Ontario

MINISTRY OF AGRICULTURE
FOOD & RURAL AFFAIRS

Johne's Disease in Sheep

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Introduction

Johne's disease (pronounced yonee's) is a disease of ruminants characterized by wasting and terminally, by diarrhea. It is caused by a bacteria called *Mycobacterium avium* subspecies *paratuberculosis*. Johne's disease has been reported in Canada in cattle for several decades. Although it has also been reported in sheep for many years, no one is certain of how widespread it is or exactly how much damage it is doing to our sheep industry.

World-Wide Distribution

Johne's disease has been diagnosed in cattle (both dairy and beef), goats, deer (fallow, red deer, white tail deer and many other species both wild and farmed), llamas, camels, other wild ruminants (moose, Rocky Mountain goats, bison, antelope, big-horn sheep) as well as sheep. The disease in sheep has been reported across North America and Europe (including Iceland). It has been a major infectious disease of sheep in New Zealand for some years but has only invaded Australia in the last decade, where it appears to be spreading rapidly. Reports of experimental infection of non-ruminant species such as mice and rabbits has led to speculation that there could be non-ruminant reservoirs of disease, particularly in the United Kingdom (UK) rabbit population.

Johne's and Humans?

In recent years there has also been speculation that *M. avium* subsp. *paratuberculosis* may also be implicated in Crohne's disease in humans. This is a disease characterized by ulceration of the intestine causing extreme pain and debilitation. While it may be an autoimmune disease, special tests that detect DNA (Polymerase Chain Reaction tests) have detected evidence of the organism in some Crohne's patients. However, to date this research has not been confirmed and the organism has not been cultured from human cases. In addition, Crohne's disease has been reported in parts of the world that do not have Johne's

disease (e.g. Western Australia). The jury is still out on this one.

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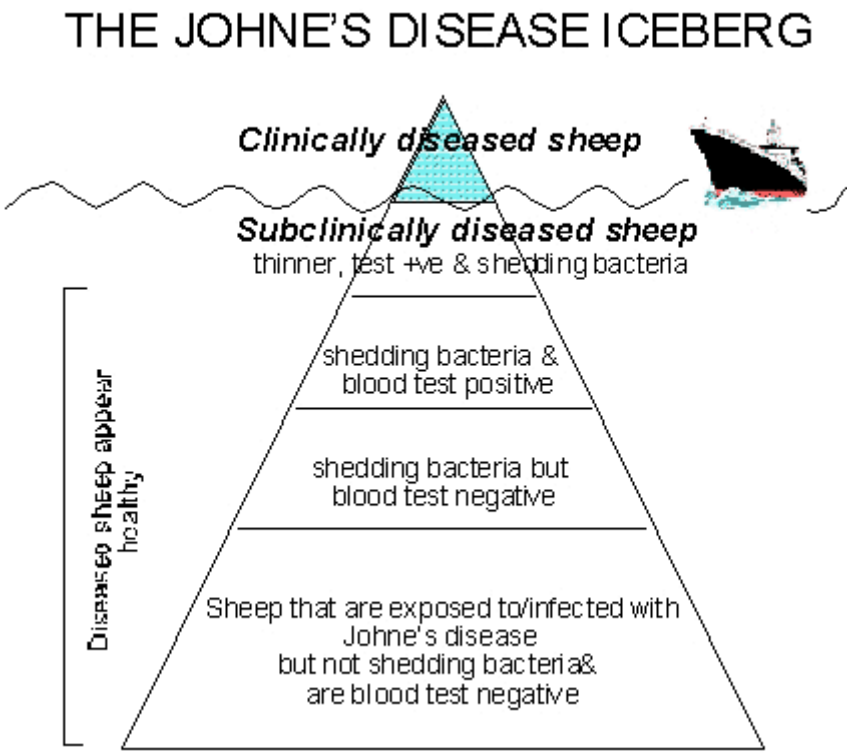
The Agent

There are three major strains of this bacteria (which is related but different from *Mycobacterium avium* subsp. *avium*, a disease of birds and rarely humans [*avium tuberculosis*]). There is a cattle strain, a sheep strain and an intermediate strain. While cattle are susceptible to all three strains, they are usually not infected with the sheep strain. Sheep usually get only the sheep strain but can also succumb to the intermediate strain. Goats usually have the cattle strain.

The Clinical Disease



Text Equivalent of Figure 1

Johne's disease in a flock or herd behaves very much like an iceberg. The disease that a shepherd may see in the flock represents only a small proportion of sheep that are actually infected. The age at which the disease becomes visually evident (i.e. wasting) likely reflects the amount of infection in the flock. If ewes are two to three years old when they become ill (as opposed to four and older), it indicates that there is a fairly high prevalence of infection in the flock, and thus a large environmental load of bacteria.

Sheep can become infected at any age, but if infected while a lamb or fetus, then the disease manifests itself as young as 18 months. An astute shepherd may notice nothing more than a ewe that seems to be a little thinner than the rest of the flock. Sometimes another stress such as lambing or mastitis will hasten the onset of more severe clinical disease. The ewe is depressed and pale and very thin and about 20% of cases develop

diarrhea. Diarrhea indicates that the sheep is nearing the end and will die soon. Thin sheep are usually culled or buried (if they die or go down due to weakness) rather than necropsied by a veterinarian. And so the disease may go unnoticed for many years.

A necropsy at this time would reveal greatly enlarged intestinal lymph nodes filled with Johne's bacteria. Intestinal changes may be mild to moderate with thickening of the gut wall. Often the lesions are quite subtle and they require the keen eye of a trained pathologist to pick up the signs. Many producers and butchers will miss the lesions.

This difficulty with diagnosing the disease is why several cases often occur in the flock before the disease is detected. By that time, the environment and several generations of sheep have been exposed to the bacteria in large doses.

Johne's disease may also be mistaken for other wasting type diseases. Bad teeth due to incisor loss (broken mouth) or uneven molar wear and gingivitis can cause considerable weight loss. Maedi Visna can cause wasting. Parasites can drag down even an adult ewe and diarrhea will further confuse the diagnosis. Internal abscesses due to caseous lymphadenitis can also cause wasting with few other clinical signs. And of course, periodic poor nutrition (e.g. poor pasture or hay) or excessive competition can lead the producer to make excuses for the thinness of some ewes.

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How the Disease is Spread in the Flock

Typically sheep become infected through eating feed contaminated with fecal material. The bacteria invade the intestine and the intestinal lymph nodes where they become established and interfere with absorption of nutrients, hence weight loss. This progression, however, takes two to seven years to go to completion, depending on the number of bacteria that infect the sheep and the age at which the sheep is infected.

When they are first infected, sheep do not shed the bacteria. This period of grace may be as short as a year or as long as 5 yrs but is often 2 to 3 yrs. Eventually the infection progresses to the point where bacteria are shed in the feces although the sheep still appear healthy and productive. This period of bacterial shedding without clinical disease may last a year or better. An infected, shedding animal may, for the time being, be the most productive ewe in the flock.

The bacteria have a very thick cell wall and can survive in the environment for perhaps as long as a year. They are resistant to disinfectants and to drying by the sun. Infected sheep on pasture will contaminate that pasture for other grazing animals. Infected sheep in a barn may defecate into feeders or waterers. Lambs born into these contaminated environments are most susceptible to infection. Dirty udders and wool tags, barn yards, bedding, etc are all sources of infection to the curious lamb. Plowing infected grazing land will dilute the bacteria and help to kill them. Snow cover will help their survival whereas sunlight, drying or exposure to intense cold will reduce their numbers. Disinfectants must be suitable against mycobacteria to be effective against Johne's bacteria. Few disinfectants work well if used in the presence of organic material.

Other Methods of Transmission

During Pregnancy

Although Johne's disease is primarily a disease of the intestine, during the advanced stages of disease the agent may spread throughout the body. Fetuses are very susceptible to infection while still in the womb. Lambs may be born infected (in cattle, up to 60% of calves

born to cows in advanced disease, were infected) and these animals may develop clinical disease at an earlier age. This means that even removing lambs at birth will not guarantee freedom from infection if the dam is infected. Milk and colostrum sometimes have small numbers of organisms present but it is not known how important milk is as a source of infection.

Semen

In cattle, the bacteria have been isolated from semen from bulls with advanced Johne's disease. To date there is no report of infection of a cow or calf from infected semen although bulls are screened in AI units. An infected bull on a farm is far more likely to infect other animals from contamination of the environment than from infected semen. In sheep, the risk is likely low, particularly when using AI since the semen is diluted.

Embryos

Embryos are free from Johne's bacteria. In a severely infected flock, embryo collection may give one of the best opportunities for preservation of valuable genetics, even when the donor ewe or ram are heavily diseased.

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Diagnosis

Direct Examination

The first diagnosis is often made at necropsy. As mentioned before, the intestinal lymph nodes become enlarged and the intestinal wall may appear thickened. Signs in sheep are more subtle than in cattle, in which the large intestine becomes quite thickened and corrugated like cardboard. Bacteria can be stained and viewed by a microscope. Sometimes the bacteria can be seen in a fecal smear, particularly in animals that have reached the diarrhea stage. To be diagnostic however, large numbers of bacteria must be seen and follow-up tests need to be done.

Bacterial Culture

This is not very successful in sheep. In cattle and goats, the bacteria can be cultured about 60% of the time when they are present in the feces. However, the bacteria are very slow growing and take 4 to 16 weeks to grow. This means that negative results take at least 4 months and then a negative result may only mean failure to grow or that the animal is still in the early stages of disease. The situation in sheep is even worse. Diagnostic laboratories in North America and elsewhere seem unable to grow the bacteria with any degree of success. Sensitivity of bacterial culture in sheep even when showing severe clinical disease is only 8% (8 animals culture positive out of 100 shedding animals). The result is that we don't even try to culture bacteria from sheep.

Serological Testing

Many serological tests are used to detect antibodies to *M. avium* subsp *paratuberculosis*. In sheep the most commonly used test is an Agar Gel Immunodiffusion Test (AGID). While a positive test result is generally correct, animals in the early stages of disease or in the advanced stages will often test negative. This means that AGID test rarely classifies a healthy sheep as infected (few false positives) but may misclassify many infected sheep and call them healthy (many false negatives).

Sheep shed bacteria in the feces for three to nine months before testing positive to the AGID test. The sensitivity for subclinical animals is less than 30% (3 out of 10 infected animals classified as infected) and is only 50% (5 of 10 infected animals classified as infected) in clinically affected animals. Animals in advanced disease sometimes lose the ability to

respond to disease because of debilitation.

Many ELISA tests (Enzyme-Linked Immuno Sorbent Assay) have been developed with an aim to improving the ability of the test to detect diseased animals. However, infected animals still slip through and sometimes animals infected with non-pathogenic *Mycobacterium* sp. will test positive, further confusing the picture.

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Other Diagnostic Tests

DNA probes are diagnostic tests that detect specific DNA. Live organisms do not have to be present, just DNA remnants. Specificity can be quite good with these tests, i.e. doesn't cross-react with other types of DNA and sensitivity can be variable. When DNA probes to *M. avium* subsp. *paratuberculosis* are used in the feces, approximately 1,000 to 10,000 bacteria per gram of feces are required to reliably detect the bacteria, compared to only 100 bacteria per gram for fecal culture (cattle data). It isn't known how well the test works in sheep but may help to detect pre-serologically positive cases. The drawback is that not all veterinary diagnostic laboratories have the correct equipment and the test is expensive to run.

There are also tests that detect cell mediated immunity (as opposed to antibodies). One is a skin test using delayed type hypersensitivity (DTH) like the TB test commonly used in humans. The second is a lymphocyte stimulation assay. The DTH test has problems with cross-reaction with other *M. avium* species that aren't pathogenic. One type of lymphocyte stimulation test (called the gamma-interferon assay) is being explored as a commercial test for cattle but hasn't been evaluated yet for sheep. In cattle, the sensitivity is thought to be between 70 and 94% with excellent specificity (almost 100%). Although there are many diagnostic tests available they all have serious drawbacks which makes early reliable detection of infected animals very difficult.

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Control & Eradication

All programs of this type are based on the ability to detect and remove diseased animals and to prevent the spread of disease within the flock. As you can see, with Johne's disease this is difficult because of the poor accuracy of the diagnostic tests. Until the spring of 1995, the Canadian government did have a voluntary eradication program based on serological testing. It was abandoned, for many reasons but mostly because the program didn't have adequate diagnostic tools. As of the summer of 1997, Johne's disease is not a reportable disease, i.e. the government is not concerned with the reporting, the control or the eradication of this disease. Estimates of prevalence then, are poor and are limited to the number of positive necropsy diagnoses at provincial diagnostic laboratories.

Because sheep producers rarely submit thin ewes for necropsy, choosing instead to market them and pocket up to $60 for a cull ewe, many diagnoses are missed. Flocks that are known to be infected likely have a high prevalence of disease. This makes the thought of eradication quite daunting.

Programs are generally based on annual or semi-annual serological testing (usually AGID) of all sheep greater than 12 months of age. Positive sheep are immediately sent to slaughter and offspring marketed. No animals should be sold where there is a risk of selling them for breeding stock (e.g. auction barns). The flock must remain closed to avoid reintroduction of disease. Often between three and five negative annual tests are required before the flock can be called low risk of disease. In a flock of 100 adult ewes greater than 12 months, at $5.00/sample (a minimum charge) plus costs of bleeding the sheep (likely not less that $150), annual costs of serology alone will be $650.

The Cost of Disease

The cost of disease is not well worked out because it will vary with type of flock (purebred vs. commercial or dairy vs. meat) but an estimate of approximately $90 per clinical case has been reported. This seems low for a purebred flock if opportunity sales are lost due to disease status of the flock. Bovine cases have been estimated at US$2,500 per clinical case.

Preventing Introduction

Because eradication is a long, difficult, expensive process, it is much better to prevent the disease from coming into the flock. How does this happen? Almost always this occurs with the purchase of breeding stock, either a ram or replacement ewes. Sheep grazing community pastures could also pick up the disease. Ruminant manure from other farms spread onto pastures or hay fields is a potential source of infection although this practice is unusual. Wild ruminants may be a source but this has not been documented. A purebred ram from an infected seedstock flock, shedding bacteria could breed for a season or even two successfully before succumbing to the disease but his legacy will be left with the flock. Johne's might not be diagnosed in that flock for up to five years, by which time the source may have been forgotten.

There currently is no national or provincial program for certifying flocks free of Johne's disease. This means that education is our best tool against this disease. Improved biosecurity, which includes closing the flock or purchasing from reputable breeders that will stand behind the health of their flock, is a beginning to slowing the spread of this disease. Countries like Australia are grappling with the possibility of depopulating infected flocks. North America does not have a vaccine but endemically infected countries like New Zealand rely on vaccination to control the losses due to clinical disease and are deciding whether to keep the disease reportable. The US is concerned about internal control but there is tremendous variation from state to state with respect to control and eradication. At this point, it is mostly buyer beware, the same as here in Canada, although some producers that have been sold infected cattle are testing the liability waters.

So Where Do We Go From Here?

There are infected seedstock sheep producers in Canada and the US. No program identifies them or protects other producers from purchasing infected stock. It is up to the industry to be concerned about Johne's and other silent, contagious diseases that can rob a flock of productivity and can be purchased in apparently healthy sheep. To prevent the spread of this and other diseases we need to stress producer education, improved biosecurity and eventually a program that can certify a flock as being low risk of disease.

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