

**“Baby Bye Bye Eye”**

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## **Introduction**

Infectious bovine keratoconjunctivitis (IBK or pinkeye) is the most common eye disease of the bovine species, with an estimated economic impact of at least \$226 million per year in the United States due to decreased weight gains.<sup>6</sup> Affected animals commonly present with blepharospasm, lacrimation, corneal edema, and corneal ulcers. The primary etiologic agent for IBK is *Moraxella bovis*, but other agents implicated in the disease include *Moraxella bovoculi*, the infectious bovine rhinotracheitis (IBR) virus, *Mycoplasma bovoculi*, *Mycoplasma bovis*, *Ureaplasma*, and adenoviruses.<sup>2,11</sup>

IBK is multifactorial, with the host, agent, and environment all playing significant roles in the disease process.<sup>6,14</sup> Predisposed cattle include those from the *Bos taurus* lineage, those with light or non-pigmented hair around their eyes, younger animals, and copper and selenium-deficient animals.<sup>11</sup> *M. bovis* is the only veterinary pathogen capable of ulcerating the cornea on its own through pili and cytotoxins, although environmental factors such as flies, tall grasses, dust, and wind play a significant role as well.<sup>2,6,11</sup>

The mainstays of treatment include antimicrobial and anti-inflammatory therapy, with tarsorrhaphy or exenteration in extreme cases.<sup>2,11,16</sup> While many antimicrobials are reportedly effective against the disease, vaccine efficacy is not well established. Therefore, the focus on prevention must be directed towards other management practices.<sup>2</sup>

## **History and Presentation**

27 is an approximately two year old Angus heifer who presented to the Mississippi State University College of Veterinary Medicine (MSU-CVM) Food Animal service on February 3, 2021 for a cloudy right eye of three weeks' duration. The owner reported that the eye had been

worsening in cloudiness over time and he believed the heifer was now blind, but no other animals were affected. The heifer was acting normally otherwise.

On presentation, 27 was anxious, alert, and responsive. She weighed 702 pounds with a body condition score of 5/9, which is considered ideal. Her vitals included a temperature of 104.1 F, pulse of 112 beats per minute, and respiratory rate of 56 breaths per minute. She appeared adequately hydrated and had normal rumen contraction. She had a decreased menace response in the right eye. The right eye contained corneal edema and an area of fibrosis with resolving keratitis centrally and ventrally (Becky Telle, DVM, DACVO, email communication, September 2021). Her elevated vitals were attributed to the stress of the trailer ride and handling and the remainder of the physical examination was within normal limits.

### **Diagnostic Approach/Differential Diagnoses**

On initial presentation to MSU-CVM, there was no evidence of fluorescein uptake in the affected eye. Fluorescein dye binds to hydrophilic surfaces, but not hydrophobic surfaces. Therefore, it will not bind to the hydrophobic epithelium of an intact cornea, but will bind to the hydrophilic stroma if the epithelium is lost, indicating a corneal ulcer.<sup>12</sup> 27's lesion was consistent with a healed ulcer.

A variety of laboratory tests are available for animals that present with active or healed corneal ulcers to obtain a definitive diagnosis of infectious bovine keratoconjunctivitis (IBK) with a specific etiologic agent. Ulcers can be swabbed along the edge of the ulcer and along the conjunctiva with a culturette and submitted to a veterinary laboratory in Amies medium for culture and sensitivity. Veterinarians should contact the laboratory prior to sample submission to learn what special handling (such as the use of a charcoal swab) might be required for *Mycoplasma* species because it is difficult to culture.<sup>2,18</sup> Polymerase chain reaction (PCR) tests

are also available to assist with IBK diagnosis. Specifically, IBK PCR tests for *Mycoplasma* species and infectious bovine rhinotracheitis (IBR) are available through the Texas A&M Veterinary Medical Diagnostic Laboratory and should be submitted as a dry swab in a red top tube.<sup>18</sup> The Kansas State Veterinary Diagnostic Laboratory offers a Bovine Pinkeye (IBK) PCR Panel which tests for *Moraxella bovoculi*, *Moraxella bovis*, *Mycoplasma bovoculi*, *Mycoplasma bovis*, and IBR. This test requires an eye swab submitted in a sterile container with 0.5 mL of sterile saline.<sup>9</sup> Fluorescent antibody tests are also described in the literature but do not appear to currently be widely available.<sup>10</sup>

Etiologies of keratoconjunctivitis in cattle include infectious bovine keratoconjunctivitis (IBK), primary infectious bovine rhinotracheitis (IBR), and malignant catarrhal fever (MCF).<sup>11</sup> 27 was not demonstrating respiratory signs consistent with a primary IBR infection, and MCF has not been reported in domestic cattle in the US since 2008. Additionally, MCF typically results in severe systemic illness.<sup>1</sup> Given the prevalence of IBK and the healed ulcer, 27 was presumptively diagnosed with IBK. Definitive diagnosis with a specific etiologic agent would only be available through culture or PCR, which the owner declined. These tests are likely not cost-effective in commercial food animal production.<sup>2</sup>

### **Treatment and Management Options**

27 was given 32 mL of oxytetracycline (20mg/kg) subcutaneously and Neomycin-Polymyxin B-Bacitracin (Neo-Poly-Bac) ointment was administered in the right eye. She was sent home with another dose of oxytetracycline to be administered in three days and instructions to return if she began squinting or her eye began tearing. The owner was also instructed to monitor the rest of the herd for similar signs. Approximately three weeks later, another veterinarian visited 27's herd. 27's corneal lesion was still present and fluorescein uptake was

present this time, due to either re-ulceration or corneal edema, as corneal edema can also cause diffuse stain uptake (Becky Telle, DVM, DACVO, email communication, September 2021). 1 mL of penicillin was administered subconjunctivally. Lidocaine was injected periorbitally and a temporary tarsorrhaphy was performed with #1 catgut suture. Approximately three weeks after the tarsorrhaphy, the veterinarian visited 27 again to find periorbital alopecia, indicating self-mutilation and a worsening disease process. A Peterson eye block was performed with lidocaine and an exenteration performed. The surgical site was closed with #2 Vicryl (Richard Hopper, DVM, DACT, email communication, September 2021). On April 1<sup>st</sup>, 2021, 27 returned to MSU-CVM for suture removal. Four cruciate sutures were removed from the surgical site, and there was no drainage or inflammation at the site, indicating appropriate post-operative healing.

Exenterations are rarely necessary for IBK lesions. Cattle with IBK may be treated with a variety of antimicrobials. One common treatment is subconjunctival penicillin. One study of ocular fluid penicillin levels after subconjunctival injections demonstrated that 2 mL of penicillin injected subconjunctivally through the skin or through the conjunctiva both resulted in peak conjunctival fluid penicillin concentrations of 8 IU/mL. However, the duration of therapeutic concentration was roughly 68 hours for the injection through the skin and 40 hours for the injection through the conjunctiva. Another study demonstrated that animals treated with palpebral subconjunctival penicillin injections (1 mL) had similar outcomes in IBK infections as animals who were not treated. In a later study, bulbar subconjunctival penicillin injections (1 mL) lowered the prevalence of IBK compared to animals not treated.<sup>3</sup>

Additional treatment options include systemic oxytetracycline, florfenicol, ceftiofur crystalline-free acid, and tulathromycin. Oxytetracycline and tulathromycin are the only labeled antibiotics for IBK in the United States.<sup>16</sup> Anti-inflammatories, such as flunixin meglumine, may

decrease pain and inflammation.<sup>2</sup> According to one study, 0.009% hypochlorous acid (Vetericyn Plus™ Pinkeye Spray) is effective in experimental IBK infections, which is a promising alternative for antibiotic-free herds.<sup>7</sup>

According to the literature, no pinkeye vaccines have proven their efficacy through clinical trials. This is believed to be due to the wide variety of different pili serogroups across the *M. bovis* species. Pili are responsible for the attachment of *M. bovis* to the corneal epithelium. Pili vaccines have not demonstrated cross-protection against different pili serogroups, while the bacteria has demonstrated its ability to display more than one type of pili. Alternatively, the *M. bovis* cytotoxin, which destroys the corneal epithelium and leukocytes, is genetically similar across the *M. bovis* species. However, no commercially available vaccines target cytotoxins.<sup>14</sup> A 2015 study of a commercially available licensed *M. bovis* vaccine (MAXI/GUARD® Pinkeye Bacterin, Addison Biological Laboratory, Fayette, MO) reported IBK was present in 59.1% of vaccinated calves and 59.6% unvaccinated calves.<sup>5</sup> A 2017-2018 study of a conditionally-licensed *M. bovoculi* bacterin (Addison Biological Laboratory, Fayette, MO) reported IBK in 27% of vaccinated calves and 21% of unvaccinated calves in 2017 and IBK in 15% of vaccinated calves and 12% of unvaccinated calves in 2018.<sup>15</sup>

Similarly, studies evaluating autogenous IBK vaccines have failed to demonstrate vaccine efficacy, but may be offered to the producer in the face of severe outbreaks or if the producer strongly desires to try a vaccine. Autogenous vaccines are created from bacteria isolated from a herd with IBK, and then administered to the same herd. They are manufactured in facilities approved by the United States Department of Agriculture.<sup>14</sup> Manufacturers include Addison Biological Laboratory and Newport Laboratories, among others. It is possible that outside of the available studies a veterinarian or producer may find anecdotal evidence to support

IBK vaccination in any given operation.<sup>14</sup> Should vaccination be chosen as a control strategy, animals should be vaccinated 4 to 6 weeks before the expected onset of an outbreak.<sup>2</sup>

Due to the lack of vaccine efficacy evident in the literature, IBK management strategies must also incorporate other practices.<sup>2</sup> Fly species implicated in the disease process include *Musca autumnalis* (face fly), *Musca domestica* (house fly), and *Stomoxys calcitrans* (stable fly).<sup>11</sup> *Musca autumnalis* has specifically been proven to transmit *M. bovis* and damage the cornea in laboratory settings and is generally considered the target of IBK management programs.<sup>13,17</sup> Flies can be a component of IBK development, but the disease can also spread in the absence of face flies. Cypermethrin products appear most effective at reducing face fly numbers and IBK cases, but the producer must ensure ear tags are removed in accordance with manufacturer guidelines.<sup>13</sup> This prevents the exposure of flies to sub-therapeutic concentrations of insecticide, which can lead to insecticide resistance. One should ensure that ear tags are labeled for face flies because most are labeled for horn flies. Additionally, no pour-on products contain face fly labels, but may help with the control of the other fly species implicated in IBK. Other options for face fly control include Tetrachlorvinphos (Rabon®), permethrin sprays, and organophosphate sprays. Tetrachlorvinphos is a feed-through larvicide. After being ingested by cattle, it is present in the manure, and works by killing larvae in the manure. Despite a producer's best efforts at fly control, the flies from nearby operations with poor fly management can travel for miles and dampen the effectiveness of the producer's fly mitigation strategies.<sup>17</sup>

Ultraviolet radiation is also a contributor to the development of IBK, so animals should be provided shade. Additionally, plant awns may traumatize the cornea and predispose the cornea to *M. bovis* colonization, so mechanical or chemical weed control may also be beneficial.<sup>13</sup> Selenium, copper, and zinc deficiencies have also been reported in herds with

frequent IBK outbreaks, so these minerals should be supplemented if the herd is in an area where deficiencies are common.<sup>2,17</sup> One study demonstrated that neutrophils from calves with adequate copper levels had higher superoxide dismutase activity than copper-deficient calves in vitro.<sup>4</sup> Superoxide dismutase is an enzyme that prevents free radical damage and is implicated in reducing the inflammatory processes of a variety of diseases.<sup>19</sup>

### **Outcome and Prognosis**

As of September 3<sup>rd</sup>, 2021, 27 has been doing well at home, is pregnant, and has had no issues since her exenteration. No other animals in the herd have been affected. The prognosis for pinkeye is generally good and some cases may resolve without treatment, although treatment is indicated because of the painful nature of the disease. Studies suggest that many cases of IBK resolve within 13-20 days when treated with antimicrobials, especially florfenicol and tulathromycin.<sup>16</sup> Most pinkeye cases are not severe enough to necessitate an exenteration, but such a procedure can be crucial to preserving animal welfare.<sup>8</sup> In 27's case, exenteration was the only option for providing relief from her diseased eye.

### **Conclusion**

Pinkeye is a challenging disease to control because of the microbial and environmental factors involved in the disease, but efforts at prevention and control should continue because its economic and animal welfare impacts.<sup>2,6,11,14</sup> While vaccination has generally proven ineffective in the literature, veterinarians and producers may choose to implement it if they find it to be anecdotally effective.<sup>14</sup> Prevention strategies center on controlling *Musca autumnalis* (the face fly), limiting exposure to UV radiation and plant awns, ensuring adequate trace mineral levels, and limiting fomite use between animals.<sup>2,13</sup> Antimicrobial treatment is often effective, but prevention strategies will always be crucial for improved animal welfare.<sup>14,16</sup>



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