JOHNE'S DISEASE
RESEARCH CONSORTIUM

ANNUAL REPORT 2011

CONTENTS

GLOSSARY:

AgR	AgResearch Limited
B+LNZ	Beef + Lamb New Zealand Limited
DCANZ	Dairy Companies Association of New Zealand
DNZ	DairyNZ Limited
ELISA	Enzyme Linked Immunosorbent Assay
JDRC	Johne's Disease Research Consortium
JML	Johne's Management Limited
JRG	Johne's Research Group
LIC	Livestock Improvement Corporation
MAP	*Mycobacterium avium paratuberculosis* – the bacterium that causes Johne's disease
MIA	Meat Industry Association
MSI	Ministry of Science and Innovation
Paratuberculosis (PTB)	Another name for Johne's disease
TLR	Toll-like Receptor
UJV	Unincorporated Joint Venture

JDRC REPORT

The Johne's Disease Research Consortium (JDRC) was established in 2008 as a joint venture between Industry and the Science community to coordinate Johne's disease research in New Zealand. The participants in the Unincorporated Joint Venture are Beef + Lamb New Zealand Limited (B+LNZ), DairyNZ Limited (DNZ), DEEResearch Limited, AgResearch Limited (AgR), Livestock Improvement Corporation (LIC), Massey University, University of Otago, Meat Industry Association (MIA), Dairy Companies Association of New Zealand (DCANZ) and the Ministry of Science and Innovation (MSI). JDRC has an annual budget of $1.7M and receives industry funding from its participants and matching funding from the MSI Research Consortia funding scheme.

The Consortium focuses on research "behind the farm gate", with the goal of developing practical tools which can be applied to produce a cost effective reduction of herd/flock and within herd/flock prevalence of Johne's disease on farm in New Zealand. JDRC contracts research services from New Zealand's leading science providers and maintains an industry focused research programme through interaction with its industry participants.

The JDRC Research Programme runs until June 2013, when both industry and government funding for the initiative will end for the current cycle of activities.

THE DISEASE

Johne's disease (or paratuberculosis) is a chronic, contagious and often fatal infection of cattle, sheep, deer, goats and wildlife caused by the bacterium *Mycobacterium avium subspecies paratuberculosis* or MAP, estimated to cost New Zealand $40-88 million annually[1]. The disease causes an autoimmune reaction that thickens the intestinal wall of an animal resulting in reduced ability to absorb nutrients, leading to wasting and ultimately death by starvation. Animals usually become infected with MAP at birth and once infected can remain "sub-clinical" with no signs of disease for a number of years. Infected animals shed the organisms in their faeces, contaminating the environment and propagating infection amongst a herd. There is currently no recognised treatment and diagnosis of disease, particularly in sub-clinical animals, is difficult.

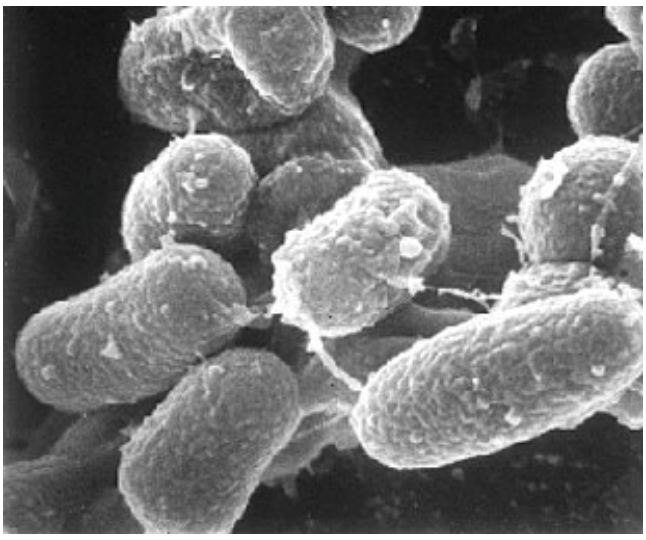
JDRC SCIENCE

The JDRC science programme has 4 major focuses: improving diagnostics, understanding the fundamentals of the disease, investigating genetic resistance to Johne's disease and disease epidemiology.

JDRC is 3 years through its 5 year programme and is at the point where tangible research outcomes are now being delivered for industry partners. An international science review has confirmed the quality of the research programme output and has provided direction for the remaining years of the programme to assure JDRC remains on target to deliver practical outcomes for farmers from the research investment.

JDRC DELIVERY

The Consortium facilitates the delivery of its scientific outcomes through its participant organisations. An important objective for JDRC in the remaining period is the development of industry wide best practice guidelines for the control and management of Johne's disease in New Zealand. JDRC is working with the Deer Industry, utilising their existing resources, to develop these guidelines across all species to provide consistent messaging for those working in the field.



[1] Brett, 1998, Johne's Disease: an economic evaluation of control options for the New Zealand livestock Industries.

HIGHLIGHTS

Landcorp Farming Limited joined JDRC as a Research Investment Partner in 2011. Landcorp is contributing both research funds and on-farm resources to the JDRC research programme.

International Science Review JDRC and the Ministry of Science and Innovation held a joint review of the science programme in 2011, hosting 4 international science experts in Wellington for the 3 day event.

SCIENCE HIGHLIGHTS

PUBLICATION OF NZ PREVALENCE DATA

Understanding the prevalence and impact of the disease on production performance is strategically valuable for New Zealand.

JDRC results suggest 72% sheep, 48% beef, >60% dairy & 47% deer farms estimated to be infected with MAP and 18% sheep, 4% beef, 22% dairy & 34% deer farms show farmer observed signs of clinical disease.

ANALYSIS OF NZ MAP STRAINS

Strain type data provide information regarding sources of infection and spread of disease.

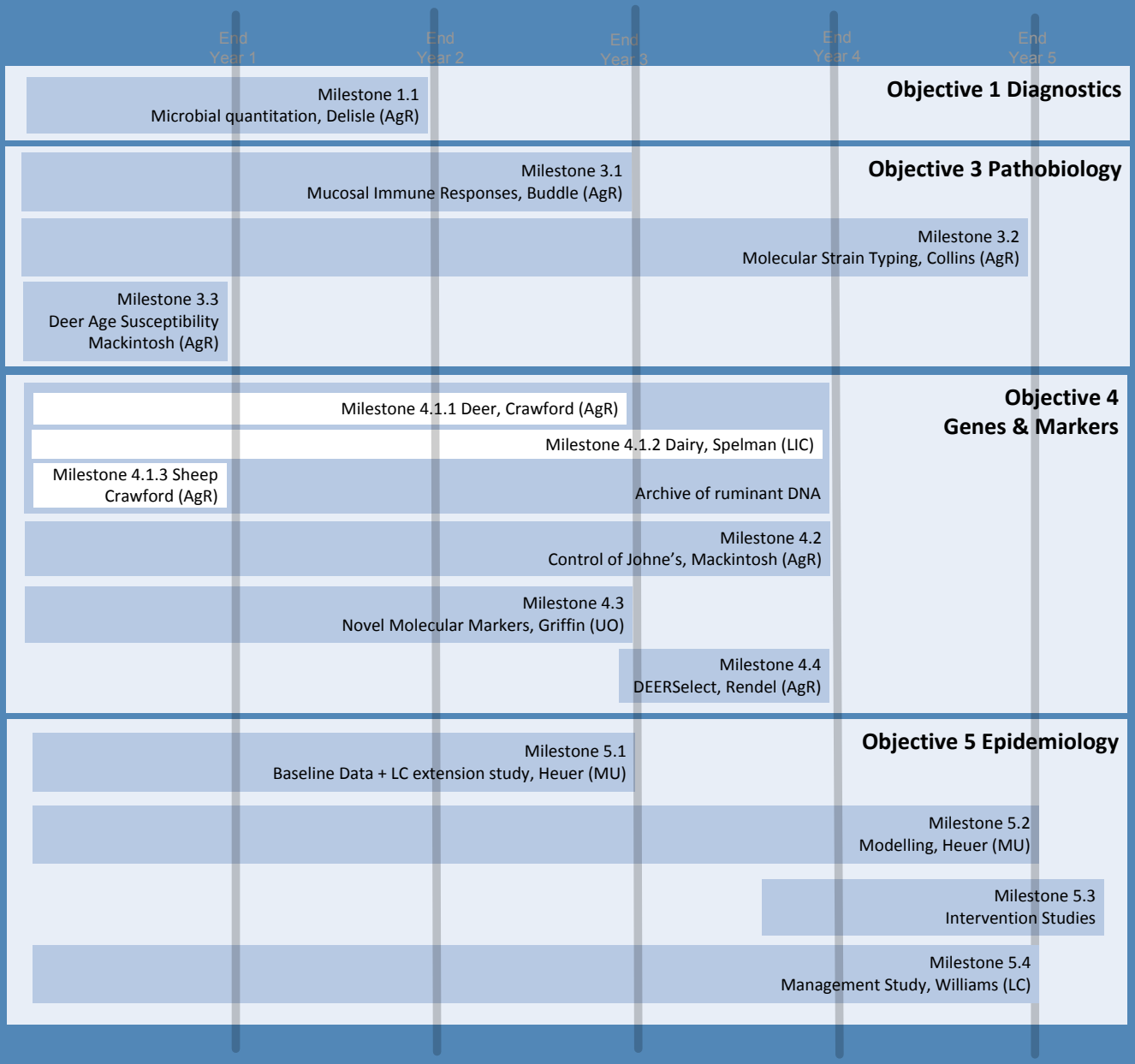
Two type C substrains and one type S sub strain of MAP were found to be responsible for the majority of infections in NZ ruminants

PARAMETERS FOR DIAGNOSTIC TESTS

Knowing the limits of diagnostic tests provides insight about when diagnostic tests should be applied and interpreting results.

Research suggests that serology and faecal culture based assays, while highly specific, have poor sensitivity and are of limited value for the early stage detection of JD in both deer and cattle.

JDRC'S SCIENCE PROGRAMME



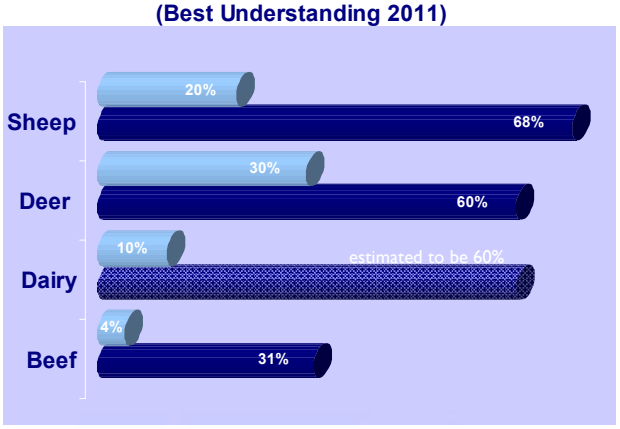
THE PREVALENCE OF JOHNE'S DISEASE

Providing an accurate estimate of the prevalence of Johne's disease in New Zealand is a critical component in understanding the steps needed to control and manage the disease. In addition to JDRC's own prevalence surveys, in June 2011 JDRC commissioned Mark Bryan of VetSouth Limited to review and benchmark the prevalence of Johne's disease in New Zealand. The review draws its findings from peer and non-peer reviewed papers, material not in the public domain and interviews of key figures involved in the study of Johne's disease in New Zealand.

The review concluded that the prevalence of Johne's disease was poorly defined and only "best estimates" of herd and within herd prevalence could be made. It is not possible to define a data set with greater accuracy due to the lack of standards for measuring and defining the disease and limitations associated with MAP diagnostic tests. Diagnostic limitations are perhaps the most influential. Tests lack sensitivity and/or specificity while some are expensive or impractical. There is also no "gold standard", a diagnostic test which correctly identifies 100% of MAP infected animals. Without a gold standard it is difficult to establish the known infection status of a population. Social pressures have also influenced the collection of data. Under the Stock Act Johne's disease was notifiable from 1931 to 2000 and there are suggestions that the disease was under reported to avoid a real or perceived stigma associated with a positive diagnosis and its impact on the ability to trade stock. To some extent this perspective still exists in some areas today.

The most comprehensive and robust prevalence data for New Zealand livestock comes from the Johne's Management Limited (JML) analysis of lymph nodes of deer at slaughter and the JDRC funded prevalence survey undertaken at Massey University from 2008-2011. These studies suggest that MAP infection is widespread and therefore it may be that detection of the bacteria may not be as important as understanding the levels of clinical disease in the livestock population and determining what factors trigger an animal's transition from subclinical infection to increased shedding and the manifestation of clinical disease. Patterns in the literature suggest that clinical Johne's disease is present at fairly low levels in New Zealand but that there is a significant tail of the population in all species where within herd prevalence (and incidence) is particularly high. Within these tails there is likely to be significant economic loss and also the greatest risk of transmission of MAP both within and into new herds and across into the food chain. JDRC research outcomes in 2012-13 are intended to bring some clarity to the understanding of the economic impact of Johne's disease in New Zealand.

HERD LEVEL PREVALENCE
(Best Understanding 2011)



JOHNE'S DISEASE IN CATTLE

The gastro-intestinal tract is the major site of infection for MAP yet few studies have been directed towards this anatomical location. In a three year study concluded in 2011 AgResearch investigated the hypothesis that MAP subverts responses in the gut immune system to ensure its survival in the host. This was found to be the case. In the study of both naturally and experimentally infected adult cows and calves severity of disease was associated with a disregulated immune response and a failure in the immune system to recognise MAP as foreign, specifically by the Toll like receptors TLR1 and TLR2, proteins which are responsible for initiating effective immune responses to the invasion of pathogens. The study has provided valuable information on markers to identify MAP infection at early and late time-points in the disease which may aid genetic studies and have application in the development of new diagnostics.

The study has also highlighted the limitations of common diagnostic tests for the early stage diagnosis of Johne's disease in cattle. In the early stage of infection immune assays (used primarily as a research tool) indicated that cattle were infected with MAP, but none of these animals were positive by common serological tests (e.g. ELISA). Serology only proved effective in the advanced stages of disease. Culture also proved to be of limited value in early stage detection as while animals showed a severe initial response on exposure to MAP, the severity of lesions, number of animals with MAP in their tissues and shedding of MAP in faeces decreased markedly after the initial infection phase. These results indicate there is limited value in testing for Johne's disease infection in young cattle using current technologies.

STRAIN TYPING

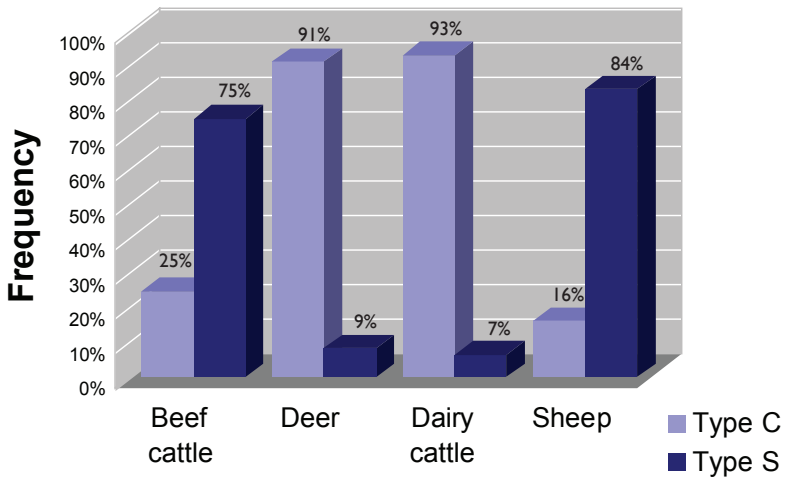
The ability to distinguish between different strains of a pathogenic bacterial species provides a basis for answering important questions about sources of infection and spread of disease and enables potential variation in pathogenicity of different strains to be more easily investigated.

Over the past three years AgResearch has developed technology to improve the ability to type strains in New Zealand. While there are two major strains of MAP, Type C and Type S, there are up to 20 sub-strains of Type C and 8 sub-strains of Type S MAP in New Zealand. In 2010-11 isolates from approximately 350 dairy, beef, sheep and deer isolates were typed using the assay, revealing previously unknown patterns of MAP strain infection in New Zealand. Historically, Type S strains were expected to come mostly from sheep and occasionally from deer and Type C strains were expected to come from cattle or from deer. The analysis has provided strong evidence that MAP is transmitted between species as a substantial number of cattle were infected with Type S strains and sheep were infected with Type C strains. Significantly, beef cattle were found to be predominantly infected with Type S strains perhaps due to intensive direct contact between sheep and beef cattle on farms. As beef cattle have notably lower rates of clinical disease than dairy cattle, which are predominantly infected with Type C strains, researchers are questioning the role of strain type in determining disease outcomes, for example is there a difference between virulence, innate resistance or immune response with differing strain types?

Other patterns noted in the data were:

- Clearly different Type C sub-strains circulating in dairy cattle than those Type C sub-strains circulating in deer
- A demonstrably different strain type profile between the North and South Islands
- A small number of samples containing more than one strain type, indicating that on some farms animals can be infected on more than one occasion, bringing an increased infection pressure in these herds and flocks.

STRAIN DISTRIBUTION



APPLYING THE KNOWLEDGE

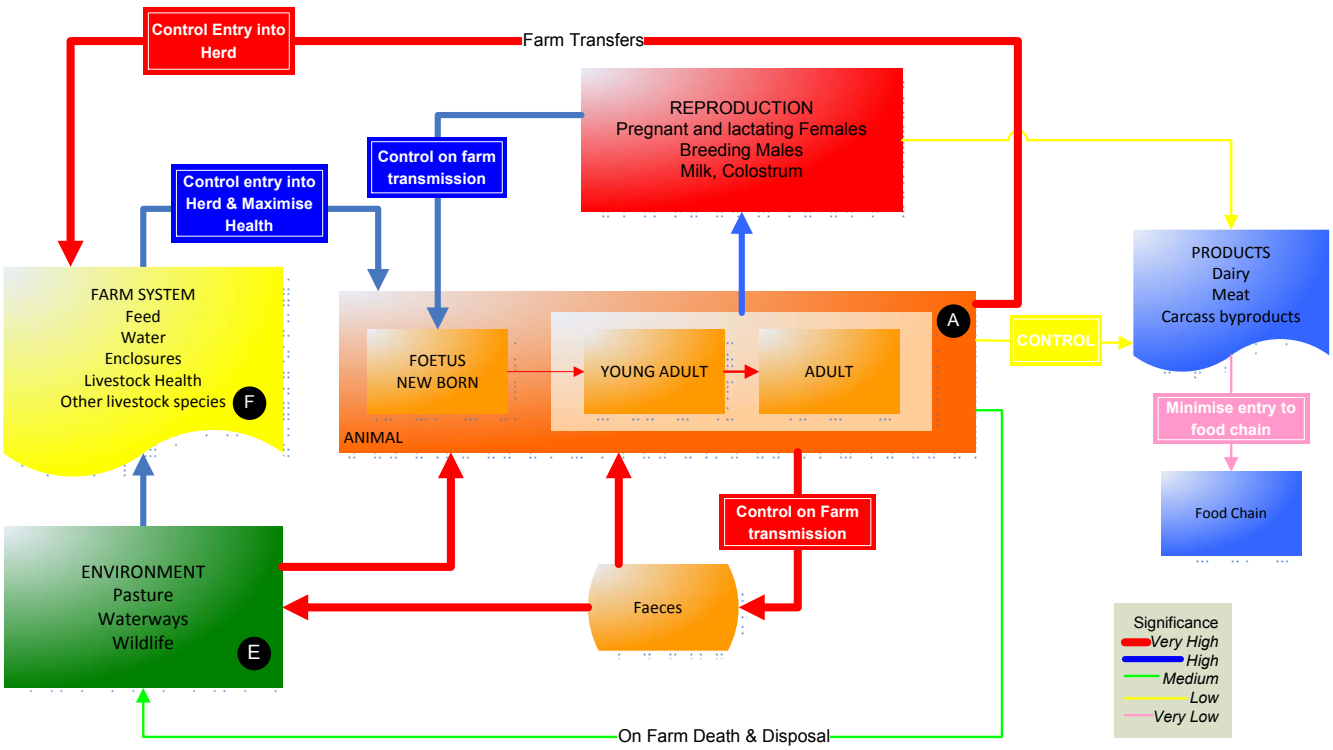
While there are still many unknown factors in the understanding of Johne's disease and its effective control and management in farm systems, the body of knowledge about the disease continues to grow and it is possible to establish a group of controls which will assist in minimising its impact on farm.

To that end, JDRC is developing resources, in conjunction with the Deer Industry's Johne's Research Group to provide practical disease control and management guidelines for Johne's disease for all ruminant species in New Zealand.

The MAP transmission diagram is a starting point in this process. It illustrates known transmission routes for the bacteria and where we understand, with varying degrees of influence and confidence, points at which we can control its transmission. Control is achieved by minimising transmission of the bacteria via these routes to reduce the impact of the disease on farm.

Three major factors have been identified as techniques for reducing the impact of MAP; controlling on-farm transmission, preventing entry of the disease into the herd and maximising herd/flock health. Within each of these categories is a schedule of actions which can be tailored for a specific livestock species to achieve maximum control over transmission in differing farming situations. JDRC is working on developing these schedules as best practice guidelines for distribution to industry.

The MAP Transmission Diagram



JDRC FINDINGS AND ACHIEVEMENTS 2008-2011

The incidence of Johne's disease shows regional variations in New Zealand, affecting deer and cattle most severely in the South Island and sheep in the North

DNA Databases have been established for deer and dairy cattle in NZ, providing resources for the development of tools for breeding animals resistant to JD.

Over 5000 dairy herds have been screened for Paratuberculosis by bulk vat milk ELISA; 1% herds were test positive and 5% herds classified as suspect

Jersey cows are three times more susceptible to Johne's disease than Holstein-Friesians

Trials have proven that young deer are more likely to develop clinical disease on exposure to challenge with MAP than older animals

National survey data indicate that both clinical and sub-clinical JD have economic consequences; in deer decreased pregnancy and weaning rates have been noted

Lists of genes have been generated which may be potential markers for signalling resistance or susceptibility to JD in cattle and deer

A reliable challenge model for inducing MAP infection in dairy cattle has been developed, traditionally an area of difficulty for researchers worldwide

Resistant and susceptible phenotypes in deer may be distinguished by the nature of their gene expression response to MAP challenge in vitro

On-farm trials suggest that resistance to JD in deer maybe highly heritable and that a proportion of deer with histopathological symptoms (lesions) can self cure

Co-grazing of livestock species effects the incidence of disease; e.g. clinical disease in one species on farm influences the likelihood of disease occurring in another species on farm

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CONSORTIUM MANAGEMENT

MS KAYLENE LARKING

JOHNE'S DISEASE
RESEARCH CONSORTIUM

For further information please contact:

Kaylene Larking
Consortium Manager
Johne's Disease Research Consortium (JDRC)
04 494 9503
Level 4, Wellington Chambers
154 Featherston Street
Wellington 6140
New Zealand
info@jdrc.co.nz | www.jdrc.co.nz

agresearch DairyNZ DEERresearch LIC Massey University beef+lamb new zealand University of Otago