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Johne's disease in deer – prospects for control

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ABSTRACT

This paper summarises current knowledge of Johne's disease (JD) in farmed deer in New Zealand and discusses prevention and control options. JD in deer is caused by "bovine strains" and "ovine strains" of *Mycobacterium avium* subsp. *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. Over 300 deer farms are known to be infected and the number is increasing. Studies have shown that the gel diffusion 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. Farms free of JD should prevent its introduction. Control options on infected deer farms are limited to management options: culling affected stock, culling test-positive animals or depopulation and restocking after 2 years. Vaccination may be the most cost-effective long term control option if a suitable vaccine can be developed. A voluntary market assurance programme for deer farms has been proposed, but implementation depends on the benefits to farmers and on the national deer farm JD prevalence being low enough to warrant it.

Keywords: deer; Johne's disease; *Mycobacterium paratuberculosis*; prevention; control.

INTRODUCTION

Johne's disease (JD) has emerged as a serious disease of farmed deer in New Zealand and overseas. The first confirmed case of JD in deer was reported in the mid-80s. Since then JD has been confirmed on over 300 deer farms and is suspected to have occurred on many more. Brett (1998) estimated that JD was costing the deer industry over $300K per annum. This figure was based on limited information and will almost certainly under estimate the losses in deer currently caused by this disease. The disease appears to be 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. The occurrence of JD lesions in mesenteric lymph nodes in deer at slaughter plants causes meat inspection problems, especially with respect to differentiating them from tuberculosis lesions. JD has been reported in deer throughout the country and deer are susceptible to both bovine and ovine strains of *Mycobacterium avium* subsp. *paratuberculosis* (*M. ptb*). 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.

This paper summarises the current state of knowledge of JD in farmed deer, explores the epidemiology, reviews current diagnostic tests and discusses prevention and control, including management options, vaccination and a Market Assurance Programme.

EPIDEMIOLOGY

JD in deer is caused by both "cattle strains" and "sheep strains" of *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 & de Lisle, 1998). These outbreaks in yearlings cause significant financial losses.

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. Most deer farms are established by deer-fencing off areas of existing sheep farms or cattle farms. 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 they are likely to similar to those for sheep and cattle and stress is very likely to play 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 cattle are 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 also likely to be important in sheep and deer. 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 test (also

known as the agar gel immuno-diffusion test) is the most reliable test for detecting 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 acid fast organisms 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 present in the macrophages. The intestine typically shows granulomatous enteritis with large numbers of acid-fast bacterial-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 gel diffusion test 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 sole basis for a control programme for JD in deer, although repeat serological testing and slaughter may assist control by reducing the number of infected animals.

Faecal culture appears to be the most sensitive means of detecting subclinical infection in deer, but it is more expensive than serological testing. 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, but the sensitivity of this technique has not been measured.

* LT test: DRL, University of Otago, Dunedin, New Zealand.

** Cervigam: CSL, Melbourne, Australia.

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

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 very wise to take all sensible precautions to prevent its introduction. Currently there are no cost effective methods to eradicate *M. ptb* from infected deer and cattle herds, and sheep flocks. To maintain JD free deer herds farmers should;

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 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.

CONTROL

Control of JD on infected deer farms are currently limited to one or more of the following options. None of these options have yet been evaluated to determine their cost-effectiveness.

Management options: a) culling affected stock, b) culling test-positive animals, c) depopulation and restocking after two years, d) changing from a breeding operation to a weaner fattening or velvet operation or e) establish a "clean" herd on another property with handreared or artificially derived offspring from deer of high genetic merit. All these options should be subjected to a rigorous cost/benefit analysis to determine the most economic and practical alternative.

Vaccination is likely to be the most cost-effective means of long-term control.

A market assurance programme may provide the means to identify and certify farms that are "free" or "low risk" of JD and be able to provide the industry with "clean:" animals

Management options

a) Cull clinically 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 most basic level of control. It relies on detecting clinically affected animals as soon as possible and culling them. It will decrease, but not eliminate, the amount of contamination from infected animals, thereby reducing the challenge to other deer.
b) Cull test-positive deer. This is more expensive but should further reduce the level of contamination by detecting some of the subclinically infected animals. The cost-effectiveness of this approach has not been determined for deer but similar methods have had limited value when applied to infected cattle herds and sheep flocks. A major limitation of this approach is the poor sensitivity of JD tests when applied to subclinically affected animals.
c) Depopulation. This would eliminate all infected animals, but the farm would have to be destocked or managed with short term "clean" grazers for at least 2 years before a breeding herd could be re-established.

Other livestock such as horses could be grazed or crops grown. "Clean" breeding 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.

d) Change the deer farming operation to weaner fattening 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.
e) Establish a "clean" herd on another property. Stud herds affected by JD have been able to transfer animals of high genetic merit to establish a new stud herd on a "clean" property using hand-reared calves and offspring that have been embryo transplanted into "clean" hinds. This is expensive and not without risks of re-infection but may be economic for high value animals.

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 provides 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 an unacceptably high incidence of significant injection site lesions in the majority of sheep and cattle. In a small trial, 6 of 15 deer injected with Neoparasec at 4 months of age had lesions ranging from 10-30 mm across when slaughtered 12 months later. The rest had no detectible lesions (Mackintosh *et al*., 2001).
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, thus potentially causing meat inspection problems. In the small trial referred to in a) there were no detectible lesions in the prescapular lymph nodes in the Neoparasec vaccinated deer.
c) It often sensitises cattle to the Tb skin test. Similarly in deer, Neoparasec caused sensitisation to the single intradermal skin test and large skin test reactions at both sites in the CCT as well as high, persistent levels of avian and bovine antibody.

The current vaccine has only a 24-hour life once it is reconstituted and is only sold in 250-dose packs. A similar live attenuated oil-adjuvanted vaccine has been used successfully in deer in the UK (Fawcett *et al*., 1995).

The Agriculture NZ Economic Evaluation (Brett, 1998) 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 AgResearch Invermay and on two commercial farms to test a new JD vaccine that does not use an oil adjuvant and appears to overcome many of the problems with injection site lesions and sensitisation to Tb tests.

Market assurance programme option

The objective of a market assurance programme 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. Overseas there are a number of JD market assurance programmes. 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. The Australian JD market assurance programme 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 original Australian National Ovine JD Control Programme (Nicholls, 1999) was similar to the cattle scheme and was based on ELISA testing of 400-500 ewes twice yearly. The scheme has recently been modified to use pooled faecal cultures, which is a more sensitive method than serology for detecting infected herds.

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 market assurance programme? Reasons include:

1. This is an essential step in reducing the spread of JD to uninfected deer farms. The proportion of NZ deer herds that are infected is unknown, but the number of infected herds is increasing.
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 should not sell weaners to "low risk" farms and will not be able to command as good a price as "low risk" farms.
4. In the future "low risk" farms may be able to export venison to a wider range of markets overseas. If M. ptb is demonstrated to be a human pathogen and cause Crohn's disease, consumers may pay a significant premium for product from uninfected herds or avoid product from animals of uncertain infection status.

There may be a number of reasons why farmers would not join a voluntary deer JD market assurance programme. Some may believe that the cost is too great for the perceived benefits. Some may not want to know their status because of a perceived stigma of having an "infected" farm. 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 to confirm it. Until effective control or eradication measures are developed, there may be little incentive for farmers to join a deer JD market assurance programme 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. Currently in New Zealand there are no restrictions on the sale of live deer from infected herds or the slaughter of infected animals for human consumption. In some countries, such as Australia, there are restrictions on the movement of stock from infected herds and flocks, a measure which is considered an essential component of a scheme to limit the spread of JD.

An important factor that will determine the viability of a JD market assurance programme is the actual prevalence of infected herds. There are over 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 market assurance programme because they are unlikely to be free of JD. Therefore it essential to obtain a reliable estimate of the herd prevalence of infection and this requires a national survey.

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