Johne's Disease in Cattle

Greg Cline, Student, VM IV
College of Veterinary Medicine
University of Missouri
Columbia, MO 65211

Introduction

Johne's disease, caused by *Mycobacterium tuberculosis*, is a problem of global proportions that causes economic losses due to decreased production, increased production costs (including veterinary care) and ultimately death incurred due to attempts at salvage, or systemic pathology. In one study, the prevalence of Johne's disease in a cross-section of Wisconsin cull cattle was 10.8%; the resulting losses from decreased production (i.e., milk yield) and forced culling exceeded 52 million dollars annually.[1]

In New England, an 18% incidence of infection in the cattle industry suggests that 129,060 cattle could be infected. If this figure is projected on a nationwide basis it could mean that 19.9 million total cattle could be infected.[2] This clearly shows that the economic importance of paratuberculosis requires that producers and veterinarians alike become well-versed on the topic.

Pathogenesis

Transmission of the causative agent of paratuberculosis is primarily through ingestion of fecally contaminated feed-stuffs. Calves are most susceptible to *Mycobacterium paratuberculosis* infection, and only a few organisms are needed to produce infection. Resistance begins to occur after approximately one month of age when relatively large numbers of the organism are needed to cause infection.[3] With the infection occurring early in life, it is interesting to note that clinical signs occur in most cases after the animal reaches or exceeds two years of age. However, under certain circumstances, usually when large numbers of organisms have been ingested, or when other stressors such as concurrent disease or poor nutrition are present, clinical illness can appear at 12-18 months of age.[4]

The lesions in cattle are primarily characterized by diffuse granulomatous changes within the bowel, with little or no evidence of necrosis.[5] Localization and multiplication of the organism in the ileum and colon causes massive cellular infiltration, which imparts a characteristic corrugated appearance of the thickened mucosa. This is a common necropsy finding, and helps to explain many of the clinical signs. When histologic evaluation of affected tissues is performed, an accumulation of epithelioid cells and lymphocytes are found in the lamina propria (Figure 1). There is evidence to suggest that these lymphocytes have an altered T-cell function mediated by an imbalance of metabolic products of arachidonic acid.[5]

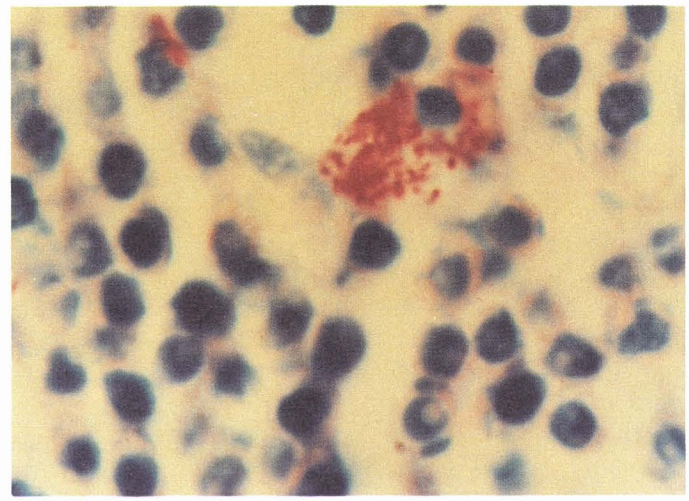

FIGURE 1. Mesenteric lymph node impression. Note the many acid fast bacilli present within the macrophage.

The resulting tissue changes are accompanied by an increased leakage of plasma proteins across the intestinal wall and malabsorption of amino acids from the intestinal lumen.[5]

Evaluation of available information regarding Johne's disease in cattle suggests the following conclusion: A massive cellular infiltration into the intestinal mucosa by disfunctioning T-cells causes mucosal thickening and malabsorption. This is compounded by a protein losing enteropathy.

With this information in mind, the clinical signs of Johne's disease become a logical sequel of its underlying pathophysiology.

Clinical Signs

The clinical signs of paratuberculosis are related to cellular infiltration of macrophages and lymphocytes. The resulting thickened intestinal walls decrease absorption, causing a chronic diarrhea and a malabsorption syndrome.[4] The resulting malabsorption syndrome, over an extended period to time, directly leads to the debilitation of the animal. The most serious component of the malabsorption syndrome is the resulting reduction in protein absorption.

In cattle, the loss of protein results in lethargy, muscle wasting, and edema. In conjunction with the previously mentioned factors, the most common clinical signs appear to be emaciation, submandibular edema, decreased milk yield, and soft, watery feces (the feces are usually without offensive odor, blood, epithelial debris, and mucous). There is usually an absence of fever or toxemia. The appetite is usually good throughout the course of the disease, but an excessive thirst may occur.[4] These clinical signs will lead to dehydration, emaciation, and weakness in the later, protracted stages of the disease. It should also be emphasized that clinical signs are most common in cattle in the two to six year-old age group.[4]

The economic implications of the loss of the infected animals in a herd situation can be staggering, particularly if the genetic potential of the affected individual warrants treatment at any cost. To date, no treatment has affected a cure.

So, what can be done?

Treatment

In the United States, treatment of a clinical case of *Mycobacterium paratuberculosis* has yet to elicit a cure. Treatments have been attempted, but the results have been only marginally successful, and high treatment costs can be incurred. In those animals in which perceived value warrants treatment, clofaziminea, a human antileprosy drug, can be utilized in an attempt to extend the infected animal's life span. Clofazimine has caused some alleviation of clinical signs in animals with clinical stages of Johne's disease.[6,7] Clofazimine will not eliminate the causative agent, and will only suppress or reduce the clinical signs associated with *Mycobacterium paratuberculosis* infection. Cows that are responsive to clofazimine should be kept on the drug for the remainder of their life to prevent relapse or reoccurrence of clinical signs.[7]

It should also be mentioned that clofazimine therapy can be coupled with intravenous johnin administration. Johnin administered intravenously has been shown to increase fecal dry matter.[8]

In most herds, prevention of clinical Johne's disease through vaccination is a more viable option than treatment. A vaccine has been developed; however, the problem with its use lies in the fact that after administration, a positive result to the caudal tail fold test for mammalian tuberculosis will be present.

The current status on the usage of the vaccine is that it may be used only by veterinary practitioners who have a permit from the state veterinarian of the state in which they practice, it can be administered only in herds with a negative herd tuberculosis test, and can be given only to calves from 1 to 35 days of age.

Vaccination has been shown to be very effective in preventing the onset of clinical signs, but does not prevent infection. In actuality, vaccination only restricts the cellular response in the intestinal wall and thus prevents the onset of clinical disease.[4] The reduction of the clinical signs of the disease also decreases the rate of fecal excretion of *Mycobacterium paratuberculosis* organisms. In one study, the ratio of excretion in calves vaccinated at 14-30 days of age fell from 19.2% to 0.4%, a reduction of 97.4%.[9] It has also been found that in herds on a vaccination program for five or more years, the number of fecal shedders per hundred dropped from an average of 10.6 to 1.2 fecal shedders/100 animals/year.[10] The use of the vaccine has even reduced the number of animals within a herd found positive for Johne's disease at slaughter from 55% to 8.7%.[10] Therefore, in certain situations, the use of the vaccine can show dramatic results.

Clinical Report

On April 5, 1989, a five-year-old Guernsey cow (#944) was presented at the University of Missouri Veterinary Diagnostic Laboratory for necropsy. Number 944 had calved on February 23, 1989 (which began her third lactation), and normally presented calf was born without assistance.

#944 was part of a 400 head closed herd that included a milking string of 155 with a rolling herd average of 19,360. Dairy Herd Improvement Association (DHIA) records
showed that for the previous lactations, #944 produced – on the 305 x 2 scale – 16,150 pounds and 15,480 pounds respectively for each lactation. The first 41 days of the third lactation, #944 produced little to no milk, with the highest yield being 15 pounds per milking. In conjunction with the tremendous decline in milk production, a chronic diarrhea was present which resulted in severe emaciation.

The cow's appetite and temperature were normal. Due to #944's severe emaciation and lack of milk production, herd owners opted for euthanasia and a full necropsy.

At necropsy the animal was found to be lean and greater than 5% dehydrated. No significant lesions were found, other than a granulomatous ileitus. Mesenteric lymph nodes were twice normal in size. Representative intestinal samples and lymph nodes were submitted for histopathologic examination; scrapings of the ileum were taken and submitted for acid fast staining.

Histopathology revealed displacement of the intestinal glands by infiltrating macrophages and lymphocytes; the lymph nodes were hyperplastic with the sinusoids con-

[a] *Geigy Laboratories, Ardsley, New York. The cost for treating a 1200 pound cow would be about 84 cents per day.*

taining numerous macrophages, some containing acid fast organisms (Figure 2). Direct microscopic examination of tissue from the intestinal scraping revealed acid fast bacilli compatible with *Mycobacterium paratuberculosis*. The final diagnosis was confirmed as Johne's disease.

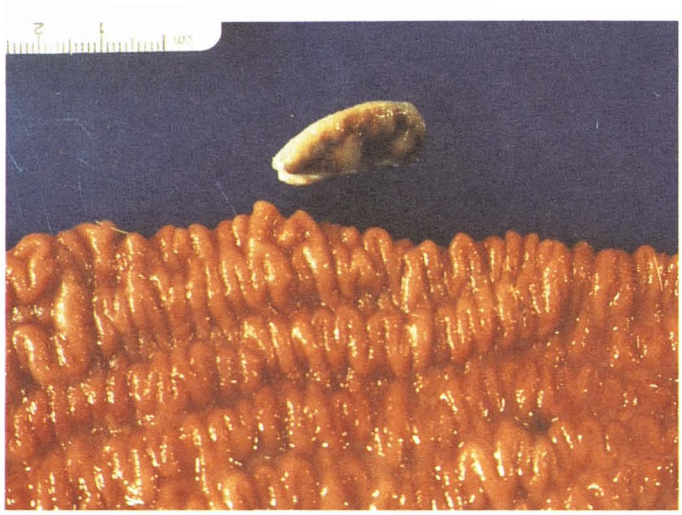

FIGURE 2. Ileum and lymph node. Note the characteristic corrugated appearance to the gut. The node is congested and enlarged.

The establishment of Johne's disease in this herd may constitute a severe problem, as cow #944's offspring are reproductively mature and lactating.

Management of the Johne's Positive Herd

The veterinarian does not always have to turn to immediate necropsy as the primary action. Utilization of all available diagnostic measures (culture, serology, histopathology, and I.V. Johnin testing) after a tentative diagnosis of Johne's is made can help to confirm the diagnosis. After positive identification, there are measures than can be instituted to save the individual and reduce the incidence in the herd.

Establishment of the tuberculosis status of the herd is imperative in that the initiation of a vaccination program cannot begin until the herd is certified tuberculosis free. Vaccination is an easy way to greatly reduce the shedding of the organism, and reduce the incidence of clinical signs. The initiation of a vaccination program would be recommended for the previously mentioned herd, due to the personnel and management practices in place. The establishment of baseline serology titers may be indicated to document the further presence of the organism within the herd. The use of clofazimine would not be recommended due to the value of the animals on this farm. Finally, close watch of preparturient cows should be instituted, so that quick removal of the neonate could be enhanced, thus reducing the transmission of the organism from dam to offspring.

Summary

Mycobacterium paratuberculosis and its clinical result, Johne's disease, has world-wide economic implications for bovine, ovine, caprine, and various wild animal-related disciplines and production systems.[11] Johne's disease can be worrisome and devastating, but it is possible to reduce economic loss through use of proper management and prevention techniques.

Acknowledgements

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Addendum

At the time of final editing of this report, cow #964 was presented to the UMC-VTH with signs consistent with Johne's disease. This cow was the first offspring of #944, the cow previously mentioned in the case report as having been diagnosed as having Johne's disease. Number 964 was near the end of gestation and a calf was delivered by Caesarean section prior to euthanasia. A pre-suckle blood sample from the calf

revealed a negative titer to Mycobacterium paratuberculosis. In this case we assume that in-utero transfer did not occur. This phenomenon has been reported in other clinical cases of Johne's disease.

The calf, at this time, is a normal healthy Guernsey female and has since been returned to the herd. The necropsy of cow #964 revealed a slight mastitis in the right rear quarter. No abnormalities were seen grossly in any of the other organ systems, including the small and large intestine. Histologically, the mesenteric and colic lymph nodes were found to have the paracortical region densely populated by small lymphocytes, also there was an increased number of macrophages and eosinophils in the medullary sinuses of the same nodes. The lamina propria of the small and large intestines was heavily infiltrated by eosinophils. No acid fast bacilli were observed in sections of the mesenteric lymph node or intestines. The final diagnosis was eosinophilic enterocolitis with an eosinophilic lymphadenitis.

These histologic findings are not diagnostic of the disease, but many of the findings are similar and suggestive of Johne's. At this time, a mycobacterial culture is pending; therefore, a diagnosis of Johne's will have to be delayed until culture results are known.

Student Clinical Reports

The AABP Board of Directors has approved a recommendation from the Forward Planning Committee to encourage students to write case reports for this journal and to award prizes.

The first prize ($200.00) is awarded to **J. A. Hoffman**, University of Missouri (see page 167).

The second prize ($100.00) is awarded to **Willem DeHoogh**, University of Illinois (see page 173).

The third prize ($50.00) is awarded equally to **Greg Cline**, University of Missouri (see page176),and **Robert McLaughlin**, Oklahoma State University (see page 180).