BOVINE KERATOCONJUNCTIVITIS

Dr. P.H. Mapham, BVSc (Hon)
Veterinary House Hospital,
339 Prince Alfred Road,
Pietermaritzburg, 3201
Tel no: 033 342 4698
Cell No: 082 771 3227
E-mail: rickm@iafrica.com

Dr. J.H. Vorster, BVSc, MMedVet(Path)
Vetdiagnostix Veterinary Pathology Services,
PO Box 13624
Cascades, 3202
Tel no: 033 342 5104
Cell no: 082 820 5030
E-mail: hendri@telkomsa.net

Introduction

Keratoconjunctivitis is a multifactorial and complex condition frequently seen in many different animal species including cattle, either as isolated and sporadic cases or occasionally as outbreaks. Clinical signs may be restricted to the eyes only as commonly seen in infectious bovine keratoconjunctivitis (IBK), or it may form part of clinical signs seen in systemic diseases. Although primary infectious bovine keratoconjunctivitis (IBK) is rarely fatal in outcome, impaired vision and pain in affected animals may result in losses. Decreased weight gain, decreased milk production, treatment costs and loss of market value of animals due to blindness or chronic eye pathology may occur. Similar figures are not available for the impact of IBK in South Africa, but a loss of 150 million dollars affecting more than 10 million calves annually has been reported in the USA\textsuperscript{7}. 
Determinants of bovine keratoconjunctivitis:

Determinants may be classified as primary or secondary, intrinsic or extrinsic and the result of a dynamic interaction of agent, host, agent and environmental factors.

The following is a brief outline of the determinants of the condition:

Primary determinants:

1. Extrinsic determinants

   - Animate
     - Endoparasitic
       - Helminths e.g. *Thelazia* spp. ("eyeworms") and *Oncocerca* sp.
     - Infectious
       - Bacteria, *Chlamyophila* sp. and Molluscites e.g., *Listeria monocytogenes* and *Moraxella bovis, Moraxella bovoculi, C. pecorum, Mycoplasma bovoculi* and other *Mycoplasma* spp.
       - Viruses e.g. IBR, BMC, BVD, parainfluenza-3 and adenoviruses
     - Ectoparasites
       - Flies and moths
   - Inanimate
     - Physical damage e.g. trauma, foreign bodies and solar radiation
     - Chemical e.g. *Euphorbia* sap, photosensitization
     - Allergenic

2. Intrinsic
   - e.g. Genetic, metabolic and behavioural tendencies

Secondary Determinants

1. Extrinsic determinants for example concurrent disease, vaccination status.
2. Intrinsic determinants for example age, nutritional status and immunological status.
This list is not comprehensive and for practical purposes this paper will concentrate on infectious bovine keratoconjunctivitis (IBK) in the absence of other clinical systemic diseases. Worldwide Moraxella bovis seems to be the most important recognized cause of disease and most of the discussion will therefore focus on this pathogen and the agent, host and environmental factors associated with it.

Epidemiology

Agent

Moraxella bovis is a Gram-negative diplobacillus with many different strains identified with varying virulence. Virulence is associated with fimbriated strains and which may include β- haemolytic corneotoxic and leucotoxic cytotoxin factors. Other virulence factors include phospholipases, iron acquisition systems, hydrolytic enzymes and proteolytic enzymes.

M. bovis needs to attach to the bovine corneal epithelium, the first step required for establishment of infection. Two functionally distinct types of pili, termed Q and I, have been identified which enhance pathogenicity. Q pili aid in the attachment of bacteria to the bovine cornea whilst I pili allows for local persistence and maintenance of an establish infection on the corneal surface. In different studies it has been demonstrated that M. bovis strains expressing Q pili type are more efficient at establishing infection, and are generally more pathogenic than strains expressing only I type pili.

Haemolytic strains of M. bovis secrete a pore forming cytotoxin which enhances the development of corneal ulcers by lysis of the corneal epithelial cells and host neutrophils. The net result is extensive release of neutrophilic enzymes leading to fragmentation and aggregation of collagen fibrils in the later stages of disease delaying corneal healing.

M. bovis has high affinity iron-uptake systems, which can remove iron from bovine lactoferrin and transferrin, which in turn support protein production and DNA and RNA synthesis.

Host factors
Several host defence mechanisms are in place and, if disrupted, may enhance infection. These include the intact healthy corneal epithelium, tear film and complement system, phagocytic cells and local secretory antibodies.

The epithelial surface of the cornea and conjunctiva is generally an effective barrier against disease. Continuous turnover of epithelial cells occurs in five to seven day cycles. As the bacteria must adhere to the epithelial cells in order to establish infection this continuous cycling inhibits bacterial adherence. The tear film represents the most important part of the non-specific defense of the ocular surface as a number of substances that have antimicrobial actions, such as B-lysine, complement, transferrin and lactoferrin are transported in tears and washing by tears may inhibit adhesion. IgA is the major immunoglobulin of the ocular surface and tears. Protective IgM and IgG (IgG1 and IgG2) were also detected in bovine lacrimal secretions.

The cornea is avascular and combined with its lack of lymphatic drainage, humoral antibodies and/or cytotoxic lymphocytes have limited access to the cornea.

It has been reported that specific strains may establish an infection in a particular herd and, by persisting in carrier animals, this particular strain may then be responsible for disease over a number of years in that particular herd. Clinically healthy carriers thus play an important role in maintaining the infection in herds by harbouring the bacteria in the ocular and nasal tracts and carrier animals may be responsible for transferring the disease into previously unaffected herds.

As infectious bovine keratoconjunctivitis is a highly contagious disease it usually occurs in epidemics; with individual cases more rarely seen. Prevalence rates in affected herds may vary and have been reported to be between 10 to 76%. Although the morbidity rate may be high, mortality rates are usually negligible. Disease is more commonly seen in young animals and is usually also more severe in these age groups. Differences in susceptibility have been associated with some breeds with Bos indicus breeds reported to be least susceptible. Animals with pigmented skin around the eye generally seem more resistant to infection.

In a recent study the association between Toll like receptor 4 single nucleotide polymorphisms (SNP’S) and the incidence of IBK was studied. Two SNP’s were identified designated Int1 and Ex3. This study showed a relationship between Int1 genotype and the incidence of IBK in American Angus cattle. In a different
study, crossbreed *Bos Taurus* steers were used to determine the association between SNP on the bovine chromosome 20 and the development of IBK\(^4\). Five SNP was found to be significantly associated with the incidence of IBK. However, some of these markers on bovine chromosomes may also be associated with various other carcass quality traits (e.g. body weight, marbling meat tenderness, fat yield etc). This remains a very interesting, but yet to be fully explored field of study.

**Environmental factors**

Disease is most common during the summer months when increased UV light exposure results in increased epithelial cell degeneration and epithelial defects which all favour establishment of infection.

Transmission of infection may be either direct or indirect. Direct transmission is through droplets from ocular and nasal secretions. Indirect means would include insect transmission by the house fly (*Musca domestica*), face fly (*Musca autumnalis*) or stable fly (*Stomoxys calcitrans*). The feeding habit of face flies results in ocular damage and increased eye secretions favouring the growth and therefore spread of infection. Noctuid eye frequenting moths were shown to also be associated with disease in South Africa by Gouws JJ *et al*\(^5\). Bacteria may survive for as long as three days on the legs of face flies which make it an ideal transmitter of infection.

Increased insect populations are reported to be associated with increased levels of transmission and mechanical irritants (grass, weeds) and crowding of animals also favours outbreaks. Outbreaks of disease have, however, been described during the winter months as well when excessive wind and dust would be predisposing factors.

Any form of stress such as transport and concurrent or prior infection with other infectious agents such as *Chlamydophila pecorum*, infectious bovine rhinotracheitis, parainfluenza-3 and adenoviruses as well as certain *Mycoplasma* spp may aggravate clinical disease.

Cattle seem to be the only reservoirs for this organism and infection does not appear to be transmitted from cattle to sheep.
Nutritional factors, for example Vitamin A deficiency, have also been suggested as possible predisposing factors.

**Clinical signs**

The severity of clinical signs and possible clearance or persistence of infection of clinical disease varies from animal to animal under field and experimental conditions, and between outbreaks of disease. Incubation may be as short as one to three days or as long as three weeks. Infection may involve eyes unilaterally or bilaterally. In the early stages of diseases lacrimation (copious watery discharge), blepharospasm and photophobia may be seen. Generally, conjunctivitis develops before keratitis and the affected conjunctivae exhibit varying degrees of hyperemia, oedema and blepharitis. With bilateral eye involvement animals may be reluctant to move. The ocular secretion soon becomes purulent and within one to two days after onset of clinical signs the centre of the cornea may become opaque (whitish to yellowish –blue) and this may spread centrifugally over the entire corneal surface. Ulceration of the cornea may develop and the peripheral areas become vascularised by proliferation of the limbal vessels over a period of few days. Some animals may recover spontaneously, and corneal ulcers may heal or be reduced by stromal regeneration leaving a corneal scar. Potential complications may be keratoconus, hypopyon, iridicyclitis or lenticular enucleation. In some animals diseases becomes chronic, and the corneal opacity may take one to two months to resolve. In a small number of cases perforation of the corneal ulcers may be seen resulting in iris prolapse and permanent blindness.

**Diagnosis**

A diagnosis of IBK would be based on the clinical history, presenting clinical signs and laboratory confirmation by means of culture. The presence or absence of clinical signs of systemic disease would be of great benefit to distinguish it from many of the differentials, especially the systemic viral infections. Samples to be collected should include a swab from the eyes, preferably collected from fresh untreated cases, in a suitable transport medium (e.g. Amies) for bacterial culture.
As sampling is relatively easy one can then also make use of the opportunity to collect samples for fungal and viral culture, and in most instance more likely collect a swab for PCR screens against most of the pathogens which may be primary concurrent or recent infections (e.g. *Chlamydophila* sp. BHV and the mycoplasmas).

**Treatment**

Topical antibiotic treatment is widely used and can effectively control the early stages of clinical disease. Concurrent topical atropine (1%) drops are useful by inducing mydriasis and cycloplegia but animals treated with atropine should not be allowed to be exposed to excessive UV light or bright sunlight following on treatment.

Systemic treatment has been advocated to be superior in some respects (safety, ease of administration, long duration) but with the downsides of high costs, restrictions in product licensing and long milk and meat withdrawal periods.

An important advantage of systemic treatment is that it may reduce the duration of the carrier state which would probably not be achieved by the other methods.

Subconjunctival injections may be cost-effective but the off label use of some antibiotics may be contraindicated in terms of possible antibiotic resistance.

Antibiotics reported to have good effect include cloxacillin, chlortetracycline and chloramphenicol. The use of several antibiotics including Penicillin G6, clindamycin, oxytetracycline, florfenicol, tilmicosin, ceftiofur, tulathromycin and fluoroquinolones have been reported.

Administration of atropine and cortisone has been reported in severe cases but the use of cortisones may be controversial.

Practical factors such as production and management systems and limitations in handling of animals, costs of drugs, licensing of drugs in different countries and meat and milk withdrawal periods for the different drugs which may be considered for use need to be taken into account in any treatment protocol.

Treatment may also be combined with the isolation of affected cattle, limiting exposure to wind, dust and UV light. If at all practical, fly control and the use of
fly repellents (e.g. dipping, spraying with insecticides, insecticide impregnated ear tags) may also be considered.

The advantages, disadvantages and experiences of the treatment methods and antibiotics as summarised above has been reported and discussed in an article by Alexander which makes for very worthwhile reading\(^1\).

**Vaccination**

Bacterial pili seem to be playing a crucial role in the development of immunity to infectious bovine keratoconjunctivitis and this phenomenon has been observed following both natural infection and vaccination with an inactivated, piliated bacterin. In contrast, vaccination of animals with non-piliated bacterins does not confer immunity to challenge with *M. bovis*. Following natural infection or vaccination animals are usually immune to ocular challenge by homologous strains. However, they do not seem to become immune to heterologous strains, although a degree of cross-immunity is reported between various strains.

The effectiveness of commercial vaccines seems to be generally low with protection rates being reported to vary from twenty to fifty percent\(^10\). Vaccine effectiveness is generally influenced by the vaccine type and the similarities between the organism used for constituting the vaccine and the particular challenge strain in an outbreak. The development of effective vaccines is an ongoing field of study.

There are several good articles which provide good insight into the recent developments in vaccine production – two examples are those written by Pietro *et al* (2008) and Burns *et al* 2008 (listed in reference below).

**Conclusion**

Snowder *et al* reported an 8.9 kg difference in weaning weight between calves affected with IBK and those that were not\(^11\). This constitutes a significant loss and together with the possibility that herds may contain carrier animals which reintroduce infection on a seasonal and opportunistic basis and this suggests that practitioners should be more aggressive in a diagnostic approach to IBK.

Thus effectively identifying such herds and eliminating the disease using aggressive systemic treatments together with control strategies of predisposing factors.
References


Multiple questions:

Which one of the following statements is correct?

1. The most important international cause of Infectious Bovine Keratoconjunctivitis is:
   a. Bovine Malignant Catarrhal fever
   b. Bovine Virus Diarhoea mucosal disease complex
   c. *Moraxella bovis*
   d. *Mycoplasma* spp.
   e. *Chlamydophila pecorum*

2. Infectious Bovine Keratoconjunctivitis is
   a. A mild sporadic disease
   b. Always a symptom of a systemic disease
   c. An insignificant factor in calf production
   d. A complex condition that may cause significant losses in cattle
   e. Not a contagious disease of cattle

3. Increased virulence of *Moraxella bovis* is associated with
   a. Fimbriated strains of the bacteria
   b. Concurrent infection with other bacteria
   c. High insect numbers
   d. Dry hot conditions
4. What is the most important defense mechanism in the bovine eye
   a. Immunoglobulin A
   b. Neutrophils and lymphocytes
   c. Highly effective lymph drainage system
   d. Lacrimal secretions
   e. Continuous turnover in superficial cells

5. Which breeds or species are most susceptible to persistent infections with *Moraxella bovis*:
   a. Sheep
   b. Goats
   c. Channel island breeds of cattle
   d. Tropical cattle breeds (*Bos indicus*)
   e. All of the above

6. Infectious bovine Keratoconjunctivitis is aggravated by
   a. Concurrent immunosuppressive infections
   b. Increased ultra violet radiation
   c. Dusty and windy conditions
   d. Nutritional deficiencies
   e. All of the above

7. *Moraxella bovis* attachment to the bovine cornea is most efficiently facilitated by which of the following:
   a. Cytotoxic factors
   b. Proteolytic enzymes
   c. Q pili
   d. All of the above
   e. None of the above
8. Which of the following is the least symptomatic of Infectious Bovine Keratoconjunctivitis caused by *Moraxella bovis*:
   a. Blepharospasm and photophobia
   b. Purulent ocular discharge
   c. Keratitis and conjunctivitis
   d. Pyrexia
   e. Clear ocular discharge

9. Cattle may become resistant to *Moraxella bovis* infections after:
   a. Vaccination with non piliated bacterins
   b. After infection with homologous strains
   c. Natural infection with *Mycoplasma bovoculi* (cross immunity)
   d. None of the above
   e. All of the above

10. Most effective treatment for *Moraxella bovis* infections are:
    a. Subconjunctival injections with penicillin G
    b. Vaccination with the appropriate vaccine
    c. Systemic treatment with appropriate antibiotics.
    d. Spraying with insecticides
    e. Treatment with non steroid anti-inflammatory preparations.