. Means and standard deviations of the (Normal) distributions of model parameters obtained by fitting to the distribution of urine magnesium flux. The results for two different rankings (A and B) of the parameters are shown.

Parameter	Rank A	Fitted Distrib μ σ	Rank B	Fitted Distrib μ σ
C_D (gm/kg Dry Matter)	1	1.97 0.16	3	2.0 0.25
S_{HG}	2	1.8 0.1	2	1.55 0.0
C_K (mmol/L)	3	15.0 5.0	1	20.0 0.0

7.2. Risk Calculation

With the parameter distributions for C_D, S_{HG} and C_K determined as described, and with all other model parameters allowed to vary according to their distributions, it is now possible to calculate the risk of tetany according to equation (1) using the criterion (2). As previously discussed, the farmer may well be interested in how the risk might vary when the environmental conditions are

perturbed in some way. To demonstrate this, in Figure 3 we show the risk of tetany as a function of the perturbation of the milk magnesium concentration from the value determined during the calibration of the model.

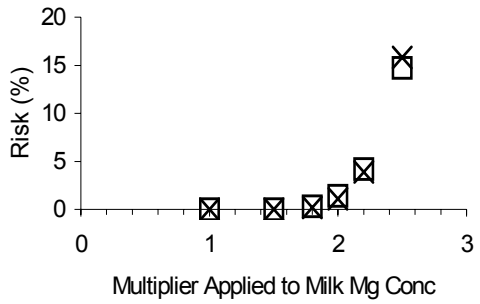

Figure 3. The risk of tetany as a function of a multiplier applied to the milk magnesium concentration. The values × were obtained using the parameters from Rank A (Table 3) and the values □ were obtained using the parameters from Rank B.

8. DISCUSSION AND CONCLUSIONS

The initial motivation for developing a model such as one describing magnesium dynamics in dairy cattle is to explore quantitatively the various mechanisms that are thought to be involved, and to provide a basis for further experimental investigations. When such a model has matured to the point that it explains the important observations and mechanisms, it is tempting to see if the model can be used in a predictive way in a practical environment - in our case to estimate the risk of tetany in a dairy herd.

The critical factor in carrying this out, is calibrating the model so that, as much as possible, its parameter distributions represent the actual herd under study. In the case of the present model, the only information available to do this is daily milk production for the herd as a whole and some sample measurements of urinary magnesium flux.

The milk production information allowed the corresponding model parameter to be estimated directly. However, urine magnesium flux is a model output so a fitting procedure had to be used. We have initially taken a very simple manual approach to this problem where we fitted each parameter one at a time independent of the others. With this approach, no meaning can be attributed to the parameter distributions that result, but it was our expectation that the effect on the subsequent risk calculations would be small. Table 3 shows that the means of the fitted distributions are not significantly affected by the order in which the parameters were fitted and Figure 3, shows little effect on the resulting risk calculation. In both cases the risk seems reasonable.

Nevertheless, we recognise the simplicity of our fitting process. We envisage some situations where the fitted parameters would be significantly affected by the order of fitting. Therefore, we plan to use a more robust approach similar to those used in discrete event modeling.

Despite the simplicity of the model calibration, we have demonstrated that our approach to using the model to estimate risk in a practical farming situation has potential. However, a number of successful field trials on a range of herds where there is some independent assessment of risk would need to be undertaken to confirm this.

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