

Are Johne's and Crohn's connected?

Science has yet to prove what causes Crohn's disease in humans. Some believe Johne's-infected animals are to blame **By Paula Mohr**



Editor's Note: *Mycobacterium avium subspecies paratuberculosis gets abbreviated different ways. The International Dairy Foods Association calls it Mpar-aTB. University of Wisconsin scientist Mike Collins calls it Mptb. United Kingdom researchers and the Paratuberculosis Awareness and Research Association call it MAP. We will, too.*

Since the majority of U.S. dairy producers still have yet to test for Johne's disease in their herds, there's one surefire way to get their attention focused on doing so: Prove that Johne's causes Crohn's disease (CD) in people. The consumer backlash would devastate dairy product and meat sales.

Considerable research links the two by association, but not causation. Also, medical doctors disagree on whether or not Crohn's is caused by a bacterial infection. Many treat it as an immune system malfunction. Only a few U.S. doctors are treating Crohn's with antibiotics directed against mycobacteria and see improvements in patients.

The premise of a link between Johne's and Crohn's isn't far-fetched. A handful of researchers around the world believe that milk, meat and water infected with the Johne's bacterium—*Mycobacterium avium subspecies paratuberculosis* (MAP)—may predispose some people to contracting Crohn's disease.

There are plenty of questions and few answers. Scientists on both sides of the fence point to studies that support their positions. Plus, milk pasteurization studies (see sidebar "Does Pasteurization Kill MAP") are divided on whether or not MAP survives heat treatment. However, no one has tested raw or cooked ground beef—mainly from culled dairy cows—for the bug. And ▶

domestic water supplies, already proven to carry *M. avium* and sicken AIDS patients, may be contaminated with infected manure runoff.

First, however, science must prove that Crohn's is caused by a bacterial infection. The National Institute of Diabetes, Digestive and Kidney Diseases is supporting research that is studying tissues of Crohn's patients and controls to identify organisms, says Dennis Lang, National Institute of Allergy and Infectious Disease.

"There's no conclusive evidence that MAP or any other bacteria is the cause of Crohn's," Lang says.

Cheryl Miller, co-director of Paratuberculosis Awareness and Research Association, says scientists at the National Institutes of Health (NIH) told members of her organization that the only way to prove MAP causes Crohn's would be to expose children to the bacterium and cure them. That type of study could ethically never take place.

Meanwhile, a growing number of scientists are wondering if there is a Johne's-Crohn's connection.

"I don't know if *M. paratuberculosis* causes Crohn's disease, but I am pretty convinced that a significant percentage of CD patients are infected with *M. paratuberculosis*," says Johne's expert Mike Collins. As a microbiology professor in the School of Veterinary Medicine, University of Wisconsin-Madison, Collins has conducted numerous on-farm and laboratory studies on Johne's for more than a decade.

In the United Kingdom (UK), John

Hermon-Taylor, professor, Department of Surgery, St. George's Hospital Medical School in London, has extensively studied MAP in humans.

"I am absolutely certain that some strains of MAP can be pathogenic for humans and can cause Crohn's disease in susceptible people," Hermon-Taylor says. "Since MAP is known to be a primary specific cause of chronic inflammation of the intestine in many different species, including primates, it would be remarkable if it did not cause disease in humans."

Collins and Hermon-Taylor point to research published in peer-reviewed scientific journals over the years that shows striking similarities between the two diseases:

- Both CD and Johne's have a long incubation period between exposure to some environmental factor and the onset of similar clinical signs (diarrhea and weight loss).
- Both Johne's and Crohn's diseases are increasing in frequency over time; genetic diseases do not. Johne's was first described in 1895 when chronic intestinal inflammation surfaced in a German cow. Eighteen years later, the first paper was published suggesting that MAP might cause chronic intestinal inflammation in people.
- Both diseases have a strong familial association, the greatest factor being whether the mother has the disease. In a recent U.S. study, doctors reported finding MAP in breast milk of lactating Crohn's patients.

• Both diseases are located in the ileum (small bowel). Both respond to the disease by developing granulomas.

Research has been slow to prove or disprove a link between Crohn's and Johne's for two main reasons: low interest and low funding, as well as the challenges in working with MAP. The bug is tough to detect and kill; it grows very slowly and it's elusive.

However, for every scientist who believes there's a link, there are those who dismiss it. Herbert Van Kruiningen, veterinary pathologist, University of Connecticut reportedly gave up the connection between Crohn's and Johne's when he realized it "did not compute." Some of his work was funded in part by NIH and the Crohn's and Colitis Foundation of America.

Dairy industry leaders downplay any alleged link between the two diseases, too, citing inconclusive research. In addition, they believe standard U.S. milk pasteurization practices effectively kill MAP.

"The vast majority of milk is pasteurized using high-temperature short-time in the U.S.," says Allen Saylor, International Dairy Foods Association. Of the various pasteurization methods, this one has proven effective in killing MAP in U.S. research.

"The regulation of equipment is very stringent and uniform across the country," Saylor adds. "It's tested every three months and sealed. I would venture to say that no place in the world has this kind of guideline." ▶

Does pasteurization kill MAP?

■ The simple answer is yes or no, depending on the researcher and the study. Preliminary results from the most recent study come from the UK, where scientists found viable MAP in 2% of the raw milk samples and 2% of the pasteurized retail milk samples from eight processors. Pasteurization time and temperature at the plants ranged from 14 to 26 seconds at 161°F.

The International Dairy Foods Association (IDFA) takes issue with this study, pointing out that the UK ag ministry admits that its own pasteurization controls are not comparable to U.S. standards. Local health officials oversee regulatory issues regarding pasteurization, which may result in lack of uniformity across the UK.

In the United States, Judy Stabel, with the National Animal Disease Center, Ames, Iowa, inoculated raw milk with MAP and processed it in a lab-sized

high-temperature, short-time (HTST) pasteurizing unit. This is the same process used in U.S. milk plants using HTST. Milk flows through a regeneration section, a heating section and a cooling section as it's heated to 161°F for 15 seconds. Plus, it flows through a curved holding tube to generate turbulence. Studies with this unit show that HTST pasteurization effectively kills MAP in raw milk.

While the research jury deliberates, more studies of milk and dairy products are in the works. The UK scientists have yet to issue a final report on their aforementioned study. Stabel and other scientists, with funding from Kraft and Dairy Management Inc., are testing dairy products such as ice cream mix and cheeses, and ultra-high-temperature milk in a two-phase project.

"We wanted a sterile product to be-

gin with so we could inoculate it with a known quantity of *M. paratuberculosis*," Stabel says. "With raw milk, you have every pathogen imaginable." The scientists will study seven heat treatments and use three strains of *M. paratuberculosis* at two inoculation levels. As of early April, Stabel says they're about 20% into Phase I. "If we're lucky, we'll be done in September," she says. In Phase II, scientists will extrapolate Phase I results and repeat them with a pilot-scale pasteurization unit.

IDFA says further pasteurization studies are under way at Cornell University, the University of Illinois and Pennsylvania State University. Food microbiologists at the University of Guelph are studying more than 600 retail milk samples and hope to have results in about a year. And the Marshfield Clinic in Wisconsin is planning to sample retail milk from several states.

The fight against Crohn's

■ Crohn's disease is a painful lifelong, progressive disease that strikes young people, usually between the ages of 15 and 24. It attacks the small bowel and results in malnutrition and wasting.

The Paratuberculosis Awareness and Research Association (PARA) estimates that at least 600,000 people in the United States suffer from Crohn's.

"At the same time that the MAP infection rate has dramatically risen in cattle, the prevalence of Crohn's in the U.S. human population has also dramatically increased," says PARA codirector Cheryl Miller. Studies show that the incidence of Crohn's rose from 100% to 400% in the 1960s and 1970s in industrialized parts of the world.

PARA estimates that U.S. Crohn's patients spend a minimum of \$5 billion annually on treatments. At least 75% of the patients require at least one surgery to remove large segments of the small and large intestine.

There are no federal research dollars allocated to determine if Crohn's is caused by MAP or other bacteria. PARA has testified before Congress for funding, as well as petitioning the National Institutes of Health to study the disease. "Our recent congressional testimony was very well received and we were told that we would get very serious consideration in the writing of the appropriations bill," Miller says.

For the past four years, PARA has talked with USDA, Food and Drug Administration and dairy leaders about their concerns. They usually were politely ignored. However, at the U.S. Animal Health Association (USAHA) Johne's disease committee meeting last October, two PARA-sponsored resolutions were approved. Both requested USDA to test for MAP in ground beef and retail milk. But the USAHA board rescinded the resolutions without explaining why.

More info online

■ For more information about Johne's and Crohn's diseases, see the following Web sites:

<http://crohns.org>

<http://johnes.org>

<http://www.iol.ie/~alank/CROHNS>

http://europa.eu.int/comm/food/fs/sc/scah/out38_en.pdf

What producers can do in the fight against Johne's

■ "If not controlled, [Johne's] may become a more troublesome scourge for future generations than tuberculosis is for the present generation of cattle owners," University of Wisconsin scientists wrote in 1924 in the *Journal of the American Veterinary Medical Association*. Prophetic words.

Johne's disease is spreading across the United States as dairy cattle move west and herds expand. A 1996 USDA survey showed 22% of herds were infected with Johne's based on ELISA testing. About 40% of the herds with 300 or more cows were infected; 20% of the herds with 100 cows or less had Johne's. Left unchecked, Johne's expert Mike Collins, University of Wisconsin, suggests that Johne's will be found in 90% of the U.S. dairy herds by 2020.

When the USDA study came out four years ago, scientists involved with the report back then said that animal production industries must give Johne's more attention, due to the potential public health concerns. Some of these scientists also serve on the U.S. Animal Health Association's national Johne's working group. This committee unveiled a voluntary Johne's certification and control program a few years ago that some states implemented 'as is' or retooled for their own use.

The National Milk Producers Federation (NMPF) also is seeking assistance for producers, but it will take several years before any impact on animal health and food safety is made. NMPF is lobbying for \$1.3 billion over seven years to support a voluntary, national Johne's indemnity program. Herds with Johne's-positive cattle would receive an estimated \$1,550/animal indemnity payment. Herds with cattle initially testing negative for Johne's would be required to continue testing to become certified Johne's-free. NMPF hopes Congress approves funds for fiscal 2002, which starts in October.

Meanwhile, producers and processors can review and implement practices to

control and eradicate Johne's. On the farm, the advice is the same given to our grandparents. A 1922 bulletin from the University of Wisconsin Agricultural Experiment Station states: "Prompt removal of all suspicious animals from the herd and care in the purchase of animals will certainly do much to limit the continued spread of this disease. . . . The prompt separation of calf and dam will, undoubtedly, prevent the infection of the former, as it does in tuberculosis."

Collins advises producers to: Test cattle before purchase. Test and remove infected cows from the herd. Limit the spread of MAP from adult to calf. Use hygienic milking techniques to reduce fecal-borne MAP in milk.

Processors should pasteurize as many dairy products as possible, Collins says. "While it might not be 100% effective 100% of the time, pasteurization definitely kills more than 99% of [MAP] in milk." Milk for nonpasteurized dairy products should come from Johne's test-negative herds. Or, the milk should be processed under conditions not suitable for MAP survival, such as low pH and aging.

