General Session IV

Infectious Diseases

Dr. George Lambert, *presiding*

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Paratuberculosis: Prevalence, Diagnosis, Prevention, and Treatment

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Paratuberculosis is an infection caused by *Mycobacterium paratuberculosis*. Clinical paratuberculosis is known as Johne's disease. Most animals acquire the infection shortly after birth, but signs of illness usually are not apparent for several years.

Paratuberculosis usually is spread from herd to herd by the purchase of infected animals that are not showing signs of the disease. We have found that cattle may shed the organisms in their feces for up to three years before exhibiting signs of the illness.

The course of *M. paratuberculosis* infection in cattle usually is approximately as follows: The cow, with a young calf, lies down in feces from an infected animal (either her own or from another animal). When the calf nurses, it ingests some of the organisms along with the milk. The organisms pass through the intestinal epithelium and are phagocytized by macrophages. However, the macrophages in young animals are naive; that is, they do not have a high level of killing ability.

The first stage after infection is a latent period before the immune response is detectable. That is, there is no recognition by the animal that it is infected. The duration of that latent period is inversely related to inoculum size. The first evidence of an immune response is the proliferation of T-lymphocytes in the lymph nodes. At the height of the lymphoprofilerative response, several events occur concomitantly. The animals develop delayed-type hypersensitivity (DTH) and the macrophages become "activated." The DTH may be detected by skin tests, thermal tests, macrophage migration inhibition tests, blastogenesis tests, etc. Some time during the DTH stage, the animal will have been exposed to enough antigen to start producing antibodies. In heavily infected animals the DTH frequently is overwhelmed so that the above tests no longer detect it, but usually the antibody levels continue to rise until death.

No endorsements are herein implied.

Prevalence:

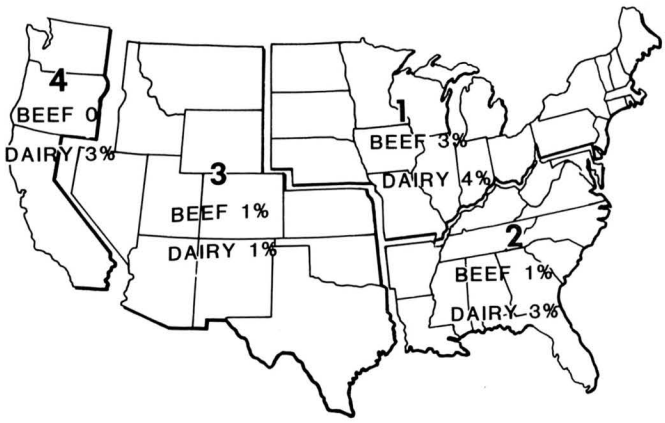
Paratuberculosis occurs worldwide. Culture of ileocecal valves from 992 cattle in Wisconsin yielded 10.8%. Samples from many sites in the intestine, mesenteric lymph nodes, and some other organs from 100 cattle in New England indicated an 18% prevalence. A national survey employing the ileocecal lymph node from randomly selected cull cattle now is being conducted in the United States. It should be noted that culture from one ileocecal lymph node will yield cultures of *M. paratuberculosis* less frequently than when assorted lymph nodes and intestinal tissues are examined in addition. Therefore, the values we are finding in the National Survey are lower than the actual prevalence, but it was not possible to collect and examine multiple specimens from each animal.

Preliminary results have yielded cultures from 3% of the 1,552 dairy cattle examined and from 1% of the 1,746 beef cattle. The infection is not distributed evenly geographically. The regional prevalences are shown in Fig. 1.

Diagnosis:

A large number of tests have been evaluated for detection of paratuberculosis animals. Unfortunately, DTH tests have not proved to be useful, because they recognize antigens that are common to other related organisms, and they are transient. Most complement fixation tests have many false positive and false negative results, plus problems with anticomplimentarity. The most sensitive test for antibody now available is the enzyme-linked immunosorbent assay (ELISA) test, but the methods for conducting ELISA tests

FIGURE 1. Regional prevalences of paratuberculosis.



are not uniform. An agar gel immunodiffusion (AGID) test is available for inexpensive tests of clinically ill animals, to confirm that their condition is due to paratuberculosis. With ELISA tests, cross-reacting antibodies must be absorbed from the serum samples by reacting them with killed *M.phlei* before the test is conducted. With AGID tests, control sera with specific antibody must be placed in wells adjacent to the wells with test sera to obtain lines of identity.

The earliest clinical sign of Johne's disease may be intermittent diarrhea. This appears to be due to an antigen-antibody reaction on the mast cells of the intestine, causing them to release histamine, and hence, cause diarrhea. Eventually, the villi of the intestine become engorged with heavily infected macrophages. In the terminal stages of Johne's disease, insufficient food can be absorbed, and water resorption from the colon is diminised, leading to a chronic diarrhea.

The "text-book picture" condition of emaciation, diarrhea, and alopecia that usually causes a producer to send the cow to slaughter because of Johne's disease is only a minor part of the true costs of paratuberculosis. Paratuberculous cows without signs of illness have about five times more mastitis, lower milk production, and longer intervals between parturitions than the noninfected animals in the same herd. In addition to these losses are costs that are difficult to assess, such as culling before peak production and losses in valuable breeding stock.

Until recently, the only reliable method of detecting infected animals was by fecal culture, which requires at least three months of incubation before a sample can be considered negative. Fecal culture will detect one-third to one-half of the currently infected animals in a herd. Animals that appear to be clinically ill usually can be diagnosed by use of the AGID test, which is less expensive than the ELISA, but much less sensitive.

The state diagnostic laboratories in most states that have large numbers of cattle have the capability to conduct fecal culturing, but most of those laboratories can handle only limited numbers of specimens. Several private laboratories are available to conduct either serological tests or fecal culturing. Two private laboratories that I am aware of are Allied Laboratories in Ames, Iowa, and Greenbriar Laboratory in Delaware, Ohio.

Prevention:

The State of Wisconsin and the American Guernsey Cattle Club have initiated programs to establish "paratuberculosis-free by culture" status, indicating the number of tests in which all adult cattle were sampled and in which no animals were found positive. Replacement animals should be purchased from herds with such status. A "second best" approach is to buy animals from herds with no history of the condition, and to conduct ELISA tests on the prospective replacements before they are added to the herd.

A bacterin has been approved by the USDA for use in vaccinating cattle, and is being produced by Fromm Laboratories in Grafton, Wisconsin. Each state must approve its use in that state, and most states that have approved it are following some version of the "Wisconsin Plan." This plan requires that before a producer can start vaccinating, the herd must be entirely free of tuberculin reactors, paratuberculosis must be demonstrated to be present by culture or histopathological examination, and the bacterin must be administered when the calf is less than 35 days old by a veterinarian approved by the state. Vaccination has been shown to reduce the prevalence of clinical Johne's disease by about 90%, and the prevalence of paratuberculous animals in the herds by about 50%. It causes many cattle to become tuberculin reactors, and eliminates the usefulness of serologic tests for detecting paratuberculous animals. A vaccination nodule, that may reach five inches in diameter, usually develops at the site of inoculation. If accidentally inoculated in the veterinarian's finger, a large and painful granulomatous lesion is likely to develop.

Treatment:

Only one drug has been found that is effective in reducing the level of infection in paratuberculous animals. This is the anti-leprosy drug called Clofazamine, or Lamprene, but it is not approved for use in the United States. It has been used on an experimental basis by our laboratory and others with some success. It is unlikely that it will ever be approved for use in food animals.

Recommendations:

After paratuberculosis has become established in a herd, strict management practices are the key to controlling it. If possible, the calves should be removed from the dam(s) at birth, and natural nursing should not be allowed. Pasteurizing the colostrum and feeding the calves milk replacer helps to break the infection cycle. The calves should be raised in separate, noncontaminated quarters. Do not use

common tools for calves and adults. Plan the parturition of beef cattle for warm weather, so that they can be outside on clean pasture. The use of calf hutches on noncontaminated soil is useful both to help control respiratory disease and prevent paratuberculosis infection. Allow young animals to graze only on pasture separate from where adults graze, and if feasible, spread manure only on ground to be used for row crops. A test-and-slaughter program can eliminate infection in a herd. Fecal culture, although slower and more expensive to conduct than serological tests, is frequently the least expensive in the long run, because it indicates which animals actually are shedding the organisms and how heavily they are shedding.