A **CONTINUING MEDICAL EDUCATION** PUBLICATION

DECEMBER 2018
ISSUE 69

TOPICS IN Ocular Antiinfectives

Update on Prevention and Management of Blebitis

Leon W. Herndon Jr., MD

Trabeculectomy remains the gold standard incisional surgery for lowering IOP in patients with medically uncontrolled glaucoma, but it carries a lifelong risk for bleb-related complications, including infection. Understanding and managing pre- and postoperative risk factors, as well as maintaining a high index of suspicion for infection, will help protect patients with blebs.

Over the past 10 to 15 years, the number of trabeculectomy procedures being performed in the management of advanced, drug-recalcitrant glaucoma is going down, in favor of glaucoma drainage device surgeries.[1-3] Indeed, as more and more minimally invasive glaucoma surgeries (MIGS) are performed for patients with varying ranges of disease severity, the frequency of trabeculectomy may continue to decline.

More research is needed to tell if the trend away from trabeculectomy is well founded and to predict how various patient types might respond to each procedure. The prospective, randomized, multicenter Tube vs. Trabeculectomy (TVT) study (N = 212 eyes) showed that both tube-shunt surgery and trabeculectomy with mitomycin C (MMC) were effective in maintaining IOP in the low teens in the first 5 years following the procedure in eyes with previous surgeries.[4] Further, patients who underwent trabeculectomy required fewer IOP-lowering medications in the first 2 years following surgery compared with patients with tubes, although that difference lost significance by the 5-year mark. Vision loss and long-term complication rates between the two groups were similar over the 5-year period.[4]

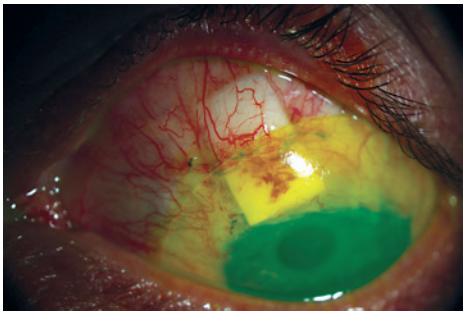

FIGURE 1 Soft bandage contact lens in place to protect eye after bleb revision (with a scleral patch graft) surgery. *(Image courtesy of Dr. Herndon.)*

1-year follow-up results from the similarly designed Primary Tube vs Trabeculectomy (PTVT) study among patients without preceding incisional ocular surgery (N = 242 eyes) revealed significantly better IOP reduction, medication burden reduction, and overall surgical success among patients treated with trabeculectomy with MMC vs tube shunt placement.[5] However, also at 1 year, adverse events and serious adverse events resulting in vision loss were more common among trabeculectomy-treated

See INSIDE for:
A Review and Update of EKC
by Nambi Nallasamy, MD

TARGET AUDIENCE This educational activity is intended for ophthalmologists and ophthalmologists in residency or fellowship training.

LEARNING OBJECTIVES Upon completion of this activity, participants will be able to:

1. Optimize peritrabeculectomy clinical care to minimize risk for bleb-related infection.
2. Recognize risk factors, signs, and symptoms of bleb-related infection.
3. Diagnose and manage individual cases of EKC.
4. Implement procedures to prevent the spread of adenovirus within healthcare facilities.

Topics in Ocular Antiinfectives is jointly sponsored by Candeo Clinical/Science Communications, LLC, and the University of Florida College of Medicine. This publication is administered by an independent editorial board and supported by an unrestricted educational grant from Shire.

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patients ($P = 0.06$ and $P = 0.03$, respectively) vs tube-treated patients.[5]

In addition to evidence that is emerging from these and other studies, the selection of surgical treatment depends on patients' desires, risk profile, and tolerance for repeated surgery if that becomes necessary—as well as on surgeons' experience, skill, and understanding of each procedure.[3] As with all interventions, potential risks and benefits must be considered in context.

Risk Factors for Blebitis

While all glaucoma filtering surgeries carry risk for complications, risk for bleb-related leak and bleb-related infection may be greater with trabeculectomy compared with other procedures, particularly when performed with an antifibrotic agent.[3,4]

Several factors thought to contribute to bleb-related infection have been identified, including placement of the bleb, the profile of the bleb, and the use of antimetabolites.[6] First, the risk of infection is significantly higher with an inferior vs a superior location of the bleb. Next, the function of the bleb can be a double-edged sword when it comes to infection risk: a thin-walled or cystic bleb allows for good filtering functioning but is associated with increased risk of bleb-related infection.

Third, use of anti-scarring agents such as mitomycin and 5-fluorouracil —increasingly popular over the past 20 to 25 years for their association with increased surgical success—have been associated with increased risk for bleb-related infection in multiple prospective studies.[7-9] This is hypothesized to be because agents such as mitomycin contribute to formation of thin-walled, avascular blebs prone to leakage and an impaired capacity to heal.[9-11] A decline in recent years in bleb-related infection has been attributed in part to more surgeons developing increased confidence and skill with perioperative antimetabolite use.[6]

Strategies for Reducing Risk

Glaucoma surgeons now pay close

TOPICS IN OCULAR ANTIINFECTIVES, ISSUE 69

STATEMENT OF NEED

The world of ocular viral and bacterial infection is continuously in flux: global travelers spread viruses and bacteria to new places; microorganisms exchange genes that affect resistance and virulence; and new medical procedures (eg, intravitreal injections) create new opportunities for ocular infection.

For these and other reasons, diagnosis and treatment continue to be challenging. For example, viral infections may be misdiagnosed as bacterial and therefore treated incorrectly. And as ongoing surveillance studies confirm, antibiotic resistance is increasing steadily among common ocular pathogens and multidrug resistance is widespread, putting old treatment paradigms into question.[1,2]

In order to make sound, evidence-based decisions, clinicians must be informed of the development of new and potentially more accurate in-office and laboratory-based techniques for the diagnosis of ophthalmic infection, including how to distinguish between viral and bacterial infections.[3,4]

With respect to treatment, clinicians need to understand current resistance patterns, the pharmacokinetics and pharmacodynamics of ocular antimicrobials for specific infectious threats, and the ways that newer agents—including those with new vehicles and those that combine antiviral and antibacterial therapies—can be optimally used.[5-7] Beyond approved therapeutic applications, an emerging body of research is accumulating data on the off-label use of antibiotics in bacterial keratitis and antimicrobial prophylaxis for ocular surgery.[8,9] Finally, managing infections caused by exotic or rare pathogens (fungal, amoebic, atypical) may require unfamiliar diagnostic and treatment modalities.[10]

Topics in Ocular Antiinfectives aims to address the evolving challenges described above, helping ophthalmologists maintain competencies and narrow gaps between actual and optimal clinical practice by providing updated information about prevalence patterns and diagnostic and treatment strategies. As an enduring resource, this ongoing series will support physicians who desire to make evidence-based antiinfective choices across a range of ophthalmic clinical and patient settings.

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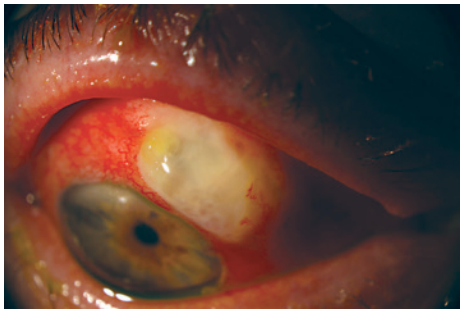

FIGURE 2 "Red-on-white" appearance of bleb is a sign of blebitis. *(Image courtesy of Dr. Herndon.)*

attention to the health of the lids and lashes preoperatively, as significant inflammation and/or microbial overgrowth may set patients up for postoperative infection.[12,13] Oral tetracyclines may be prescribed adjunctively to manual scrubs before surgery. Helping patients establish a workable and successful eyelid hygiene practice ahead of filtration surgery goes a long way to ensuring successful outcomes and habits over the long term.

Some eyecare providers advocate prescribing topical antibiotics prior to surgery, but the practice has not proven to be beneficial in decreasing the risk of bleb-related infections. A short course of postoperative antibiotic and corticosteroids (typically dosed QID for several weeks, until the bleb is well formed) is common practice, but the long-term use of antibiotic drops after surgery is not recommended.[7] Long-term antibiotic prophylaxis may do more harm than good by changing the flora of the ocular surface and selecting for resistant organisms; this has been demonstrated in studies of topical antibiotic prophylaxis of intravitreal injection in the treatment of age-related macular degeneration.[14,15] My practice for infection prophylaxis for trabeculectomy patients is to prescribe an affordable broad-spectrum antibiotic (eg, trimethoprim/polymyxin) in the immediate postoperative period only.

Bleb Leaks

A bleb leak, essentially an opening to microbes, is the number one causative factor associated with bleb-related infections.[13] Thus, vigilant monitoring for bleb leaks is essential throughout the life of a patient who has undergone a glaucoma filtering surgery. Fluorescein dye helps visualize a bleb leak. Once identified, a bleb leak requires treatment with topical antibiotics, a bandage contact lens, or ultimately bleb revision surgery if it persists.

A diffuse, low bleb is typically amenable to treatment with a bandage soft contact lens, which provides tamponade, or counter-pressure, against outward flow and creates a barrier against blink-related trauma. In my practice, I typically describe a bandage contact lens as a "clear band-aid" designed to protect the bleb from the direct trauma of blinking and to allow the bleb to heal. Learning that they do not have to handle or remove the bandage contact lens themselves is frequently reassuring to patients (Figure 1).

After placing the lens, I prescribe a prophylactic topical antibiotic for use while the lens is in place, and I ask the patient to return to the office in 2 weeks, generally a sufficient amount of time for the bleb to resolve. While not a part of my practice, some practitioners employ aqueous suppressants to decrease the amount of aqueous flow through the leak.

Counseling Patients

Most patients who undergo trabeculectomy do not experience bleb leaks and infection. However, it is important that patients preparing for surgery understand that they are at risk for bleb-related infection for the rest of their life, and that, due to a host of factors—including antimetabolite-induced bleb wall thinning and cumulative blink-related trauma—the risk generally increases over time. As such, eyecare providers of patients with blebs should emphasize the need for ongoing vigilance and carefully educate patients regarding symptoms and signs of a potential leak or infection. Anything that seems unusual, whether mild and nonspecific (eg, blurred vision or mild irritation, which may indicate an early bleb-related infection) to more severe (eg, decreased vision or eye pain), should prompt a return to the office promptly for evaluation.

CORE CONCEPTS

- Patients who have undergone trabeculectomy, and their doctors, should be highly vigilant for signs and symptoms of blebitis.
- Eye pain, decreased vision, or any new ocular symptom should raise concern for bleb-related infection.
- Risk for bleb-related infection can be reduced with careful attention to eyelid hygiene.
- Blebitis treatment includes round-the-clock broad-spectrum antibiotic drops, antibiotic ointment at night, and a bandage contact lens.
- Follow-up should occur daily at first then spaced out as indicated.

Diagnosing Blebitis

Recognizing signs of blebitis facilitates timely intervention and is critical to caring for patients with blebs. First, clinicians should remember that "blebitis" is something of a misnomer in that it refers to infection, not just inflammation. Bleb-related infections may present in one or more of three stages—early blebitis, blebitis, and endophthalmitis—and may occur at any time in the months, years, or decades after surgery.

Early blebitis is characterized by conjunctival injection or redness around the bleb; also, the bleb may lose its transparency and become milky in appearance during the early stage. Anterior chamber inflammatory reaction may be absent or mild. Any of these findings, including an isolated finding of mild peri-bleb redness, should raise concern for early infection (Figure 2).

In mid-stage blebitis, (generally just called "blebitis"), bleb redness and opacity become more marked and the anterior chamber reaction more pronounced. Anterior chamber reaction may range from mild to hypopyon. In early blebitis and blebitis, infection is confined to the bleb. Bleb-associated endophthalmitis is differentiated from

blebitis by the presence of cells in the vitreous. Although rare, bleb-associated endophthalmitis carries the potential for visually devastating consequences.[6]

Whether or not to swab suspected blebitis is somewhat controversial. Bleb culture yield is generally low; however, a positive result may be useful in guiding choice of antimicrobial therapy.

Management

Empiric antimicrobial therapy for the treatment of blebitis should be broad-spectrum and include activity against *Staphylococcus* and *Streptococcus* species, which are the most common pathogens associated with bleb-related infections.[16] *Haemophilus*, *Corynebacterium*, *Enterococcus*, and other bacteria have been demonstrated from blebitis cultures.[11,16] My practice is to employ a fourth-generation fluoroquinolone eyedrop dosed one drop every 30 minutes throughout the day while awake, and a broad-spectrum antimicrobial ointment at bedtime.

Blebitis patients should be advised to follow up with the clinic daily until resolution is evident and progression to endophthalmitis is ruled out. For suspected endophthalmitis, prompt referral to a glaucoma or retina specialist for emergency management could be vision-saving.

Bleb leak is often the culprit of blebitis. Once a bleb-related infection is successfully treated, a bleb leak, if present, can be surgically repaired. Patients with a persistent leak despite initial revision may require additional surgery, with the risk for bleb failure (and the need for additional IOP-lowering procedures) increasing with each procedure.[17]

Conclusion

Trabeculectomy ranks consistently among the most effective and most common procedures for major IOP reduction but carries the risk of bleb-related infection.[3,10] Routine eye care for patients with blebs involves, first and foremost, staying vigilant for signs of infection at every visit. Knowing and mitigating risk factors, recognizing common signs and symptoms, prompt diagnosis and treatment, and collaborating with glaucoma and/or retina specialists when warranted are also critical.

Leon W. Herndon Jr., MD, is an ophthalmologist and glaucoma specialist at Duke Eye Center, in Durham, NC. ***Dr. Herndon has received grant/research support from Glaukos and is a consultant for Aerie Pharmaceuticals, Sight Sciences, and Glaukos. He is also on the speakers bureau for Glaukos. Medical writer Noelle Lake, MD, assisted in the preparation of this manuscript.***

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A Review and Update of EKC

Nambi Nallasamy, MD

Adenovirus is one of the most contagious pathogens ophthalmologists encounter in clinical practice, capable of inciting severe keratoconjunctivitis and other complications in individuals and groups. Rapid identification and containment are essential; management options are limited but evolving.

Epidemic keratoconjunctivitis (EKC) is one of several highly contagious forms of ocular adenoviral infection associated with significant morbidity and occasional community- or healthcare-related outbreaks.[1]

Effective EKC management addresses symptom relief, prevention of sequelae, and prevention of viral spread to others.

Clinical Features and Morbidity

EKC typically presents as follicular conjunctivitis with onset of signs and symptoms approximately 7 to 8 days following initial exposure. Patients may recall recent direct or indirect contact with someone with a red eye. Symptoms include acute onset of watery ocular discharge, foreign body sensation, photophobia, chemosis, hyperemia, pain, itching, and eyelid swelling, with symptoms starting in one eye and then spreading to the fellow eye within 2 to 4 days.[2] Ipsilateral preauricular lymph nodes may be enlarged and palpable.

Progression of EKC may result in formation of painful conjunctival membranes or pseudomembranes, differentiated by either a tendency to bleed (membranes) or not bleed (pseudomembranes) when peeled by a clinician. If allowed to persist, membranes may lead to the formation of subepithelial fibrosis, symblepharon, or other sequelae.[3]

Within 2 to 4 days of the onset of EKC symptoms (or about 10 days from initial exposure), the cornea may become involved, starting as scattered punctate epithelial erosions, then coalescing to produce larger epithelial infiltrates; subsequently these may be replaced by focal subepithelial infiltrates which represent a delayed type hypersensitivity reaction to viral antigens.

Subepithelial infiltrates appear as small round grayish lesions, which typically increase in number during initial weeks, then slowly fade by week 4 or 5.[2] Subepithelial infiltrates may, however, persist for weeks or months after their onset and contribute to visual disturbances such as glare or halos around lights; further subepithelial infiltrates may lead to corneal scarring and decreased visual acuity.

Epidemiology

Molecular Epidemiology

While not feasible in clinical practice, identifying the specific adenoviral serotypes in EKC is beneficial to public health efforts aimed at determining a source of an outbreak, mapping its spread, and implementing and monitoring containment.[4] As a result, clinical correlates of adenovirus serotypes and genotypes have come to light.

Of the 55 known human adenovirus (HAdV) serotypes, serotypes 3, 4, 7, 8, 19, and 37 are the most common etiologic agents in conjunctivitis, and 8, 19, and 37 in EKC specifically.[5] Compared with other serotypes, infection with adenovirus serotypes 5 (HAdV-5) and 8 (HAdV-8) is more commonly associated with the presence of subepithelial infiltrates. Adenovirus serotype 8 is the serotype most commonly associated with the development of uveitis, a rare complication of EKC. Further, HAdV-8 subtype H is associated with a higher incidence of keratitis compared with other subtypes.

Transmissibility

Adenovirus transmission occurs via direct contact with ocular secretions of an infected individual or via indirect contact with a contaminated surface or fomite, such as towels, pillows, multiuse eye drop bottles, examining room chairs, and medical instruments, on which adenovirus has been shown to remain viable for up to 30 days.[4] Less commonly, adenovirus spreads via swimming pool water or sexual contact.

Adenovirus remains transmissible for a period of about 2 weeks following onset of symptoms and is particularly contagious within the first few days of symptoms. Because of this, healthcare providers who have been diagnosed with EKC are advised to avoid contact with patients for 2 weeks.

EKC Outbreaks

While not a reportable disease to the Centers for Disease Control (CDC), clusters of cases in an ophthalmology practice or network of practices, hospital, other healthcare setting or geographic area should be reported to local and state health authorities for investigation and containment.[4,6] By looking back on the details of recent EKC outbreaks as reported by the CDC, important lessons regarding modes of transmission and corrective procedures snap into focus.[4,6]

For example, a 2015 outbreak in West Virginia of at least 23 cases (including patients, family members of patients, and clinic staff) was linked to a contaminated surface within a single ophthalmology practice. Environmental samples uncovered HAdV-8 on an exam chair hand rest, a slit-lamp chin rest, a tonometer, and other sites.[4] Ophthalmology practices were also central to HAdV-8 outbreaks in Florida (37 cases), Minnesota (70 cases), and New Jersey (about 300 cases).[6] The Florida outbreak involved an eye care provider who continued to work despite experiencing EKC symptoms.

In 2009, an HAdV-19 outbreak in Illinois involved twelve premature infants, two family members, two neonatal intensive care unit (NICU) staff members, and two ophthalmology team members, one of whom was an ophthal-

mology resident who failed to take leave while symptomatic. All twelve affected infants had undergone retinopathy or prematurity examination by the ophthalmology team with reusable and improperly cleaned instruments within a month of the outbreak; and virus was detectable on the ROP equipment cart. The NICU was forced to close to new admissions for 3 weeks for disinfection.[6]

Morbidity related to EKC outbreaks has been significant. Among patients affected by the Florida outbreak, 22% developed keratitis and required long-term corticosteroids. In Minnesota, 53% developed keratitis or corneal erosions, 41% developed membranous conjunctivitis, and 40% had visual compromise as a result of their infection.[6]

Measures taken to contain past EKC outbreaks and prevent future ones have included the following infection-control protocols, which should be written down and distributed within the practice:[4,6]

- Improved staff hand hygiene practices
- Improved equipment cleaning and reprocessing
- Use of cleaning agents effective against HAdV, such as sodium hypochlorite
- Use of disposable equipment when possible
- Cleaning of all touched surfaces between symptomatic patient encounters with virocidal agent, such as sodium hypochlorite
- Separation of infectious and suspected infectious patients from others in waiting areas
- Dedicating an exam room for conjunctivitis patients
- Limiting use of multidose eyedrop vials
- Mandatory leave for infected staff
- Patient education regarding EKC transmission prevention

Clinical Diagnosis

EKC is primarily a clinical diagnosis. Clues in the history and physical examination that differentiate EKC from other infectious processes include the presence of follicular conjunctivitis involving the inferior tarsal conjunctiva, preauricular lymph node enlargement, and recent contact with someone with a red eye. Subepithelial infiltrates and an associated upper respiratory tract infection may also be present; however, their absence does not preclude EKC. EKC is less likely to be associated with pharyngeal symptoms, oral mucosal changes, or diarrhea, which point toward a non-EKC viral etiology.

Differentiating viral from bacterial causes of conjunctivitis is important to clinical decision-making but can be challenging based on symptoms alone, especially early in the course of disease. In a prospective cohort study of patients presenting with acute conjunctivitis (N = 184), copious unilateral or bilateral discharge upon awakening in the morning (eyes "glued" shut) was independently predictive of bacterial etiology (as demonstrated by bacterial culture); ocular itchiness and prior history of conjunctivitis predicted viral etiology.[7]

Diagnostic tests

Gold standards for viral identification are viral cellular culture with confirmatory immunofluorescence assay (CC-IFA) and polymerase chain reaction (PCR), both of which are highly accurate but require expensive equipment and a surplus of time, which most eye care providers do not have. Point-of-care adenovirus detection tests are far more practical. A positive test confirms EKC in real time, enables timely implementation of control measures, and spares patients unnecessary antibiotic exposure when bacterial conjunctivitis is the presumed cause.

SAS Adeno Immunoassay (Meridian Bioscience Inc.), a 20-minute assay for detecting adenovirus in ocular and nasopharyngeal specimens, is available in Europe.[8] RPS AdenoPlus (Rapid Pathogen Screening Inc.)—an improved version of RPS AdenoDetector associated with a 90% sensitivity and 96% specificity rate compared with CC-IFA—is available in the US.[5] Additionally, since results correlate somewhat with infectivity, a negative follow-up AdenoPlus test (indicating fewer than 50 viral particles per tear sample) in a patient who initially tested positive may be used as support for a safe return to work or school.

CORE CONCEPTS

- Severe EKC may be associated with painful conjunctival membranes, pseudomembranes, or keratitis; subepithelial infiltrates may persist and impair vision.
- Adenovirus serotypes 8, 19, and 37 are the most common causes of EKC.
- Eye care practices with inadequate room and instrument sterilization practices have contributed to past EKC outbreaks.
- Cold compresses and removal of membranes may reduce discomfort.
- No antiviral treatment is indicated.
- Antiinflammatory treatment may be indicated in severe cases.

Management

Preventing Spread

Preventing HAdV spread within the healthcare setting is an essential first step in the management of EKC. This is accomplished by meticulous and consistent hygienic precautions, including hand-washing with soap and water, paper towel use, and appropriate cleaning of environmental surfaces and instruments with sodium hypochlorite or other chlorine-releasing agent (not 70% isopropyl alcohol solution) between patient encounters, particularly when there is suspected or documented EKC.

A 2006 study showed that germicides effective against HAdV-8 dried on medical devices and environmental surfaces included 0.55% ortho-phthalaldehyde, 0.2% peracetic acid, 2.4% glutaraldehyde, 2.65% glutaraldehyde, 6,000 ppm chlorine (1:10 dilution of sodium hypochlorite of Clorox), 1,900 ppm chlorine (Clorox Clean-up), and 79.6% ethanol with 0.1% quaternary ammonium compound (Lysol disinfectant spray). Agents inactive against surface HAdV included 3% hydrogen

peroxide, 70% isopropyl alcohol, 10% povidone-iodine and others; these should not be relied upon for containment or prevention of outbreaks.[9]

Preventing viral spread also requires identification and surveillance for new cases by AdenoPlus testing.

Symptomatic Relief

Supportive care and symptomatic relief are mainstays of EKC treatment, as the disease is generally self-limited and there are currently no antiviral drugs approved for treatment of adenovirus infection. In the clinic, removal of conjunctival membranes with forceps may improve ocular comfort and reduce the risk for development of subepithelial fibrosis, symblepharon, or other deleterious sequelae.[3]

Sunglass wear to reduce photophobia and cold compresses may also provide relief. Patients and family members should be advised that cold compresses can harbor viable adenovirus particles and should be handled with care so as to avoid intrahousehold EKC transmission.

Antiinflammatories

Topical corticosteroids are a logical option to reduce pain, inflammation, and risk for sequelae in patients with EKC; but they also enhance viral replication and shedding, potentially increasing risk of disease spread. Corticosteroids carry other well-known risks, including cataract formation in phakic individuals and elevated intraocular pressure and glaucoma. However, in severe EKC cases—such as those complicated by membranes or pseudomembranes, iridocyclitis or uveitis, severe keratitis, or persistent subepithelial infiltrates with decreased vision—a short course of low-potency topical corticosteroid should be considered.

Alternatives to corticosteroids have been proposed. Nonsteroidal antiinflammatory agents (NSAIDs) have not been shown to increase viral shedding, rendering them a seemingly safer alternative for inflammation control. However, NSAIDs have not been shown to improve symptoms, so they are generally not recommended in the management of EKC. There is some evidence that topical cyclosporin A (in concentrations ranging from 0.05% to 2%) may promote the regression of subepithelial infiltrates in patients with EKC and be a viable steroid-sparing antiinflammatory option.[2,10,11]

Antiinfectives

Study of antiviral treatment for EKC has centered around trifluridine, cidofovir, and povidone-iodine. Topical trifluridine, a highly effective treatment against herpes simplex virus, has not been shown to be more effective than artificial tears in the treatment of adenoviral conjunctivitis and is not recommended for treatment of EKC.[12] Cidofovir has been shown to decrease adenoviral activity but is limited by toxicity to conjunctival and skin cells. Although cidofovir might conceivably be better tolerated at lower concentrations, this has not been tested, and cidofovir is also not currently recommended in the treatment of EKC.

Povidone-iodine has activity against a wide range of potential pathogens including bacteria, fungi, and viruses. It is also inexpensive. A number of studies have looked at the role of povidone-iodine in the treatment of viral conjunctivitis. Povidone-iodine may have a therapeutic effect in early stages of adenoviral conjunctivitis due to greater potency against free (compared with intracellular) adenovirus.

Topical antibacterial agents—either alone or in combination with a corticosteroid—are not indicated for suspected or confirmed viral conjunctivitis and should be avoided. Antibiotics may be appropriate, however, as prophylaxis against superinfection in eyes with a large epithelial defect in the cornea or following removal of membranes or pseudomembranes.

Future Directions

A combination povidone-iodine 0.6% and dexamethasone 0.1% (PVP-I/dexamethasone) is currently in phase 2 clinical trials for the treatment of adenoviral conjunctivitis. A recent article in the *American Journal of Ophthalmology* presented findings from a randomized, controlled, double-masked trial comparing PVP-I/dexamethasone with PVP-I alone and vehicle control in the treatment of acute AdenoPlus-confirmed conjunctivitis.[13]

The investigators found that clinical resolution at day 6 of treatment was significantly higher among patients treated with PVP-I/dexamethasone compared with no treatment, 31.3% vs 10.9% (P = 0.0158). Further, adenoviral eradication was also statistically improved among patients treated with PVP-I/dexamethasone compared with untreated patients at days 3, 6, and 12 of treatment (P < 0.02 for all).

These results indicate that a combination PVP-I/dexamethasone drop may be a useful treatment for EKC in the future, particularly in instances in which aggressive antiinflammatories are warranted (eg, highly symptomatic patient, presence of membranes, persistent subepithelial infiltrates). Interestingly, the study also showed that the povidone-iodine-only group had significantly greater adenoviral eradication rates at day 3 of treatment (although not at day 6 or 12) compared with control (32.0% vs 8.7%; P = 0.005). Whether povidone-iodine monotherapy has a role in EKC management will require further study.

Conclusion

Preventing the spread of EKC within families, communities, and healthcare centers remains an essential component of EKC management. Symptomatic treatment, supportive care, and antiinflammatory treatment in severe cases are standard. The broad-spectrum antiseptic agent povidone-iodine in combination with dexamethasone has met its endpoints in a phase 2 study.

Nambi Nallasamy, MD, practices at Bascom Palmer Eye Institute in Miami, Florida. He states that in the past 12 months, he has not had a financial relationship with any commercial organization that produces, markets, resells, or distributes healthcare goods or services consumed by or used on patients relevant to this manuscript. Medical writer Noelle Lake, MD assisted in the preparation of this manuscript.

NALLASAMY REFERENCES *continue on page 8*

EXAMINATION QUESTIONS TOPICS IN OCULAR ANTIINFECTIVES, ISSUE 69

This CME activity is sponsored by the University of Florida College of Medicine and is supported by an unrestricted educational grant from Shire. Participants must score at least 80% on this exam in order to receive credit. The University of Florida College of Medicine designates this enduring material for a maximum of 1 *AMA PRA Category 1 Credit*™. To take this exam and obtain credit, please take the test online at **http://cme.ufl.edu/ed/self-study/toa/**. Expires: November 30, 2019.

1. Which of the following agents demonstrated both clinical resolution of adenoviral conjunctivitis and enhanced adenoviral eradication compared with control in a recent phase 2 study?
   A. Povidone-iodine
   B. Povidone-iodine plus dexamethasone
   C. Cidofovir
   D. Trifluridine

2. Which of the following is NOT a risk factor for blebitis?
   A. Superior bleb position
   B. Adjunctive 5 fluorouracil
   C. Bleb leak
   D. Thin-walled bleb

3. Pathogens most commonly associated with bleb-related infections include:
   A. *Haemophilus* and *Bacillus* spp.
   B. *Haemophilus* and *Streptococcus* spp.
   C. *Staphylococcus* and *Streptococcus* spp.
   D. *Corynebacterium* and *Acanthamoeba* spp.

4. Which of the following findings is least indicative of EKC?
   A. Bilateral exudates
   B. Hyperemia
   C. Lid involvement
   D. Enlarged lymph node

5. Healthcare providers diagnosed with EKC should refrain from patient contact for:
   A. 48 hours
   B. 72 hours
   C. 1 week
   D. 2 weeks

6. Which of the following was NOT a mode of transmission of recent EKC outbreaks in the US?
   A. Contaminated tap water
   B. Improperly sterilized examination instruments
   C. Symptomatic healthcare provider
   D. Contaminated ophthalmology suite

7. Strategies for reducing risk for bleb-related infections include:
   A. Vigilance and surveillance for leaks
   B. Educating and encouraging consistent eyelid hygiene
   C. Prescribing long-term topical antibiotics
   D. A and B

8. Choosing a surgical approach to medically unresponsive glaucoma might reasonably involve:
   A. Patient tolerance for repeat surgeries
   B. Surgeon skill level
   C. Patient risk profile
   D. All of the above

9. The Tube vs. Trabeculectomy (TVT) study was:
   A. A longitudinal observational cohort study
   B. A prospective, randomized comparison study
   C. A retrospective risk factor analysis of Medicare database
   D. Discontinued early due to wide margin of superiority of tube shunt procedures over trabeculectomy with MMC

10. Which is the most common adenovirus serotype associated with EKC outbreaks?
    A. HAdV-1
    B. HAdV-4
    C. HAdV-8
    D. HAdV-12

NALLASAMY *continued from page 7*

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