Mycoplasma bovis

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Mycoplasma bovis (*M bovis*) was first diagnosed in Ireland over 20 years ago. There is little recent information available on the prevalence of the disease in the country. However, the University College Dublin's (UCD's) Herd Health Group has observed an increase in the number of herd health investigations subsequently attributed to *M bovis* in the last 36 months.

A large proportion of these herds have a history of recent expansion. *M bovis* can have devastating consequences in an outbreak scenario but may be subclinical in endemic herds. *M bovis* is a highly specialised pathogen, known as an atypical bacteria due its lack of cell wall and therefore is an inaccessible target of many antibiotics *M bovis* has several features such as immunomodulatory mechanisms and the ability for biofilm formation as well as many other virulence factors that enhance its pathogenicity and make so difficult to deal with on farms. M bovis is recognised as part of the bovine respiratory disease complex (BRD) and can be present on its own or often in combination with other infectious agents. *M bovis* is capable of exerting pathogenic effects on many organ systems, common clinical presentations include mastitis, arthritis and otitis in calves. A number of other clinical presentations have been reported, such as its role in keratoconjunctiivits and meningitis but are much less common.

SOURCE AND SPREAD

The source of *M bovis* is assumed to be introduction of asymptomatic carriers into previously naïve herds and disease transmission occurs if/when shedding occurs. Presumably stress and immunosuppression may have a role in the shedding of the disease from previously asymptomatic carriers. Although there are still many gaps in the current understanding of *M bovis*, particularly with regard to its epidemiology, there are a number of key features that make this pathogen especially difficult to deal with. *M bovis* is excellent at colonising mucosal surfaces especially those of the upper respiratory tract and tonsils. The upper respiratory tract is thought to be the primary site of colonisation after infection via the aerosol route and the mammary gland is the primary site of colonisation following intra-mammary infection. *M bovis* is capable of persisting with or without causing clinical disease for variable periods of time making shedding patterns difficult to predict. Due to its persistence on mucosal surfaces it can therefore be seen as a commensal and makes the understanding of patterns of disease spread and persistence, as well as diagnosis difficult. *M bovis* however, may also be very pathogenic and once colonised *M bovis* can be found in multiple body sites in the early stages of infection and bacteraemia has been found in some experimental studies post infection. The pathogenic effects are the usually seen following this early disease (if there is a clinical manifestation at all) and immunity develops in some weeks. Once colonized, *M bovis* may be shed from the animal for varying amounts of time and also shed unpredictably and intermittently hence why spread is so difficult to predict. *M bovis* can be spread within herds readily by nose to nose contacts via nasal secretions, aerosols, indirect contact such as via food and water, fomites, in the parlour as a contagious mastitis pathogen on milkers hands/equipment, etc., or by ingestion of infected milk.

M bovis is commonly found in pneumonia cases and *M bovis* associated pneumonia can occur at any age. It has been associated with outbreaks in feedlot cattle and sometimes is followed by an outbreak of polyarthritis following the initial respiratory presentation. *M bovis* is capable of inciting pneumonia alone or as part of the bovine respiratory disease complex where viral infections incite the initial insult damaging the respiratory mucosa, reducing ciliary activity and weakening the immune defences of the respiratory tract. The immune status of the animal is important in the development of mycoplasma pneumonia; failure of passive transfer is a risk for the increased severity of respiratory disease in young calves. Similar to the rest of the pneumonia pathogens; nonspecific respiratory defences can be compromised by many risk factors, such as viral pathogens, changes in environmental temperature, heat or cold stress, overcrowding, transport, poor air quality and poor nutrition predisposing to pneumonia. *M bovis* is often identified at post mortem, characteristic signs include multifocal pyogranulomatous inflammation with centres of caseous necrosis although there is a range of pathology associated with the disease. Lesions are different pending stage of the infection and severity. If animals survive mycoplasma associated pneumonia, poor thrive and weight gain may be a sequelae. *M bovis* pneumonia is often accompanied by cases of polyarthritis particularly in feedlot scenarios but can also be associated with cases of otitis.

M bovis is often identified as a mastitis pathogen, similarly to other disease states it can be present subclinically or manifest as severe clinical mastitis at individual or group level. Some of the key features of mycoplasma mastitis include; it is highly contagious, it often affects more than one quarter, it causes a noticeable reduction in milk production, it is often poorly responsive to treatment, milk can be purulent and odourless, or it can have grossly abnormal secretions often settling out when the sample is left to stand, it is also possible to exist subclinically with little/no changes visible in the milk or indeed in the somatic cell count yet still be shed through the milk in

some cases. Several other disease states, such as arthritis, joint problems or respiratory disease can accompany mycoplasma mastitis. Expanding herd sizes, as well as buying in animals/animals returning to the herd after being reared elsewhere, are potential risk factors for mycoplasma mastitis. Cases have been documented among dry cows and the protocol used at drying off cows can be a potential source of spread in some cases. The lack of a designated, well segregated, (nowhere near youngstock) hospital pen was also found to be a risk factor for the spread of mycoplasma mastitis in herds. Diagnosis is important including strain typing to confirm that the species is *M bovis* and even further molecular typing would be useful if it were available. Some level of immunity to *M bovis* lesions following an initial exposure, is thought to exist for infections spread by the nose to nose route, that at least confer some protection stopping the infection crossing the blood milk barrier for example, following a further insult. However, immunity to infections spread via the intramammary route where infections are centred on colonisation of the mammary gland is not well understood, it is hypothesised that cows do not get immunity and are susceptible to re-infection via this route and indeed some will never cure after first infection. Equally well in experimental studies, cows with mycoplasma mastitis have been shown to have mycoplasma present in the upper respiratory tract (URT). This is an area of ongoing research. Arthritis, synovitis and periarticular infections may be a potential manifestation of *M bovis*. These conditions usually accompany some other manifestation such as pneumonia or mastitis but can occur independently. The clinical signs are typical of those of septic arthritis but the severity depends on the case and degree of joint pathology. If a true septic arthritis the clinical signs can be severe and the welfare of the animal severely affected. However it is possible to have periarticular involvement. Each case should be judged on an individual basis. The author recently investigated a dairy herd outbreak with polyarthritis followed by mastitis. Several of the severely lame animals had to be culled on welfare grounds but many cows who were not severely lame and did not have mastitis but had visibly swollen joints and periarticular swelling recovered, suggesting that the clinical presentation rather than just the presence or absence of clinical signs should be used in determining cases for treatment, monitoring or culling.

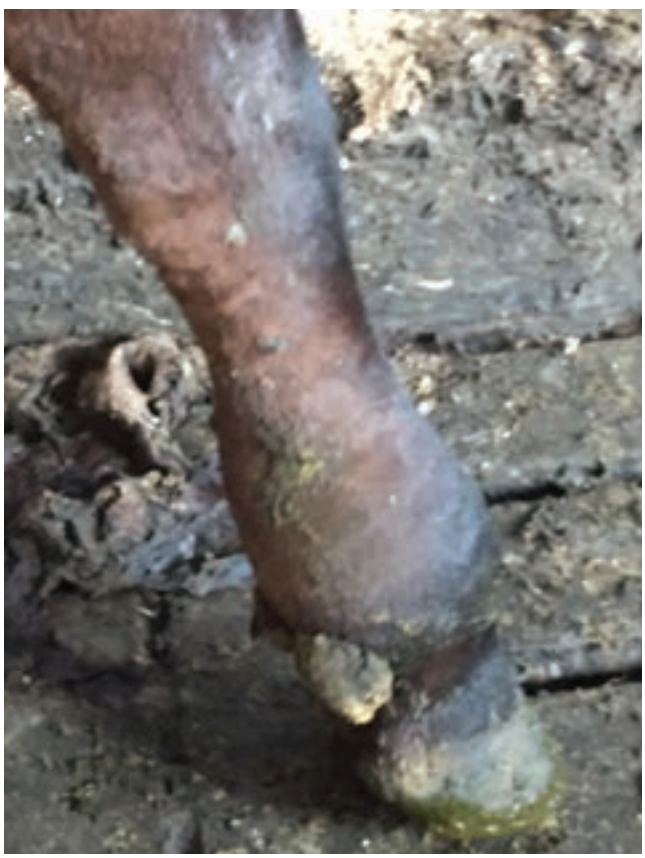
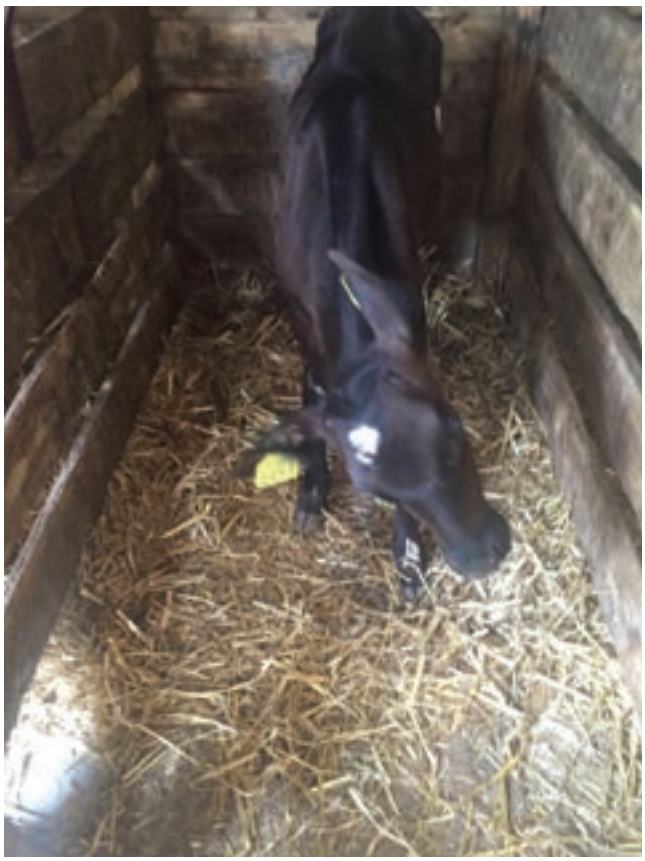


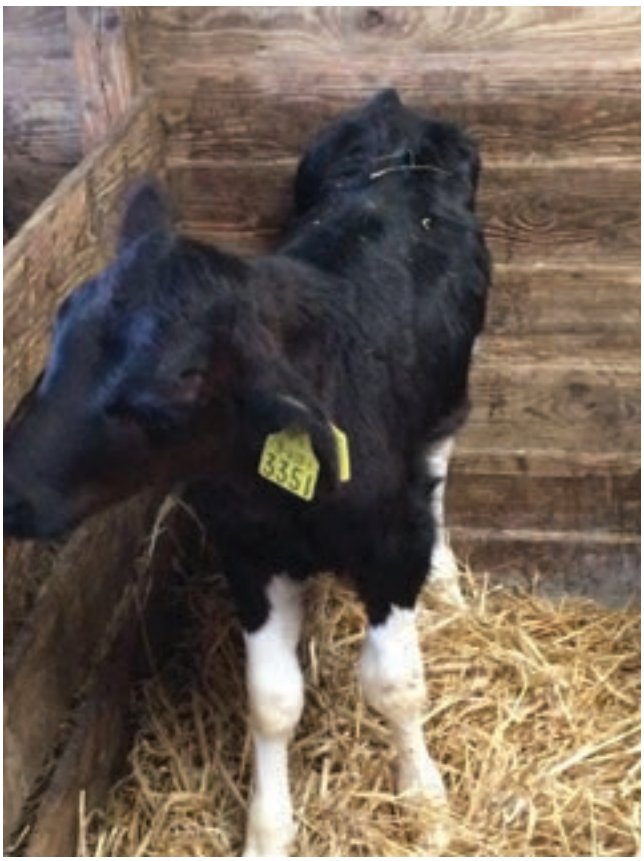
Figure 1: Septic arthritis and visibly swollen joints are symptoms of *M bovis*.

M bovis also is now emerging as the most common cause of otitis media in calves, it can occur in both dairy and beef calves and again can occur sporadically or as group outbreaks. The route of *M bovis* infection in young calves is thought to be ingestion of milk or colostrum infected with *M bovis* from cows shedding the pathogen from the mammary gland, although direct contact, aersol and fomites are also potential routes of infection. After infection, *M bovis* colonises the upper respiratory tract primarily, but can colonise any mucosal surface. Otitis media in calves is thought to result from ascending infection via the Eustachian tube, extension of infection from otitis externa or via the haematogenous route. Infection via the Eustachian tube is accepted as the most likely route by which *M bovis* infections reach the middle ear. Otitis media infection frequently can advance to otitis interna with varying degrees of dysfunction of the vestibulocochlear nerve including nystagmus, head tilt and ataxia. Lesions of the facial nerve are thought to occur due to the anatomical position of the facial nerve and the middle ear. Lesions of the vestibulocochlear nerve are due to infection in the inner ear. In very advanced cases extension of infection can spread to the meninges and along nerves to other brain areas.

DIAGNOSIS

Low sensitivity of diagnostic tests for *M bovis*, intermittent shedding, subclinical infection and the technicalities associated with isolation of *M bovis* all complicate diagnosis. It is however important to confirm diagnosis and presence of *M bovis* in suspected clinical outbreaks. Diagnosis of mycoplasma in clinical material such a milk samples (individual quarter, composite or bulk tank samples), joint aspirates and bronchoalveolar lavage samples can be done by culture or polymerase chain reaction (PCR). Both are readily available in Ireland. Culture requires specialised mycoplasma growth media used at the lab and rapid transit to the lab is important. For nasopharyngeal swabs, a special transport media such as aerobic or special mycoplasma transport medium is required. Any culture for mycoplasma needs to be speciatied to *M bovis*, other mycoplasma species do exist





Figures 2 and 3 show the effects of *M bovis* on the facial nerves of the cow.

in Ireland and it is important to confirm if the pathogen is truly *M bovis*. Tissue samples should be fixed in formalin for histology examination or for immunohistochemistry (to determine the presence of mycoplasma organisms in tissue). Samples should be refrigerated if processing within two days or alternatively, frozen. The presence of mycoplasma inhibitors in tissue may compromise diagnosis and if processing is to be delayed swabs or bronchoalveolar lavage (BAL) fluid may be preferable if stored at 4°C as mycoplasma detection in post-mortem tissue samples once tissue is disturbed, declines rapidly. Serology for *M bovis* is also available in Ireland however is not as useful in clinical diagnosis as presence does not necessarily attribute cause, additionally some clinical cases may develop high titres, some may not, some case may also develop antibody titres that remain high long after the event and maternal derived antibodies (MDA) can give rise to high titres in calves. Group-level serology with high titres that map to seroconversion coincident with disease may be useful in diagnosis. Serology is useful in a screening tool and can be used in youngstock screens (post-MDA) or surveillance as part of a biosecurity programme.

TREATMENT

There are a number of antibiotics reported to be effective against *M bovis* such as certain fluoroquinolones and macrolides for example. However, the disease is often already chronic before treatment is initiated and is often unrewarding. Very early detection and prompt, aggressive treatment may potentially be successful in some cases. There is a number of industry led and also experimental trials on antimicrobial efficacy with some positive outcomes however there is a lack of robust research on treatment of naturally occurring mycoplasma disease. It is accepted that mycoplasma arthritis usually has a poor response to treatment if established in the joint with associated severe pathology, but should be judged on a case by case scenario. Mycoplasma mastitis also has poor cure rates and treatment is rarely advised. Regardless of the organ system/s involved it is important that each individual case and the animal's welfare is considered. Due to the common failure of antibiotic treatment, once a diagnosis is established efforts to contain the disease are usually more focused on control.

CONTROL

Control of *M bovis* in herds is challenging and depends on the nature and severity of the clinical presentation. Reducing concurrent stressors and any potential causes of immunosuppression are important in infected herds and prevention using biosecurity and operating a closed herd is obviously the first choice to prevent entry in the first place. However if mycoplasma is a problem, many of the principles of infectious disease control apply to its control. In herds with problems with respiratory disease, the principles around prompt identification, segregation and treatment of infected cases, controlling concurrent infections and promoting optimal housing and husbandry conditions as well as minimising stress are all applicable. For specific problems regarding arthritis, it is difficult to

apply a herd level approach and no one solution suits all farms. There are some specific control measures aimed at reducing the infectious pressure and maximising the immunity of the herd that may be used.
Some potential options for prevention of *M bovis* infection in pre-weaned calves include: reducing the level of exposure to *M bovis*; maximise calf immunity; and control mycoplasma mastitis.

REDUCING THE LEVEL OF EXPOSURE TO *M BOVIS*

- Reduce exposure in milk - pasteurize milk or feed milk replacer;
- Reduce exposure in colostrum - avoid pooling of colostrum; pasteurise colostrum;
- Reduce exposure to airborne *M bovis* – assess stocking rate; adequacy of calf housing design to maximise air quality; segregate sick calves;
- Prompt treatment of sick calves; barrier nursing of sick calves;
- Feed the youngest calves on the farm first;
- Optimise hygiene of calf pens but also equipment for feeding – review current practice and assess adequacy.

MAXIMISE CALF IMMUNITY

Use best practice with regard to colostrum – feed adequate volumes of good-quality colostrum soon after birth; assess passive transfer intermittently through calving season; Feed an adequate amount of milk or milk replacer to ensure the calves are on an optimum plane of nutrition.
Control of mycoplasma mastitis is difficult and again depends on the farm specific presentation. There is no blueprint for an approach to control but some measures may include:

- Segregation of infected cows, whether it is respiratory presentation, arthritis or mastitis; will help break the infection cycle;
- Segregated cows with mastitis would need at least three consecutive monthly negative cultures before considering re-entry to the herd;
- Chronic mycoplasma mastitis cows will likely need to be culled; it is often the case that clinical cases that become culture negative can remain as intermittent, clinical shedders;
- In the face of an outbreak, bulk-tank samples (potentially pre and post milking of the segregated batch) can be submitted for PCR testing weekly (or as things improve; monthly) to monitor the success of the management changes;
- The utmost attention to in parlour milking routine should be followed in the face of mycoplasma mastitis and the principles of control of contagious mastitis pathogens applied;
- Check all cows for mastitis and all cases of mastitis should be submitted for culture/PCR;
- Post-milking teat disinfection is important and should follow Animal Health Ireland Cellcheck guidelines, adequate amount of the correct product should be applied diligently;
- Milk-infected cows last;
- If cluster flush is not present, cluster dipping between cows may need to be considered or at least;
- The utmost care must be followed during drying-off procedure.

The diagnosis of *M bovis* appears to be increasing in recent times. UCD herd health group have investigated a number of mycoplasma-related herd problems recently and it is undoubtedly a problem on some Irish farms. There are lessons to be learned and each presentation is different and no one herd approach suits all circumstances. Despite often high morbidity, there are some cases that recover and go on to be productive healthy cows. It is important to first confirm diagnosis and then herd controls will be specific to each herd outbreak. Given the severity and grave consequences experienced by some herds and the immense welfare concerns associated with this disease, it is important as an industry that we are aware of the disease and its consequences.

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