

Transmission of Paratuberculosis

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Prenatal Transmission

The causative organism of paratuberculosis, *Mycobacterium paratuberculosis*, inhabits the intestinal tract and mesenteric lymph nodes of infected cows. While paratuberculosis has generally been regarded as an enteric infection, there is now evidence that the organism can disseminate to extra-intestinal sites such as uterus, supramammary lymph nodes, udder, sexual organs of bulls, and may be excreted directly in milk and semen.^{1,2,4-8,12,14-16,18} Recent studies would suggest that the likelihood of dissemination increases as extent of infection increases. Most clinical cases are likely to be disseminated.

Trans-placental or *in-utero* infection of fetuses with *M. paratuberculosis* was first reported in 1935, and was initially met with incredulity by the scientific community.¹ However, subsequent studies confirmed these findings, and showed that 20 to 40% of fetuses from infected cows were infected *in-utero*.^{3,7,9,11,13,16} In general, these were studies of fetuses obtained from infected cows manifesting clinical signs of paratuberculosis (weight loss, diarrhea) in other words, cows in advanced stages of the infection. However, the majority of infected cows in a herd do not manifest clinical signs of the disease, even though they may be shedding large numbers of organisms in feces.

A recent study of fetuses from asymptomatic cows confirmed that *in-utero* transmission can occur in those cows, but with less frequency than has been reported for symptomatic cows. Culture of fetal tissue for *M. paratuberculosis* was positive in only 8.6% of fetuses from asymptomatic (infected) cows, compared with the 20 to 40% reported previously for symptomatic cows. The likelihood of fetal infection was dependent on the severity of the infection as measured by the number of organisms excreted in the feces, as all infected fetuses came from "heavily infected cows."¹⁶ These findings suggest that fetal infection in "light shedders" (<10 colonies/culture tube) is unlikely, and it may not be necessary to cull the most recent calf from such a cow, provided that steps are taken to prevent post-natal transmission from the infected cow (albeit "light" infection) to calf. Under no circumstances should a pregnant heavily infected (as identified by fecal culture or positive AGID or ELISA serologic test result) or symptomatic cow be kept

in the herd in hopes of obtaining the calf prior to culling--the cow sheds billions of organisms into the environment, contaminating critical areas such as the calving pens, and the calf has a strong chance of being infected *in-utero* and should not be kept as a replacement.

Post-natal Transmission

After a long incubation period (years), infected cows begin to shed detectable quantities of *M. paratuberculosis* organisms in their feces, in barely detectable quantities at first, and then in gradually increasing numbers as the infection becomes well established. A cow with clinical signs of paratuberculosis may shed billions of organisms each day. These organisms have the ability to persist in the environment for up to a year, and are thus available to infect susceptible animals.

It is generally regarded that young calves are the most susceptible to infection with *M. paratuberculosis*, although the specific numbers of organisms required to establish infection for specific age groups has not been determined.^{10,19} In most herds, it is generally assumed that infected cows were infected as calves, probably soon after birth in most instances. This is often a source of frustration for farmers enrolled in control programs, who may need to be reminded that the animals detected on the most recent test were probably infected 2 or more years ago as calves, possibly before control measures were initiated.

Greater susceptibility of newborn calves may be related to the "open gut" during the first 24 hours following birth, wherein macromolecules (such as immunoglobulins from colostrum) can penetrate the mucosa for absorption--perhaps the mucosal barrier against *M. paratuberculosis* is also reduced during this time. In one experiment involving inoculation of 2 year old heifers with feces from symptomatic cows, *M. paratuberculosis* organisms were found adherent to the mucosa of the ileum, but organisms were not found within the mesenteric lymph nodes four weeks after inoculation.¹⁷ These animals could not be followed long-term to determine if infection was established. Finally, exposure of adult cattle is usually of less concern because of the long incubation period of the organism. Adult cattle, if infected,

are likely to be culled for other reasons before the 2 to 3 year (or longer) incubation period has elapsed and shedding of the organism in detectable quantities begins. There are anecdotal reports of fecal culture negative adult cows being sold to infected herds, and developing clinical paratuberculosis, which suggests that if the exposure dose is high enough, older cattle are also susceptible.

Post-natal transmission of *M. paratuberculosis* to the calf results from oral ingestion of the organism by the calf. The most likely source of fecal contamination of the calving stall, either by the calf's dam, or a previous occupant that was shedding the organism unbeknownst to the farmer. One likely source is the udder of the calf's dam. There is great opportunity for fecal contamination of the udder, and if the calf is permitted to suckle, it will ingest *M. paratuberculosis* organisms. Calves that are housed in the cow barn or fed manger sweepings from the adult cows are more likely to become infected. Contamination of feeding utensils with adult cows' manure, and fecal contamination of the handler's shoes or clothing could present a possible source of infection. Direct manure contamination of feed (animals defecating in feed bunk), contamination of trench silos with manure runoff, and use of manure scraping equipment (front end loader) for handling feed represent other ways that animals may be exposed to contaminated feces.

Finally, even if steps are taken to prevent the above methods of transmission, some cows shed the *M. paratuberculosis* organism directly in their milk.^{1,2,14,15,18} As with *in-utero* transmission, dissemination of the organism from the GI tract to the udder, is more likely to occur in the more advanced stages of the infection. In previous studies, up to 35% of symptomatic infected cows have shed the organism directly in milk, whereas 19% of asymptomatic heavy shedders and only 3% of light shedders had the organism in their milk.¹⁵ While colostrum was not tested, presumably shedding of the organism in colostrum would be comparable. Thus, if colostrum of infected cows is fed to calves, this could serve as a potential source of infection. Some herds have attempted to avoid this route of infection by pasteurizing colostrum or using commercial colostrum replacers/supplements in lieu of feeding colostrum. In most herds, if cattle are tested annually and positive animals are culled promptly, colostrum from "heavy shedders" is unlikely to be used. If known infected cows are not culled, their colostrum should not be used.

Other Methods of Transmission

Other proposed methods of infection include transmission in semen of infected bulls, transmission by embryo transfer, transmission from wildlife ruminant

reservoirs, and transmission by veterinary procedures such as rectal examination.

There is evidence that *M. paratuberculosis* organisms can be found in the semen and accessory sex organs of infected bulls.^{6,7} It has also been shown that inoculation of the uterus with *M. paratuberculosis* organisms can result in infection of the cow. The role of herd bulls used in natural service is still unknown, but it is unlikely for infection to result from artificial insemination as most bulls are tested periodically for paratuberculosis.

Embryo transfer has been investigated as a possible means of transmission of paratuberculosis. It has been shown that *M. paratuberculosis* organisms can be found in uterine washings from infected cows, and that organisms adhere to embryos *in-vitro*.¹² Thus, it would be theoretically possible for an embryo flushed from an infected cow to be infected, resulting in an infected fetus. However, embryo transfer from infected cows has not resulted in infected calves. Similarly, implantation of an infected embryo could theoretically transmit the infection to the recipient cow, but this has not occurred in practice. Therefore, embryo transfer from infected cows is generally regarded as safe for the offspring and the recipients. Inadvertent use of infected recipient cows is more likely to result in fetal infection, via transplacental infection after implantation.

Although wild ruminants such as deer are susceptible to *M. paratuberculosis* and may serve as a sylvatic reservoir, contact of feces from deer is most likely to be with adult cattle or heifers at pasture. Young, more susceptible calves are unlikely to contact these infected deer. The pelleted nature of the deer feces might make dissemination of the organisms in the environment and consumption by grazing cattle unlikely, and it is suspected that deer do not represent a major source of infection for cattle.

There have been no studies on the possibility of transmission of the organism by rectal examination. The ability of the organisms to penetrate the rectal mucosa compared to the mucosa of the ileum is unknown.

Transmission to Herds

The above methods represent the major ways the organism is transmitted between animals within an infected herd, especially oral exposure of calves to feces from infected cows. How is the organism introduced to new herds, or in other words, how does the infection spread from herd to herd? There is no question that the majority of herds that acquire *M. paratuberculosis* do so through purchase of infected animals. Because of the long incubation period, infected cows may show no signs of the infection for many years, and may even test negative on serologic and fecal culture tests. Such a "car-

rier" animal may then be purchased as a herd replacement, and later serve as a source of infection in the new herd when it begins to shed the organism. Purchase of asymptomatic "carrier" animals represents the major threat to the biosecurity of certified test-negative herds, and the program regulations call for immediate testing of purchased animals. Every effort should be made to made to maintain a closed herd, or to purchase animals from a certified test-negative herd.

Summary

Infection of the calf soon after birth by oral ingestion of *M. paratuberculosis* organisms from feces of infected cows is the most important method of transmission of paratuberculosis. The severity and rate of progression of the disease are dependent on the quantity of organisms in the exposure and the age of the animals. A young calf ingesting a large dose of organisms will likely progress to clinical paratuberculosis within 2 to 4 years. On the other hand, an older heifer exposed to only a small number of organisms may never progress to clinical disease. Similarly, it is probably possible to overwhelm age-related resistance by introduction of a large dose of organisms to the adult cow. Other means of transmission such as transplacental and direct excretion in the milk are a concern primarily in advanced stages of infection when heavy fecal shedding is detected.

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