

Infectious bovine keratoconjunctivitis: a practical yet evidence-based approach to treatment and prevention on dairy farms

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Abstract

While it has long been accepted that *Moraxella bovis* is the cause of infectious bovine keratoconjunctivitis (IBK), there is growing evidence that *Moraxella bovoculi* and/or *Mycoplasma bovis* may be involved in some outbreaks on some farms, and that more than one organism may often be involved. All 3 organisms can be found in the eyes of healthy cattle and are likely commensal organisms in the bovine eye. Interactions between these organisms in the pathogenesis of IBK are only beginning to be understood. The disease triangle (host – pathogen – environment) is a conceptual model that is especially useful to practitioners dealing with IBK for all 3 are equally important and must be considered. Corneal damage is likely a prerequisite for initiation of IBK in most cases. Therefore, efforts to eliminate causes of corneal damage are critical elements of success. While there are surprisingly few studies supporting vaccination as a control measure, vaccination against both *Moraxella bovis* and *Moraxella bovoculi* is recommended. Treatment is relatively straightforward.

Key words: infectious bovine keratoconjunctivitis, pinkeye, *Moraxella bovis*, *Moraxella bovoculi*, *Mycoplasma bovis*

There is abundant, though interestingly not conclusive, evidence to support the generally accepted view that *Moraxella bovis* causes infectious bovine keratoconjunctivitis (IBK).^{4,24} *Moraxella bovoculi* and *Mycoplasma bovis* are also likely involved in some outbreaks on some farms, though the evidence supporting this is less clear. All three organisms can be isolated from the eyes of healthy cattle and are likely commensals – i.e. part of the “normal” bovine ocular microbiota.^{4,8}

Moraxella bovis and IBK

The pathogenesis of *Moraxella bovis*-associated IBK is a 3-step process: corneal damage, followed by microbial adhesion, and then cytotoxicity. While there may be exceptions,²⁶ some degree of insult or damage to the corneal surface seems to generally be a necessary precursor for the development of IBK.^{11,20} Indeed, the disease model for the study of IBK – mildly abrading or otherwise (e.g. using ultraviolet radiation) damaging the cornea followed by instillation of a pathogenic strain of *Moraxella bovis* – very consistently leads to classical IBK. Potential causes of corneal damage in the field include the female face fly (*Musca autumnalis*), dust, sawdust, sand, sunlight (UV radiation), young animals eating from large round bales, and grazing in tall grass.

Moraxella bovis readily attaches to damaged corneal surfaces by means of attachment pili. Subsequent cytotoxicity is mediated by cytolysin, which is a hemolytic, leukotoxic, pore-forming protein,²³ and other factors. The time from initial adhesion to full thickness corneal invasion and infection can be less than 48 hours.²⁶

Moraxella bovoculi and IBK

Moraxella bovoculi has genes encoding for pili.⁶ However, it is not known whether pilin expression by *M. bovoculi* is prerequisite for establishing colonization of the ocular surface.⁶ In a recent study, *Moraxella bovoculi* failed to produce signs of IBK (0/10 calves) using the standard scarification and inoculation technique, whereas in the same study, *Moraxella bovis*-inoculated calves were clinically affected (9/10 calves).¹⁶ Electron microscopy studies suggest that *Moraxella bovoculi* may attach poorly to the corneal surface but attach well to *Moraxella bovis*.¹ *Moraxella bovoculi* growth may outpace that of *Moraxella bovis*. This suggests a hypothetical scenario wherein *Moraxella bovis* attachment is necessary to “get things started” followed by *Moraxella bovoculi* “taking over.” If true, then this implies both that timing of ocular culture is critically important vis-à-vis interpretation of culture results, and that vaccination against both *Moraxella bovis* and *Moraxella bovoculi* is necessary for protection.

Mycoplasma bovis and IBK

Mycoplasma bovis may cause a conjunctivitis syndrome that is clinically distinct from and does not necessarily progress to IBK.²⁷ Conversely, *Mycoplasma bovis* may enhance colonization of bovine eyes by *Moraxella bovis*,²⁷ and therefore be involved in the pathogenesis of some outbreaks of IBK. Cattle do seem to develop some degree of natural ocular immunity against *Mycoplasma bovis*²¹ though no commercial vaccine is available.

IBK pathogens: Commensal or contagious?

Appropriate steps to prevent IBK depend at least somewhat upon whether the infectious agents are commensal or contagious organisms. Evidence that the organisms are commensals include that *Mycoplasma spp.* and *Moraxella spp.* are common in the bovine ocular microbiota,⁸ and that both *Moraxella bovis* and *Moraxella bovoculi* can be cultured from the eyes of healthy cattle.⁴

Conversely, Brown et al stated that *M. bovis* has to be transmitted in sufficient quantities for IBK to occur, and preventing transmission remains the single most important factor in controlling the disease.¹⁰ Bruce Addison, quoting John Angelos (though it may be that neither of these researchers still believe the following to be true) stated that one should “Never write a paper or give a presentation without emphasizing that these bugs are extremely contagious.”² Anecdotal reports involving farms that had never had IBK which then experienced an outbreak contemporaneous with that of a nearby farm (potentially spread by face flies) are suggestive of contagiousness, though other factors could also be explanatory. Perhaps the answer

lies somewhere in between, i.e. that pathogenic variants could arise within commensal populations, and then be spread in a contagious manner.

IBK Prevention – environment

The disease triangle (host – pathogen – environment) is applicable to pinkeye – see Figure 1. The disease triangle is like a 3-legged stool – if any one of the legs fails, then the stool fails. Every popular press article ever written on IBK in beef cattle contains the words “control flies and clip pastures”. Most of us speed past that and hope the article will suggest some new easy fix. However, given that corneal damage is generally a necessary first step in the pathogenesis of IBK, environment should not be overlooked. Careful investigation can reveal environmental causes of corneal damage. The following examples are from the author’s experience.

On an extensive corral-based calf ranch in southwest U.S., the herdsman was complaining of an ongoing IBK problem. As we spoke, scraping and hauling of manure from a pen nearly half a mile away was occurring and approximately one truck per minute was driving on the dirt road along the western border of the facility. As I visited with the herdsman my eyes were stinging from the dust. The herdsman stated that even when pens were not being scraped that the road was heavily travelled.

During a visit to a northeastern heifer raiser in a converted free-stall barn, the barn was being bedded with sawdust from a mechanical “shooter”. The owner wanted to go outside of the barn to continue our conversation regarding ongoing IBK. After asking him to remain during the process and experience the eye irritation, it was relatively easy to convince him to use a different bedding method.

On a dairy farm just east of one of the Great Lakes where heifers were consistently breaking with IBK at 5 months of age after entering “the barn on the hilltop” that was bedded with fine sand, I suggested to the owner that irritation from wind-blown sand might be part of the problem. Later, I was visiting with the herd veterinarian regarding the issue and he said: “Yeah, I hate going up there. My eyes always hurt after going in that barn.”

Finally, on a dairy farm in the Midwest where they housed heifers from 60 to 150 days of age in an open-fronted barn where the feed rail faced due east, heifers consistently broke with IBK at about 120 to 150 days of age. Feed was delivered to this barn once per day at about daybreak. Thus, every day heifers were looking directly into the rising sun as they ate. Remember, UV light is one of the mechanisms of inducing corneal damage in the IBK disease model. Asking the owner to remove his hat and look east for more than even one minute was revelatory.

Environmental modifications are often difficult, but difficult is not the same as impossible.

Female face flies swarm around the muzzle and eyes of cattle and feed on ocular and other secretions. These flies have sharp microscopic mouthparts that they use to irritate ocular tissues to stimulate tear production.²² This irritation/damage can be sufficient to allow *Moraxella bovis* to attach to the cornea.

If one accepts the hypothesis that a particularly pathogenic variant of an IBK pathogen is important (i.e. that the pathogen is contagious), then fly control is also important from the standpoint of limiting entry of pathogens to an operation as well as control of spread within it. *Moraxella bovis* can be recovered from the gut of face flies and they regurgitate *Moraxella bovis* while feeding on eye secretions.²² Face flies are strong flyers

and can travel several miles to find a host and/or food source.⁹ Regardless of whether transmission of IBK pathogens from animal-to-animal or farm-to-farm is important, the damage to the cornea caused by *Musca autumnalis* makes control of this pest critical toward preventing IBK.

IBK prevention – host

Assuming that nutrition (protein, energy, vitamin and mineral) is adequate and that animals are not exposed to inordinate stressors, increasing resistance via vaccination is the main host intervention. IBK can sometimes affect animals at an age (< ~3 months) when maternally derived antibody can interfere with vaccination. Vaccination of pregnant cows prior to parturition is a commonly used method to provide protection to calves in the face of maternal antibody, and that has been shown to at least provide some protection against IBK in calves.⁷

Most *Moraxella bovis* vaccines are directed against the attachment pili. Unfortunately, *Moraxella bovis* can and does switch surface pili, and antibody pressure can induce pilus switching¹⁸ leading to apparent vaccine failure. An obvious solution would thus be to build a vaccine containing many different pili/pilus epitopes. However, the inclusion of “too many” different pili would likely lead to antigenic competition.²³ That is, the immune system would “see” so many antigens that it would only respond to some. How many is too many is not yet well-defined.

A recent review²² concluded “there is no evidence that vaccines against infectious bovine keratoconjunctivitis are effective in the field.” However, that statement was based upon only 2 studies, one of which was quite small, and the other did not include a booster. If one accepts the hypothesis that *Moraxella bovis* and *Moraxella bovoculi* are commonly co-involved in the pathogenesis of IBK, then perhaps it may be that vaccination against both is necessary to achieve clinical efficacy in the field.

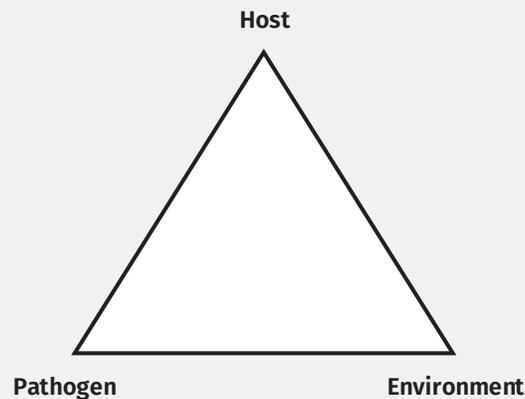
IBK treatment

The goals of IBK treatment should be to improve animal welfare (it is not unreasonable to assume that calves with IBK are experiencing pain), decrease disease severity, shorten disease duration, and decrease the fraction of animals with permanent corneal damage. There is little to no evidence to support the use of topical treatments, palpebral or bulbar subconjunctival antimicrobial injections, palpebral subconjunctival injection of both an antimicrobial and a corticosteroid, eye patches, or third eyelid flaps (tarsorrhaphy). Indeed, many of these interventions have been studied and shown to not be efficacious.^{3,25} Furthermore, a 1ml (300,000 units) subconjunctival injection of procaine penicillin G was shown to lead to detectable penicillin in the milk of treated lactating dairy cows for up to 22 hours post-injection.¹⁹

200 mg/mL oxytetracycline is labeled for the treatment of IBK and has been shown to be effective.¹⁴ Elimination of ocular *Moraxella bovis* infection probably depends more on reaching therapeutic drug concentrations in the infected ocular tissues than in tears¹⁵ and oxytetracycline is selectively concentrated in ocular tissues including the epithelium of the conjunctiva and lacrimal gland ductules, reaching concentrations in each tissue that exceed those in serum.¹⁵ Based upon the preceding, practitioners should have strong evidence of antimicrobial resistance or lack of efficacy of oxytetracycline prior to considering alternatives.

Tulathromycin is also labelled for the treatment of IBK and has been shown to be effective.¹⁷ Florfenicol has been shown to be

Figure 1:



Host factors:

- Age
- Immunity
- Colostrum
- Exposure
- Vaccination
- Nutrition
- Protein, energy
- Vitamins, minerals
- Peri-ocular pigment

Pathogens:

- *Moraxella bovis*
- *Moraxella bovoculi*
- *Mycoplasma bovoculi*
- *Bovine Herpesvirus-1*

Environmental factors:

- Eye irritation / corneal damage
- Face flies
- UV radiation
- Dust, sawdust, sand
- Eating hay from large bales
- Tall grass / weeds
- Pathogen spread
- Headlocks etc.
- Stocking density

effective^{5,12} and is labelled for IBK in Canada, but not the U.S. Similarly, ceftiofur efficacy has been demonstrated¹³ but ceftiofur is not labelled for IBK in the U.S.

Conclusion

While much is known about the pathogenesis, prevention and treatment of IBK, there is still much to learn. Practitioners should consider host, environmental and pathogen factors with equal regard when designing prevention programs.

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