

# TOPICS IN Ocular Antiinfectives

## Advances in Understanding and Managing Blepharitis

Preeya K. Gupta, MD

*It is well accepted that microbial overgrowth can play an etiological role in anterior blepharitis and can aggravate posterior blepharitis. Recent research implicates an imbalance in the ocular surface microbiome and further supports the need for both acute and long-term maintenance treatment for this common condition.*

Rigorous epidemiological studies of blepharitis are lacking, but most ophthalmologists and optometrists likely see eyelid inflammation in one form or another on a daily basis. Although mixed presentations are relatively common, we divide blepharitis subtypes according to anatomical location: anterior blepharitis, which affects the anterior eyelid margin, eyelashes and follicles, and periocular skin; and posterior blepharitis, which affects the posterior eyelid margin and chiefly the meibomian glands. Blepharitis can affect patients of any age range, from pediatric to geriatric and everyone in between, but prevalence generally increases with age.<sup>1-4</sup> In a survey published in 2009, clinicians reported finding blepharitis in 37% to 47% of

their patients, and subsequent authors have agreed that it is one of the most commonly encountered ophthalmic conditions.<sup>1,2,5</sup>

Though both anterior and posterior blepharitis are complex, potentially multifactorial conditions, anterior blepharitis is often thought to be related to microbial colonization on the eyelids, whereas posterior blepharitis is generally an inflammatory, non-infectious process, typically associated with meibomian gland dysfunction (MGD).<sup>6</sup>

### Impact and Sequelae

All forms of blepharitis are important to recognize and treat because while they can wax and wane in severity, most of the time, these conditions are

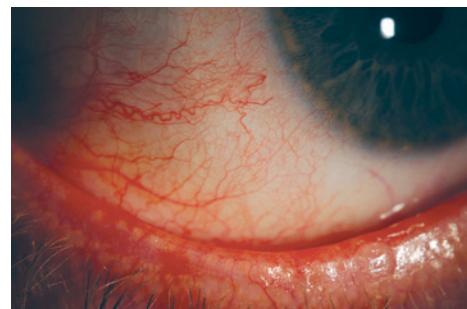


FIGURE 1 MGD with marked eyelid vascularity and conjunctival injection. (Image courtesy of Dr. Gupta.)

chronic—leading not only to bothersome symptoms of irritation and redness, but also to potential long-term sequelae.

Over time, for example, MGD can lead to tear film disruption, ocular sur-

### See INSIDE for:

#### Intracameral Antibiotics in Cataract Surgery

by Neal H. Shorstein, 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. Develop a risk-stratified plan for long- and short-term blepharitis treatment.
2. List potential approaches to *Demodex* infestation.
3. Describe current trends and practice patterns of antibiotic prophylaxis against endophthalmitis during cataract surgery in the US.
4. Improve prophylaxis of endophthalmitis in cataract surgery with appropriately selected intracameral antibiotics.

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### CME REVIEWER

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face inflammation, and gland atrophy, producing more severe symptoms and making the disease process more difficult to treat.<sup>6</sup> Chronic inflammation related to anterior blepharitis can also lead to structural damage and scarring of the lids and lashes, and may be associated with corneal issues, such as neovascularization or superficial keratitis.<sup>6</sup> Mixed anterior/posterior blepharitis presentations can arise, in part, because of chronic eyelid inflammation leading to meibomian gland damage and/or dysfunction (Figure 1).

The potential for reduced visual function—either transiently, due to increased tear evaporation, or over a longer term, due to corneal infection—further

supports a strategy of early diagnosis and management of blepharitis.

## Diagnostic Process

We employ formal screening questionnaires for many of our patients who are at risk for dry eye disease (DED) or report a suggestive symptom. For blepharitis specifically, responses to the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire have been found to correlate with clinical measures of MGD.<sup>7</sup>

A recent publication details the development and evaluation of the BLerharitIS Symptom (BLISS) measure, a screening instrument comprised of two multi-item symptom scales, covering

“irritation” (itching, burning, puffy eyelids, irritated eyes, red eyes) and “debris” (crusty eyes, flaking from eyelids, eyelids stuck, and debris).<sup>8</sup> These capture most of the classic complaints of blepharitis, including discomfort, fatigue, and irritation, crusting of the lids and lashes, as well as eyelash changes and loss. It is not uncommon for patients with blepharitis to complain of fluctuating vision, even though this might not be revealed by normal visual acuity testing.

As a simple initial screen, the technicians in our clinic are trained to ask patients whether they experience any redness, irritation, or fluctuating vision, which casts a relatively wide net for ocular surface diseases. A positive response

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### 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.<sup>1,2</sup>

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.<sup>3,4</sup>

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.<sup>5-7</sup> 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.<sup>8,9</sup> Finally, managing infections caused by exotic or rare pathogens (fungal, amoebic, atypical) may require unfamiliar diagnostic and treatment modalities.<sup>10</sup>

*Topics in Ocular Antimicrobials* 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 antimicrobial choices across a range of ophthalmic clinical and patient settings.

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can trigger further in-office testing.

For patients with primarily anterior blepharitis, common signs are debris along the lash line, erythema of the lid margin, with or without swelling, and with chronic disease, increased vascularization. Patients for whom *Demodex* infestation is a contributing factor will usually have cylindrical dandruff surrounding the lash follicles: as *Demodex* mites, typically *Demodex folliculorum*, colonize the follicles, the consequent distention, irritation, and hyperkeratinization lead to these characteristic cuffs.<sup>9</sup> Infestation with *Demodex brevis*, which colonizes sebaceous and meibomian glands, may lead to posterior blepharitis, MGD, and keratoconjunctivitis.<sup>9,10</sup>

In addition to *Demodex* overgrowth, rosacea and seborrheic keratosis are dermatologic findings commonly associated with blepharitis. Indeed, studies have also shown a strong association between rosacea and *Demodex* infestation.<sup>9,11</sup> Some researchers suggest that bacteria related to *Demodex*, rather than the mites themselves, may play a significant role in the pathophysiology of dermatologic rosacea and blepharitis.<sup>9,12</sup>

## Role of Microbial Colonization

Research comparing the periocular and ocular surface microbial communities of patients with and without blepharitis have found differences in both relative amounts and genera of bacteria.<sup>6,12</sup> It is thought that overcolonization of bacteria on the eyelids of patients with blepharitis leads to a hypersensitivity and inflammatory reaction of the eyelids and ocular surface. Not only the presence of bacteria, but also the lipolytic enzymes produced by bacteria like *Staphylococcus aureus* and *Staphylococcus epidermidis*, contribute to the clinical picture of blepharitis by degrading meibomian gland lipids and releasing irritating fatty acid byproducts.<sup>6</sup>

Further, some research indicates that differences in the diversity of eyelid and ocular surface microbial communities exist between patients with and without blepharitis.<sup>12</sup> In a study published in 2012, Lee and colleagues found that the most common ocular flora on blepharitis-affected and normal ocular

surfaces were *Propionibacterium*, *Staphylococcus*, *Streptophyta*, *Corynebacterium*, and *Enhydrobacter*. For eyelash samples from subjects with blepharitis, relative proportions of *Streptophyta*, *Corynebacterium*, and *Enhydrobacter* were higher, and of *Propionibacterium*, lower, than for lash samples from healthy subjects. In tear samples, the relative proportion of *Staphylococcus* was higher for blepharitis subjects.<sup>12</sup> These researchers concluded an overall balance between ocular surface microbes is likely necessary for ocular surface health, and that the disruption of that balance could be a cause or consequence of blepharitis.

Thus, many treatments for blepharitis are aimed at reducing and/or rebalancing the bioburden on the eyelids and periocular skin.

## Phases of Treatment: Acute and Long-Term

Again, since blepharitis has a tendency to wax and wane, with episodic flares and a chronic, ongoing inflammatory process, treatment can be thought of in two phases: immediate interventions and long-term maintenance. A patient who is acutely irritated, with signs of redness, swelling, and crusting needs relatively quick-acting therapy to bring down the inflammation and address the infection; but he or she will also require maintenance treatment to help “normalize” the lids and ocular surface and, hopefully, reduce the frequency of flares over time.

For an acute presentation, assuming there is no infectious lesion or other contraindication to corticosteroid use, I often initiate treatment with a short course of combination antibiotic/corticosteroid ointment (eg, neomycin/dexamethasone, tobramycin/dexamethasone, tobramycin/loteprednol etabonate, or prednisolone acetate/sulfacetamide). A single-agent topical antibiotic ointment, such as bacitracin or erythromycin, can also be beneficial, but where possible, addressing both the bacterial overgrowth and the associated inflammatory reaction is ideal. Combination agents are best suited for use in brief pulses to address disease flares, due to the risks of long-term steroid use.

## CORE CONCEPTS

- Blepharitis is among the most common ophthalmic conditions encountered in daily practice.
- Over time, blepharitis can lead to structural damage to the eyelids, meibomian glands, and eyelash follicles, as well as the cornea.
- As a chronic, often waxing and waning disease, blepharitis requires both acute and ongoing management.
- Formal and informal symptom screening for blepharitis can help catch the disease earlier.
- Bacterial overgrowth is often an etiological factor in blepharitis, and it is likely that not just overgrowth, but also a lack of diversity may be especially important.
- Eyelid hygiene products containing hypochlorous acid solution can effectively reduce overcolonization without negatively impacting bacterial diversity.

In general, I weigh the risks and benefits of using antibiotic and steroid therapies in terms of three factors: severity, chronicity, and damage to surrounding structures. For a patient with very severe, chronically waxing and waning anterior blepharitis and associated eyelid damage, ongoing anti-infective and anti-inflammatory therapy is probably worthwhile to limit disease flares and continued damage. A patient with chronic rosacea blepharitis, who is at higher risk for developing corneal and/or meibomian gland damage, may likewise be a good candidate for ongoing topical treatment. On the other hand, someone with relatively mild disease and perhaps one or two flares a year can be better maintained with ongoing hygiene and acute management as needed.

Topical formulations tend to be preferable to systemic, in order to minimize both side effects and the likelihood of generating resistance; but a number of oral antibiotics can be useful in managing blepharitis, including doxycycline, minocycline, or azithromycin.<sup>6</sup> I try to

involve patients as much as possible in discussions of their treatment options and potential risks; and I explain that with long-term use of antibiotic/corticosteroid combinations, we must be diligent about monitoring intraocular pressure and cataract development.

## Eyelid Cleansing Alternatives

Maintenance treatment of blepharitis—eyelid hygiene and, where appropriate, therapies to improve meibum quality and flow—is usually initiated in conjunction with acute treatment. Many eyelid cleansing products are commercially available in distinct formulations.

A recent randomized, double-masked, contralateral eye trial compared a dedicated eyelid cleanser (TheraTears® SteriLid®) to diluted baby shampoo (Johnson's® No More Tears®).<sup>5</sup> Forty-three patients with blepharitis used the eyelid cleansers twice daily (one cleanser for each eye, randomly assigned) for 28 days. Both the dedicated eyelid cleanser and the diluted baby shampoo led to improved blepharitis signs and symptoms, but the dedicated eyelid cleanser was associated with a significantly greater reduction in the Symptom Assessment in Dry Eye (SANDE) score, and significantly more patients expressed a preference for the dedicated cleanser than the baby shampoo. With the dedicated cleanser, a significant reduction in MMP-9 expression was measured; whereas with the baby shampoo, levels of the goblet cell mucin MUC5AC decreased.<sup>5</sup>

Thus, while eyelid hygiene with baby shampoo may be better than nothing, depending on a patient's presentation and sensitivities, one of the commercially available dedicated eyelid cleaners is worth considering. For patients with anterior and/or posterior blepharitis, hypochlorous acid is particularly effective at reducing bacterial overgrowth. In one recent study, the application of a hypochlorous acid/saline solution significantly reduced the bacterial load on the eyelids without appreciably affecting the diversity of bacteria present.<sup>13</sup>

Hypochlorous acid solution has efficacy against *Demodex*-associated blepharitis, however, products contain-

ing tea tree oil are especially effective at eradicating *Demodex* from the lid margin.<sup>9</sup> The compound terpinen-4-ol was found to be the component of tea tree oil most effective against *Demodex* and has been incorporated into commercially available eyelid wipes, which I routinely use in patients with *Demodex*.<sup>14</sup>

A number of procedures aimed at improving eyelid health have emerged over the past several years, most of which are intended to address MGD. In cases of MGD, procedures like thermal pulsation and meibomian gland probing may be appropriate to consider in patients who have tried conventional therapies. A micro-exfoliation device is available for the treatment of anterior blepharitis, which can help to debride the crusting associated with anterior blepharitis, and particularly the cylindrical dandruff caused by *Demodex*.

## Challenges and Future Directions

In contrast to in-office procedures, a major limitation of most blepharitis treatments is their reliance on consistent, ongoing patient commitment. Often, a blepharitis treatment regimen will be multi-step, involving eyelid hygiene twice a day, the application of a warm compress once or twice daily, and/or ointment in the evening, etc., which challenges adherence. Ideally, future treatments for blepharitis would put less of a daily burden on patients—once-daily administration of a drug, for example, or a procedure that could be performed every 6 months.

Some of the pharmaceutical avenues being explored for blepharitis treatment employ innovative formulations and combinations of molecules that have long been available. Pelletier and colleagues have published case reports of successful rosacea- and *Demodex*-associated blepharitis treatment using low-dose povidone iodine (0.25% and 1%) in a gel formulation with dimethylsulfoxide (DMSO).<sup>15,16</sup> Povidone iodine is an antiseptic with broad-spectrum activity and a long history of use in ophthalmology; DMSO can act as a solvent and penetration enhancer.<sup>15,16</sup>

A few different formulations of

manuka honey have been or are being evaluated for the treatment of blepharitis and MGD/evaporative DED.<sup>17,18</sup> Manuka honey (*Leptospermum* species) has antibacterial and antiinflammatory properties and eyedrop, gel, and microemulsion cream formulations show promise as potential adjunctive therapies for DED and/or blepharitis.<sup>17,18</sup>

Blepharitis is an undoubtedly common condition—and one that may, in its early stages, be easy to miss. But early recognition and prompt, continued management are key to minimizing damage and sequelae in its later stages.

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# Intracameral Antibiotics in Cataract Surgery

**Neal H. Shorstein, MD**

*Accumulating evidence shows that intracameral antibiotics are beneficial in reducing the risk of endophthalmitis in cataract surgery, but the challenge for US surgeons remains how to source the product and feel confident about its safety.*

Acute endophthalmitis is a severe, vision-threatening postoperative complication of cataract surgery caused by bacterial infection. Recent Medicare and IRIS registry data show an incidence between 0.8 to 1.4 cases per 1000 surgeries.<sup>1</sup> Perioperative antibiotic prophylaxis, in conjunction with other preventive measures such as povidone-iodine application just prior to surgery, have been the mainstay for reducing the risk of postoperative infection. There are a variety of antibiotic agents and routes of delivery in common use around the globe, but there is no uniform consensus of an optimal regimen.

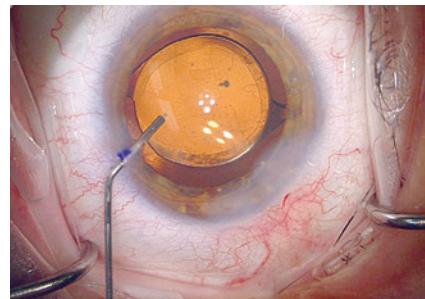
At the present time, the clinical study of intracameral antibiotic injection by the European Society of Cataract and Refractive Surgeons (ESCRS) stands as the only large-scale, randomized, controlled trial showing the efficacy of any antibiotic regimen for the prevention of endophthalmitis. Published in 2007, the landmark study reported a 5-fold reduction in endophthalmitis rates with

injection of cefuroxime into the anterior chamber.<sup>2</sup> Since then, and particularly with the advent of an approved product in Europe, intracameral antibiotic injection at the conclusion of cataract surgery has become standard practice in that region (Figure 1). In the US, application of perioperative topical antibiotics remains the most common form of antibiotic prophylaxis for cataract surgery, but the practice pattern has begun to change with intracameral antibiotics gaining broader acceptance.

## A Shifting Trend?

According to American Society of Cataract and Refractive Surgery (ASCRS) member surveys, the number of US surgeons using intracameral antibiotics has been growing over the past decade. In 2007, 14% of respondents said they routinely injected intracameral antibiotics.<sup>3</sup> By 2014, 36% of respondents reported injecting drug.<sup>4</sup> In the most recent survey, in 2016, 40% respondents were performing intracameral antibiotic injections during routine cataract surgery and more than 30% were planning to do so within the next 12 months.<sup>5</sup>

While there seems to be a trend towards increasing use of intracameral antibiotics, the majority of surgeons continue to rely on topical antibiotic prophylaxis for cataract surgery—despite



**FIGURE 1** Injection of intracameral antibiotic at the conclusion of cataract surgery. (Image courtesy of Dr. Shorstein.)

the absence of high-certainty evidence supporting its effectiveness. More than 90% of survey respondents said in 2007 that they were using topical antibiotics, and that has changed little over time.<sup>3,4</sup>

Hidden in these numbers is a growing practice among surgeons to forego topical antibiotic drops altogether and replace them with intracameral injection instead. In the 2007 ASCRS survey, 2% of respondents reported that they were not using any perioperative topical drops.<sup>3</sup> That number was 4% in 2014 and 10% in 2016.<sup>4,5</sup> In Sweden, over 85% of cataract surgery eyes receive antibiotic prophylaxis by injection alone.<sup>6</sup> For these surgeons, intracameral prophylaxis works so well that additional topical antibiotic drops offer no marginal benefit. This is precisely what recent evidence supports.

## The Evidence

In a preliminary observational study published in 2013, my colleagues and I reported a statistically significant 10-fold reduction in endophthalmitis

rates after adoption of intracameral antibiotics (with or without perioperative topical drops) at one Kaiser Permanente facility in Northern California.<sup>7</sup> The results corroborate the beneficial effect of intracameral antibiotics as shown in the ESCRS study and other comparative cohort studies from around the world.<sup>2,8,9</sup> Notably, the incidence of endophthalmitis (0.49 in 1000) in more than 2000 patients who received no topical drops but a single intracameral injection at the conclusion of surgery was about 50% lower than the recent Medicare and IRIS registry rates, suggesting that intracameral antibiotics alone may be effective. In the Swedish study noted above, the rate of endophthalmitis was 0.29 per 1000 surgeries with the preponderance of prophylaxis being intracameral antibiotic injection alone.<sup>6</sup>

More recently, in a larger comparative study that evaluated over 300,000 phacoemulsification procedures performed at multiple medical centers in Northern and Southern California, we found that topical fluoroquinolones and polymyxin/trimethoprim drops reduced the endophthalmitis rate by about half compared to the cohort of patients (4.5%) that had no record of a pharmacy dispensing of an antibiotic.<sup>10</sup> The group that received intracameral injection had an additional reduction in endophthalmitis by 42%. More interesting, we could not detect any statistical benefit of adding topical antibiotic drops to intracameral injection.

## An Enduring Barrier

One major reason why US surgeons have been slow to adopt intracameral antibiotics is the need to compound the medication for injection. No FDA-approved antibiotic preparation is available yet for endophthalmitis prophylaxis. This hurdle, according to the ASCRS surveys, has prevented many surgeons from adopting an intracameral regimen. The fear is that compounded products are at risk of contamination or dilution errors, which may lead to serious complications, such as toxic anterior segment syndrome (TASS) or iatrogenic endophthalmitis. In Europe, where a pre-packaged cefuroxime product indicated

specifically for injection during cataract surgery came onto the market in 2012, 74% of surgeons reported injecting intracameral antibiotic in the 2 years that followed.<sup>11</sup> That number is reported to be even higher now. There is little doubt that, in addition to the influence of the ESCRS study, what set the European countries on a different path was the availability of a commercial product.

Following the notorious fungal meningitis outbreak from contaminated products compounded by a New England pharmacy, Congress passed the Drug Quality and Security Act in 2013. The regulations created a new type of compounding pharmacy known as a 503b outsourcing facility. Unlike traditional, neighborhood (503a) pharmacies, these facilities are registered with the FDA, are held to higher production standards, and provide for the preparation and shipping of large batches of drug without the need for patient-specific prescriptions. The outsourcing facilities must submit samples for testing and stability studies and follow current good manufacturing processes. For US surgeons who have adopted intracameral antibiotics for endophthalmitis prophylaxis, 503b pharmacies provide the highest level of safety short of commercial manufacturing. Nevertheless, some surgeons are still hesitant to inject a non-FDA approved drug as reflected in the surveys.

## The Intracameral Agents

For ophthalmologists interested in the intracameral approach, one important consideration is which antibiotic to inject. In Europe, the choice is easier as cefuroxime is currently the most rigorously studied and is available commercially. As most of the organisms that cause endophthalmitis are gram-positive,<sup>12</sup> cefuroxime, a second-generation cephalosporin, covers most of the common causative organisms, except for *Enterococcus*. In Sweden, where intracameral cefuroxime has been injected for over 20 years, the endophthalmitis pathogen profile has shifted towards more cefuroxime resistance, including a higher frequency of *Enterococcus* infections.<sup>13</sup>

## CORE CONCEPTS

- ▶ Intracameral antibiotic injection at the conclusion of cataract surgery is more effective for the prevention of endophthalmitis than topical application alone. Current evidence favors intracameral antibiotics alone over combined use of intracameral and topical antibiotics.
- ▶ Both compounded cefuroxime and moxifloxacin (preservative- and thickener-free) are effective and safe for intracameral injection.
- ▶ Routine use of intracameral vancomycin is not recommended because of the risk for HORV.
- ▶ Regardless of the mode of antibiotic prophylaxis, proper wound closure and management is critical to reduce the risk of post-cataract surgery infection.
- ▶ Use of intracameral antibiotics in the US has shown a steady trend of increasing over the past decade, but widespread adoption of the prophylactic measure is hampered by the lack of a commercial, approved product.

In the US, in the absence of an injectable formulation of cefuroxime, surgeons tend to favor compounded moxifloxacin.<sup>4</sup> In the large California cohort study, we examined the risk of infection associated with specific intracameral agents and found no discernible difference in effectiveness in our patient population between cefuroxime and moxifloxacin.<sup>10</sup> A third-generation fluoroquinolone, moxifloxacin has a broad spectrum of activity against both gram-positive and gram-negative organisms, including *Enterococcus*.

No one knows yet how the pathogen profile will change over the years with wide adoption of intracameral moxifloxacin injection. There is good

evidence, however, that in the last 20 years, fluoroquinolone resistant coagulase-negative *Staphylococcus* (CoNS), the most frequent cause of culture-positive endophthalmitis, is on the rise.<sup>14</sup> A recent report of the MIC90 (ie, the minimum inhibitory concentration required to inhibit 90% of isolates) of this organism was as high as 64 µg/mL—far above the level of drug that penetrates from topical instillation.<sup>15,16</sup>

The good news with intracameral moxifloxacin is that, depending on the dose, typical aqueous levels can reach as high as 1500 µg/mL and remain above the MIC for most organisms for hours.<sup>17,18</sup> For many surgeons, delivering a single, highly concentrated dose of antibiotic directly to the site of potential infection for eradication of the most potential pathogens is a reasonable approach.

A few short years ago, an argument could be made that vancomycin is the best intracameral choice for endophthalmitis prevention. All causative, gram-positive organisms are susceptible,<sup>12</sup> and it stays above killing concentrations in the anterior chamber for many hours.<sup>19</sup> Any potential exuberance over this magic bullet has been greatly tempered by the recent reports of a rare, yet serious vancomycin-associated complication known as hemorrhagic occlusive retinal vasculitis (HORV).<sup>20-22</sup> Caused by a delayed hypersensitivity reaction to vancomycin, HORV usually leads to very poor visual outcomes. Prompted by reports of the adverse event, the ASCRS and the FDA have each issued an advisory warning against the routine use of prophylactic intraocular vancomycin.<sup>23,24</sup>

## Getting Started

Surgeons or surgery centers looking to get started with intracameral injection should first examine their historical endophthalmitis organism profile before choosing an antibiotic agent. The majority of cases of post-cataract surgery endophthalmitis in the US involve *Staphylococcus epidermidis*, the most significant CoNS species, with a smaller proportion of cases involving *Staphylococcus aureus*, *Streptococcus* species, *Enterococcus*, and

other gram-positive organisms.<sup>12,25,26</sup> In general, gram-negative cases are rare. In most cases, current evidence indicates that both cefuroxime or moxifloxacin injection are equivalent.<sup>10</sup> Facilities with relatively higher rates of infection from *Enterococcus* or gram-negative pathogens, however, may benefit more with moxifloxacin injection as a first-line drug. In either case, having both agents available in case of allergy to one or the other assures the maximum number of patients are able to receive intracameral treatment.

My own prophylactic regimen is a single cefuroxime injection at the conclusion of surgery. I typically prescribe no perioperative topical drops of any kind and I follow the intracameral antibiotic injection with subconjunctival triamcinolone.<sup>27</sup> If a patient reports allergy to a penicillin analogue or a cephalosporin, I inject moxifloxacin (0.3 to 0.4 ml of 100 µg/ml moxifloxacin). For the very few patients reporting an allergy to both penicillin and a fluoroquinolone, upon further inquiry, most will report a rash rather than anaphylaxis to the penicillin analogue. In this case, the risk of anaphylactic reaction to cefuroxime (with its distinctive side chain) is low.<sup>28,29</sup>

The combination of intracameral antibiotic injection and subconjunctival triamcinolone is a drop-free approach that eliminates compliance issues to ensure that adequate drug reaches the target site and remains in place for an adequate period of time. Studies have shown that more than 90% of patients make mistakes when self-administering eye drops after cataract surgery, including touching the eye with drop bottle tips.<sup>30</sup> This may induce a wound gape leading to the introduction of infective organisms into the eye.<sup>31</sup> A drop-free perioperative strategy may avoid risk of infection through contamination of eye dropper tips and introduction of organisms through the clear corneal wound. In addition, the single injection method can avoid the risk of selecting out resistant bugs from multiple topical instillations of lower concentration of drug.<sup>14</sup>

No discussion of endophthalmitis prevention would be complete without

mentioning the importance of effective wound construction and management. Wounds that are too short increase the chances of fluid ingress and introduction of pathogens.<sup>32</sup> This may render any antibiotic prophylaxis ineffective. Finally, leaving the eye somewhat firm at the conclusion of surgery helps to keep the clear corneal wound apposed<sup>33</sup> while hydrating the wound with balanced salt solution or with the intracameral antibiotic has additional potential benefit.<sup>34,35</sup>

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## EXAMINATION QUESTIONS TOPICS IN OCULAR ANTIINFECTIVES, ISSUE 68

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: July 31, 2019.

1. Which symptom survey has been shown to correlate with clinical measures of MGD?
  - A. CLDEQ
  - B. SANDE
  - C. SPEED
  - D. NITBUT
2. Which of the following procedures may be a valuable anterior blepharitis treatment?
  - A. Vectored thermal pulsation
  - B. Blepharoplasty
  - C. Crosslinking
  - D. Microexfoliation/eyelid debridement
3. Which of the following organisms is thought to be responsible for most post-cataract surgery endophthalmitis cases?
  - A. S. Epidermidis
  - B. Enterococcus
  - C. Streptococcus
  - D. MRSA
4. All of the following may have efficacy against Demodex infestation except:
  - A. Tea tree oil
  - B. Baby shampoo
  - C. Povidone iodine and dimethylsulfoxide
  - D. Hypochlorous acid solution
5. In the US, the most widely used mode of antibiotic prophylaxis for preventing endophthalmitis in cataract surgery is:
  - A. Topical antibiotic drop application
  - B. Periocular antibiotic injection
  - C. Intracameral antibiotic injection
  - D. Irrigation with antibiotics during surgery
6. Which of the following bacterial genera have been found more commonly on eyelids affected by blepharitis?
  - A. Propionibacterium
  - B. Streptophyta
  - C. Bacteroidetes
  - D. Leptospermum
7. Which of the following statements is true about intracameral antibiotic injection for endophthalmitis prophylaxis in cataract surgery?
  - A. It lacks prospective evidence for its efficacy
  - B. It is the preferred antibiotic regimen in the US
  - C. It is more likely to select for resistant organisms than topical antibiotics
  - D. Its effectiveness depends on proper wound closure
8. Which of the following antibiotics is available in the US as a commercial formulation approved specifically for intracameral prophylaxis?
  - A. Cefuroxime
  - B. Moxifloxacin
  - C. Vancomycin
  - D. None of the above
9. Vancomycin is not recommended for routine surgical prophylaxis because:
  - A. It has a narrow spectrum of antimicrobial activities
  - B. It can cause a hypersensitivity reaction leading to vision loss
  - C. It is ineffective against MRSA
  - D. It is too expensive and in short supply
10. Possible sequelae of blepharitis include:
  - A. Corneal neovascularization
  - B. Meibomian gland atrophy
  - C. Keratitis
  - D. All of the above

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