Johne's disease: Clinical approach to a control program
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Paratuberculosis (Johne's disease) has emerged as one of the most prevalent and costly infectious diseases of dairy cattle today. It also affects the beef cattle industry, particularly purebred cattle breeders. Previous updates on paratuberculosis have comprehensively reviewed many facets of the causative agent, Mycobacterium paratuberculosis, and the disease. Although they are excellent compilations of facts and recommendations, few of these article have dealt with practical issues of how to deal with M. paratuberculosis-infected herds. In my opinion, several key factors have been ignored in deciding which type of control program is best suited to each cattle enterprise. Consequently, the purposes of this presentation and article are: 1) to outline a rational approach to assess a paratuberculosis problem, and 2) to develop a practical plan to control or eradicate the disease that is tailored to each farm.

Facts about the pathobiology of paratuberculosis are documented in the literature cited above. Recommended control measures are consistent with those of other publications and have been reinforced by personal experience. I recommend 3 questions to pose to the herd owner, give 6 facts about paratuberculosis that owners must understand and on which decisions for the herd should be based, and 3 steps to follow in structuring a control/eradication program. (Certain facts are stated as generalizations to simplify the discussion.)

Fundamental paratuberculosis facts:

✓ Paratuberculosis must be managed as a herd problem, not just as an individual animal disease.

✓ Paratuberculosis is an infectious disease. The rate of infection in a herd will only increase with time unless something is done to intervene.

✓ Paratuberculosis can and must be controlled to improve a herd's productivity and profitability. New diagnostic tests and recent findings on the epidemiology of paratuberculosis make it feasible to cost-effectively intervene to halt, then reverse the spread of the infection.

In my experience, some practitioners are unaware of new information about paratuberculosis and/or refuse to accept the facts listed above. The result is that, aside from making an occasional clinical diagnosis of paratuberculosis and recommending culling of the animal, little is done to deal with the problem at the herd level. It is also true that herd owners are often unwilling to address the problem until they see how economically devastating the infection can become. Consistent with modern approaches to production animal medicine, many factors other than the pathobiology of the disease and the accuracy of diagnostic techniques must be considered in formulation of a rational paratuberculosis control program.
Three questions to ask herd owners:

Question 1:  
**What is their primary business objective?**

Commercial milk producers will not be seriously urt economically by paratuberculosis, provided the infection rate in the herd (prevalence) is <5%. The disease causes 5 to 25% reduction in milk production and shortens the productive life of a cow in a herd. While there are little data on the effect of paratuberculosis on feeder cattle, it is not likely that the growth of feeder cattle is affected from birth to market age.

Breeders and owners of registered cattle provide seedstock for other herds and, thus, have an obligation to prevent transmission of *M. paratuberculosis*. Essentially every herd that becomes infected with *M. paratuberculosis* does so by purchase of an infected cow or bull. Consequently, herds of breeding cattle, or any herd that sells herd replacements, should become *M. paratuberculosis*-free for the benefit of the industry.

Question 2:  
**How long does the owner intend to stay in business?**

Paratuberculosis is among the slowest progressing infectious diseases of cattle. It takes a considerable number of years for clinical disease to become evident after introduction of the infection into a herd, and it takes a similarly long period, ≥5 years, to eradicate the infection, depending on how aggressively eradication is pursued. In today's business climate, for dairy producers in particular, unless the owner intends to keep his/her herd for >5 years, little profit will be realized from a paratuberculosis control program.

Question 3:  
**How aggressively does the owner want to tackle Johne's?**

Many factors enter into this decision; type of cattle business, profitability of the particular enterprise, indebtedness and cash flow, knowledge and understanding of paratuberculosis, and perceptions of the client, or perhaps those of his/her neighbors, about the disease. Veterinarians should try to provide the most accurate current knowledge about paratuberculosis. It is up to owners to decide how much they can afford to spend to control the infection. The difficulty comes in evaluating the long-term benefits of investment in paratuberculosis control. Definitive calculations of the cost-benefits of Johne's disease control are not yet possible or, in my opinion, even necessary. So many intangible factors enter into the financial decision making process that no economist or banker can provide all of the answers.

*The critical role for veterinary practitioners is that of a teacher/consultant. Practitioners must educate their clients about the pathobiology and epidemiology of Johne's disease and the available options for control of the infection. To do this it is imperative that practitioners have current and accurate information, plus a solid understanding of the complexities of paratuberculosis and its control.*
Facts about paratuberculosis to stress to owners:

✓ Paratuberculosis decreases milk production of subclinically infected cows as early as first lactation.

✓ Paratuberculosis shortens the productive herd-life of cattle.

✓ Young cattle are more susceptible to *M. paratuberculosis* infection than are older animals. The critical window of susceptibility is roughly the first 6 months of life.

✓ *M. paratuberculosis* principally is transmitted by the fecal/oral route, but can also be transmitted in utero and from milk of infected cows, more so from cows with late-stage infections. Calves born to infected cows have a higher likelihood of becoming infected than do calves born to non-infected cows.

✓ The *M. paratuberculosis* infection rate in herds will increase with time unless something is done to intervene.

✓ Control of paratuberculosis takes time and requires management changes to minimize the chances of infecting calves, AND culling of *M. paratuberculosis*-infected adults from the herd. Culling only clinically ill cows with paratuberculosis is NOT sufficient to control spread of the infection.
To control of paratuberculosis, take the following steps:

Step 1: **Determine the infection rate in the herd.**

The number of clinical cases of Johne's disease that develops in a herd each year is a very rough indication of herd infection rate. Assuming the clinical cases are infected cows which were born and raised in the herd (not purchased), for every clinical case of paratuberculosis there are likely to be an additional 5 to 10 cows with subclinical *M. paratuberculosis* infection. The age of animals with clinical disease may indicate the infection pressure in the herd (dose of *M. paratuberculosis* to which young animals are exposed). When many of the clinical cases occur in first-calf heifers, there is likely something seriously wrong with the way calves are being raised for replacements, such as heavy exposure to infective feces or extensive use of raw milk in feeding calves.

The best way to measure the herd infection rate is by use of an objective diagnostic test. The entire adult herd should be tested (all animals ≥2 years old). Either a serum antibody test like the ELISA or fecal culturing could be used. Both tests have sensitivity of about 50% for detecting subclinical infections. Consequently, if 5% of a herd tests positive (apparent prevalence), it should be assumed that twice as many cows in the herd, 10%, are actually infected (true prevalence).

Step 2: **Survey the management practices on the farm.**

Emphasis should be placed on manure management and contact between calves and the adult herd. The level of hygiene in calving areas, frequency of cleaning the areas, and how promptly calves are removed from the cow are directly related to the probability a calf will become *M. paratuberculosis*-infected. Ideally, calves should be raised in an area free of adult fecal contamination for at least the first 6 months of life.

Feeding of waste milk to calves is a second, often overlooked practice that can transmit *M. paratuberculosis*. Use of milk replacer for all calves is a simple solution to the problem; however, colostrum too can contain the organism. Routine use of diagnostic tests on the herd can help by identifying cows that are more likely to be infected; then, feeding their colostrum and milk to calves can be avoided.

Step 3: **Outline a control/eradication program consistent with the economic capabilities of the owner and the findings from steps 1 and 2.**

Several excellent recent reports have summarized paratuberculosis control practices, and most of these recommendations are intuitively obvious. So many recommendations are often listed, however, that there are too many to be implemented immediately and the herd manager and veterinarian can feel overwhelmed. The five paratuberculosis critical control points listed on the following pages are the most effective and least expensive, and should be the foundation of any control or eradication program.
Critical control points for paratuberculosis in dairy herds.

#1 - Calving.

Generally, on most farms the largest benefits will be realized from changes in calving practices. This is frequently one of the farm management areas given least attention, and improvements in hygiene and the overall quality of calf rearing practices will minimize *M. paratuberculosis* transmission and may decrease several other common calfhood disease problems, such as diarrhea and pneumonia. Prompt removal of calves from cows and housing calves in clean hutches placed in a dry and well ventilated location on the farm is a simple, easily implemented, and low-cost way to control new paratuberculosis infections on a farm. Calves should only be fed colostrum from paratuberculosis test-negative cows.

#2 - Calf rearing.

On farms serious about paratuberculosis control, no raw milk should be fed to calves. Milk replacer products exclusively should be used to feed calves up to weaning. This is often a difficult management practice to change. Unfortunately, switching from milk to milk replacer may lead to increases in other calfhood disease problems. Inability to use milk for feeding calves is one of the many hidden costs of Johne's disease to herd owners.

#3 - Test-and-cull.

Every paratuberculosis control program should invest in methods to identify and cull infected cows in a herd, in particular those shedding *M. paratuberculosis* in their feces. Cattle infected with *M. paratuberculosis* shed millions to billions of *M. paratuberculosis* in their feces daily, and the organism can remain viable for over a year, depending on environmental conditions. These fecal-contaminated environments are the most common sources of infection for calves.

The choice of diagnostic test is complicated by economic considerations. Because of the variable subsidy structure for services at veterinary diagnostic laboratories across the country, it is hard to generalize as to which test is most cost effective. In principle, the best test is one that detects fecal shedders of *M. paratuberculosis*. These cattle are in more advanced stages of the disease, more infective, and more likely to transmit the infection to their calves in utero or through their milk. Conventional culture, BACTEC culture, and DNA gene probes are all techniques available to detect fecal shedders. While these techniques are usually more expensive than serologic tests (costing in the range of $8 to $25/animal), they detect the more infectious animals and occasionally detect infected animals missed by serologic tests.

**ELISA is the least costly and most accurate serological test.** It is the most cost-effective means of assessing the herd infection rate. Many, but not all, fecal shedders of *M. paratuberculosis* will test ELISA-positive. For a minimal investment of roughly $4/cow, a herd owner can thus measure the prevalence of paratuberculosis, then begin to cull the test-positive animals. Note: not all Johne's
ELISAs are the same. These comments pertain only the USDA-licensed *M. paratuberculosis* Antibody Test Kit® (IDEXX Laboratories, Inc.)

For herd owners wishing to make the most rapid progress in controlling paratuberculosis, the best testing regimen is one that uses the ELISA plus fecal culturing to detect as many infected cows as possible. The tests could be performed concurrently or on an alternating basis. Test frequency as short as every 6 months is advocated by some experts, but testing once a year is probably sufficient. The most aggressive test-and-cull program is one in which the test-positive cow and its daughters are culled from the herd.

#4 - Farm sanitation.

After the risk of fecal or milk transmission of *M. paratuberculosis* to calves is minimized through management changes and a regular test-and-cull program is established, other potential avenues for *M. paratuberculosis* transmission on a farm should be corrected. The most common problem is fecal contamination of feed for the adult cattle by use of common equipment for feces and feed handling or feed bunk designs that allow fecal contamination. Free-stall barns seem more prone to these problems than do stanchion or tie-stall barns. Another potential source of *M. paratuberculosis* transmission is drinking from surface waters contaminated with feces from the adult herd. Although adults are considered refractory to *M. paratuberculosis* infection, a sufficient dose probably can cause infection and disease.

#5 - Prepurchase testing.

Before purchase, replacement cattle should be tested by ELISA or fecal culturing and only come from herds that have negative paratuberculosis test results on the whole herd. It is economically foolish to invest in a paratuberculosis-control program if reintroduction of the infection to the herd is not scrupulously avoided. The risk of buying *M. paratuberculosis*-infected dairy cattle is roughly 1 in 10 on the basis of recent surveys. The only reasonable means of reducing this risk is to buy tested cattle and, because of the sensitivity of existing tests for paratuberculosis, it is important to buy only test-negative cattle from herds with no or few test-positive animals.

DO NOT VACCINATE

Vaccination of cattle against paratuberculosis is not on this list of recommendations. Although it may have served a purpose in the past, recent information indicates it is of limited value in controlling *M. paratuberculosis* infections, causes a false sense of security in owners, is a serious health risk for veterinarians, and prevents use of serologic tests in a herd.
Johne's disease: View of the future

New diagnostic tests

Two new tests which may see increasing use in paratuberculosis diagnosis and control are discussed below. Today, these tests are primarily used for research purposes. However, I think they will be used increasingly for routine herd screening and/or clinical diagnosis confirmation.

GAMMA INTERFERON ASSAY

Principle of the test:
Mycobacterial diseases like tuberculosis in humans and cattle are primarily diagnosed today by skin testing. Skin testing is done by injection of very small amounts of mycobacterial antigens, called PPD, intradermally. After 48-72 hours, the site of PPD inoculation is examined for evidence of swelling. Swelling indicates that the animal is sensitized to the antigens that were inoculated. Specifically, it indicates that the animal has a cell-mediated immune response to mycobacteria. Comparative cervical testing of cattle is used to discriminate between cattle infected/sensitized to \(M. \text{ bovis}\), the cause of TB in cattle, and \(M. \text{ avium}\) a common soil saprophyte.

Gamma interferon (IFN\(\gamma\)) is a substance released by cells (mostly T lymphocytes) that serves to activate other cells of the immune system (generally macrophages). Release of IFN\(\gamma\) by T lymphocytes after exposure to PPD is considered to be an indication of infection or prior exposure of an animal to mycobacteria. The IFN\(\gamma\) assay has been made into a test kit that can be used as a laboratory test that gives the same kind of information as does a skin test for TB. The IFN\(\gamma\) test has also been made into a kit for diagnosis of \(M. \text{ paratuberculosis}\) infections. Preliminary data indicates that it has good sensitivity and high specificity (>95%) and that it usually becomes positive in infected animals before other tests for paratuberculosis do. Thus, it might be a good test for screening heifers before breeding or calving.

Evaluation of the IFN\(\gamma\) assay for paratuberculosis is not yet complete, but early results of studies at the University of Wisconsin on both naturally and experimentally \(M. \text{ paratuberculosis}\)-infected cattle are promising.

BACTEC CULTURE

The BACTEC system is a radioisotope-based detection technique for isolation, identification and sensitivity testing of mycobacteria that has become standard in human clinical microbiology laboratories. BACTEC methods have not been widely employed in veterinary diagnostic laboratories, however, and few studies have reported use of BACTEC methods for detection of \(M. \text{ paratuberculosis}\). Discussion of the advantages and disadvantages of this technique will be restricted to the radiometric method with filter concentrated samples as reported by Collins et al. in November 1990.
BACTEC culture has the same advantages as conventional culture as a diagnostic test for paratuberculosis.

**High specificity**  Isolation of *M. paratuberculosis* from an animal is considered definitive for diagnosis of the infection. Lacking the ability to produce mycobactin, a siderophore all other mycobacteria use to obtain iron from their environment under natural conditions, *M. paratuberculosis* can be considered an obligate parasite of mammalian cells, usually macrophages. Since recovery from infection is not known to occur, the organism also can be considered an obligate pathogen. Thus, isolation of *M. paratuberculosis* from clinical samples as a method for diagnosis of paratuberculosis is 100% specific.

**Detects infectious animals**  Animals excreting *M. paratuberculosis* in their feces are those most likely to transmit the infection to other animals. Fecal excretion has been correlated with increased likelihood of excretion of *M. paratuberculosis* in milk and colostrum, and transmission of the infection to fetuses in utero. Fecal excretors of *M. paratuberculosis* are generally the animals more likely in advanced stages of the infection and those more likely to soon progress to clinical disease. Consequently, for control of paratuberculosis, detection of fecal excretors of *M. paratuberculosis* is important.

**Allows further testing of the infecting strain of *M. paratuberculosis***  Culture-based methods have the distinct advantage, over all other methods of paratuberculosis diagnosis, of isolating the specific strain of *M. paratuberculosis* causing the infection. With the organism in culture, further studies can be performed that will aid in understanding the biology (eg, antibiotic sensitivity) and molecular epidemiology of this pathogen. Such studies are critical to advancements in paratuberculosis research.

Advantages unique to the BACTEC culture method are:

**Lower limit of detection and higher sensitivity than conventional culture**  The combination of selective concentration of *M. paratuberculosis* using a large-pore filter that retains clumped organisms, a culture medium supplemented with selective antibiotics, and a radioisotope-based growth indicator system, permits detection of as few as 3 *M. paratuberculosis* per gram of clinical sample. Broth-based bacteriologic media are generally able to recover lower numbers of organisms from clinical samples than are solid agar media. Broth culture media are preferred over agar media for recovery of organisms injured by exposure to heat or chemical treatments, such as decontaminants.

**More rapid detection of *M. paratuberculosis***  Detection time in the BACTEC system is directly related to the number of *M. paratuberculosis* in the inoculum. When high numbers of *M. paratuberculosis* were present in tissues of infected animals, growth of the organism was detected in 3 days. Growth of *M. paratuberculosis* from bovine fecal samples from clinically normal cattle is typically detected after 28 to 35 days of incubation. For practical reasons, cultures are declared negative after 7 weeks incubation without detection of growth.
Commercially available, quality controlled and comparable in price to conventional culture

The base medium, BACTEC 12B, is commercially available. A single vial of the medium per sample is sufficient for routine radiometric cultures, replacing the need for multiple tubes of conventional culture media. The approximate cost for a vial of BACTEC 12B, with egg yolk and antibiotic supplements, is $4.00 as compared to four tubes of Herrold's egg yolk agar (recommended procedure) valued at approximately $6.00 (preparation costs included). Becton-Dickinson, the company producing the BACTEC system, generally provides the BACTEC 460 instrument to laboratories at no charge in exchange for a long-term contract to purchase a specified number of units of the BACTEC 12B culture medium.

Sealed vessel prevents dehydration of the medium

Prolonged incubation required for conventional cultures often results in dehydration of the medium making it unsuitable for growth of mycobacteria. Another problem faced with conventional culture methods, is contamination from sources other than the specimen itself. Both of these problems are avoided by use of BACTEC 12B medium which is contained in a sealed vessel.

Automated and objective growth detection

Because growth of *M. paratuberculosis* is detected by an instrument, it does not depend on the eyes of an experienced clinical microbiologist. In addition, cultures can be read with less investment in time by the technologist.

The BACTEC culture method is used at the University of Wisconsin as the sole method for isolation of *M. paratuberculosis* from clinical samples. Identification of mycobacterial isolates is done by DNA probe and HPLC analysis of mycolic acid extracts from the cell wall. Use of these sophisticated identification methods is generally only necessary for mycobacterial isolates obtained from zoological animals. In 1994 at the University of Wisconsin, over 4,000 BACTEC cultures were done on clinical fecal and tissue samples.

*Mycobacterium paratuberculosis: a possible zoonotic pathogen*

Association of *M. paratuberculosis* with Crohn's disease

*(From Proceedings of the U.S. Animal Health Association, October, 1994)*

Crohn's disease is one of two similar diseases of the human intestinal tract called inflammatory bowel disease. It is a chronic, incurable, low-grade inflammation of the terminal ileum that afflicts roughly one million person in the U.S.¹ The incidence of Crohn's disease is difficult to estimate because it is not a reportable disease, however, approximately 20,000 to 25,000 new cases are thought to occur in the U.S. each year. The incidence, 4-11/100,000, is similar in most developed countries and records indicate the incidence is increasing.² The highest attack rate is in people 15 to 30 years old. Investigators interpret this to imply human exposure to some agent or environmental factor(s) in early childhood that lead to the disease. Patients with Crohn's disease suffer from diarrhea, chronic weight loss, abdominal pain, and general malaise. In Crohn's disease, the wall of the terminal ileum is thickened by a diffuse granulomatous inflammatory response that bears marked resemblance to that induced by a mycobacterial infection. Anti-inflammatory drugs like steroids are usually used to treat
the symptoms of Crohn's disease. This treatment is consistent with the prevailing opinion that a major component, if not the cause, of the Crohn's disease is autoimmune-mediated. Treatment temporarily alleviates the symptoms of Crohn's disease but does not result in a cure, and patients must resign themselves to medical management of the condition for the duration of their life. As the degree of intestinal pathology progresses, it is common for Crohn's patients to require surgical removal of a segment of the affected bowel.

Crohn's disease and Johne's disease (bovine paratuberculosis) are remarkably similar in clinical signs and intestinal pathology. However, because *M. paratuberculosis* is readily cultured from animals with Johne's disease but not from humans with Crohn's disease, B.B. Crohn et al.\(^3\) and most gastroenterologists and Crohn's disease researchers since his time, have considered Crohn's disease to have an etiology not related to mycobacteria. In the late 1980s, investigators began reporting isolation of *M. paratuberculosis* from patients with Crohn's disease.\(^4-8\) They found that the organism was frequently present in these patients in a cell wall-deficient state called a spheroplast.\(^9\) These spheroplasts lack the normal tough cell wall characteristic of mycobacteria and are thus very fragile and easily destroyed by disinfectants. The inability of spheroplasts to survive harsh chemical treatments typically used to process clinical specimens for isolation of mycobacteria may explain the long history of failure to grow *M. paratuberculosis* from specimens from Crohn's disease patients. Without a cell wall, spheroplasts can not be stained or therefore seen in tissue sections by histopathology, possibly explaining failure to *see* mycobacteria in biopsies from affected human bowel tissue.

Genetic probes provided new tools with which to examine the assumption that *M. paratuberculosis* was the cause of Crohn's disease. Results of application of gene probes to tissue samples from patients with Crohn's disease are causing the medical community to reconsider whether mycobacteria, and *M. paratuberculosis* in particular, might not be the cause of this disease.\(^8,10-14\)

Data supporting the hypothesis that *M. paratuberculosis* causes Crohn's disease are as follows: Isolation of *M. paratuberculosis* from a patient with Crohn's disease was reported in 1984.\(^5\) This isolate, when orally inoculated into infant goats, caused Johne's disease.\(^15\) Since that time, isolation of *M. paratuberculosis* from Crohn's patients has been reported from almost every developed country.\(^16\) In 1992, using newly developed genetic probes, Sanderson et al.\(^14\) reported that 26 of 40 (65%) of Crohn's patients studied harbored *M. paratuberculosis* in their intestinal tissues. July, 1994, Danish workers, using genetic probes for *M. paratuberculosis*, reported finding evidence of the organism in fresh intestinal tissues in 11 of 24 (46%) Crohn's patients, confirming the findings of the British workers.\(^17\) French investigators reported similar findings; 72% of 18 Crohn's patients tested positive for *M. paratuberculosis* by IS900 PCR amplified probe.\(^12\) Using new tests for serum antibodies to *M. paratuberculosis*, workers in Spain, England, and Italy have found that Crohn's patients have a significantly higher rate of positive results than do control patients.\(^18-20\)

Data not supporting this hypothesis come from laboratories that have failed to consistently isolate *M. paratuberculosis* from Crohn's patients, or failed to find differences in the frequency of antibody titers to *M. paratuberculosis*, or other mycobacteria, between Crohn's patients and suitable controls.\(^21,22\) Critics of such reports argue that such studies are heavily dependent on the accuracy of laboratory
tests used, the expertise of the technologist performing the assays, and the experience of the investigators in working with fastidious mycobacteria such as *M. paratuberculosis*.

Epidemiological studies have shown no correlation between occupational exposure to animals and the incidence of Crohn's disease. However, recent information suggests that *M. paratuberculosis* may have a wider environmental distribution than previously thought, or be a food-borne microbial pathogen, confounding studies of occupational risk factors for Crohn's disease.

*Mycobacterium paratuberculosis* is found in milk of infected cows. In October, 1993, Chiodini reported data on the thermal tolerance of *M. paratuberculosis* suggesting that it can survive pasteurization far better than other mycobacteria. At the Fourth International Colloquium on Paratuberculosis held in Cambridge, England, July, 1994, a food microbiologist from Ireland also reported that *M. paratuberculosis* can withstand pasteurization conditions. At that meeting, British workers reported that 21 of 336 (6.25%) of cartons or bottles of milk purchased from retail outlets throughout central and southern England tested positive for *M. paratuberculosis* using gene probes. While genetic probes can not distinguish dead from living organisms, when coupled with other reports, it seems plausible that the pasteurized fluid milk supply could be contaminated with viable *M. paratuberculosis*.

The ability of *M. paratuberculosis* to survive pasteurization may not be required for it to be found in dairy products still viable. Cheese products could contain the organism. Only 38% of milk used in the manufacture of cheeses is subjected to any heat treatment. Furthermore, when milk is heated prior to production of many cheese products, the heating regime (65°C for 15-18 sec) is far less rigorous that used for pasteurization of milk for fluid consumption, and well below that necessary to kill *M. paratuberculosis*.

Dairy products may not be the only means for exposure of humans to *M. paratuberculosis*, however. Studies on the tissue distribution of *M. paratuberculosis* in infected animals indicate that it is present in blood and many organs of the body. Thus, red meat also could contain *M. paratuberculosis*. In addition, surface water contamination by *M. paratuberculosis*, and survival of after treatment of water for domestic consumption, could theoretically expose humans to this organism. This theory is not only plausible, but has precedence. *Mycobacterium avium*, first cousin to *M. paratuberculosis*, occurs in domestic water supplies, and domestic water is considered to be a principle means by which AIDS patients acquire intestinal infections by this mycobacterial pathogen. Lastly, when considering possible mechanisms for exposure of humans to *M. paratuberculosis*, the dairy industry should not be the only focus of attention. Paratuberculosis also occurs in beef cattle, sheep, goats, camelids and many exotic ruminants.

While the evidence for a causal relationship between *M. paratuberculosis* and Crohn's disease is not yet over-whelming, it is sufficiently strong that animal industries and the veterinary profession should take action. If *M. paratuberculosis* becomes established as the cause of Crohn's disease, or even an important complicating infection, and investigations confirm that it is present in foods of animal origin, the magnitude of the paratuberculosis problem as a food safety issue will be profound.
Because paratuberculosis is most prevalent in dairy cattle, and because \textit{M. paratuberculosis} is known to be excreted in milk of infected cows, the diary industry may be first and hardest hit.

Research is needed to address many pressing questions such as:

- Does \textit{M. paratuberculosis} survive after pasteurization using commercial equipment rather than laboratory scale systems?
- Can gamma irradiation or other milk processing methods kill \textit{M. paratuberculosis}?
- Do the \textit{M. paratuberculosis} strains isolated from humans originate from dairy cattle, other humans, or other animals?
- Are present paratuberculosis control recommendations able to effectively eliminate the infection from herds?
- Could antibiotics be used for chemoprophylaxis of calves to limit the rate of infection?
- Can more effective vaccines be developed?
- Do cattle genetics play a role in determining susceptibility of animals to \textit{M. paratuberculosis}?

These and many more questions remain to be answered about paratuberculosis. Bovine paratuberculosis is sufficiently prevalent and costly to warrant increased effort to control the disease for animal production industry profitability reasons alone. If \textit{M. paratuberculosis} is added to the growing list of food-borne microbial pathogens of humans, control of paratuberculosis in animals used for food production may change from a recommendation to a requirement.

References related to Crohn's disease association with \textit{M. paratuberculosis}: 


Paratuberculosis Diagnostic Services Available
at the University of Wisconsin
School of Veterinary Medicine

- Consultation - Call Mike Collins at:
  Office phone: 608-262-8457
  E-mail: CollinsM@SVM.VetMed.Wisc.Edu
  Lab phone: 608-263-6920
  (experienced staff can answer questions)
  Lab FAX: 608-265-6463 (=26-JOHNE)

- Literature:
  - Client handouts;
    A summary of Johne's disease with color pictures.
  - Practitioner literature; for more detailed background information.
  - Scientific literature; clinical and basic research articles.

- Testing:
  - Serum antibody ELISA (USDA-licensed kit from IDEXX)
    Cattle, bison, buffalo and goats @ $5.00/serum
  - Gamma interferon assay for bovine paratuberculosis
    (USDA-licensed kit from IDEXX)
    Bovine samples @ $25.00/sample (appointment required)
  - BACTEC fecal cultures performed @ $16/sample
  - Mycobacterial isolates identified by DNA probes and HPLC @ $25 ea.

- Information on the Web!
  http://www.vetmed.wisc.edu/pbs/johnes/

Charges are the same for Wisconsin and non-Wisconsin veterinarians and based on rates effective July 1, 1996 (subject to change).