Johne's Disease in deer – current situation and future directions

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Abstract

This paper summarises the current state of knowledge of Johne's disease (JD) in farmed deer in New Zealand, the assessment of losses associated with JD, discussion of prevention and control options, options for a Market Assurance Programme (MAP) and plans for a deer farm prevalence survey

JD in deer is caused by both "cattle strains" and "sheep strains" of *Mycobacterium paratuberculosis* Two clinical syndromes are recognised, sporadic cases in mixed age deer and serious outbreaks, affecting up to 15% of groups, in 8 to 15 month old deer. The number of known infected herds is rapidly increasing.

Previous studies have shown that the gel diffusion (GD) test is the most reliable test for confirming JD in clinically affected deer However, none of the currently available serological or cell-mediated immunological tests is sufficiently sensitive or specific for detecting subclinical paratuberculosis in deer to be useful for control of JD

Clinical JD in deer is estimated (based on 1998 figures) to cost the deer industry approximately $341,000 (ranging from $205,000 – 4,875,000) per annum

Farms free of JD should prevent its introduction. Control options on infected deer farms are currently limited to culling affected stock, culling test-positive animals or depopulation and restocking after 2 years

A voluntary Market Assurance Programme for deer farms has been proposed, but its implementation depends on the national deer farm JD prevalence being low enough to warrant it. A national survey based on bulk faecal cultures from 100 deer farms throughout New Zealand is currently being planned

Introduction

Johne's disease (JD) has emerged as a serious disease of farmed deer in New Zealand (and overseas). The New Zealand Deer Farmers Association has acknowledged that it has the potential to be more serious than tuberculosis The recently completed report on JD commissioned by the Chief Veterinary Officer acknowledges that, of all the farmed animals, the least is known about JD in deer (Brett, 1998)

The first confirmed case of JD in deer was reported in the mid-80s Since then JD has been confirmed on over 200 deer farms and is suspected to have occurred on many more The JD Review estimated that JD costs the deer industry over $300K per annum. But the disease is rapidly spreading and there have been an increasing number of serious outbreaks in yearlings occurring Sporadic losses of adult deer are also occurring with increasing frequency

JD has been reported in deer throughout the country and deer appear susceptible to both cattle and sheep strains of *M paratuberculosis* JD is widespread in sheep and cattle, especially dairy cattle, in NZ With time, it has the potential to affect the majority of NZ deer farms due to the movement of deer between farms, the use of cattle and sheep to graze excess pasture on deer farms and the fact that deer farms are usually created or expanded by taking in land grazed by sheep or cattle.

There is also increasing concern over the possible connection between JD and Crohn's disease in humans and the potential for this to cause trade embargoes on products from infected animals or farms

This paper summarises the current state of knowledge of Johne's Disease (JD) in farmed deer. It explores the epidemiology of JD, reviews current diagnostic tests, summarises the economic assessment of losses associated with JD undertaken by Agriculture New Zealand and discusses prevention, possible control options, a Market Assurance Programme (MAP) and plans for a deer farm prevalence survey

Epidemiology

JD in deer is caused by both "cattle strains" and "sheep strains" of *Mycobacterium avium* ss *paratuberculosis* (*M ptb*) Two clinical syndromes are recognised, a) sporadic cases in mixed age red deer and b) serious outbreaks, affecting up to 15% of groups, in 8 to 15 month old deer (Mackintosh and de Lisle, 1998) The numbers of newly infected herds recorded by the AgResearch Wallaceville laboratory from samples submitted for culture were 4, 7, 22, 27, 46, 43, 36 and 27 for the years 1992 to 1999, respectively To date they have isolated a total of 445 strains from deer on 222 properties However, these are preliminary figures because they do not include a number of deer that have had JD-like lesions that were culture negative but PCR positive for *M ptb* The figures are also likely to be underestimated due to under-reporting by farmers, veterinarians and inspectors at Deer Slaughter Plants (DSPs) Very few submissions have been received from field veterinarians With the number of cases of JD lesions appearing in DSPs it seems likely that there have also been clinical cases occurring on farms If so, have farmers not sought veterinary advice when they encountered clinical cases of JD or have vets not submitted samples from these animals? The majority of submissions have been from samples taken at meat inspection in DSPs where tuberculosis is suspected It appears that DSPs do not submit samples if they are confident that the lesions are due to JD based on lesion appearance, location and herd history, but there is a risk that some cases of Tb may be overlooked. Some cases of JD in deer may also have been missed in DSPs if there has been no gross enlargement of the mesenteric lymph nodes, because the jejunal and ileal lesions in deer may not be obvious on gross examination It appears from personal observation and anecdotal reports from vets and farmers, that there have been an increasing number of multiple cases of clinical JD occurring on deer farms, especially in rising yearling animals. In these cases, typically affected deer were in poor condition, had rough coats, scoured and had green faecal soiling around the tail Once affected they lost weight over a few weeks and died or were euthanased

M ptb may be introduced to deer farms by faecal contamination from infected sheep, cattle, deer or possibly wildlife such as rabbits. Some local environmental spread from runoff is also theoretically possible Many deer farms are established by deer-fencing off areas of existing sheep farms or cattle farms *M ptb* organisms are thought to persist in the environment for up to 2 years, although the number of viable organisms probably declines exponentially, so the greatest risk is in the first 3 to 6 months The use of sheep on deer farms to assist with pasture management and weed control is an additional risk

The exact risk factors for the development of clinical JD in deer are not known, but it is likely that stress plays a major role in exacerbating the disease. Sheep and cattle generally do not develop clinical disease until they are 2 - 4 years old, although under experimental conditions young lambs (<14 days old) exposed to very heavy challenges (>10^9 colony forming units) developed severe disease in under 6 months It is assumed that the earlier and the heavier the challenge, the more likely it is that animals will become infected and develop clinical disease. Older animals appear to become more resistant to infection and are much less likely to develop disease. The development of clinical signs of JD in deer as young as 8 months of age suggests a heavy early challenge. Genetic susceptibility to JD plays a role in dairy cattle (Koets et al , 1999) and it is likely to be important in sheep and deer as well The relative susceptibility of deer to JD, compared with sheep and cattle is not known The level of shedding by infected deer, the amount of environmental contamination and the likelihood and degree of contamination of the hind's udder, have not been established. There may also be behavioural factors, such as coprophagia, that increase the level of exposure

Diagnosis

Clinical JD

Previous studies (Mackintosh, 1999, Mackintosh et al , 1999) have shown that the gel diffusion (GD) test (also known as the agar gel immuno-diffusion or AGID test) is the most reliable test for confirming JD in clinically affected deer On a limited number of samples it showed a sensitivity of >90%. The ELISA and the complement fixation test showed poor sensitivity (20-40%) in these cases. If necropsies are carried out on severely affected animals that are euthanased or die, it is important to recognise that JD in deer may not look the same as in sheep or cattle. There is often no obvious thickening of the terminal ileum and ileo-caecal valve area, although histopathological examination usually reveals masses of AFOs in the intestinal mucosa However, the jejunal lymph nodes are usually enlarged and frequently contain firm, white or cream, caseous and sometimes gritty lesions up to 20-30 mm in diameter The lacteals draining the jejunum are often thickened and cord-like. It appears that in deer JD has a predilection for the anterior and mid sections of the jejunum, and early lesions tend to be confined to these areas and the anterior nodes of the jejunal or mesenteric chain. Histopathological examination of affected areas typically reveals extensive areas of invasion of affected lymph nodes by macrophages, often with foci of calcification and/or caseation and numerous small acid fast organisms (AFOs) present in the macrophages. The intestine typically shows granulomatous enteritis with large numbers of AFO-laden macrophages in the mucosa and often extending into the serosa However, it is important to submit fresh material for culture and/or polymerase chain reaction (PCR) testing because other members of the *M avium/intracellulare* group can cause gross and microscopic lesions that are indistinguishable for JD (Mackintosh et al , 1997)

Subclinical M. ptb infection

A previous study (Mackintosh et al , 1999) showed that the sensitivity of the GD in subclinically affected animals was <50%, and the CFT and ELISA were no better. Cell-mediated tests such as the skin test (using Johnin or avian PPD), the lymphocyte transformation test* and gamma interferon tests** all suffer from poor specificity because of cross reactivity between *M ptb* and other closely related members of the *M. avium/intracellulare* group to which domestic livestock are commonly exposed. In fact, none of the currently available serological or cell-mediated immunological tests are sufficiently sensitive or specific to provide the basis of a control programme for JD in deer

Faecal culture appears to be the most sensitive means of detecting subclinical infection in deer, but it is expensive PCR testing can also be carried out on faeces, but it is currently not as sensitive as culture The use of bulk faecal culture in sheep has demonstrated that this may be a cost-effective means of detecting infection in groups of animals The sensitivity of culture is reduced by bulking faeces and this limits the number of faecal samples that can be bulked. In the National JD Control Programme in Australia, in order to detect infection on a farm, up to 100 sheep faecal samples are bulked together and up to 10 bulked samples are cultured per sheep flock

Economics

Agriculture New Zealand (Brett, 1998) conducted an economic evaluation of JD and possible control options for cattle, sheep and deer in New Zealand Economic models were developed for each industry, based on a model developed for the Victorian dairy industry to assess the productivity losses caused by the disease The exact incidence of JD and the prevalence and impact of subclinical infection are not known and therefore assumptions were made, based on limited available information, and a range of probable outcomes given A summary of results is shown in Table 1

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* LT test: DRL, University of Otago, Dunedin, New Zealand
** Cervigam: CSL, Melbourne, Australia

Table 1. Summary of losses per year to the various livestock industries associated with JD (E. Brett, 1998).

Industry	Cost per clinical case ($)	Minimum cost ($'000)	Most likely cost ($'000)	Maximum cost ($'000)
Dairy	1,616	3,800	18,923	31,744
Sheep	70-75	918	9,910	14,063
Deer	**1,080**	**205**	**341**	**4,875**
Beef	720	62	-	6,238
Total		4,985	29,176	56,920

Clinical JD in deer is estimated (based on 1998 figures) to cost the deer industry approximately $341,000 (ranging from $205,000 – 4,875,000) per annum However, the cost could become very much greater than this if the rate of increase of JD infected deer farms continues to rise at the current or higher rate The estimates are based almost entirely on losses from clinical disease and nothing from subclinical infection It was estimated that the cost per clinical case was $1080 per year. The model was based on sporadic losses of mixed age animals, as seen in the sheep and cattle industry. Losses associated with a serious outbreak (12%) of JD in yearlings were estimated to cost $24,731 per year It would only take 14 such outbreaks in a year for the losses to exceed the "most likely cost" of $341,000 per year for NZ The actual number of outbreaks that occur each year is not known, but at least seven occurred in 1997 (Mackintosh and De Lisle, 1998)

Non-tariff trade barriers and/or the establishment of a link between JD in livestock and Crohn's disease in humans could result in serious disruption to our overseas markets for venison and/or velvet and cause even more serious losses "Perceived risk" is likely to be far more damaging than "real risk"

Prevention

If JD has never been diagnosed in a deer herd and the farmer has no reason to suspect that his herd is infected, it would be wise to take all sensible precautions to prevent its introduction This means

a) Keep a closed herd, avoid buying in animals and use AI to bring in new blood lines
b) Only purchase animals from "low risk" herds. A Market Assurance Programme (MAP) would provide a mechanism for assessing risk and provide a premium for replacements from low risk herds.
c) Avoid grazing sheep or cattle on the deer farm unless they are known to come from flocks or herds that are low risk The risks of grazing sheep or cattle could be minimised by;
    i) using low risk sheep, such as JD vaccinated lambs Alternatively handreared sheep or cattle, which have had not exposure to JD, could be used
    ii) grazing beef cattle, which are less likely to carry JD than dairy cattle
    iii) leaving as long a break as possible between sheep and subsequent deer grazing
    iv) grazing only adult deer, especially velveting stags or deer that are soon to be slaughtered, after the sheep

Control

Control options on infected deer farms are currently limited to either culling affected stock, culling test-positive animals, depopulation and restocking after two years or changing from a breeding operation to a weaner finishing or velvet operation. All these options should be subjected to a rigorous cost/benefit analysis to determine the most economic and practical alternative

1 Cull affected deer It may also be prudent to cull the offspring of JD affected hinds, as there is a high risk that they have been infected by their dams This is the cheapest and least effective level of control It relies on detecting clinically affected animals as soon as possible and culling them. It will minimise, but not eliminate, the amount of contamination from infected animals, thereby reducing the challenge to other deer.

2 Cull test-positive deer This is more expensive but should further reduce the level of contamination by detecting infected animals before they develop clinical signs. Unfortunately none of the tests is more than 50% sensitive and therefore repeated testing would have to be carried out every 6-12 months The current tests are most unlikely to eliminate all subclinically infected animals

3. Depopulation This would eliminate all infected animals, but the farm would have to be destocked of hinds for at least 2 years Other livestock such as horses could be grazed or crops grown "Clean" animals would have to be obtained for restocking the farm after 2 years This option is likely to be too expensive and impractical for many commercial operations

4 Change the deer farming operation to weaner finishing or velveting stags. Weaners would have to be bought in from sources "free" of JD Velveting stags could be bought in as older animals, preferably from a farm "free" of JD

Vaccination

There are currently no JD vaccines licensed for use in deer in New Zealand Neoparasec*, which is licensed for use in sheep, goats and cattle, can be used only in cattle herds free of Tb, and requires written approval from a MAF Veterinary Officer, because of the possibility that vaccination could interfere with the AHB National Pest Management Strategy for Bovine Tb Control. Neoparasec appears to provide significant protection against clinical JD in sheep and cattle, even when given at 12 weeks of age, and it is likely to be similarly effective in deer. Unfortunately the vaccine, which contains live attenuated *M. ptb* strain 316F and is oil-adjuvanted, has a number of undesirable side effects

a) It causes injection site lesions in the majority of sheep and cattle and is likely to affect deer in the same way

b) It causes lesions in the draining lymph node in around 10% of sheep. These lesions have a histological appearance similar to Tb and they may contain acid fast organisms (AFOs), thus potentially causing meat inspection problems. If such a lesion was found in deer at slaughter, it could result in either condemnation of the carcass, downgrading for "local" trade at half the price/kg or holding in storage for weeks until it is cleared by culture or PCR

c) It may cause vaccinated deer to react to the Tb skin test

The current vaccine has only a 24-hour life once it is reconstituted and is only sold in 250-dose packs

A live attenuated oil-adjuvanted vaccine has been used successfully in deer in the UK (Fawcett et al., 1995). The Agriculture NZ Economic Evaluation reviewed a number of control options and concluded that vaccination would be the most viable if a safe, effective vaccine was available For a vaccine to be registered for deer it must be shown to be safe, effective, have few side-effects, not cause serious loss of value of the carcass, and not interfere with Tb control. Trials are currently underway in deer at Invermay to test possible vaccines

Market Assurance Programme option

The objective of a Market Assurance Programme (MAP) is to classify tested herds according to their disease-risk status and is similar to the classification of herds in the Tb control scheme. Once herds have achieved a "low risk" status, they can be confident that losses due to JD are extremely unlikely and they will be in a favoured position to supply deer to other farms wishing to source animals with a minimal risk of *M ptb* infection

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Neoparasec Merial, New Zealand Ltd, P O Box 76 211, Manukau City.

Overseas cattle and sheep MAPs

Overseas there are a number of JD MAPs A Dutch National Cattle JD Control Programme (Benedictus et al , 1999) has a series of herd status levels from 1 to 10. namely 1-4 (infected/unknown), 5 (owner declaration of no JD), 6 (negative ELISA for cattle 3+ years old), 7-10 (negative pooled faecal culture for all cattle 2+ years old). For herds that have worked their way through the scheme it is considered that, if the bulk faecal culture system is ~40% sensitive and 99.9% specific, then there is a 95-99% chance the tested herd is free of JD after 4 years of negative cultures. There are strict management rules, especially related to purchasing, calf rearing/access to colostrum etc) The Australian JD MAP for cattle is similar to the Dutch scheme and classifies herds according to their disease status, but is based on ELISA testing blood samples from the adult herd It is estimated that there is a >95% probability of detecting infection if it is present in >2% of adult animals Herds progress from Monitored Negative status 1 (MN1) to MN3 over 4 years of testing Again there are rules regarding movement, purchasing and grazing The Australian National Ovine JD Control Programme is similar to the cattle scheme and is based on ELISA testing of 400-500 ewes twice yearly A recent trial showed that pooled faecal cultures are more sensitive than serology and the scheme may change to this form of monitoring.

A New Zealand deer MAP

A voluntary Market Assurance Programme for deer farms in New Zealand has been proposed, but its implementation depends on farmer "ownership" and support

Why should NZ deer farmers support a deer JD MAP? Reasons include:

1 This is the first essential step in reducing the spread of JD to uninfected deer farms. The proportion of NZ deer herds that are currently infected is believed to be still relatively low, but the number of newly infected herds is increasing rapidly

2 Progressive farmers will recognise the value of knowing their status so that they can manage their herd accordingly If "low risk", the farmer should recognise how valuable that status is and can take all precautions to prevent the introduction of JD If "infected", then an appropriate control programme can be implemented.

3 A "low risk" status will enhance the value of a farmer's stock and enable deer to be sold at a premium "Low risk" animals will be sought after as replacements, especially for herds that are starting up or expanding. On the other hand, "infected" farms will not be able to sell weaners to "low risk" farms and will not be able to command as good a price as "low risk" farms

4 It has been suggested that, in the future, importing countries may not buy produce from JD infected farms and it may be necessary for a farm to demonstrate "freedom" from JD to gain access to certain markets

There may be a number of reasons why individual farmers would not join a voluntary deer JD MAP Some may believe that the cost is too great for the perceived benefits Some may not want to know their status because of the stigma associated with an "infected" status They may believe that a status of "untested" is better than "infected" They may know or suspect that their herd is infected and do not want spend money to confirm it Until effective control or eradication measures are developed, there may be little incentive for farmers to join a deer JD MAP unless there is a very large premium for "low risk" animals or there are restrictions on the movement of animals from "infected" or "untested" herds.

One of the most important factors that will determine the viability of a JD MAP is the actual prevalence of infected herds There are 200 – 300 deer farms (~5% prevalence) on which JD has been confirmed by culture and /or PCR. However, the true prevalence is likely to be somewhat greater If the true prevalence is too high, then few farmers will be interested in joining a voluntary MAP because they are unlikely to be free of JD. Therefore it desirable to obtain a reliable estimate of the herd prevalence of infection and this requires a survey.

National Deer Farm Prevalence Survey

In order to estimate the true prevalence of JD, representatives of the Deer Branch, NZVA and the Deer Farmers' Association decided to explore the possibility of a National Deer Farm Prevalence Survey A small working party of Massey University and AgResearch scientists is currently addressing the problem.

There are a number of key questions to consider.

1 Should it be a random farm survey (potentially the most accurate but also the most expensive) or a DSP-based survey (cheaper but unlikely to give a true prevalence)?

2 How many farms should be sampled for an accurate estimate?

3 How will the farm status be assessed?

4 How much will it cost and who will fund it?

Question 1: The working party decided that only a farm survey would provide an accurate estimate of the true prevalence of infected herds. However, the collection of DSP data on the prevalence and severity of lesions and the age of affected animals could provide valuable additional information.

Question 2 Statistical modelling showed that if the prevalence of infected herds is around 5%, then there is a >95% chance that at least one will be shown to be infected if 100 farms are sampled Or in other words, if the true prevalence is around <5% then 100 farms should be sampled to have a good chance of getting an accurate estimate of the prevalence, assuming that there is a sensitive means of detecting herd infection

Question 3 None of the serological tests appears sensitive enough for a cost-effective means of detecting infected farms Faecal culture is the most sensitive test, but is too expensive on an individual basis Bulk faecal culture, if it can be shown to be sufficiently sensitive in deer, offers the most viable alternative The working group decided that a small preliminary study to validate the faecal sampling methodology (ie how many deer faecal samples could be bulked together and still retain adequate sensitivity) is an essential prerequisite to a National Survey

Question 4 The cost depends on the final trial design, but assuming that ten bulked samples are cultured from 100 randomly selected farms, and including the costs of sample collection, data analysis and the costs of the preliminary study, then the overall cost is likely to be over $150,000 The question of who will fund this remains unanswered.

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References

Benedictus, G., Verhoeff, J , Schukken, Y H , Hesselink, J W 1999. Dutch paratuberculosis programme· history, principles and development Proc Sixth Int Colloq On Paratuberculosis Melbourne Australia pp 9-21

Brett, E 1998 Johne's disease an economic evaluation of control options for the New Zealand livestock industries Agriculture New Zealand Report

Fawcett, A R , Goddard, P J , M[c]Kelvey, W A C , Buxton, D , Reid, H W , Greig, A , Macdonald, A.J 1995 Johne's disease in a herd of farmed red deer Vet Rec 136 165-169

Koets, A P, Adugna, G., Janss, L G., van Weering, H J , Kalis, C H J , Harbers, A , Ratten, V P M G., Schukken, Y H 1999 Genetic variation in susceptibility to *M a paratuberculosis* infection in cattle Proc Sixth Int Colloq On Paratuberculosis Melbourne Australia pp169-175

Mackintosh, C G., Webster, J , Corson, I , Masters, B., Pearse, A J , Littlejohn, R 1997 An outbreak of avian tuberculosis in red deer Deer Branch, NZVA, Proc Course No 14 243-250

Mackintosh, C G., de Lisle, G W 1998 Johne's disease. the current situation in New Zealand deer. Deer Branch, NZVA, Proc Course No 15 175-182

Mackintosh, C G 1999 Update on investigations into giagnostic tests for Johne's disease in red deer Deer Branch, NZVA, Proc Course No 16 145-150

Mackintosh, C G., Reichel, M P, Griffin, J F T, Montgomery, H, de Lisle, G W 1999 Paratuberculosis and avian tubercul,osis in red deer in New Zealand clinical syndromes and diagnostic tests Proc Sixth Int Colloq On Paratuberculosis Melbourne Australia pp 449-457

Nicholls, M A 1999 National ovine Johne's disease control program The Australian experience Proc. Sixth Int Colloq On Paratuberculosis Melbourne Australia pp 22-32