Questions and Confusion surrounding Johne's Disease

What is Johne's Disease ?

Johne's disease is a chronic inflammatory bowel disease that causes wasting and deaths in domesticated ruminants and it is found worldwide in cattle, goats , deer and sheep. The disease is caused by infection with *Mycobacterium avium* (subspecies) *paratuberculosis* (MAP) which belongs to the group of organisms that cause tuberculosis (*Mycobacterium bovis*).

How is the disease manifest ?

Infection with MAP may be present for prolonged periods before clinical disease is manifest. Sheep, goats and cattle do not normally develop clinical disease until they are 2-3 years old while deer may develop clinical disease within the first year. This has important ramifications for animal production as meat producing animals that have late onset disease may reach target slaughter weights without being impacted on by MAP. MAP becomes a more important issue in these animals as it can impact on reproduction and meat recovery from adult animals. In the case of deer, where there is early onset disease, MAP becomes a more important confounder as it may affect young animals used for venison production. Normally only a very small proportion of animals infected by MAP develop clinical johne's disease ("The Iceberg Effect" for infection) so many farms that are infected by MAP are unaware of its presence, unless there is a significant outbreak of clinical disease. Outbreaks of disease may occur if there are groups of animals that are uniquely susceptible because of a specific genotype or if there are environmental stressors (nutritional, environmental. Consequently, disease may be more evident in stud herds, when there is an aggregation of specific genotypes in purebred animals, rather than in outbred production herds.

Can Johne's Disease or MAP infection be diagnosed accurately ?

We now have serological tests (*Paralisa*^{TM}) that can accurately identify infected and diseased animals, and molecular techniques (*PCR*) that can precisely estimate the numbers of bacteria in gut tissues or faecal samples. These diagnostic techniques can be used cost effectively to eliminate disease and control infection within affected herds or flocks, when MAP is present. We also have accurate histological tests that can estimate the presence and severity of disease in individual animals. Current technology allows for the control of infection at a herd level and identification of seriously diseased animals that shed large numbers of bacteria ("supershedders")

Is there a risk that diseased animals could contaminate the food chain ?

There is a high risk that diseased animals will have contaminated carcasses and meat products obtained from these animals will contain MAP. As supershedders may contain more than 10^8 of bacteria per Gm of faeces, the risk of environmental contamination and spread of MAP Animals that contain low grade MAP infection are unlikely to produced contaminated meat products. Overall diseased deer tend to shed higher numbers of MAP

than cattle or sheep so the risk of environmental or carcase contamination with MAP may be greater then for other farmed ruminants. While our laboratory initially attempted to develop diagnostic assays that would identify the maximum number of infected animals, our view now is that the majority of infected animals shed no bacteria or low numbers (10^4) and these animals can be retained within the herd, providing "supershedders" are removed. This is particularly relevant when testing high value stud animals, where low shedders do not pose a problem for disease spread, yet they may represent a resilient group, that can contain infection and will not progress to disease.

Why would MAP infection within a herd be of concern ?

While MAP infection may produce clinical Johne's disease in a small proportion (<5%) of animals, subclinically infected animals that harbor significant levels of infection may be affected and have impaired growth rates or reproductive efficiency (both lowered by 10%). In a recent group of hinds tested on a seriously infected commercial deer farm, we found 12% reactors in pregnant hinds and a 45% reactor rate in a matched mob of dry hinds.

Animals with clinical Johne's disease present a much greater challenge for the farmer and meat processor, for the following reasons:

1. There is a welfare issue allowing food producing animals to progress to develop a chronic wasting disease, in conflict with NZs "Clean' Green, Happy animal" image.
2. No clinically affected animal should **ever become part of the food chain**, because of the risk of carcass contamination with MAP, and the contingent loss in meat quality. There can be a significant loss of capital stock, that may compromise farming viability on seriously affected farms. Ideally all subclinically affected animals should be culled before they develop chronic wastage and pose a threat to the food chain.

Is MAP in the food chain a health hazard ?

While there is NO significant scientific study that Proves a link between MAP and human disease there are numerous studies that show an association between MAP and Crohn's disease in humans. While my personal view is that the jury is out, we must be careful to ensure that "Absence of evidence" is not used as "Evidence of absence". The striking observations that are based in science are:

1. Crohn's disease (CD) in humans has identical pathology to Johne's disease (JD) in animals, apart from the onservation that one can see bacteria in JD but not in CD.
2. Numerous published have shown bacterial genes specific for MAP are present in gut tissues and blood from CD patients.
3. The liklelihood of isolating MAP from humans with CD is 8-12 times higher than normal controls.
4. There is convincing scientific evidence from many international studies the MAP is found in association.
5. Ten years ago, scientists who claimed there was a link between MAP and CD were regarded as 'cranks', whereas now they are now considered 'mainstream'.

Points that argue against MAP causing CD are:

1. Gastroenterologists worldwide generally do not claim that MAP causes CD.
2. Nobody has yet found the smoking gun that links MAP causally with CD. This will be difficult to ever prove unequivocally , unless we directly infect human subject with MAP; which is the standard scientific method to establish a causal link between a specific organism and a human disease. This experiment is unlikely to receive Ethical approval.

Should we be concerned about MAP as a human health hazard ?

YES – because the marketplace is driven by 'perception', rather than 'reality', and science has established the association between MAP and CD, in many independent studies.

It's a 'no brainer', that there should be strategies to control MAP infection in domestic livestock because of the coalescence of multiple risks, involving animal welfare, farming efficiency and food security.

Strategies to control MAP infection in domestic livestock ?

1. Lab diagnostics can be used to control MAP at a herd level, but while they are cost-effective they are expensive and must be used continually as while they control disease they do not eradicate MAP.
2. Vaccines are not an option because of their limited efficacy and interference with routine TB control schemes.
3. Selection for heritable resistance provides a future option that if used in tandem with diagnostics could result in complete containment, and roll back of MAP infection in domestic livestock.

What is the evidence for heritable resistance or susceptibility to infectious disease ?

1. For more than 200 years there has been clear evidence that susceptibility to infection is heritable in animals and humans.
2. For the past 50 years there has been evidence that resistance to infection is heritable.
3. Extensive genomic studies carried out over the past 20 years show that susceptibility/resistance involves multiple genes (10-100).
4. We have recently shown that susceptibility to MAP infection involves specific cell systems affected by multiple genes.

How come we have found breeds of deer that have polarized resistance or susceptibility to MAP, when others have been less successful studying cattle and sheep ?

1. We have been able to access unique pure breeds of deer from Pell Forest Estate where the founder genetics has remained pure and likely contains a high proportion of homozygotes.

2. The fact that Peel Forest has a serious outbreak of MAP infection that lasted for a decade has allowed us to indentify polarized breeds that are either susceptible or resistant to MAP.
3. The widespread use of ET gives confidence that the phenotypes are due to the genotype of the individual rather than different rates of exposure to pathogens.
4. We have established that R or S phenotypes are highly heritable in progeny from R or S stags.
5. We have recently characterized the genes (cell systems) that result in the S phenotype.
6. **We desperately need research funding to characterize the genes that result in the R phenotype. If no money is forthcoming all research will cease at the end of 2012.**

We believe that deer are an ideal generic model to discover the critical genes and cells systems involved with heritable resistance, that will not only relate to MAP infection but other infectious disease.

Selection for disease resistance will become one of key the traits included in next generation progeny testing of livestock that will involve Multi-trait selection systems. Do we continue or leave it to somebody else who has the funding ????

Apologies that this is a rough unedited draft. I am happy to clarify any issues that may arise.

Frank Griffin (31/08/12)