REVIEW OF "TEST AND CULL" AS A MANAGEMENT PROCEDURE FOR THE CONTROL OF JOHNE'S DISEASE

September 2010

By Kaylene Larking

Executive Summary

"Test and Cull" is a management procedure that seeks to minimize transmission of disease in a herd by culling of infected animals as soon as possible. The success of the technique is dependent on the ability to accurately and cost- effectively detect disease in infected animals.

This report documents a review of "Test and Cull" as a management technique for Johne's disease for the Johne's Disease Research Consortium (JDRC) Board and was prepared from submissions made by NZ based researchers and practitioners.

The report notes that the major limitation impeding the utility of the procedure is the lack of a sensitive, specific and cost-effective test for accurately detecting infected animals and that further work is required to improve the confidence, sensitivity and specificity of diagnostics. Evidence also suggests that the technique is highly unlikely to be cost effective for reducing disease prevalence. The review concludes that given current understanding regarding "Test and Cull" that culling of test positive animals on the basis of results from diagnostic tests alone is not recommended. Majority opinion both within New Zealand and internationally suggests that culling should only be considered for animals which can be confidently identified as high shedders which need to be removed from the herd as they pose a severe risk for disease transmission on farm.

Contents

Definitions:

ELISA	Enzyme- linked immunosorbent assay
JDRC	Johne's Disease Research Consortium
MAP	*Mycobacterium avium paratuberculosis* – the bacterium that causes Johne's disease
Paratuberculosis	Another name for Johne's disease
PCR	Polymerase chain reaction
PTB	Paratuberculosis
qPCR	Quantitative polymerase chain reaction

Background

"Test and Cull" is a management procedure that can be employed for the control of Johne's disease where animals that are test positive for *Mycobacterium avium paratuberculosis* (MAP) are removed from a herd by culling. It seeks to minimize transmission of the disease by removal of infected animals from a herd as early as possible.

"Test and Cull" is not unique to Johne's disease. It can and has been applied to the control of other livestock diseases, but its success is dependent on the availability of cost effective tests that are sensitive and specific for infection. "Test and Cull" has proven effective for eliminating tuberculosis from most cattle and deer farms in New Zealand,[1] but there are only limited examples where the procedure alone has been successfully used for the eradication of a disease. The utility of the procedure may be in targeted application aimed at reducing the impact of disease by culling highly affected animals, thereby decreasing the risk of disease transmission.[2]

The Johne's Disease Research Consortium (JDRC) Board has requested that a review be undertaken of the current understanding of the use of "Test and Cull" as a management procedure for Johne's disease.

Methodology

The following were invited to prepare a submission for JDRC's evaluation of "Test and Cull" as a management procedure for Johne's disease in New Zealand (those listed in bold chose to respond). The responses have been summarized in the following report and represent the majority view of the submissions. Quotations from the submissions are noted in italics and referenced in footnotes.

Dr John Aitken
Dr Penny Back and Dr Hinrich Voges
Dr Mandy Bell
Dr Bruce Buddle
Dr Adrian Campbell
Dr Des Collins
Dr Allan Crawford
Dr Geoff DeLisle
Prof Frank Griffin
A.Prof Cord Heuer
Dr Colin Mackintosh
Dr Geoff Nicoll
Dr Solis Norton
Prof Peter Wilson

A full copy of the submissions has been appended to the report, with the exception of a paper supplied in Confidence by Massey University, in advance of publication. The appendix is not required reading.

Discussion

Potential reasons for Test and Cull

In a submission from Massey University[2] the following points were noted as potential reasons for employing a "Test and Cull" strategy:

1. *"Eradication of disease at herd, regional or national level.*
2. *Management targeted to minimise the spread of disease within and between farms*
3. *Management within farm to minimise the economic impact*
4. *Market requirements either for export (trade barriers) or local markets (confirmation of freedom of disease in live animals)".*

In order for implementation to be justified or successful, the authors consider that the following criteria need to be fulfilled:

- That a highly sensitive and predictive test is available which detects a high proportion of clinically and sub-clinically infected animals and which is capable of accurately determining the disease-free status of replacements.
- That the disease is causing or could potentially cause greater economic losses than the cost of culling
- That alternative means of control are not effective or cost-effective as a substitute for culling (e.g. management, genetics or vaccination).
- That the role of all MAP reservoirs (e.g. environment and wildlife) in transmission of the disease as understood.
- That the "drivers" for implementation (i.e. the market for live animals and/or product) are real and justified

These were common themes in all of the submissions and the following addresses current information relating to these criteria. The review also includes comments regarding application of the technique both in New Zealand and internationally.

Diagnostics:

Central to the use of Test and Cull, is the ability to **accurately diagnose the disease status of animals in herds and flocks**. It is widely acknowledged that all of the currently available diagnostic procedures employed for the detection of paratuberculosis have limitations. It is also noted that the effectiveness of diagnostic techniques can vary between different animal species:

Culture: Culturing is the process of detecting MAP bacteria in samples, by allowing the organism to grow on either solid or liquid media. While generally considered the most accurate test available (80-98%) it is expensive and because the bacteria grow slowly, time consuming. This technique is rarely used by practitioners on farm.[12]

PCR (polymerase chain reaction)
PCR checks samples for the presence of gene segments from the MAP organism. There are limitations with the specificity of this test and while the technology is improving a positive PCR result generally indicates further testing is warranted.

ELISA (Enzyme linked immunosorbent assay) or Paralisa
The ELISA tests blood (serum) or milk samples for antibodies produced in response to MAP bacteria in the animal. The test is rapid and less expensive than culture but it is also less sensitive and there is a potential for MAP-positive animals to test negative and vice versa.

All of these tests are most effective for identifying animals that have clinical disease, when an animal is most likely to have mounted a significant immune response and be shedding large quantities of bacteria in their faeces. These animals present a severe contamination risk to the rest of the herd. What is most difficult with any of the current tests is reliable diagnosis of subclinical disease, however this is critical to the successful implementation of a "Test and Cull" program, to ensure infected animals are removed from a herd as early as possible to avoid transmission of MAP to non-infected animals[3]. It is also noted that it is necessary to subject a herd to repetitive testing over long periods of time to accurately determine infection status, a costly investment for most farms.

Canterbury Health Laboratories is investigating alternative diagnostic pathways and other biological markers for Johne's disease that may be more cost-effective and reliable in the detection of infected animals than those currently employed. The work is commercially sensitive, and has reached a stage where the group is deploying some of these approaches in pilot studies. [4]

Economics

Computer Simulation studies carried out both in New Zealand[8] and overseas[5] have indicated that "Test and Cull" is unlikely to be an economically viable procedure for the control of Johne's disease, particularly in smaller herds and flocks. Models calculating the economic impact of "Test and Cull"[6] balance the cost of production losses against the cost of purchasing and rearing replacement animals as well as the expense of long term repetitive testing to detect the presence of the disease on farm.

Barkema et al[7] noted that costs associated with "Test and Cull" "*are typically higher than the economic benefits*".

Alternative Control Methods

"Control of clinical and sub-clinical diseases, including reduction of the spread of contagious pathogens can be achieved by preventive measures such as vaccination, strategic application of chemotherapeutics, risk reduction, or by treatment of clinically affected animals".[2] Good Management practices (e.g. hygiene, minimizing exposure of young animals to MAP) are also recognized as control strategies for paratuberculosis. It is outside the scope of this review to compare the merit of these strategies against "Test and Cull", except to note that simulation studies carried out both in New Zealand[8] and the Netherlands[6, 9] have shown that improved farm management is predicted to reduce prevalence rates more effectively than "Test and Cull".

Role of MAP reservoirs

Known reservoirs for MAP include pasture, waterways and wildlife. It is well documented that MAP survives for long periods of time in the environment under optimum conditions, e.g. 18 months on pasture. What is not well understood is what role these MAP reservoirs play in the transmission of disease and little data exists to predict their impact accurately.

Drivers for implementation:

The current drivers for implementation of "Test and Cull" for the eradication or reduction of MAP prevalence in New Zealand are primarily economic. There are no market barriers for live animals or animal products, either nationally or internationally.

Australia, the United States and some countries in Europe all have voluntary control programs for paratuberculosis. In Australia the control program limits the trade of animals in an attempt to reduce disease prevalence, which has met with limited success. In the EU, Denmark controls MAP to improve animal health while Belgium and the Netherlands are controlling paratuberculosis for the purpose of food safety and securing trade access for products.[10]

New Zealand Practice:

In New Zealand the use of "Test and Cull" is primarily seen in deer farming operations, where the affects of Johne's disease have the most impact. "Test and Cull" is rarely discussed in the context of sheep, beef and dairy cattle.

DEER:
While there is vigorous debate amongst researchers regarding the use of "Test and Cull" as a management tool for paratuberculosis in deer, parties appear to agree that the tool may have benefits on farms where there is a high degree of clinical disease, [1,2] however there are real limitations associated with use of the tool that must be acknowledged and managed.[1,2,11] Few practioners recommend that culling decisions are based on testing alone, but that test results need to be balanced against a range of on farm information (multi factor approach) to ensure the most effective solution is implemented for the farmer.[12]

"The cost-effectiveness of the Paralisa in deer herds is dependent on the existing incidence of clinical disease, the seroprevalence in the herd, environmental and management factors, the value of the stock (especially if they are stud animals or the individual farmer is risk aversive). It is up to each farmer, his advising veterinarian and the laboratory to undertake a risk/benefit analysis for each farm and undertake the most appropriate control programme".[1]

The central disagreement in the "Test and Cull" debate in New Zealand is the ability of current tests, particularly the Paralisa, to reliably detect MAP infected animals. Paralisa is the most frequently employed diagnostic used for detecting MAP infection in deer in New Zealand.

Those employing or recommending "Test and Cull" on farm are confident that the Paralisa test is useful for identifying the most heavily infected animals for targeted removal from the herd as they see a good correlation between the level of antibody response and the severity of disease in an animal. They also see a positive correlation between high Paralisa antibody levels, the number of MAP organisms detected by qPCR and "time to positive" in the BACTEC culture system.[1] Field study data suggests significant shifts in the infection status on some, but not all farms where the technique has been applied. The approach has not been successful in reducing infection in herds with low incidence of clinical disease. [2]

Those who are not in favor of the application of "Test and Cull" are concerned that the sensitivity and specificity of any of the current test methods is still unacceptably low, resulting in unnecessary culling occurring at high cost to the farmer. Coupled with this the opponents believe that international evidence would suggest "Test and Cull" is rarely effective for eradication of paratuberculosis. The argument is that further peer review of the diagnostic test is required to validate the approach before implementing the strategy on farm.

Landcorp Farming Limited has been trialing the effect of a whole herd "Test and Cull" policy in their sire breeding operations since 2008. In 2010/11 they have restricted testing to yearlings and 2 year old animals only. All test positive animals (>50 elisa units) have been culled in these herds over the past 2 years. The prevalence of sero positive females has dropped dramatically on these farms, but this has been at great cost to the company, as in some cases up to 40% of a herd had initially tested positive for the disease. Landcorp notes that the strategy is not economical and could not be applied to the majority of their commercial operations. In part Landcorp have committed to the trial as they believe that they are one of the few farms in NZ that could support the losses associated with the technique in order to evaluate on-farm effectiveness. At this point in the trial they are more supportive of a multi factor control program where "Test and Cull" is used more as a means to remove high shedders from herds.[13]

Sheep and Cattle:
As noted above, "Test and Cull" is rarely discussed in a New Zealand context for the control of Johne's disease on farm, however computer simulation studies, carried out to model the effect of differing control strategies in New Zealand dairy herds[8] indicated that annual test and cull of herds was prohibitively expensive and not cost effective as a sustained control strategy for the disease. The most effective tool for reducing disease prevalence in a cost effective manner was improved farm management.

International Evidence:

"There is no example anywhere in the world in any species where using "Test and Cull" to eradicate paratuberculosis has been successful or cost-effective in either pastoral or intensive farming situations. Of particular relevance is the experience with ovine JD in Australia where attempts were made to eradicate the infection in a pastoral environment, but without success ".[2]

Internationally "Test and Cull" is recognised as a management tool that can be employed to control MAP but the majority opinion is that use of the procedure alone will not eradicate the disease and is highly unlikely to be cost effective.

A US study completed in 2008[14] has shown that good herd management combined with culling high shedding animals may be effective for controlling MAP transmission, but in the case of poor management, culling of both low and high shedding animals is likely required to control the disease.

The best practice for control of the disease is suggested to be a combination of management techniques that aim to reduce the risk of transmission of the disease.[3] By necessity these techniques involve the removal or isolation of infectious animals from a herd or flock and therefore culling infected animals can play an important role in management programs. The US Johne's Disease Information Centre[15] notes that the practice of "Test and Cull" is *"essential for the successful control of Johne's disease in herds or flocks in a reasonable period of time"*. It is noted however that

the routine culling of a test-positive animal is not generally recommended unless there is clear signs of clinical disease. The generally accepted practice is to test and manage; culling clinical animals and isolating suspects from the rest of the herd/flock, particularly younger animals who are most susceptible to infection.

Recovery from Disease

There is evidence, both from JDRC studies in deer[16] and international studies in sheep[17] that a proportion of infected animals can recover from Johne's disease symptoms, after mounting a significant immune response to the disease and/or shedding organisms in their faeces. Such "resilient" animals are an asset in a herd/flock, but without repeated testing and/or management would potentially be culled in a traditional "test and cull" management scheme.

Conclusions

It is the conclusion of this review that given the current understanding regarding the utility and limitations associated with the use of "Test and Cull" as a management procedure for Johne's disease that that culling of test positive animals on the basis of results from diagnostic tests alone is a highly unfavorable practice. Majority opinion both within New Zealand and internationally suggests that culling should be targeted and only considered for animals which can be confidently identified as high shedders which need to be removed from the herd as they pose a severe risk for disease transmission on farm. "Test and Cull" under current conditions will not eradicate Johne's disease and is highly unlikely to be economic. Further work is required to improve confidence, sensitivity and specificity of diagnostics.

The review of "test and cull" as a procedure has noted a number of issues which hinder the utility of the technique and which require additional research (this is not a complete list):

- The lack of accurate disease prevalence data
- Poor sensitivity and specificity of current diagnostics tests
- Evaluation of the economic impact of disease (both clinical and sub-clinical) in New Zealand

References

[1] Submission to JDRC re use of "test-and-cull" as a management procedure for the control of Johne's disease in NZ. Dr Colin Mackintosh. AgResearch Invermay, August 2010.

[2] Test and Cull as a management procedure for the control of Johne's disease in New Zealand. Submission to Johne's Disease Research Consortium, August 2010. Prof. P Wilson and A. Prof. Cord Heuer, Massey University.

[3] Paratuberculosis, Organism, Disease, Control, Edited by M. Behr and D. Collins. CABI, 2010, ISBN 978-1-84593-613-6. Paratuberculosis Control Measures in Europe. Douwe Bakker

[4] Dr John Aitken, Personal communication, September 2010.

[5] The importance of culling in Johne's disease control. Lu Z, Mitchell RM, Smith RL, Van Kessel JS, Chapagain PP, Schukken YH, Grohn Y. J Theor Biol. 2008 Sep 7;254(1):135-46. Epub 2008 May 16.

[6] Development of the Dutch Johne's disease control program supported by a simulation model. H. Groenendaal et al. Preventive Veterinary Medicine 60 (2003) 69–90.

[7] Paratuberculosis, Organism, Disease, Control, Edited by M. Behr and D. Collins. CABI, 2010, ISBN 978-1-84593-613-6. Global Prevalence and Economics of Infection with *Mycobacterium avium* subsp. *paratuberculosis* in Ruminants. Herman W. Barkema, Jan Willem Hesselink, Shawn L.B. McKenna, Geart Benedictus and Huybert Groenendaal.

[8] Simulating control strategies for Johne's disease in New Zealand dairy herds. S Norton, H Groenendaal, C Heuer, Proceedings, 8th International Colloquium on Paratuberculosis, 2005.

[9] A simulation of Johne's Disease Control. H. Groenendaal et al. Preventive Veterinary Medicine 54 (2002) 225–245.

[10] Report on the 10th International Colloquium on Paratuberculosis, Minneapolis, USA, 9-14 August 2009, JDRC #130519. Kaylene Larking and Dr Lindsay Burton

[11] Dr Solis Norton, Johne's Management Limited, Personal Communication, September 2010

[12] Dr Amanda Bell, Personal Communication, August 2010.

[13] Dr Geoff Nicoll, Landcorp Farming Limited. Personal Communication, September 2010.

[14] The importance of culling in Johne's disease control. Lu Z, Mitchell RM, Smith RL, Van Kessel JS, Chapagain PP, Schukken YH, Grohn Y. J Theor Biol. 2008 Sep 7;254(1):135-46. Epub 2008 May 16.

[15] University of Wisconsin Johne's Disease Information Centre, http://www.johnes.org/. Content by Dr Michael Collins and Dr Elizabeth Manning.

[16] Study Confirms genetic links to Johne's disease resistance, Dr Colin Mackintosh, Deer Industry News, Issue 43, August/September 2010

[17] Dr Richard Whittington, Personal Communication, September 2010

Appendix: Submissions

Contents

Email correspondence regarding Test and Cull as a Management Procedure

From: Kaylene Larking [mailto:Kaylene.Larking@beeflambnz.com]
Sent: Friday, 6 August 2010 12:15 p.m.
To: Buddle, Bryce; c.heuer@massey.ac.nz; Mackintosh, Colin; Collins, Des; Crawford, Allan; Frank Griffin; DeLisle, Geoff; hvoges@lic.co.nz; Rory O'Brien; rspelman@lic.co.nz; Wilson, Peter; Hein, Wayne
Subject: JD test and cull

Team,

The JDRC board are interested in current thinking about the use of "test and cull" as a management procedure for the control of Johne's disease in New Zealand. If you would like to comment for the board could you please reply to me by email by Friday 03 September 2010. All responses will be included in a report to the JDRC board that will be tabled for the October board meeting. I would also be interested in any recent publications with information on the topic that you consider valuable.

Kind regards

Kaylene

1. Response from Dr Des Collins, AgResearch

From: Collins, Des [mailto:Des.Collins@agresearch.co.nz]
Sent: Monday, August 09, 2010 4:28 PM
To: Kaylene Larking
Subject: RE: JD test and cull

Hello Kaylene

The book I edited on Paratuberculosis contained 3 chapters on control measures in USA, Europe and Australia. All three chapters give some insights into "test and cull" and anyone who is serious about understanding this approach should at least have read these.

Des Collins

2. Response from Dr Bryce Buddle, AgResearch

From: Buddle, Bryce [mailto:bryce.buddle@agresearch.co.nz]
Sent: Monday, August 09, 2010 3:11 PM
To: Kaylene Larking
Subject: RE: JD test and cull

Hi Kaylene

In response to your request, enclosed are some comments about the use of "test and cull" as a management tool based on results from our current study.
Regards
Bryce

Comment on a "test and cull" strategy for control of Johne's disease in cattle
As part of our contract for the Johne's Disease Research Consortium we have been monitoring peripheral blood immune responses in naturally-infected cows and experimentally-infected calves. A total of 24 naturally-infected cows were selected principally on the basis of a positive serological test and 22 of the 24 cows had a positive serological test. *Mycobacterium avium subsp. paratuberculosis* (MAP) was isolated from gut tissues of all animals. All of the sero-positive animals were scouring, had body scores of 1-3 and had moderate to severe histopathological lesions. The animals were culled mid-lactation or at the end of the lactation due to poor milk production. The two serological negative animals had body scores of 3 and had been culled from Johne's disease infected herds due to poor milk production. These two

animals had no distinct histopathological Johne's disease lesions and no acid-fast bacilli were identified in gut sections, although MAP was isolated from gut tissues. These results indicate that serological tests will detect moderate to severely infected cattle, but not necessarily animals at an earlier stage of infection.

In a second study, 5-8 week old calves were experimentally infected with MAP to study early stage immune responses and to establish a reproducible experimental model to determine the validity of gene markers for disease resistance/susceptibility. MAP was isolated from the faeces of 19 of the 20 experimentally infected calves between 2 to 4 months post-challenge, while no MAP were isolated from the faeces of the 11 control calves. Serological responses were negative in all calves at 0, 2, 4 and 6 months post-challenge indicating that antibody is not a reliable indicator of early MAP infections. Peripheral blood cellular immune responses were detectable from 5 of 20 experimentally-infected calves at 5 months post-challenge and from 19 of 20 at 7 months post-challenge. Cellular immune responses such as the release of interferon-gamma from MAP-stimulated blood cultures can detect infected animals earlier stage than serological tests but do not identify infected calves when they first start shedding MAP. The cellular immune assays are considerable more expensive than serological tests. It is important to state that the calves were only shedding low numbers of MAP at 2-4 months post-challenge.

In summary, serological tests can be used to identify moderate to severely MAP-infected cattle which should reduce contamination in the environment and reduce the likelihood of infection of young calves. However, serological tests or even cellular assays will not identify animals at the early stage of infected so cannot be used to eradicate the disease.

Bryce Buddle 9 August 2010
Principal Scientist
AgResearch, Hopkirk Research Institute

3. Response from Massey University

From: Heuer, Cord [mailto:C.Heuer@massey.ac.nz]
Sent: Saturday, August 07, 2010 3:38 PM
To: Kaylene Larking
Cc: Wilson, Peter; lindsay.burton@fonterra.com
Subject: RE: JD test and cull

Your inquiry obviously calls for a response from our group. The two supporting pieces of evidence support my points. The underlying simulation model is described by Groenendaal et al. Prev.Vet.Med 54:225-45 (2002).

1. Test&cull have so far never been financially attractive for JD control in dairy cattle (attached references).
2. The graph below shows the simulation results from our model which was adapted to NZ dairying conditions in a PhD completed in 2007 (Norton et al.), the modified Groenendaal model. The cost:benefit discounted over 20 years is on the x-axis (NPV = net present value); the y-axis is the prevalence of MAP infection after 20 years adjusted for test inaccuracy ('True prevalence'). The simulation evaluated various test&cull strategies with/-out management practices aiming at reducing exposure of calves to infection (early cow/calf separation, calving hygiene, individual calf pens).
3. The bottom line of test&cull from this study: none of the test&cull based control strategies had a positive economic outcome. Bi-annual faecal culture and early removal of offspring (MO) reduced prevalence close to zero while still returning negative return to investment. The only strategy with a positive NPV was management + vaccination (not shown).
4. The abstract pasted further below is a reference for similar results in NL.
5. The fundamental problem with T&C is that the currently available tests are either not sensitive enough, too expensive and taking too much time (FC), or insensitive AND producing false positives (ELISA), hence too many uninfected animals need to be replaced: replacement is very costly since every replacement costs a new born calf + 2 years of rearing.
6. The current challenge therefore is to develop and evaluate better tests. An opportunity exists with the faecal PCR: we know it has a short turnaround time (1-3 days) – and if a positive PCR reliably identifies high shedders (and is negative for low shedders and non-infected animals), then it may become economically viable by only picking the animals that have the greatest impact on the prevalence in the herd.
7. Remember the discussion we had in our last teleconference: Otago's PCR was said to 'correlate well with the Paralisa, so we do not need a PCR since the Paralisa is cheaper, fast and accurate'. Rory sent me his data 15 minutes after the conference to substantiate the point made by Geoff DL. However, the data clearly demonstrated that 40% of all samples with high Paralisa results (>100) were PCR negative or very low shedders. In a real life herd, this poor

prediction would become even worse because the prevalence of high shedders would be a lot lower than in this set of selected samples with a high rate of shedders. Hence, there is currently no evidence that neither Paralisa (deer) nor an ELISA (sheep, cattle) has any merit for positive economic returns when used for T&C. I made that point in more detail in an email to Lindsay a day after the tele-discussion.

8. Last point: we therefore propose to study animals (deer, cattle, sheep) from an early age up to death or culling to verify whether any test (Elisa, Paralisa, PCR) has any good predictive value for high shedders at any advanced age or state of infection (JDRC years 3-5). A necessary pilot for that is the comparison of culture and PCR on available samples. This is the justification for the PCR study proposal.

Massey University

Submission

to

Johne's Disease Research Consortium

August 2010

Test and cull as a management procedure for the control of Johne's disease in New Zealand

T

By: Professor Peter Wilson and Associate Professor Cord Heuer
Institute of Veterinary, Animal and Biomedical Sciences
Massey University
Palmerston North

A submission in response to the call for opinion from the JDRC, August 6, 2010

1. Preamble

Test and cull has been applied to the control of some diseases of livestock, such as tuberculosis. However, there are limited examples where test and cull alone has been successful in eradicating disease because of epidemiological, logistical and economic considerations. Targeted test and cull may have applications other than eradication, such as reducing the impact of disease by removing high-shedding hosts, recovering value of animals which are predicted to proceed to become clinically affected or fatal cases, and decreasing the risk of transmission of disease between farms by live animals by sale/transfer of test negative animals only.

It is tempting to advocate test and cull for paratuberculosis in livestock. However, decisions should be based upon full understanding of the potential reasons for test and cull, and clear and thoroughly researched criteria, including epidemiology, bacteriology, pathobiology, economic impact and the role of alternative strategies. Adoption of test and cull should be preceded by simulation modelling to estimate its effectiveness in each species, and for each purpose. It is apparent that more robust estimates of disease and infection prevalence would be required to ensure that models are robust.

2. Potential reasons for test and cull

2. Eradication of disease
- Herd, regional or national level

3. Management targeted to minimise the spread of disease within and between farms
4. Management within farm to minimise the economic impact
5. Market requirements
- Export markets imposing tariff or non-tariff trade barriers on live animals and/or products
- Local markets for live animals (stud and commercial) as being "free" of disease

3. Requirements for successful test and cull schemes

The appended paper provides background to the criteria for a successful test and cull programme. ("**Factors of importance for test and slaughter approaches to disease control and management"** by C Heuer, PR Wilson, to be published in CERVETEC2010, the proceedings of the conference of the Deer Branch NZVA, 2010.)

3.1 Eradication of disease

The criteria for eradication using a test&cull strategy are:

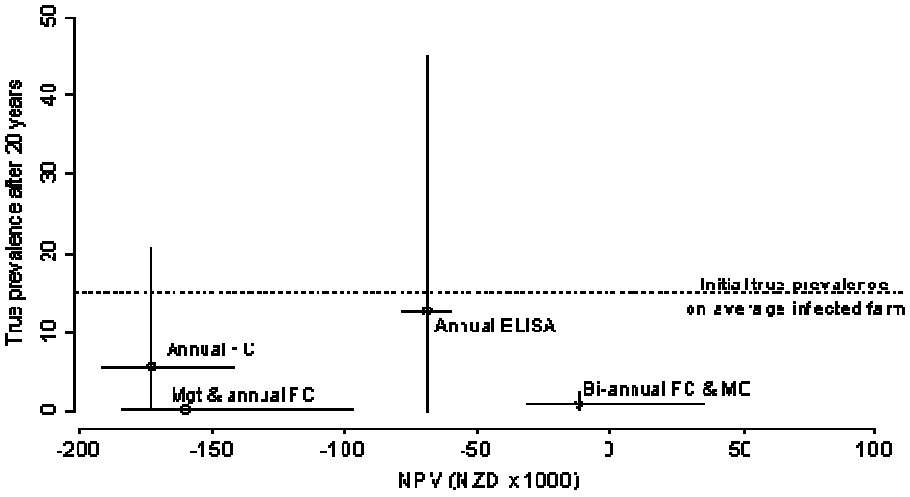
- The pathogen is undesirable at national level due to concerns about food safety, or at herd level due to continued economic loss.
- Highly sensitive tests are required
    - Which detect a high proportion of clinically and sub-clinically infected animals
    - Which are capable of accurately determining the disease-free status of replacements
    - That are validated for all livestock hosts (given the multi-species nature of NZ farming)
- Highly specific tests are required
    - which minimise wastage of uninfected animals
- The disease is causing or could potentially cause greater economic losses than the cost of eradication
    - Costs include replacements, lost production, lost genetics, and the cost of testing *per se*
- The organism does not survive for long periods in the environment (note: this is one of the more important features of paratuberculosis to consider in relation to eradication, since Ptb has a long survival time in the environment under optimum conditions)
- An infection prevalence that is low enough to justify eradication
    - Current evidence suggests the infection prevalence of Ptb in livestock in NZ and elsewhere is high (i.e. >50% of herds and flocks)
- There is no reservoir in wildlife species that can transmit the disease to livestock
    - Or that it is controllable in those wildlife hosts
    - Or that those hosts can be eradicated
- The "drivers", i.e. the market for live animals and/or product, are real and justified
- Alternative means of control are not effective or cost-effective as a substitute for eradication
    - E.g. vaccination, management factors, environmental factors, genetics for resistance

None or few of these factors are consistent with the known biology, diagnostics, economics or epidemiology of infection and disease associated with paratuberculosis in farmed livestock in New Zealand.

Furthermore, there is no example anywhere in the world in any species where eradication of paratuberculosis has been successful or cost-effective in either pastoral or intensive farming situations. Of particular relevance is the experience with ovine JD in Australia where attempts were made to eradicate the infection in a pastoral environment, but without success.

Further supporting comments:
The underlying simulation model is described by Groenendaal et al. Prev.Vet.Med 54:225-45 (2002).

9. Test&cull has so far never been financially attractive for JD control in dairy cattle (attached references).
10. The graph below shows the simulation results from our model which was adapted to NZ dairying conditions in a PhD completed in 2007 (Norton et al.), the modified Groenendaal model. The cost:benefit discounted over 20 years is on the x-axis (NPV = net present value); the y-axis is the prevalence of MAP infection after 20 years adjusted for test inaccuracy ('True prevalence'). The simulation evaluated various test&cull strategies with/-out management practices aiming at reducing exposure of calves to infection (early cow/calf separation, calving hygiene, individual calf pens).
11. The bottom line of test&cull from this study: none of the test&cull based control strategies had a positive economic outcome. Bi-annual faecal culture and early removal of offspring (MO) reduced prevalence close to zero while still returning negative return to investment. The only strategy with a positive NPV was management + vaccination (not shown).
12. The abstract pasted further below is a reference for similar results in NL.



Preventive Veterinary Medicine 60 (2003) 69–90
Development of the Dutch Johne's disease control program supported by a simulation model

Huybert Groenendaal a,b,∗, Mirjam Nielen a,
Jan Willem Hesselink c
a *Department of Farm Management, Wageningen University, P.O. Box 9101, 6700 HB Wageningen, The Netherlands*
b *Center of Animal Health and Productivity, School of Veterinary Medicine, University of Pennsylvania, New Bolton Center, 328 W. Street Road, Kennett Square, PA 19348 1692, USA*
c *Animal Health Service, P.O. Box 9, 7400 AA Deventer, The Netherlands*

Abstract
The development of a simulation model, 'JohneSSim', was part of a research program aimed at designing a national Johne's disease control program for The Netherlands. Initially, the focus was mainly directed towards different compulsory 'test-and-cull' strategies. However, the results from the JohneSSim model showed that eradication of Johne's disease based on such strategies would not be possible within 20 years and that it was also economically unattractive. However, improved calf management seemed to be more effective in reducing the prevalence within the same time period. Simulation of a strategy using an 'ideal test' (80% sensitivity in all infected animals)
showed a considerably faster decrease in prevalence. However, this strategy proved to be economically unattractive because of the high culling rate of (young) test-positive animals. The simulation model was also adapted to study beef cow herds. However, the results indicated that none of the strategies were able to reduce the mean true prevalence to almost zero for such herds. Only strategies based on 'separation of calves and adult animals' proved to significantly reduce the prevalence but such a
strategy is unpractical and uneconomic for Dutch beef cow herds. Due to this finding and the relative low number of Dutch beef cow farms, first priority has been given to the development of a Johne's disease control program for dairy farms. Based on the results of the 'JohneSSim' model, the new national voluntary Johne's disease control
program for dairy, Paratuberculosis Program Netherlands (PPN), started in September 2000. The PPN is based on a stepwise improvement of calf hygiene, with little dependency on 'test and culling'. The model results indicated that, if dairy farmers consistently carried out the necessary management adaptations, PPN considerably decreased prevalence and that it was economically more attractive than any previous plans.
Recommendation: *Our submission is that it is not feasible, either currently or in the foreseeable future, to consider a test and cull strategy for eradication of paratubercuolsis in any livestock species New Zealand.*

3.2 Management targeted to minimise the spread of disease within and between farms

Disease can spread within and between farms by movement of livestock between farms, by environmental contamination via waterways and run-off, and potentially by wildlife, assuming that transmission can occur via that pathway.

Criteria for justifying and minimising spread of infection include:

- Proof that transmission occurs via the environment
- Proof that wildlife play a significant role in the transmission of infection
- A test or tests that are highly predictive of transmission, either via faecal shedding of organisms, of vertical (*in-utero)* or pseudo-vertical (via milk) transmission.
- This format of control may be economically justified in dairy herds (Groenendaal et al 2003 (see above)

No evidence is currently available that render any of these criteria as valid and applicable to paratuberculosis in farmed livestock situations in New Zealand, or elsewhere.

3.3 Management within farm to minimise the economic impact

Including clinical and/or subclinical losses.

Test and cull may play a role in minimising the impact of clinical and subclinical paratuberculosis. This approach aims at eliminating the impact of disease rather than eradicating it. This could be realised under the following conditions:

- A highly sensitive and predictive test is available
    - A test detecting all animals that will become clinically diseased or lose production with a high level of confidence, within the testing interval
    - A test that accurately identifies animals that may exacerbate the transmission of infection at levels that will cause clinical disease in herd- and flock-mates i.e the so-called "multi-bacillary" of "super-shedders"

    - A test identifying breeding animals that will pass infection to progeny via *in utero* or pseudo-vertical transmission.
- Demonstration that economic losses justify the cost of interventions
    - And that alternatives to test and cull are not as cost-effective
    - The cost of the intervention include replacements, lost production, lost genetics, and the cost of testing *per se*
- Replacement animals can be reliably determined as not at risk of disease
    - This requires that factors precipitating disease of subclinical losses are known, can be predicted, and can be eliminated
- Sufficient research has been conducted to determine the effectiveness and cost-effectiveness in different circumstances, to provide likelihood estimates that this approach will or will not work.

In the case of paratuberculosis, these criteria cannot be met currently for any livestock species, and significant research input into understanding the biological parameters would be needed to validate this approach to paratuberculosis control. Theoretically, the strategy most likely to be feasible would be the detection and culling of super-shedders, once it is established that horizontal transmission is the most important route.

Understanding the economic impact of infection and disease are critical to a test and cull strategy. Currently insufficient economic data are available for any livestock species in New Zealand.

One fundamental problem with T&C is that the currently available tests are either not sensitive enough, too expensive and taking too much time (FC), or insensitive AND producing false positives (ELISA), hence too many uninfected animals need to be replaced: replacement is very costly since every replacement costs a new born calf + 2 years of rearing.

The current challenge therefore is to develop and evaluate better tests. An opportunity exists with the faecal PCR: we know it has a short turnaround time (1-3 days) – and if a positive PCR reliably identifies high shedders (and is negative for low shedders and non-infected animals), then it may become economically viable by only picking the animals that have the greatest impact on the prevalence in the herd.

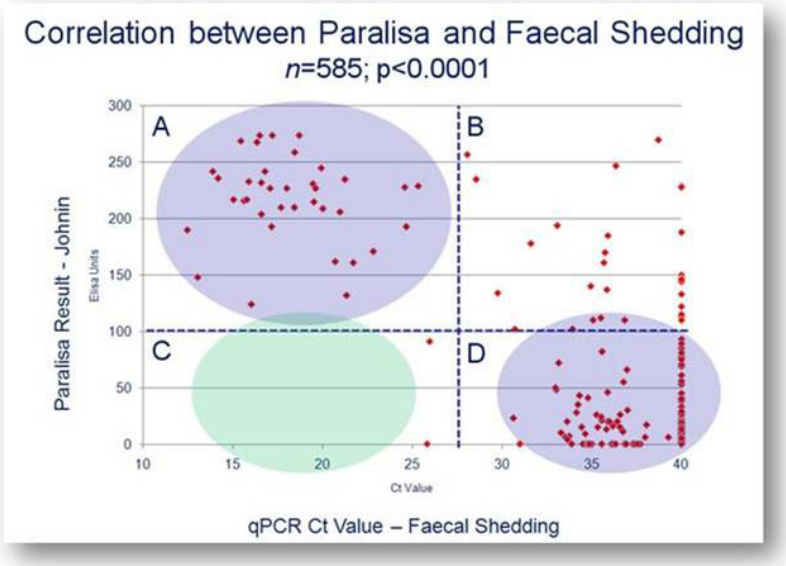
4. General comment

It is understood that some deer farmers are currently practising a test and cull policy, and that there is anecdotal information that this is successful. However, there is no researched data to that effect, and indeed, there are examples including those based on personal experience of one of the authors (PRW), that this approach has not been successful in reducing the prevalence of infection, at least in a herd with a low incidence of clinical disease. Anecdotal information from other farming and veterinary sources supports this observation. Recent research at Massey University demonstrating that 45% of deer were infected, as determined by lymph node culture, and that more than 60% of herds are likely to be infected suggests that a test and slaughter strategy is unlikely to be successful in this species in many circumstances. It remains to be determined what situations this strategy could be economically successful.

Lack of prevalence data in sheep and cattle industries, and lack of sensitive validated tests hampers understanding of the disease, and limits our ability to begin to predict the economic impact or cost-benefit off testing regimes in those species. However, it is unlikely that even the availability of highly sensitive tests will be cost effective in test and cull policies on most farms, and then may be cost effective only in identifying the most contagious animals.

Discussion during the last JDRC science provider teleconference included that Otago's PCR was said to 'correlate well with the Paralisa, so we do not need a PCR since the Paralisa is cheaper, fast and accurate'. Rory O'Brien sent his data 15 minutes after the conference to substantiate the point made by Geoff DL (figure below). However, the data clearly

demonstrated that about 40% of all samples with high Paralisa results (S/P>100) were PCR negative or very low shedders. In a real life herd, this poor prediction would become even worse because the prevalence of high shedders would be much lower than in this set of selected samples with a high rate of shedders. Hence, there is currently no evidence that either Paralisa (deer) or an ELISA (sheep, cattle) has any merit for positive economic returns when used for T&C. This point has been made in more detail in an email to Lindsay Burton a day after the tele-discussion.



The point of discussion was that a PCR wasn't required because Elisa tests can predict shedding quite as well. Looking at the upper horizontal half of the plot, there are 37 correct and 25 incorrect Paralisa predictions of high PCRs, resulting in a predictive value of 37/62 (60%). If used for culling, 40% Paralisa>100 would be light or negative shedders, thus removed and replaced due to low specificity for the purpose of identifying high shedders. In this dataset, the proportion of shedders is much higher than can be expected in even a heavily infected herd. In a situation with a lower prevalence of shedders, the PPV would decrease further.

Massey data from non-infected or sub-clinical dairy cows look like this (4 herds, 3 years, Norton et al):

		Culture		
		pos	neg	total
ELISA	pos	24	17	41
	neg	57	2000	2057

Even though the specificity of ELISA against culture is much higher than Paralisa against PCR in your data, the PPV is just about the same 24/41 (58%), and this is due to the low prevalence of MAP infection among these cows. The Kappa value (0.37) shows that there is only poor to moderate agreement between the tests. Again, the ELISA can't be used to predict shedding. The bottom line therefore is that the PCR has great potential as an alternative to ELISAs or culture.

The Massey group therefore proposes to study animals (deer, cattle, sheep) from an early age up to death or culling to verify whether any test (Elisa, Paralisa, PCR) has sufficient predictive value for high shedders at any advanced age or state of infection, i.e. whether the test can predict the infection, shedding or disease outcome for an animal or the herd (JDRC years 3-5). A necessary pilot for that is the comparison of culture and PCR on available samples. This is the justification for the PCR study proposal.

5. Conclusion

It is the opinion of the writers that there is little or no justification for consideration of test and cull for eradication on a farm, national or regional scale in any livestock species.

Test and cull may have benefits for the management of disease on individual deer farms with high clinical disease incidence, and if the subclinical impact of infection can be demonstrated to justify the intervention. This is provided the predictive value of Paralisa and PCR in terms of identifying "multi-bacillary shedders" is validated robustly. Additionally, more robust data is needed in terms of the sensitivity of the Paralisa in sub-clinically infected animals, and the predictive value of that test in determining which animals become clinical cases, or lose production sub-clinically. Current research at Massey University suggests that the sensitivity of the Paralisa is around 20% for the purpose of identifying sub-clinically infected animals ***(Note: This study has only just been completed so it is requested that the data remain confidential to JDRC until we have completed discussion with the Otago University Disease Research Laboratory).***

Tests currently available for management of the infection in sheep or cattle have similar sensitivity as the Paralisa. Thus the sensitivity of presently available tests is insufficient to justify their use in a test and cull strategy at the individual herd/flock level. Furthermore, given the extent of the unknowns about the infection in those species, and the biological difficulties with control, it is questionable whether investment into development of tests for these species would be economically justified.

13. Recommendation

If JDRC gives further consideration to test and cull, it is recommended to undertake detailed modelling to evaluate the required test specifications for various strategies for each livestock species. This would take into account all the issues raised above, and provide guidance as to the likelihood of biological and economic effectiveness in each, for different purposes.

Note: It would be necessary to research robust data on clinical disease prevalence in each species, and also the subclinical infection prevalence in sheep and cattle since that data is currently lacking.

4. Response from Dr Amanda Bell (phone conversation)

As a veterinary advisor for Johne's disease management Dr Bell considers test and cull as a useful tool in the management of Johne's disease but it must be coupled with experience and knowledge. Culling of animals on the basis of testing alone in isolation from other information gathered regarding herd and animal status, should never be considered.

- The JML veterinary network recommend gross level application of test and cull and trains their vets to have a rudimentary level of understanding about the procedure
- The paraElisa is not a definitive test for Johne's disease
    - paraElisa test should never be quoted as a positive/negative reading alone but should always have a number assigned to them for interpretation.
    - There is a gap in understanding regarding what paraElisa results actually mean, but broadly speaking Dr Bell has happy there is sufficient evidence that very high paraelisa results correlate to high shedders. ParaElisa results can be banded; rough bands are >100 animals to be concerned about, 50-100 possibly suspect, <50 no concern.
    - It is noted that animals that have ParaElisa results above 120-150 are inevitably shedding and should likely be culled even if they are not sick due to the risk they present to the herd. At anything less than 120 it is not known if an animal without symptoms would progress to clinical disease or would be resistant to developing disease and an asset to the herd. Animals should therefore not be culled on the basis of the paraElisa test number alone. A lot of other information would be considered before a management strategy was recommended.
- Other important factors which must be considered before deciding which management strategy to employ include:
    - Death rates
    - Environmental factors
    - Time of year
    - Prevalence rates in different classes of animals on a property
    - regarding test and cull
- Regarding the use of alternative tests it is noted that:
    - Blood PCR may be useful for expensive animals, but is costly and will not be widely used
    - There is little benefit in Faecal culture for on farm testing for the status of Deer in the field. It is costly compared to ParaElisa and will inevitably find MAP. In addition farmers do not like collecting faecal samples.

5. Response from Dr John Aitken

RESEARCH INTO MYCOBACTERIUM PARATUBERCULOSIS INFECTION

OVERVIEW

If a graph were to be plotted showing expenditure on Johne's disease in New Zealand over the last ten years, and this were to be compared to a graph showing rate of infection against a similar period, both graphs would likely show a similar upward trend.

This trend can be interpreted in a number of different ways, but in general such an observation would indicate that expenditure so far has not resulted in control of disease spread.

Understanding of virulence of the agent is also lacking, and some researchers have made the assumption that Mycobacterium paratuberculosis (MAP) is highly conserved and all strains will have similar virulence characteristics. Other studies on pathogenic bacteria (ie TB, Staph aureus, E.coli) demonstrate the fact that the microbial world is in constant change, generally driven by selective pressure, and resulting in major variations in pathogenesis and virulence within species.

It is also important to note that disease presentation seems to be more severe in deer than in cattle, so there may also be evolutionary changes in the various hosts.

In an infection control model, these changes are not directly relevant, as Johne's Disease (JD) is now prevalent throughout New Zealand and rates appear to be increasing. The main priority now is to control spread and contain the outbreak as far as possible. Eradication is a secondary goal.

EPIDEMIC SPREAD

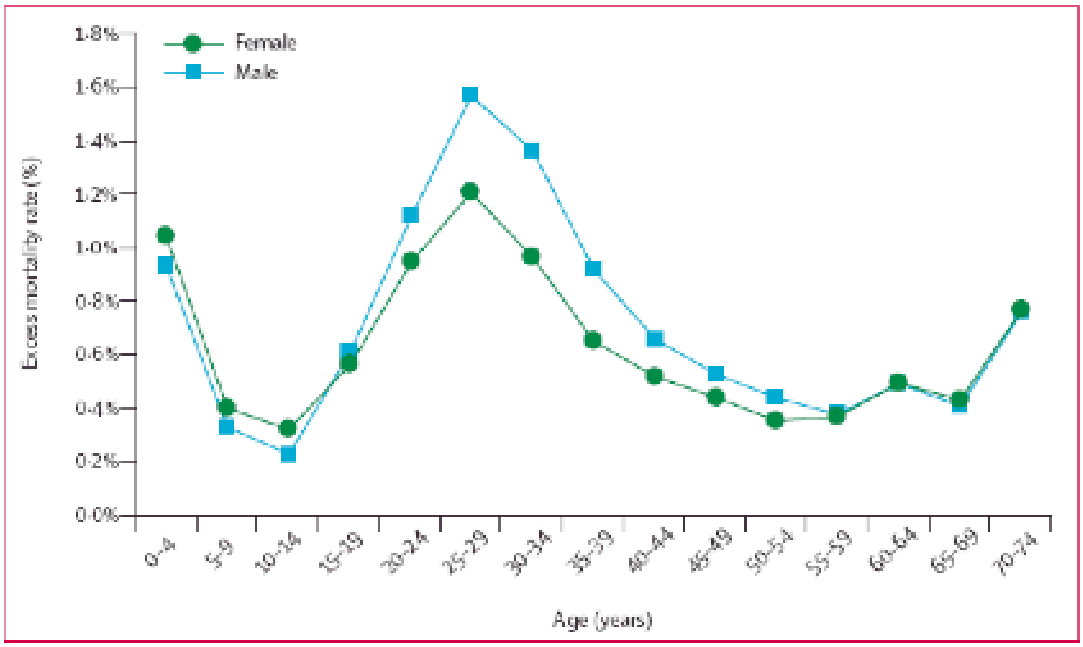


Figure 1: Median excess mortality by age and sex for the 1918–20 pandemic, based on data from 13 countries with available complete age-specific mortality data

The above graph shows a typical trend for an infectious event. As the outbreak spreads there are more opportunities for an individual to contract the disease, hence the accelerating rate of infection in the mid-stage of the outbreak.

A graph of acquisition rates for JD will indicate where New Zealand farmers are in terms of JD infection. I suspect that the curve will be accelerating, although this is uncertain, as no precise definition of JD infection has yet been established. This is known as the "Blind men looking at the Elephant" phenomenon. Each person will appraise the situation in terms of their own particular perspective.
To plot accurately the rate of infection, a set of definitions is a basic requirement for any epidemiologist.
Tracking rates of infection is essential to judge the impact of any intervention. Implementation of measures without tracking outcomes is pointless.
Time is of the essence, and rapid responses will be needed. A nationally driven and controlled study is probably not required, and may take too much time.

GOAL

The ultimate purpose, or aim of the endeavour should be clarified. If there is a goal to control JD in New Zealand, then this is much easier that trying to eradicate the disease.
Some researchers maintain that MAP is ubiquitous in animals in NZ. If this is correct, then that is strong evidence for different virulence determinants amongst MAP strains. The more virulent strains may be causing outbreak events, while the less virulent strains may confer a degree of protection. This is hypothetical, and largely irrelevant, but does indicate the need for a new approach to diagnosis.

Despite a great deal of money being poured into Mycobacterium paratuberculosis infection in New Zealand, the definition of what constitutes a case of Johnes disease remains elusive.

DIAGNOSTIC TESTING

What constitutes a reliable test? Medical laboratories are well practiced in judging the effectiveness (sensitivity and specificity) of tests in real-time. This is because their patients are in a position to voice complaints, and mortality rates can be readily interpreted by the media and reported to the public.

As an example, the HIV epidemic is a good model.
The first step was to identify the causative agent and then develop a test to identify probable carriers. (ELISA)
Identification of the agent quickly led to an understanding of the mode of transmission. This led to safe-sex guidelines. These were initially implemented locally without national coordination.
The problem of false positive ELISA tests was solved by the availability of PCR, which was used to confirm the presence of HIV virus. Later adaptations of PCR utilised quantitation of virus particles to track treatment.

That experience shows the approach to an infectious disease outbreak is multi-factorial.

1. Screening.

A test is required to identify potential carriers. This should be pre-mortem

2. Confirmatory

A test is needed to confirm the presence of the infection using a fundamentally different target. One of the problems at the moment is that both the skin test and the antibody tests target the same immune response.

3. Control.

There are several requirements for animal interventions. The two main requirements are a reliable, accurate and cost effective test regime, and a farm-based intervention related to the situation on the individual farm. Geographical and environmental factors are variable and local solutions will be more readily adopted.

Interruption of transmission.

With MAP infection the moment this is elimination of the animal based on the test result.

If this approach was adopted by public health authorities, the flaws would quickly become apparent.

In the case of both TB and HIV, the infectious curve was already declining because of public health interventions before the discovery of antimicrobial treatments The deer industry will need to quickly develop industry-relevant practical and cost-effective interventions on a local basis.

SPECIFIC TESTS

- Clinical

It is always true that the primary test for disease status is to look at the host. Clinical examination is key to test and cull. If the animal is showing the symptoms associated with extensive shedding then cull, and cull quickly.

- Culture

Culture is a reliable indication of Mycobacterium paratuberculosis carriage.

A positive faecal culture will, however, not indicate disease status, as carriage is common and shedding may be intermittent. The culture test takes 12 weeks to complete, and time is often a factor in infection control. The use of broths is not quantitative, despite the enthusiasm shown by some advocates. Rate of growth of Mycobacterium species is dependent on a number of factors, including strain type, decontamination regime, shedding status, etc

- ELISA

The problems with serological diagnosis of mycobacterial disease in humans and animals are well described. As infection progresses, immune status of the host animal may change. Individuals with overwhelming human TB infections may manifest negative skin testing as a result of the “swamping” of the immune system. Carriage of related Mycobacterium species may confound the antibody signals and result in false positive reactions. Skin tests are subject to similar caveats

- PCR

PCR of faeces is unreliable, as carriage of MAP may occur in animals with no symptoms, normal clinical appearance, and an absence of disease.

Quantitation of MAP in faeces via PCR is also unreliable, because of the tendency to intermittently shed bacilli in subclinical animals. A positive PCR test, may however, indicate presence of MAP, and this may be important in a herd, or in an animal recently imported onto a farm that is currently JD clear.
PCR is more expensive than other tests, and should provide more value, however cost-effectiveness is a primary governor on usage. (resource utilisation control)
And this is yet to be examined.
PCR of peripheral blood is much more useful, and has the additional advantage that if the test is positive, haematogenous spread (rather than carriage) is more likely. It may be useful in the control of breeding stock.
Given that culture has a long turnaround time, PCR can also be useful in the validation of screening and confirmatory tests where these are required quickly.

- Biomarkers

These are used extensively in the diagnosis of human disease as an adjuvant to clinical examination, serological tests, and PCR. They are cheap, add additional valuable clinical perspective and are a interim step before PCR is contemplated. Their use in animal pathology is largely unexplored.
We have been working in this area in conjunction with other scientists affiliated with our group.

LIFE CYCLE OF MAP

A precise understanding of the modes of transmission in animals in New Zealand would considerably advance efforts to control JD. Once a model is defined, then testing of the hypothesis using standard infection control interventions will provide insights into methods of control. We have developed a model for MAP transmission, and have been trialling interventions in order to understand relationships of specific control measures to outcomes.

SUMMARY

- An accurate case definition is required
- Mode of transmission needs to be understood in terms of an outbreak model and farmers need to be educated on controls available to prevent spread.
- Any approach must have the ability to measure outcomes.
- Tests currently available are either insufficiently reliable or expensive
- Interventions on the farm are piece-meal throughout the country

DIRECTIONS

- Much of what has been done so far has been directed at estimating, either directly or indirectly, the extent of the problem. New initiatives should focus on interventions. Measurement of the extent and magnitude of the problem will not, by itself, reverse the trend.
- We are exploring the transfer of technical delivery from human to animal health, and have carried out pilot studies on different approaches to diagnosis.
- Research initiatives should be measured against performance goals, set by industry, not the researchers
- Environmental control at the farm level should be a top priority for research.

- Research projects should be coordinated and be under central industry dominated control.
- Interpretation of diagnostic tests without clinical input is not useful
- Outcome measures should be defined and related to interventions to assess performance.

There is an old saying “Never mistake motion for action”
Our approach so far has been to form technical and clinical teams and act quickly at a local level.

6. Response from Dr Solis Norton, Johne's Management Limited

From: solis norton [mailto:solis.norton@johnes.org.nz]
Sent: Thursday, September 09, 2010 9:45 AM
To: Kaylene Larking
Subject: RE: JD test and cull

Hi Kaylene,

My thoughts on the use of test-and-cull as a method of control for JD in farmed animals (not specifically deer).

Test-and-cull methods for the control of JD are a valuable tool but won't lead to acceptable levels of control if not combined with on-farm management techniques. Testing and removing positive animals from the herd is the ideal way of tackling the worst of the problem (tip if the iceberg) and reducing the rate of contamination as a consequence. But this technique is limited by test sensitivity and inevitably becomes uneconomic at some point as prevalence decreases. It is only through careful on-farm management and observation over time (with further testing of suspect animals) that the subclinically infected animals missed by the test will be removed and the contamination rate driven down still further.
Driving down the contamination rate to a point where there is less than one new infection for each existing infection indicates that the disease transmission rate is less than one and this puts us on a path to eradication, in theory. Either way, control should be considered a multi-year plan since short term or half hearted attempts will almost certainly fail.

I think the key on-farm management techniques besides testing are maintaining a closed herd, testing any animals that must be brought into the herd, minimising the exposure of young animals to the main sources of MAP like faeces (and milk??), and being aware of other potential sources of MAP.

I'm sure the attached article will have been covered in the literature review you spoke of but I'll send it up all the same. I think it captures the essence of the limitations of control based solely on testing and the benefits of management and while the figures presented are probably indicative of the truth, they won't be perfectly accurate.

I think the website http://www.johnes.org/general/control.html captures my view (with the possible exception of the milk bit) well: "Protect your young stock by making sure they don't swallow milk, water or other feed that contains MAP from adult manure. Find and remove infected adult animals to keep your premises free of MAP contamination."

Hope this is of some help, I'm happy to expand on any points if you would like.

Regards –

Solis Norton
BAgSci, MApplSci, PhD (Veterinary Epidemiology)
Project Manager, Johne's Management Limited (JML)
541 Castle street, PO box 6475, Dunedin 9059

Phone: 03 4740506 Mobile: 027 5552882 Freephone: 0800456453
email: solis.norton@johnes.org.nz

7. Response from Dr Colin Mackintosh, AgResearch

Submission to JDRC re use of "test-and-cull" as a management procedure for the control of Johne's disease in NZ

Colin Mackintosh, BVSc, PhD. AgResearch Invermay

Introduction
"Test-and-cull" is traditionally used to eliminate infected animals from a herd or flock of animals and is dependent on a test or tests that is/are sensitive and specific for infection and is cost-effective. For example "test-and-cull" has been effective for eliminating tuberculosis from most cattle and deer farms in New Zealand. It relied on a skin test using bovine tuberculin (PPD), which primarily measures cell-mediated immunity and detects infected animals very soon after challenge, it is quite sensitive and moderately specific, and is relatively inexpensive.

Paratuberculosis eradication
In the case of paratuberculosis there are no tests that are comparable to skin testing for tuberculosis. Skin testing for paratuberculosis is not specific enough because of widespread sensitization to avian tuberculosis, which antigenically very similar to MAP. Individual faecal culture is not sensitive enough and is quite expensive. No antibody tests are sensitive enough for eradication. Therefore test-and–slaughter is not currently feasible.

Paratuberculosis Control
Cattle: Test-and-slaughter may be used as a control measure to reduce production losses due to paratuberculosis. For example in the USA faecal smears, quantitative faecal culture and qPCR are being used to identify supershedders in some herds, in order to reduce the level of environmental contamination and therefore the rate of spread within herds. This is either from individual screens of cattle or from initial pooled faecal samples and then individual cultures of animals within pools showing high counts. ELISA tests have also been used in dairy herds on the basis that, although the sensitivity is not very high, it is detecting animals that are the most heavily infected.

There is increasing desire to reduce the level of infection and environmental contamination on dairy farms in light of the possible link between MAP and Crohn's disease in humans. If the link is proven then there will be increased pressure to minimize the level of infection in herds by culling the most heavily infected animals.

Deer: In New Zealand the Paralisa test has been shown to be very useful for removing the most heavily infected animals, because there is a good correlation between level of antibody response and the severity of the disease in the animal. Similarly it has been shown that there is a positive correlation between high Paralisa

antibody levels and number of MAP organisms in faeces as detected by qPCR and "time to positive" in the BACTEC culture system. It has also been shown that a high proportion of Paralisa positive pregnant hinds have infected foetuses due to intra-uterine transmission. Thus culling deer with high antibody levels is an effective means of reducing the transmission of MAP on farm. The use of the Paralisa appears to be most cost-effective in herds where there is a high incidence of clinical Johne's disease, especially in young animals. This is because the hinds are infecting the young deer either in utero, or from infected milk, or from close grazing between hind and calf. The elimination of the most heavily infected hinds, which are Paralisa positive, appears to dramatically reduce the incidence of clinical disease in the next crop of weaners and lowers the prevalence of infection in the replacement hinds.

The cost-effectiveness of the Paralisa in deer herds is dependent on the existing incidence of clinical disease, the seroprevalence in the herd, environmental and management factors, the value of the stock (especially if they are stud animals, and the risk-aversiveness of the individual farmer. It is up to each farmer, his advising veterinarian and the laboratory to undertake a risk/benefit analysis for each farm and undertake the most appropriate control programme.

In some cases it may be cost-effective to use qPCR or culture on faeces to identify animals that are shedding and cull all of them or perhaps the most serious shedders.

Sheep: It is probably not cost-effective to use test-and-slaughter to aid in the control of Johne's disease in sheep flocks unless there is a high incidence of disease and the animals are of high value.

References to support this submission can be supplied.

8. Response from Livestock Improvement Corporation

From: pback@lic.co.nz [mailto:pback@lic.co.nz]
Sent: Friday, September 03, 2010 2:25 PM
To: Kaylene Larking
Subject: Fw: JD test and cull

Hi Kaylene,

Hinrich and I have had a quick chat re this email that was sent out. Unfortunately H is currently away so I have bullet pointed our thoughts. He will be back week starting 27th Sept if you have any questions for him.

- Does testing add any benefit when we know the limits of the test as it currently is?
- What value is there with the cost of having to do ongoing screening?
- Could predominately be controlled in dairy herds with management rather than testing - particularly focusing on separation of calves from areas where mature stock is run from birth is crucial.
- Identification of super-spreaders to reduce bug load and potential risk of infection - farmers are used to this concept with controlling BVD so could be used with JD?

Dr Penny Back
Project Manager R & D
Private Bag 3016 (Cnr Ruakura & Morrinsville Roads, Newstead)
Hamilton 3240 NEW ZEALAND
Ph: 07 856 0801
Fax: 07 856 0640
Web: www.lic.co.nz