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Beth Carlson, DVM Deputy State Veterinarian, North Dakota State Board of Animal Health Johne's (pronounced "yo-knees") disease is an incurable, progressive wasting disease found in ruminants worldwide, caused by the bacterium *Mycobacterium avium*, subspecies *paratuberculosis* (also known as MAP, paratuberculosis). This bacterium is closely related to the ones that cause tuberculosis in cattle and humans. H.A. Johne, a German veterinarian, first described this disease in 1895; his name is used as the common name for this disease.

Historically, Johne's disease has been considered a "dairy" disease, but all ruminants are susceptible, including sheep, goats, bison, deer and elk. In dairy and beef cattle, Johne's is a slowly progressive disease that costs the producer through excessive culling, suboptimal milk production, decreased fertility and death loss. It also is a possible cause for litigation if knowingly infected cattle breeding stock are sold as noninfected animals or without disclosing that information.

For every clinical (symptomatic) case of Johne's disease in a herd, multiple animals are likely to be infected with the disease without showing any clinical signs or symptoms (asymptomatic). The real problem is subclinical (below the surface) or asymptomatic animals. This "iceberg" effect of Johne's can significantly impact your production system and diminish your profits. Unfortunately, there is no cure for Johne's disease. Antibiotics, medications or dietary changes cannot cure the infection. No vaccines are commercially available in the United States.

Clinical Signs/Symptoms

Cattle

Johne's-affected cattle usually exhibit signs between 2 and 5 years of age, but animals can be much older (10 to 15 years of age) and much younger (as young as 10 months). Males, females or sterilized animals can all be affected. The animals may appear unhealthy and thin, are often weak and typically do not have a fever. Appetite often remains normal. The diarrhea is initially mild, then becomes severe, often described as "water-hose" or "pipestream." Diarrhea may be intermittent at the onset of clinical signs. As the diarrhea becomes more severe, the animal will start to lose protein through the gastrointestinal tract and may eventually develop bottle jaw edema.



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Goats and Sheep

Small ruminants primarily have chronic weight loss despite a healthy appetite. It may take years before clinical signs are observed. Males, females and sterilized animals can all be affected. Profuse diarrhea is not common in small ruminants as it is in cattle and may be pasty. The clinical signs often resemble infection with internal parasites. Lymph nodes along the GI tract become enlarged.

Transmission

Johne's disease is usually transmitted through the fecaloral route, where contaminated colostrum, milk, water, feed or manure is ingested. In utero transfer (while still inside the mother) is also possible. It is often contracted when the animal is very young (up to 30 days of age, or even 6 months in goats) and probably within the first 24 hours of life while the gut is "open" to absorb colostral antibodies. After the gut closes, infection becomes dose-dependent as the animal ages and more bacteria are needed to cause infection.

Specialized cells in the wall of the intestine take up the bacteria. Normally, an invading bacterium would be killed, priming the immune system to strengthen itself against future invasion. However, some of the organisms that cause Johne's disease are able to survive this process. As time passes, more and more specialized cells are recruited to try to kill the bacteria, causing the intestinal wall to thicken. The thickening of the intestinal wall causes poor absorption of nutrients.

Animals affected with Johne's disease eventually shed the organism in their manure, with the number of organisms increasing through time. The bacterium can live for up to 18 months in soil or manure, depending on environmental conditions.

The bacterium also can be found in the semen of infected bulls. Theoretically, Johne's transmission via natural service is possible but has not been proven. In general, artificial insemination (AI) is not believed to pose a large risk for the spread of Johne's in a typical production setting but could be a risk if the animals(s) have not been tested.

Annual whole herd testing or testing of a subset of the whole herd is important to enable early detection of the disease.

Clinical Course

Animals that are infected early in their lives show no evidence of Johne's disease for an extended period of time. The time from initial infection to onset of clinical signs (diarrhea and weight loss) is generally 2 to 5 years. This is radically different from other diseases; in those, the time from infection to time of illness is generally less than 14

After this incubation period, infected animals may begin shedding the Johne's-causing bacterium in manure at very low levels or intermittently, but in some normal, healthyappearing animals, large numbers of bacteria can be shed. In most cases, the number of bacteria shed increases with increasing age of the animal. At some point, the animal may develop clinical Johne's disease, with diarrhea and weight loss.

Due to the long incubation period, producers may not realize the herd is infected with Johne's until years later, if ever. Before animals reach the point of chronic diarrhea and weight loss, they may already have been culled for other reasons, including mastitis, poor production or reproductive failure (the "iceberg" effect).

Diagnosis

Due to the complexity of the disease, it is important to discuss testing strategies with your veterinarian. Additionally, we recommend talking with your veterinarian and the laboratory for assistance interpreting all Johne's disease test results. Diagnostic tests for Johne's disease identify the bacterium that causes the disease, Mycobacterium avium ss. paratuberculosis (MAP), or antibody to the MAP infection in the blood or milk. There are three main laboratory tests: 1) polymerase chain reaction (PCR), 2) enzyme-linked immunosorbent assay (ELISA) and 3) culture.

The NDSU Veterinary Diagnostic Laboratory (NDSU VDL) performs PCR and ELISA tests. It no longer does culture as the organism grows very slowly and can take up to 4 months to grow. The PCR and ELISA tests allow for much faster turnaround time, enabling timely and appropriate management decisions.

PCR is an organism-based test that detects MAP DNA in fecal or tissue samples. The PCR used at the NDSU VDL is very sensitive and can be performed rapidly on individual samples (fecal samples or tissues from dead animals) or pooled fecal samples from up to five individuals. On individual fecal samples, the NDSU VDL report will include the Ct value that is used as guidance on the shedding status of the animal. While the PCR assay is quicker than

culture, it may detect nonliving genetic material that does not represent a true infection, such as a pass-through infection.

Pooling samples for PCR testing is typically more costeffective if suspicion is low. The pooling of fecal samples must be done at the NDSU VDL. If a pool tests positive (or "detected"), all animals in the pool will be tested individually, for an added cost. The producer and veterinarian need to discuss whether pooling is appropriate for the herd in question.

The ELISA looks for antibodies in the blood or milk of the animal. It is a good way to screen a herd and test a large number of animals while keeping costs down. This will give an indication of the incidence of infection in a herd.

ELISA results are numeric; generally, the higher the number generated by the test, the more likely the animal is truly infected and shedding. However, ELISA testing can produce false positives that are best confirmed by retesting in a few weeks or confirming with a fecal PCR. ELISA test kits are available for milk samples from individual cows as well.

In animals with symptoms of Johne's, PCR and ELISA tests are equally effective. For asymptomatic animals, ELISAs tend to be less sensitive than PCR or culture because antibody production usually ramps up later in the course of infection. That could happen months or years after an animal has been shedding the bacteria in feces.

As with all diagnostic tests, false positive and false negative results can occur; thus, whole-herd testing is strongly recommended if any animal in the herd has been diagnosed with Johne's disease. When designing a diagnostic strategy for an animal or group of animals, the best procedure is to confer with the laboratory being used and your veterinarian. Many factors are involved in deciding which diagnostic plan is appropriate. This will optimize results and keep costs reasonable.

Prevention

The number one way to avoid introducing Johne's disease into your herd is to be as certain as possible that animals brought into the herd are not infected. A second way is to work with a producer who knows the level of Johne's disease in their herd and follows good infection control practices and then purchase test-negative animals from test-negative dams. It is OK to ask the seller to show you test results/lab reports and if they have been testing for multiple years.

Remember that Johne's disease is a herd problem, and knowing the test status of numerous adults in the source herd will give you a much better sense of the risk of

purchasing an infected animal than the one test result you might get on the single animal you wish to buy. A single test on an individual animal may not detect every infected animal.

A better option is to determine a herd's Johne's disease status by a whole-herd test of female animals more than 2 years of age and bulls over 1 year of age. Ideally, only buy from those herds in which all animals test negative and involve your veterinarian in any discussion of laboratory results.

Some states (including North Dakota for cattle) have voluntary Johne's control programs that can help defray the cost of testing but may be host species-dependent. Please check your state for Johne's control programs and which species are supported. These programs establish the Johne's status of the participating herds. Again, ask prospective sellers if they participate in a Johne's control or testing program and to see results. Testing and maintaining a "clean" herd is expensive and time-consuming, but it is also a good marketing tool.

Control

If Johne's is present in a herd, control requires a long-term commitment. The most effective method is identifying infected animals through systematic testing and implementing management changes. This twopronged attack centers on removing infected animals to decrease shedding in the herd and protect the youngest, most susceptible animals. This will take time, patience, commitment and money, but Johne's can be eradicated from the herd or flock.

Voluntary Johne's programs in most states are designed to help producers control Johne's and provide a wealth of expertise to help herd managers.

Johne's control programs will vary from herd to herd. Involve your veterinarian at the onset of your control program.

Herd size, geographic location, type of enterprise, number of infected animals, herd/flock management and herd/flock size need to be taken into account. No one program will work for all operations, but some control measures will be universal:

- Cull clinical or shedding Johne's animals immediately. If an animal is symptomatic and tests positive, please DO NOT sell or give it away and make Johne's someone else's problem. The best practice is to cull and send the animal to slaughter (following proper withdrawal times for any vaccines or drug treatments).
- ☐ Use colostrum or milk from test-negative dams/ewes/ does.

☐ Follow the Johne's control program outlined by your state or veterinarian.
☐ Test dams/ewes/does prior to birthing and maintain a Johne's-free birthing zone.
☐ Any male, female or sterilized animal can be affected. Often bulls are forgotten or not tested; however, they should be routinely checked.
☐ Maintain clean and dry birthing areas, pens, or pastures.
☐ If using semen for AI, make sure bulls/rams/bucks have tested negative for Johne's.
☐ Manure should not be applied to land where animals graze or where feed is produced. Apply manure on non-pasture and non-hay land to avoid reintroduction via fecal-oral transmission.
□ Keep biosecurity practices in mind. These are practices to prevent or minimize the spread of harmful pathogens and include but not limited to: thoroughly washing/ disinfecting hands, boots, and equipment; working with healthy animals first and moving to sick animals; DO NOT reuse a sleeve/glove on different animals. Read NDSU Extension's "Site Visits: Biosecurity Practices for Professionals Working in Animal Agriculture" (AS2244) for more information.
☐ Limit access to low-lying wet areas where the Johne's organism can survive for over a year.
☐ Do not contaminate milk/water/feed for young stock with manure.
☐ When dams exhibit clinical signs of Johne's disease, the probability that the calf was infected in utero is about 20%. Do not retain or sell these calves as replacement heifers.
☐ Early removal of a high-value calf/kid/lamb from an infected dam in the first few hours of life may be helpful in reducing the incidence of infection. However, that assumes no in utero transfer occurred which is more likely possible in clinically ill animals.
☐ Calves, lambs and kids should be kept away from potentially infected adults and manure for at least the first 6 months of life.

- ☐ Things like bottles, tools, feed dishes and troughs should be washed thoroughly with soap and water, rinsed and dried before applying a tuberculocidal disinfectant according to manufacturers' instructions. Organic material deactivates the disinfectants.
- ☐ Do not feed on the ground. Feed should be placed in bunks, racks or other elevated feeding devices.
- □ Please be wary of "free" or "giveaway" animals. A "free" animal is not necessarily "free." It is not unusual for free or cheap animals to introduce Johne's (or other pathogens) to a herd or flock.
- ☐ Testing an animal before introduction can help reduce the chances of spreading Johne's; however, due to the nature of the bacterium, animals can test negative (PCR and ELISA) but still carry the bacteria.

Outcome

Johne's disease is very difficult to eliminate from a herd and will take a long-term commitment to testing and management changes. It is possible for an individual animal to test negative over multiple years and then test positive. However, Johne's can be eradicated from a herd, but even then, Johne's management does not end. To prevent reinfection, producers must remain vigilant. In addition to testing any sick animals, any new animals should be screened and tested if appropriate. Annual whole herd testing or testing of a subset of the whole herd is important to enable early detection of the disease.

For more information on the North Dakota Voluntary Johne's Control Program, contact the North Dakota Department of Agriculture – State Board of Animal Health by calling 701-328-2655. For more information on Johne's testing performed at the NDSU Veterinary Diagnostic Laboratory, contact the NDSU VDL by calling 701-231-8307.

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