# Infectious Bovine Keratoconjunctivitis Management

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**Abstract**

Infectious bovine keratoconjunctivitis is a disease that affects many herds in the US, however, the epidemiology of the disease is complicated and control is frustrating for many producers. This article discusses putative causes of IBK and approaches to understanding the causes of success and apparent failure in IBK control programs.

**Résumé**

La kératoconjonctivite bovine infectieuse (KBI) est une maladie qui frappe plusieurs troupeaux aux É.-U.; toutefois, l'épidémiologie de la maladie est complexe et la lutte contre la maladie se révèle éprouvante pour bon nombre de producteurs. Le présent exposé traite des causes présumées de la KBI et de démarches destinées à comprendre les causes de succès et d'échec apparent des programmes de lutte contre la KBI.

## Introduction

Infectious bovine keratoconjunctivitis (IBK) is one of the most common and economically important diseases of pre-weaned calves in the United States. Calves with IBK have a spectrum of clinical signs from tearing to corneal rupture. A survey of 2,700 beef production operations in the United States found that, of calves born alive in 1996, 1.1% (+/- 0.1) of unweaned calves more than three weeks old were affected with IBK, making it second only to diarrhea as the most prevalent condition affecting this age group.[4] In addition, over 11% of operations reported pinkeye in calves over three weeks of age. Treatment, injury from extra handling and devaluation at market due to eye disfigurement add to economic costs of IBK. Based on economic impact, IBK ranked fourth in importance by producers.[4] Internal and external parasites were considered the most important.[4] In a study conducted in Missouri, 45% of herds reported endemic IBK. [26] Within herds, the average prevalence of IBK was 8%.

## Causes of IBK

*Moraxella bovis* (*M. bovis*) is normally considered the cause of IBK. [7] However, it is often easier to understand the epidemiology and successes and failures in management of IBK using the concept of necessary, component and sufficient causes. A necessary cause is one without which the disease cannot occur. However, exposure to a necessary cause is rarely sufficient to cause disease. Instead, necessary causes combine with other component causes to be sufficient cause of the disease. Diseases named after organisms, such as tetanus and salmonellosis, are examples of diseases with necessary causes. For diseases that do not include an organism name, such as IBK and undifferentiated bovine respiratory disease, there is no necessary cause and animals can be thought of as developing the disease due to a combination of component causes being sufficient to cause the disease. Some texts refer to predisposing factors or risk factors, and these qualify as component causes.

## Is *M. bovis* a Necessary Cause of IBK?

Despite its predominance in IBK, is seems likely that a small percentage of IBK cases are associated with other organisms, therefore it is unclear if *M. bovis* is a true necessary component of all IBK cases.[7,15,18,19] Biological company literature and case reports, although not field studies or challenge studies, have suggested that *Moraxella ovis (M. ovis)* is an infectious organism associated with some outbreaks of IBK.[10] Other studies have suggested *Mycoplasma bovoculi* may play a role in the disease process.[21-23] In a longitudinal study involving 159 beef calves, calves colonized with *M. ovis* early in summer were less likely to subsequently develop IBK during the summer months.[28] Among 58 *M. ovis*-positive calves, nine (15%) subsequently developed IBK, while 32 of 101 (32%) *M. ovis*-negative calves subsequently developed IBK.[28] In the case control study, *M. bovis* was recovered from 49 of the 143 (34%) cases, and 32 of 114 (28%) non-clinical pasture mates (exact p value =0.34). *M. ovis* was recovered from 64 of the 143 (44%) pinkeye cases and 30 of 114 (26%) non-clinical pasture mates (exact p value =0.003).[28] A case-control study from Australia reported a higher prevalence of *Neisseria catarrhalis* which was not differentiated from, and therefore may have included, *Neisseria ovis* (*N. ovis*; reclassified as *M. ovis),* in pinkeye cases (25.5%) compared to normal animals (10.5%).[29,30] The authors also reported a similar relationship existed, with higher prevalence of *M. bovis* in pinkeye cases (27.5%) compared to normal non-clinical animals (6.5 %).[29,30] Based on the study design, it was not possible to determine whether these associations could be due to secondary invasion rather than initiating cause. Several other studies have reported recovery of *N. ovis*, *B. ovis* or *M. ovis* from populations of cattle with or without IBK, but none included appropriate controls and are therefore not useful in attributing causation.[6,10,29,30] Other descriptive studies of the microbial flora of cattle eyes failed to mentioned *M. ovis (N. ovis, N. catarrhalis)*, but likely these studies were not looking for the organism, which does not rule out the possibility that organism was present.[8,15,17-19]

Experimental studies failed to show a causal relationship between *M. ovis* and IBK. In experimental studies, eight week-old C57/B16 mice infected with *M. ovis* and negative controls showed no signs of disease compared to 100% (7/7) incidence of keratitis in mice infected with *M. bovis*.[23] Furthermore, experimental studies with nine colostrum-deprived calves ranging in age from four to six months old, which were inoculated with *M. ovis* alone or in conjunction with *Mycoplasma bovoculi*, failed to produce signs of keratitis.[23] Although these studies do not eliminate the possibility that *M. ovis* is a causal organism associated with outbreaks to date there is limited evidence of a causal role in IBK. Recently, there have also been reports of haemolytic gram-negative cocci isolated from cases of IBK, with the proposed name of *Moraxella bovoculi* sp. *nov*.[3]

## What are Component Causes and Sufficient Causes of IBK?

For IBK, component causes such as breed, age, ultraviolet radiation, presence of face flies, dust and trauma are important for the development of disease. Figure 1 contains schematics of hypothetically sufficient causes of IBK. Sufficient causes can be thought of as combinations of components sufficient to cause the disease. It is possible within a herd for several sufficient causes to be at work affecting different animals. Unfortunately it is not possible to empirically determine the sufficient cause for any one herd or animal. However, understanding the concept of sufficient causes can help us understand why control programs for IBK may succeed or fail. For illustration purposes, assume a herd has 30% prevalence of IBK in calves, of which two-thirds of cases are caused by sufficient cause 1 (SC1), and one-third by sufficient cause 2 (SC2) (Figure 1). One option for control of IBK would be to eliminate the necessary cause in this herd, i.e. remove *M. bovis* which occurs in SC1 and SC2. If vaccination were 100% effective, then both sufficient causes of IBK would be disrupted and, theoretically, IBK would not occur. Alternatively, the herd may decide to forgo vaccination and use a vigorous fly control program. A vigorous fly control program would disrupt only SC2, and prevent the occurrence of one-third of the cases of IBK. Unfortunately for the veterinarian and producer, 20% of animals still develop IBK due to SC1 and the control program will appear ineffective. Obviously it is not possible to know the sufficient cause in each animal, or if they truly differ between animals within a herd and between herds. However, given the number of risk factors identified for IBK, it provides a framework for working with herds with endemic IBK. This concept of sufficient causes may help explain why in some years control measures appear to be effective and other years ineffective. For example, in one year the majority of cases may be associated with SC2 and therefore a vigorous fly control program is protective, while the next year SC 1 may predominate and the control program appears ineffective.

## Control Options for Managing IBK

Another important concept for working with IBK control is primary, secondary and tertiary prevention practices (Figure 2).[16] Primary prevention options are directed towards preventing exposure to causal factors, such as vaccination and quarantine. Secondary preventive practices intervene after the disease has occurred but before pathology (clinical disease) is obvious, and aim to intervene early in the disease process. Tertiary preventive practices are implemented after clinical disease is diagnosed and attempt to limit the outcome of the disease, i.e. prevent death or decreased productivity.

Vaccination is a commonly used primary preventive practice in veterinary medicine. Depending on the mechanism of immunity, vaccines may offer primary protection by rendering the animal immune to the level of the challenge by *M. bovis* under field conditions.[16] Using the sufficient causes in Figure 1 as an illustration, effective vaccination against a necessary cause (or major component cause) such as *M. bovis* would be the

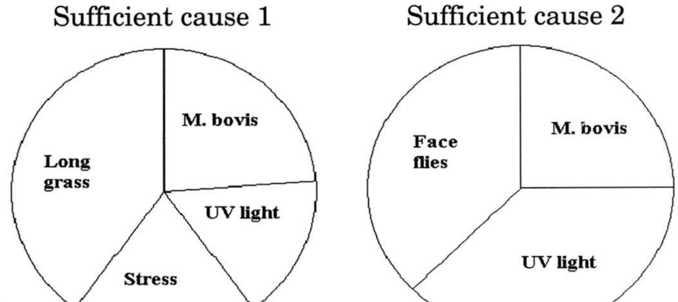


**Figure 1.** Schematic of hypothetical sufficient causes of infectious bovine keratoconjuntivitis.

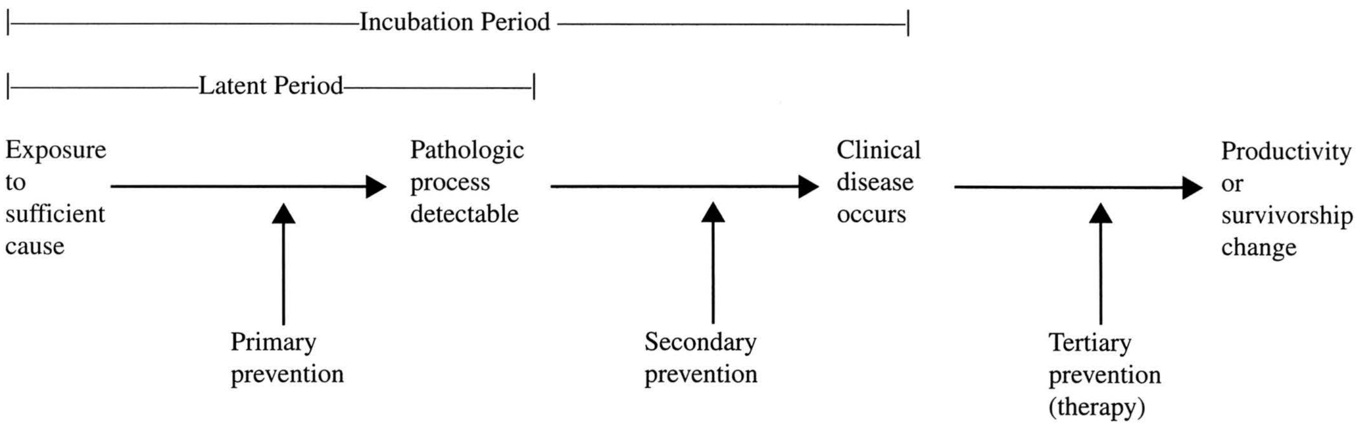


**Figure 2.** Schematic of the timing of preventive, secondary and tertiary preventive practices with respect to the disease process.[16]

most effective primary preventive practice. However for IBK, multiple commercial vaccines are available with no consensus on vaccine efficacy. There is no shortage of studies that describe the use of vaccines against *M. bovis*-associated IBK. In a recent review, we identified over 120 trials that evaluated vaccines against *M. bovis.*[9] As these trials vary enormously by study design (challenge versus field), *M. bovis* organism, adjuvant, dose, frequency of administration and study population, it is not possible to generalize about efficacy. However, numerous study design flaws in these reports reduced the evidentiary value of the majority of the studies identified. Only 15 trials reported using randomization and blinding and of these, three (20%) reported a significant association between vaccination and pinkeye occurrence.[1,14] In the studies reporting effective vaccines, the risk ratios varied from 0.25 (RR 95% CI: 0.11, 0.58) to 0.38 (0.18, 0.79).[1,14] One of the studies evaluated a vaccine product that is not yet commercially available.[14] When the outcomes of all studies were considered, regardless of the use of randomization or blinding, 48 of 123 trials (39%) reported significantly protective vaccines (RR 95% CI <1). Based on these data, it seems unlikely that vaccination is the solution to all IBK problems. It is possible that the vaccines do work on some herds, due to the differences in sufficient causes.

As mentioned, ideally disease control programs should use primary prevention practices against a necessary cause as this will be most effective. However, in lieu of vaccination against *M. bovis* it can be frustrating to eliminate other component causes. For example, SC1 may not be amenable to disruption, as UV light cannot be controlled, nor, frequently can long grass. Fly control has been proposed as a method of IBK control, and anecdotal reports are favorable. However, no studies with proper controls have directly evaluated the impact of fly control on IBK incidence. A similar lack of published studies is true for other recommendations, such a pasture clipping to reduce trauma due to long grasses.

Secondary prevention practices for IBK refer to detection of the disease process as early as possible, before clinical disease occurs. Screening for elevated somatic cell counts in milk prior to visible changes in milk consistency is an example of a secondary intervention for mastitis. Due to the short course of disease, there are unlikely to be any realistic secondary preventive practices for IBK unless a herd owner mass-medicates all calves in a group because a threshold number of cases has been identified. In this situation, treatment may occur after the disease process has begun, but before it is detected in a percentage of calves.

Tertiary control programs occur after disease has been diagnosed and aim to limit the disease impact, therefore antibiotic therapy can be thought of as a tertiary preventive practice. The cost of IBK on production is substantial. The economic losses occur through decreased growth rates, as affected calves display an average of 37-40 lb (17-18 kg) decrease in weaning weight.[5,24,25] Furthermore, lower performance in post-weaning cattle has also been documented: specifically, lower average daily gain, 365-day weight and final weight.[24,25] In a study conducted in 2004- 2006 in five Iowa herds with 1879 calves, affected individuals weighed 26 lb (11.8 kg) less than unaffected calves.[20] Calves with a single affected eye weighed an average 19 lb (8.6 kg) less than unaffected individuals.[20] Calves with bilateral infections weighed, on average, 40 lb (18.2 kg) less than unaffected animals.[20] These data suggest rapid treatment during an outbreak should reduce losses to IBK. In a review of antibiotic therapies that assessed lesions at day 21, antibiotic treatment was frequently successful at decreasing the number of lesions at day 21 (Table 1).[27] Unfortunately, no antibiotic regime was reported more than once in the literature reviewed, therefore it was not possible to determine how much variation in response to therapy could be naturally expected. Table 1 refers to number of lesions in animals at day 21, and because of a relatively high self-cure rate, some antibiotics appear to be ineffective. These studies should have been able to document treatment efficacy using weight change during the study period, but this outcome was rarely reported.[27] Other studies looking at time to lesion healing earlier than day 21 would suggest most antibiotic therapies decrease the time to healing.

## Conclusion

Cases of IBK within a herd and between herds may be associated with different sufficient causes, making it difficult to assess the impact of disease prevention programs. The majority of high quality studies evaluating *M. bovis* vaccines and IBK occurrence do not report efficacy. Antibiotic treatment with oxytetracyline and florfenicol are effective treatment choices for IBK. More studies are needed to assess weight changes in cattle of treatment interventions.

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**Table 1.** Regimen specific summary statistics from randomized control clinical trials included in systemic review of antibiotic treatment of naturally occurring pinkeye. An event was defined as an unhealed corneal ulcer at approximately 20 days post-treatment

| Trial | Treatment | Adverse event rate | P value* |
|---|---|---|---|
| Angelos *et al* (2000) SC[2] | Florfenicol (18.2 mg/lb [40 mg./kg]) SC on day 0 and 2 | 3/37 (8%) | 0.01 |
| | 0.9% NaCl IM on day 0 and 2 in equivalent volume of florfenicol given at 9 mg/lb (20 mg/kg) | 15/46 (32%) | |
| Angelos *et al* (2000) IM[2] | Florfenicol (9.1 mg/lb [20 mg/kg]) IM day 0 and day 2 | 0/43 (0%) | 0.00 |
| | 0.9% NaCl IM on day 0 and 2 in equivalent volume of florfenicol given at 9 mg/lb (20 mg/kg) | 15/46 (32%) | |
| Dueger *et al* (2004)[11] | Ceftiofur (3 mg/lb [6.6 mg/kg]) SC on day 0 | 6/64(9%) | 0.13 |
| | Purified coconut oil extract and cottonseed oil (0.01 mL/lb [0.03 mL/kg]) SC | 13/66 (20%) | |
| George *et al* (1988)[13] | Oxytetracycline (9.1 mg/lb [20 mg/kg]) IM twice in 72 hours | 3/35 (8.5%) | <0.01 |
| | No treatment | 21/33 (64%) | |
| Eastman *et al* (1998)[12] | Procaine penicillin G 300 IU subconjunctivally in the bulbar conjunctiva on day 0 and between days 2-4 | 2/40 (5%) | 0.15 |
| | No treatment | 7/40 (17.5%) | |

*Fisher's exact test for binomial proportions.

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