

UPDATED EDITION

**Diagnostic & Treatment  
Algorithms for  
Ocular Surface Disease States**

**Conjunctivitis**  
*Part two of an ongoing series*

New paradigms in the understanding and  
management of conjunctivitis.

Supported by an Unrestricted Grant from **BAUSCH + LOMB™**

Dear Colleagues:

In a series of monographs, first issued in 2008 and updated in 2011, we present diagnostic and treatment algorithms for ocular surface disease states. In this monograph, we will discuss new paradigms in the understanding and management of conjunctivitis.

Keeping in mind the best interests of you, our colleagues, we are proud to offer a summary of our consensus on the

most effective ways to address conjunctivitis in the typical optometric practice. Our hope is that you find the information contained here to be as useful as we intended it to be. Stay tuned for part 3 of this 2011 series, which will cover dry eye.

Our thanks go out once again to Bausch + Lomb for their support with this project.

— The Authors

## About the Authors



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# PART 1: Epidemiology and Etiology of Conjunctivitis

Conjunctivitis is one of the most common reasons for acute eye-related primary care visits. At a leading cornea service (Wills Eye Hospital), blepharoconjunctivitis was the most common diagnosis in children, accounting for 15% of all pediatric referrals.<sup>1</sup> Some forms are highly contagious, while other forms, such as allergic conjunctivitis, are non-infectious.

The term conjunctivitis is a non-specific term that simply means inflammation of the conjunctiva resulting in hyperemia, general discomfort and other symptoms. A

diverse range of etiologies—viral, bacterial, allergic, toxic contact lens-related, lid and dermatologic—result in similar presentations that can be challenging to differentiate.

In this monograph, we will provide practical, evidence-based guidance to assist the clinician in making the differential diagnosis and appropriately managing the range of clinical presentations.

### Allergic Conjunctivitis

Allergic conjunctivitis is an important and growing health problem, characterized by its hallmark symptom: itch-

ing. Seasonal and perennial allergic conjunctivitis, often accompanied by rhinitis, account for the vast majority of ocular allergy cases. These are caused by Type I IgE/mast cell reactions to airborne allergens such as pollen, mold, pet dander and dust mites. Less common, but potentially more challenging forms include giant papillary conjunctivitis (GPC), vernal keratoconjunctivitis and atopic keratoconjunctivitis. This panel previously published an in-depth monograph on ocular allergy ([http://www.revoptom.com/email/2011\\_allergy](http://www.revoptom.com/email/2011_allergy)).

pdf);<sup>2</sup> therefore, we will not address allergic conjunctivitis in any detail in the current monograph, except to alert the clinician to consider allergy in the differential diagnosis.

### **Viral Conjunctivitis**

Viral conjunctivitis is a common condition characterized by conjunctival redness and inflammation. Any ocular discharge is typically watery. Although it may be caused by a wide array of viruses, the most common is adenovirus, particularly in adults. By several accounts, adenovirus accounts for more than 60% of infectious conjunctivitis cases.<sup>3,4</sup>

Two types of adenoviral conjunctivitis exist: 1) pharyngoconjunctival fever (PCF), which is usually seen in children, accompanied by mild sore throat and a low-grade fever. It is self-limiting, typically resolving within two weeks without treatment.

2) Classic adenoviral conjunctivitis, also known as epidemic keratoconjunctivitis (EKC), commonly causes acute follicular (often hemorrhagic) conjunctivitis in children and adults. It generally begins in one eye and spreads to the fellow eye within a few days. Symptoms can be quite severe, although not sight-threatening. Palpable preauricular or submandibular lymphadenopathy is common and an extremely helpful diagnostic sign.

Dosso's work using *in vivo* confocal microscopy suggests that the immune system, in the form of dendritic cells, is

highly active early on in the EKC infection, but that the conjunctival inflammatory component in both epithelium and stroma is massive and lasts for some time in the deeper layers of the stroma.<sup>5</sup> EKC can be highly contagious by direct contact for as long as the eye is red and the watery discharge persists. Clinicians should use proper procedures to avoid spreading the virus to themselves,

staff or other patients.

Viral conjunctivitis may also be caused by Herpes simplex virus (HSV), picornavirus, influenza A, Epstein-Barr, Newcastle disease and others. HSV cases can recur and may lead to significant corneal complications.

### **Bacterial Conjunctivitis**

Acute bacterial conjunctivitis, especially in children, is

## **Tips for an Effective Patient History and Exam**

When a patient presents with a red eye, include these questions in a thorough history to aid in differential diagnosis:

- When did the symptoms start?
- Are they in one eye or both?
- Are they getting better or worse?
- Have you ever experienced this before?
- Do your eyes itch?
- Has there been any discharge from the eye? If so, what kind and how much?
- Have you had an upper respiratory infection recently?
- Have you had a fever or felt warm?
- Have you had any recent trauma or surgery in that eye?
- Do you wear contact lenses?
- Have you been around anyone else with a red eye?
- Does anyone in your family have a history of frequent red eye?
- Have you had any problems with light sensitivity or decreased vision?

During your exam, don't neglect the following steps:

- Evert the lids
- Examine the periorbital skin closely and note any lesions on face or scalp
- Palpate for preauricular and submandibular lymph nodes.



Acute bacterial conjunctivitis.

one of the more common eye disorders seen by primary care providers and is said to account for 1% to 4% of all primary care consultations.<sup>6</sup> Bacterial conjunctivitis is characterized by conjunctival injection, often associated with mucopurulent discharge. Symptoms usually begin in one eye, but may spread to the other.

In young children, bacterial conjunctivitis may be accompanied by upper respiratory infections and/or acute otitis media. Patients with ectropion or entropion, nasolacrimal duct obstruction, prior trauma or dry eye disease are more predisposed to bacterial infection.

The most common pathogens implicated in bacterial conjunctivitis are *Haemophilus influenzae* and *Streptococcus pneumoniae* in children and *Staphylococcus aureus* in adults.<sup>6-8</sup> Methicillin-resistant *S. aureus* (MRSA) is emerging as a more important pathogen, even in non-hospitalized populations. *Staphylococcus epidermidis*, *Streptococcus viridans*, *Moraxella catarrhalis* and Gram-negative intestinal bacteria are also common.

Although it may be highly contagious, serious complications of bacterial conjunc-

tivitis are rare. The most common presentations are self-limiting in immunocompetent patients.

• **Hyperacute bacterial conjunctivitis.** Hyperacute bacterial conjunctivitis, characterized by lid swelling, rapid onset and progression of symptoms, as well as copious purulent discharge, is more serious and may lead to corneal ulceration and loss of vision.

This condition is typically caused by *Neisseria gonorrhoeae* or *Neisseria meningitidis* and is predominantly found in newborns born to mothers with gonorrhea or adults who have become infected through sexual contact. These patients usually require systemic and topical drug therapy and are probably best co-managed with a primary care physician.

• **Adult inclusion conjunctivitis.** Another rare, but clinically significant form of bacterial conjunctivitis is caused by *Chlamydia trachomatis* (trachoma). Although more common in developing countries, it is sometimes seen in some poor and immigrant communities in the developed world. In the United States, *Chlamydia* most commonly manifests not as trachoma, but as adult inclusion conjunctivitis or as a sexually transmitted disease. This condition is often missed or misdiagnosed.

• **Blepharitis.** Blepharitis, or inflammation of the eyelids, is a common, typically bilateral ocular surface disease

entity. The pathophysiology of blepharitis is complex and not fully understood. It likely involves some interaction of abnormal lid-margin secretions, microbial organisms and tear film abnormalities.<sup>9</sup> The condition is chronic, but episodic, and is often associated with skin conditions such as dermatitis, rosacea and eczema. Additionally, the debris and inflammatory components released in blepharitis may lead to secondary conjunctivitis and tear film problems, making the individual more prone to dry eye and other ocular inflammatory conditions. In a landmark article in 1982, McCulley identified six primary types of blepharitis: staphylococcal; seborrheic; seborrheic/staphylococcal; meibomian seborrhea; seborrheic blepharitis with secondary meibomitis; and primary meibomitis.<sup>10</sup>

Blepharitis includes infectious and seborrheic blepharitis, primarily affecting the anterior lid margins and eyelashes. It can be inflammatory, bacterial, viral or even parasitic. Most frequently, however, the underlying cause is staphylococcal, which then triggers an inflammatory reaction responsible for patient symptoms.<sup>11</sup> It is particularly common in people of Northern European descent with light skin and eyes. Meibomian gland disease (MGD) will be discussed briefly here, but covered in much more detail by this panel in the next monograph on dry eye.

## Clinical Pearl

*Barrier protection (wearing gloves) and hand washing are important when examining patients with red eyes of unknown etiology. Infectious conjunctivitis spreads easily and rapidly and can result in needless infection of other patients, as well as lost clinic time for the doctor and staff. Wearing gloves also conveys the significance of potential contagion to the patient and reinforces the recommendation to stay home from school or work.*

### Nonspecific Inflammatory Conjunctivitis

Nonspecific conjunctivitis that is inflammatory in nature can have a varied clinical presentation. It may be related to dry eye, trichiasis, entropion or ectropion, but the most common cause, at least in the contact lens wearer, is contact lens-induced acute red eye (CLARE).

CLARE is often a complication of extended (overnight) lens wear. Although generally self-limiting, the condition is more rapidly controlled with intervention by the practitioner,

in addition to temporary discontinuation of contact lenses.

Researchers originally thought CLARE was related to corneal hypoxia. CLARE has been reported in less than 4% (and in some studies, less than 1%) of silicone hydrogel continuous wear patients, compared to up to 34% of hydrogel extended wear patients.<sup>11</sup> However, it is now believed to be an acute inflammatory reaction to the presence of bacteria under the lens.<sup>12</sup>

The pathogens responsible for CLARE are often the same

as those implicated in microbial keratitis, although the mechanism is different. In a recent review article, Sweeney and colleagues showed that inflammatory keratitis (CLARE) and infectious keratitis do not share a pathogenic continuum.<sup>13</sup> CLARE is not a risk factor for subsequent infection; the two are different disease entities.

CLARE can however resemble infiltrative keratitis in signs and symptoms. In this monograph, we primarily address CLARE without associated significant corneal involvement.

To help you make the differential diagnosis, take a look at the general guide to major signs and symptoms of the leading causes of red eye presentation at [www.revoptom.com/email/diffdiagnosis.pdf](http://www.revoptom.com/email/diffdiagnosis.pdf). For more specific information on the diagnosis and management of conjunctivitis, read on.

## Part 2: Diagnosis and Management Of Conjunctivitis

### Viral Conjunctivitis - PCF: Diagnosis

Pharyngoconjunctival fever (PCF) occurs predominantly in children. The patient will have a history of low-grade fever, upper respiratory infection, a scratchy or mildly sore throat, and perhaps some malaise. It is almost always unilateral.

Palpable preauricular or submandibular lymphadenopathy is an important

diagnostic clue that points to viral etiology. Adenopathy is almost always present in EKC and occasionally in PCF, especially more severe cases.

### Viral Conjunctivitis - PCF: Management

While routine PCF may seem minor to the clinician, it can be a significant event for the family, particularly if

a child has been sent home from school or daycare.



Courtesy of Ron Melton, O.D.

Pharyngoconjunctival fever usually occurs in children and is almost always unilateral.

Although there are no antiviral products approved for the treatment of adenoviral ocular infections, we believe that topical ganciclovir may become standard of care for these infections in the future. There is good basic science<sup>14-16</sup> and some small pilot studies<sup>17,18</sup> to support such use.

PCF can be treated with supportive therapy (cool compresses and artificial tears) and ganciclovir ophthalmic gel 0.15% (Zirgan, Bausch + Lomb), dosed 5 times per day until the first follow-up visit (usually at 1 week), then 3 times per day for another week. It is important to educate the family that the child is contagious as long as the redness and watery discharge persist.

Check the lids and face carefully to rule out herpes simplex dermatitis. As long as the clinician has confirmed the absence of any lid involvement, a low-dose steroid such as loteprednol etabonate 0.2% (Alrex, Bausch + Lomb) is a safe way to reduce inflammation from viral conjunctivitis. In more severe cases with corneal involvement, an antibiotic/steroid combination such as Zylet (loteprednol etabonate 0.5% / tobramycin 0.3%, Bausch + Lomb) may be needed.

### **Viral Conjunctivitis - EKC: Diagnosis**

Classic adenoviral conjunctivitis usually presents with acute symptoms, including watery discharge, that worsen over a few days. This acute

red eye usually begins in one eye, with the fellow eye becoming afflicted in 2 to 4 days. A unilateral or bilateral acute red eye(s) with a serous watery discharge and preauricular lymph node swelling on the more involved side are

Courtesy of Ron Melton, O.D.



Classic case of EKC with asymmetrical conjunctival injection.

the key diagnostic indicators for identifying the presence of EKC. There is usually no history of upper respiratory infection, which is important in distinguishing it from PCF. The patient will sometimes recall having been exposed to someone else with a red eye.

Generally, the vision will be slightly decreased, depending on the amount of associated inflammation and the duration of the infection. This can also facilitate diagnosis, because other causes of conjunctival hyperemia do not necessarily affect vision.

Significant periorbital edema, especially in the more involved eye, is another good indicator that the condition is viral, because one typically sees little swelling in a case of bacterial conjunctivitis.

On exam, the clinician will often see small conjunctival vesicular hemorrhages, particularly on the inferior bulbar conjunctiva and sometimes large subconjunctival hemorrhages. Although the presence of follicles and papillae

generally do not help much in the differential diagnosis, a lot of follicles accompanied by watery discharge is cause to suspect viral etiology. The corneal presentation varies, depending on the stage and severity of the viral infection.

A new diagnostic tool, the RPS Adeno Detector (Rapid Pathogen Screening, Inc.), can be helpful in assessing conjunctivitis patients and determining the best management approach, particularly when it is unclear whether the etiology is viral or bacterial.

### **Viral Conjunctivitis - EKC: Management**

EKC is primarily an infection with a secondary (but major) inflammatory response. Appropriate management depends on the presentation, timing, severity and effect on vision.

Traditionally, supportive therapy alone (cold compresses, artificial tears) has been considered standard of care. However, as with PCF, Zirgan can now be used as primary therapy. Anecdotally, we have seen that this greatly increases patient comfort compared to supportive therapy alone, and the pilot studies mentioned previously have shown faster recovery and lower rates of infiltrates.<sup>17,18</sup>

Tabbara, for example, compared the effects of ganciclovir ophthalmic gel 0.15% with the instillation of preservative-free artificial tears in 18 patients with adenoviral keratoconjunctivitis. The 9

## Clinical Pearl

*If you see a conjunctivitis patient with non-specific pain in one eye, particularly in a patient over 50 years old, be suspicious of herpes zoster. The sensation may be described as pain, tenderness, burning, numbness or a tingling sensitivity. Begin your normal therapy, but tell the patient that you want to see them again if any lesions appear on the eyelids, skin or scalp.*

subjects treated with ganciclovir had a mean recovery time of 7.7 days, compared to 18.5 days in the control group.<sup>17</sup> In addition, 22% of the ganciclovir group, vs. 77% of the tears group developed subepithelial opacities. These results are consistent with our current clinical experience, in which early treatment with topical ganciclovir often reduces ocular morbidity and may prevent or modify the severity of subepithelial infiltrates.

The benefits of routine use of ganciclovir for adenoviral infection, including preventing the contagious spread of EKC, far outweigh the risks, given its high safety profile. However, if the patient is moderately symptomatic, or one sees sub-epithelial infiltrates and reduced visual acuity later in the course of EKC, a steroid such as loteprednol etabonate 0.5% (Lotemax, Bausch + Lomb) may be extremely helpful.

Infiltrates may appear that compromise a patient's vision. In this instance, consider prescribing Lotemax q.i.d. for one month (or in some cases, longer), with a follow-up visit scheduled one to two weeks after beginning

the steroid. Clinicians can taper the steroid if desired, but it is not necessary. In the preregistration clinical trials of this medication, no tapering was done.<sup>19,20</sup>

Some have argued that steroids slow down the healing rate with active viral conjunctivitis, extending the period of infection. Patients with significant symptoms prefer symptomatic resolution over non-treatment, even if the duration is slightly longer. Ultimately, it is the clinician's responsibility to consider the severity of the presentation and then intercede therapeutically based on that assessment. An alternative that has been proposed for treatment of adenoviral conjunctivitis is povidone-iodine (Betadine 5% Sterile Ophthalmic Prep Solution, Alcon).

In a large, prospective clinical trial in 2002, Isenberg and colleagues found povidone-iodine 1.25% ophthalmic solution, given q.i.d. for a week, to be ineffective against viral conjunctivitis.<sup>21</sup> The anecdotal experience of some clinicians, however, suggests that a higher concentration of povidone-iodine (5%) given as a single bolus in the office may be very effective in eradicating the virus and preventing sub-epithelial infiltrates. This has not yet been tested in formal trials, but enjoys widespread clinical use.

Those who use povidone-iodine recommend first anesthetizing the eye with 0.5% proparacaine HCl (Ophthetic, Allergan), then instilling several drops of Betadine 5%. The clinician should rub along the closed eyelid with a gloved finger and, after 60 seconds, lavage the eye with sterile saline irrigation solution. Lotemax, used q.i.d. for 4 to 5 days, will hasten tissue normalization and enhance patient comfort. More research on this topic is needed to provide us with clear guidance for clinical care.

The literature does not sup-

## Topical Antiviral Options

### Trifluridine

- Old drug
- Nonselective toxicity
- Potentially toxic
- More frequent dosing
- Refrigerate until opened
- Thimerisol preserved
- Solution (7.5 ml bottle)
- Viroptic and generic
- Samples not available

### Ganciclovir

- New drug
- Infected cell-specific
- Very low toxicity
- Less frequent dosing
- No refrigeration needed
- BAK preserved
- Gel (5 gram tube)
- Zigan by B+L
- Samples available

port any role for nonsteroidal anti-inflammatories (NSAIDs) in the management of viral conjunctivitis.<sup>22</sup> NSAIDs were not shown to be any more effective than artificial tears.

In a typical case, therefore, we recommend Zirgan or povidone-iodine, with or without a steroid, depending on the severity of the clinical presentation. In rare instances when there is epithelial compromise or significant corneal involvement, a combination antibiotic-steroid may be needed.

### **Herpetic Conjunctivitis: Diagnosis**

Herpes simplex conjunctivitis usually presents with lid involvement first, often leading to secondary conjunctivitis. Ulceration of the lid margin and/or vesicles on the peri-orbital skin (or elsewhere on the face) are the clearest signs of a herpes infection; in their absence it can be more difficult to diagnose. In any conjunctivitis case with significant, active watery discharge where there is no involvement of the other eye, we recommend looking closely at the lids at the slit lamp or under bright ambient light for indications of herpes simplex virus such as vesicular rash.

Herpes zoster conjunctivitis is predominantly an inflammatory condition, accompanied by lesions on the face or scalp. The earliest indication of herpes zoster may be dermatomal pain, as some patients present with conjunctivitis before any lesions appear.

### **Herpetic Conjunctivitis: Management**

Although herpes simplex and herpes zoster are both viruses that can result in conjunctivitis, they are treated quite differently. Herpes simplex, in the presence of lid or facial lesions, is primarily an infectious process that responds well to systemic antiviral therapy. If there are any signs of periorbital or dermatological involvement, treat with an oral antiviral such as acyclovir (Zovirax, GlaxoSmithKline), valacyclovir (Valtrex, GlaxoSmithKline) or famciclovir (Famvir, Novartis). All are available generically now, making cost less of an issue for patients.

In addition, we treat herpetic ocular disease, whether keratitis or conjunctivitis, with Zirgan.<sup>23,24</sup> This recently approved antiviral has replaced treatment with trifluridine drops (Viroptic, Monarch Pharmaceuticals) because ganciclovir has a number of advantages over trifluridine, including comfort, toxicity and frequency of dosing (see "Topical Antiviral Options" on the previous page).

Although some clinicians use Zirgan alone for ocular surface herpetic disease without lid involvement, others prefer to maintain the systemic antiviral along with ganciclovir in all cases. In particular, patients with primary HSV infection, immunocompromised patients and children may benefit from oral antivirals in addition to topi-

cal therapy.<sup>25</sup> Mismanagement of herpes simplex conjunctivitis with topical steroids can make it worse and lead to corneal involvement.

By contrast, a red eye in the setting of first division trigeminal herpes zoster is a secondary inflammatory ocular manifestation—either inflammatory keratoconjunctivitis or inflammatory uveitis—that must be treated aggressively with topical corticosteroids such as Pred Forte (prednisolone acetate ophthalmic suspension, USP 1%, Allergan) or Lotemax, concurrent with systemic antiviral medications.



Classic bilateral bacterial conjunctivitis.

Courtesy of Ron Meitlan, O.D.

### **Acute Bacterial Conjunctivitis: Diagnosis**

The ocular discharge is a key factor in the diagnosis of bacterial conjunctivitis. The discharge will be mucopurulent and significant enough to mat the eyelashes together, particularly upon awakening. Be aware that it is also common for dry eye patients to feel that their eyes are "stuck shut" in the morning, but in the eye with conjunctivitis, the onset of this symptom will be sudden, usually worse in one eye, and noticeably worse than normal, even if the patient also suffers from dry eye. At the slit lamp, the



clinician will usually be able to see microparticulate debris in the lacrimal lake.

Patients may complain of burning, stinging and photophobia. Corneal involvement is usually proportional to photophobic symptoms. The presentation can be unilateral, bilateral, or begin in one eye and spread to the other. We do not see a consistent pat-

tern in bacterial conjunctivitis, unlike viral EKC where one eye is always more involved.

In mild to moderate cases, there will almost always be more inflammation and bulbar injection inferiorly than superiorly. In severe cases, though, the injection may be more diffuse. Examine the tear film carefully for microparticulate debris, especially infe-

riorly, which can be indicative of bacterial etiology.

### **Acute Bacterial Conjunctivitis: Management**

We manage bacterial conjunctivitis with antibiotic therapy alone, provided that secondary inflammation is limited. We are fortunate to have many antimicro-

## **The MRSA Threat**

By and large, optometrists need not worry about rampant methicillin-resistant *Staphylococcus aureus* (MRSA) conjunctivitis. However, large national surveillance programs have shown that the incidence of MRSA may be on the rise, so clinicians should maintain a healthy awareness of the potential for methicillin-resistant *S. aureus* and be prepared to treat suspected cases.<sup>31-33</sup> In addition, current resistance trends should be considered before initiating empiric treatment of common eye infections.

If an eye does not respond to your typical initial management of bacterial conjunctivitis, first reassess the accuracy of your diagnosis. If you are still convinced it is bacterial conjunctivitis, MRSA should be considered. Even though we rarely culture conjunctivitis in clinical practice, this might be a good time to do so.

When MRSA conjunctivitis is diagnosed or suspected, it is appropriate to add Polytrim (trimethoprim/polymyxin B, Allergan) to your regimen. This drug is also available generically. In severe cases of bacterial conjunctivitis and in postoperative management of suspected MRSA infection, fortified vancomycin may be the antibiotic of choice. Besivance may also be appropriate, as recent data suggest that besifloxacin has potent activity against resistant organisms.

The Antibiotic Resistance Monitoring in Ocular microOrganisms (ARMOR) study has found that antibacterial resistance is a significant concern in ocular isolates of *S. aureus* and coagulase-negative staphylococci (CNS) and that there are significant differences in the potency of commonly used antibiotics against these organisms.<sup>27,28</sup>

For example, of the 228 *S. aureus* isolates collected, 50% were MRSA, 40% were ciprofloxacin non-susceptible (CIP-NS) and 36% were both MRSA and CIP-NS. By the MIC<sub>90</sub> values, besifloxacin, vancomycin and imipenem were the most potent, while ciprofloxacin, tobramycin and azithromycin were the least potent. Go to [www.revoptom.com/email/MICactivity.pdf](http://www.revoptom.com/email/MICactivity.pdf) to view a table of MIC ( $\mu\text{g}/\text{mL}$ ) activity of besifloxacin and comparators against *S. aureus*. Against MRSA, besifloxacin maintained potency with an MIC<sub>50</sub>/MIC<sub>90</sub> of 0.5/1  $\mu\text{g}/\text{mL}$  (moxifloxacin: 2/8  $\mu\text{g}/\text{mL}$ ; ciprofloxacin: 8/256  $\mu\text{g}/\text{mL}$ ).<sup>32</sup>

Of the 165 collected CNS isolates, 57% were methicillin-resistant (MRCNS), 40% were CIP-NS and 34% were both MRCNS and CIP-NS. According to the MIC<sub>90</sub> values, imipenem, besifloxacin and vancomycin were the most potent agents, while levofloxacin, trimethoprim and azithromycin were the least potent.<sup>32</sup>

A smaller percentage of *S. pneumoniae* isolates were nonsusceptible to commonly used topical ocular antibiotics. According to the MIC<sub>90</sub> values, imipenem and besifloxacin were the most potent agents, while trimethoprim and azithromycin were the least. And among the *H. influenzae* isolates tested, 100% were susceptible to all the antibacterial drugs tested.<sup>32</sup>

bial agents available to us for treating mild to moderate bacterial conjunctivitis, including the fluoroquinolones, macrolides, aminoglycosides and other antibiotic classes. The newest antibiotic option for the treatment of bacterial conjunctivitis is Bausch + Lomb's besifloxacin ophthalmic suspension, 0.6% (Besivance). Laboratory studies have shown Besivance to be rapidly bactericidal.<sup>26,27</sup> In clinical studies, this new antibiotic has been effective and well-tolerated in adults and children age 1 and older.<sup>28-30</sup> Most any of these would be an appropriate intervention.

In moderate to severe bacterial conjunctivitis cases, we prescribe an antibiotic on an aggressive schedule initially—every two hours while awake—to gain control over the infection. After a couple of days, the dosing can be dropped back to q.i.d. for another four to five days. In short-term treatment like this, the clinician does not need to be overly concerned about complications that can arise from longer-term use, such as ocular surface toxicity from aminoglycosides.

Antibiotic drops alone may not be enough to address all the clinical signs/symptoms seen in moderate to severe cases. After first getting the infection under control and determining that the eye is responding, clinicians should re-assess signs and symptoms. If there is a significant amount of secondary conjunctival inflammation,

the condition may be better managed with a combination antibiotic/steroid that can both eradicate the bacteria and suppress the conjunctival inflammation.

Certainly, the old paradigm that corticosteroids should never be used in treating bacterial conjunctivitis no longer holds true. Much more is known about the role inflammation plays in bacterial conjunctivitis. It makes sense to add steroid therapy during the course of treatment as long as the infective component is being effectively addressed.

The one exception to this is the contact lens wearer with active bacterial conjunctivitis. In such a patient, consider the use of a broad-spectrum antibiotic and avoid any steroid or combination therapy, due to concerns about potential MRSA infection (see "The MRSA Threat" on page 9) and greater risk of corneal sequellae.

Courtesy of Ron Melton, O.D.



The redness in hyperacute bacterial conjunctivitis is more severe than in routine acute bacterial conjunctivitis.

### **Hyperacute Bacterial Conjunctivitis**

Distinguishing hyperacute from routine acute bacterial conjunctivitis is a matter of degree. The redness will be more severe, the amount

of discharge will be profound—perhaps the most purulent discharge you have ever seen—and there may be significant ocular swelling, papillae and node activity. Marked eyelid edema and erythema are nearly always present.

These cases are typically caused by streptococcal or gonococcal bacteria. They can be very aggressive and affect both eyes, although unilateral presentation is more common.

Hyperacute ocular infections should be cultured. Clinicians with limited access to culture plating should have a mini-tip culturette on hand for cases such as this. Gonococcal hyperacute conjunctivitis is potentially quite dangerous. In a child, sexual abuse should be suspected. Check the cornea carefully, as some research indicates that these pathogens can penetrate an intact epithelium within as little as 48 hours.

The patient with a hyperacute bacterial conjunctivitis of gonococcal origin should be treated with a single 1-gram dose of intramuscular ceftriaxone (Rocephin, Hoffman-LaRoche) as well as topical fluoroquinolone drops, and followed on a daily basis until the infection is under control.

For nongonococcal hyperacute conjunctivitis, a topical fluoroquinolone, such as moxifloxacin, gatifloxacin or levofloxacin can be used at an initial dosage of one drop every hour. Systemic treatment options include

## Clinical Pearl

With *Chlamydia conjunctivitis*, find out if the patient has been exposed to domesticated birds, particularly parakeets. A sizeable number of U.S. parakeets carry the *Chlamydia* organism in their bodies as *Chlamydia psittacosis*, which causes a clinically identical picture to sexually transmitted disease. Treatment is the same: one 1000-mg dose of oral azithromycin.

ampicillin (various), amoxicillin, amoxicillin/clavulanate potassium (Augmentin, GlaxoSmithKline) or a second-generation cephalosporin such as cefuroxime (Ceftin, GlaxoSmithKline).

### Adult Inclusion Conjunctivitis (*Chlamydia*): Diagnosis

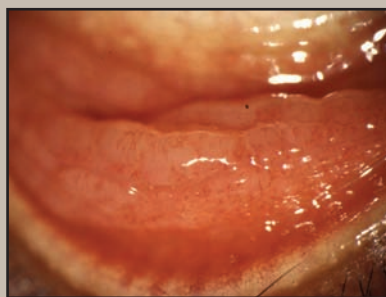
Adult inclusion conjunctivitis, caused by *Chlamydia*, often manifests as a lingering, low-grade red eye with scant mucous discharge. The patient may have been self-treating for some time. Often, these cases are seen on referral from a general practitioner who treated the patient unsuccessfully with a topical eye drop that did not resolve the condition.

In reviewing the signs and symptoms, this patient may seem to have both a viral and a bacterial infection at the same time. A key point in the differential diagnosis is the asymmetry of the follicles between the two eyes. With fluorescein staining, one eye may have giant inferior follicles, while the other eye has a limited follicular response, if

any. One may also see a very inflamed upper tarsal conjunctiva with papillary hypertrophy once the upper lid is everted.

If *Chlamydia* is suspected, it is important to ask if the patient has changed sex partners or had a new sex partner in the last few months. The patient may also have noticed burning on urination, although as many as 50% of those with *Chlamydia* are asymptomatic.

Many optometrists are uncomfortable asking such personal questions, but there is no need to be embarrassed about clinically relevant details. One approach is to tell the patient that you suspect he or she has a sexually transmitted disease, so the questions don't seem out of the ordinary. Another



Giant follicles to the inferior palpebral conjunctiva classic for chlamydial conjunctivitis.

approach is to thoroughly review systems, starting at the top with headaches, moving on to upper respiratory and breathing problems, gastrointestinal issues, and sexual partners/urination.

### Adult Inclusion Conjunctivitis (*Chlamydia*): Management

Adult inclusion conjunctivitis is the ocular manifestation of a systemic condition; it must be addressed with systemic medication. There is no need for topical therapy, other than artificial tears if desired.

Key to successful management of *Chlamydia* conjunctivitis is concurrent treatment of both sexual partners so that they don't re-infect one another. For compliance and efficacy, the ideal treatment is a single 1000-mg dose of oral azithromycin,<sup>34</sup> although 3- and 5-day courses of azithromycin have also been shown clinically to be effective.<sup>35</sup>

It is incumbent upon us to coordinate the management of this condition with the patient's gynecologist or personal physician. *Chlamydia* is one of the leading causes of female infertility. Our patients—and their sexual partners—need medical care and counseling for the non-ocular aspects of this sexually transmitted disease. *Chlamydia* should also be reported to the local health department, which can be done online on a state-by-state basis.

Courtesy of Ron Melton, O.D.

## Blepharitis: Diagnosis

Blepharitis is a chronic, long-term problem often associated with lid margin erythema, crusting, scaling or discharge accompanied by symptoms of foreign body sensation, stinging, burning or ocular discomfort. In the early stages of this common eyelid disease, patients may have mild or no symptoms. What usually prompts them to see an eye doctor is that the eye has become inflamed and more symptomatic. Once that happens, we need to treat both the infectious and inflammatory components of the condition.

## Blepharitis: Management

Effective management of blepharitis not only improves patient appearance and comfort, but is essential in preventing complications and optimizing outcomes in cataract or refractive surgery.<sup>36-39</sup>

For very mild cases of infectious blepharitis, some practitioners treat with high quality lid scrubs (Ocusoft lid scrubs, for example, have been shown to significantly reduce *Staphylococcus epidermidis*) and a steroid ointment alone. A more conservative approach is to always treat with a regimen that includes an antibiotic. We recommend beginning with a combination antibiotic-steroid to address both the infectious etiology and the underlying inflammatory component.

A highly lipophilic drug such as Zylet, that can

address the oil gland/lipid dysfunction, is our drug of choice for blepharitis. This combination has been shown to have similar efficacy to tobramycin 0.3% / dexamethasone 0.1% (TobraDex, Alcon), with much less risk of increasing IOP.<sup>40</sup> Loteprednol etabonate, alone or in combination with tobramycin, has a lower risk of IOP elevation compared with ketone corticosteroids owing to its rapid hydrolysis to inactive metabolites.<sup>41</sup> It also lacks the ability to form Schiff base intermediates with lens proteins, a common first step in catarac-



Anterior blepharitis with generalized redness to the lid margins.

togenesis.<sup>41</sup> Zylet has been shown to have better ocular comfort and tolerability than TobraDex.<sup>42</sup>

Another option is a topical antibiotic such as Besivance plus a steroid drop such as Lotemax or Zylet rubbed into the lids and lashes with lid scrubs rather than instilled into the eye. After or concurrent with appropriate antibiotic treatment, some patients may benefit from one to two weeks of Lotemax ointment at bedtime to eliminate residual inflammation.

In moderate to severe blepharitis, longer-term therapy will likely be required.

Therefore, the clinician will want to use a regimen that includes the safest steroid possible so that the patient can be treated long enough to eradicate the bacteria and also to control the underlying inflammation. Blepharitis patients can be placed, for example, on a course of Zylet q.i.d. for two weeks, then b.i.d. for another two to four weeks as necessary for improvement of signs and symptoms.

Long term lid hygiene and artificial tears are recommended to keep chronic blepharitis under control. Commercial lid scrubs or baby shampoo are effective at providing a clean eyelid environment to limit blepharitis activity. The commercial lid scrubs appear to be better for patient acceptance and compliance in maintaining clean lids and lashes.

Recently there has been a great deal of anecdotal discussion about the anti-inflammatory properties of topical azithromycin (AzaSite, Inspire Pharmaceuticals) in blepharitis care.<sup>43</sup> This antimicrobial agent has been shown to be more effective than warm compresses alone in treating inflammation,<sup>44</sup> but not as effective as TobraDex ST.<sup>45</sup> One would not expect its anti-inflammatory properties to approach those of a steroid. Indeed, it did not meet the primary efficacy endpoint in clinical trials for treatment of blepharitis, and this year, the FDA specifically said that claims implying that AzaSite



Courtesy of Ron Melton, O.D.

Classic case of PKC with inferior phlyctenules.

can restore ocular surface health are misleading because this has not been demonstrated by substantial evidence or clinical experience. AzaSite is indicated for the treatment of bacterial conjunctivitis. Another older antibiotic, doxycycline, also has some documented anti-inflammatory properties, but it is not considered a substitute when a steroid is indicated.

Patients with blepharitis often have dry eye syndrome as well, in which case the anti-inflammatory component of a combination drop can also be beneficial in treating the dry eye.

### PKC: Diagnosis

Phlyctenular conjunctivitis (PKC) is seen most commonly as a secondary condition in young girls with staphylococcal blepharitis, although it may also be caused in rare cases by tuberculosis. Patients will present with a scratchy, foreign body sensation, ocular redness and sectoral rather than generalized conjunctival injection, mimicking episcleritis. There is typically no discharge.

PKC may be unilateral, but there is usually some involvement bilaterally. Although phlyctenular conjunctivitis can occur without obvious associated disease, patients with

phlyctenules may exhibit concurrent evidence of either dermatologic or systemic disease.

In adults, phlyctenules may be associated with rosacea, secondary to dry eye and staphylococcal blepharitis. If the eyelid appears healthy and there is no evidence of staphylococcal blepharitis, you should query the patient about breathing problems, and perhaps even obtain a chest X-ray to rule out tuberculosis.

### PKC: Management

Therapy depends on etiology. In individuals who are suspected of having tuberculosis, diagnosis should make use of a purified protein derivative (PPD) skin test, chest radiograph, and sputum cultures if necessary. These individuals should be referred for comanagement to their primary physician or to an infectious disease specialist.

Though antituberculin agents are systemically administered, the ocular lesions are appropriately treated with topical steroids. In most instances, patients respond to a potent topical corticosteroid q.i.d. for three to four days, and subsequently tapered according to the clinical response.

When patients are suspected of having underlying staphylococcal disease, both inflammatory and bacterial components can be managed with a combination antibiotic-steroid such as Zylet. Initial doses should be administered every 2 to 4 hours, depending on severity, for the first

24 to 48 hours, then four times daily after that. In most instances, patients obtain dramatic relief from symptoms and can diminish use of the drug in 7 to 10 days. If the patient is experiencing significant pain and discomfort, a steroid ointment such as Lotemax ointment at night, in addition to the antibiotic/steroid combination during the day, can help to relieve inflammation and pain.

Because of the association of *Staphylococcus* with eyelid disease, lid therapy should be instituted. Antibiotic ointments such as bacitracin or bacitracin-polymyxin B can be used twice daily in conjunction with warm compresses and eyelid scrubs. The tetracyclines are effective in treating phlyctenular keratoconjunctivitis. Doxycycline, 100 mg twice daily for 4 to 6 weeks, is another common therapy. When other etiologic agents, such as intestinal parasites, *Chlamydia*, gonococci and HSV are suspected, patients should receive appropriate systemic medications.

### Non-Specific Inflammatory Conjunctivitis: Diagnosis

Patients may present with low- to moderate-grade conjunctival injection. Typically, they will say their eye "doesn't feel right" or perhaps friends have said their eyes look red. The eye is a little red and irritated but not bothering the patient too

much. Assuming that dry eye has been ruled out first, this presentation is nearly always inflammatory in nature.

If the patient is a contact lens wearer and has been sleeping in the lenses, CLARE is the most likely diagnosis.

Allergy and environmental causes, irritative conjunctivitis or mechanical conjunctivitis should also be considered.

CLARE is distinguished by a history of contact lens wear, a unilateral red eye with minimal or no corneal involvement, and mild watery discharge. There is no pre-

mine whether there has been a change in solutions or wearing pattern.

### **Non-Specific Inflammatory Conjunctivitis: Management**

In non-specific ocular surface inflammatory disease of any type, as long as the cornea is clear and there is no epithelial compromise, there is no need for an antibiotic; the condition is best managed with topical corticosteroids. If the cornea has significant epithelial compromise, one

to five more days is recommended. This aggressive dosing schedule helps to resolve symptoms by quickly addressing the inflammation. If the patient is experiencing significant pain and discomfort, a steroid ointment such as Lotemax ointment at night, in addition to the antibiotic/steroid combination during the day, can help to relieve inflammation and pain.

Recurrent episodes of CLARE are common, so patients should be strongly encouraged to follow a daily wearing schedule.

### **Clinical Pearl**

*Consider adding low-dose doxycycline in the following types of blepharitis cases:*

- *Very advanced*
- *Chronic, recurrent*
- *Associated with rosacea*
- *Significant eyelid telangiectetic vascular activity.*

auricular or submandibular lymph node involvement. Patients nearly always experience photophobia. In fact, a surprising level of pain and photophobia, given the low-level of hyperemia, is highly characteristic of CLARE.

Although it is often associated with overnight wear, simple overwear—too many hours in a day—can also be the culprit. CLARE is more common in people who have been wearing lenses longer, have some dryness issues or have had a prior occurrence. The clinician should probe the patient for more detail on contact lens history to deter-

mine whether there has been a change in solutions or wearing pattern.

mine whether there has been a change in solutions or wearing pattern. The major exception to this rule of thumb is the contact lens wearer. Sterile corneal infiltrates are not the result of infection, and studies indicate that even in contact lens wearers, a topical corticosteroid alone may have a role in treatment.<sup>42</sup> However, because lens wear may predispose patients to ocular infections, the conservative clinician may wish to employ a combination antibiotic-steroid in the setting of CLARE.

In such patients, a combination product such as Zylet every 2 hours for 24 to 48 hours, then q.i.d. for four

### **Conclusions**

With careful questioning and a thorough examination, clinicians can accurately differentiate among the various types of conjunctivitis. Appropriate treatment in many cases requires us to address both the infectious and inflammatory components of the condition, in order to treat the underlying cause and fully resolve patient symptoms.

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## Case: Classic CLARE

Ron Melton, O.D.

A 31-year-old male presented complaining that he woke up in the middle of the night with acute onset of painful, red left eye with photophobia and profuse tearing. The discomfort was so severe he could not work the next day. The patient was a smoker in good general health who wore two-week continuous wear disposable hydrogel lenses.

At the slit lamp, the left eye had Grade 3 conjunctival injection. The cornea was slightly edematous, more pronounced in the periphery, consistent with classic microcystic corneal edema. The right eye had just trace injection of the conjunctiva, likely secondary to contact lens wear.

Intraocular pressure (IOP) and pupillary function were normal. Visual acuity in the left eye was impaired at 20/40. Fluorescein staining showed mild diffuse superficial punctate keratitis in the left eye, with negative staining of the periphery, again consistent with mild

microcystic corneal edema. There were no significant findings in the right eye.

I diagnosed contact lens-induced acute red eye (CLARE). Lens wear was discontinued until resolution of symptoms. Loteprednol etabonate 0.5%/tobramycin 0.3% (Zylet, Bausch + Lomb) was prescribed, one drop every 2 hours while awake, for 2 days and on Day 3, the patient was seen for follow up. IOP was normal. There was a good clinical response including resolution of corneal edema and inflammation without evidence of further corneal involvement. The photophobia was gone.

The Zylet was tapered to one drop q.i.d. for an additional 5 days (7 days total treatment). After assessing the contact lens fit, I recommended a silicone hydrogel daily wear lens to be started once the treatment recommendations were completed.



Courtesy of Ron Melton, O.D.

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