Mastitis Due to *Mycoplasma bovis* Insights

PEER REVIEWED

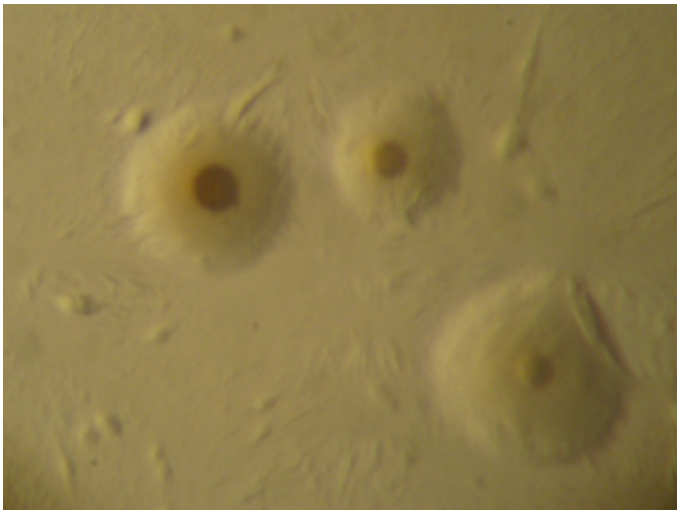
Mycoplasmosis in dairy cattle is an increasing problem that is closely related to herd size. The increased frequency of mastitis due to *Mycoplasma bovis* in the USA and the EU has been linked to herds with more than 500 cows.[1] Along with mastitis, the incidence of other diseases associated with *M. bovis* is also increasing, including pneumonia, otitis and arthritis in calves.[2]

Mycoplasma mastitis prevalence has increased in the last 15 years. In most cases, mastitis tends to manifest itself in its subclinical, non-severe form, usually affecting one quarter, detected in the milk bulk tank.[3] Recently, some outbreaks of acute mastitis have been identified in the UK, the Netherlands and Italy.[4]

Cows infected with mycoplasma spread the infection both vertically through milk and horizontally to other animals through aerosols, direct contact, milking systems or objects contaminated with the infectious organisms (fomites) such as bedding, water or feed. Recent research shows that mycoplasma can survive for months in moist bedding sand and in other organic materials that are not exposed to direct sunlight.[5]

What are Mycoplasmas?

- Mycoplasmas are bacteria with an external lipoprotein-based membrane (very similar to cytoplasmic membranes) instead of a cell wall. For this reason, antibiotics whose mode of action is destruction of the cell wall have no effect on these bacteria.



Mycoplasma bovis colonies. Courtesy Dr Veronica Rojas and Dr Rosa Elena Miranda,
Microbiology Dept, Veterinary Faculty, Nat University of Mexico (UNAM)

- Mycoplasmas are the smallest organisms capable of independent replication, varying in size from 0.125 – 0.82 microns (one-tenth the size of common bacteria). They are too small to be seen using standard microscopy.
- Mycoplasmas evolved from other bacteria (probably gram-positive bacteria) through a process of "degenerative evolution", which entails a loss of non-essential genes.[6]
- Mycoplasmas survive thanks to their highly efficient pathogenic mechanisms.

Why Mycoplasma is a Problem:

Mycoplasma is considered a "silent" pathogen in cattle. While it is less aggressive than other viruses or bacteria, it irritates tissues, distracts the immune system and creates favourable conditions for other pathogens to invade and create disease.[7] Difficulty in diagnosing mycoplasma has led clinicians to underestimate their destructive power.

Studies of 28 BRD outbreaks between 1999 and 2010 in Germany and France reveal that M. bovis is highly prevalent in cattle.[8]

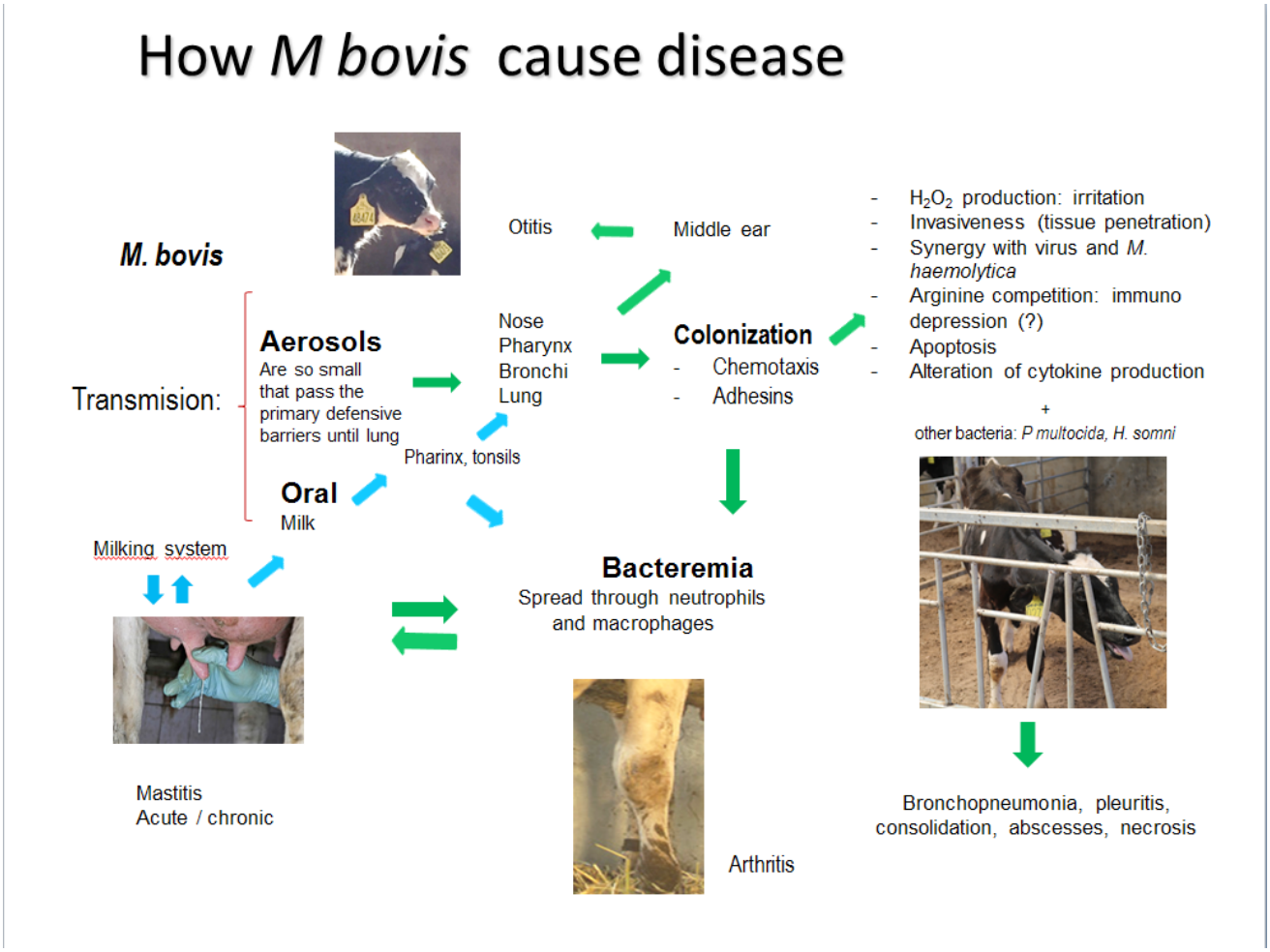
How *M. bovis* Contributes to Disease:

Mycoplasma is a persistent pathogen once established on the farm. Its ability to survive in the environment for extended periods, and its contagiousness, make it a formidable foe. Once the animal is infected, mycoplasma has numerous mechanisms to generate disease:

1. **Spreading to different tissues:** Mycoplasma can move through the tissues via a chemotactic response to sugars and amino acids. Their cytoskeletal-like filaments seem to bind to the cell membrane to create a network in the cell.[9]
2. **Colonisation:** Attachment through accessory proteins enables mycoplasma to bind to animal cells, specifically to sialic acid residues of sialo-glyco conjugate on the host cell membranes.[10] This mobility and its ability to adhere is critical for *Mycoplasma*, allowing it to move to ideal locations within the host and colonise various tissues.
3. **Immune system evasion:** The persistence of mycoplasma is due to its ability to modify its external membrane proteins, believed to contribute to immune system evasion. This is the principal reason the development of a vaccine for *M. bovis* has proven so elusive.[11]
4. **Ciliostatic effect:** Mycoplasmas are thought to produce hydrogen peroxide. This compound, along with superoxide derivatives, produces a ciliostatic effect in trachea cell cultures which allow bacteria to spread.[12]
5. **Invasiveness:** By penetrating the epithelial barriers, *M. bovis* reaches the blood stream causing bacteremia. Mycoplasma's ability to colonise serosal cavities leads to tenosynovitis or arthritis.[13]
6. **Synergistic interaction with other pathogens.** Mycoplasmas facilitate the infection of viral and other bacterial pathogens, mostly in the respiratory tract, contributing to the bovine respiratory disease complex (BRD).[14]

7. **Persistency of *Mycoplasma bovis* in the environment.** Once thought to have relatively short lifespans, as mentioned before, mycoplasma can survive for long periods in humid environments with organic material between 15˚C and 20˚C. They can also live for up to four months in sand bedding.[15]

How These Mechanisms Interact to Produce Disease:



Diagnostic:

- Due to the protagonist role of other bacteria/viruses in clinical diseases, mycoplasma is often overlooked during diagnosis. This may be due in part to the inherent difficulty of cultivating these bacteria in the lab.
- Currently, indirect tests are used to diagnose mycoplasma infections: ELISA, PCR, denaturing gel, electrophoresis, even bacteriology (which is complicated and requires several days).
- Sensitivity tests first require a bacteriological culture, followed by testing of the MIC. Although this takes some time, data can later be used as historical support for treatment of future infected animals.

Treatment:

The common use of βlactams for mastitis treatment does not work against mycoplasma. But, a variety of other antibiotics are used to treat mycoplasma in bovines including: tetracyclines, macrolides, lincosamides, florfenicol and fluorquinolones. However, the long withdrawal periods of new macrolides and florfenicol means they are not always suited for mastitis treatment. Traditionally, mycoplasmal mastitis has not been treated, although infected animals continue to infect others intermittently. But due to the increased incidence of mycoplasmal mastitis, the need for treatment has grown. Not even culling will prevent further infections.[16]

Few studies have been carried out to demonstrate the efficacy of Enrofloxacin in mycoplasma mastitis.[17] Enrofloxacin has been approved to treat mycoplasmosis associated with BRD, bovine otitis and arthritis.[18] The use of Enrofloxacin in mycoplasmal mastitis is not presently approved.

The Eight Best Practices for Mycoplasma Control:

Every farm should:

1. Check acquired animals (including calves), as these can be infected and spread the disease on the farm.
2. Check the milk bulk tank regularly (at least every three months) to monitor the disease.
3. Ensure proper hygiene. Both bedding and all items involved in the milking procedure should be as hygienic as possible.
4. Reduce stress. Welfare and cow comfort are important and stress is a predisposing factor for mycoplasma outbreaks.

On farms where Mycoplasma is suspected or diagnosed:

1. Take samples for mycoplasma in clinical and subclinical mastitis on the farm. Send the samples to the lab. Currently PCR is the fastest and most sensitive test.
2. Determine antibiotic sensitivity.
3. Culling is the best option when few animals are detected as carriers. If possible, treat clinical cases based on historic records of antibiotic sensitivity.
4. Clean and disinfect barns that held the infected animals. For bedding recycling, disinfect with sodium hypochlorite (0.5 %) and chlorhexidine (2 %) which has been shown to be efficacious.

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