Equine fungal keratitis (EFK) is a major concern in equine veterinary practice, particularly in certain geographic regions, such as the southeastern US, where it represents a significant cause of equine blindness. With vision loss occurring in as high as 58.3% of diagnosed cases, EFK represents a formidable threat to equine ocular health. This review aims to outline the prevalence of EFK, offer insights into current treatment practices, elucidate diagnostic and therapeutic hurdles, and underscore the urgency of advancing clinical approaches to reduce vision loss and improve outcomes in EFK.

**Epidemiology and Etiology**

**Prevalence**

Reports of the prevalence of EFK exhibit significant variation, with the highest reported caseloads concentrated in the northern and southeastern US. For example, Utter et al documented 30 cases diagnosed with EFK in a single year at the University of Pennsylvania, while Sherman et al reported an average of 7.3 cases per year diagnosed with EFK at North Carolina State University.

Reed et al conducted a study spanning 23 years at the University of California-Davis Center for Equine Health and reported that 0.04% of all equine admissions were diagnosed with EFK during this period. Similarly, Wada et al found a comparable frequency with 0.01% of all horses presenting to Japanese Racing Association Hospitals being diagnosed with EFK. When focusing on prevalence among all equine ophthalmology admissions, the frequency of EFK increases to a median of 6% (range, 2% to 16%) across various institutions.

Importantly, the available literature suggests that approximately 30% of all equine ulcerative keratitis (UK) cases and 50% of all equine infectious keratitis (IK) cases are attributed to a fungal etiology. However, total EFK prevalence is likely underrepresented by these data. For instance, in a 9-year study including 178 UK cases, Verdenius et al reported positive microorganism identification in only 36% of all cases. Currently available data do not include cases where fungal elements are present but not identified (eg, deep stromal ulcer, insufficient sampling, the owner declined diagnostics) or instances of previous use of prolonged antifungal therapy before referral resulting in a true lack of fungal presence.

Additionally, only 2 comprehensive retrospective analyses of EFK prevalence have been published within the last decade, both originating from Northern Europe. While increasing incidence of fungal keratitis (FK) over time has been demonstrated in human ophthalmology, a lack of modern retrospective analyses of
EFK prevalence prevents identifying similar changes in EFK incidence over time.16,17

**Causative pathogens**

The most common causative agents of EFK include a range of filamentous fungi and yeasts, notably *Aspergillus* spp, *Fusarium* spp, *Candida* spp, *Penicillium* spp, *Microsporum* spp, and *Cryptococcus* species.3–14 Among these, filamentous fungi represent the majority of identified causative agents, with *Aspergillus* accounting for a global prevalence ranging from 33% to 73%.3–14 *Fusarium* spp are also significantly featured in 6% to 45% of cases.3,5–7,9–13 Yeasts, notably *Candida* and *Cryptococcus*, exhibit a lower reported prevalence, ranging from 4% to 10%.5,7,12,14 Additionally, less commonly reported pathogens such as *Rhizopus*, *Alternaria*, and others highlight the diversity of fungal species implicated in FK.3,6,7,9,12 Mixed infections involving bacterial agents are reported in an average of 33% of cases (range, 4% to 56%), with *Staphylococcus*, *Streptococcus*, *Pseudomonas*, and *Bacillus* spp being the most commonly identified bacteria.3–11,14

**Clinical Presentation**

**Clinical signs**

Equine fungal keratitis presents with a range of clinical signs indicative of ocular discomfort and inflammation, including, commonly, blepharospasm, along with purulent or mucoid discharge and epiphora.4,5 Secondary uveitis often accompanies EFK, with signs ranging from mild, such as localized corneal edema and faint aqueous flare, to severe, including diffuse corneal edema, hypopyon, fibrin deposition, iritis, and profound miosis.5,8,11 Even in the absence of uveitis, deep corneal edema and corneal neovascularization are common.5,8

**Lesions**

Equine fungal keratitis lesions manifest a spectrum of features reflecting the disease’s severity and progression. These can range from corneal opacification and superficial punctate epithelial defects to deep ulceration, often accompanied by stromal abscessation or fungal plaque formation (Figure 1).4,5 Classic features of EFK lesions include white or multicolored appearance with feather-like margins, resembling “cake frosting” in the case of fungal plaques.4,5 Furrowing at the lesion margin is commonly observed and historically is associated with fungal involvement and severe disease progression.5,8,11 Lesions may progress from superficial to stromal over time, with fungal hyphae observed migrating into the subepithelial stroma as the disease advances.18 *Fusarium* species are significantly more likely to be associated with stromal ulcers compared to *Aspergillus*.3 Corneal stromal abscess can also develop, likely when overlying epithelium covers the initial wound resulting in deeper corneal fungal growth and inflammation.

**Diagnostic Methods**

**Clinical diagnosis**

A comprehensive ophthalmic examination, necessarily consisting of slit lamp biomicroscopy, indirect and direct ophthalmoscopy, and the application

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**Figure 1**—Clinical manifestations of equine fungal keratitis. **A**—Superficial punctate fungal keratitis (arrows). **B**—Superficial fungal plaque. **C**—Superficial stromal fungal keratitis with surrounding furrow. **D**—Deep fungal keratitis with temporal furrow. **E**—Deep fungal corneal stromal abscess (arrowhead) with secondary uveitis.
of fluorescein stain to the cornea to detect epithelial defects, is important in all horses presenting with suspected keratitis. Notably, while trauma is commonly associated with EFK and fluorescein stain retention is expected, epithelial nonulcerative keratomycosis and stromal abscesses may not initially stain with fluorescein.\textsuperscript{12} It is important to note that the clinical features of EFK are often nonspecific and thus cannot be used to distinguish EFK from other differentials, such as bacterial stromal keratitis.

**Culture**

Fungal culture swabs are recommended for all cases of IK in horses. Collection of several samples from the lesion periphery, where the infection is likely active, is advised to enhance diagnostic accuracy. While culture results typically require 1 to 2 weeks for assessment, they may take up to 4 weeks or longer for definitive analysis.\textsuperscript{19}

**Cytology**

Studies\textsuperscript{5,6,14,20} examining the role of cytology in fungal diagnosis consistently demonstrate its efficacy in identifying fungal elements, particularly in cases where fungal cultures yield negative results. Beyond its role in fungal identification, cytology has proven valuable in discerning other potential causes of keratitis, such as eosinophilic keratitis, foreign body reactions, or carcinoma.\textsuperscript{19} Utter et al\textsuperscript{6} also noted that positive identification of fungi on cytology at the initial examination of the horse was significantly associated with the eye requiring surgery, suggesting that cytological results might help guide clinical decisions regarding the need for surgical intervention.

**Histopathology**

Histopathology offers high sensitivity in visualizing fungal elements within corneal tissue samples. In addition to identifying fungal elements, histopathology enables the assessment of local tissue damage, inflammatory response, and the presence of deep-seated fungal elements that may not be accessible in cytology or culture sampling (Figure 2). In cases where culture and cytology fail to detect fungal involvement despite clinical indications, histopathology has demonstrated its utility in identifying fungal elements within corneal tissues.\textsuperscript{5,8,12}

**Polymerase chain reaction and DNA sequencing**

Polymerase chain reaction coupled with DNA sequencing is a promising diagnostic tool for EFK, providing rapid and accurate species identification crucial for targeted antifungal therapy. The precision of PCR in speciating fungi via amplification and sequencing of specific DNA regions, such as the internal transcribed spacer 1 and 2, surpasses conventional culture and cytology methods, which often struggle to accurately identify fungal species.\textsuperscript{19} This is crucial considering different species of fungi within the same genera can exhibit variations in disease virulence and antifungal susceptibility.\textsuperscript{3} In clinical settings, PCR has demonstrated its use in diagnosing EFK with several studies\textsuperscript{11,21,22} leveraging PCR and sequencing to speciate fungi and validate culture results. Importantly, fungal DNA may also be detected in culture-negative and healthy corneas, emphasizing the need to consider normal corneal flora when interpreting PCR results.\textsuperscript{19} While PCR has proven valuable in diagnosing FK, it should not be solely relied on due to potential false-positive results and its inability to distinguish normal flora from infection.

**In vivo confocal microscopy**

In vivo confocal microscopy (IVCM) is a rapid, noninvasive method providing real-time visualization of fungal elements within the corneal layers. In vivo confocal microscopy is effective for ulcerative and nonulcerative lesions and detecting fungi in superficial and deep corneal layers and is particularly useful for deep stromal abscess cases where traditional sampling may fail.\textsuperscript{12,23} However, IVCM has limitations in identifying yeast organisms due to their small size and similarity to inflammatory cells.\textsuperscript{20}

**Antifungal susceptibility testing**

Antifungal susceptibility testing (AST) is a laboratory technique that assesses the susceptibility of fungal isolates to antifungal drugs by measuring the inhibitory effect of these drugs on fungal growth. While AST plays a vital role in EFK management,
its use is associated with several challenges, such as the limited availability of trained personnel and the absence of standardized breakpoints set by organizations such as the Clinical and Laboratory Standards Institute or the European Committee on Antimicrobial Susceptibility Testing. The lack of official breakpoints often results in discrepancies in categorizing fungal isolates as sensitive or resistant, complicating the interpretation and application of AST results in clinical settings. Studies evaluating AST and clinical outcomes have found a low correlation between in vitro sensitivity testing and actual clinical responses. In vitro resistance in the face of clinical efficacy is frequently observed.3–13

**Current Therapeutic Approaches**

**Medical management**

The primary objectives in the medical management of EFK are to eliminate infectious agents, address secondary uveitis, manage inflammation, and enhance corneal wound healing. Ultimately, these efforts aim to preserve the structural integrity of the globe and vision, while restoring ocular comfort to the affected horse. According to the recent literature, approximately half of all EFK cases are managed through medical therapy alone. This approach has proven to be generally effective, achieving success in an average of 69% of cases (range, 18% to 100%).

**Antifungal agents**

Topical and systemic antifungal agents play an important role in the medical management of EFK, serving as the frontline defense against fungal pathogens directly affecting the cornea. The primary goal of using antifungals is to eradicate the fungal infection while minimizing ocular damage.

**Azoles**

The primary mechanism of action of azoles involves the inhibition of 14-α-demethylase, an enzyme critical to the synthesis of ergosterol, an essential component of the fungal cell membrane. By disrupting ergosterol production, azoles impair the structural integrity of the fungal cell membrane, leading to cell death.

**Miconazole**

Miconazole is a first-generation imidazole that, despite the development and availability of newer-generation azoles, continues to be widely used in the treatment of fungal infections due to its broad-spectrum antifungal activity, favorable tolerance profile, and effective penetration of the cornea. Administered topically, miconazole has been successfully used to treat subepithelial keratomycosis, superficial stromal ulcers, and deep stromal abscesses caused by *Candida*, *Aspergillus*, and *Fusarium* species.

**Voriconazole**

Voriconazole is a second-generation triazole. Topical 1% voriconazole exhibits excellent corneal penetration and reaches aqueous humor concentrations sufficient for clinical efficacy. Coupled with a good safety profile and a broad spectrum of activity against filamentous fungi and yeast organisms, voriconazole has become the drug of choice for treating EFK, largely replacing older antifungals like miconazole and fluconazole. Voelter-Ratson et al8 conducted a comparative analysis between horses treated with and without voriconazole to assess for differences in outcome since the introduction of voriconazole to the practice, revealing that 75% of horses treated with voriconazole experienced positive visual outcomes compared to 58.3% of horses receiving other antifungals.

**Fluconazole**

Fluconazole is a third-generation triazole widely recognized for its excellent corneal penetration and broad spectrum of action against nonfilamentous fungal organisms. Recent in vitro studies have indicated low susceptibility to fluconazole among predominant pathogens such as *Aspergillus* and *Fusarium*, suggesting prevalent resistance. Consequently, clinicians are more often opting for newer azoles with superior susceptibility, such as voriconazole.

**Itraconazole**

Itraconazole is another member of the triazole class with a broad spectrum of action that includes most yeasts as well as *Aspergillus*. Utter et al identified itraconazole as the drug of choice for treating ulcerative EFK in Pennsylvania, particularly in cases of severe and recalcitrant infection.

### Table 1—Minimum inhibitory concentrations (µg/mL) of azole drugs to clinically relevant fungal species.

<table>
<thead>
<tr>
<th>Species/strain</th>
<th>VOR</th>
<th>MIC</th>
<th>ITR</th>
<th>FLU</th>
<th>POS</th>
<th>PRO</th>
<th>LUL</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Aspergillus</em> spp</td>
<td>0.05 to 4</td>
<td>&lt; 0.03 to 10</td>
<td>0.38 to 2</td>
<td>&gt; 156 to &gt; 256</td>
<td>&lt; 0.03 to 1</td>
<td>6.25 to &gt; 156</td>
<td>0.001 to 0.06</td>
<td>3, 8, 12, 13, 31, 34, 40</td>
</tr>
<tr>
<td><em>A. flavus</em></td>
<td>0.05 to 4</td>
<td>0.38 to 1.5</td>
<td>&gt; 156</td>
<td>0.19 to 0.38</td>
<td>&gt; 156</td>
<td>6.25</td>
<td>0.001 to &lt; 0.03</td>
<td>3, 12, 34, 40</td>
</tr>
<tr>
<td><em>A. fumigatus</em></td>
<td>0.06 to 1.25</td>
<td>&lt; 0.03 to 10</td>
<td>0.75 to 2</td>
<td>&gt; 156 to &gt; 256</td>
<td>&lt; 0.03 to 1</td>
<td>6.25</td>
<td>0.001 to &lt; 0.03</td>
<td>3, 8, 12, 13, 31, 34, 40</td>
</tr>
<tr>
<td><em>Fusarium</em> spp</td>
<td>1 to &gt; 16</td>
<td>8 to &gt; 16</td>
<td>&gt; 156</td>
<td>&gt; 16</td>
<td>32</td>
<td>0.002 to &lt; 0.03</td>
<td>3, 13, 34, 40</td>
<td></td>
</tr>
<tr>
<td><em>F. falciforme</em></td>
<td>1 to 6.25</td>
<td>16</td>
<td>&gt; 156</td>
<td>32</td>
<td>0.002</td>
<td>3, 40</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>F. keratoplasticum</em></td>
<td>4 to 8</td>
<td>&gt; 156</td>
<td>32</td>
<td>0.002</td>
<td>3, 40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>F. proliferatum</em></td>
<td>1.25 to 4</td>
<td>16</td>
<td>32</td>
<td>0.002</td>
<td>3, 40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Mucor</em> spp</td>
<td>&gt; 156</td>
<td>&gt; 156</td>
<td>32</td>
<td>0.002</td>
<td>3, 40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Penicillium</em> spp</td>
<td>0.5 to 2</td>
<td>&lt; 0.003</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Cladosporium</em> spp</td>
<td>0.25 to 2</td>
<td>&lt; 0.003</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are reported in µg/mL.

FLU = Fluconazole. ITR = Itraconazole. LUL = Luliconazole. MIC = Miconazole. POS = Posaconazole. PRO = Prothioconazole. VOR = Voriconazole.
where Aspergillus was the predominant isolated causative pathogen. Limitations to the use of itraconazole included limited efficacy against Fusarium species, poor corneal penetration, and a lack of commercially available ocular formulation.29

Polyenes
Polyenes act by directly binding to ergosterol, which disrupts the integrity of the fungal cell membrane, resulting in leakage of cellular contents and eventual fungal cell death.25 This distinctive mechanism of action distinguishes polyenes from antifungals targeting specific enzymes or internal cellular processes, rendering them particularly effective against a broad spectrum of FK pathogens, including resistant strains.

Natamycin
Natamycin suspension (Natacyn) is the only US FDA-approved formulation for treating ophthalmic fungal infections. However, its use is limited by its poor corneal penetration. In vitro studies13,25,29 suggest that natamycin is uniquely effective against Fusarium species, demonstrating lower MICs to this pathogen than other polyenes and most azoles (Table 2). Brooks et al30 identified natamycin as the treatment of choice for iris abscesses with intralenticular fungal invasion. Despite its limited corneal penetration, Galera and Brooks31 argue for the use of natamycin as a highly active agent of choice for deep stromal abscesses in cases accompanied by corneal debridement.

Amphotericin B
Amphotericin B (AMB) often exhibits the lowest in vitro MICs among clinically relevant fungi when compared to other polyenes (Table 2). However, despite its potency, Mustikka et al12 reported in vitro resistance to AMB in 80% of tested Aspergillus isolates and 100% of Fusarium isolates, while Reed et al7 reported resistance in Papulaspora. Considering the potential for resistance development, the use of AMB should be carefully considered, especially given its ocular toxicity and reputation for marked ocular irritation.33

Adjunctive therapies
Nonsteroidal anti-inflammatories are often necessary to control ocular discomfort and reduce inflammation associated with anterior uveitis. Systemic flunixin meglumine is most widely employed, although phenylbutazone may also be used. Flunixin meglumine is regularly dosed at 1 mg/kg orally, IV, or IM twice a day or as needed.4,5,7,10,11 Additionally, protease inhibitors, such as autologous serum or EDTA 1%, are used to modulate the inflammatory response and promote corneal healing. Topical anticholinergics, such as atropine 1%, may also be employed to dilate the pupil and alleviate ciliary spasm, thus reducing pain and discomfort associated with anterior uveitis and helping to prevent synchiae formation.

Topical antibiotics are crucial in managing secondary bacterial infections that often accompany EFK. Ofloxacin and tobramycin are currently the most employed antibiotics for the treatment of mixed EFK.5,9–11 Other regularly used topical antibiotics included moxifloxacin, chloramphenicol, cefazolin, and ciprofloxacin.5,10,11,26 Additionally, a topical triple antibiotic ointment such as neomycin, polymyxin B, and bacitracin zinc formulation can be easily incorporated into treatment regimens suspected of concurrent bacterial infection.7,10,11,26

Surgical management
Surgical intervention is a critical aspect of managing severe or complicated cases of EFK, particularly when medical therapy fails or the structural integrity of the eye is compromised. Recent literature3–13 indicates that surgical intervention is pursued in an average of 41.6% of EFK cases, with approximately 70.2% of surgical interventions achieving a positive visual outcome (range, 12.5% to 83.3%). Typical criteria for indication of surgical intervention include nonresponsiveness to medical treatment, corneal ulcer penetration beyond 50% of the stromal depth, or a globe at risk of losing structural integrity, such as descemetocele formation or perforation.5,7,10 Utter et al12 reported that patients appeared to be better candidates for surgery when treated with aggressive medical therapy overnight before surgery. Common surgical interventions include superficial keratectomy, anterior lamellar keratectomy, and penetrating keratoplasty, which may be performed with or without the use of grafts or a conjunctival flap.3,11,34

Table 2—Minimum inhibitory concentrations of polyene and echinocandin drugs to clinically relevant fungal species.

<table>
<thead>
<tr>
<th>Species/strain</th>
<th>Polyene drugs</th>
<th>Echinocandin drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AMB</td>
<td>NAT</td>
</tr>
<tr>
<td>Aspergillus spp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A flavus</td>
<td>0.5 to 16</td>
<td>2 to 1,000</td>
</tr>
<tr>
<td>A fumigatus</td>
<td>1 to 16</td>
<td>16 to 70</td>
</tr>
<tr>
<td>Fusarium spp</td>
<td>0.5 to 3</td>
<td>2 to 8</td>
</tr>
<tr>
<td>F falciforme</td>
<td>2 to 4</td>
<td>0.125 to &gt; 1,000</td>
</tr>
<tr>
<td>F keratoplasticum</td>
<td></td>
<td>0.125 to 70</td>
</tr>
<tr>
<td>F proliferatum</td>
<td></td>
<td>6.25 to 32</td>
</tr>
<tr>
<td>Mucor spp</td>
<td></td>
<td>1.25 to 4</td>
</tr>
<tr>
<td>Penicillium spp</td>
<td></td>
<td>6.25</td>
</tr>
<tr>
<td>Cladosporium spp</td>
<td>0.25 to 4</td>
<td></td>
</tr>
</tbody>
</table>

Values are reported in µg/mL.
AMB = Amphotericin B. AND = Anidulafungin. CAS = Caspofungin. NAT = Natamycin. NYS = Nystatin.
Outcome

Visual outcomes of EFK over the past 20 years exhibit considerable variability. A positive visual outcome, defined through evaluations of corneal scarring, menace response, and behavioral observations, is achieved in an average of 67.8% of cases (range, 41.7% to 100%), while globe retention averages higher at 77% (range, 50.8% to 100%). However, the prevalence of vision loss and the decision for enucleation present ongoing challenges in EFK management. Loss of vision has been reported in as high as 58.3% of cases in the last 2 decades, with an average of 32% of horses experiencing vision loss across the available literature. The current average enucleation rate is 19.43%, ranging from 0% to 40.7%. The highest rate of enucleation in recent studies was reported by Mustikka et al who found that 40.7% EFK cases over 11 years resulted in enucleation. Most enucleations from this study occurred in medically managed cases, of which 82% failed to respond to therapy and progressed to enucleation.

Factors Associated with Visual Outcome

Causative pathogen

Recent studies have found no correlation between treatment outcome and infection caused by Fusarium versus Aspergillus species, despite Fusarium demonstrating significantly higher in vitro MICs to most common antifungals (Table 1). However, some distinct trends among these fungal genera have been identified. Sherman et al identified an insignificant trend toward successful surgical management in Aspergillus cases over Fusarium cases, while Martinez et al identified a trend toward longer healing times in Aspergillus infections. Similarly, Cullen et al reported that Fusarium cases were significantly more likely to heal with medical therapy compared to Aspergillus cases, although the overall rate of enucleation remained the same due to improved healing with surgical management in Aspergillus cases.

Regarding bacterial pathogen involvement, Sherman et al found no significant difference in treatment outcome or the type of surgical intervention required between cases with only fungal involvement versus those with bacterial coinfection. Berkowski et al and Cullen et al similarly reported no difference in visual outcomes between cases of mixed infection and those caused by fungal pathogens alone.

Medical versus surgical management

The only report of a significant impact of surgery on visual outcome has come from Mustikka et al in a report on EFK in Finland that positively associated surgical intervention with visual recovery (88% recovery in surgical cases vs 18% recovery in medical cases). Reports on how surgical intervention affects treatment duration are conflicting, with Mustikka et al finding that treatment duration was significantly longer for surgically treated cases versus medically treated cases (36 vs 20 days), while Reed et al report no significant difference but a subjective trend toward more rapid resolution in surgically treated cases (37 vs 46 days). Although significance was not evaluated, findings by Utter et al strongly support longer treatment duration in surgically managed cases versus surgical cases (83 vs 33 days).

Advancements in Treatment

Novel antifungals and combination drug therapy

Luliconazole is a third-generation imidazole widely used as a topical treatment for dermatological fungal infections. Previous work from our laboratory has demonstrated luliconazole’s potent in vitro antifungal activity against EFK-derived fungal isolates of Aspergillus and Fusarium, with MICs at least 25-fold lower than other antifungal drugs (Table 1). Recent work by Arimoto et al demonstrated luliconazole’s efficacy against Fusarium in a rabbit model of Fusarium solani FK. Poor solubility remains a significant hindrance to the practical use of luliconazole; however, integration of modern nanoemulsion formulation techniques may provide an effective ocular formulation.

Echinocandins, primarily caspofungin and anidulafungin, work by inhibiting the synthesis of β-(1,3)-d-glucan, weakening the fungal cell wall and leading to cell death. They offer greater specificity for fungal cells and potentially lower toxicity compared to other antifungal agents. Echinocandins are known for activity against Candida and Aspergillus species and have demonstrated low MICs against EFK isolates of Aspergillus and Fusarium in vitro (Table 2).

Among the polyene drugs, AMB is the most commonly used drug of this class but can be associated with significant adverse effects, prompting the development of lipid formulations that offer improved tolerability without compromising efficacy. Ghosh et al evaluated liposomal AMB compared to the conventional drug in a rabbit model of Aspergillus flavus and Candida albicans FK. Fungal burden was found to be significantly lower in the liposomal formula-treated group compared to the conventional AMB-treated group.

Multidrug antifungal protocols are also being studied that may allow less frequent drug administration and reduce antimicrobial resistance compared to monotherapy. Scotty et al investigated a combination treatment including natamycin, tobramycin, cefazolin, and serum against clinical EFK isolates of Aspergillus and Fusarium, as well as bacteria common to EFK infections. Their findings demonstrated significantly greater inhibition of Aspergillus and Fusarium spp with the drug combination compared to natamycin alone and enhanced inhibition of Streptococcus with the drug combination compared to tobramycin alone.
Targeted Drug Delivery

Injections
Injectable targeted drug therapy offers a promising approach to the management of fungal keratitis, presenting a localized and potentially effective treatment, with fewer side effects than systemic or topical antifungals.

Smith et al.15 conducted a retrospective analysis of 6 cases involving deep stromal abscess suspected of fungal involvement, treated with an intrastromal injection of 5% voriconazole solution (22.5 mg) alongside traditional medical treatment. All 6 horses achieved complete healing without significant complications, although mild, linear stromal scars associated with needle tracts were observed. The authors recommended intrastromal voriconazole injection as an alternative to traditional therapy for deep stromal ulceration. A voriconazole-loaded gel, administered via subconjunctival injection, has also been investigated as a potential long-term treatment, but voriconazole was only detectable in the tear film for 3 hours.42

Subconjunctival injection of AMB is an adjunctive therapy to topical antifungals and is used in challenging cases of filamentous FK.3,10,12 In their studies, Sherman et al.10 suggested a dosing regimen of 62.5 μg every other day for 3 doses, which was used in 12.3% of their EFK patient population, while Mustikka et al.12 proposed a single 1-mg dose, delivered to 6.6% of their patients.

Photodynamic Therapies

Photoactivated chromophores
Photoactivated chromophore for keratitis-corneal cross-linking (PACK-CXL) involves applying riboflavin eye drops followed by UV light to induce cross-linking of corneal collagen, aimed at stabilizing melting corneas. Its potential utility in EFK was explored in a study by Hellander-Edman et al.43 which evaluated PACK-CXL in standing, sedated horses to address stromal melting associated with infectious or UK. The procedure, using epithelial debridement, riboflavin instillation, and UVA light exposure over 2 hours, was well tolerated in 9 horses. The therapy halted stromal melting within 24 hours in 1 horse with FK, with complete ulcer healing in 9 days.45 However, in a second FK case, the procedure was unsuccessful, leading to hyphal penetration into the anterior chamber in the enucleated eye 4 days later.45

A notable limitation of PACK-CXL is its superficial corneal penetration, limited to the top 300 μm of the cornea, potentially reducing its efficacy against deep-seated organisms.45,44 Additionally, the lengthy treatment time, lasting up to 2 hours, may pose practical challenges and limit its feasibility in certain clinical settings. Cross-linking is also not recommended for corneas thinner than 400 μm due to the risk of UVA damage to posterior ocular structures.45

Cold atmospheric plasma
Cold atmospheric plasma (CAP) is an innovative antifungal therapeutic, offering a nonchemical alternative that directly targets fungal cells without the need for the use of exogenous photosensitizers. Cold atmospheric plasma is generated by applying a low-current voltage to a gas such that the electrons become energized, without producing significant thermal output. When CAP is applied to microbes, such as fungi, CAP-generated reactive oxygen and nitrogen species interact with the microbial cell at the membrane, cytosolic, and DNA levels to induce cell damage and apoptosis.45 Cold atmospheric plasma demonstrated antifungal activity against many common FK pathogens in vitro, including Aspergillus flavus, Aspergillus fumigatus, and Pseudomonas aeruginosa.46-49 Early ex vivo works using rabbit models of IK and CAP treatment are associated with improved clinical signs and reduced fungal and bacterial loads.47-49

Conclusions

Fungal keratitis remains a significant concern in equine ophthalmology, representing approximately 30% of all equine UK cases. Among IK cases in horses, fungal involvement is identified in nearly 50% of cases, indicating a substantial burden on equine ocular health. While EFK remains a significant clinical challenge, ongoing advancements in diagnostics and therapeutics offer promise for improving outcomes. However, continued research efforts are needed to further elucidate the epidemiology, pathogenesis, and optimal management strategies for this condition.

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