

Living With Johne's Disease

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Continuing our focus on diseases of importance on your farm, Dr Philip Hywel Jones, veterinary expert on Johne's disease gives some answers to frequently asked questions about the disease.

What is Johne's disease?

Johne's disease (or paratuberculosis) in cattle is a chronic wasting disease which is characterised by chronic, long-term diarrhoea and weight loss. On post-mortem examination, the terminal part of the small intestines (ileum) typically shows severe thickening. When viewed under a microscope, the same region of the intestines shows loss of structure and large numbers of red-staining (acidfast) bacteria can be seen within the tissues. Figures 1 and 2 show the microscopic appearance of normal intestines and intestines taken from an animal with Johne's disease.

Johne's disease occurs all over the world. The disease causes considerable economic losses to the dairy industry due to reduced milk yield and increased culling of infected animals. A recent study indicated that approximately 1.5% of dairy herds in England and the Welsh borders had had at least one clinical case of Johne's disease during both 1993 and 1994. Clinical cases of Johne's disease, however, only represent the tip of the iceberg – at any given time, many animals are infected with the causative organism but they may not develop clinical signs of the disease for several years.

What causes Johne's disease?

Johne's disease is caused by a bacterium called *Mycobacterium avium* subspecies *paratuberculosis* or, more simply, *Mycobacterium paratuberculosis*. This organism grows very slowly and, in the laboratory, takes at least three to four months to isolate. In contrast, most other bacteria, such as *E coli*, take a mere 18-24 hours to grow. Under natural conditions, *M paratuberculosis* is unable to multiply outside the host but it is able to survive in the environment for periods in excess of one year. The organism has a waxy cell wall which makes it relatively resistant to physical factors such as heat, cold, sunlight, etc and to many of the commonly used disinfectants.

Which animals are most likely to show signs of the disease?

All breeds of cattle are susceptible to Johne's disease although Channel Island breeds seem to have a higher predisposition to the condition than other breeds. Clinical signs of the disease generally develop when cattle are two to five years of age. There is some evidence to suggest that stressful events such as calving and high milk yield can trigger the development of clinical signs although the mechanism for this effect is not fully understood.

How do you know if an animal has Johne's disease?

The clinical signs of Johne's disease in cattle are characterised by chronic diarrhoea and weight loss. Animals showing clinical signs can shed large numbers of *M paratuberculosis* in the faeces resulting in considerable contamination of the local environment. In advanced stages of the disease, cattle may develop 'bottle jaw' (sub-mandibular oedema) because the plasma protein concentration is reduced as a result of the diarrhoea. In the terminal stages, animals become debilitated and eventually die. There is no evidence to suggest that animals can recover spontaneously once they have become infected.

Can animals carry the infection without being obviously clinically affected?

Cattle become infected with *M paratuberculosis* during the neonatal period but do not show clinical signs of Johne's disease until they are several years old. Following infection, animals typically go through three distinct stages. In the first stage, animals are infected but do not shed the organism in the faeces. In the second stage, animals shed the organism in the faeces but do not show clinical signs. Finally, in the third stage, animals shed the organism in the faeces and show clinical signs. The numbers of organisms shed by subclinically infected animals are considerably lower than clinically affected animals but the subclinical phase of the disease can last for several years without being detected. Furthermore, the organism can survive for many months, if not years, in the environment. As a result, subclinically infected animals are likely to represent a significant source of environmental contamination.

The epidemiology group at the University of Liverpool examined the extent of subclinical infection in the UK in a recent study. Abattoir samples were taken from cull cows and young cattle and examined for the presence of *M paratuberculosis*. None of the animals was showing clinical signs of Johne's disease at the time of slaughter. The results indicated that 3.5% of cull cows and 2.0% of young cattle were subclinically infected with the *M paratuberculosis*.

Can animals other than cattle carry Johne's disease?

Johne's disease generally occurs in ruminants such as cattle, sheep, goats, deer and camelids. In sheep and goats however the disease is not associated with diarrhoea. Furthermore, in sheep, the presence of a thick fleece can hide the dramatic weight loss which occurs in clinically affected animals.

Isolated cases of Johne's disease have also been reported in pigs, horses and non-human primates and *M paratuberculosis* has been isolated from rabbits. The strains of *M paratuberculosis* that occur in sheep tend to be more difficult to isolate than the strains that occur in cattle. However, DNA studies have found no differences between the strains that occur in cattle, sheep and goats. In addition, some studies have identified infections in sheep and goats that were grazing with infected cattle. At present, it should be assumed that transmission of *M paratuberculosis* can occur between different species.

How do cattle catch Johne's disease?

Experiments have shown that adult cattle are relatively resistant to infection with *M paratuberculosis*. Young calves, however, are susceptible and can become infected whilst in the uterus or by ingesting the organism during the neonatal period. In practice, the most important mode of transmission is the oral route. Adult cattle infected with *M paratuberculosis* shed the organism in colostrum, milk and faeces. Neonatal calves can, therefore, become infected by suckling an infected dam or by ingesting bedding or other material which is contaminated with faeces from an infected animal.

Can you treat the disease successfully in sick animals?

Treatment of Johne's disease is possible but is generally not very effective. Several antibiotics have been used to treat Johne's disease but infected animals require long term treatment which, in most cases, is not economically viable. In addition, treated animals may continue to shed the organism after the start of treatment and, therefore, continue to be a potential source of infection. Treatment of Johne's disease should only be considered in extremely valuable animals and when isolation facilities are available.

Does treatment eradicate the infection?

At present, the drugs used to treat cases of Johne's disease merely control the clinical signs rather than produce a definitive cure.

Does your understanding of the infective process help to construct control programmes?

The ingestion of contaminated faeces by young calves is the most important method of transmitting Johne's disease. As a result, control measures should aim to block this route of infection. Adults that are shown to be infected with *M paratuberculosis* should be removed from the herd regardless of whether or not they are showing clinical signs. It is important to remember, however, that laboratory tests will not identify all infected animals. Infected animals that are not shedding the organism at the time of the test will inevitably start doing so at a later date. Subclinically infected animals do not shed as many organisms as animals showing clinical signs but they may be responsible for a considerable degree of environmental contamination. Furthermore, the organism is able to survive for long periods in

the environment. As a result, it is important to prevent calves coming into contact with faeces from adult animals and to prevent calves having access to areas of the farm where adult animals have been kept. Calving should take place in a clean environment and calves should be removed from the dams as soon as practically possible. A recent study in the UK identified that offering hay to young calves had a protective effect against Johne's disease – this effect may have been produced by reducing the amount of time that calves spent chewing contaminated bedding. It is also worth considering culling calves that are subsequently shown to be from infected dams. A calf that suckles an infected mother is at a very high risk of becoming infected but evidence of the infection may not be identified for several years. On balance, it may be worth culling the calf at an early age.

Is vaccination an appropriate part of control?

Vaccination against Johne's disease does not eliminate infection from a herd although it has been shown to reduce the occurrence of clinical signs and to reduce faecal shedding of *M paratuberculosis*. As a result, vaccination may help to limit the economic losses associated with Johne's disease but it should be used in conjunction with, rather than instead of, other control measures.

M paratuberculosis is very closely related to the organism that causes avian tuberculosis (*M avium*). The compulsory intradermal skin test used by MAFF to control bovine tuberculosis in the UK uses tuberculin from *M avium* as the negative control. Vaccination against Johne's disease can, therefore, affect an animal's response to the intradermal skin test. As a result, any farmer who wishes to vaccinate his herd against Johne's disease requires permission from MAFF.

Are the tests for the infective agent completely sensitive, or is it possible to have animals carrying the disease organism which test clear?

Several tests are available to identify whether an animal is infected with *M paratuberculosis*. The tests either look for the presence of the organism directly or measure the animal's immunological response to the organism. Culturing *M paratuberculosis* from faecal samples is considered to be the best means of positively identifying an animal that is infected with the organism. However, the organism grows very slowly and it can, therefore, take several months to obtain the results of the test. More recently, a technique Polymerase Chain Reaction (PCR) has been developed which can identify the DNA from the organism. This test is much more rapid but the process can be inhibited by the presence of faeces. Several other tests are also available which look for the presence of antibodies against *M paratuberculosis* in blood samples.

None of the tests described above is able to detect all infected animals in a herd. The main problem arises because the disease develops very slowly. Animals that become infected with *M paratuberculosis* may not shed the organism in the faeces or produce measurable levels of antibodies

for many months. As a result, a negative test result does not guarantee that the animal is free from infection.

Is eradication of the disease from a herd, a region or a country achievable?

The control of Johne's disease at any level, whether it be herd, region or country, has proved to be extremely difficult. Several countries around the world have recently introduced schemes that aim to eradicate the disease but, at present, it is too early to be able to evaluate the success and feasibility of such programmes.

What is the risk of re-introduction of the disease into a 'clear' herd?

At the farm level, the introduction of suitable control measures can reduce the economic losses associated with Johne's disease but, at present, it is unlikely that a herd will ever be completely 'clear'. The lack of a diagnostic test that reliably identifies infected animals is a major limitation when attempting to eradicate the disease from a herd. In addition, the *M paratuberculosis* is able to survive for very long periods in the environment and so simply removing infected animals does not eliminate the disease from the premises. Finally, the recent isolation of *M paratuberculosis* from rabbits may indicate that there is a wildlife reservoir for the causative organism.

Does the disease have any human implications?

In 1913, a Scottish physician named Dalziel recognised that the pathology associated with Crohn's disease in humans is very similar to the pathology associated with Johne's disease in cattle. There is, however, one major difference between the two diseases – the large number of acid-fast bacteria found in Johne's disease are absent from Crohn's disease. In the 1980s a group of American scientists lead by Chiodini was able to culture *M paratuberculosis* from biopsy samples taken from a small number of patients with Crohn's disease. Since that time, numerous other studies have been performed to confirm these findings but the results of these studies have often been inconclusive. In addition, it must be emphasised that simply isolating *M paratuberculosis* from cases of Crohn's disease does not prove that *M paratuberculosis* causes Crohn's disease. At present, the existence of a casual link between *M paratuberculosis* and Crohn's disease remains a highly controversial issue.

Philip Hywel Jones graduated from Bristol University of Bristol in 1991, spent two years in mixed practice in South Wales and returned to Bristol to study for his PhD. He was awarded a Research Training Fellowship in Epidemiology from the Wellcome Trust in 1997, spent a year studying for the degree of Master of Preventative Veterinary Medicine at the University of California, Davis before returning to Liverpool University last year to study Johne's disease.