



JOHNE'S DISEASE – DAIRY

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Johne's Disease a Focus of RDQMA Study

Mycobacterium avium subspecies *paratuberculosis*, the organism known to cause Johne's disease, was among organisms studied by the Regional Dairy Quality Management Alliance which tracked endemic disease dynamics over time in Northeast dairy herds with well-characterized animals and herd management practices. The RDQMA project is in cooperation with USDA.

Since starting its research, the RDQMA has identified MAP super-shedders on study farms and have recognized the role that super-shedders play in the creation of passive shedders.

"Over time, many passive shedders become infected with MAP in their intestinal tissues (adult infection)," states the RDQMA report. "We recognized that virtually all active shedders have the potential to become super-shedders and super-spreaders of MAP."

In the most recent study, researchers sought to estimate the effect of Johne's disease status on individual cow milk production using longitudinal data collected over a four-year period from three U.S. dairy herds enrolled in the RDQMA project. Quarterly ELISA serum testing, biannual fecal culture and culture of tissues at slaughter helped determine Johne's disease status: uninfected, low shedding or high shedding. Milk production data were collected from the Dairy Herd Improvement Association, with the effect of Johne's disease status on milk production analyzed.

Highlights of the RDQMA report:

- "Johne's disease status was

found to have a significant effect on milk production, and this effect was not uniform across Johne's disease status categories. Our data indicate that cows that eventually will show low and high shedding of MAP are out-producing MAP-negative animals in the herd. Although latent animals produce more milk than uninfected animals, that difference decreases over time in the latent infection state."

- "When an animal starts shedding low levels of MAP, the model predicts an initial milk production that is slightly higher than that of uninfected herdmates, but there is a greater rate of decrease in milk production compared with the latently infected animals."

- "Animals in the high-shedding category have a meaningfully lower milk production than uninfected herdmates, with large decreases in production over time when remaining in the herd."

- "Greater milk yield is evident during latency compared with uninfected herdmates, but the discrepancy in yield decreases as the disease progresses over time. This MAP-induced decrease in milk production is supported by the clinical progression of Johne's disease."

- "As the organism invades the intestinal epithelium and begins to affect nutrient absorption, feed efficiency decreases and milk production in negatively affected."

- "This analysis provides strong support that Johne's disease status affects milk production in all infected animals, with increasing losses in milk production as disease progresses."

- Culling decisions should be



RDQMA finding: Johne's disease status affects milk production in all infected animals, with increasing losses in milk production as disease progresses.

made "on an individual animal, economic level, particularly since animals shedding MAP also spread the infection through environmental contamination."

Looking Closer at Super-Shedders

To better understand the epidemiology of Johne's disease and MAP dynamics in dairy cattle, researchers used a DNA-based molecular subtyping technique. Using this technique with the observed MAP shedding level, they evaluated whether low shedders of MAP were passive shedding (pass-through) animals or whether they were truly infected and whether these animals were possible infected by the super-shedders within the herd.

From among the 142 isolates from fecal and tissue samples from the

(continued on page 4)



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Researchers Team with Producers in Battle Against Johne's

When the National Animal Health Monitoring System released its comprehensive report on Johne's disease in 1997, the majority of dairy producers had only a general idea of what the disease was, and fewer still thought it affected their herds. But with an estimated 50% of the dairy animals in Michigan infected with Johne's disease, there was no doubt it was a serious industry priority.

Several Michigan State University researchers sought out funding to learn more about this economically damaging animal health issue, which has an estimated \$200 million annual impact on the U.S. dairy industry.

Central to the initial research efforts was Dan Grooms, MSU associate professor of large animal clinical sciences and a large animal veterinarian. Along with learning more about the disease, Grooms and his colleagues from MSU and other universities would work for several years to determine the best management practices to employ on a dairy farm to prevent the spread of the disease and lower the percentage of animals infected (prevalence rate).

In 2003, researchers and veterinarians from the MSU Department of Animal Science, College of Veterinary Medicine and the Diagnostic Center for Population and Animal Health, and the Michigan Department of Agriculture joined researchers from 16 other states to monitor dairy herd management practices. The Michigan team was chosen to be a part of the USDA's National Johne's Disease Demonstration Project. The purpose of the national project was to evaluate the long-term feasibility and effectiveness of management-related practices designed to control infection by *Mycobacterium avium paratuberculosis* (MAP), the causative organism for Johne's disease.

Grooms selected seven herds to serve as his Johne's disease demonstration herds. The herds, located in various regions of the state, underwent whole-herd testing to measure



Calf management was the top priority of a seven-herd Michigan research project focused on best management practices to prevent the spread of Johne's disease and lower the percentage of animals infected.

baseline levels of infection. From there, a disease risk assessment was conducted, and management practices were put in place to help control on-farm spread of the disease.

"We know that animals are most susceptible to Johne's infection at a very young age, so calf management was our first priority," he says. "There is no cure for Johne's, so the best way to manage the disease is to prevent it."

At the same time that Grooms was assembling his herds for the demonstration project, Galen Schalk, a dairy farmer in Hillman, Mich., encountered his herd's first diagnosed case of Johne's disease.

"I had heard about Johne's disease but thought, 'That's not me,'" Schalk says. "We have had a closed herd since 1974, so because I was not bringing new animals into the herd, I didn't feel we were at risk for the disease."

The first Johne's test from the Schalk's herd, run at the request of his veterinarian, came back positive for Johne's. The diagnosis concerned Schalk, who contemplated how many other cases he might have in the herd, so when Grooms approached him to be part of the Johne's disease demon-

stration project, Schalk did not hesitate to sign up.

"I had a very minimal understanding of Johne's and minimal prevention practices when we started with this project," Schalk says.

The first round of fecal cultures from the Schalk herd came back with a 21% prevalence rate among the 168 animals tested; the second year, 2004, the rate jumped to 42%. The more Schalk learned about the disease and the test results on his herd, the more he realized that he had seen cows develop clinical signs of the disease in the past but hadn't realized it was Johne's.

(continued on page 3)

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Johne's Battle (continued)

"We would have cows get really thin and drop in productivity, so we would cull them from the herd," Schalk says. "Now I know they were Johne's animals."

Seeing the high prevalence rate, Schalk was eager to eliminate the problem as quickly as possible. Schalk, Grooms and other MSU scientists put together new management strategies to help control the disease.

The area of highest concern on the Schalk farm was the calving area. Cows calved on a manure pack, which created the perfect environment for disease organisms to survive and spread to newborn calves. Though the Schalks had already drawn up building plans for a new transition barn, they opted instead to construct a new maternity and housing area for close-up cows.

"It was good that we were already looking to put up a new building because we really needed a better place for the animals to calve in," Schalk says.

Along with building the new maternity area, Schalk started withholding the colostrum from Johne's-positive cows and feeding newborn calves colostrum from only non-infected cows.

"Johne's can be transmitted to the calf through the colostrum or from the contaminated environment," Grooms says. "Knowing which cows are positive for Johne's is critical in stopping the disease from spreading."

The new maternity area also provided an opportunity for each cow to calve in its own pen and allowed Schalk time to clean and disinfect each pen between calvings. Because animals contract Johne's disease early in life, properly caring for calves is one of the most critical steps in preventing disease transmission, even though measuring immediate results from changing management practices is difficult.

"Even though we culled a number of animals during the first two years of the project, we still need to manage for the disease because we know some of the older animals are carriers," Schalk says.

Visually identifying the Johne's carriers helps Schalk manage the disease. Schalk now tags all animals that test positive for Johne's disease with a special red neck chain. Any heifers born to positive dams are also tagged with the red neck chain until they receive a negative test reading.

"It is not perfect," Schalk says. "Occasionally an animal is born early in the close-up area and not in the assigned calving pen, but we are really making progress."



Researcher Dr. Dan Grooms notes that "this project shows us that, though there is no cure for Johne's disease, with proper management, farmers can prevent the spread of the disease on their farms and reduce its prevalence over time."

Animals can shed the organism that causes Johne's even if they are not showing clinical signs of the disease. Research indicated that the disease-causing organism is shed through the manure. So Schalk implemented another critical management practice -- taking preventive measures to ensure that no manure comes in contact with animal feed.

To prevent cross-contamination, the Schalks bought a second skid steer and use one only to clean and scrape manure and the other only to handle and move feed. They also make sure not to cross over feed alleys with equipment to minimize the risk of any manure on the tires coming into contact with the feed.

Since the Schalk herd became part of the Johne's demonstration project, the prevalence of Johne's in the herd has dropped to less than 5%.

The results on this herd are similar to the outcomes realized by the other test herds.

"We saw a reduction in the number of Johne's-positive animals in all the herds we worked with," Grooms says. "This project shows us that, though there is no cure for Johne's disease, with proper management farmers can prevent the spread of the disease on their farms and reduce its prevalence over time."

As the demonstration project

winds down, Schalk is looking ahead to how he will continue implementing the recommended management practices on his farm. Now that he has the prevalence rate down to less than 5 percent, he will continue to test the herd to monitor for any new infections.

"We were surprised to learn that we had the disease at all. If we don't continue to test the herd, we won't know if we're continuing to make progress," Schalk says.

Funding for Grooms' position with an emphasis on cattle disease management was made possible by the Animal Agriculture Initiative at MSU. The AAI was established in 1996 as part of the grass-roots-driven Revitalization of Animal Agriculture in Michigan Initiative.

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Vaccine Project Underway

With only one USDA-approved vaccine available to help protect against Johne's disease, many veterinarians and producers would like more available vaccines—particularly since the current approved vaccine has limitations and is not approved for use in all states. With funding from USDA-APHIS-VS, the Johne's Disease Integrated Program has undertaken an effort to identify viable vaccine candidates and evaluate those with the greatest potential for commercial development.

"The project is in the initial stages of a three-step process," states Tiffany Cunningham with JDIP. "Currently, JDIP is in Phase I of the vaccine-testing program and has added an additional participating institution, AgResearch Limited, to the program."

As part of Phase I of the program, scientists have submitted strains of live vaccine candidates and recombinant proteins, and a laboratory at The Pennsylvania State University is coordinating the cultures and growing the strains that have been received. The strains will then be distributed to candidate vaccine-

testing centers at the University of Wisconsin and the University of Minnesota for blinded evaluation.

"The JDIP Epidemiology and Biostatistics Core at Cornell University will analyze the results of the testing in a blinded manner and identify the 'best candidates'," Cunningham states. "Once the analysis is complete and the blind is opened, all of the program participants will receive the data at the same time."

During Phase II of the vaccine-testing program, "best candidates" will be evaluated using a mouse model. If all goes as planned, two laboratories will conduct the infection and protection studies in the mouse.

Phase II will involve the "best candidates" identified through the mouse studies being evaluated using a goat model.

"This will provide data similar to that from cattle, but the data will be available in a much shorter time frame and at a lower cost," states Robab Katani, a JDIP scientist with The Pennsylvania State University.

"The coordinated three-stage

evaluation will take approximately three years to complete. It is expected that this rigorous screening process will identify one or more viable candidates to move forward for commercial development."

RDQMA *(continued)*

three farms were 15 different strains: 9 types on Farm A, 7 types on Farm B and 6 types on Farm C. The results indicated herd-specific infections: a clonal infection in Herd C with 89% of animals sharing the same strain (Type 2) and different strains in Herds A and B.

Type 4 was the most predominate one on Farm A (59%), and most super-shedder isolates belonged to this type.

Farm B was found to have a variety of strains from a limited number of isolates, and animals from which these samples were collected were purchased from different sources.

On Farm C, 100% of the infected cows shed the same strain as that of contemporary super-shedders. On Farm A, 17% to 70% of cows shed the same strain as that of contemporary super-shedders. Tissues from about 82% of cows other than super-shedders were culture-positive for MAP, indicating a true infection.

Based on results of MAP strain-typing and shedding levels, at least 50% of low shedders have the same strain as that of a contemporary super-shedder.

"The results of this study indicate that very few cows had characteristics of a possible pass-through animal. Many more cows were truly infected," the researchers stated in their report. "Sharing of the same strain of low shedders with the contemporary super-shedders suggest that low shedders may be infected by the super-shedders."

The next RDQMA research project: model the efficacy of vaccination against Johne's disease.

The Johne's Disease Integrated Program, often referred to as JDIP, is a comprehensive consortium of scientists whose mission is to promote animal biosecurity through the development and support of projects designed to enhance knowledge, promote education, develop real-world solutions and mitigate losses associated with Johne's Disease. By joining together, efficiencies through collaborative research can be achieved and intellectual and physical resources critical to overall success can be shared. The consortium includes leading scientists in the field, drawn from the world's top academic and government institutions representing the diverse disciplines of microbiology, immunology, pathology, molecular and cellular biology, genomics, proteomics, epidemiology, clinical veterinary medicine, public health, extension and public policy.

Funding from USDA-CSREES-NRI allows JDIP to provide competitive awards for meritorious research, education and extension projects addressing Johne's disease. Approximately \$1 million will be distributed in the current funding cycle, with \$400,000 designated for Johne's disease diagnostics projects, and the remainder available across the remaining JDIP Core and Project areas.