DUTCH SOCIETY FOR VETERINARY EPIDEMIOLOGY AND ECONOMICS
VEEC

ENDEMIC DISEASES
Proceedings 19th Annual Meeting held on February 15th 2007
Faculty of Veterinary Medicine

Editors: A. Bouma and Y. Melger
Thank you for opening the proceedings of the 19th annual meeting of the Dutch Society for Veterinary Epidemiology and Economics (VEEC) organized by the Faculty of Veterinary Medicine of Utrecht University.

This year’s topic of the morning session of our annual meeting is “endemic diseases”. Although exotic diseases like Avian Influenza and Blue tongue, zoonoses and food borne diseases seem to attract the majority of the attention of scientists and society, it is good to realize that our animals still suffer most from endemic diseases and the farmers from the accompanying losses. Thus, after having addressed the majority of our recent meetings to the diseases first mentioned, it seemed like a good idea to focus this year’s meeting on endemic diseases. We will focus on the patterns of diseases and the consequences in terms of performance as well as economic losses. For this reason we are pleased that Christine Fourichon from the University of Nantes, James Wood from Cambridge University, and Ruud Huirne from the Animal Sciences Group Wageningen UR want to share their ideas with us.

In the afternoon program, which has a variety of interesting subjects, we will young scientists the opportunity to briefly present their recent work.

I thank Annemarie Bouma and Yoox Melger for organizing this meeting and preparing the proceedings. Furthermore I would like to thank The Faculty of Veterinary Medicine for their hospitality.

On behalf of the board of the VEEC I wish you a pleasant and stimulating conference.

Arjan Stegeman
President VEEC
CONTENTS

RESEARCH IN EPIDEMIOLOGY OF ENDEMIC DISEASES TO SUPPORT HEALTH MANAGEMENT DECISIONS IN DAIRY HERDS
Christine Fourichon 7

ECONOMIC ASPECTS OF DISEASES IN PIG PRODUCTION, WITH EMPHASIS ON ENDEMIC AND PRODUCTION DISEASES
Ruud Huirne 13

MODELLING THE TRANSMISSION OF EQUINE INFLUENZA
James Wood 17

VITAMIN E AND OXIDATIVE STATUS OF DAIRY COWS
Ruth Bouwstra 19

MONITORING SUBCLINICAL MASTITIS IN THE NETHERLANDS: TWO EXAMPLES
Bart van de Borne 23

MODELLING OF VECTOR-BORNE DISEASES
Nienke Hartemink 29

A CONCEPTUAL FRAMEWORK FOR EXPLORING TRADEOFFS BETWEEN PREVENTION, MONITORING AND CONTROL OF AVIAN INFLUENZA
Natasha Longworth 33

TRANSMISSION OF EIMERIA ACERVULINA IN BROILER CHICKENS
Francisca Velgers 43

CERTIFICATION- AND-SURVEILLANCE PROGRAMMES FOR PARATUBERCULOSIS IN DAIRY HERDS
Maarten Weber 47
RESEARCH IN EPIDEMIOLOGY OF ENDEMIC DISEASES TO SUPPORT
HEALTH MANAGEMENT DECISIONS IN DAIRY HERDS

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1. INTRODUCTION

Management of endemic infectious diseases in dairy herds mainly relies on individual farmers decisions. They need information to chose control actions worth to implement in the context of their own farm and have to assess: (i) what is the risk for their farm to introduce a pathogen and have a long-lasting infection, (ii) what are the possible consequences of a herd infection, and (iii) what are the costs associated with the infection and with its control. The objective of this paper is to illustrate how epidemiologic studies provided pieces of knowledge to support decisions for the control of endemic diseases, with the example of BVDV (Bovine Viral Diarrhoea Virus) in France.

2. DESCRIBING DISEASE RISKS AND EFFECTS FROM FIELD DATA

Surveys and quantitative epidemiology methods were used to estimate herd level prevalence, incidence and risk factors of BVDV infection in dairy herds in Brittany. Estimates were used in a Markov chain model to predict the trend of prevalence at the regional level assuming no changes in risks. In 2000, 42% of the herds were BVDV-free. It was shown that without any action, at the regional level, the prevalence would reach an equilibrium close to 50% of infected herds (Joly et al., 2001).

In a cohort study on significant risk-factors were use of a bull for mating, presence of a fattening calves unit, presence of a bull steers unit, buying cattle for fattening, pasture contact with other herds for heifers (OR from 2.7 to 4.8) (Delquigny, 2002). Risks associated with cattle movements or pasture contacts varied between regions, e.g. in the Cher district high risk contacts result mainly from contacts between herds at pasture (Ezanno et al., 2006; Sautereau, 2005).

Estimates of production effects of the infection put forward an increase in foetal loss, a decrease in milk yield and an increase in milk somatic cells in BVDV-positive herds, but no effect on fertility at AI (Table 1). Carry-over effects on milk yield and somatic cells were evidenced for at least one year after herd status definition (Beaudeau et al., 2004, 2005; Robert et al., 2004).

Table 1. Estimated production effects of BVDV infection in a dairy herd

<table>
<thead>
<tr>
<th>Results of consecutive ELISA on bulk milk over 1 year</th>
<th>Interpretation and assumed herd status</th>
<th>Effect on % of late return to service (repeat AI &gt; 25d)</th>
<th>Effect on milk yield</th>
<th>Effect on bulk milk somatic cell count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seroconverting Positive</td>
<td>New infection</td>
<td>RR = 1.12</td>
<td>-0.3 kg/d</td>
<td>+12 000 cells / ml</td>
</tr>
<tr>
<td>Highly positive</td>
<td>Previous infection, virus likely to still be present</td>
<td>RR = 1.11</td>
<td>-0.6 kg/d</td>
<td>+25 000 cells / ml</td>
</tr>
<tr>
<td>Positive</td>
<td>Previous infection</td>
<td>RR = 1.03</td>
<td>-0.4 kg/d</td>
<td>+15 000 cells / ml</td>
</tr>
</tbody>
</table>
3. UNDERSTANDING DYNAMICS OF THE VIRUS TRANSMISSION AND PERSISTENCE WITH EPIDEMIOLOGICAL MODELLING

A stochastic simulation model was used (Viet et al., 2004). It consisted of two processes: one modelling the herd dynamics (demography, structure and management) assuming the dairy herd as a multigroup population (semi-Markov process) and the other modelling the transitions between BVDV statuses (Markov process). Animals were assumed to be raised in groups according to their age. Herd size was controlled by sale of female calves and culling, according to birth and death of animals. An individual-based approach was used to take into account individual characteristics influencing the occurrence of events (movements between groups, transitions between BVDV statuses, vertical virus transmission). The transiently infective animals were assumed to be able to transmit the virus to susceptible animals only in the same group whereas the PI animals were assumed to transmit the virus to susceptible animals both within their group and in other groups.

In the modelled herd, actions to avoid virus transmission from herd’s neighbourhood were assumed to be in place. PI animals were assumed to be detected before any movement between herds and not to be sold. In such a context, the most probable remaining origin of virus introduction is the purchase of immune dams carrying a PI foetus which cannot be detected by available tests. The virus introductions were simulated as the purchase of immune heifers carrying a PI foetus, 20 days before calving. Virus reintroduction over time was either ignored, or simulated at an intermediate or high frequency according to observed data (Ezanno et al., 2006). Four scenarios representing four strategies were studied: (1) no other action, (2) prevention of contacts between animals of different groups of age, (3) test-and-cull of PI animals, and (4) combination of (2) and (3). The prevention of contacts between animals was modelled by setting transmission rates between different groups to zero. The test-and-cull programme consisted of monitoring the herd, and, in case of a positive herd result, screening for detecting and eliminating PI animals. Every 6 months, the antibody level in the bulk-milk was measured by an ELISA test. If the percentage inhibition was higher than 60% (corresponding to a prevalence of immune cows higher than 30%), a virus spread was assumed. Then, screening for PI animals was based on consecutive combined tests for antibody and virus detection, defined per category of animals, in order to mimic existing zoosanitary schemes.

The initial herd consisted of 38 cows, 13 bred heifers, 18 heifers before breeding, and 3 female calves, all of which were susceptible (all male calves were sold out at 10 days of age). The virus spread was simulated over 10 years. For each strategy, 600 replications were run.

Effects of strategies on virus elimination considered three categories of criteria:
- The interval between virus introduction in the herd and detection of infection from monitoring bulk-milk antibodies.
- The occurrence of and the time to virus clearance. Clearance was defined as the absence in the herd of any shedding animal or dam carrying a PI foetus. The probabilities of virus persistence within the herd (as opposed to clearance) were represented by Kaplan-Meier curves. The distributions of time to clearance were compared between scenarios, stratifying by time of bulk-milk antibody detection (or level allowing detection in case of strategies with no monitoring). Herds already cleared at the time of bulk-milk antibody detection were excluded from this latter analysis.
- The extent of the infection in the herd. The total number of contaminated animals in the herd during 10 years was calculated for each replication.

Monitoring bulk-milk antibodies every 6 months allowed the detection of BVDV infection within one year after virus introduction in most cases when there were contacts between groups of animals of different ages, but could also result in very late detection (Table 2). Detection was postponed after at least 2 years when absence of contacts between groups of animals limited virus transmission within the herd. In case of late detection, the herd was often already cleared from the virus when the seroconversion of the lactating cows was evidenced.
Table 2. Number of replications per interval from virus introduction to detection of bulk-milk antibodies (out of 600 per scenario, after excluding very early clearance) and % of replications with herd not yet cleared at the time of detection

<table>
<thead>
<tr>
<th>Time from virus introduction to detection of bulk-milk antibodies - in days</th>
<th>190</th>
<th>370</th>
<th>550</th>
<th>730</th>
<th>910</th>
<th>1090</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test-and-cull of persistently infected animals, no increased biosecurity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NUMBER OF REPlications DETECTED</td>
<td>120</td>
<td>135</td>
<td>25</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>% NOT CLEARED BEFORE DETECTION</td>
<td>98.3</td>
<td>96.3</td>
<td>84.0</td>
<td>25.0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Test-and-cull of persistently infected animals combined with prevention of contacts between groups in the herd</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NUMBER OF REPlications DETECTED</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>178</td>
<td>8</td>
</tr>
<tr>
<td>% NOT CLEARED BEFORE DETECTION</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>24.7</td>
<td>0</td>
</tr>
</tbody>
</table>

Clearance occurred earlier with test-and-cull programme than with do-nothing, and persistence was further reduced by prevention of contacts in the herd, especially in the first two years after virus introduction (Fig. 1). Extent of infection was only slightly reduced by test-and-cull programme, whereas prevention of contacts resulted in a drop in the number of contaminated animals (Fig. 2). Test-and-cull programme reduced time to clearance (Fig. 3 and 4). In herds still infected at time of (possible) detection of antibodies in bulk-milk, the probability of virus persistence lasting more than 4 years decreased from >25% to <5%. When combined with prevention of contacts, test-and-cull programme reduced time to clearance, but later than three years after virus introduction. In this scenario, because of very early clearance or clearance before virus be detected, only 7% out of 600 replications could benefit from decreased persistence associated with test-and-cull programme.

When possible virus reintroduction was included in the model, the test-and-cull programme strongly reduced the probability of virus persistence in the herd over time. The effect of the programme on distribution of dates of virus detection, virus persistence and extent of the infection also varied according to the level of contact between animals of different age groups (Viet et al., 2006).

A sensitivity analysis on a comparable stochastic compartmental model showed that the transmission parameter for animals in different groups, which depends on the contact structure in the herd, explains the highest proportion of variance in the model outputs (Ezanno et al., 2007).

After a purchase of a non-PI dam carrying a PI foetus, a zoo-sanitary scheme based on test-and-cull reduces persistence of BVDV in a herd, but this effect may be limited or delayed due to late detection of infection. If late detected, the herd is likely to be free of PI animals at cows’ seroconversion. In Brittany (Western France), PI animals were found in only 28% of seroconverting herds (Joly, unpublished data), suggesting that virus introduction may often have occurred more than one year before. Shortening virus persistence by detecting and eliminating PI animals may in fact be limited to a small proportion of cases, nevertheless at a regional level, benefits from reduced risk of virus introduction in other herds should also be considered.

Prevention of contacts between groups appears to be very efficient in limiting both duration and extent of infection. Nevertheless, in many commercial herds, total prevention of contacts between age groups is not possible. Anyway, it should be recommended as it is one of the very influential determinants of virus persistence in a herd.

Model simulation allows the investigation of how BVDV control strategies interact with herd management and provides relevant data to assess their efficiency in various herd situations. In the contexts of either low or high risk of virus introduction, zoo-sanitary schemes appear to reduce overall duration of herd infection.
Figure 1. Probability of virus persistence for four strategies (600 replications by strategy)

Figure 2. Extent of the infection for four strategies: number of contaminated animals during the simulated 10-year period (600 replications by strategy)

Figure 3. Time to clearance by time of detection of bulk-milk antibodies for test-and-cull (right) vs. no action (left)

Figure 4. Time to clearance by time of detection of bulk-milk antibodies for prevention of contacts with (right) vs. without (left) test-and-cull
4. QUANTIFYING ECONOMIC LOSSES WITH ECONOMIC MODELLING

Costs of a BVDV infection in a dairy herd were calculated by partial budgeting. Total disease costs included extra expenditures for treatment of sick animals and losses resulting from production effects of the virus. Production effects were calculated for a 100-cow herd and included the effects of BVDV infection on reproduction, milk yield, milk somatic cells, calf mortality, and occurrence of diseases in calves and cows. The partial budget model calculates losses in a farm with management, production costs, and prices representative of western France situation and resulting from total production effects at the herd level across one year. Extra-expenditures for extra diseased animals were based on current treatment costs as charged by veterinary practitioners in western France.

Overall costs (losses plus expenditures) resulted in a decreased gross margin of 10.7 and 19.0 € per 1000 litres of milk for an average and severe infection, respectively. With a milk quota system allowing no lease of quota, assuming adjustment of the herd size by the farmer to produce the quota, decrease in gross margin was limited to 7.9 and 13.9 € per 1000 litres of milk (Fourichon et al., 2005).

5. REFERENCES


1. INTRODUCTION

In The Netherlands, pig production is an important economic activity within agriculture. Approximately 21 million pigs are produced annually, of which more that 50% is exported either alive as piglet or hog, or as meat. Obviously, livestock diseases can have a major impact on this economic important activity. Livestock diseases can be categorized in various ways. In principle, populations should be free of highly contagious diseases such as Classical Swine Fever (CSF) and Foot-and-Mouth Disease (FMD). Furthermore, certain enzootic diseases can potentially be eradicated, like Aujeszky’s Disease (AD). Finally, there are enzootic production diseases such as respiratory diseases and fertility problems, which are hard or even impossible to eradicate. From a financial-economic point of view, major aspects, which should be considered, are whether or not diseases have an impact on only individual farms, if the pig sector is predominantly affected or if the financial-economic impact goes beyond this level of the economy, and if the country is net-exporting for pig meat. Taking this into account, livestock diseases can be categorized as follows:

− Diseases which will affect all primary producers and related industry, and which can also have a financial-economic impact on other parts of society (i.e. the consumers): CSF and FMD are typical examples;
− Diseases which are important for the whole pig production sector, but which will have a less dramatic impact outside the sector: such diseases include those for which sector wide programs for eradication and prevention can be established, such as AD;
− Diseases which are predominantly important at the level of the individual farm, such as respiratory diseases.

Each of these diseases has a different financial-economic impact, and studying these diseases should include very specific aspects.

The aim of this presentation is to present the various financial-economic considerations for the different categories of diseases mentioned. This is done by presenting the main methodological aspects in short, accompanied by a practical example.

2. EPIZOOTIC PIG DISEASES

Control of epizootic pig diseases such as FMD and CSF are subject to European Union (EU) legislation, which include stamping-out of affected premises and the establishment of zones with transport stand-still, which have a radius of at least 10 km (the so-called Surveillance zone). Hence, if such outbreaks occur in densely populated areas, a large number of pig producers will be affected economically for a relatively long period of time, because transports to and from their premises is prohibited. Moreover, there is the risk of an export ban on animals and products, particularly in cases when vaccination is used as an additional control measure. In such cases, prices for both consumers and producers will be affected, particularly if the country is net-exporting.
The build-up of the financial-economic costs of epizootic pig diseases include:

- Direct costs, e.g. for compensation to affected farmers;
- Consequential costs, which can be split-up into (1) direct consequential costs (caused by e.g. welfare slaughter and idle production factors), and (2) indirect consequential costs (caused by increased or decreased prices);
- Costs which occur during the period of recovery after the epizootic, e.g. if prices have changed due to starting-up production or regaining export markets.

A research addressing these issues was carried out by Mangen and Burrell (2005). They analyzed the financial-economic impact of CSF control in The Netherlands for various scenarios taking into account (1) the pig density of the region affected, (2) whether or not export bans were imposed and (3) 4 different types of control strategies. They clearly showed the impact of an export ban on pig products. In case these bans were imposed, particularly small outbreaks in sparsely populated pig areas, which are from an epidemiological point of view ‘best case’ scenarios, could lead to high costs for collective pig producers. In contrast, consumers would benefit from the price decrease. Another finding was that large outbreaks in densely populated pig areas without export bans would result in a benefit for the collective producers.

With regard to the latter, it should be realized that within the group of collective pig producers differences can be very large: from very dramatic losses of producers within the Surveillance zone which cannot continue their production to large gains due to high prices for farmers outside the Surveillance zone.

### 3. ENDEMIC DISEASES AT THE LEVEL OF THE PIG PRODUCTION SECTOR

Endemic diseases can be distinguished into diseases, which can potentially be eradicated, and those for which eradication is not a feasible option from a veterinary point of view. Eradication can be carried out on individual farms, in which case the farmer takes the decision. However, such decision can also be taken at the level of the pig sector. In both cases, usually the following aspects are considered: the benefits of eradication (i.e. reduced avoidable costs due to diseases) and the costs of eradication. However, other important aspects should also be addressed: the costs for increased bio-security and monitoring, the risks of re-introduction of the disease and the costs associated with that event. Self evidently, the latter highly depend on the demographic features of the region affected, e.g. the pig density and the production ratio piglet/hog (this is particularly important if animal movements are allowed within the affected area).

Saatkamp et al. (2005) studied to financial-economic consequences for the Dutch pig production sector with regard to Aujeszky’s Disease (AD): going from article 9 (freedom of AD with vaccination) to article 10 (freedom of AD without vaccination). A cessation of vaccination would result in a reduction of the annual costs for the collective producers of approximately 16 m€ (i.e. no costs for vaccination and certification of farms that have the permission not to vaccinate). Moreover, securing access to markets that have already the article 10-status is an additional benefit. These benefits should be weight against the costs associated with re-introduction of the AD virus in a fully susceptible population, and the probability hereof. In this respect, the results showed the economic importance of the ratio piglet/hog in the affected area. If AD would occur in high density areas, the preferred control strategy from a veterinary point of view would be (given the adopted constraints of non-vaccination and not stamping-out): vaccination within a considerable larger area around infected premises than 10 km. However, from a cost point of view, vaccination within a smaller area should be preferred, particularly of relatively high ratios of piglet/hogs are considered. Hence, the direct costs of a bit more prolonged outbreak are more than outweighed by a reduction of the costs associated with marketing piglets originating from the affected area. Prediction of the probability of re-introduction of the AD virus appeared to be very difficult. Nevertheless, they concluded that from a financial-economic point of view obtaining the article 10-status would be sensible.
4. PRODUCTION DISEASES AT PIG FARMS

In comparison to e.g. cattle farms, on pig farms particularly the phenomenon of small margins, large numbers and therefore large financial-economic effects of enzootic livestock diseases exist. Even small deviations of production parameters, particularly feed conversion ratio (FCR), can cause considerable costs, particularly if feed prices are high.

The financial-economic consequences on the net return to labor and management of changes of production parameters in pig production can be calculated relatively easily (Dijkhuizen et al., 1997). This is due to the relatively straight-forward production pattern (i.e. simple input-output relations), the large part of the variable costs in the total costs and the fact that production occurs on small areas of land with relatively a large amount of in-bought production means (i.e. little problems in valuation). The problem of estimation of the financial-economic costs of enzootic pig diseases arises from the fact that usually the animals suffer from a complex of various agents, which often interact with each other. This holds particularly for respiratory diseases (Stevenson, 1998), which are assumed to be the most important veterinary problem in hog production (Martens, 2002). This particularly impedes cost-benefit analyses of e.g. treatment or vaccination.

Giebels (2002) calculated the impact of deviations of production parameters from the average figures on the net return to labor and management on Dutch hog farms. He showed that a deviation of e.g. 10% of the FCR caused an impact on the net return to labor and management of 40%, indicating a huge impact on the farmers’ income; this impact can of course be reduced or increased due to lower or higher feed prices. Similar deviations of e.g. daily weight gain and mortality rate had an impact of only 6% and 2% respectively. Hence, enzootic diseases which affect the FCR are particularly important in pig production.

5. CONCLUSIONS

From this short overview, some conclusions can be drawn:

− With regard to epizootic pig diseases such as CSF and FMD:
  o the financial-economic impact for the pig production sector is particularly determined by price effects on animals and products; if these occur, due to e.g. export bans or a prolonged period of economic recovery of the sector, the impact for the collective producers can be very large whereas consumers can face a temporary gain;
  o also, the area where outbreaks occur and the control strategy applied have a considerable impact on the financial-economic costs;

− With regard to disease problems at the sectoral level such as AD:
  o There can exist a difference in benefits and (potential) losses between farmers, hence conflicts of interest;
  o Demographic features can have an important impact on the total financial-economic costs of e.g. re-introduction of these diseases;

− The economic impact of pig diseases on the farm level:
  o Is usually hard to estimate because of the complexity of the disease problem as such;
  o Deviations from production parameters on the net return to labor and management can be estimated relatively easily.

6. REFERENCES

MODELLING THE TRANSMISSION OF EQUINE INFLUENZA: MATHEMATICAL MODELLING IN A MULTIDISCIPLINARY PROGRAMME MAXIMISES THE BENEFITS ANS INSIGHTS

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Equine influenza is a highly contagious respiratory disease with a pathogenesis and ecology similar to infection in man. The principle strain of influenza virus currently infecting horses is A/H3N8. The virus causes occasional epidemics, which are often international in spread as well as more sporadic local outbreaks, particularly where groups of young horses are congregated. International movement of horses, far easier than for any other domesticated species, contributes significantly to the spread of infection. Antigenic drift, with clear evidence of immunologically driven selection, is an important feature of equine influenza. Compulsory vaccination policies are imposed by some authorities and while this has been generally successful in preventing large scale epidemics amongst such populations, antigenic drift has resulted in significant problems of vaccine failure. The OIE makes annual recommendations for the strain composition of equine influenza vaccines.

The presentation will include a review of modelling work done on equine influenza transmission and control by a number of different research scientists and a description of ongoing work in this area. Parsimonious models, which incorporate data derived from a multidisciplinary programme of research into the disease, have increased our understanding of the transmission and control of the disease, as well as having given considerable insight into diagnosis and surveillance and support for the conclusions from the panel making recommendations for the OIE.
VITAMIN E AND OXIDATIVE STATUS OF DAIRY COWS

Comparison Of The Oxidative Status Between Oral Vitamin E Supplemented And Non-Supplemented Cows Under Field Conditions

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1. INTRODUCTION

Vitamin E supplementation around calving is associated with enhanced health of dairy cows (Smith et al., 1997, LeBlanc et al., 2002, Politis et al., 2004). When free radical generation exceeds anti-oxidant capacity, oxidative stress develops. Around parturition lipid peroxidation increases (Brzezinska-Slebodzinska et al., 1994, Bernabucci et al., 2005, Castillo et al., 2005), indicating a higher level of oxidative stress which subsequently can lead to reduced health in cattle (Miller et al., 1993). Serum α-tocopherol in cows decreases in the last month before calving (Brzezinska-Slebodzinska et al., 1994, LeBlanc et al., 2004). Vitamin E, as the primary lipid-soluble antioxidant is important for the body’s defence against oxidative stress (Ibrahim et al., 1997). Combining these findings it is reasonable that the link between vitamin E supplementation and improvement of health is reduced oxidative stress. The oxidative status of vitamin E supplemented and non-supplemented dairy cows was evaluated as well as the relationship between serum levels of vitamin E and oxidative stress parameters.

2. MATERIALS AND METHODS

Ninety eight Holstein Friesian dry cows were selected from 26 different commercial herds in The Netherlands. The daily vitamin E intake of the fifty-two supplemented cows was 1000 international units; the control cows were not supplemented. All cows were sampled once between 0 and 28 days before calving. Vitamin E, cholesterol and triglycerides levels were analyzed and the ratio of α-tocopherol to cholesterol was calculated. The markers of oxidative status measured were 1) the intracellular working enzymatic anti-oxidants superoxide dismutase (SOD) and glutathione peroxidase (GSHpx) 2) the low-molecular weight antioxidants uric acid and vitamin E 3) the extracellular working anti-oxidant albumin and 4) the non-antioxidants: malondialdehyde (MDA), a degradation product of lipid peroxidation, protein thiol oxidation level (pSH), reactive oxygen metabolites (ROM), iron (Fe) and the ferric reducing ability of plasma (FRAP). Parameters were chosen because they are all implicated in the pathways of the oxidative stress cascade and are directly or indirectly correlated to vitamin E. Data were analyzed using the statistical program SPSS 12.0.1 for Windows. The oxidative status of the two groups was compared using one sampled T-test for each parameter.

3. RESULTS

The mean concentration of serum α-tocopherol in the control group was significantly lower than in the supplemented group as was the ratio of α-tocopherol to cholesterol. Significant differences in serum MDA, pSH, Fe and uric acid levels were observed between the two groups.
Table 1. Mean values and standard deviation (SD) of α-tocopherol, cholesterol, triglycerides, ratio α:ch, GPx, SOD, Albumin, Fe, Uric acid, PSH, MDA, ROM, FRAP in the control group and the vitamin E+ group

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
<th>Vitamin E+ group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-Tocopherol (µmol/l)</td>
<td>6.68 (1.80)</td>
<td>9.02 (2.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>2.44 (.510)</td>
<td>2.35 (.573)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>0.29 (.098)</td>
<td>0.30 (.080)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Ratio α:ch¹ (mmol/l)</td>
<td>2.76 (.619)</td>
<td>3.82 (.715)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>GSHpx² (U*/l)</td>
<td>7.30 (6.18)</td>
<td>7.11 (3.05)</td>
<td>n.s.</td>
</tr>
<tr>
<td>SOD³ (U*/l)</td>
<td>188 (89.3)</td>
<td>194 (81.1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>37.3 (2.79)</td>
<td>37.3 (2.45)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Fe (µmol/l)</td>
<td>30.3 (7.39)</td>
<td>33.2 (6.46)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Uric Acid (µmol/l)</td>
<td>22.7 (9.37)</td>
<td>30.2 (9.91)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>pSH⁴ (µmol/l)</td>
<td>192 (39.0)</td>
<td>166 (25.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MDA⁵ (µg/l)</td>
<td>15.0 (3.01)</td>
<td>11.6 (4.74)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ROM⁶ (U⁸/ml)</td>
<td>64.3 (19.8)</td>
<td>58.1 (18.6)</td>
<td>n.s.</td>
</tr>
<tr>
<td>FRAP⁷ (µmol/l)</td>
<td>325 (11.3)</td>
<td>326 (6.70)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Haemolytic index</td>
<td>42.5 (60.0)</td>
<td>32.2 (27.2)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

¹ratio α-tocopherol:cholesterol (ratio α:ch)
²glutathione peroxidase (GSHpx)
³superoxide dismutase (SOD)
⁴protein thiol oxidation (pSH)
⁵malondialdehyde (MDA)
⁶reactive oxygen metabolites (ROM)
⁷ferric reducing ability of plasma (FRAP)
⁸U. Carr. is an arbitrary unit; 1 U. Carr. is equivalent to 0.08 mg of H2O2/100 mL

4. DISCUSSION

The aim of this study was to compare the oxidative status of orally vitamin E supplemented and non-supplemented housed cows under field conditions in the four weeks period before calving. As expected levels of serum α-tocopherol are influenced by the concentration of vitamin E in the diet, although correlation was low. The significant difference in serum MDA levels observed between the two groups suggests that in the control group higher levels of free radicals are present which cause more lipid peroxidation than in the vitamin E+ group. The MDA levels around parturition have been analyzed in a previous report (Castillo et al., 2005) and are in accordance with the results obtained by (Turk 2005) on serum paraoxonase activity of dairy cows, showing an increase of oxidative stress during the transition period. As we did, (Castillo et al., 2005) also observed a great inter-individual variation in MDA levels. Interpretations of the MDA results are therefore difficult and require further research.

5. CONCLUSION

Results of the present study demonstrated that MDA is a useful parameter to define a part of the oxidative status and the relation between supplementation and lipid peroxidation. But to determine the total oxidative status under field conditions and the exact influence of vitamin E on other oxidative stress parameters, further research is required.
6. REFERENCES


MONITORING SUBCLINICAL MASTITIS IN THE NETHERLANDS: TWO EXAMPLES

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1. INTRODUCTION

Mastitis, the inflammation of the udder, has two appearances. In the mild clinical appearance, the cow has clots in the milk while in more severe cases redness of the udder, fever and a swollen udder can also be seen. Subclinical mastitis (SCM) is the non-visible appearance of the disease and can, among others, be measured by somatic cell counts (SCC) in the milk (Pyörälä, 2003; Schukken et al., 2003). In 2005 a national five-year udder health program was started in the Netherlands to decrease mastitis incidence by founding the UGCN (Dutch Udder Health Centre) to execute the five-year program (Van der Zwaag et al., 2005). The UGCN is a centre in which research and practice meet to execute research and to implement knowledge at dairy farms in the Netherlands. In a previous study, the private practitioner was identified to be the farmers first contact person regarding mastitis (Jansen et al., 2004). Also, practitioners visit their farms at least four times a year for the obligatory 3-monthly visits, and often more frequently. The practitioner was therefore chosen to be the person to implement the udder health program at their farms, supported by the UGCN with information and tools to improve udder health.

A baseline survey, based on cow SCC (CSCC) measurements, was conducted to assess the prevalence of SCM, to set a definition of SCM incidence, and to estimate the SCM incidence rate in lactation with that definition in the two years preceding the five-year program. In this paper, the results of this baseline survey of SCM incidence rate will be presented. In addition, the results of an analysis of the bulk milk SCC (BMSCC) of 10 private practices, who started with the udder health program, will be shown.

2. MATERIALS AND METHODS

2.1 Monitoring Cow Somatic Cell Counts

In the baseline survey, CSCC of all cows from all Dutch dairy herds participating in the test day recording were available for analysis. Farms with 10 or more animals and over 5 test day records per year were selected from the dataset. To calculate SCM prevalence, data on 1,845,975 cows on 18,605 farms were used for the analysis. Full lactations (>280 days) were additionally selected from these data, to estimate the lactational incidence rate of SCM. One lactation was randomly selected for analysis from cows having two lactations. These selections resulted in 1,011,065 cows on 18,494 farms, and represent approximately 85% of the total number of cows and 80% of the farms in the Netherlands.

SCM prevalence was calculated as the proportion cows at risk in a herd when CSCC was above 250,000 for multiparous cows and when CSCC was above 150,000 for heifers. Negative binomial models with repeated measures (Proc Genmod, SAS 9.1) were fitted against the data to estimate SCM prevalence as the number of cows above the threshold related to the log total number of cows tested at a test day. Incidence rates were calculated as the number of new SCM infections divided by the number of days at risk, both assessed at the herd level. A new infection of SCM was defined as a pattern of change from below to above a certain threshold. Five different thresholds (Group A) and four different patterns of change (Group B) were evaluated (Table 1). The number of days at risk was calculated as the non-infected days during lactation (Figure 1). Generally, the days until the next test day were assumed to be at risk if CSCC was below the threshold. If the first CSCC in lactation is below the threshold, the days from calving until the first test day in lactation are also assumed to be at risk and vice versa; if the first CSCC
in a lactation is above the threshold the days from calving until the first test day in lactation, the cow is assumed to be infected. Also, at the end of lactation, half of the days between the last and the assumed next test day, assessed at the herd level, are assumed to be at risk if the last CSCC measurement is below the threshold and vice versa.

Negative binomial models (Proc Genmod, SAS 9.1) were used to calculate the SCM incidence rates as the number of new infections per herd against the log number of days at risk as the offset.

![Figure 1](image)

Figure 1. A visualisation of the days at risk for a pattern of change from two consecutive CSCC < 200,000 cells/ml to one CSCC above the cut-off value.

2.2 Monitoring Bulk Milk Somatic Cell Counts

By the end of 2004, 10 private practices were asked to participate in the five-year program and to improve udder health at their farms as much as possible. All practices agreed on participation. The udder health program was started on these practices in January 2005 with a meeting to inform their farmers about the program. The 10 pilot practices received practical information and tools to improve udder health at their farms. All farms in their practice received newsletters about udder health, checklists, and instruction cards on treatment, CMT, sampling protocols and so on. Farmers were also asked to participate in study groups on mastitis, organised by their own practitioner. Off the 1378 farms belonging to the 10 practices, 434 farmers agreed upon participation in these study groups, which started in February 2005.

BMSCC were collected from all the farms belonging to these practices. These were compared to BMSCC from all the farms belonging to 20 control private practices, matched on region and size. These control practices had up to 2319 herds servicing. The control practices and farms didn’t receive any extra information about how to improve udder health. The log BMSCC of herds not participating in the udder health program (control) was compared to herds participating in study groups (intervention-active) and to herds in the pilot practices not participating in study groups (intervention-passive), using a linear mixed model (Proc Mixed, SAS 9.1). The year before intervention (January 2004 – December 2004) was compared to the beginning of the program (January 2005 – October 2005) and the remaining part of the analytical period (November 2005 – April 2006). The log BMSCC was adjusted for seasonality, by adding a sinus and cosinus to the model, and for repeated measurements, using the autoregressive correlation structure. Group and period effects were analysed as fixed effects and as an interaction term. The log BMSCC was additionally corrected for a random effect of the private practice.

3. RESULTS

3.1 Monitoring Cow Somatic Cell Counts

The average SCM prevalence was 23.3 in 2003 and 2004, using the currently used threshold and pattern of change in the Netherlands (1x < 150,000 for heifers and 250,000 for multiparous cows, 1 > 150,000 for heifers and 250,00 for multiparous cows). SCM was most prevalent in August and least prevalent in December/January (Figure 2). SCM prevalence was generally higher in 2003 than in 2004.
Herd SCM incidence rates ranged from 13.4 (500,000 cells/ml) to 64.8 (100,000 cells/ml) new SCM infections per 10,000 cowdays at risk (Table 1), depending on the used threshold. The herd-incidence rates were 17.2 (500,000 cells/ml), 4.6 (250,000 cells/ml), 1.9 (200,000 cells/ml) lower and 34.2 (100,000 cells/ml) higher, compared to the currently used threshold in the Netherlands. The SCC pattern used to identify a new SCM infection also affected the SCM incidence rate (Table 1). The highest incidence rate of SCM was observed if the pattern used was definition B-1 (1 CSCC < 200,000, 1 CSCC > 200,000). The lowest incidence rate was according to definition B-4 (2 CSCC < 200,000, 2 CSCC > 200,000). Excluding cows with SCC above the threshold 2 test days before and were below the threshold the previous test day, decreased the incidence rate by 6.0 new infections per 10,000 cow-days at risk (definition B-1 versus definition B-2). If new infections had to have at least 2 consecutive CSCC above threshold (definition B-1 vs definition B-3) incidence rates decreased by 21.8 new infections per 10,000 cow-days at risk. Finally, if a new infection had to be preceded by 2 consecutive CSCC below threshold, followed by 2 consecutive CSCC above threshold (definition B-3 vs definition B-4), incidence rates decreased another 1.6 new infections per 10,000 cow-days at risk.

Table 1. Average within herd-incidence of subclinical mastitis for different thresholds of CSCC$^1$ and patterns of new infections for all herds participating in the test day recording in the Netherlands in 2003 and 2004, based on selected full lactations.

<table>
<thead>
<tr>
<th>Group</th>
<th>Definition</th>
<th>Intercept ($\alpha$)</th>
<th>Herd-incidence rate$^2$ (/10,000 cowdays at risk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A$^1$</td>
<td>1. Threshold = 500,000 cells/ml</td>
<td>-6.6181</td>
<td>13.4</td>
</tr>
<tr>
<td></td>
<td>2. Threshold = 250,000 cells/ml</td>
<td>-5.9532</td>
<td>26.0</td>
</tr>
<tr>
<td></td>
<td>3. Threshold = 150,000 for heifers and 250,000 for multiparous cows</td>
<td>-5.7892</td>
<td>30.6</td>
</tr>
<tr>
<td></td>
<td>4. Threshold = 200,000 cells/ml</td>
<td>-5.7301</td>
<td>32.5</td>
</tr>
<tr>
<td></td>
<td>5. Threshold = 100,000 cells/ml</td>
<td>-5.0388</td>
<td>64.8</td>
</tr>
<tr>
<td>B</td>
<td>1. 1 CSCC &lt; 200,000, 1 CSCC &gt; 200,000</td>
<td>-5.5584</td>
<td>38.5</td>
</tr>
<tr>
<td></td>
<td>2. 2 CSCC &lt; 200,000, 1 CSCC &gt; 200,000</td>
<td>-5.7297</td>
<td>32.5</td>
</tr>
<tr>
<td></td>
<td>3. 1 CSCC &lt; 200,000, 2 CSCC &gt; 200,000</td>
<td>-6.3938</td>
<td>16.7</td>
</tr>
<tr>
<td></td>
<td>4. 2 CSCC &lt; 200,000, 2 CSCC &gt; 200,000</td>
<td>-6.4951</td>
<td>15.1</td>
</tr>
</tbody>
</table>

$^1$Cow somatic cell count.

$^2$Incidence is calculated as $e^{\alpha}$*10,000.

$^3$Used pattern: 2 CSCC < threshold to 1 CSCC > threshold.
3.2 Monitoring Bulk Milk Somatic Cell Counts

BMSCC for the 3 groups analysed are shown in Figure 1. The statistical analysis showed a significant seasonal effect (P<0.0001), with the log BMSCC being highest in the summer and the log BMSCC being lowest in the winter. Log BMSCC were higher in the beginning (P=0.0523) and significant higher (P=0.0023) in the remaining part of the program, compared to the year preceding the program. Overall, log BMSCC of farms in the study groups (intervention-active) and farms in pilot practices, not participating in study groups (intervention-passive) did not deviate from the log BMSCC of farms in the control practices. However, the interaction term showed that farms in the study groups (intervention-active) had a significant log BMSCC decrease in the beginning (P=0.0170) and remaining part of the program (P=0.0023), compared to the period before intervention on these farms.

Figure 3. BMSCC in herds participating in study groups (intervention-active; n = 434), herds not participating in study-groups (interaction-passive; n = 944) and herds in control practices (control; n = 2319) in the year preceding the program (2004) and during the beginning and the remaining part of the program (2005-2006).

4. DISCUSSION

Both examples show the possibility to monitor SCM by SCC, either at the cow or herd level. However, monitoring SCM incidence rates by CSCC measurements heavily depends on the definition chosen (Table 1). To monitor the five-year program, the current threshold of SCM was chosen because of an acceptable and workable sensitivity and specificity (Dohoo and Leslie, 1991; Schepers et al., 1997). The pattern of change of 2 consecutive CSCC below threshold to 1 CSCC above threshold was chosen to identify a new SCM infection during the udder health program. All infections, even if they cause just 1 high CSCC (e.g. *E. Coli*, (De Haas et al., 2004)) are monitored with this definition. This pattern also avoids double counting of infections with an intermitted shedding pattern (e.g. *Staph. Aureus*, Sears et al., 1990). The SCM incidence rate in full lactations was 30.6 per 10,000 days at risk in 2003 and 2004 in the Netherlands.

The results regarding BMSCC in the first year in the 10 pilot are promising for the rest of the project, although large differences in BMSCC between farms and practices are observed (data not shown). An obvious decrease in log BMSCC was observed for farms participating in the study groups (intervention-active). However, farms not participating in the study groups (intervention-passive) did not show a decrease in log BMSCC. The challenge for the next coming years will be to trigger these farms to improve udder health at their farms, as all the farms in the Netherlands will be introduced to the udder health program in February 2007. Focus will be on communication strategies to motivate farmers to improve udder health, by personalisation of the message, increasing farmers’ knowledge and by giving them feedback on their performance.
5. ACKNOWLEDGEMENTS

This study is part of the five year udder health program of the Dutch Udder Health Centre and was financially supported by the Dutch Dairy Board. The data in these analyses were kindly provided by NRS and Milk Control Station. The comments of Gerben de Jong and Wim Swart were also highly appreciated by the authors.

6. REFERENCES


MODELLING VECTOR-BORNE DISEASES

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1. INTRODUCTION

The basic reproduction number, or \( R_0 \), is one of the most important concepts in the field of infectious diseases epidemiology (Anderson & May 1990; Diekmann & Heesterbeek 2000). It is defined as the average number of secondary cases that is to be expected from one infectious individual placed in a population of susceptible individuals and it is a measure for the success of invasion into a population. If the value of \( R_0 \) is higher than 1, an outbreak of the disease is possible, whereas if \( R_0 \) is smaller than 1, the disease will die out.

For vector-borne disease the interpretation of \( R_0 \) is less intuitive than for directly transmittable diseases because there are different types involved in transmitting the infection, i.e. hosts and vectors. The average number of hosts infected by a vector and vice versa, the number of vectors infected by a host, should then be 'averaged'. A framework has been developed for the derivation of \( R_0 \) in the case of more than one type; the so-called next-generation matrix (NGM) (Diekmann & Heesterbeek 2000; Diekmann et al. 1990).

We illustrate the use of this methodology for two vector-borne disease systems. The first example concerns West Nile virus. This virus is principally maintained in a bird-mosquito transmission cycle: birds are considered to be the primary hosts, and ornithophilic mosquitoes the primary vectors (Hayes et al. 2005). However, there is experimental evidence for direct transmission between birds (Komar et al. 2003; McLean et al. 2001) and for direct transmission between mosquitoes (Baqar et al. 1993; Dohm et al. 2002; Goddard et al. 2003; Higgs et al. 2005). The importance of these routes of transmission in nature is not known. We use the next-generation matrix methodology to get an impression of the relative importance of the various transmission routes for the establishment of the disease.

The second example concerns two tick-borne pathogens that are transmitted by the European tick species Ixodes ricinus: Lyme borreliosis and tick-borne encephalitis (TBE). The ticks have three post-egg life stages: larva, nymph and adults. During each of these stages, the tick takes one blood meal on a warm-blooded host, before moulting into the next life stage (or in case of a female adult, before laying eggs). The pathogens are transmitted during these blood meals: from tick to host, or from host to tick, or even from one tick to another if tick feed closely together on the same host. Transovarial transmission from the female adult tick to her offspring is also possible. We constructed a next-generation-matrix based on a model with tick eggs, larvae, nymphs, female adults and two host types (competent and non-competent hosts).

Again, we use the next-generation matrix methodology to gauge the relative importance of the various transmission routes, from tick to host and vice versa (known as systemic transmission), between ticks (known as non-systemic transmission) and transovarial transmission (TOT). This illustrates that the next-generation matrix methodology can be applied to very complex pathogen transmission systems.

2. MATERIAL AND METHODS

2.1 General next-generation matrix methodology

The first step in deriving an expression for \( R_0 \) is to identify the different types-at-birth in the system, i.e. to categorize individuals by their state at the moment they become infected. These types-at-birth differ with respect to their ability to produce secondary cases (infectivity, contacts, life history, and transmission route). For vector-borne diseases, there are typically at least two types-at-birth (host and vector), but in some cases there are more.

The second step is to construct a next-generation matrix for the system under study. The next-generation matrix for a system with \( m \) types-at-birth has \( m \) columns and \( m \) rows. Each of the elements \( k_{ij} \) represents
the expected number of new cases of type-at-birth $i$ caused by one infected individual of type-at-birth $j$ during its entire infectious period. The third step is to calculate the dominant eigenvalue of this next-generation matrix. This eigenvalue has been proven to equal the basic reproduction number.

2.2 West Nile virus
For the West Nile virus example, we derived the next-generation matrix of the system. As the system consists of two types-at-birth, the mosquitoes (type-at-birth 1) and the birds (type-at-birth 2), the next-generation matrix is a 2 by 2 matrix:

$$K = \begin{bmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{bmatrix}$$

where element $k_{11}$ refers to the mean number of mosquitoes infected by one infected mosquito, element $k_{12}$ to the mean number of mosquitoes infected by one infected bird, etc. The next-generation matrix was parameterized with literature data. The basic reproduction number $R_0$ was calculated for the situation with and without bird-to-bird and mosquito-to-mosquito transmission to investigate the difference that the additional transmission routes make. Further details are discussed in Hartemink et al (a, in preparation).

2.3 Tick-borne diseases
As ticks can have four types at the moment they become infected, we need four different types-at-birth for the ticks and one more for the competent host (the non-competent cannot become infected, and therefore not a type-at-birth, they are just ‘diluting’ the infectious bites of the ticks):

1=egg
2=larva
3=nymph
4=adult
5=host (systemic infection only)

We then have the following next-generation matrix:

$$K = \begin{bmatrix} k_{11} & k_{12} & k_{13} & k_{14} & 0 \\ k_{21} & k_{22} & k_{23} & 0 & k_{25} \\ k_{31} & k_{32} & k_{33} & 0 & k_{35} \\ k_{41} & k_{42} & k_{43} & 0 & k_{45} \\ k_{51} & k_{52} & k_{53} & 0 & 0 \end{bmatrix}$$

Some of the elements are zero, as not all types-at-birth can give rise to all other types-at-birth, for instance a systemically infected host (type 5) can not infected tick eggs, so element $k_{15}$ equals zero.

As ticks bite only once per life stage, we did not use a ‘biting rate’ as is often done in vector-borne disease models that regard mosquitoes or other biting insects. Instead, we based the elements of the matrix on the following ‘ingredients’:

- Survival probabilities from stage to stage
- Transmission coefficients
- Mean number of hosts encountered
- Mean number of (co-feeding) ticks encountered

The approach is described in detail in Hartemink et al (b, in preparation).

The next-generation matrix was parameterized with literature data. Parameter values that could not be found in literature, were estimated by an expert.
3. RESULTS

3.1 West Nile virus
Comparing the \( R_0 \) for the situation with and without reveals that bird-bird transmission could make a difference between an epidemic outbreak and an epidemic fading out, but only in situation where few mosquitoes per bird.
The contribution of mosquito-to-mosquito transmission appears to be negligible at the levels that have been reported under experimental conditions so far.

3.2 Tick-borne diseases
With the obtained matrix, we can easily calculate \( R_0 \) for different sets of parameters. As an example we show how the duration of the systemic infection, which is very short for TBE and very long for Lyme, influences the value of \( R_0 \). Assuming all other parameters to be equal, we plot the values of \( R_0 \) for two diseases with a short and long duration of systemic infection, respectively (solid lines in fig. 1). We plot the values of \( R_0 \) against the fraction of blood meals taken by ticks on competent hosts, as this fraction is not known and yet very important, as blood meals taken on non-competent hosts are ‘wasted’ from the pathogen’s point of view, thereby ‘diluting’ the disease transmission. A longer period of systemic infection in the competent host results in a higher value of \( R_0 \).

We also calculated the values of \( R_0 \) for a situation without any non-systemic transmission (by setting all elements in the next-generation matrix that refer to non-systemic transmission to zero), and plotted the curves for the two diseases (Fig. 1, dotted lines). This shows that a disease with a short duration of systemic infection in the competent host, such as TBE, may depend critically on the non-systemic transmission route, as without this route the \( R_0 \) value does not exceed 1. In contrast, a disease with a long period of systemic infection (e.g. Lyme) can establish without non-systemic transmission, even in areas with a low proportion of hosts competent for systemic transmission.

The difference in duration of systemic infection in the competent host may explain the fact that some diseases depend mainly on non-systemic transmission (e.g. TBE) and others mainly on systemic transmission (e.g. Lyme).

Figure 1. \( R_0 \) values versus the fraction blood meals taken on hosts that permit systemic transmission for different scenarios: both systemic and non-systemic transmission (solid lines), only systemic transmission (dotted), long duration of infection (thin lines), short duration of infection (thick lines).

4. DISCUSSION
We illustrated that the next-generation methodology provides a useful tool to study infectious diseases with complex dynamics, such as vector-borne diseases. Basic reproductive numbers can be used to obtain risk assessments for certain areas and predictions for effect of control measures or of environmental change. Climate change is likely to have a large impact in vector-borne diseases, as the survival of cold-blooded animals like ticks and insects, heavily dependent on environmental conditions (Altizer et al. 2006). The effect of changes in climate can be explored by linking the survival probabilities or biting rates of the vectors to climatic factors. Mathematical models can only make accurate predictions if all the relevant factors are taken into account. For vector-borne diseases, factors like seasonality and (spatial)
heterogeneity should be taken into account, as these may be essential in determining the disease dynamics (Altizer et al. 2006; Bacaër & Guernaoui 2006; Randolph et al. 1999).

5. REFERENCES


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A CONCEPTUAL FRAMEWORK FOR EXPLORING TRADEOFFS BETWEEN PREVENTION, MONITORING AND CONTROL OF AVIAN INFLUENZA

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1. INTRODUCTION

Until fairly recently, highly pathogenic avian influenza (HPAI) was considered a rare poultry disease with only 17 outbreaks in the forty years between 1959 and 1998 (Alexander, 2000). Since 1999 an unprecedented number of outbreaks have caused significant socio-economic losses and in some cases human illness and loss of life.

Avian Influenza (AI) is a contagious viral infection which can affect all species of birds. AI viruses are classified according to pathogenicity and subtype and almost all combinations of subtypes have been isolated from wild birds. HPAI viruses can cause mortality of up to 100 per cent in poultry flocks, while low pathogenic avian influenza (LPAI) causes much milder disease. HPAI viruses have been restricted to subtypes H5 and H7 and current theories suggest that highly virulent viruses emerge from LPAI viruses by mutation, and that mutation occurs in poultry flocks and not in wild birds (EFSA, 2005). AI (defined as all H5 and H7 subtypes or viruses with a pathogenicity index greater than 1.2) is a notifiable avian disease in the Terrestrial Animal Health Code of the World Animal Health Organisation (OIE) which provides a standard for the regular reporting of animal diseases. The genetic pool for AI viruses is primarily in aquatic and shore birds which are responsible for the perpetuation of these viruses in nature. Current evidence suggests that wild birds and particularly migratory birds play a role in the introduction of LPAI into new areas; the role that they might play for HPAI and in particular H5N1 is the subject of continuing debate (Olsen et al., 2006). In addition to all species of birds, AI viruses can also infect mammalian species, including humans.

Outbreaks of HPAI and even LPAI can have a significant impact on countries, depending on the size and length of the outbreak. Economic impacts include both direct losses (the costs of the eradication strategy and organisational factors) and consequential losses due to movement restrictions and market disruptions. Direct losses caused by the 2003 HPAI outbreak in the Netherlands were estimated at 270 million euro, while consequential losses were much higher at 750 million euro (Landman and Schrier, 2004). Other impacts arise from the animal welfare considerations of disease outbreaks and control methods, and the psychological impacts for farmers and backyard poultry holders. Though rarely quantified, these ‘intangible’ impacts of animal disease outbreaks can be large and pervasive (Bosman et al., 2005 and Haaften and Kersten, 2002).

In contrast to many other contagious animal diseases such as Foot-and-Mouth Disease (FMD), AI viruses can have a direct impact on human health. AI viruses can be transmitted to humans causing a range of illness from conjunctivitis and influenza-like illness to severe respiratory disease and death. To date (until 27 December 2006), 261 human cases of H5N1 have been confirmed by the World Health Organisation (WHO), of which 157 were fatal. Although this represents a very high mortality rate, it is unclear how many human cases remain undetected. Current evidence of human infections of H5N1 is consistent with bird-to-human transmission, possible environment-to-human transmission and limited, non-sustained human-to-human transmission (The Writing Committee, 2005). In general, the human infections have resulted from close direct contact with live or dead poultry (Perdue and Swayne, 2005). Given the widespread nature of outbreaks of H5N1, relatively few people have become infected and only a very small percentage have become clinically ill (Perdue and Swayne, 2005). In addition to the direct health risks of AI viruses, a much bigger health threat is posed by the possibility of a pandemic influenza strain arising from reassortment between avian and human influenza viruses. A pandemic influenza strain could also arise from adaptation (mutation) of an AI virus to humans. Reassortment could take place in a human
co-infected with an AI virus and a seasonal human influenza virus, or in other mammalian mixing vessels such as pigs. The likelihood of a pandemic influenza strain arising from AI viruses is unknown. Two of the influenza pandemics in the 20th century (1957 and 1968) arose from genetic reassortment of avian and human influenza viruses, while the third may have been the result of the adaptation of an avian strain to humans (De Jong and Hien, 2006). The risks of pandemic influenza clearly influence the strategies used to manage both HPAI and LPAI in poultry.

Decision-makers at the national and supranational level in the European Union will need to select future strategies for managing AI. An overall management strategy will consist of elements of prevention, monitoring and control. In selecting an overall strategy two questions can be considered: (1) what is the optimal combination of prevention, monitoring and control and (2) which measures should be chosen to achieve this combination? To date, most analyses of strategies for contagious animal diseases have focused on the second question and have not considered the potential trade-offs that exist between prevention, monitoring and control. In this paper we present a conceptual framework appropriate for considering the first question. An overview of the framework is presented and a simple example is used to explore the implications of human health risks for the allocation of resources. Following the conceptual framework, we highlight a number of important characteristics of the decision problem. Particular attention is given to perceived risk in the context of human health risks. At the end of this paper we present a brief overview of methods that can be used to assess specific strategies and measures. These methods can be used to address the second question and will be the focus of further research.

2. CONCEPTUAL FRAMEWORK

Choosing an appropriate overall strategy for prevention, monitoring and control of Avian Influenza is a complex problem. A schematic outline of this decision problem for countries within the European Union (EU) is provided in Figure 1. The schema clearly highlights the interrelatedness of prevention, monitoring and control actions and places the epidemiological system within a wider socio-economic perspective.

Figure 1 Schematic overview of the decision problem for management of avian influenza
The key elements of this schema are indicted on the left of the Figure: states, events, influencing factors and actions. The domestic, commercial poultry population of a region or country can be in one of three mutually exclusive states at any one time: AI-free, the High Risk Period (HRP), or the post-HRP. Transitions between states take place following the occurrence of a particular event. The normal situation is AI-free where the disease is not present in the domestic population. Following disease introduction, the population enters the HRP. The HRP is defined as the period following introduction of the virus until detection and notification. During the HRP the virus is present but undetected in the population and virus spread occurs largely unhindered. The length of the HRP is an important determinant for the subsequent development of the epidemic. Following detection and notification of the disease the population enters the post-HRP state and control measures are implemented. This period continues until the disease is eradicated and the population re-enters the AI-free state.

The timing of events and therefore the length of time that a population spends in each state is affected by a number of influencing factors, as shown in Figure 1. These factors differ according to the event and population state. By addressing these factors, actions can influence the timing of events. An action is defined as a group of measures with the same common purpose; a measure is a specific activity. Examples of measures within the action of control include ring-vaccination, pre-emptive culling and transport restrictions. Three types of actions are considered: prevention, monitoring and control. Prevention is defined as all measures aimed at reducing the likelihood of disease introduction into the domestic population; monitoring includes all measures related to the surveillance of the domestic population aimed at reducing the HRP and control includes all measures aimed at controlling disease spread and eradicating the disease as quickly as possible. An overall strategy is a combination of specific measures for each of these three actions.

Within this scheme the key elements depict the epidemiological system. Decision-makers must consider the epidemiological system in the context of the socio-economic system. The total annual impact of AI is a combination of the impacts of a disease outbreak and the measures implemented. Impacts are classified into five categories: epidemiological, economic, social-ethical, human health and environmental. From a decision-making perspective, not all categories of impact will be important and importance will differ across time and space. Importance is determined by two aspects, the size of the impact and the value given to the impact by individual and societal preferences.

An economic concept that captures the two dimensions of importance is that of utility. Utility is a theoretical measure of happiness or satisfaction. In theory, any element can contribute to utility – consumption of a particular good, the state of the environment, individual health state etc. According to neo-classical economics, individuals make decisions so as to maximise their individual utility. In the context of Figure 1, we can consider that individuals’ utility (in relation to AI) is a function of some or all of the five categories of impacts. A social welfare function (SWF) represents a conceptual measure for the aggregated welfare of society, which is some aggregation of the utilities of individuals in society. An optimal strategy for prevention, monitoring and control of AI would be one where society’s social welfare (aggregated utility) is maximised, or equivalently where society’s disutility is minimised. Social welfare is appropriate as a conceptual framework for problems at the level of society; recent experience with outbreaks of contagious animal diseases has illustrated that such diseases are not only a problem at the level of the domestic population aimed at reducing the HRP and control includes all measures aimed at controlling disease spread and eradicating the disease as quickly as possible. An overall strategy is a combination of specific measures for each of these three actions.

Figure 2 provides an overview of these economic concepts. The possibilities curve (PC) represents the feasible combinations of prevention and control efforts, given technical and resource constraints. The SWF portrays the level of social welfare associated with a particular combination of prevention and control. As depicted in Figure 2, SWF curves to the right and above (such as SWF3) represent higher levels of social welfare. The optimal combination of prevention and control arises where the SWF is tangent to the possibilities curve, point f. This is the highest level of social welfare achievable given the possibilities curve. Point g represents an inefficient combination of prevention and control, while point e represents an efficient allocation but a higher level of welfare can be obtained by shifting from point e to f (a shift from SWF3 to SWF4).

In Figure 2 the possibilities curve is represented as a continuous convex curve, which suggests that zero levels of prevention or control are possible. In reality there is some base level of prevention and control required by legal constraints, this restricts the area of the possibilities curve where we can feasibly
operate. The shape of the possibilities curve reflects the degree of substitutability between prevention and control, the degree to which resources (labour and capital) can be switched from one action to the other.

Figure 2 Theoretically optimal allocation of prevention and control efforts to maximize social welfare

3. FRAMEWORK APPLICATION – A SIMPLE EXAMPLE

Using the concepts presented in Figure 2, the potential differences between epizootic animal diseases with and without risks for human health can be illustrated. Consider the situation for an epizootic animal disease without implications for human health, such as Classical Swine Fever (CSF) or FMD. The feasible combinations of prevention and control are given in Figure 3 by the possibilities curve PC_E and the applicable social welfare function is SWF_E, representing some aggregation of the utilities of individuals. For an epizootic animal disease individual utilities could be a function of the economic losses and gains, the level of animal welfare, the psycho-sociological impacts of an outbreak and so forth. The optimal levels of prevention and control are P_E and C_E (point e).

Now consider the situation for an epizootic animal disease with zoonotic aspects, such as AI. Initially, assume that the technical and resource constraints for prevention and control are similar to that for non-zoonotic epizootic animal diseases, therefore PC_E = PC_Z. However the presence of possible adverse effects for human health has an impact on the shape of the social welfare function. In addition to those factors listed for non-zoonotic epizootic animal diseases, individual utility functions will also be a function of the expected health state of individuals. The effect of health risks on the social welfare function will depend on how individuals value health in relation to other factors such as money income or animal welfare and how large the possible health effects could be. One possible function is depicted in Figure 3 by SWF_Z. The optimal combination of prevention and control in this case is P_Z and C_Z (point f) representing a shift of resources from control to prevention when compared to the non-zoonotic situation. The assumption that technical and resource constraints are the same for both zoonotic and non-zoonotic epizootic diseases may be inappropriate. If this assumption is relaxed, the new possibilities curve could be represented by PC_Z, which depicts a situation where a higher level of prevention is not technically possible but higher levels of control are possible (relative to the non-zoonotic disease) through either
technical advances or increased resources. The expansion of the possibilities curve allows a higher level of social welfare to be achieved, point $g$ in Figure 3, consistent with the same level of prevention but a higher level of control. Alternatively, it could be envisaged that control of zoonotic epizootic diseases could face more stringent constraints: additional measures relating to safety of individuals involved in control and the potential lack of supply of labour would shift the possibilities curve to the left (not shown in Figure 3).

Figure 3 An example of the conceptual framework for epizootic diseases with and without zoonotic aspects

The above exposition highlights the potential role that human health aspects can play in decision-making for epizootic animal diseases. Ignoring the impact of human health on individual and societal welfare (that is, assuming that the appropriate social welfare function is still $SWF_E$ when the true social welfare function is $SWF_Z$), the same allocation of prevention and control would be obtained as for a non-zoonotic disease but as depicted in Figure 3, this would result in a much lower level of social welfare ($SWF_Z$).

Obviously, a concrete analysis requires a large amount of information regarding the form of the individual utility functions and aggregating social welfare function, the impacts of AI outbreaks on these functions, and the effectiveness and costs of prevention, monitoring and control measures. In addition research, the conceptual framework presented has been extended by specifying further the relationships in the form of an analytical model. Of the range of possible impacts, only a subset of financial-economic and human health impacts have been included in individual utility functions. The model consists of three sets of equations. The first set define the effectiveness of prevention, monitoring and control in reducing the likelihood of virus introduction and the size and length of an epidemic. A second set of equations define the effect of management actions and the characteristics of the epidemic on the attributes in the utility functions. The third set of equations aggregates the individual utility functions into a social welfare function. Two states of nature are used (virus-absent and virus present) and the expected social welfare function is maximised across both states subject to a budget constraint. This model is being used to explore the potential role of risks to human health in the allocation of resources between prevention, monitoring and control in a number of scenarios.
4. IMPORTANT CHARACTERISTICS OF THE DECISION PROBLEM

A number of characteristics of the decision problem can be identified which should be taken into consideration in any theoretical or practical framework. These include: the level of decision-making, stakeholders, variability and uncertainty and elements of risk and risk perception. Each of these elements and their potential implications are discussed. Particular attention is given to risk perception.

**Level of decision-making:** AI is an OIE notifiable disease and also subject to regulations at the EU level. In December 2005 a new Council Directive was adopted (2005/94/EC) which lays out the measures to be taken in the event of an outbreak of AI. This repeals the existing legislation governing control of AI, Directive 92/40/EC. Although effective, Member States are only required to implement the new Directive as of 1 July 2007. The Directive provides the possibility to adopt additional measures where required; to date these measures have focused on preventative measures. The conceptual framework presented here is consistent with the level of decision-making. EU regulations restrict the operating area of the possibilities curve, as discussed in section 2.

**Stakeholder groups:** A wide range of stakeholder groups can affect and/or are affected by the management strategy for AI. This includes stakeholders in the production chain (breeders, multipliers, businesses with layers or broilers, slaughterhouses etc.), stakeholders who provide auxiliary services (transporters, feed suppliers, veterinarians etc.), and consumers. For AI, stakeholder groups also include owners of susceptible animals (backyard poultry owners, zoo’s etc.) and the general public due to the risk for human health. These stakeholder groups are likely to hold a wide range of opinions regarding appropriate strategies and be impacted in different ways. A strategy which has taken the preferences of these stakeholder groups into account is more likely to be accepted.

**Variability and uncertainty:** Variability is the effect of chance and is a property of the system under consideration, while uncertainty is the lack of knowledge about the parameters which characterise the same system (Vose, 2000). Both the likelihood of introduction of AI and the subsequent development of an epidemic are inherently variable processes. In addition to variability, there exist a large number of uncertainties in the current level of knowledge regarding introduction and spread of AI viruses. This body of knowledge is constantly being updated in response to ongoing research and new experiences with AI outbreaks.

**Risk and risk perception:** The traditional paradigm for decision-making under uncertainty in economics is that of subjective expected utility (SEU) maximisation, decisions are made by assessing the likelihood and consequences of the possible outcomes of alternative choices and integrating this information through expectation-based calculus (Loewenstein et al., 2001). A large body of evidence in the fields of behavioural economics, psychology and risk analysis suggests that the expected utility theory is a poor predictor of decision-making under uncertainty. People depart systematically from this rational approach. For example many studies have shown that people have difficulties in interpreting low probabilities (Kunreuther et al., 2001) and that in some situations people appear to either neglect or be insensitive to changes in probabilities (Sunstein, 2003). Tversky and Kaheman (1974) conceptually characterise these departures by suggesting that people rely on heuristic principles which reduce the complexities of assessing probabilities and values. Therefore people do not only rely on probabilities and consequences in making decisions in risky situations. In this line, a growing body of research highlights the role that emotions play in making decisions (see e.g. Loewenstein et al., 2001; Slovic et al., 2004 and, Wardman, 2006). The common theme is the interaction between a cognitive rational process based on the analysis of likelihood and consequence and a feeling-based evaluation based on emotions. The interaction of these dual processes determines behaviour. Although generally considered complementary (emotions play an informational role in decision-making), emotions can also induce individuals to depart from what they consider is the best course of action (Loewenstein et al., 2001). People’s emotional reactions to risk are determined by factors such as the vividness of the potential consequences, time-course of the decision, personal exposure to, or experience with, outcomes and past history of conditioning (Loewenstein et al., 2001).

These findings appear particularly relevant for considering how individuals assess and value the risks associated with AI: both the risks in terms of economic losses but also risks for human health. Sunstein (2003) considers the aspect of probability neglect in the face of terrorism and suggests that fear causes people to only focus on the bad outcome and ignore the likelihood of occurrence. Similar phenomena could be expected in regard to AI and the risks of pandemic influenza. These findings suggest that the
SEU, which underlies the conceptual framework presented here, does not adequately explain people’s behaviour in situations under risk. However it is still useful as a basis for decision-making at the national and supra-national level, as long as due consideration is also given to the role emotions might play in individual decisions.

5. DISCUSSION

In this paper we suggest that decision-makers must address two questions in choosing an overall management strategy for AI. The first question – what is the optimal combination of prevention, monitoring and control – is the focus of the conceptual framework presented. In most research on strategies for prevention, monitoring and control of contagious animal diseases, each action is considered individually and there is rarely any integration. The framework presented here highlights the value in first considering how resources should be allocated between the three actions before addressing which particular measures are optimal for each action. Such an approach can lead to a more efficient allocation of resources for both research effort and practical implementation of management strategies. In considering the integration of these three actions, attention should be paid to critical factors which may influence the allocation and trade-offs. We suggest that for AI, one of these critical factors will be how society assesses and values the risks to human health. In this regard, the role of risk and perceived risk is identified as a crucial characteristic of the decision problem. This aspect is complicated by the dual nature of the risk to human health of AI viruses: the risk of direct transmission and illness and the risk of pandemic influenza. These two risks have different likelihoods and different consequences for both individuals and society; however for pandemic influenza both the likelihood and the possible outcomes are largely unknown. Emotions such as dread and fear are likely to play an important role in the assessment and valuation of pandemic influenza. In the context of terrorism, Sunstein (2003) suggests that the presence of fear leads to phenomena such as probability neglect, where people focus only on the consequences and ignore the likelihood of their occurrence. Although he considers that basing government decisions on emotion-driven assessments will lead to sub-optimal outcomes for governments, he acknowledges that fear, anxiety and worry present a real cost to society. A similar approach seems applicable for AI. That the presence of fear and worry in a society has real costs has already been demonstrated for AI, many EU member states have seen a large drop in the consumption of poultry products as a response to consumer concerns regarding the risk of AI infection via consumption of poultry products. Understanding the role the emotions play in these decisions will be important for improving risk communication regarding the risks of AI for human health.

The conceptual framework is relevant for epizootic animal diseases both with and without zoonotic aspects. Using a simple example it was shown how using the same analysis for both types of animal diseases could result in sub-optimal allocation of resources for diseases with zoonotic implications. Depending on the magnitude of the risks to human health and how these risks are valued by society, the optimal allocation of resources is likely to favour prevention relative to a non-zoonotic disease. To further explore the role of risks to human health in decision-making, this framework has been further developed into an analytical model. This will allow further analysis of the critical factors affecting the optimal allocation of prevention, monitoring and control for AI.

For a concrete analysis of specific strategies a practical framework is needed which approximates the conceptual framework and takes specific characteristics of the decision problem into account. Two alternative approaches for assessing specific options are cost-benefit analysis (CBA) and multiple criteria decision-making methodologies (MCDM). CBA consists of identifying, quantifying and monetising all the costs and benefits of different alternatives and is the most widely used technique for evaluating policies and projects. CBA is considered as a relatively objective method for assessing policies with an established literature for quantifying and monetising impacts. It is based on the criterion of potential compensation; if winners can potentially compensate the losers a particular alternative represents a Pareto-improvement. In reality, monetisation of all impacts is very difficult and rarely attempted. CBA has been widely used in the field of contagious animal diseases (e.g. Berentsen et al., 1992; Risk Solutions, 2005). Multiple criteria decision methods (MCDM) or multiple criteria analysis (MCA) are general terms for a large group of techniques for decision-making in situations of multiple criteria. Seo and Sakawa (1989) define two phases in MCDM: an analytical (objective) and a judgemental (subjective) phase. The analytical phase is concerned with determining the non-dominated alternatives and the judgemental phase is concerned with identifying the most preferred of these options. Conceptually this is very similar to the framework presented in this paper. In terms of the decision characteristics highlighted
in this paper, both CBA and MCDM adequately address the decision-perspective, while the flexibility of MCDM techniques makes them particularly suitable for addressing the aspects of stakeholders and risk perception. Variability can be addressed in both methods (though this is rarely done) and uncertainty is usually taken into account with sensitivity analysis. Although the flexibility of MCDM techniques provides considerable advantages, it also gives rise to method-uncertainty, with different techniques resulting in different outcomes for the same problem. Finally, the focus of CBA is towards finding the best solution while MCDM techniques are generally process-oriented and aimed at providing an analysis of the decision problem.

Both CBA and MCDM require quantification of effects although some MCDM techniques allow for qualitative assessment. An assessment of combined prevention, monitoring and control strategies requires epidemiological models for the processes of virus introduction and virus spread. Analysis of prevention strategies can be undertaken using a pathway model (e.g. De Vos et al., 2004; Sutmoller et al., 2000). This approach quantifies the probability of virus introduction into a region or country by considering the probability of virus introduction of individual pathways. A large variety of mathematical models have been used to model transmission of disease between animals or herds and to assess monitoring and control strategies; these models differ in complexity, assumptions, whether or not they are spatially explicit, and whether they are deterministic or stochastic. One approach is the use of spatially explicit and dynamic Monte Carlo simulation models which explicitly model individual contacts between farms (e.g. Jalvingh et al., 1999; Karsten et al., 2005; Mangen et al., 2001; Nijlen et al., 1999). The latter models are particularly suited as a basis for estimating the economic impact of epidemics and different control strategies but require estimation of a large number of parameters.

In this paper we have stressed the importance of first considering the allocation of resources between prevention, monitoring and control before considering specific measures. In addressing this question, an analysis of the decision problem and a conceptual framework are presented. In further research this conceptual framework will be further refined and a practical assessment approach will be developed.

6. ACKNOWLEDGEMENTS

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TRANSMISSION OF *EIMERIA ACERVULINA* IN BROILER CHICKENS

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1. INTRODUCTION

Development and evaluation of new intervention strategies against coccidiosis, e.g. vaccination, is necessary, because of increasing resistance of *Eimeria* spp against anticoccidial drugs in the feed (Chapman, 1997; Peek and Landman, 2003), objections of consumers and legislative restrictions against medicated feed. Transmission experiments have been carried out for many viral and bacterial infections in animal populations to study infection dynamics and for use in development and evaluation of intervention strategies populations (Bouma et al., 2000; De Jong and Kimman, 1994; Feberwee et al., 2005; Geenen et al., 2004; Keeling et al., 2003; Klinkenberg et al., 2002; Stegeman et al., 1997; Van der Goot et al., 2003; Velthuis et al., 2002) However, for protozoan infections like coccidiosis, quantification of transmission parameters has not been described to this date. For *Eimeria* spp. transmission of the parasite has characteristics that make it different from many viral or bacterial infections. The infectious stages of *Eimeria* spp. are oocysts that have to sporulate in the litter. Oocysts can remain viable in the litter for several weeks (Williams, 1995). Therefore transmission of the parasite from an inoculated to a contact chicken can have a considerable time lag and re-infection from the litter in both inoculated (or previously infected) and contact birds can occur. These factors have to be considered when analyzing transmission dynamics in parasites like *Eimeria*. In this paper our efforts to create a model to quantify transmission of *Eimeria acervulina* oocysts between broilers is described. A pairwise transmission experiment was carried out, where one inoculated bird was housed together with one contact bird. Infectivity in both inoculated and contact birds was measured by determining presence and number of oocysts excreted in the individual droppings.

2. MATERIALS AND METHODS

Sixty-four one-day-old male SPF broiler chicks, tagged for identification, were used in the experiment. At the age of six days (D6 of the experiment) the birds were randomly assigned to five groups (Table 1).

Table 1. Outline of the experimental design: experimental groups, number of chicks per group and *E. acervulina* inoculation dose.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of chicks</th>
<th>Description</th>
<th>Inoculation dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>17</td>
<td>Contact</td>
<td>Tap water</td>
</tr>
<tr>
<td>I1</td>
<td>17</td>
<td>Inoculated</td>
<td>50 sporulated oocysts</td>
</tr>
<tr>
<td>S2</td>
<td>10</td>
<td>Contact</td>
<td>Tap water</td>
</tr>
<tr>
<td>I2</td>
<td>10</td>
<td>Inoculated</td>
<td>500 sporulated oocysts</td>
</tr>
<tr>
<td>Control</td>
<td>10</td>
<td>Control</td>
<td>Tap water</td>
</tr>
</tbody>
</table>

The inoculated birds (I-birds) were orally inoculated with either 50 or 500 sporulated *E. acervulina* oocysts suspended in 0.9 ml of tap water, depending on the experimental group. Chicks of the control group and contact birds (S-birds) received only 0.9 ml of tap water on D6. After inoculation on D6 the chicks were housed together in groups on wired floors. On D7 pairs of S1- and I1-chicks and pairs of S2- and I2-chicks were randomly assigned to floor pens. Control birds were housed individually in floor pens.
that were randomly allocated between the pairs, to detect possible environmental coccidial infections. Groups, number of chicks per group and inoculation dose are outlined in Table 1.

Droppings were collected daily from D10 up to and including D37. To determine course of infection and oocyst excretion in individual birds, each individual chick was placed daily in a clean cardboard box for approximately one to two hours, near the end of the dark period. After the lights were turned on, most of the chicks produced a dropping within this period (“single dropping”). A previous study by our group has shown that oocyst counts of single dropping samples are a reliable quantitative measure of oocyst production during coccidial infections (Velkers et al., submitted). To quantify oocyst production, a modification of a McMaster counting chamber technique according to Long and Rowell (1958) was used, as described by Velkers et al. (submitted). When no oocysts were found in the McMaster slide, the sedimentation flotation technique was carried out, according to a modification of the technique according to Long et al. (1976).

Transmission parameter $\beta$ was quantified using the stochastic susceptible-infectious-recovered (SIR) model described for example by Becker (1989). A binomial distribution of probability of infection per quarter of a day was made to obtain the maximum likelihood estimation for transmission rate $\beta$. This probability distribution was based on the number of infections per number of birds at risk per quarter of a day. Transmission rate $\beta$ was estimated, using a modification of the transient state algorithm as described by Velthuis et al. (2002) The transient state algorithm included the assumption that the infected bird had not recovered by the end of the experiment.

3. RESULTS

3.1 E. acervulina oocyst excretion patterns
Inoculated chicks of group 1 shedded oocysts from on average D11 (range D10-D14) to D28 (D25-D31). Contact chicks of group 1 produced oocysts from D16 (D14-D18) to D28 (D20-D31). In all inoculated chicks of group 2 oocyst production started on D10 and was terminated on D29 (D25-D36). Contact chicks of group 2 shedded oocysts from D16 (D15-D17) to D29 (D18-D32). In both groups, oocyst excretion of the inoculated chicks showed a higher second (higher) excretion peak, which coincided with the start of shedding (D16) of the contact chicks (Figure 1).

Figure 1. Average oocyst production in $^{10}\log \ (OPG+1)$ for group 1 (50 oocysts) and group 2 (500 oocysts).

3.2 Transmission rate $\beta$
Since the analysis is still in progress only preliminary results are presented. Using a modification of the transient state algorithm of Velthuis et al. (2002), $\beta$ was 2.5 day$^{-1}$ (95% CI 1.4-4.0) for the 50 oocyst group and 3.2 day$^{-1}$ (95% CI 1.8-5.0) for the 500 oocyst group. This implies that for example for the low inoculation dose the average number of new infections per day equals 2.5. Another way of interpreting the same figure is that a contact animal will on average become infected after 9.6 hours (1/2.5 day).
4. DISCUSSION

These results show that transmission of coccidiosis from an inoculated to a contact animal was successful for both inoculation doses in all pairs. Furthermore, the second excretion peak in inoculated birds suggests that inoculated birds are actually reinfected by their own excreted oocysts. Since excreted oocysts can remain infectious for many months in the litter (Williams, 1995) the duration of the infectious period for inoculated birds is difficult to define. Therefore, a basic reproduction ratio $R_0$ could not be calculated. The transmission rate $\beta$ was slightly higher for the 500 oocyst group compared to the 50 oocyst group. This model will be used in future experiments to evaluate the effect of intervention strategies for coccidiosis and might be used to analyze transmission in similar infections.

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CERTIFICATION-AND-SURVEILLANCE PROGRAMMES FOR PARATUBERCULOSIS IN DAIRY HERDS

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1. INTRODUCTION

Paratuberculosis (Johne’s disease) is a chronic inflammatory bowel disease, primarily affecting ruminants, and is caused by Mycobacterium avium subsp. paratuberculosis (Map). Clinical signs of paratuberculosis include reduced milk production, persistent diarrhoea, weight loss and progressive emaciation. The economic effects of paratuberculosis, of course, depend on the likelihood of a herd being infected, and the economic impact on infected herds (Weber, 2006). The likelihood of a Dutch dairy herd being infected is considerable: the herd-level true prevalence (95% CI) has been estimated (using serological tests) at 0.31 to 0.71 (Muskens et al., 2000), at 0.54 (0.46, 0.63; van Schaik et al., 2003) and at 0.32 (0.21, 0.46; Broekhuijse, 2004). The direct economic impact in infected herds has been estimated at on average $35 per cow for a typical 100-head US dairy herd (increasing to $72 per cow after 20 years; Groenendaal and Galligan, 2003) and at £27 per cow in Scottish herds (Stott et al., 2005). More important than direct losses, a milk price reduction for infected herds can result from consumer concerns about the zoonotic potential of Map. The issue of a potential role of Map in the pathogenesis of Crohn’s disease in humans has not yet been resolved, and milk is a possible route of transmission of Map to humans (Grant, 2005).

Certification-and-surveillance programmes can contribute to a reduction of the economic effects of paratuberculosis, by enabling low-risk trade of cattle and reducing the between-herd transmission of Map, by assuring confidence of consumers in dairy products, and by alerting farmers to an infection present in their herds before losses due to clinical disease arise. In the Netherlands, a certification-and-surveillance programme for paratuberculosis in dairy herds was initiated in 1998 (Benedictus et al., 2000). However, the uptake of the programme amongst farmers was rather low: by the end of 2002 only 1231 of approximately 25,000 Dutch dairy were participating. The uptake was low, because the programme was felt to be too expensive and incentives to participate were lacking. Therefore, several studies were performed to optimize and differentiate the certification-and-surveillance programmes towards the needs of various groups of dairy farmers. The concepts and approach followed in these studies may equally apply to other infectious diseases and other countries. Therefore, this paper aims to provide an overview of these studies.

2. PROGRAMMES TO ENABLE LOW-RISK TRADE OF CATTLE

Trade of cattle is the main route of between-herd transmission of Map (Sweeney, 1996). Consequently, cattle in herds in which animals were introduced from other herds, are more likely to be test positive (van Weering et al., 2005). For many herds, a closed herd management is feasible. A one-year study (Sept 2001 – Aug 2002; Velthuis, 2004) revealed that 55% of Dutch dairy herds in which young stock were raised were closed. However, trade of cattle between herds may be necessary to achieve goals of farmers, such as optimizing production. Then, availability of certified Map-free herds as a source of non-infected cattle becomes important. Farmers purchasing stock may reduce the risk of introducing Map by purchasing the stock from certified ‘Map-free’ herds. Farmers aiming to sell breeding stock may get a better price for their stock if they participate in a certification-and-surveillance programme for ‘Map-free’ herds. Certification-and-surveillance programmes for ‘Map-free’ herds have been set-up in several countries such as the USA, Australia and the Netherlands (Bulaga and Collins, 1999; Benedictus et al.,
2000; Jubb and Galvin, 2000; Kennedy and Allworth, 2000). Herds in the Dutch programme can obtain ‘Map-free’ status following five annual herd examinations with negative results only, the first by ELISA and the second to fifth by pooled faecal culture (Benedictus et al., 2000). Until 2003, surveillance of ‘Map-free’ herds was done by annual herd examination by pooled faecal culture (Table 1).

To identify attractive alternative certification schemes (i.e. the initial assessment of herds) for obtaining the ‘Map-free’ status in the Dutch programme, various alternative schemes were studied with a stochastic simulation model (JohneSSim; Groenendaal et al., 2002). Within-herd transmission and economics of Map infection in a population of closed Dutch dairy herds were simulated. The use of the model for this purpose was validated by comparing model results with results of a field study in 90 dairy herds (Weber et al., 2004). Key output parameters were the animal-level true prevalence of (‘invisible’, because undetected) Map infections in the group of ‘Map-free’ herds, and costs of the programme. The simulations showed that an alternative scheme in which herds obtain ‘Map-free’ status after four negative biennial herd examinations by pooled faecal culture was most attractive. With this alternative scheme, the costs of achieving ‘Map-free’ status as well as the animal-level prevalence in ‘Map-free’ herds were lower in comparison with the standard scheme (Fig 1; Weber et al., 2004).

Figure 1: Animal prevalence at reaching the ‘Map free’ status (i.e. number of infected animals / total number of animals in all herds that recently reached the ‘Map free’ status) and median (range 10% - 90%) total (A) and annual (B) discounted costs until the ‘Map free’ status is reached with two certification schemes (Weber et al., 2004). The standard scheme consisted of five annual herd examinations, the first by ELISA and the second to fifth by pooled faecal culture. The alternative scheme consisted of four biennial herd examinations by pooled faecal culture.

To identify attractive alternative schemes for surveillance of ‘Map-free’ herds, various alternative schemes were studied with the JohneSSim model (Weber et al., 2004) and with a mathematical S-I model (van Roermund et al., 2002). In comparison with the standard surveillance scheme (annual herd examinations by pooled faecal culture), none of the alternative schemes resulted in both lower annual costs and a lower animal-level prevalence of undetected Map infections in the pool of ‘Map-free’ herds. However, a higher animal-level prevalence in the pool of “Map-free” herds is not necessarily problematic, as long as (1) the animal-level prevalence is substantially lower than in the general dairy population to ensure that there is an added value to cattle purchased from ‘Map-free’ herds, and (2) the population of ‘Map-free’ herds is sustainable on the long term. A criterion for sustainability of a population of disease-free herds that is frequently used is that an (undetected) infection in any of these herds does not result in a cascade of infections to other herds in the population. More formally, that means that the between-herd transmission rate \( R_h \) (which is the average number of secondary infected herds resulting from an initially infected herd in a large population of susceptible herds) should be smaller than one. Then, only small outbreaks might be expected (Graat et al., 2001).

To study whether any alternative surveillance schemes, that were cheaper than the standard scheme of annual herd examinations by pooled faecal culture, met the \( R_h < 1 \) criterion, a deterministic mathematical model for the within- and between herd transmission of Map was developed (van Roermund et al., 2002). The model described transmission following introduction of Map into a population of (previously) Map-free herds. The model showed that \( R_h \) was linearly dependent on the herd-contact rate if a random herd-contact structure was assumed (Fig. 2). An alternative scheme that consisted of biennial herd examinations by pooled faecal culture resulted in a higher \( R_h \) at a given rate of cattle transfers between herds. However, over a three-year period the observed rate of cattle introductions into ‘Map-free’ herds was 0.33 per 100 cattle present per year (Weber et al., 2006), and at this rate \( R_h \) was substantially lower.
than 1 (Fig. 2; van Roermund et al., 2002). Therefore, it is likely that the population of ‘Map-free’ herds is sustainable with the standard as well as the alternative surveillance scheme. This was also confirmed in another modelling study that took into account both introduction of infected cattle and environmental infections as a way of introducing Map into herds (Ezanno et al., 2005).

Based on the aforementioned study results, in 2003 the surveillance scheme for Dutch ‘Map-free’ herds was relaxed from annual herd examinations to biennial herd examinations by pooled faecal culture (Table 1).

![Figure 2: Between-herd transmission rate $R_h$ as a function of animal transfers between herds, assuming an uniform herd size and random contacts between herds (van Roermund et al., 2002). Standard scheme for surveillance of ‘Map-free’ herds: annual herd examinations by pooled faecal culture. Alternative scheme: biennial herd examinations by pooled faecal culture. The vertical line indicates the observed rate of cattle introductions into ‘Map-free’ herds over a three-year period (Weber et al., 2006).](image)

Table 1. Test schemes used in the Netherlands for the certification procedure (i.e. the initial assessment of herds) and the surveillance procedure of the ‘Map-free’ programme and the ‘Paratuberculosis Programme Netherlands’. In the certification and surveillance procedures, a positive ELISA result was confirmed by individual faecal culture (IFC). A positive pooled faecal culture (PFC) is followed by individual faecal culture of the positive pool. Farmers are advised to cull test positive cattle and their lastborn calf.

<table>
<thead>
<tr>
<th>Years</th>
<th>Certification test</th>
<th>Certification animals</th>
<th>Surveillance test</th>
<th>Surveillance interval</th>
<th>Surveillance animals</th>
<th>Control test</th>
<th>Control interval</th>
<th>Control animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>'Map-free' herds</td>
<td>1998 - 2003</td>
<td>ELISA / All, ≥3 yr / PFC</td>
<td>1 yr</td>
<td>All, ≥2 yr</td>
<td>-- b</td>
<td>-- b</td>
<td>-- b</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PFC ^</td>
<td>All, ≥2 yr</td>
<td>PFC</td>
<td>2 yr</td>
<td>All, ≥2 yr</td>
<td>-- b</td>
<td>-- b</td>
<td>-- b</td>
</tr>
<tr>
<td></td>
<td>ELISA ^</td>
<td>All, ≥3 yr / PFC</td>
<td>2 yr</td>
<td>All, ≥2 yr</td>
<td>ELISA</td>
<td>1 yr</td>
<td>All, ≥3 yr</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PFC ^</td>
<td>All, ≥2 yr</td>
<td>PFC</td>
<td>2 yr</td>
<td>All, ≥2 yr</td>
<td>IFC</td>
<td>2 yr</td>
<td>All, ≥2 yr</td>
</tr>
</tbody>
</table>

^ The certification procedure of ‘Map-free’ herds initial assessment of scheme E consists of five annual herd examinations (the first herd examination by ELISA followed by IFC of ELISA-positive animals; the 2nd through 5th examination by pooled faecal culture followed by individual faecal culture of positive pools).

^ In the programme for ‘Map-free’ herds no specific control procedure is prescribed for test-positive herds; however, the most frequently used control procedure consists of annual herd examinations by individual faecal culture, or pooled faecal culture followed by individual faecal culture of positive pools.

^ Farmers can freely choose between the two test schemes of the ‘Paratuberculosis Programme Netherlands’.

^ As an alternative to herd examinations by serum-ELISA including all cattle ≥3 years of age, farmers are also allowed to test all lactating cattle using a milk-ELISA (including lactating cattle <3 years of age).
3. PROGRAMMES TO ASSURE THE QUALITY OF DAIRY PRODUCTS

The most effective way to reduce any potential human health risk of exposure to Map through consumption of dairy products is to control and prevent paratuberculosis in the national dairy herd (O’Reilly et al., 2004). Therefore, the potential losses to dairy farmers due to consumer concerns about milk safety might be reduced by implementation of a milk quality assurance programme. The goal of a milk quality assurance programme is to reduce the concentration of Map in milk delivered to the dairy plant, rather than elimination of Map from the herd. Therefore, such a milk quality assurance programme might be run at considerable lower costs than a programme to enable low-risk trade of cattle.

To identify attractive milk quality assurance programmes and to evaluate the effects of preventive management measures taken in participating herds, three modelling studies were performed (van Roermund et al., 2005; Weber et al., 2005b; Velthuis et al., 2006). In these studies assumptions were made on the contamination of milk with Map at various stages of the infection-and-disease process (Table 2), and on the maximum acceptable concentration of Map in bulk milk from certified herds. Because no data were available on human exposure to Map and a dose-response curve between exposure and the probability of human disease (if any), it was assumed that no viable Map organisms should be present after commercial pasteurisation. Then, based on the results of pasteurisation studies, the maximum acceptable concentration of Map in bulk milk from certified herds was set at $10^3$ Map per litre. Thus, in these modelling studies, herds were certified as ‘Low-Map bulk milk’ if there was a high probability of having less than $10^3$ Map per litre of bulk milk.

The epidemiological and economic effects of preventive management measures and various test schemes for a bulk milk quality assurance programme were studied in a simulated population of closed dairy herds with the JohneSSim model (Weber et al., 2005b). Output of the model was the proportion of dairy herds that was certified as ‘Low-Map bulk milk’, the distribution of the concentration of Map in bulk milk of ‘Low-Map bulk milk’ herds, and the costs of the programme. Assuming a herd-level true prevalence of 30%, the model results indicated that 90% of all participating herds would be test-negative and therefore certified as ‘Low-Map bulk milk’ at a certification procedure (i.e. initial assessment) by ELISA of all cattle ≥3 years of age. The distribution of the concentration of Map in bulk milk from herds that were test-negative and test-positive at the certification procedure is shown in Fig. 3. If this certification procedure was followed by a surveillance procedure consisting of biennial herd examinations by ELISA of all cattle ≥3 years of age, >96% of ‘Low-Map bulk milk’ herds were <$10^3$ Map per litre of bulk milk at any point in time. However, in the control procedure in test-positive herds, culling based on faecal culture was more effective than culling based on ELISA. Preventive management measures considerably increased the number of ‘Low-Map bulk milk’ herds over time. Average total discounted costs for 20-year participation in a programme consisting of certification by ELISA, surveillance by biennial ELISA and control by biennial faecal culture were €16·10^3 per herd. Additional preventive measures increased these costs to €40-10^3 per herd.

Table 5. Assumptions in two modelling studies (van Roermund et al., 2005; Weber et al., 2005b) on the concentration of Map-bacteria in milk for each stage of the infection-and-disease process in adult cattle. (Total Map in milk = direct shedding + faecal contamination * Map in faeces. Faecal contamination was assumed to be 0.04 gram/litre milk.)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Proportion of animals with each stage</th>
<th>Direct shedding of Map in milk (organisms per litre)</th>
<th>Map in faeces (organisms per gram)</th>
<th>Total Map in milk (organisms per litre)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Latent infected</td>
<td>0.8</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lowly infectious</td>
<td>0.2</td>
<td>0</td>
<td>$10^2$</td>
<td>4</td>
</tr>
<tr>
<td>Highly infectious</td>
<td>0.6</td>
<td>$10^2$</td>
<td>$10^2$</td>
<td>$10^2$</td>
</tr>
<tr>
<td></td>
<td>0.24</td>
<td>$10^2$</td>
<td>$10^3$</td>
<td>5·$10^2$</td>
</tr>
<tr>
<td></td>
<td>0.16</td>
<td>$10^2$</td>
<td>$10^3$</td>
<td>4·$10^2$</td>
</tr>
<tr>
<td>Clinical disease</td>
<td>10^4</td>
<td>10^9</td>
<td>4·$10^3$</td>
<td>4·$10^3$</td>
</tr>
</tbody>
</table>

(Total Map in milk = direct shedding + faecal contamination * Map in faeces. Faecal contamination was assumed to be 0.04 gram/litre milk.)
To study epidemiological effects of various test schemes in a bulk milk quality assurance programme in a population of dairy herds between which cattle are transferred, a new deterministic mathematical model was developed (van Roermund et al., 2005). Input parameters of this model were tuned with those used in JohneSSim. The within-herd dynamics of paratuberculosis in each herd was described by the transmission rate $\beta$, which default value was based on simulations with JohneSSim. Assumptions on animal transfers between herds were based on actual data from the Netherlands. The model output included the proportion of dairy herds that were classified as ‘Low-Map bulk milk’ over time, and the average concentration of Map in bulk milk of ‘Low-Map bulk milk’ herds over time. The model results indicated that a closed herd management and taking preventive management measures were very important for a herd to increase the probability of being classified as ‘Low-Map bulk milk’. If cattle were transferred between herds, the proportion of ‘Low-Map bulk milk’ herds was markedly decreased. For instance, without additional preventive management measures, 30% to 40% of herds were classified as ‘Low-Map bulk milk’ after 8 years if cattle were transferred between herds, compared to 75% to 80% if no cattle were transferred between herds. Furthermore, cattle transfers between herds increased the average concentration of Map in bulk milk from ‘Low-Map bulk milk’ herds, especially if no additional preventive management measures were taken.

A decision tree analysis was performed to determine the conditions under which participation in a bulk milk quality assurance programme would be economically attractive for farmers (Velthuis et al., 2006). In this analysis, the decisions ‘should I join the programme?’, and ‘should I continue joining the programme, given the test results so far?’ were studied, while the decision criterion was the expected monetary value. The result of the analyses was that the preferred decision was not to participate if there was no incentive to do so. A milk price differentiation between ‘Low-Map bulk milk’ herds and other herds was studied as an incentive. In case a farmer would commit to 7 test rounds if entering a programme consisting of certification by a single herd examination by ELISA, surveillance by biennial herd examinations by ELISA and control in test positive herds by annual herd examinations by ELISA, the preferred decision changed to ‘participate’ at a milk price differentiation of €0.90 to €5.50 per 1000 kg of milk (depending on whether or not preventive management measures were taken, and whether or not the herd was closed). For a similar programme with control in test positive herds by annual herd examinations by individual faecal culture, this was €1.90 to €9.80 per 1000 kg of milk.

Based on the results of the aforementioned studies, herd examinations by ELISA for the certification and surveillance were considered to effectively ensure the quality of ‘Low-Map bulk milk’. A new programme, the ‘Paratuberculosis Programme Netherlands’ was started in January 2006, in which farmers can freely choose between two test schemes (Table 1). In this new programme, test-negative herds are designated ‘Status A’ (instead of ‘Low-Map bulk milk’), while test-positive herds are designated ‘Status C’ (if any test-positive cattle are still in the herd) or ‘Status B’ (if all test-positive cattle have been culled).
4. PROGRAMMES TO ALERT FARMERS TO A (SUB)CLINICAL INFECTION

Surveillance of the paratuberculosis status may benefit farmers with herds in which no prior diagnosis of clinical or subclinical paratuberculosis has been established, because this would enable them to take appropriate corrective actions (Collins et al., 2006). Therefore, surveillance of the paratuberculosis status may be beneficial, even if the farmers would not benefit from a ‘Map-free’ status (for instance, if no breeding stock is sold to other herds) or from a ‘low-Map bulk milk status’ (for instance, if the dairy plant does not pay a premium for milk from herds with such status). However, for this purpose, the programmes for ‘Map-free’ and ‘Low-Map bulk milk’ herds are too expensive, because it was clearly shown by Vethuis et al. (2006) that, without incentives such as a milk price differentiation, the farmers’ preferred decision is not to participate in these programmes. Therefore, cheaper surveillance schemes should be used for this purpose. For this purpose, laboratory confirmation of all suspected clinical cases should be sought, for instance by post mortem examination, bacterial culture of faecal samples or serology. Furthermore, culture of environmental faecal samples is an appropriate method for this purpose (Collins et al., 2006). Culture of environmental faecal samples can detect 76% to 90% of herds with at least one positive culture result of pooled faecal samples collected from individual cattle (Raizman et al., 2004; Fyock et al., 2005; Lombard et al., 2005). The sensitivity of culture of pooled environmental faecal samples in Dutch dairy herds is currently being studied.

5. DISCUSSION

In this paper, an overview was given of studies performed to optimize and differentiate the certification-and-surveillance programmes towards the needs of various groups of dairy farmers. Dairy farmers trading cattle may benefit from a certification-and-surveillance programme for ‘Map-free’ herds. The programme was optimized by changing the interval between herd examinations in the surveillance procedure from one to two years, based on the results of the study by van Roermund et al. (2002). The certification scheme was unchanged, because with the cheaper alternatives it took longer to obtain ‘Map-free’ status (Weber et al., 2004) – and that would also delay any potential benefits from being certified as ‘Map-free’.

All dairy farmers may benefit from a milk quality assurance programme, if such a programme contributes to preventing concerns about the safety of dairy products. The ‘Paratuberculosis Programme Netherlands’ was based on the modelling studies mentioned and started in January 2006. The programme is regarded positively by farmers, and numbers of participating herds meet the expectations: over 1000 dairy herds were participating at the end of 2006 (i.e. within a year after the start of the programme). However, incentives for farmers, such as a premium for milk from ‘Low-Map bulk milk’ herds are needed to economically justify participation (Vethuis et al., 2006). Because of possible consumer concerns about the zoonotic potential of Map, the dairy processing industry may be most interested in providing such incentives. In a ‘Strategy for the control of Mycobacterium avium subspecies paratuberculosis (Map) in cows milk’ the British Food Standards Agency considered ‘The Agency believes that precautionary action to reduce human exposure to MAP should start now and should not be dependent on waiting for the link [between Map and Crohn’s disease] to be proved or disproved’ (Food Standards Agency, 2002). Future studies might result in further recommendations for adaptations of the Dutch paratuberculosis programmes towards farmers’ needs. Directions of further studies include the contact structure between herds, shedding of Map before adulthood, slaughterhouse sampling and bulk milk assays.

A three-year study on cattle transfers between ‘Map-free’ herds showed an underdispersed contact structure between these herds (Weber et al., 2006). Therefore the assumption of a random contact structure in the modelling study by van Roermund et al. (2002) is conservative, and provides potential for a further relaxation of the surveillance of ‘Map free’ herds and differentiation of this surveillance towards the risk that herds pose to other herds. Herds from which cattle are transferred to many other herds, and therefore pose a greater risk towards the disease-free status of the population, may be tested more frequently than other herds. A further modelling study is projected within the EU project ‘ParaTB-tools’ to determine the extent to which relaxation and differentiation of the surveillance scheme are warranted.

An analysis of results of individual faecal culture on samples submitted to the Animal Health Service between 1996 and 2002 indicated that some young stock may be infectious: in high-prevalence herds (i.e. >10% of individuals faecal culture positive) an estimated 5% to 14% of cattle became culture positive before two years of age, depending on breed and herd size (Weber et al., 2005a). Also, transmission of Map between calves was shown in an experimental study (van Roermund and de Jong, 2005). However, in various models of paratuberculosis transmission in dairy herds it was assumed that cattle only become
infectious after two years of age (van Roermund et al., 2002; Weber et al., 2004; van Roermund et al., 2005; Weber et al., 2005b). Transmission between calves may result in higher within-herd prevalences of Map in any infected ‘Map-free’ and ‘Low-Map bulk milk herds’. However, due to these higher within-herd prevalences, such infected ‘Map-free’ and ‘Low-Map bulk milk’ herds are more likely to be detected as infected at herd examinations of the surveillance scheme. Therefore, the effect of transmission between calves on the ‘quality’ of the ‘Map-free’ and ‘Low-Map bulk milk’ status is unsure. However, this effect will be studied within the framework of the EU project ‘ParaTB-tools’.

Slaughterhouse sampling (that is, collecting serum or meat-drip samples at slaughter) and bulk milk sampling are established sampling methods within certification-and-surveillance programmes for other bovine infectious diseases such as infectious bovine rhinotracheitis, leptospirosis and leucosis. Such sampling methods may also be usefulness in establishing a herd status with respect to paratuberculosis. Studies to determine the suitability of such sampling methods are projected within the framework of, again, the EU project ‘ParaTB-tools’.

In summary, an overview of studies performed on certification-and-surveillance programmes for paratuberculosis was given in this paper, and directions for future research were indicated. We conclude that the performed studies provided the decision-makers with information on the cost-effectiveness of these programmes for paratuberculosis. However, the approach followed in these studies is not unique to paratuberculosis or to the Netherlands, and therefore may be applied similarly to other infectious diseases and other countries.

6. REFERENCES


