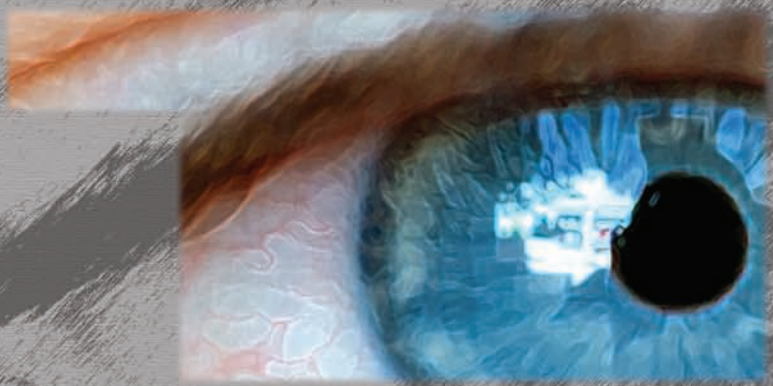
A Supplement to

REVIEW OF OPTOMETRY

June 15, 2007

2007 Clinical Guide



TO OPHTHALMIC DRUGS

by Ron Melton, O.D., and Randall Thomas, O.D.

INTRODUCTION

Dear friends and colleagues,

Can you believe that optometrists write as many prescriptions for allergy medicines as our surgical counterparts? It's true, and that is very exciting. When this statement comes true for glaucoma meds, we will have truly arrived—and public health will be very well served.

As a profession, we continue to season well. Our prescription-writing patterns continue to demonstrate that, while still the junior partner, our growth rate is very strong. Patient care and practice growth are inseparable, so as we do more to serve our patients, they reciprocate by expanding our practices. It's a wonderful "win-win" scenario.

There is steady, albeit slow growth within the ophthalmic pharmaceutical pipeline. We continue to long for new classes of compounds and new cures, but enduring patience seems to be the order of the day. For the *2007 Clinical Guide to Ophthalmic Drugs*, we have new formulations of current allergy medicines, and a prostaglandin upgrade that we will highlight. This year, we want to re-emphasize the combination drugs, as a masterful understanding of these classes can be enormously helpful to many, many patients. We'll also share some new insights to patient care enhancement which we think can further optometric practice maturation.

Also in this edition, we have enclosed a couple of tear-out forms that we think will help promote and improve O.D. communications with primary-care physicians—an extremely important aspect of the patient care continuity.

We are deeply grateful to all of you who have shared with us your appreciation of this drug guide. It makes it all worthwhile.

Our very best wishes to all of you,

Sincerely,

Randall Thomas, O.D., M.P.H.

Ron Melton, O.D.

Educators in Primary Eye Care, L.L.C.
www.eyeupdate.com

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Call for Clinical Conundrums
Got a problematic patient? Having difficulty determining a diagnosis? Can't come to a conclusion on a course of therapy?
Send your clinical questions to Drs. Melton & Thomas at: DrugGuide@jobson.com. They'll publish your question—and their answer—in next year's *Clinical Guide to Ophthalmic Drugs*.

ENHANCING PATIENT CARE: THE OD-MD LINK

Some family physicians and other M.D.s have no idea of the scope of optometric training and care. To change this, we must communicate with these doctors.

We just returned from a conference where a family doctor, whose brother was an O.D., attended our lectures. He told us he would like to work more closely with the O.D.s in his service area, especially with regard to his patients with diabetes, but he had become frustrated and discouraged with the near-nonexistent O.D. to M.D. communication.

Furthermore, he said he was very willing to send all sorts of eye problems to O.D.s in his city, but only one optometrist had approached him to establish a mutually beneficial relationship to address patient care. On the other hand, three different area ophthalmologists take him to professional ball games, golf, dinner, etc., from time to time.

Is there any intelligent reason we do not pursue these beneficial relationships with other health-care providers?

It gets worse. A rheumatologist in our area has a brother who is an O.D. in another state. When this doctor first established his practice, he gladly recommended that his patients see their O.D. for Plaquenil evaluations; but, after a year of a frustrating lack of communication from the O.D.s in the community, he now steers his patients to area ophthalmologists who consistently communicate their findings to the referring/prescribing M.D. How sad is this?

For the sake of your patients and the sake of your practice, start working with your local physicians.

Now, let's be realistic. Optometry is a foreign entity to the medical community at large. In medical school and residency training, all eye and vision problems are handled by ophthalmology. When these new physicians enter our cities, towns and communities, they encounter a whole new breed of provider with whom they are not familiar: the optometric physician. These new M.D.s do seem to understand that O.D.s "fit eyeglasses and contact lenses," but they have no idea of the scope of training and clinical competence we O.D.s can provide.

For example, we encountered a family physician at a function recently. He recounted to us how his wife and daughter, "just love their optometrist." He, however, had never sent any of his diabetic patients to that O.D. Why? Because he was completely unaware that O.D.s performed diabetic eye evaluations! We were delighted to have the opportunity to educate this physician about our profession, and he was equally delighted to know that he could start sending his patients with diabetes (and other medical eye needs) to his family's optometrist.

We don't know what percentage of primary-care physicians would be willing to partner with an O.D., and it really doesn't matter. What does matter is that we, as a profes-

sion, need to begin to step out of our little boxes and interact with the medical community—first, to complement and enhance patient care; and second, to grow our practices.

Established physicians have established referral relationships that are very difficult to alter (although that does not mean we shouldn't try). However, when new physicians come to town, take the initiative and invite them to lunch, preferably within their first month; some will eagerly accept, while others may not. The result may be very rewarding, or it may be disappointing. One thing is certain: nothing ventured, nothing gained.

Written communication with doctors in the community can be technologically challenging. In our practices, we contract with a local medical transcription service to type our letters. The service's dictation/transcription system allows us to simply dial a local or toll-free telephone number from any phone and give our verbal dictation. The service then transcribes our dictation and returns the drafts to our office via a secure site. The letters are either printed out for our review, or we can review them on screen, and make any necessary changes. Our staff prints the letters out on our letterhead, we sign them, and they are mailed. Copies are generated for the patient charts. There are lots of medical transcription services out there. Bottom line: Call your personal physician, any medical specialist, or an ophthalmologist to find out how their correspondence is handled; find a reliable service and get onboard.

We generate letters on all our patients with medical problems to their referring physicians, except when a patient is referred for a diabetic eye or Plaquenil evaluation. In those instances, we simply fill out an in-house form that takes perhaps 20 to 30 seconds to complete. We then fax these forms to the referring doctors, and place the originals in the patient charts. These forms save us both time and the cost of a postage stamp. We have included the Plaquenil form (*page 5*) and the diabetes form (*page 6*) that we use. Please feel free to use them "as is,"

Examples of Letters to Referring Physicians

Remember, be concise and to the point. Notice that there are no refraction numbers because they are meaningless to physicians. Speak their language.

EXAMPLE LETTER ON ADENOVIRAL INFECTION

Dear Doctor,

Ms. Rickard has been a long-time patient in our office. She developed red eyes about a week and a half ago, and has been using an eye drop for the past several days given to her by you. However, Ms. Rickard could not recall the name of the drop. When her eye redness had not resolved within the expected period of time, you sent her here for consultation.

Ms. Rickard's entering visual acuity was 20/30 right eye and 20/50 left eye with her eyeglasses. Both eyes were Grade 1 injected. There were no palpable preauricular lymph nodes. Her corneas were clear with no fluorescein staining. She did give a history of a mostly watery discharge during the course of her problem. Her anterior chambers were deep and clear. Eyelid eversion was normal in both eyes.

It is my impression that Ms. Rickard is at the tail end of a low virulence expression of an adenoviral infection. I placed her on Alrex Ophthalmic Suspension to be used QID x 1 week. Alrex is a moderate-strength, topical corticosteroid. I anticipate that Ms. Rickard will do fine and have no sequelae to her probable adenoviral infection.

Thank you for sending Ms. Rickard over for consultation. If I can be of any further help to you in any way, please do not hesitate to call.

Sincerely,

EXAMPLE LETTER ON MACULAR DEGENERATION

Dear Doctor,

This is my fourth time to see Mr. Jones in the office. As you know, he is taking deferoxamine 3 to 4 times weekly for his liver treatment.

Mr. Jones is correctable to 20/25 right eye and 20/20 left eye. He maintains an icteric sclera. His slit lamp examination is entirely normal. Ophthalmoscopic examination reveals healthy optic nerves with a 0.1 cup in each optic nerve head. There is some mild, geographic atrophic macular degeneration in the right eye, and a rough textured appearance to the macula in the left eye. Although uncommon at the young age of 47, this does not appear to be anything associated with the deferoxamine therapy. His visual field testing is nearly normal in both eyes. There is no evidence of any type of optic neuropathy associated with the deferoxamine. I have updated Mr. Jones's eyeglasses and have asked to see him back on an annual basis.

I trust this information is helpful to you. I wish you well in your overall care of this nice gentleman.

Sincerely,

(cont'd on next page)

EXAMPLE LETTER ON ORDERING LABS

Dear Doctor,

I have been seeing Ms. Rainski in the office since November 1997. She has a history of recurrent episcleritis. At her most recent visit, she expressed some concern as to the underlying etiology of this recurrent problem. She has no history of lupus or gout. It was felt, however, that a systemic evaluation was in order. In the meantime, I have treated her with Lotemax (a potent, topical ophthalmic corticosteroid) every two hours for several days, and then QID x 1 week. When Ms. Rainski returned in one week, she was 90% improved.

Ms. Rainski does have some mild arthritis, malaise, and some general achiness. We ordered a CBC, sed rate, ANA, anti-DNA, RF, and TSH. As you can see from the enclosed copies of this focused workup, her only positive test is a smooth pattern ANA at a ratio of 1:60. I am surprised that the ANA was positive, and yet the anti-DNA was negative. I am sure you can explain that better than I.

I want to make you aware of this information since you are Ms. Rainski's primary care physician. I trust this information is helpful to you. If you have any information on your end that you feel would be helpful to me in my portion of her care, I would appreciate you passing it along. I do wish you well in your overall care of this nice lady.

Sincerely,

EXAMPLE LETTER ON CHRONIC BLEPHARITIS

Dear Doctor,

I saw Mr. Rink in our office April 1, 2004 upon your referral. He complained of having a flare-up of a red, painful right eye for the past several days. He complains of having this problem occur about every six months for the past ten years. Mr. Rink has used an antibiotic/steroid eyedrop off and on for years for this condition.

Mr. Rink's slit lamp examination reveals a classic, peripheral, sterile corneal ulcer secondary to staphylococcal exotoxin erosion of the superficial epithelial tissues. He has low-grade staphylococcal blepharitis in the right eye, as well. The left eye appears to be normal.

I explained to Mr. Rink the underlying problem is his chronic blepharitis and instructed him in how to properly, carefully, and meticulously keep his eyelids as clean as is humanly possible. If we can keep Mr. Rink's lids clean, and can decrease the population of the staphylococcal bacteria on his eyelid margins, I think we will be able to prevent, or at least minimize, recurrent toxic erosion to his peripheral cornea. I prescribed Zylet (a newer combination antibiotic/steroid eyedrop) to use three or four times a day as needed. In addition, I have placed him on Polysporin Ophthalmic Ointment at bedtime for the next two to three weeks in an attempt to diminish resident eyelid staph.

I thank you for your kindness in sending Mr. Rink for consultation. I trust this information is helpful to you, and wish you well in your overall care of this nice man.

Sincerely,

or make any changes that you feel will enhance their usefulness to you in your service to your patients. You can also download these forms from our web site www.eyeupdate.com.

A note about letters: Be direct and succinct. All that a primary-care physician wants to know is the essentials—nothing more. This is a real pearl, and it needs to be heeded. In general, PCPs know little about the eye. Keep the language in your letter clear, basic, and to the point.

Here, we have selected some actual letters that we have written to help give you a flavor for the character such letters should take. (Names of doctors and patients in these letters are fictitious.)

We, as a profession, possess a tremendous knowledge base. We have the ability to perform a scope of professional services for our patients that go far beyond refractive care. Unfortunately, it seems this is a well-kept secret that we are not even sharing with our own patients, let alone their physicians!

Surely, we all know optometric physicians who have prosperous, diverse and thriving practices. Ask yourself, "What are these doctors doing that I'm not?" You'll likely find that they have put in the time and effort to actively engage and educate their patients about the services and expertise they offer. They have labored to build and maintain strong relationships with other physicians in their community, and to keep the lines of communication open with their referral sources. In other words, they are their own best advocate.

The opportunity for you to do likewise is there. If you aren't satisfied with the number or types of patients you are seeing, YOU are the only one who can change that. Lunches and letters are a good start. ■

SAVE TIME — SNIP THIS!

Clip out these forms, affix your letterhead, or use "as is." Fill it out and fax to the referring physician.

PLAQUENIL EYE EVALUATION REPORT

Date _____

Patient Name _____ DOB _____

Prescribing Doctor _____ Fax # _____

Consulting Optometrist _____

Plaquenil dose _____mg _____ Patient's weight _____

Visual acuity: right eye 20/_____ left eye 20/_____

Slit lamp exam: Normal _____ Other _____

_____

Fundus exam: Normal _____ Other _____

_____

Macular Visual field Testing (10-2): Normal _____ Other _____

_____

Recheck: 1 year _____ Other _____

Comments: _____

_____

_____

Thank you very much for entrusting your patients to us for their eye care.

DIABETIC EYE EVALUATION REPORT

Date _____

Patient Name _____ DOB _____

Primary Care Provider _____ Fax # _____

Endocrinologist _____ Fax # _____

Consultant Optometrist _____

Duration of Known Diabetes _____

Most recent A1c _____ % ☐ A1c unknown by patient

Visual acuity: right eye 20/_____ left eye 20/_____

Slit lamp exam: Normal _____ Other _____

_____

Dilated fundus exam:
No diabetic retinopathy _____ right eye _____ left eye

Other findings: _____

_____

Recheck: Annually _____ Other _____

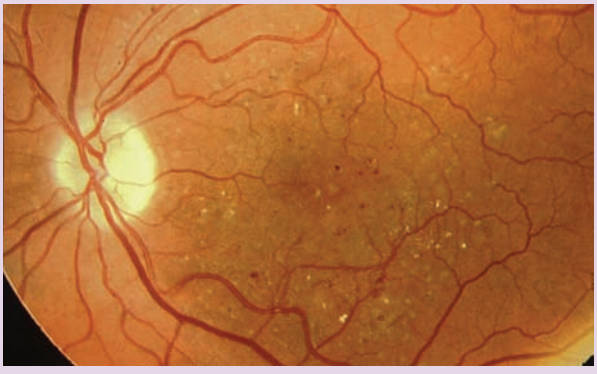
Comments: _____

_____

Thank you very much for entrusting your patients to us for their eye care.

Update on Diabetes Mellitus[1]

• Definition: fasting plasma glucose greater than 126mg/dl.
• 5% to 10% of diabetic patients have Type I diabetes mellitus (insulin-dependent).
• 90% to 95% of diabetic patients have Type II diabetes mellitus (treated with oral medicines, and occasionally with insulin also).
• Approximately 15 to 18 million Americans have diabetes, and about 250,000 of these people are under age 20.
• Native peoples are disproportionately afflicted.
• Risk factors for development or progression of diabetic retinopathy:
  – *Severity of hyperglycemia*
  – *Duration of diabetes*
  – *Systemic hypertension*
  – *Hyperlipidemia*
• After retinopathy is present, the severity of hyperglycemia, rather than duration of diabetes, seems to confer greater risk for progression.
• Intensive control of blood glucose is associated with a much-decreased risk for retinopathy and other complications.
• Based on the Wisconsin Epidemiology Study of Diabetic Retinopathy, patients with Type I diabetes will express retinopathy at an approximate rate of 25% after five years, 60% after 10 years, and 80% after 15 years. As many as 25% of these diabetic patients will have proliferative diabetic retinopathy.
• In the same Wisconsin study, Type II patients expressed retinopathy somewhat similarly, but those controlled without the need for insulin unsurprisingly fared better than those requiring the addition of insulin. Bottom line: There is a direct relationship between the duration of diabetes and the incidence of retinopathy.
• Development of hemorrhages and exudates occurs 50% faster when cholesterol and/or triglyceride levels are above normal.
• Intensive treatment and control of glycemic levels in Type I patients reduces the risk of developing retinopathy by about 75% and slows progression of established retinopathy by about 50%.
• Similar intensive control in Type 2 patients reduces the risk of developing retinopathy by about 25%, and a similar reduction in risk was achieved by keeping blood pressure below 150/85.
• The number of patients referred by their primary-care physician for ophthalmic care (only 34% to 65%) is far below consensus expert guidelines. (*We urge all O.D.s to work vigorously to develop relationships with primary-care physicians in an effort to address this major shortcoming.*)
• When should patients with diabetes have their first diabetes-oriented eye examination?
  – *Type I:* within five years of the diagnosis.
  – *Type II:* at the time of diagnosis, because the time of onset is difficult to determine and may precede the diagnosis by a number of years.
• Pregnancy: Diabetes mellitus is legendary for progression during pregnancy in some patients. Therefore, all diabetic pregnant patients should be examined close to the time of conception. A second examination should be performed during the first trimester. Another examination is needed if retinopathy was detected, or had progressed on the initial or first trimester visit. These standards hold true for all expecting diabetic patients, whether their diabetes is Type I or Type II.
• Clinically significant diabetic macular edema (CSME) is a clinical diagnosis, but can be assessed via OCT. Fluorescein angiography is usually not needed, but can help guide laser therapy in the setting of CSME.



Background diabetic retinopathy with macular involvement.

• International Clinical Classification of Diabetic Retinopathy (ICCDR):
  – *Mild nonproliferative diabetic retinopathy*: microaneurysms only.
  – *Moderate nonproliferative diabetic retinopathy*: more than microaneurysms, but less than severe nonproliferative diabetic retinopathy.
  – *Severe nonproliferative diabetic retinopathy,* which may include any of the following:
    ✶ more than 20 intraretinal hemorrhages in each of four quadrants
    ✶ definite venous beading in two or more quadrants
    ✶ prominent IRMA (intraretinal microvascular abnormalities) in one or more quadrants.
  – *Proliferative diabetic retinopathy,* which is diagnosed when one or both of the following is present:
    ✶ neovascularization
    ✶ vitreal or preretinal hemorrhage
• Regarding diabetic macular edema (DME), it is a clinical diagnosis, made with biomicroscopic ophthalmoscopy. The OCT very eloquently quantifies the degree of macular thickness as altered by the macular edema. The clinical significance of DME is largely dictated by the proximity of hard exudates to the center of the macula.

• Regarding the laser treatment of CSDME, the main goal and outcome is "preventing moderate vision loss rather than improving vision, although in some cases vision can improve." It is focal/grid laser application that is applied to the edematous macular tissue (as opposed to panretinal photocoagulation).
• It is recommended that eye doctors "educate all patients about diabetes and stress the value of controlling blood glucose (measured by hemoglobin A1c) as well as blood pressure control."

Be a Part of the Diabetic Care Team

Of all parameters of diabetic care, by far the greatest shortfall is the recommended annual dilated eye examination. This begs the questions: Are the patients not receiving timely eye care? Or, are the provider optometrists not communicating their findings back to the primary-care physician and/or endocrinologist?

The answer is probably "yes" to both questions. As O.D.s, we have little control over the first part of the problem; however, we can immediately rectify the second. We, as a profession, have an ethical and moral imperative to enter into the mainstream of the team approach to diabetic patient care by apprising the primary-care physician of our mutual patients' eye status. This is easily accomplished via a "Diabetic Eye Evaluation Form," which can be filled out in approximately 30 seconds. (*See page 6, or visit our web site, www.eyeupdate.com, to download the form, affix to your letterhead, and use for this purpose.*) The form can then be faxed to the appropriate physician(s).

One major hesitation to such communication by many optometrists is the fear of encountering the following scenario:

[*Primary-Care Physician*:] "Mrs. Jones, I notice that you are seeing an optometrist for your eye care. These 'people' are not medically trained. Since you have diabetes, I want you to start seeing an ophthalmologist."

Thus, optometrists hesitate to communicate with primary-care physicians due to the fear of perhaps encountering prejudice on the part of some M.D.s who may refer the diabetic eye patient to an ophthalmologist for ongoing care. Some medical doctors view optometrists as practitioners "trained to fit eyeglasses," not realizing (or recognizing) that O.D.s are thoroughly trained and capable in the care not only of the diabetic eye, but most eye diseases.

The key to avoid the loss of your patient (and still communicate important information about patients' ocular status with the primary care physician) is proactive education on two levels. First, educate your patients. Be sure they understand that you are a doctor, trained and competent in diabetic eye care. If your patient sees a primary-care physician with whom you do not yet have a professional relationship, you might forewarn that the PCP may attempt to send him/her to another eye doctor. Reassure the patient that you have the expertise needed to follow him/her for eye problems associated with diabetes.

It is equally important, if not more so, to at least attempt to educate other members of your medical community about the scope of professional care you can offer. Develop a practice information packet and send it along to the primary-care physician with your examination findings; place a phone call to the office and invite the physician to lunch so you can become acquainted. This is especially fruitful with newer physicians who have not already established referral networks. Remember, most doctors (and many of our patients) are under the impression that optometrists "only fit eyeglasses and contact lenses." This is a serious under-representation of our scope of professional services and it can be a drawback for our patients—but it's a situation we can easily correct if we have the will and the perseverance.

1. Update on Diabetes and Eye Care 2006. National Eye Institute and Duke University.

Quality Reporting Guidelines for Diabetic Retinopathy

The 2007 Physician Quality Reporting Initiative (PQRI) guidelines can be seen at www.cms.hhs.gov/PQRI. These 74 unique guidelines, issued by the Centers for Medicare and Medicaid Services (CMS), cover all elements of medical care. The stated goal for these guidelines is to achieve the clinical standards outlined therein 80% of the time. Two of these standards are critical to the care of patients with diabetes mellitus:

Diabetic Retinopathy: Documentation of Presence or Absence of Macular Edema and Level of Severity of Retinopathy

Description: Percentage of patients aged 18 years and older with a diagnosis of diabetic retinopathy who had a dilated macular or fundus exam performed which included documentation of the level of severity of retinopathy and the presence or absence of macular edema during one or more office visits within 12 months.

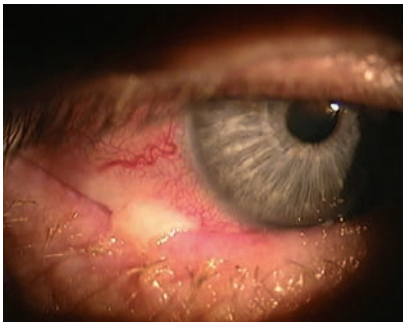
Diabetic Retinopathy: Communication with the Physician Managing Ongoing Diabetes Care

Description: Percentage of patients aged 18 years or older with a diagnosis of diabetic retinopathy who had a dilated macular or fundus exam performed with documented communication to the physician who manages the ongoing care of the patient with diabetes regarding the findings of the macular or fundus exam at least once within 12 months. (*Emphasis added.*)

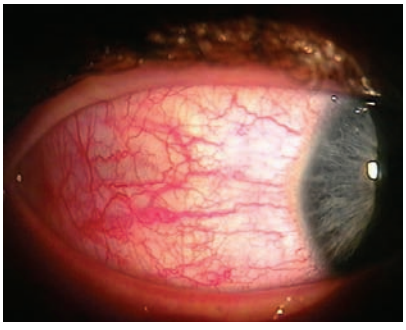
As can be seen, continuity of care can be greatly enhanced when primary-care providers have meaningful feedback from specialty-care providers, notably O.D.s.

ANTIBIOTICS

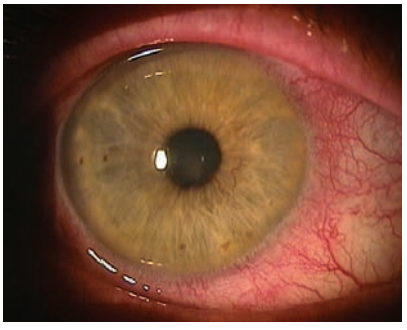
Rather than prescribing an antiobiotic that will "do no harm" in a red eye, nail the diagnosis first, then prescribe with precision.



The evident mucopurulent discharge is pathognomic for bacterial conjunctivitis.



Although not always consistent, such a relative limbal-sparing conjunctival injection pattern is common to bacterial conjunctivitis.



In contradistinction to the eye at left, the injection pattern in the eye above shows considerable hyperemia in the paralimbal region, with relative sparing of the forniceal conjunctiva. This patient has advanced iridocyclitis.

Everybody loves antibiotics. They are considered a cure-all for most medical maladies, but they aren't. Parents commonly prevail upon the doctor to give their child an antibiotic, even though the condition is viral. Even more common is the doctor (eye or other) who is unsure of the diagnosis, and therefore prescribes an antibiotic because "it will do no harm," in hopes that the condition (whatever it is) will improve with time.

It's frustrating that topical antibiotics are still heavily prescribed. This is particularly poignant as their only clinical indication is bacterial infection, one of the least common entities we encounter in clinical practice. Such infections are more common in children than in adults.

The reality is that the "red eye" almost always represents some sort of inflammatory condition, thus calling for a topical corticosteroid, or at least an antibiotic-steroid combination.

The most common indication for writing an antibiotic prescription is for a patient presenting with acute mucopurulent discharge. An absolute indication for antibiotic use is in patients with microbial keratitis, although such presentations are thankfully rare.

It must be stressed that most presumed "corneal ulcers" are nothing more than sterile leukocytic infiltrates that usually merit a combination product such as Zylet or TobraDex—or generic Maxitrol, if cost is an issue.

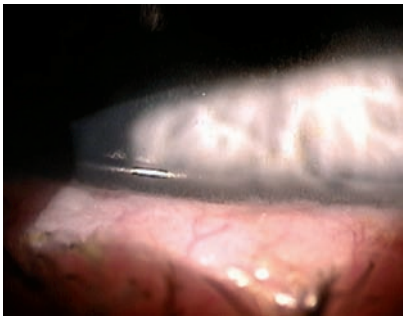
Not knowing the diagnosis is poor justification to write for an antibiotic. Red eyes are either infectious or inflammatory, and inflammation is by far the more common presentation. If the cornea is not compromised, and there is no mucopurulence, then a steroid (or even a combination drug) would be an approach far more likely to benefit the patient.

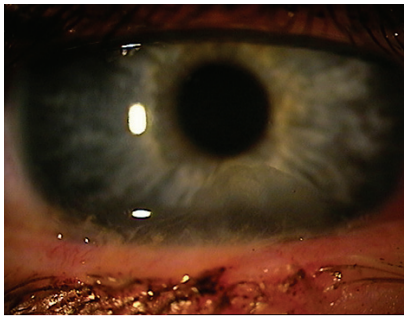
That said, let's now characterize the various antibacterial drugs with the goal of optimum selection.

Sodium Sulfacetamide

Bacteria synthesize folic acid from para-aminobenzoic acid, or PABA. Folic acid is a necessary component for normal cell physiology.

Sulfa drugs, which are bacteriostatic, inhibit this production of folic acid. Because sulfa drugs are chemically similar to PABA, com-





Not all patients with bacterial infection present with obvious mucopurulence. Careful examination of the lacrimal lake, which is normally optically empty, may reveal hundreds of microparticulant discharge/debris particles. This can help seal the diagnosis.

petitive inhibition of folic acid production occurs, resulting in bacterial death.

Though sulfas are broad-spectrum drugs, a high percentage of commonly encountered staphylococcal organisms are resistant, as are most *Pseudomonas* species. Sulfas do not work well against infections that produce copious amounts of purulent exudate, probably because there is much PABA in these discharges, which tends to negate the drug's mechanism of PABA competition. Also, many patients are allergic to sulfa drugs.

For these reasons, sulfa drugs, once a mainstay of treatment, are now very poor choices. Much more effective are Polytrim, tobramycin or a fluoroquinolone.

The one exception is childhood bacterial infection when the child will not cooperate with eye drop therapy. Most childhood bacterial infections are caused by *Streptococcus pneumoniae* or *Haemophilus influenzae*, and 10% sodium sulfacetamide may not be effective against it. This is why Polytrim remains our choice for children who will accept eye drops.

Sodium sulfacetamide is available in solution (10%, 15%, and 30%) and ointment (10%). It is marketed by numerous companies. The 30% solution stings sharply on instillation and is rarely used.

There are times when a patient is seen for a very mild or self-limiting conjunctivitis and you sense the patient desires to be treated rather than simply reassured. Because the sulfa drugs are generic, inexpensive and sting upon instillation, they can serve as virtual placebo therapy in such cases.

The Enduring Value of Generics

When an ophthalmic drug becomes generic (i.e., loses patent protection), all marketing promotion ceases. Of course, the drug remains as viable as ever, but with the absence of samples and active promotion, it generally withdraws into the recesses of our brains. However, one point that merits explanation is the enduring value of many generic drugs. Drugs such as bacitracin, polymyxin B, and the aminoglycosides are like the Energizer Bunny—they just keep going and going.

The explanation for this is very straightforward; they are not used systemically for a variety of reasons. Any antibiotic used orally will ultimately develop resistance. Since the above-mentioned antibiotics are not used systemically, they remain very viable for topical ophthalmic use.

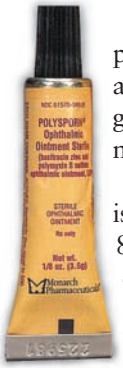
Bacitracin

This drug, which is bactericidal, works by destroying cell walls. Its antimicrobial spectrum of activity is similar to erythromycin, but has greater activity against most gram-positive bacteria. Its effectiveness and low likelihood of provoking toxic or allergic reactions would make it a drug of choice for treating gram-positive bacteria, except that it is only available as an ophthalmic ointment. We do recommend its use for the first week or two in treating moderate to advanced cases of staphylococcal blepharitis in addition to providing aggressive eyelid hygiene. Its only practical use, in our opinion, is in select cases of blepharitis management. It is generically available.

Although bacitracin has been around since 1943, it maintains excellent activity against a host of gram-positive organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA). An article in April's *American Journal of Ophthalmology* states: "For patients exposed to healthcare facilities who are at higher risk of infection from nosocomial MRSA, we recommend … considering a fourth-generation fluoroquinolone or bacitracin for preoperative prophylaxis."[1]

Bacitracin and Polymyxin B

This is an excellent broad-spectrum antibiotic combination that enjoys widespread use in eye care. As bacitracin is highly effective against gram-positive organisms, polymyxin B is a potent killer of gram-negative bacteria, including *Pseudomonas*. It works by destroying the cell membrane's structural and functional integrity, resulting in cell death. Resistance, toxicity and allergic reactions are rare.

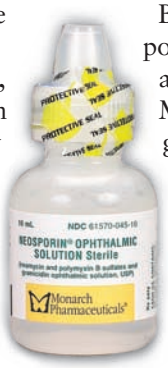


Doctors can use this drug safely in most bacterial infections. In blepharitis therapy, since polymyxin B is nontoxic, Polysporin can be substituted for bacitracin should the pharmacy not have bacitracin. Unfortunately, it is only available in the U.S. as an ointment, which limits its practical use in adults. It is marketed as **Polysporin** ophthalmic ointment by Monarch Pharmaceuticals and numerous generic manufacturers. Interestingly, Polysporin ophthalmic solution is available in Canada.

Bacitracin, Polymyxin B and Neomycin

This is a very effective combination antibiotic available both as solution and ointment. The characteristics of bacitracin and polymyxin B are covered above. Neomycin, an aminoglycoside, kills a broad spectrum of bacteria by inhibiting protein synthesis. It is effective against most gram-positive and gram-negative bacteria, with the notable exception of *Pseudomonas*.

This preparation's Achilles' heel is its potential for toxicity. About 8% of all patients experience a delayed, type IV hypersensitivity reaction to neomycin. If the patient has not been exposed to the drug before, the reaction can occur within five to ten days after therapy has been initiated. If the patient has been previously sensitized, the reaction can happen more quickly, usually within 12 to 72 hours.



If such a classic neomycin hypersensitivity reaction were to occur, you would usually see erythema and mild edema of the eyelids, conjunctival injection, and possibly superficial punctate keratitis. The reaction usually is most pronounced in the inferonasal region of the eye, because gravity and blinking concentrates the drug there. The treatment is to discontinue the drug.

The reaction typically resolves on its own within a few days. Consider prescribing cold compresses and/or mild topical steroids, such as Alrex, for two to four days.

Bacitracin (or gramicidin) with polymyxin B and neomycin is available as **Neosporin** from Monarch Pharmaceuticals, and generically. Neosporin is basically Polysporin plus neomycin, except that Neosporin is available as a solution and an ointment. In the solution, gramicidin replaces bacitracin, since bacitracin is unstable in water. In terms of activity, gramicidin is virtually identical to bacitracin, but is more water soluble.

Because newer antibiotics are now available that are less toxic and equally or superiorly efficacious, Neosporin is rarely used.

Topical Antibiotic Drugs

BRAND NAME	GENERIC NAME	MANUFACTURER	PREPARATION	PEDIATRIC USE	BOTTLE/TUBE
Fluoroquinolones					
Ciloxan, and generic	ciprofloxacin 0.3%	Alcon, and generic	sol./ung.	≥ 1 yr./ ≥ 2 yrs.	2.5ml, 5ml, 10ml/3.5g
Ocuflox, and generic	ofloxacin 0.3%	Allergan, and generic	solution	≥ 1 yr.	5ml, 10ml
Quixin	levofloxacin 0.5%	Vistakon Pharm.	solution	≥ 1 yr.	2.5ml, 5ml
Vigamox	moxifloxacin 0.5%	Alcon	solution	≥ 1 yr.	3ml
Zymar	gatifloxacin 0.3%	Allergan	solution	≥ 1 yr.	2.5ml, 5ml
Aminoglycosides					
Tobrex, and generic	tobramycin 0.3%	Alcon, and generic	sol./ung.	≥ 2 mos.	5ml/3.5g
Genoptic, and generic	gentamicin 0.3%	Allergan, and generic	sol./ung.	N/A	1ml, 5ml
Polymyxin B Combinations					
Polytrim	polymyxin B/trimethoprim	Allergan, and generic	solution	≥ 2 mos.	10ml
Polysporin	polymyxin B/bacitracin	Monarch, and generic	unguent	N/A	3.5g
Neosporin	polymyxin B/neomycin/ gramicidin	Monarch, and generic	sol/.ung.	N/A	10ml/3.5g
Other Antibiotics					
AzaSite	azithromycin 1%	Inspire Pharm.	solution	≥ 1 yr.	2.5ml
Ilotycin, and generic	erythromycin 0.5%	Dista, and generic	unguent	≥ 2 mos.	3.5g
AK-Tracin, and generic	bacitracin 500u/g	Akorn, and generic	unguent	N/A	3.5g, 3.75g

General Observations and Clinical Pearls

• For bacterial conjunctivitis or prophylaxis, we generally select an aminoglycoside or a fluoroquinolone. When treating an infectious keratitis, we use a fourth-generation fluoroquinolone or fortified antibiotic.

• If we use an aminoglycoside by day and desire an ointment at bedtime, we would choose either Ciloxan or Polysporin. If we use a fluoroquinolone by day and desire an ointment at bedtime, we would choose Polysporin. It is extremely rare to encounter a condition where both an eyedrop and ointment are needed.

• We have never experienced aminoglycoside corneotoxicity. Perhaps if dosed frequently for more than one week, and/or the patient has untreated tear film dysfunction, then such an event could occur, but that would be very rare. Fluoroquinolones have considerably less corneotoxic potential than aminoglycosides.

• Whether an aminoglycoside or one of the fluoroquinolones is selected is not a pivotal decision. The key to effecting a clinical cure centers on "frequency of administration." As best as can be anticipated, prescribe a dosing frequency commensurate with the nature of the disease entity.

– *For moderate to severe bacterial conjunctivitis*, dose every two hours until control is achieved, then consider decreasing to q.i.d. for four to six more days.
– *For hyperacute bacterial infections*, dose hourly along with Polysporin ointment at bedtime until control is achieved. Once under control, stop the ointment and reduce eyedrops to q2 hours for four days, then q.i.d. for four days. Consider concurrent oral Augmentin (amoxicillin/clavulanate potassium, GlaxoSmithKline) at 875mg b.i.d. for a week if the condition warrants.
– *For garden variety bacterial conjunctivitis*, dose q2 hours for two days, then q.i.d. for four to five more days.
– *For high probability or firmly diagnosed bacterial keratitis*, dose hourly along with Polysporin ointment at bedtime. Cycloplege with 5% homatropine or 0.25% scopolamine two or three times daily. Once the infection shows evidence of control, stop the ointment and decrease the eye drops to q2 hours for four days, then q.i.d. for four days. If there is any epithelial toxic SPK, use preservative-free artificial tears p.r.n. and GenTeal Gel at bedtime.
– *For staphylococcal blepharitis*, use bacitracin or Polysporin ointment at bedtime for two weeks, along with proper hygiene. If there is secondarily associated eyelid margin inflammation as evidenced by considerable erythema to the eyelid margin, then TobraDex ointment at bedtime for two weeks would be appropriate. TobraDex ointment at bedtime is also an excellent choice for angular blepharitis, or any expression of tissue maceration or erosion to the eyelid tissues.
– *For subacute dacryocystitis*, Keflex (cephalexin, Dista) 500mg b.i.d. or Augmentin 875mg b.i.d. p.o. for one week, along with warm compresses, would be warranted.

Trimethoprim with Polymyxin B

Trimethoprim, a diaminopyrimidine, achieves bacteriostasis by interfering with folic acid production, but later in the pathway than sulfa drugs. Specifically, it interrupts the synthesis of tetrahydrofolic acid, the metabolically usable form of folic acid.

Trimethoprim is active against most common gram-positive and gram-negative ocular pathogens. It is inactive against *Pseudomonas*, which is why polymyxin B is added to trimethoprim. Since *Streptococcus pneumoniae* and *Haemophilus influenzae* are common pathogens in children, this drug is an excellent pediatric choice. To wit, pediatricians are the largest prescribers of trimethoprim with polymyxin B.

Adverse effects are very rare. The recommended frequency of administration is one drop every three hours (q3 hours) while awake. This is a bit more frequent than the more common four-times-a-day schedule. As with most other antibiotic agents, treatment should continue over seven to ten days.

Trimethoprim sulfate (0.1%) with polymyxin B is marketed as **Polytrim** ophthalmic solution by Allergan, and generically. This is an excellent antibiotic that enjoys widespread use in treating bacterial conjunctivitis in children and adults.

Azithromycin

We are all familiar with azithromycin (Zithromax, Pfizer) by use of the famous Z-Pak or Tri-Pak. Azithromycin is a macrolide antibiotic possessing broad-spectrum action against most common gram-positive pathogens as well as *Chlamydia* species. Like all macrolides, its mechanism of action is inhibition of protein synthesis.

In eye care, we use azithromycin primarily to treat chlamydial conjunctivitis, and typically prescribe it as a single 1,000mg oral dose. In primary-care medicine, azithromycin is used (and overused) to treat upper and lower respiratory diseases and sinusitis.

Now, azithromycin is available as a 1% ophthalmic antibiotic solution under the brand name **AzaSite**, manufactured by InSite Vision and licensed to Inspire Pharmaceuticals, Inc. On the plus side, azithromycin possesses the ability to achieve high tissue concentrations, and because of its unique viscous vehicle, DuraSite, ocular surface residence time is prolonged, which should further enhance tissue penetration.

This dual characteristic allows for less frequent instil-

lations. Dosage is one drop twice daily (about every eight to 12 hours) for two days, then once daily for five more days. This regimen should enhance user-friendliness, and therefore result in better compliance. On the negative side, azithromycin has been very heavily prescribed for many years, and therefore has been experiencing growing resistance.

In the Phase III studies, post-treatment cultures were negative on day six in 88.5% of azithromycin-treated eyes vs. 66.4% of vehicle-treated eyes. When success was defined in more clinically relevant terms (i.e., discharge and conjunctival hyperemia), 63.1% of azithromycin-treated eyes (vs. 49.7% of placebo-treated eyes) were cured at day six. As an aside, this is generally why we often treat bacterial conjunctivitis with a combination drug, such as Zylet, TobraDex or generic Maxitrol—such drugs address both the infection and the associated inflammation.

If the patient has an allergy to erythromycin—the prototypic macrolide—then avoid use of any other macrolide, such as azithromycin.

AzaSite 1% ophthalmic solution comes in a 5ml bottle containing 2.5ml of the medicine. It is preserved with a low concentration (0.003%) BAK. It is a Pregnancy B drug, and is approved for patients as young as age 1.

So, in the ocean of antibiotics, there is yet another fish in the sea. Whether AzaSite performs in a manner beneficial to our patients, or fills a special niche, will only become known after a year or two of widespread clinical use. At least initially, we plan to use AzaSite to treat pediatric bacterial conjunctivitis and mild to moderate cases of adult bacterial conjunctivitis.

A final note: Since chlamydial conjunctivitis is an ophthalmic expression of systemic disease, this condition must be treated with the *oral* form of azithromycin.

Chloramphenicol

This agent achieves bacteriostasis by inhibiting protein synthesis. It is available in both solution (0.5%) and ointment (1%) form. It is effective against a broad spectrum of bacteria, but is not active against *Pseudomonas*. Because it is lipid-soluble, it has excellent penetration through the cornea.

However, a few cases in the literature implicate chloramphenicol in aplastic anemia deaths, and some believe that even the small, topical doses in ocular therapy could trigger bone marrow aplasia in genetically susceptible individuals.

Because there are many good alternatives, it might be difficult to defend a malpractice suit arising from complications due to this drug. While it is a very good drug in a wide variety of ocular infections, for medico-legal reasons, we never use it. However, note that chloramphenicol is the workhorse ophthalmic antibiotic in Europe and Australia, being successfully prescribed over a million times a year. Chloramphenicol is marketed by several companies.

Erythromycin

Erythromycin, which is also bacteriostatic, works by inhibiting protein synthesis. The topical form is effective against many gram-positive and some gram-negative organisms. However, if used over several days, staphylococcal resistance may develop. The drug is only available as 0.5% ointment. For these reasons, erythromycin is not a drug of choice for active therapy.

However, because it is so gentle, it is an excellent prophylactic antibacterial when pressure patching corneal abrasions. Furthermore, any time there is corneal compromise from virtually any condition, where both lubrication and antibacterial prophylaxis are desired, erythromycin is an excellent choice.

Erythromycin ophthalmic ointment is commonly used in labor and delivery suites for neonatal prophylaxis. Topical erythromycin was most commonly known by its original brand name **Ilotycin**, by Dista. Erythromycin ophthalmic ointment is now generically available from numerous manufacturers in a 1/8oz. tube and in a 1g unit-dose tube.

Is Chloramphenicol OK After All?

In 1982, a landmark article was written by F.T. Fraunfelder linking aplastic anemia deaths to topical ophthalmic chloramphenicol.[1] This effectively killed the chloramphenicol market in the United States.

This same author revisited the topic in January 2007.[2] Newer information revealed that high-performance liquid chromatography does not detect chloramphenicol in the blood. This drug is heavily prescribed in Ireland, England, Australia, and the Far East. Indeed, it is, "one of the most widely prescribed topical antibiotics in the world."[2]

Regarding a link between aplastic anemia and chloramphenicol, the expert assessment is "probable;" however, there is no proof of causality. The general guideline: Do not use chloramphenicol if there is a personal or family history of blood dyscrasia.

In summary, chloramphenicol is, "efficacious, affordable, broad spectrum, and very rarely causes blood dyscrasias."[2]

1. Fraunfelder FT, Bagby GC Jr, Kelly DJ. Fatal aplastic anemia following topical administration of ophthalmic chloramphenicol. Am J Ophthalmol 1982 Mar;93(3):356-60.
2. Fraunfelder FW, Fraunfelder FT. Scientific challenges in postmarketing surveillance of ocular adverse drug reactions. Am J Ophthalmol 2007 Jan;143(1):145-149. Epub 2006 Nov 13.

New Perspectives on Fluoroquinolones

While methicillin has not been used clinically for many years, it is the gold standard for in vitro efficacy in the setting of highly resistant strains of *Staphylococcus aureus*, a common ocular pathogen. A growing concern within the infectious disease community, as well as the eye-care community, is a bacterial pathogen widely known as MRSA (methicillin-resistant *Staphylococcus aureus*).

An article in the November 2006 *American Journal of Ophthalmology*, "In Vitro Activity of Fluoroquinolones, Vancomycin, and Gentamicin Against Methicillin-Resistant Staphylococcus Aureus Ocular Isolates," provided an updated perspective on this issue.[1] Following are quotes (and/or in-context paraphrases) from this excellent and timely article:

- "Alarmingly, ocular bacterial isolates are exhibiting increasing resistance to ophthalmic fluoroquinolones. … The present study data demonstrate that ocular surface MRSA isolates have a relatively high percent of in vitro resistance to the fourth-generation of fluoroquinolones." These isolates "were nearly universally susceptible to vancomycin and gentamicin."
- "One of the limitations of many ophthalmic studies that look at antibiotic efficacy is that standard routine antibiotic susceptibility values and susceptibility interpretations reported from the clinical microbiology laboratory are based on the achievable blood serum concentrations of the antibiotic. These values may not be directly relevant to topically-applied ophthalmic antibiotic preparations. It is known that direct application of topical agents to the eye surface initially provides high concentrations of the agent but that these levels are generally dissipated rapidly from the tear film."
- "It is possible that antibiotic resistance determined by standard in vitro MIC (minimal inhibitory concentration) values could be overcome when high levels of an available antibiotic are instilled in topical ophthalmic preparations."
- "Topical fourth-generation fluoroquinolones should not be regarded as an antibacterial panacea … as the devastating effects of rapidly progressive ocular MRSA infection despite treatment with fourth-generation fluoroquinolones have been described."

First and foremost, in most circumstances the fourth-generation fluoroquinolones are indeed highly efficacious when properly administered. The purpose of discussing the topic of resistant organisms is that such infections, while uncommon, do exist; eye doctors need to recognize such events and be prepared to prescribe alternative therapy.

This article appropriately emphasized that laboratory-based in vitro susceptibility testing has limited in vivo application. To wit, it clearly has been shown that topical ophthalmic therapy can readily eliminate bacterial pathogens found to be "resistant" in vitro. The key to successful antibacterial therapy is frequent (usually hourly) instillation of the chosen topical antibiotic, since tear and blinking dynamics rapidly diminish the residence and concentration of the drug.

If you encounter resistance when using a fluoroquinolone, then consider (pharmacy-compounded) vancomycin or an aminoglycoside (commercially available or concentrated via a compounding pharmacy). This has been shown to be highly successful in the setting of MRSA resistance. For perspective, systemic MRSA infections have been shown to be virtually 100% susceptible to systemically-prescribed trimethoprim with sulfamethoxazole (Septra and Bactrim are common brand names); we hypothesize that topical applications of trimethoprim with polymyxin B (Polytrim) could be another useful medicine ophthalmically. We would recommend an aminoglycoside as the alternative drug of first choice because it is readily available, and also "saves" vancomycin for infections where it is the only effective agent.

The article concludes: "MRSA ocular isolates exhibited a relatively high rate of in vitro resistance to all fluoroquinolones tested, including the fourth generation. In contrast, MRSA isolates were found to be highly sensitive to vancomycin and gentamicin."

Bottom line: First, make an accurate diagnosis. Then choose your antibiotic of choice and have it instilled at a dosage frequency deemed appropriate. Last, be prepared to change medicines if you encounter resistance.

Has the use of fourth-generation fluoroquinolones decreased the rate of post-cataract endophthalmitis? A nice article in the April 2007 issue of *Ophthalmology* did not find any change in such events since the advent of these newer antibiotics. The authors were unclear as to exactly why this was the case, but felt that, "The possibility of emerging resistance must be considered."[2]

They went on to say: "It is disconcerting to see a possible trend of bacterial resistance to these agents, as was observed with third-generation fluoroquinolones after their widespread and indiscriminate use."

1. Kotlus BS, Wymbs RA, Vellozzi EM, Udell IJ. In vitro activity of fluoroquinolones, vancomycin, and gentamicin against methicillin-resistant Staphylococcus aureus ocular isolates. Am J Ophthalmol 2006 Nov;142(5):72.
2. Moshirfar M, Feiz V, Vitale AT, et al. Endophthalmitis after uncomplicated cataract surgery with the use of fourth-generation fluoroquinolones: a retrospective observational case series. Ophthalmology 2007 Apr;114(4):686-91.

Gentamicin and Tobramycin

Both of these aminoglycosides are broad-spectrum antibiotics, which are bactericidal by inhibiting protein synthesis. They are most effective against gram-negative bacteria, especially *Pseudomonas* species, but are also effective against most gram-positive bacteria. These drugs are available in solution (0.3%) and ointment (0.3%).

Being aminoglycosides, they can cause allergic reactions similar to those seen with neomycin, but are much less likely to do so.

Aminoglycoside toxicity is legendary, but very uncommon. Clinical signs include epithelial breakdown (superficial punctate keratitis, or SPK), injection in the inferior cul-de-sac, and a weepy erythema and edema of the eyelid tissues. These responses are usually not serious and mostly occur after the drug is used in excess of a week or two. In our years of clinical practice, we have never seen such an occurrence at our hands. For short-term use, these drugs are excellent, cost-effective choices for treating bacterial infections.

One of the practical advantages of these drugs is their generic availability. This has allowed us to prescribe a highly effective antibiotic when expense to the patient was of particular concern.

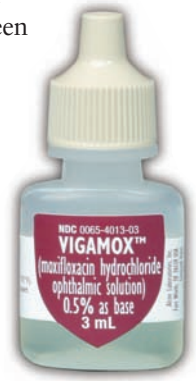
Fluoroquinolones

Just as prostaglandins reign supreme in the care of glaucoma, and steroids reign supreme in inflammation control, so do the fluoroquinolones enjoy near-absolute dominance in managing bacterial infections, particularly of the cornea.

There are, for all practical considerations, five ocular fluoroquinolone solutions:

- **Ciloxan** (ciprofloxacin 0.3%, Alcon and generic)
- **Ocuflox** (ofloxacin 0.3%, Allergan and generic)
- **Quixin** (levofloxacin 0.5%, Vistakon Pharmaceuticals)
- **Vigamox** (moxifloxacin 0.5%, Alcon)
- **Zymar** (gatifloxacin 0.3%, Allergan)

All of these drugs perform very similarly, with the two 8-methoxy fluoroquinolones (Vigamox and Zymar) outperforming the others against certain gram-positive organisms. The absolute key in using any topical antibiotic is "frequency of administration" of the eyedrop. Dosing every few minutes initially (for severe infections) or hourly (for moderate infections) achieves sufficiently high minimum inhibitory concentrations (MIC) to achieve bacterial control in virtually all cases. Then once clinical control has been achieved, decreasing the dosing frequency for a few more days generally assures a complete clinical cure. Never taper an antibiotic below q.i.d. as such potentially subtherapeutic levels could foster development of resistance. The ultimate key in preventing resistance is simply to avoid using any antibiotic unless there is a clear indication to do so.



Since the 8-methoxy fluoroquinolones are the rage these days, we will dissect them here:

Vigamox	Zymar
• 0.5% concentration	• 0.3% concentration
• pH of 6.8	• pH of 6.0
• Non-preserved	• BAK-preserved
• 3ml transparent bottle	• 5ml opaque bottle

Both are absolutely excellent drugs, with Vigamox preferred by a nose; mostly because of proven enhanced penetration.[2,3] There is also an increasing trend to migrate toward preservative-free products, and away from BAK when there is an option.

In summary, when faced with a moderate to severe bacterial eye infection, use Zymar or Vigamox, and use it aggressively. Lastly, do not lose sight of the fact that bacterial eye infections in adults are uncommon events. Know your diagnostic target before you select your armament! ■

1. Solomon R, Donnenfeld ED, Perry HD, et al. Methicillin-resistant Staphylococcus aureus infectious keratitis following refractive surgery. Am J Ophthalmol 2007 Apr;143(4):629-34.
2. Solomon R, Donnenfeld ED, Perry HD, et al. Penetration of topically applied gatifloxacin 0.3%, moxifloxacin 0.5%, and ciprofloxacin 0.3% into the aqueous humor. Ophthalmology 2005 Mar;112(3):466-9.
3. Kim DH, Stark WJ, O'Brien TP, Dick JD. Aqueous penetration and biological activity of moxifloxacin 0.5% ophthalmic solution and gatifloxacin 0.3% solution in cataract surgery patients. Ophthalmology 2005 Nov;112(11):1992-6. Epub 2005 Sep 23.

CORTICOSTEROIDS

The epidemiology of eye disorders is largely one of inflammation. For this reason, this class of drugs is the most important to master.

The ability of steroids to suppress inflammation (clinical efficacy) is based on two factors: *potency* (as compared on a mg-per-mg basis) and *bioavailability* (the ability to penetrate into target tissues).

The most clinically effective of the ophthalmic corticosteroids are loteprednol and prednisolone. As such, they enjoy the most widespread use.

Loteprednol

Almost all of the traditional generation corticosteroids are ketone-based formulations. Loteprednol ushered in an entirely new generation of corticosteroids using an ester base. The keystone to this new formulation is that the human body possesses abundant esterases, but has no ketones. Ketone-based steroids such as prednisolone and dexamethasone linger in tissues, which renders good therapeusis but concurrently places patients at risk for undesirable side effects such as posterior subcapsular cataracts and increased IOP. In contrast, ester-based steroids provide a potent anti-inflammatory effect, then enzymatic degradation of the steroid occurs, minimizing the potential for development of adverse side effects.

With all steroids, the key to a clinical cure is frequency of instillation. It is difficult to give specific clinical guidance in written text because the frequency of instillation (and indeed, the steroid prescribed) may vary considerably depending on the nature and severity of the clinical condition. That said, we usually treat most significant inflammatory conditions with **Lotemax** (loteprednol 0.5%, Bausch & Lomb) every hour or two for a few days until the condition comes well under control. We then taper down to q.i.d. for a few days, then b.i.d. for a few days, then stop.

Since Pred Forte is slightly more efficacious than loteprednol, we use Pred Forte to

Topical Corticosteroid Drugs

BRAND NAME	GENERIC NAME	MANUFACTURER	PREPARATION	BOTTLE/TUBE
Maximum Strength Steroids				
Inflamase Forte, and generic	prednisolone sodium phosphate 1%	Novartis	solution	5ml, 10ml, 15ml
Lotemax	loteprednol etabonate 0.5%	Bausch & Lomb	suspension	2.5ml, 5ml, 10ml, 15ml
Pred Forte, and generic	prednisolone acetate 1%	Allergan, and generic	suspension	1ml, 5ml, 10ml, 15ml
Vexol	rimexolone 1%	Alcon	suspension	5ml, 10ml
Moderate Strength Steroids				
eFlone	fluorometholone acetate 0.1%	Novartis	suspension	5ml, 10ml
Flarex	fluorometholone acetate 0.1%	Alcon	suspension	2.5ml, 5ml, 10ml
FML, and generic	fluorometholone alcohol 0.1%	Allergan	suspension	1ml, 5ml, 10ml, 15ml
FML S.O.P.	fluorometholone alcohol 0.1%	Allergan	ointment	3.5g
Pred Mild, and generic	prednisolone acetate 0.12%	Allergan	suspension	5ml, 10ml

treat most cases of uveitis and severe episcleritis. Otherwise, we use Lotemax for the remaining host of ocular inflammatory conditions.

Loteprednol is formulated as an ophthalmic suspension. It is available in two concentrations: 0.5% as Lotemax and 0.2% as Alrex.

Alrex is approved for treating allergic conjunctivitis, and works well for this condition. For most cases of ocular allergy, we initiate therapy with an antihistamine/mast cell stabilizer, such as Patanol. But if there is any evident inflammation (such as conjunctival injection or chemosis), we would unhesitatingly prescribe Alrex (or even Lotemax).

Prednisolone

Studies show that prednisolone has the greatest anti-inflammatory efficacy of all topical ophthalmic steroids, and that prednisolone acetate 1% as **Pred Forte** (Allergan) is the most effective of the topical ophthalmic steroids for the treatment of uveitic and corneal inflammations.[1] It is well suited for treating severe forms of ocular inflammation such as episcleritis, iritis, chemical/thermal burns of the cornea, and other severe ocular inflammatory conditions. Prednisolone in suspension form is the most effective drug for treating iridocyclitis, due to its ability to penetrate the cornea.

As with any steroid, prescribe frequent instillation schedules until the inflammation is under control, then begin to taper the therapy based upon the nature of—and the response of—the individual condition.

Prednisolone eye drops are available in 1% and 1/8% concentrations, of which the 1% is by far the more clinically useful. No ointment form is available.

Be sure to instruct your patients to shake any suspension formulation prior to each instillation. This instruction should be given verbally as well as indicated on your prescription. Some pharmacists will occasionally dispense a generic product, even if you have signed above "Dispense as Written." Remember that when absolute maximum effect is required, nothing surpasses Pred Forte.

Dexamethasone

In its approved concentration, dexamethasone is less clinically effective than prednisolone and has a greater propensity to raise intraocular pressure, making it a drug of second choice.

It is available in suspension (0.1%) and solution (0.1%). **Maxidex** (Alcon) is the common suspension form of dexamethasone. **Decadron** (Merck) is the common solution. These eyedrops are rarely used in clinical care because of suboptimum efficacy and the potential for undesired side effects.

Fluorometholones

Fluorometholones are a unique class of corticosteroid formulations. They possess good to excellent anti-inflammatory properties, while having a diminished propensity to cause secondary IOP increase.

Why Taper Steroids?

To understand why it's necessary to taper steroids, rather than halt them abruptly, we must first understand the body's system for regulating natural steroids in the bloodstream.

The hypothalamus produces a substance called corticotropic releasing factor, or CRF.

This substance travels to the anterior pituitary and triggers the release of adrenocortotropic hormone, or ACTH. This substance causes the adrenal cortex to up-regulate the production of hydrocortisone and corticosterone, the naturally occurring steroids.

When the level of the natural steroids in plasma increases, the production of ACTH declines. This negative feedback system helps maintain homeostasis of hydrocortisone and corticosterone.

When a patient takes synthetic steroids over a long period of time, the adrenal cortex slows its production of physiologic steroids. This can result in atrophy of the adrenal cortex and even suppression of pituitary function. This is one reason why steroids must be gradually tapered—it gives the adrenal cortex time to start producing the normal level of natural steroids again. To abruptly stop synthetic steroids could potentially leave the body with abnormally low levels of steroids.

Though this phenomenon is more pronounced with systemic steroids, it can occur with topically administered ophthalmic steroids, as well. One study demonstrated that 0.1% dexamethasone sodium phosphate ophthalmic solution, one drop four times a day for six weeks, resulted in a decreased level of the natural steroids.[1] Of course, only rarely would such a protracted dosing schedule be prescribed.

A more important reason for tapering ophthalmic steroids is the rebound effect of local inflammation. Remember that steroids suppress, but do not resolve, the underlying inflammation. Abruptly discontinuing topical steroids may allow the suppressed inflammation to bounce back. A good rule of thumb: taper dosage frequency by about a 50% reduction once inflammation control is achieved. One example: q1h for two days; q2h for two days; q.i.d. for four days; b.i.d. for four days. Or, q.i.d. for one week, then b.i.d. for four more days.

1. Krupin T, Mandell AI, Podos SM, Becker B. Topical corticosteroid therapy and pituitary-adrenal function. Arch Ophthalmol 1976 Jun;94(6):919-20.

There are two formulations of fluorometholone, the alcohol and the acetate. Both are useful in some primary inflammatory conditions.

• ***Fluorometholone alcohol***. This product is a good, moderate-strength ophthalmic suspension. It is used very commonly to treat a host of mild to moderate ocular surface inflammatory conditions. It is also a rational choice in treating chronic inflammations requiring long-term (beyond three to four week) therapy such as low-grade chronic iridocyclitis, and some cases of ocular allergy. Its usefulness in chronic care lies in its reduced tendency to cause secondary IOP increase. Although chronic use of any steroid can result in increased IOP, the fluorometholone class of steroids is less likely to do so than traditional ketone-based products.

Fluorometholone alcohol is available in both 0.1% and 0.25% sus-

Relative Clinical Efficacy of Steroids

Here, based on our clinical experience and the comparative information we have available, we grade the relative efficacy of the topical steroids:

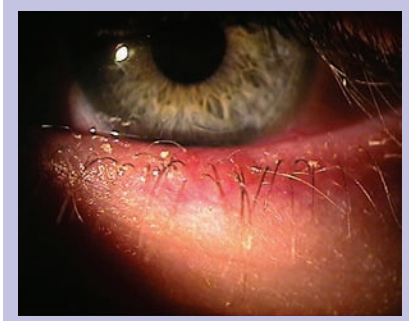
Hydrocortisone 1%	1
Prednisolone 1/8%	2
Medrysone 1%	2
Loteprednol 0.2%	2.5
Fluorometholone alcohol 0.1%	3
Dexamethasone 0.1%	4
Fluorometholone acetate 0.1%	4
Rimexolone 1%	4.5
Loteprednol 0.5%	4.5
Prednisolone 1%	5

Anti-inflammatory Therapy for the Eyelids

The two most common eyelid inflammatory conditions are anterior blepharitis and eczematoid contact blepharodermatitis. Regarding blepharitis, the cutaneous tissues of the external aspect of the eyelid may or may not be inflamed; that is determined by clinical observation—are the tissues the normal skin coloration, or is there obvious redness to these tissues? The more important question is, what is the best way to restore these tissues to normal?

STAPHYLOCOCCAL BLEPHARITIS

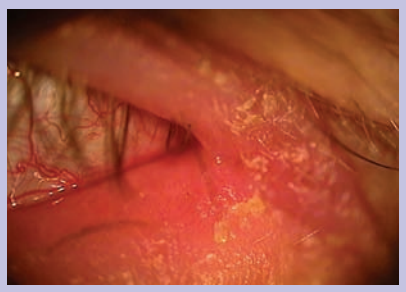
Staphylococcal species can produce exotoxins that cause tissue inflammatory responses, while seborrheic blepharitis generally does not evoke significant cutaneous response. The staph exotoxins can produce general cutaneous erythema (and, to a lesser extent, edema). In advanced cases, the exotoxins can also lead to ulcerative blepharitis.



Most cases of staphylococcal blepharitis result in significant eyelid inflammation, which can be treated with an antibiotic/steroid combination.

The two-pronged approach to treating staphylococcal blepharitis is to use a combination antibiotic/steroid ointment, such as **TobraDex** (tobramycin/dexamethasone, Alcon). This therapeutic approach accomplishes two goals: it minimizes resident staph populations; and it simultaneously suppresses the associated tissue inflammation. When expense is a concern, a generic equivalent of **Maxitrol** (neomycin/polymixin B/dexamethasone, Alcon) ophthalmic ointment can be prescribed.

Have patients with problematic staph blepharitis rub the prescribed ointment in the eyelid margins twice daily for two to five days, then just at bedtime for one to three more weeks. For cosmetic concerns, recommend a light application in the



Tissue inflammation, as evidenced by 'angular blepharitis,' can be healed with an antibiotic/steroid combination.

mornings, and then a more liberal application at bedtime. Carefully educate patients as to the target tissues, and use your finger or a cotton swab to show exactly where the eyelid margin is. Provide this demonstration in addition to verbal direction: "right along the base of the eyelashes where they come out of the eyelid."

Lid scrubs can, and should, be a major component to the control of both staphylococcal and seborrheic blepharitis. Some doctors employ these scrubs initially; others get the tissues under control medically, then introduce lid scrubs as a hygienic maneuver to maintain the health of the eyelid tissues long-term. We have been impressed with eyelid cleaners, such as **SteriLid** (Advanced Vision Research), and have now largely abandoned use of baby shampoos. We have heard of many misadventures with baby shampoos, and are glad to have these newer, blepharitis-specific eyelid hygiene products available for our patients.

CONTACT BLEPHARODERMATITIS

Now let's turn our attention to the itchy and/or irritated eyelid. With very rare

exception, these patients are women. Contact blepharodermatitis, or eczematoid blepharodermatitis, is most commonly a delayed, type 4 hypersensitivity reaction to some substance. The most common offender seems to be the formaldehyde breakdown products of eyelid cosmetics, particularly fingernail polish. Contact blepharodermatitis is also seen with neomycin, poison oak/ivy, and various other, often idiopathic, sensitizing agents.

Contact blepharodermatitis can be easily treated with topically-applied corticosteroid formulations, such as triamcinolone or fluorometholone.

There can be tissue erosion as evidenced by lateral canthal maceration and irritation. All these eyelid afflictions are the result of tissue inflammation, and naturally respond to topical corticosteroid suppression. There are numerous such corticosteroid medications available. We choose to keep our clinical toolbox simple, so we have two workhorses for these conditions:

• ***FML (fluorometholone, Allergan) ophthalmic ointment***. This is the only standalone ophthalmic corticosteroid available. FML works well clinically, but has three limiting factors: it is expensive; it comes only in a 1/8oz. tube; and is available only as an ointment (as opposed to a lotion or cream). The 1/8oz. size is generally sufficient to treat most cases of eyelid dermatitis, however.

• ***Triamcinolone cream***. Our favorite by far is the "non-ophthalmic" drug, triamcinolone. This is a low- to moderate-potency corticosteroid that has three advantages: it is inexpensive as a generic; it comes in a large, 4oz. tube; and is available as an ointment, lotion, and cream. It is available in three concentrations—0.025%, 0.1%, and 0.5%. We chose to prescribe the 0.1% concentration early on and have stayed with it because of its excellent clinical performance. Our female colleagues advised us to use a cream vehicle, so we always prescribe triamcinolone 0.1% cream when anti-inflammatory therapy is indicated.

Whether to prescribe FML ophthalmic ointment or 0.1% triamcinolone cream is a very practical decision. If the patient is new, or in any way appears potentially particular, hard to please, questioning, or apprehensive, we prescribe FML. If, on the other hand, the patient is well known to the practice, has a trusting relationship with us, and is rational and reasonable, then we prescribe triamcinolone cream.

As a non-ophthalmic formulation, the triamcinolone tube has, in standard-sized font, a statement saying: "not for ophthalmic use." We have even had pharmacists tell patients, "You're not supposed to use this near your eyes." To quell any uncertainty about this on the patient's part, we are always proactive in telling our patients for whom we prescribe triamcinolone about this statement, and reassure them we have successfully used the medication with hundreds of our patients over the years. We have never had any problem in any way whatsoever with this approach. It is a sound, rational, well-proven, cost-effective treatment for achieving tissue restoration in patients with clinically significant inflammatory conditions of the eyelid skin.

You may ask, "But what about thinning of the eyelid skin with steroid use?" Steroid preparations certainly have the potential to cause thinning, but in our 50-plus combined years of clinical practice, we have never seen this occur with 0.1% triamcinolone cream. Two main reasons for skin thinning are: use of "high-potency" formulations (which this is not), and/or prolonged or repeated use. We never prescribe high-potency corticosteroids (such as betamethasone), and we advise the patient not to continue use of the medication for longer than the prescribed time. Although triamcinolone comes in a 4oz. tube, we carefully inform our patients to use the medicine "as directed," i.e., two or three times a day for three to four days, then just at bedtime for four to six more days.

To repeat: We have had excellent success using this approach, and are excited that such an easy, simple, cost-effective medicine is available. While OTC hydrocortisone may work well for very mild cases of blepharodermatitis, for the cases we see in our offices, we always prescribe FML or triamcinolone 0.1% cream.

What about steroid-sparing therapy such as Protopic (tacrolimus, Astellas Pharma) or Elidel (pimecrolimus, Novartis)? These agents are broadly macrolide immunosuppressants. They work by inhibiting T-lymphocyte activation. These drugs are approved as "second-line" therapy for mild to moderate atopic dermatitis. Via expert opinion we have obtained from our colleagues in the dermatologic community, these preparations do not perform as effectively as corticosteroid preparations. But, they are occasionally used when long-term dermatitis suppression is indicated. Bottom line, we see little or no reason to prescribe these agents in light of the excellent success we have had with time-honored, traditional approaches as we have just described.

In summary, the care of patients with anterior blepharitis and contact/eczematoid blepharodermatitis is straightforward, and is easily treated with conventional medical approaches. In the case of blepharodermatitis, should the patient exhibit multiple recurrences, consider a consult with an allergist or dermatologist.

Regarding posterior blepharitis (meibomitis), warm soaks followed by eyelid massage are good initial approaches. A three- to nine-month course of oral doxycycline (or minocycline) may be needed to achieve success if initial methods fail. We generally prescribe a 50mg tablet once daily, and monitor the patient every three months until clinical control is achieved.

pensions, and 0.1% ointment. The 0.25% suspension offers little, if any, clinical advantage over the 0.1%, and is rarely used. These are marketed under the brand name **FML** (Allergan), and are also available generically.

• ***Fluorometholone acetate***. This is the more clinically active form of the more familiar FML. Fluorometholone acetate is marketed as **Flarex** ophthalmic suspension (Alcon), and **Eflone** ophthalmic suspension (Novartis Ophthalmics), and is available generically. The acetate formulation confers upon fluorometholone greater clinical efficacy (which may or may not be needed for each individual case), while still enjoying the relative IOP-sparing effect of the fluorometholones. Its clinical effectiveness is about midway between FML and 1% prednisolone acetate.

The Very Few Steroid Contraindications

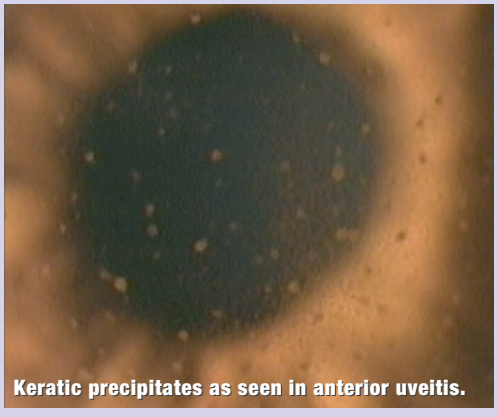
• *Herpes simplex infectious epithelial keratitis*. However, steroids are often indicated when managing stromal immune forms of herpetic keratitis.

• *Acute bacterial infections*. The only exception: when treating bacterial infections and there is much associated inflammation. In this case, a good combination antibiotic/steroid such as Zylet or TobraDex is often a wise choice.

• *Significant epithelial compromise*. Again, the only exceptions are cases in which the breach of epithelial integrity is the result of inflammation. Here, a good combination antibiotic/steroid may be needed to potentiate re-epithelialization.

Steroid Indications

Below are examples of when steroids may be indicated:


Keratic precipitates as seen in anterior uveitis.

- Iritis, iridocyclitis
- Episcleritis
- Chemical trauma
- Corneal infiltrates
- Angular blepharitis
- Peripheral corneal erosions
- U.V. keratitis
- Phlyctenulosis
- Contact blepharodermatitis
- Glaucomatocyclitic crisis
- Vernal keratoconjunctivitis
- Thygeson's superficial punctate keratitis
- Stromal keratitis
- Epidemic keratoconjunctivitis
- Uveitic glaucoma
- Ocular trauma
- Staphylococcal exotoxin blepharoinflammation
- Postoperative care
- Eczemoid blepharitis
- Corneal microcystic edema

… and a host of other nonspecific ocular inflammatory conditions.

The indications for this product are essentially the same as for the other corticosteroids. It is generally wise to adhere to recognized "community standards of care" in drug selection. Keep this medico-legal principle in mind when using any drug.

Rimexolone

Rimexolone is a potent, relatively safe preparation and is close to—but not as efficacious as—1% prednisolone acetate; yet its decreased propensity to raise intraocular pressure is very similar to that of the fluorometholones. It is marketed as **Vexol** 1% ophthalmic suspension (Alcon).

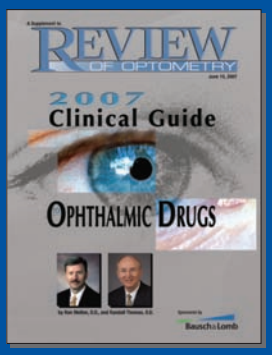
The uniqueness of Vexol is that it is the first steroid to be approved by the FDA for postoperative inflammation control. (Pred Forte is the gold standard for this purpose, yet has no FDA indication for such a use.) Rimexolone is also approved for the treatment of anterior uveitis.

In summary, corticosteroids are the mainstay of medical therapeutics in office-based eye care. At least 80% of the prescriptions we write within the context of acute eye care are for a steroid or combination antibiotic-steroid medicine. It is not that we have a particular love for steroids, but we greatly enjoy seeing our patients with acute red eye recover quickly.

Nothing achieves this goal better than a corticosteroid medication when the condition is inflammatory in nature. ■

1. Leibowitz HM, Kupferman A. Antiinflammatory Medications. In: Holly FJ, ed. Clinical Pharmacology of the Anterior Segment. Int Ophthalmol Clinics 1980;20(3):117-134.

Current Therapy in Ocular Disease



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CLINICAL CASES FOR COMBINATION DRUGS

Perhaps half of all inflamed eyes require a combination drug, rather than an antibiotic or steroid alone.

This class of ophthalmic drugs is highly useful and rivals the pure topical corticosteroids in the treatment of the acute red eye. As with most drugs, there are clear indications and clear contraindications, with a gray zone in between.

In order to prescribe a combination drug with clinical precision, one has to have a masterful understanding of both antibiotics and corticosteroids. As many as half of all red eyes that we see are treated with a combination drug, rather than either a steroid or antibiotic alone. This observation clearly acknowledges two clinical realities:

- The need for topical antibiotics alone is relatively low, and
- Almost all acute red eyes have a significant inflammatory component.

So, how does the astute clinician choose between a pure steroid and a combination drug? The answer is relatively straightforward, but, as always, there are exceptions to generalizations. The pivotal issue is the integrity of the corneal epithelium. If the corneal epithelium is intact, there is little or no reason for prophylaxis against opportunistic bacterial pathogens. This is because an intact epithelium is itself a firewall of defense. If there is significant epithelial compromise, then a combination drug may perfectly match the clinical need.

Corticosteroid/Antibiotic Combination Drugs

BRAND NAME	MANUFACTURER	STEROID	ANTIBIOTIC	PREPARATION	BOTTLE/TUBE
Blephamide	Allergan	prednisolone acetate 0.2%	sodium sulfacetamide 10%	susp./ung.	2.5ml, 5ml, 10ml/3.5g
Cortisporin	Monarch	hydrocortisone 1%	neomycin 0.35%, polymyxin B 10,000u/ml	suspension	7.5ml
Dexacidin	Novartis	dexamethasone 0.1%	neomycin 0.35%, polymyxin B 10,000u/ml	suspension	5ml
FML-S	Allergan	fluorometholone 0.1%	sodium sulfacetamide 10%	suspension	5ml, 10ml
Isopto-Cetapred	Alcon	prednisolone acetate 0.25%	sodium sulfacetamide 10%	susp./ung.	5ml, 15ml/3.5g
Maxitrol	Alcon	dexamethasone 0.1%	neomycin 0.35%, polymyxin B 10,000u/ml	susp./ung.	5ml/3.5g
NeoDecadron	Merck	dexamethasone 0.1%	neomycin 0.35%	solution	5ml
Poly-Pred	Allergan	prednisolone acetate 1%	neomycin 0.35%, polymyxin B 10,000u/ml	suspension	5ml, 10ml
Pred-G	Allergan	prednisolone acetate 1%	gentamicin 0.3%	susp./ung.	2.5ml, 10ml/3.5g
TobraDex	Alcon	dexamethasone 0.1%	tobramycin 0.3%	susp./ung.	2.5ml, 5 ml/3.5g
Vasocidin	Novartis	prednisolone sodium phosphate 0.25%	sodium sulfacetamide 10%	solution	5ml, 10ml
Zylet	Bausch & Lomb	loteprednol 0.5%	tobramycin 0.3%	suspension	2.5ml, 5ml, 10ml

Remember that the conjunctiva will be inflamed in any patient presenting with an acute red eye. Simply put, the eye is red because it is inflamed. Also, the conjunctiva will be inflamed in almost all cases in which keratitis is present. With either keratitis (with an intact epithelium) or non-infectious conjunctivitis, we almost always use a topical steroid.

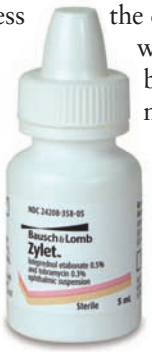
If the accurate diagnosis of bacterial conjunctivitis is made, the decision is whether to prescribe an antibiotic or a combination drug. The prime determinants are twofold:

1) the severity of the infection, and

2) the degree of conjunctival injection.

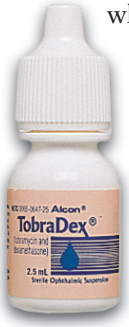
If the infection presents with marked mucopurulence, we would likely treat with a pure antibiotic, such as moxifloxacin (and perhaps even culture if the infection was severe). If the infectious expression was only mild to moderate, the degree of conjunctival injection would be the overriding issue in choosing between an antibiotic and a combination drug such as **Zylet** (loteprednol/tobramycin, Bausch & Lomb), **TobraDex** (dexamethasone/tobramycin, Alcon), or **Maxitrol** (dexamethasone/neomycin/polymyxin B, Alcon). We stress again that bacterial infection is uncommon, especially relative to the numerous expressions of non-infectious conjunctivitis.

An exception is the patient who presents with what appears to be a low grade bacterial conjunctivitis (i.e., minimal discharge), yet with moderate to marked conjunctival injection. The patient usually complains that the affected eye was "stuck together when I woke up." Commonly, by the time the patient arrives at your office, any excess debris may have been cleaned from the lids and lashes. Further, blinking has moved considerable mucopurulent debris down the naso-lacrimal system so that the objective slit lamp findings reveal only minimal microparticulant debris in the lacrimal lake; a clear, non-staining cornea; and/or a red eye. Here is where a combination product is used mainly to address the conjunctival inflammation, while concurrently eliminating any infectious component, even when the cornea is uninvolved. When there is significant corneal epithelial compromise, we almost always use a combination drug. For most cases, the choice of drug class is that simple.



The first blockbuster, highly effective combination antibiotic/corticosteroid was Maxitrol, containing neomycin, polymyxin B and dexamethasone. Maxitrol became a real workhorse in primary eye care. However, the occasional neomycin reaction, while not a major issue, prompted investigation into a "new and improved" combination drug.

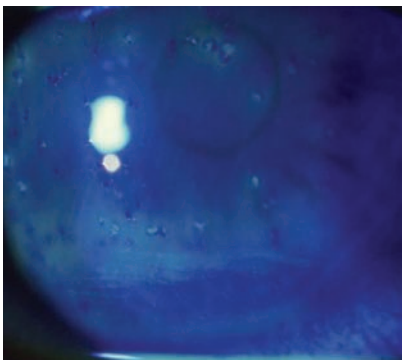
Thus was born TobraDex, which replaced the neomycin and polymyxin B with tobramycin. This drug, like Maxitrol, enjoyed market dominance, though from time to time, and again not a major issue, intraocular pressure increases prompted an investigation into a "new and improved" combination drug.



Thus was born Zylet. Keeping the highly efficacious tobramycin, the dexamethasone was replaced with a newer generation, ester-based corticosteroid, loteprednol. Now with Zylet, we have excellent antibiosis along with the safety and potency of loteprednol. It is available in 2.5ml, 5ml and 10ml bottles.

Now that we have 90% of this topic covered, we need to spend the bulk of this article discussing other various exceptions and modifications to this rather simple decision tree. The best way to teach the concepts for drug class choice is perhaps by looking at a few specific clinical entities:

Thygeson's Superficial Punctate Keratopathy (SPK). This not-so-uncommon keratitis is seen in young to middle-aged patients. The classic symptoms are foreign body sensation, photophobia and lacrimation. This idiopathic condition has cycles of exacerbation and remissions over the course of 10 to 20 years, until it finally abates. It is during these exacerbations when symptoms prompt the patient to seek medical attention. This usually



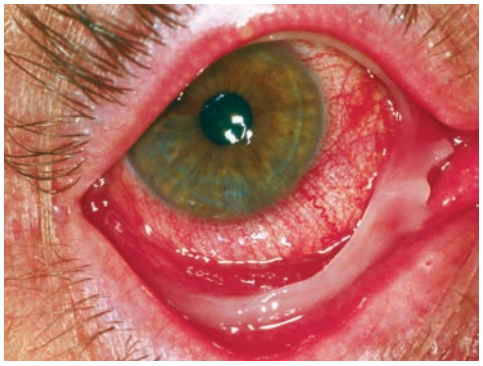
A classic presentation of the corneal staining pattern of Thygeson's SPK. (The fellow eye was nearly identical.) This is one of the unusual cases of keratitis in which a modestly-potent corticosteroid, such as Alrex (q.i.d. for one week; b.i.d. for one to two more weeks), quickly brings resolution in most cases.

bilateral keratitis shows several tiny, usually central, subtle (but readily seen) staining defects with fluorescein dye. (Note that about 20% of cases are unilateral, so differentiating Thygeson's from herpes simplex must be done; here is where corneal sensitivity testing can be useful. Also, the Thygeson's eye will generally be white, or minimally injected, whereas the herpetic eye will generally be considerably injected.)

If the patient is significantly symptomatic, a topical corticosteroid readily suppresses the keratitis and its attendant symptoms. If the presenting symptoms are tolerable, then artificial tears and patient education are likely all that is needed. However, the teaching point here is that even though there is some punctate staining in acute Thygeson's SPK, all that is needed is a topical steroid. This is the uniform recommendation in authoritative textbooks.

While 1% concentrations of topical steroids are indicated in most inflammatory eye conditions, Thygeson's is steroid sensitive. Therefore, our drug of choice in these cases is Alrex (loteprednol 0.2%, Bausch & Lomb). We generally treat symptomatic patients q.i.d. for one week, then b.i.d. for one to four weeks, until the phase of exacerbation subsides. Artificial tears complement virtually all acute ocular surface conditions, but there is no need for an antibiotic.

Epidemic Keratoconjunctivitis (EKC). If the EKC is severe, and especially if tarsal conjunctival membranes have formed, there can be epithelial compromise. The key here is to physically peel away these membranes, as they exert toxic and mechanical trauma to the epithelium. Be sure to wear gloves when performing this procedure, as minor bleeding often results.



Development of thick membranes can be seen in more advanced cases of EKC. After instillation of topical anesthetic, these membranes (note both superior and inferior tarsal) were peeled away with minimal bleeding. Zylet was then used q2h for two days, then q.i.d. for four days.

These membranes are a marker of intense inflammation, and as such, corticosteroid therapy is of paramount importance. We generally use Lotemax (loteprednol 0.5%, Bausch & Lomb) q.i.d. for a week. By the end of this period, natural healing will likely have occurred and the steroid can be stopped, or tapered to b.i.d. for a few more days. While a combination drug, such as Zylet, TobraDex or generic Maxitrol, could be used here, we almost always use a pure topical steroid. Aminoglycoside toxicity on an already toxic ocular surface is probably not a practical concern, but could be in instances in which the patient has concurrent dry eye.

In many advanced cases of EKC, subepithelial infiltrates (which do not stain) can develop. When these cause symptomatic, visual compromise, a steroid will readily clear this unique, immune keratitis. This generally requires two to four months of tapering therapy. Our routine has been to use Lotemax q.i.d. for one month, t.i.d. for one month, b.i.d. for one month, and then once-daily for one month. It usually takes two to four months for sufficient viral antigen to be physiologically leeched from stromal residence. So when the steroid taper is completed, any small infiltrates that might reform should be symptomatically minimal, or silent.

Of note, antibiotics and combination drugs have little or no role in treating patients with adenoviral infections because concurrent bacterial infection is exceedingly rare.

For several years now, we have successfully treated symptomatic patients with acute, grade II or higher EKC with a 60-second treatment of 5% Betadine Sterile Ophthalmic Prep Solution (povidone/iodine, Alcon) followed by ocular surface lavage. This accomplishes two objectives. First, eradication of the bulk of the adenoviral load has-

Pearls for Using Combination Drugs

- Anytime you see any process at or near the limbus, it is inflammatory in nature. Herpetic infection can present at this area, but will typically be linear (as opposed to oval) in morphology.
- In any acute, unilateral red eye with a serous discharge, be sure to rule out herpetic keratitis.
- Never (or rarely) taper combination drugs below q.i.d. because subtherapeutic levels of antibiotic set the stage for antibiotic resistance.
- In the context of a red eye with a mild secondary iritis, instill a short-acting cycloplegic agent, particularly if a pure antibiotic is used. A combination product will generally eliminate such an iritis without the need for a cycloplegic, though this is a fine clinical point.

tens acute symptomatic recovery. Second, since the virus particles residence time has been considerably truncated, the potential for viral antigenic (stromal immune) keratitis is largely pre-empted.

Note: since Betadine stings, always pre-treat the cornea with a drop of proparacaine. Furthermore, to diminish any patient discomfort, we generally instill a drop or two of Voltaren (diclofenac sodium, Novartis Ophthalmics) or Acular LS (ketorolac tromethamine, Allergan) before, and again after the treatment.

Following the in-office treatment as described above, we always prescribe Lotemax, usually q.i.d. for four to six days, to dampen or eliminate any residual inflammatory keratoconjunctivitis.

Herpes Simplex Keratitis (HSK). Here is another condition that commonly demonstrates considerable epithelial compromise.

Since corticosteroids cause local immunosuppression, their use is contraindicated—an exceedingly

Contact Lens-Associated Keratitis

Confusion abounds in eye care regarding the diagnosis and treatment of contact lens-related keratitis, although in most cases, these clinical presentations are rather straightforward. Of course, our greatest concern is vision loss from a central bacterial corneal ulcer. The good news is that such ulcers are exceedingly rare. The problem, however, is threefold: 1) corneal infiltrates are quite common occurrences; 2) there is a lot of uncertainty among eye doctors as to the differentiation of corneal lesions; and 3) the ever-looming concern, "Is this the beginning of a potentially vision-threatening ulcerative process?" This last point is particularly worrisome when a positive epithelial defect is present.

Corneal hypoxia is the most common cause of corneal infiltrative events, but with the advent of the super oxygen-permeable silicone hydrogel lenses, we hope to see a dramatic decrease in the hypoxic-related keratitis.

Hypoxia can result in a cascade of events that result in leukocytic chemotaxis into the anterior stromal tissues. Once ample leukocytic recruitment occurs, exocytotoxic chemicals can lead to retrograde demise of some of the overlying epithelium as evidenced by a positive fluorescein staining defect. It is these circumstances that lead many doctors to erroneously assume the worst and start the patient on a course of topical antibiotics. While this does no harm, it does no more good than simply discontinuing the use of the contact lenses, which, of course, is the first step of treatment for all contact lens-related eye problems. A steroid, in combination with an antibiotic, is perfectly suited to suppress the immune/inflammatory response, while protecting the cornea against any opportunistic bacterial infections.

There are numerous parameters to evaluating the differential diagnosis of leukocytic infiltration (largely from hypoxia) versus stromal opacification lesions (largely from bacterial infection). (*See "Infectious Ulcers vs. Sterile Infiltrates," on page 28A.*)

Let's look at some risk factors for ulcerative keratitis so that we can better quantify the likelihood of such occurrences:

- Poor tear film function
- Uncontrolled staphylococcal blepharitis
- Smoking
- Swimming while wearing contacts (esp. in fresh water)
- Being under age 22 ±

While this is not an exhaustive list, it gives us some red flags by which we can exercise our clinical judgment, and enhance our patient education.

If you truly feel your patient has an infectious lesion, then start them on a fluoroquinolone such as Vigamox or Zymar every 15 minutes for three to six hours, then hourly until bedtime. We have our patients instill generic Polysporin (or Neosporin) ointment at bedtime. Follow your patient daily and modify therapy based on the clinical response.

There is a less intensive approach that can be used if you think your patient has a leukocytic infiltrate, but are still concerned about possible infection. Here, use any fluoroquinolone or aminoglycoside hourly until the patient is seen back the next day to assess the clinical course. In either diagnostic circumstance, (bacterial infection or leukocytic infiltration), improvement will most always be evident, mainly because lens wear has been discontinued.

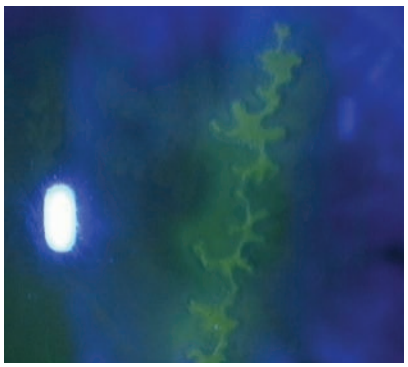
Naïve practitioners who witness such improvement may wrongly deduce that the lesion must have been an infective process, and be glad they used an antibiotic. Once again, infiltrates are very common, and bacterial keratitis is very rare.

The most appropriate therapeutic response to an immune/inflammatory condition (e.g., a leukocytic/sterile infiltrate) is a steroid. Since a small epithelial defect may or may not be present, or clinical judgment may be wrong (if the lesion actually is an early infectious disease process), we always prescribe an antibiotic/steroid combination drug, such as Zylet, TobraDex, or generic Maxitrol to treat these conditions. To this day, tobramycin remains an excellent, broad spectrum bacterial antibiotic.

Prescribe the combination drug to be used q2h for two days, then q.i.d. for four days (mainly to quiet the inflammation and allow the eye to calm down).

Each doctor must evaluate each patient's condition carefully and prescribe with as much precision as possible. As stated at the outset, treatment of contact lens-associated keratitis is rather straightforward in most cases. In ambiguous cases, treat conservatively until the diagnosis becomes clear. For perspective, we have seen less than a handful of cases of microbial keratitis between the two of us.

well-known principle. No authoritative textbook recommends the use of a prophylactic antibacterial agent in such cases. As clinicians, we do not know why the herpetic corneal defect does not invite opportunistic bacterial pathogens; we just know that antibacterial therapy is not needed, unless there is clear evidence of concurrent bacterial infection.



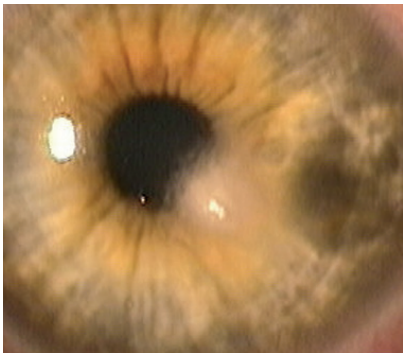
Herpes simplex keratitis

Topical **Viroptic** (trifluridine, Monarch Pharmaceutical), perhaps in conjunction with preservative-free artificial tears, is the only therapeutic intervention warranted for herpes simplex epithelial keratitis. Oral antivirals, such as acyclovir (400mg five times daily for seven days) can be used if there is trifluridine resistance, or if the patient has developed an allergic response to trifluridine.

Corneal Abrasions. Most such defects heal within a day or two, regardless of any therapeutic maneuvers. To our knowledge, no studies have prospectively followed "no treatment" of abrasions, but it would be interesting to know the absolute need for prophylactic antibiotic use, which is standard practice in these situations. We imagine the rate of infectious keratitis would be very small. However, since antibiotics are safe, there is no mandate to take unnecessary risks.

Conservative therapy with antibiotics has evolved into the standard of care for corneal abrasions. There are, however, circumstances—most notably delay in seeking care—in which the abraded eye is considerably inflamed. While fungal infection is always a *rare* possibility if the traumatic agent was vegetative, 99.9% of the time fungus is not a player.

That being said, we have occasionally used a short-acting cycloplegic agent and a combination drug in "hot" eyes with corneal abrasions. The steroid component calms the tissues and thus potentiates corneal re-epithelialization. A further note for the fungal worriers out there: if the delay in seeking care is only two to four days, fungal involvement at this point is unlikely, since fungi are usually slow growing and would take many more days to proliferate to symptomatic proportions.



Fungal (*fusarium*) infection with stromal infiltrate.

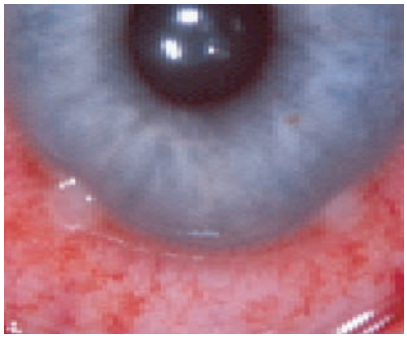
Now, if the patient gives a history of vegetative trauma, and reports that the abrasion initially healed over a day or two, but is now (perhaps a week later) presenting with a hot eye and stromal infiltrates, consider fungal etiology. However, such symptoms are still most likely associated with a cell-mediated immune response to the initial trauma rather than a fungal infection. The salient features of a fungal keratitis are:

- History of corneal injury (vegetative matter)
- Slowly progressive
- Hypopyon in advanced cases
- Not very painful (relatively)
- Feathery border (hyphate-like)
- Slightly raised, dirty-white infiltration
- Satellite lesions
- Partial or complete ring
- Secondary anterior uveitis

For perspective, in our combined 50 years of intense clinical experience, we have seen a grand total of two cases of fungal infection following corneal abrasion, both of which were treated successfully.

If, however, the traumatic vector of the corneal abrasion was inorganic, and there is marked inflammation, a combination product could be considered. More conservatively, use a pure antibiotic a day or two, then if the traumatic keratoconjunctivitis fails to subside or if symptoms worsen, add a steroid.

Phlyctenular Keratoconjunctivitis (PKC). Most usually seen in young girls, this staphylococcal hypersensitivity response commonly targets the limbal tissues as one or two raised, whitish lesions, which stain lightly with fluorescein. Nothing else looks like a phlyctenule.



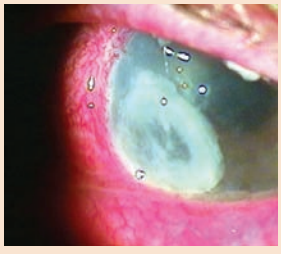
These classic, limbally expressed phlyctenules were treated with Zylet (q2h for two days; then q.i.d. for five days) with quick resolution.

While one would think staphylococcal blepharitis would always be evident, such is not empirically the case. Certainly, if blepharitis is present, initiate proper care, but first treat the inflammatory keratoconjunctivitis. When there is a staining defect at the corneolimbus, a prophylactic antibiotic is counterproductively conservative.

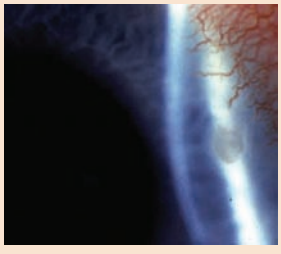
The key clinical feature is the inflammatory component—the eye is red. Here, a combination product is probably wise. Use a combination drug every two hours for a day or two, then q.i.d. for four to six days, and then stop.

Staph. Marginal "Ulcers" (much more appropriately called "peripheral inflammatory epithelial defects"). These are uncommon events that have a similar pathophysiology to PKC and sterile infiltrates. In these cases, the staphylococcal exotoxins begin to erode a section of the peripheral corneal epithelial tissues. The eye is red with accentuation of a sector of bulbar conjunctival inflammation adjacent to the affected cornea. The foci of compromised epithelium

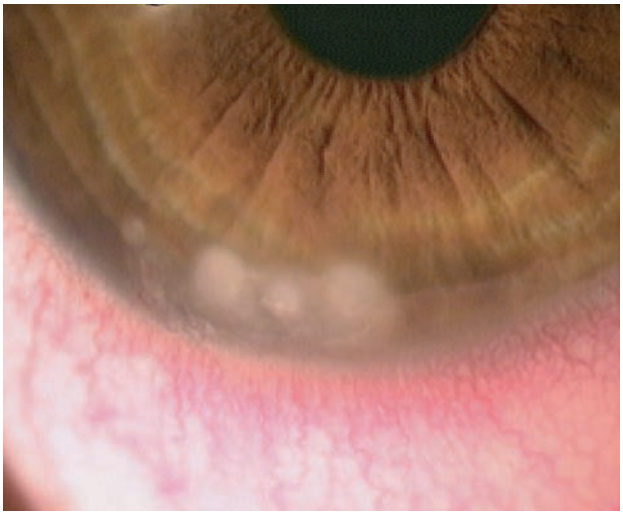
Infectious Ulcers vs. Sterile Infiltrates

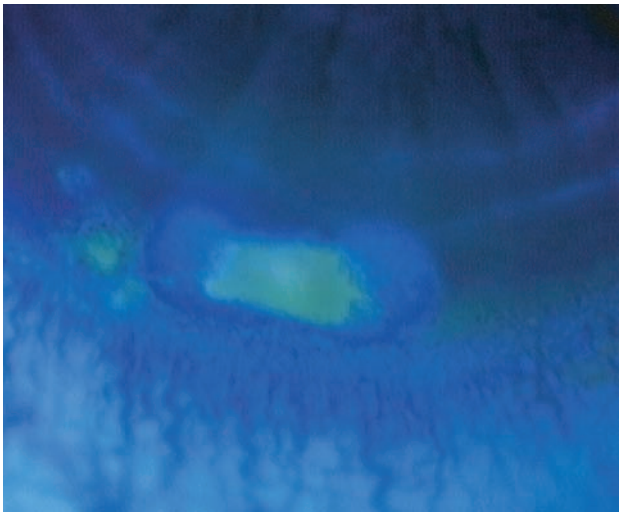


Is it an ulcer or an infiltrate? At left is an infectious ulcer. At right is a sterile infiltrate.



ULCER	INFILTRATE
Rare	Common
Usually painful	Mild pain
Tends to be central	Tends to be peripheral
Size of epithelial staining defect closely mirrors the size of the underlying stromal lesion	Epithelial staining defect size relatively small compared to underlying stromal infiltrate
Cells in anterior chamber	No cells (or minimal cells) in anterior chamber
Generalized conjunctival injection	Sector skewed injection pattern
Usually solitary lesion	Can be multiple lesions
Possible tear lake debris	Clear tear lake





Peripheral anterior stromal infiltrates may or may not exhibit overlying epithelial compromise (as evidenced by positive fluorescein staining). This contact lens wearer presented with a typical 'infiltrate,' which was treated with Zylet (q2h for two days, then q.i.d. for four more days).

stains brightly with fluorescein dye. There may be a few cells in the anterior chamber. The epithelium is broken down as a result of the underlying anterior stromal inflammatory process, thus causing retrograde compromise to the overlying epithelium.

Once this subepithelial inflammation is subdued by the corticosteroid component in a combination drug, re-epithelialization is potentiated. An antibiotic alone in this case is almost worthless. While an antibiotic can serve to protect against opportunistic bacterial potential, it will do nothing to curb the inflammatory process.

As with PKC, a combination product is perfectly suited to address the inflammatory process while simultaneously guarding the cornea against the possibility of bacterial infection. Therapeutic management is as described for PKC.

Keratoconjunctivitis Sicca (KCS). We have all seen dry eye patients with slit lamp-observable, coarse SPK. Also known as punctate epithelial erosions, SPK represents a break in epithelial integrity that theoretically provides a foothold for bacterial adherence and subsequent penetration. Yet, antibiotic intervention is rarely, if ever indicated.

Acknowledging the participation of inflammation in the pathogenesis of many cases of dry eye-related SPK, topical steroid and/or Restasis (cyclosporine, Allergan) therapy is often employed (along with artificial tears, etc.) in the successful management of KCS.

We have never read of an antibiotic role in the management of KCS.

In summary, select a pure antibiotic when the clinical picture is portrayed by evident mucopurulent discharge, or there is evident (or high risk for) corneal infection.

Select a combination drug in the absence of the above two findings when there is mild to moderate epithelial compromise near the limbus along with considerable conjunctival inflammation.

Select a pure steroid if the eye is red and the corneal epithelium is intact. We might default to a combination drug if the patient is a contact lens wearer, but such would depend upon the individual situation.

We have discussed many exceptions to these general guidelines. The primary purpose of this article is to encourage the reader to limit the prescribing of an antibiotic for the gamut of red eyes and recognize that most red eyes are inflammatory in nature.

Most importantly, prescribe with precision! ■

CALL FOR CLINICAL CONUNDRUMS

Got a problematic patient? Having difficulty determining a diagnosis? Can't come to a conclusion on course of therapy? Send your clinical conundrums to Drs. Melton & Thomas at: DrugGuide@jobson.com. They'll publish your question—and their answer—in next year's *Clinical Guide to Ophthalmic Drugs*.

ALLERGY DRUGS

Allergic conjunctivitis prompts many office patient encounters. New and modified anti-allergy drugs provide patient-friendly dosing and over-the-counter availability.

Optometric physicians write roughly equal numbers of prescriptions for anti-allergy medicines as do our surgical counterparts. This is appropriate prescriptive behavior, similar to the observation that primary care physicians write for more allergy medicines than specialty physicians. Slowly but steadily, optometric prescribing is approaching a rational and appropriate level.

New and Revised Drugs

The ocular allergy management landscape has indeed changed in 2007. Alcon has released a higher concentration (0.2%) of olopatadine, marketed as Pataday. It is the first topical antihistamine/mast-cell stabilizing drug to be approved for once-daily dosing.

While once-daily instillation is always a welcome dosing schedule, it will be especially convenient for contact lens wearers because they can instill Pataday a few minutes prior to insertion of the lenses, and then enjoy all day relief.

While the drug is not approved for use with contact lenses, we see no reason why any of the anti-allergy preparations cannot be safely used with either disposable contact lenses or RGP lenses.

Further news on the allergy front is the transformation of ketotifen to over-the-counter medication, which has previously been the prescription product Zaditor. Ketotifen is now available OTC under two brand names: Alaway (Bausch & Lomb),

Ocular Allergy Medicine Profile

BRAND NAME	GENERIC NAME	MANUFACTURER	PEDIATRIC USE	BOTTLE SIZE(S)	DOSING
Acute Care Products					
Acular LS	ketorolac tromethamine 0.4%	Allergan	3 years	5ml, 10ml	q.i.d.
Alaway (OTC)	ketotifen fumarate 0.025%	Bausch & Lomb	3 years	10ml	b.i.d.
Alrex	loteprednol etabonate 0.2%	Bausch & Lomb	12 years	5ml, 10ml	q.i.d.
Elestat	epinastine HCl 0.05%	Allergan	3 years	5ml	b.i.d.
Emadine	emedastine difumarate 0.05%	Alcon	3 years	5ml	q.i.d.
Optivar	azelastine hydrochloride 0.05%	MedPointe	3 years	6ml	b.i.d.
Pataday	olopatadine hydrochloride 0.2%	Alcon	3 years	2.5ml	q.d.
Patanol	olopatadine hydrochloride 0.1%	Alcon	3 years	5ml	b.i.d.
Zaditor (OTC)	ketotifen fumarate 0.025%	Novartis	3 years	5ml	b.i.d.
Chronic Care Products					
Alamast	pemirolast potassium 0.1%	Vistakon Pharm.	3 years	10ml	q.i.d./b.i.d.
Alocril	nedocromil sodium 2%	Allergan	3 years	5ml	b.i.d.
Alomide	lodoxamide tromethamine 0.1%	Alcon	2 years	10ml	q.i.d.
Crolom	cromolyn sodium 4%	Bausch & Lomb	4 years	10ml	q.i.d.
Opticrom	cromolyn sodium 4%	Allergan	4 years	10ml	q.i.d.

and Zaditor (Novartis Ophthalmics). For patients who have no issues with b.i.d. dosing, or those who have no prescription drug benefits, these relatively inexpensive OTC products should nicely meet their needs. Certainly, they are vastly preferred over topical vasoconstricting products.

Allergic conjunctivitis is a common condition prompting office patient encounters. Many of these patients present with true ocular allergy as a result of environmental allergen exposure. Many others present with secondary allergic symptoms because they have subnormal tear film dysfunction. The latter group of patients express itchy eyes because their impaired tear function does not adequately dilute and/or wash away environmental allergens. Indeed, a large number of these patients presenting with itching/burning eyes simply have "dry eyes," and are rendered asymptomatic with appropriate intervention(s) for insufficient tear film function. Therefore, it is important that we first rule out dry eye when patients present with symptoms compatible with allergic conjunctivitis.

If the history and examination clearly yield a diagnosis of allergic conjunctivitis, simply prescribe one of these four antihistamine/mast cell stabilizers b.i.d. p.r.n.:

Antihistamine/Mast Cell Stabilizers

- **Alaway** (ketotifen, Bausch & Lomb)
- **Elestat** (epinastine, Allergan)
- **Optivar** (azelastine, MedPointe)
- **Pataday** (olopatadine, Alcon)
- **Patanol** (olopatadine, Alcon)
- **Zaditor** (ketotifen, Novartis)

All of these perform well. The only two distinguishing features are: once-daily dosing of Pataday; and over-the-counter availability of Alaway and Zaditor.

Prior to the advent of these newer generation antihistamines with some mast cell stabilizing properties, pure antihistamines were the workhorses in allergic eye disease as well as in the treatment of lid myokymia (lid twitch). These antihistamines were **Livostin** (levocabastine, Novartis) and **Emadine** (emastadine, Alcon). As of December 2004, Novartis stopped production of Livostin, so now Alcon's Emadine is the sole representative of this class. For lid myokymia, we generally prescribe Emadine q.i.d. for one week, then b.i.d. for one to two weeks. We have had nearly as good results with antihistamine/mast cell stabilizing agents, but prefer the pharmacologic action of a pure antihistamine in the setting of myokymia.

Some patients with ocular allergy present with clinical inflammation above and beyond symptomatic itching. These patients are best served by a topical steroid. **Alrex** (loteprednol 0.2%, Bausch & Lomb) or **FML** (fluorometholone alcohol, Allergan) every two hours for two days, then q.i.d. for a week, then b.i.d. or once-daily for several more days or weeks can be enormously beneficial to this subset of allergy patients.

If the clinical expression is more pronounced, then consider Lotemax, rather than Alrex or FML. Since loteprednol is extraordinarily safe relative to the older ketone-based steroids, we see no reason to be timid with corticosteroid suppression when patients need a steroid.

The February 2005 issue of *EyeWorld*, a publication of the American Society of Cataract and Refractive Surgery, had a special issue on ocular allergy. We provide the following quotes and commentaries on this topic, and on other topics in the remainder of this chapter:

"Clearly, it appears that topical steroids do indeed have a role in some patients with ocular allergy; a treatment modality in the past largely avoided by most for fear of secondary steroid complications," says Stephen S. Lane, M.D.[1]

Mast Cell Stabilizers

Mast cell stabilizers have no role in acute allergy expression. These drugs have no active therapeutic properties! They simply chemotherapeutically make the mast cell membrane stable in the face of antigenic exposure, and therefore prevent the subsequent release of allergy-causing chemical mediators.

There are two advanced formulations of this drug class:

- **Alamast** (pemirolast, Vistakon Pharmaceuticals)
- **Alocril** (nedocromil, Allergan).

Prescribe them q.i.d. for a week, then b.i.d. p.r.n. We no longer use the first generation products **Crolom, Opticrom** and **Alomide**, since these more advanced formulations

have become available.

Again, for acute allergy expression, try a steroid. Mast cell stabilizers are for long-term preventive and maintenance therapy. Says John D. Sheppard, M.D.: "I can get as much out of a drop every other day of Lotemax or Pred Forte as I can four times a day with Alamast."[2]

For patients with known allergy triggers, such as cat exposure, mast cell stabilizers can be taken q.i.d. for one week prior to the anticipated exposure to prevent or minimize a subsequent allergic response.

Mast cell stabilizers, when used appropriately, can virtually eliminate the outbreak of allergic reactions. These drugs work by inhibiting the degranulation of mast cells, preventing them from releasing histamine and other allergy mediators. They are completely safe medications that can be used for weeks or months without any significant side effects. Since they are preserved, there is a low risk of toxicity, especially in patients with compromised tear function.

Here's what the experts have to say about using mast cell stabilizers with contact lenses and for dry eye: "Using mast cell stabilizers alone to combat contact lens-associated allergies is often a mistake, but physicians still run into that and other pitfalls associated with the drug." (More on contact lenses and allergies later.) "Another common misuse of mast cell stabilizers is for dry eye, simply because of a missed diagnosis. The most common mistake physicians make is to believe the mast cell stabilizer is going to work quickly for severe disease. In fact, mast cell stabilizers are better suited as a maintenance drug."[2]

Advise Against Vasoconstrictors

Discourage patients from using over-the-counter (OTC) anti-allergy drugs that include vasoconstrictors. In our experience, most patients using OTC vasoconstrictor products have dry eyes with low-grade, secondary conjunctival hyperemia.

We strongly advise against the use of any and all OTC vasoconstrictors because their short duration of action often encourages multiple instillations. This, in turn, may result in rebound conjunctival hyperemia, and exacerbate the redness they are trying to eliminate.[3]

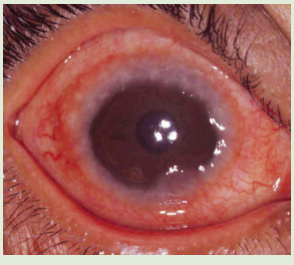
"In the past, we have been limited in our treatment of this frustrating problem to vasoconstrictors, decongestants, and antihistamines," Dr. Lane says.[1] "While sometimes helpful, these treatments are most often unsatisfactory and in many cases (especially the over-the-counter medications) lead to toxicity from either the agent or the preservatives they contain."

We have for many years urged patients not to use OTC vasoconstrictors for their ocular surface redness, be it from allergy or dry eyes. The goal should be to prevent red eyes from allergy and dryness, not just to "whitewash" the eyes when they become red.

Children with Ocular Allergy

Regarding allergic conjunctivitis in children: "The single best morsel of advice I can give to the parents of an allergic child is to wash their child's hands frequently. Children just won't stop rubbing their itchy eyes," Dr. Sheppard says.[4] "So many of the oral anti-allergy drugs have a significant drying effect on the eye. That just creates more

Cyclosporine for VKC Coming Soon?



Limbal vernal conjunctivitis.

In May, the FDA approved orphan drug designation for Vekacia, a proprietary cationic emulsion of cyclosporine A for the treatment of vernal keratoconjunctivitis (VKC) in children. The drug is produced by Novagali Pharma, of Evry, France.

In Phase III clinical trials, Vekacia reduced both signs and symptoms of VKC, and the drug was safe and well tolerated, the company says. Note that this is the same drug as Restasis (cyclosporine, Allergan), but of a higher concentration—Restasis is cyclosporine 0.05% whereas Vekacia is cyclosporine 0.1%.

Vekacia is the first drug intended specifically for treating VKC. Previous research has found that cyclosporine A inhibits eosinophilic infiltration by interfering with the type IV allergic reaction in the conjunctiva.[1] Signs of edema, follicles, giant papillae and corneal complications improved after one month of treatment with cyclosporine 0.1% administered t.i.d.[2] But the cationic oil-in-water emulsion vehicle, as used in Vekacia, resulted in significantly (11-fold) improved corneal and conjunctival delivery compared with cyclosporine 2% in an olive oil vehicle.[3]

We have not yet had the opportunity to try this therapy. In any case, we will continue to use Lotemax or Pred Forte as first-line treatment to get VKC under control, and perhaps use this new drug only if the the steroid therapy failed, or to maintain control once such had been achieved by the steroid.

1. Fukushima A, Yamaguchi T, Ishida W, et al. Cyclosporin A inhibits eosinophilic infiltration into the conjunctiva mediated by type IV allergic reactions. Clin Experiment Ophthalmol 2006 May-Jun;34(4):347-53.
2. Fujishima H, Takano Y, Murat D, et al. 0.1% Cyclosporine eye drops for patients with vernal keratoconjunctivitis. ARVO poster (5845/B408); May 10, 2007.
3. Lambert G, Rabinovich-Guilatt L. Cationic oil-in-water emulsion as an improved cyclosporine ocular vehicle for vernal keratoconjuctivitis sicca (VKC). ARVO poster (2301/B999); May 07, 2007.

problems in addition to the frequent behavioral changes seen in children taking antihistamines orally," he says.

If a topical antihistamine/mast cell stabilizer fails to achieve relief, then certainly try a pulse dose course of Lotemax every two hours for four days; then use both Patanol and Lotemax b.i.d. for a week. At the end of this short pulse of corticosteroid, the condition should be sufficiently controlled such that the antihistamine/mast cell stabilizer alone can maintain asymptomatology as long as necessary. With children, use the least amount of steroid the least amount of times to accomplish the greatest good.

Contact Lenses and Ocular Allergy

It is well known that contact lens wearers are disproportionately bothered by allergy. This begs the question of safety and efficacy of using Pataday, Zaditor, Optivar or Elestat with contact lenses. No problem. Just to be conservative, have the patient instill the morning drop a few minutes prior to insertion; the afternoon drop can go right on top of the contact lens.

To quell hyperacute allergic reactions, use potent topical corticosteroids (Lotemax, Inflamase Forte, Vexol, fluorometholone acetate 0.1%, or prednisolone acetate 1%) every hour or two for a day or two. In these more marked expressions, cold compresses can be immensely helpful in restoring calm.

Once you've neutralized the marked inflammatory response using one of the potent corticosteroids, then, if indicated, switch to an appropriate anti-allergy medication to continue to suppress any chronic expression of disease.

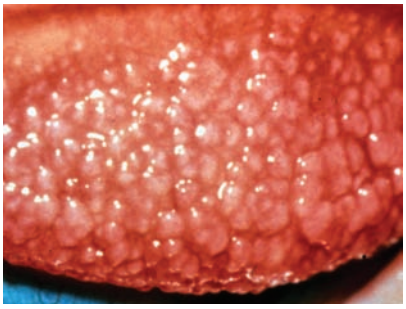
What to do with an allergic contact lens wearer in a case of severe papillary conjunctivitis? "You really need to crank out the big guns if patients don't stop using contacts.

Pearls for Ocular Allergy

- The price of various popular anti-allergy eyedrops can vary considerably. We urge you to have your staff consult two or three pharmacies near your office to get price quotes on your ten most prescribed medicines. Trust us, you will be amazed—not just in how the cost for the same medicine varies from pharmacy to pharmacy, but at the cost difference between competitive products.
- Try getting your patients with dry eye complaints off oral antihistamines. They can cause or exacerbate ocular surface dryness, which can be counterproductive to eye allergy relief.
- Many patients who present to the eye doctor have concurrent allergic rhinitis and/or allergic sinusitis. Many of these patients might achieve comparable or better relief from their symptoms with the popular steroid nasal sprays than from the oral antihistamines.
- Antihistamine/mast cell-stabilizing eyedrops can render a therapeutic effect to allergic rhinitis by virtue of their accessibility to these tissues via nasolacrimal drainage and local distribution.
- Steroid nasal sprays rarely cause ocular side effects, but patients on high-dose pulmonary inhaler delivery systems can, on occasion, experience ocular hypertension and/or PSC cataracts from their use.
- Most q.i.d. allergy meds can maintain a good therapeutic effect at b.i.d. dosing following a q.i.d. loading period of one to two weeks. We have also found that patients using b.i.d. allergy medicines for a couple of weeks can often be maintained at q.d. dosing.
- Discourage patients from rubbing their itchy eyes. Rubbing causes mast cell degranulation, which perpetuates the allergic cycle.

In other words, you should use a steroid that really will reverse as much as possible the underlying pathology of the cobblestone or severe papillary conjunctivitis. Once the patient is stabilized and has a fairly normal looking tarsus, it's fine to switch back to using the mast cell stabilizer, with a gradual steroid wean."[2]

We have advised the use of steroids in these instances for years and could not agree more!



Severe papillary conjunctivitis.

"If you want the efficiency of an anti-immunologic agent, one might even consider very infrequent use of the 'big daddy'—the steroid—to control swelling, vasodilation, migration of eosinophils, and release of granules from the mast cell," Dr. Sheppard says. "That is all accomplished by the topical application of a steroid, which might be done in the evening after removing the contact lenses as infrequently as every other day during the peak of the allergy season once the initial symptoms have been controlled."[2]

He adds, "I think once a day, or once every other day with the tremendous activity you achieve with a steroid, you are really creating a continuous level of immunosuppression, or down-regulation of the allergic response. With the more frequent use of the antihistamine and multiaction topical anti-allergy agents, you require the more frequent application perhaps twice a day. Even at every other day, we all know we can accomplish quite a bit with oral steroids once the initial episode has been brought under control as maintenance therapy."

Fortunately, most allergy expressions can be controlled with a topical antihistamine. When such therapeutic intervention insufficiently subdues the allergenic expression, pulse dosing with Lotemax can reduce the pathologic expression below the antihistamine efficacy threshold. An example of pulse dosing in this context could be every two hours for three days, then q.i.d. for a week. Hopefully, the steroid will have nicely subdued the inflammatory response so that a topical antihistamine/mast cell stabilizer can keep the patient asymptomatic.

Another approach to using steroids like Lotemax was discussed previously; that is, a drop every morning (at least 10 minutes before inserting contact lenses) and a second drop after contact lenses are removed in the evening. Such b.i.d. dosing could supplement topical antihistamine/mast cell stabilizers during contact lens wear.

This approach could be modified to just a drop of Lotemax near bedtime for a few weeks if needed to get these more challenging patients through the worst of the allergy season. As always, use the least amount of medicine possible to provide maximum patient care. Please understand, we do not ever prescribe steroids frivolously, but we are not timid in our use of these awesome drugs when needed.

In closing, dry eye is epidemic and the most common cause of the "itchy-burnies." True allergy is the near-exclusive cause of isolated itching. Cold compresses and refrigerated eye drops can be helpful. Most patients do very well with one of the antihistamine/mast cell stabilizers. ■

1. Lane SS. As spring blossoms with allergy symptoms, consider these treatment options. EyeWorld 2005 Feb:3.
2. Best strategies to treat CL users that have allergies. EyeWorld 2005 Feb:43-44.
3. Soparkar CN, Wilhelmus KR, Koch DD, et al. Acute and chronic conjunctivitis due to over-the-counter ophthalmic decongestants. Arch Ophthalmol 1997 Jan;115(1):34-8.
4. Young M. To combat allergies in children, it's avoidance, then treatment. EyeWorld 2005 Feb 2005: 37.

Ovaries and the Ocular Surface

There may be a unique expression of the itchy-dry eye that is associated with polycystic ovary syndrome (PCOS), the most common endocrine abnormality in women of reproductive age. PCOS afflicts approximately 4 million women in the U.S., and is generally characterized by ovulation failure, hyperandrogenism, and polycystic ovaries.

Critical ocular clinical features include: conjunctival hyperemia; itching; dryness; excessive mucous production; foreign body sensation; photophobia; burning; and contact lens intolerance. These signs and symptoms tend to appear approximately three years following the diagnosis of polycystic ovary disease.

While these signs and symptoms clearly overlap with dry eye and allergic eye disease, "We suspect that the unusual coupling of itching and dryness is a distinct clinical entity associated with hormonal imbalance, and we have designated this condition, the *itchy-dry eye associated* syndrome (IDEA)," the authors write.[1] This ovarian-associated syndrome tends to respond poorly to traditional dry eye or allergic therapy, which can also be a clue that the clinical presentation is not a typical case of dry eye and/or allergy.

"In conclusion, itchy-dry eye symptomatology in PCOS seems to be a distinct clinical entity that shares many characteristics with dry eye and ocular allergic disease, but has the unique feature of a concomitant endocrinopathy."[1]

1. Bonini S, Mantelli F, Moretti C, et al. Itchy-dry eye associated with polycystic ovary syndrome. Am J Ophthalmol 2007 May;143(5):763-771. Epub 2007 Mar 23.

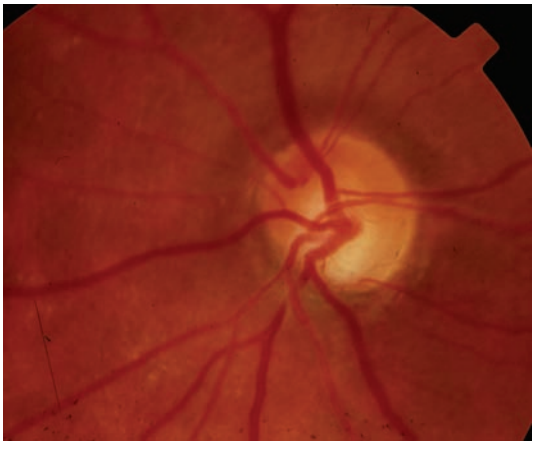
GLAUCOMA

The arsenal of glaucoma therapies is robust, with the addition of a preservative-free prostaglandin. But, the question of *when* to initiate glaucoma therapy remains.

We are now at a point where we have sufficient topical medicines to achieve "non-progression," or "minimal acceptable progression" in most patients with glaucoma. In fact, one could argue that the greater public good would be to divert all glaucoma pharmaceutical R&D funds into glaucoma detection programs.

As there is only one notable development in glaucoma medication this year, we present an abbreviated, "just the facts" chapter. For those in a "catch-up mode," see our web site (www.eyeupdate.com) for further details on each of the glaucoma drugs.

The prostaglandins have truly captured the hearts of optometrists and ophthalmologists, and for good reason. It is amazing that one drop per day of a highly-diluted prostaglandin can cause sufficient cytoarchitectural remodeling within the uveoscleral tissues to enable a 30% reduction in IOP. For balance and perspective, for 25 years we have had once-daily beta-blockers that can produce a 20 to 25% reduction in IOP via aqueous production inhibition. That's impressive, as well. In our experience, we have found that target IOP can be reached and maintained in +/-80% of glaucoma patients with one or the other (or both) of these two medicines. That's really pretty simple when you think about it. Of course, the most difficult challenge is getting patients to faithfully use their medicines as prescribed.



Note the inferior erosion of the neuroretinal rim in this case of advanced glaucoma. The patient was asymptomatic to her superior total altitudinal visual field defect.

Help Your Patients Get Their Drops

The attentive physician is aware that cost is a major determinant of compliance.[1] There are some patients who can afford Betimol (or a generic, non-selective beta-blocker), but cannot afford a prostaglandin. Since the issue of cost may well be pivotal for some patients, be wise in assessing your patients' abilities to be compliant with treatment from a cost perspective. Keep in mind that every pharmaceutical company has an indigent drug program that allows truly needy patients to receive glaucoma drugs at little or no cost. We recommend that every optometrist and ophthalmologist obtain a complimentary copy of the "Directory of Ophthalmic Pharmaceutical Assistance Programs for the Medically Underserved." This directory is available upon request from:

Eye Care America
Public Service Programs
P.O. Box 429098
San Francisco, CA 94142-9098
(877) 887-6327
www.eyecareamerica.org

1. Patel SC, Spaeth GL. Compliance in patients prescribed eyedrops for glaucoma. Ophthalmic Surg 1995 May-Jun;26(3): 233-6.

Xalatan (latanoprost, Pfizer) should be stored under refrigeration at the pharmacy. This is because there remains some uncertainty regarding its long-term (a year or more) stability at room tempera-

ture. Once a patient receives the Xalatan, it can be kept on the nightstand or in any other convenient place of the patient's choosing. None of the glaucoma medicines should be stored in direct sunlight, or in an enclosed place where temperatures may become excessively hot.

Travoprost has two formulations: first-generation **Travatan** (Alcon) and the newer, updated BAK-free **Travatan Z** (Alcon). (The "Z" is marketing-speak for zero BAK). Both formulations have demonstrated to perform equally at reducing IOP. Given that BAK has the potential to cause epithelial toxicity, any effort to decrease ocular surface exposure is pharmacologically virtuous. This is especially promising in the setting of dry eye conditions. Both formulations come in 2.5ml and 5ml bottles.

Now that Travatan has been upgraded to Travatan Z, we anticipate that the latter will be the exclusively prescribed version of travoprost.

Time of prostaglandin instillation should not be a concern. While the prostaglandins are best suited for evening instillation, the difference in effect is very small. Since compliance is a far greater issue, patients should instill their prostaglandin drops when it is most convenient for them to do so.

In summary, the optometric profession is perfectly positioned to positively impact glaucoma care. Glaucoma is most often diagnosed during the course of routine eye examinations. This provides us with both great responsibility and opportunity for early diagnosis and appropriate intervention. For the betterment of our respective communities, we should redouble our efforts to diagnose and manage glaucoma within our practices. ■

Topical Glaucoma Drugs

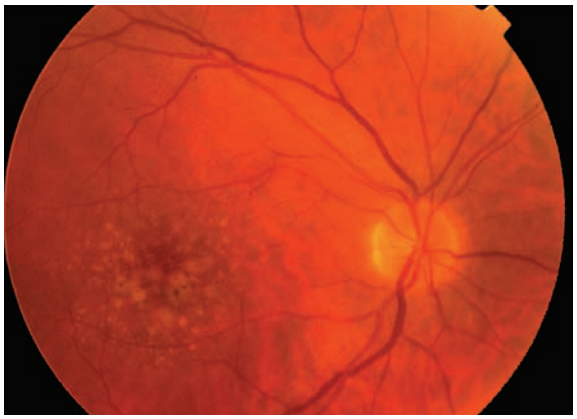
BRAND NAME	GENERIC NAME	MANUFACTURER	CONCENTRATION	BOTTLE SIZE
Beta Blockers				
Betagan, and generic	levobunolol hydrochloride	Allergan	0.25% 0.5%	5ml, 10ml 2ml, 5ml, 10ml, 15ml
Betimol	timolol hemihydrate	Vistakon Pharm.	0.25% 0.5%	2.5ml, 5ml, 10ml, 15ml 2.5ml, 5ml, 10ml, 15ml
Betoptic-S	betaxolol hydrochloride	Alcon	0.25%	2.5ml, 5ml, 10ml, 15ml
Istalol	timolol maleate	Ista	0.5%	5ml
Timoptic, and generic	timolol maleate	Merck, and generic	0.25% 0.5%	unit-dose, 2.5ml, 5ml, 10ml, 15ml unit-dose, 2.5ml, 5ml, 10ml, 15ml
Timoptic-XE, and generic	timolol maleate	Merck, and generic	0.25% 0.5%	2.5ml, 5ml 2.5ml, 5ml
Prostaglandin Analogs				
Lumigan	bimatoprost	Allergan	0.03%	2.5ml, 5ml, 7.5ml
Travatan	travoprost	Alcon	0.004%	2.5ml, 5ml
Travatan Z	travoprost	Alcon	0.004%	2.5ml, 5ml
Xalatan	latanoprost	Pfizer	0.005%	2.5ml
Alpha Agonists				
Alphagan P, and generic	brimonidine brimonidine	Allergan, generic	0.1%, 0.15%, 0.2%	5ml, 10ml, 15ml 5ml, 10ml, 15ml
Iopidine	apraclonidine	Alcon	0.5% 1%	5ml, 10ml unit-dose
Carbonic Anhydrase Inhibitors				
Azopt	brinzolamide	Alcon	1%	5ml, 10ml, 15ml
Trusopt	dorzolamide	Merck	2%	5ml, 10ml
Carbonic Anhydrase Inhibitor/Beta Blocker Combination				
Cosopt	dorzolamide/timolol	Merck	2%/0.5%	5ml, 10ml

AGE-RELATED MACULAR DEGENERATION

The new measures for Medicare's Physician Quality Reporting Initiative speak directly to patient care in the setting of macular degeneration. Measure 13 states that patients over age 50 with a diagnosis of age-related macular degeneration should have at least one antioxidant vitamin or mineral supplement prescribed/recommended within 12 months of diagnosis. This clearly follows the guidelines from the National Eye Institute's Age-Related Eye Disease Study (AREDS).[1]

These new Medicare guidelines acknowledge what we have been doing clinically for several years now. In our practices, we routinely recommend PreserVision gel caps (Bausch & Lomb) b.i.d. for all nonsmokers, and PreserVision Lutein (Bausch & Lomb) b.i.d. for those who smoke, or have a recent history of smoking. AREDS demonstrated that such therapeutic supplementation slows the rate of progression by about 25% in many patients.[2] While not an ideally robust intervention, it is the most effective benefit we can offer patients with the dry/atrophic form of age-related macular degeneration.

There is a newer, simpler technique for assessing the risk of developing advanced AMD. This comes as a refinement from AREDS. The important progression risk factors are the presence of large drusen (i.e., 125µm or larger) and/or pigment abnormalities. For reference, a venule at the disc margin is about 125µm in size. Regarding RPE pigmentary changes, these changes are either present or absent, and require no quantification. The use of this newer system for assessing risk of advancement or progression is as follows:[3]



Drusen in dry AMD. Two major interventions for these patients: smoking cessation and use of PreserVision.

Each eye is evaluated separately, and the score for both eyes is combined. One point is counted if large drusen are present, and one point for pigment change, for a possible total score of 4 points for both eyes combined. Patients with a score of 4 points have a 50% risk of developing advanced AMD over five years; 3 points a 25% chance; 2 points a 12% chance, and with a score of 1, only a 3% chance.

While this system seems very simple, it has been proven valid, and it allows clinicians to easily assess risk, which in turn enables us to more knowledgeably counsel our patients.

As a general guideline, we recommend PreserVision to most of our patients who display any significant expression of age-related macular degenerative changes. We also encourage these patients to increase their consumption of dark green leafy vegetables. For those patients on Coumadin (warfarin, Bristol-Myers Squibb), we strongly encourage them to consult with their physicians prior to making such a

Quality Reporting Guidelines for AMD

The 2007 Physician Quality Reporting Initiative (PQRI) guidelines can be seen at www.cms.hhs.gov/PQRI. These 74 unique guidelines, issued by the Centers for Medicare and Medicaid Services (CMS), cover all elements of medical care. The stated goal for these guidelines is to achieve the clinical standards outlined therein 80% of the time. Two of these standards are critical to the care of patients with macular degeneration:

Age-Related Macular Degeneration: Age-Related Eye Disease Study (AREDS) Formulation Prescribed/Recommended

Description: Percentage of patients aged 50 years and older with a diagnosis of age-related macular degeneration who had the AREDS formulation prescribed/recommended within 12 months.

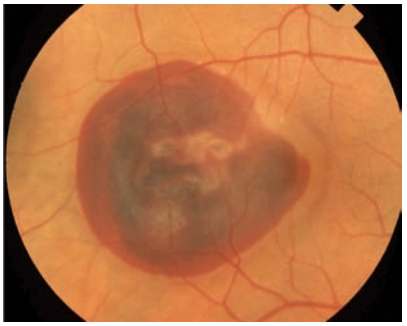
Age-Related Macular Degeneration: Dilated Macular Examination

Description: Percentage of patients aged 50 years and older with a diagnosis of age-related macular degeneration who had a dilated macular examination performed which included documentation of the presence or absence of macular thickening or hemorrhage AND the level of macular degeneration severity during one or more office visits within 12 months.

change in their diets, since the vitamin K in these vegetables can alter their coagulation profiles. Lutein and vitamin K are both present in dark green leafy vegetables, but lutein supplements do not contain vitamin K. Therefore, lutein supplements are safe with regard to coagulation function.

If patients with advanced atrophic degenerative changes convert to hemorrhagic (or exudative/wet) forms of macular degeneration, then a retinal specialist should be consulted for an assessment of the benefit of intravitreal Lucentis (ranibizumab, Genentech Inc.) or Avastin (bevacizumab, Genentech Inc.) injections. ■

1. Bressler NM, Bressler SB, Congdon NG, et al.; Age-Related Eye Disease Study Research Group. Potential public health impact of Age-Related Eye Disease Study results: AREDS report no. 11. Arch Ophthalmol 2003 Nov;121(11):1621-4.
2. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol 2001 Oct;119(10):1417-36.
3. Four-point scale developed to simplify AMD risk assessment. Ocular Surgery News 2007 Jan 22.



Wet, or hemorrhagic, AMD is best prevented. But newer anti-VEGF drugs, such as Avastin or Lucentis, can be enormously beneficial for some patients.

A New Drug to Combat Cigarette Smoking

"Eye-care practitioners, particularly optometrists, should consider asking their adolescent patients whether they smoke and provide advice on quitting to smokers."
***— British Journal of Ophthalmology, May 2007*[1]**

Smoking is the leading cause of preventable morbidity and mortality in industrialized countries.[2] As health-care providers, we have, at the very least, a supporting role in primary prevention of tobacco-related disease. Since smoking also increases the risk of macular degeneration and exacerbates the course of diabetes mellitus, we have a fiduciary role as well in joining with our patient's primary-care physician to encourage smoking cessation.

(On a side note, we would do well to have our staff check the blood pressure on our patients over 40 years old. As with glaucoma, there is a huge population with undiagnosed systemic hypertension out there. Offering blood pressure checks as part of our spectrum of care would be an enormous service to our patients.)

Chantix (varenicline, Pfizer) is new drug that aids in smoking cessation. It is a nicotinic acetylcholine receptor agonist, and is also pharmacologically able to block nicotine receptor binding. This dual action helps dampen both cravings and withdrawal symptoms. There is also some dulling of the sense of smoking satisfaction while on Chantix. Interestingly, there are no contraindications to this drug.

Chantix was FDA-approved in May 2006, and may offer smokers the best chance yet to stop smoking. Chantix is a 1mg tablet that is taken twice daily for 12 to 24 weeks following a one-week, lower-dose induction phase. In clinical trials, 44% of subjects abstained entirely from smoking during the 12 weeks of therapy.[3] At one year, however, the success rate is less than 25%. Still, this drug appears to achieve the highest cure rates of any pharmacologic intervention to date.

Every day in our practices, we encounter patients who smoke. As part of our patient care, we inform them of the availability of new drugs that may help them if they would like to stop smoking. Every day, we write the name "Chantix" on the back of our business cards, give them to our smoking patients, and ask them to discuss this new medication with their doctor on their next visit. This is at the very least a nudge, and a step in the right direction. For more information, go to www.chantix.com.

Another smoking cessation drug, **Zyban** (bupropion, GlaxoSmithKline) was the first non-nicotine medication approved by the FDA. Bupropion is perhaps better known by its original brand name Wellbutrin, which is indicated for the treatment of depression. Zyban/Wellbutrin works by inhibiting neural re-uptake of dopamine and/or norepinephrine. The dopamine relieves craving; the norepinephrine dampens nicotine withdrawal. Other commonly employed approaches are nicotine replacement products, such as skin patches, gums, nasal sprays and lozenges.

In summary, there are a number of pharmacologic agents available to help our patients stop smoking. Our role is to be at least casually knowledgeable about these interventions and to make our smoking patients aware of new medicines as they come to market. We encourage you to write the name Chantix on your business card with the active hope that your patients will discuss it with their physicians. It's good for your patients, and it's just another example of how optometrists can work as a team with other members of our medical community to promote public health.

1. Moradi P, Thornton J, Edwards R, et al. Teenagers' perceptions of blindness related to smoking: a novel message to a vulnerable group. Br J Ophthalmol 2007 May;91(5):605-7.
2. Mokdad AH, Marks JS, Stroup DF, Gerberding JL. Actual causes of death in the United States, 2000. JAMA 2004 Mar 10;291(10):1238-45.
3. Jorenby DE, Hays JT, Rigotti NA, et al.; Varenicline Phase 3 Study Group. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. JAMA 2006 Jul 5;296(1):56-63.

THE DYSFUNCTIONAL TEAR FILM

The vast majority of patients with dry eye woefully underutilize their artificial tears. In this section, we offer an algorithm for engaging the dry eye patient.

There are two key points to consider in current dry eye therapy. First, punctal occlusion seems to be underutilized. Second, many doctors are initiating therapy with **Restasis** (cyclosporine, Allergan) before doing an "inflammation detection" trial with a topical corticosteroid. It is very difficult to identify which patients will benefit from cyclosporine and which will not. Since a valid therapeutic trial with cyclosporine can take as long as three to four months, we suggest the following initial approach: Have the patient try **Lotemax** (loteprednol 0.5%, Bausch & Lomb) q.i.d. in the more symptomatic eye for two weeks. If the patient derives considerable benefit, this strongly indicates that inflammation is playing a clinically significant role in that individual's tear film dysfunction. At this point, consider a trial of Restasis, or simply continue Lotemax b.i.d. for another month or two, then once daily for a few months. This latter option is much more cost effective.

Punctal Plugs

Punctal plugs do seem to be helpful for many patients. For those patients with moderate tear volume, plugs can offer significant symptomatic relief. However, if the tear volume is scant, the main benefit that plugs may offer is prolonging the residence time of artificial tears. Patients with scant lacrimal lakes must use the recommended artificial tear frequently (at least every four hours); otherwise, tear film stagnation caused by the punctal plugs may concentrate pro-inflammatory cytokines in the tear film and actually exacerbate signs and symptoms of dry eye. In such cases, pulse dosing with Lotemax q.i.d. for two weeks, then b.i.d. for two weeks, along with frequent instillation of artificial tears, should be accomplished prior to plugging the inferior puncta.

Since plug extrusion is a common problem, always attempt to insert the largest-size plug that can be fitted. Use punctal gauge devices to determine the optimal size.

Anti-inflammatory Therapy

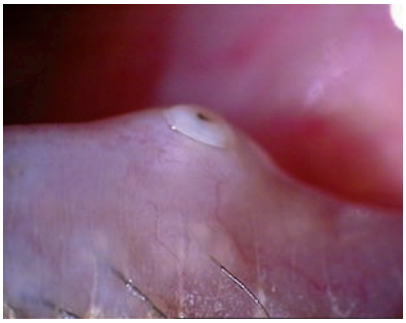
Photophobic, painful and injected eyes are inflamed. These eyes almost invariably respond to pulse dosing with Lotemax or FML q.i.d. for two to four weeks, along with frequent use of artificial tears. While most patients with ocular surface drying do not overtly manifest inflammation, they may still benefit significantly from immunosuppressive intervention. This can be accomplished with Lotemax, Restasis, or perhaps with a several-months' course of orally-adminis-

A Prescription Artificial Tear

Focus Laboratories, Inc., based in North Little Rock, Ark., has developed an artificial tear product whose most unique distinguishing feature is that it is available by prescription only.

FreshKote sterile ophthalmic solution contains polyvinyl pyrrolidone 2.0%, polyvinyl alcohol 0.9% (87% hydrolyzed), and polyvinyl alcohol 1.8% (99% hydrolyzed), along with Amisol clear, and other buffers and electrolytes. The manufacturer states that, "This patented blending enhances ocular surface wettability, delays tear evaporation, assists ocular surface healing, and treats all three layers of the tear film." It is preserved with disodium edetate dihydrate and Polixetonium, and comes in a 15ml bottle. The approximate retail price is $30.

We are in the process of our own informal clinical trials, and will be able to offer our clinical perspectives in next year's Drug Guide. For more information, visit the FreshKote web site at www.freshkote.com. As we have said over the years, it is important to try all new products in the clinical setting so that a consensus of professional opinion can evolve quickly and appropriate decisions can be made to maximize health care.



Punctal plugs are an underutilized modality in the care of patients with insufficient tear volume.

tered doxycycline or omega-3 essential fatty acid supplementation.

Biomedical research has confirmed that inflammation plays a clinically significant role in many patients with precorneal tear film dysfunction. Generally speaking, the greater the signs and symptoms, the more success we have had with topical inflammation therapy. Note that concurrent use of artificial tears is always implemented.

If you have decided upon a therapeutic trial with an anti-inflammatory medication, there are two ways to proceed: with either topical corticosteroids or topical cyclosporine. Since corticosteroids (we usually use Lotemax) have an onset of action much faster than cyclosporine, initiate anti-inflammatory therapy q.i.d. with the steroids. When the patient returns in a month, the clinical response (or lack thereof) will indicate whether this patient's dry eye is characterized by clinically significant inflammation.

If the steroid trial was significantly beneficial, two choices are available: Either continue the Lotemax b.i.d. for one month then taper to once-daily for a month or two (along with artificial tears), or continue the Lotemax b.i.d. for a month along with Restasis b.i.d. Since it usually takes Restasis at least a month to render a meaningful effect (and two to four months in many patients), front-loading with the steroid quantitatively diminishes the expression of inflammation and seems to potentiate the therapeutic effect of Restasis.

A drop or two of Lotemax for two to four months should be both safe and effective in virtually all patients.

Our experience has shown that some patients do well for months, then become acutely symptomatic. Pulsing with Lotemax q.i.d. for one week, then b.i.d. for a week or two can regain control for many more months. Since Restasis is a slow-onset drug, it is not suitable for pulse dosing. If the time period between acute symptomatic exacerbation becomes too short, then either continue the Lotemax at b.i.d tapered to q.d. after a week or two, or Restasis at b.i.d. for several months. Periodically stop the medicine to assess how the patient does without it. Always attempt to use the least amount of medicine to care for the patient. ■

Therapeutic Options for Dry Eye

	THERAPY	USAGE
Mild Options:	• Artificial tears alone, and/or • Punctal plugs alone, and/or • Omega-3 fatty acid supplementation	Two of these may be needed concurrently.
Moderate Options:	• Artificial tears used frequently • Gel formulation at bedtime • Punctal plugs • Omega-3 fatty acid supplementation • Restasis trial for 3-6 months	Two or three of these interventions may be necessary to achieve control.
Severe Options:	• More viscous, preservative-free artificial tears used frequently • Lotemax q.i.d. for 1 week, then b.i.d. for a month (to observe for significant inflammatory component) • Long-term Restasis if Lotemax brought relief • Oral doxycycline; 100mg/day for 2 weeks, then 50mg/day for 6 months • Omega-3 fatty acid supplementation for 3 to 6 months • Punctal plugs, once the above measures have been in effect for a month or two • Moisture shields or moisture goggles	Since punctal plugs have the potential to concentrate inflammatory cytokines, try first to get the ocular surface tissues at least partially rejuvenated prior to plugs. Of course, intervention is highly variable among patients.

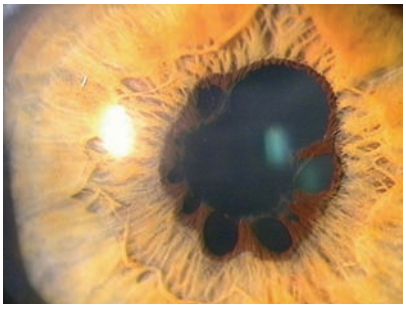
Each therapeutic intervention can influence (hopefully positively) the effects of other therapeutic maneuvers. For example, punctal plugs may enable the patient to decrease the frequency of artificial tear instillation. Omega-3 fatty acid supplementation may likewise diminish the need for artificial tears. Of course, if a patient were to be highly compliant with artificial tears, then perhaps the need for punctal plugs and/or omega-3 supplementation would be precluded. There is a dynamic state of flux in managing dry eye disease. Each intervention may complement other maneuvers, so a precise clinical algorithm for managing dry eye disease is impossible because of the enormous individual variability of both the disease process as well as response to therapy.

CLINICAL PEARLS IN PATIENT CARE

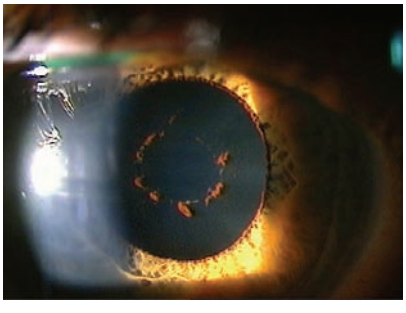
Thomas Jefferson was the prototypical "lifelong learner," and we should emulate his constant pursuit of knowledge. To that end, here we offer pearls that we've learned.

As part of our lectures, we are privileged to answer many hundreds of questions and offer our perspectives on a wide range of issues germane to optometric practice. Here, we share a number of these clinical pearls and pointers. Some are strictly informative. Others are meant to stimulate thought. But all are focused on helping you sharpen your skills.

• Synechia in the context of anterior uveitis can be problematic as it can increase IOP, and resulting in anisocoria in bright or dim light. Inability to dilate the pupil in the future (for example, in the patient with acute onset of flashes and/or floaters) could preclude the needed clinical evaluation.



Synechiae commonly result from delay in seeking care and suboptimal dosing of a cycloplegic drug and/or topical corticosteroid.



After four days of proper care, the synechiae are all broken.

Most of the time, synechiae can be broken during the presenting visit. But in some cases, the synechial breakage occurs after a few days of appropriate treatment. We normally treat synechiae with a couple of drops of 1% tropicamide along with a couple of drops of 2.5% phenylephrine (sometimes 10%, if needed) at presentation.

If the synechiae break within an hour or so, fine; if not, and the IOP is below 30mm Hg, then we prescribe Pred Forte (*not* a generic substitution, primarily because of the potential for a poorer quality product) to be used hourly while awake, along with either 0.25% scopolamine or 5% homatropine three to four times each day. Very rarely is there a need to prescribe FML ophthalmic ointment at bedtime.

We usually find the synechiae have broken by the patient's first follow-up in three to five days, but there are those recalcitrant cases in which the synechiae remain permanently. While certainly not desirable, as long as the IOP remains normal, it is an acceptable situation.

In our experience, it is usually the patient who has been misdiagnosed prior to coming to definitive care, the undertreated patient (either through mismanagement or poor patient compliance), and the patient who simply thought, "it would get better," and delays seeking care who have the truly stubborn synechia that can result in a permanently fixed pupil.

• Acne rosacea is most commonly expressed between the ages of 30 and 50, mostly afflicting white patients. The mainstay of therapy is an oral tetracycline antibi-

• The National Rosacea Society has available an excellent brochure, "Coping with Rosacea." Copies can be obtained by e-mailing rosaceas@aol.com. Visit the web site at www.rosacea.org. We have found that many, if not most, of our patients with posterior blepharitis also have rosacea. This brochure has helped us more comprehensively manage our patients with this disease.

otic, such as doxycycline or minocycline, for several months to a year or so, depending upon the clinical response. There are patients who only present with ocular signs—exemplified by evident telangiectatic vessels on the top portion of the eyelids (best seen on the inferior eyelid), tear film dysfunction, possibly corneal neovascularization, and multiple, subtle paralimbal infiltrates—and show no evidence of cutaneous disease; i.e., true ocular rosacea.

Rarely, younger children can be afflicted. If the child is less than 10 years of age, oral erythromycin at a dosage of 20mg/kg has been shown to be highly therapeutic.[1] But when dosing patients older than 10 years, we generally use doxycycline or minocycline at 50mg per day. Topical corticosteroid eyedrops, such as Lotemax, may also be needed to help quiet any expression of corneal inflammatory disease. Be aware that rosacea can present at almost any age, and a portion of acne rosacea patients will not have any skin disease to help elucidate the diagnosis.

Oral therapy commonly needs to be maintained for several months, with pulse dosing of a topical steroid if there are any flare-ups. Artificial tears are routinely employed to manage any associated keratoconjunctivitis sicca.

• **Patients with lattice degeneration of the retina are at risk for subsequent retinal tears or breaks** that could lead to detachment if not treated at the time of the rent. However, this risk is less than 1%, and so patient reassurance, not fear, should be given. Obviously, the patient should be thoroughly educated regarding the symptoms of a retinal tear, break or detachment, and the chart so documented.

On the "glass is half-empty" side of the equation, one-third of patients who have a retinal detachment also have lattice degeneration.

• **It is definitely time to do better than just record a cup-to-disc (C/D) ratio.** We challenge you to never again write down just a C/D ratio, but to include an accurate description of what you see on clinical examination. Some examples follow:

"0.6 C/D with central, shallow cup"

"0.7 C/D with erosion of the superior temporal rim"

"0.5 C/D with deep central cup and uniform pink neuroretinal rim"

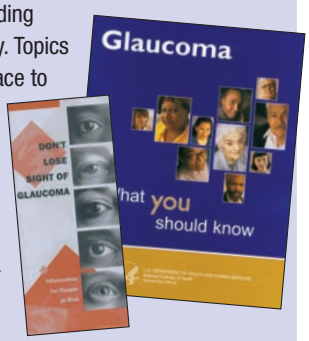
"0.4 C/D with temporal pallor"

Such characterizations are not as important with small cups, unless the optic nerve is small. Jost Jonas, M.D., a well respected expert on the optic nerve, states that in routine practice, the clinician conduct a quick, crude estimate of whether the disc in question is average-sized (medium), smaller-than-average, or larger-than-average.[2]

Many times, a cup is not precisely 0.6 or 0.7, but may be more accurately quantified as 0.65. Such wonderful attention to detail is yet another indication of astute attentiveness to the anatomy of the optic nerve head.

Too many optometrists and ophthalmologists do a surprisingly poor job of truly characterizing the optic nerve head. Let's work together to raise the bar and set a new standard of documenting the optic nerve. Remember, among the three million Americans who have glaucoma, as many as half of them remain undiagnosed. We feel very strongly that if we all discipline ourselves to critically analyze and characterize the optic nerve head, such diagnostic oversight would largely cease.

• **Receiving benefits paid for with your federal tax dollars isn't quite as good as free, but it's about as close as it gets.** Your National Eye Institute in Bethesda, Md., has a very nice array of excellent patient education brochures available at no cost upon your electronic request. These are all well written and they are "politically correct" regarding optometry vis-à-vis ophthalmology. Topics are wide ranging from commonplace to esoteric. We urge you to peruse the web site, www.nei.nih.gov, to see the available offerings. Most of the informational pieces can be ordered in packets of 50 on a monthly basis, as needed. In glaucoma, for example, the NEI has brochures for people "at risk" and for people "with glaucoma." It's good to have both pamphlets available for your patients.

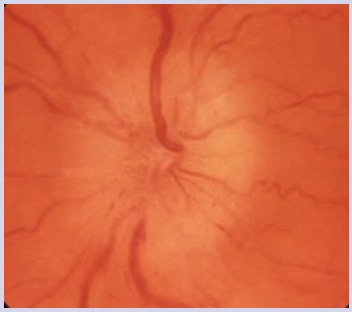


• **These will cost you, but ophthalmology/optometric journals have enormous potential for your lifelong professional growth.** Thomas Jefferson was the prototypical "lifelong learner," and we should emulate his constant pursuit of knowledge. While most of us receive optometric literature, precious few of us draw upon other ophthalmic literature on a monthly basis. We subscribe to five ophthalmology journals, and the knowledge gleaned has enormously benefited our clinical care. We strongly recommend you choose at least one of the journals available via www.ophsource.com. It's an investment with lasting dividends.

• **Finally (and this is completely free!), visit our web site**, www.eyeupdate.com, for practical, clinically-oriented information that we think you will find helpful in your day-to-day practices.

ED Drugs and AION: Still a 'Maybe'

• Erectile dysfunction and the drugs used to treat this condition have generated considerable discussion in the lay and professional press. The prime issue as it relates to vision is: Do these drugs pose a risk to vision via anterior ischemic optic neuropathy (AION)? The answer is, "maybe," but the consensus opinion is that while there is an association, these drugs are probably not causal.



A swollen optic disc, surrounded by multiple flame-shaped hemorrhages, is characteristic of NAION.

In the October 2005 *American Journal of Ophthalmology*, Frederick Fraunfelder, M.D., states, "Since millions have taken these medications with risk factors for AION, this may be an expected coincidence… Postmarketing surveillance … has produced no data to date which confirms a 'certain' relationship between AION and erectile dysfunction medications."[1]

An editorial in that same issue states, "Most, but not all, of these patients had underlying anatomic or vascular risk factors for development of NAION, including: small C/D ratio (crowded disk), age over 50, diabetes, hypertension, coronary artery disease, hyperlipidemia, and smoking."[2] They go on to say, "a possible association [exists] … but a causal relationship has not been established conclusively."

ED medicines are basically phosphodiesterase-5 (PDF) inhibitors. Phosphodiesterase-6 is found in the retina and is thought to partially explain some of the visual phenomena occasionally experienced by patients taking one of the drugs in this class. These include Viagra (sildenafil, Pfizer), Levitra (vardenafil, Bayer), and Cialis (tadalafil, Lily ICOS). Since nonarteritic anterior ischemic optic neuropathy is seen most commonly in patients with small optic nerve heads and/or minimal cupping, i.e., "the disk at risk," the optometrist's role is to be aware of all of their patients' medicines. Any patient using PDF inhibitors should be advised of the possible risk of AION if they have "high risk optic nerve heads."

With more than 200 million ED drug prescriptions written for (and presumably used by) more than 23 million men, we would think any true cause-and-effect relationship would be evident. We can't imagine that it will be much longer until definitive data are available to seal this question.

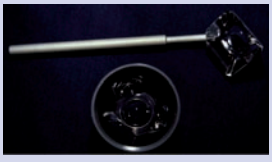
1. Fraunfelder FW. Visual side effects associated with erectile dysfunction agents. Am J Ophthalmol 2005 Oct;140(4):723-4.
2. Lee AG, Newman NJ. Erectile dysfunction drugs and nonarteritic anterior ischemic optic neuropathy. Am J Ophthalmol 2005 Oct;140(4):707-8.

• Follow patients with ischemic central retinal vein occlusion (CRVO) monthly for the first six months. On each visit, look carefully for neovascularization of the iris, do a quick four-mirror gonioscopic examination to look for angle neovascularization, and check the IOP prior to dilation. If neovascularization of the iris (NVI), of the disk (NVD), or elsewhere (NVE) develops, then send the patient to a retinologist for panretinal photocoagulation. After the first six months, check CRVO patients quarterly for one year, then annually.

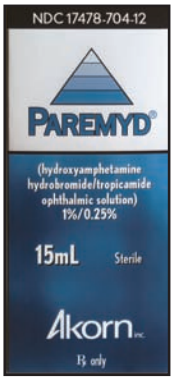
• Culturing is a common topic, yet uncommonly indicated. Culturing should, however, be considered in the following situations:

- *Severe purulent conjunctivitis*
- *Chronic or recurrent conjunctivitis unresponsive to standard therapy*
- *Neonatal ocular infection*
- *Central or moderate-sized corneal ulcers*
- *Postoperative ocular infection*
- *High suspicion for fungal keratitis*

• The four-mirror goniolens is a workhorse in our practices. Its exclusive virtue is its usefulness for examining the iridocorneal angle, most always related to glaucoma assessment. Only topical anesthesia is needed, and the tear film serves as the interface solution. It is quick, efficient, and patient-friendly.



• When dilating patients with potentially occludable iridocorneal angles, it is probably best to dilate them in the morning with either Paremyd (0.25% tropicamide/1% hydroxyamphetamine hydrobromide, Akorn) or 0.5% tropicamide. It is relatively easy to reverse the dilatory effects of these two medicines, and should angle-closure occur, there would be plenty of time to move through the management protocol and arrange for a YAG laser photoiridotomy. It is vitally important to challenge these narrow angles in a controlled clinical setting. A worst-case scenario would be for one of your patients to be on a remote vacation and have a spontaneous occlusion. This could prove to be a litigiously unhappy patient because the doctor failed to diagnose a potentially blinding condition in a proactively timely manner.



• **High-sensitivity (hs) C-reactive protein (hs-CRP), like erythrocyte sedimentation rate (ESR), is a nonspecific barometer of system inflammation.** Both of these tests are blood derived and therefore require venipuncture to collect samples for laboratory analysis. The results of the tests can be obtained within a few hours at almost any medical diagnostic laboratory.

CRP has both acute and chronic implications. Optometrists use CRP almost exclusively in the diagnostic workup of patients suspected of having giant cell arteritis (GCA) as a companion test with ESR. The CRP test typically elevates more rapidly in response to inflammation and decreases more rapidly in response to oral steroid therapy. The normal threshold within the context of GCA is less than 2.45mg/L.

As for CRP's role in chronic disease, it can be a helpful indicator of risk for cardiovascular disease. The following information from our hospital laboratory succinctly describes the role of hs-CRP in cardiovascular risk assessment:

"CRP is a nonspecific marker of inflammation, and a variety of conditions may cause elevated levels. CRP values above 8.0mg/L are associated with clinical inflammation.

"The cardiovascular risk profile may not apply to patients with other known sources of inflammation. hs-CRP interpretation for cardiac risk is based on 'quintiles of risk.' The recommended quintiles are as follows:

Quintile 1	*Lowest risk*	*0.1 - 0.6mg/L*
Quintile 2	*Low risk*	*0.7 - 1.1mg/L*
Quintile 3	*Moderate risk*	*1.2 - 1.9mg/L*
Quintile 4	*High risk*	*2.0 - 3.8mg/L*
Quintile 5	*Highest risk*	*3.9 - 15.0mg/L*

"Patients with elevated hs-CRP concentrations are more likely to develop stroke, myocardial infarction, and severe peripheral vascular disease. Simultaneous measurement of hs-CRP and lipids predict future vascular risk better than lipid measurements alone. In women, hs-CRP concentrations may be influenced by hormonal status."

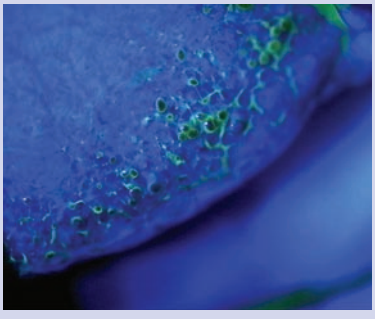
• **Uncommonly, a patient will present with foreign body sensation resulting from a tarsoconjunctival concretion** that has eroded through the overlying conjunctival epithelium. (Such a concretion is composed of hyaline-like material, and is not calcific in origin.) The microerosion resulting from the protruding concretion is readily observed with fluorescein staining upon eyelid eversion. Any erosion that has symptomatically eroded will preferentially stain with sodium fluorescein dye.

Removing the lesion is rather straightforward. Just instill a drop or two of proparacaine or Fluress (fluorescein/benoxinate, Akorn). Also, instilling a drop of 2.5% phenylephrine can be useful to minimize the potential for a microbleed, as these occasionally occur in concretion removal.

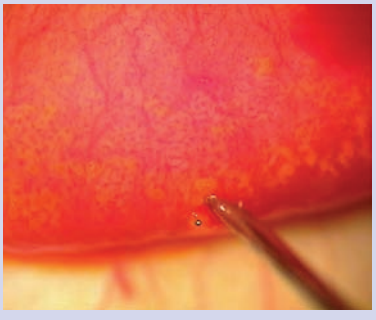
Then use a "golf club spud," or other instrument of your choice, and begin gently picking away at the erosion site until the firm concretion dislodges.

The concretion invariably comes out as a single chunk. Some minor bleeding may occur, but this quickly stops once the tarsal conjunctiva is reapposed to the globe.

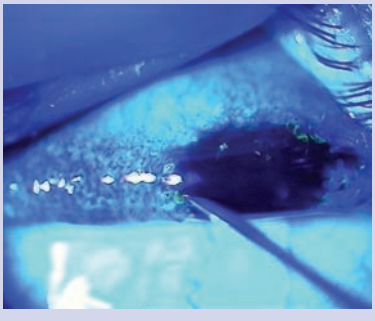
Following the procedure, consider instilling a drop or two of antibiotic solution, or a small amount of antibiotic ointment. Follow-up care is simply PRN.



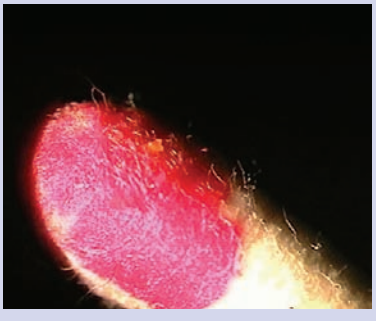
Example of eroding, symptomatic aggregates of concretions, which must be removed to bring relief and comfort to the patient.



Use a needle to remove a symptomatic eroding concretion.



When removing concretions, microbleeds are common. They can be reduced somewhat by pretreatment with 2.5% phenylephrine.



The removed concretion is seen here affixed to the cotton swab.

Clinical Pearls

• **Diagnosing glaucoma in highly myopic (10D to 18D) individuals can be rather challenging.** It has been shown that the major anatomic weakness in highly myopic patients is lamina cribrosa thinning, not thinning of the retinal nerve fiber layer. Therefore, "OCT, CSLO, and GDx are not useful to discriminate nonglaucomatous and glaucomatous subjects that have high myopia."[3] Furthermore, "clinicians often must rely on an examination of the optic disc in order to diagnose glaucoma in high myopes," and, "the contour of the retinal vessels on the disc is often the sole indicator of the surface topography." Therefore, "clinicians must assume each highly myopic optic disc to be glaucomatous until proven otherwise."

In addition, "the optic disc in highly myopic eyes is oval, elongated, and obliquely oriented to a significantly greater degree than in any other group. The cup is also remarkably shallow." So, "evaluating the parapapillary atrophy in myopia will not assist in the diagnosis of glaucoma."[4]

Hopefully, these perspectives will help guide your diagnostic decisions in the setting of myopia.

• **In patients with 7th facial nerve palsy (Bell's palsy), or any condition resulting in incomplete blink or eyelid closure, always determine whether Bell's *reflex* is intact.** With forceful orbicularis eye closure, the eye(s) should reflexively roll up and out within the orbit.

The way to assess the presence of absence of the Bell's reflex is to have the patient look down, then use your thumbs to raise and pin the upper lids to the superior orbital rim. Then, while the patient is looking in primary gaze, ask that s/he forcefully attempt to close his/her eyes. If the Bell's reflex is intact, the eyes will roll up and out; if absent, they will remain in primary gaze. There is much less risk of corneal desiccation with an intact reflex. If the reflex is absent, more aggressive lubrication may be needed to protect against ocular surface drying.

• **Many people with macular degeneration also take Coumadin (warfarin, Bristol-Myers Squibb) for anticoagulation.** Most are keenly aware that dark green, leafy vegetables should be avoided because of their vitamin K content. This can be perceived as a concern by the patient when we recommended a product containing lutein, since many patients also understand this substance is found abundantly in dark green, leafy vegetables. Certainly, it is a justifiable concern, so we need to explain to these patients that while both vitamin K and lutein have many common sources, the latter does not affect the INR (coagulability profile).

When patients present with symptoms compatible with posterior vitreous detachment (PVD)—such as sudden onset of flashes, floaters, cloud, curtain, and/or a spider-web appearance in their vision—give careful biomicroscopic attention to the retrolenticular anterior vitreous (Berger's space). Very often (but not always) if there is an associated retinal tear or break, red blood cells (RBCs) and/or debris will be evident in this portion of the vitreous cavity. This "tobacco dust" or "paprika" appearance (known formally as Shaffer's sign), commands an exhaustive examination of the peripheral retina. In evaluating Berger's space, a critical step is to compare the fellow eye so as not to be misled by baseline non-RPE, non-RBC debris that may occasionally be seen in normal vitreous. As a general rule, in most eye conditions, it is wise to compare the fellow eye.

• **"One third of conclusions in major medical journals are later found to be inaccurate,"** reveals the January 2007 *American Journal of Ophthalmology*.[5] This is interesting—and disconcerting—to say the least.

• **A word of perspective to those who have acquired the Optos Instrument:** While it is good technology (similar to the glaucoma scanning devices), it is not comprehensive in its diagnostic ability.

There are several circumstances that come to mind in which either a magnified stereoscopic view or a thorough peripheral examination is indicated. Three such instances are when assessing for: an optic nerve head or a retinal lesion; early diabetic retinopathy; or a symptomatic posterior vitreous detachment. It may be best in these special circumstances to pharmacologically dilate the pupil, and carefully study the "at risk" tissues.

Amiodarone, the O.D., and the Cardiologist

• **Amiodarone (Cordarone, Wyeth-Ayerst) universally causes a verticillate deposit in the corneal epithelium, which can, on rare occasions, slightly decrease vision.** However, this drug also has the potential to cause an optic neuropathy. This highly infrequent ocular side effect is seen bilaterally, since it is thought to be a response to the systemic medicine. The optic neuropathy presents as a papillitis, and can occasionally be confused with anterior ischemic optic neuropathy. The time between the patient starting amiodarone and the time of expression of optic neuropathy is variable with no consistent pattern. Furthermore, there is no relationship to dosage. After stopping the amiodarone, some patients improve; others do not.

Verticillate deposit in the corneal epithelium caused by amiodarone.

Medicolegally, a "causal" relationship has been established between amiodarone usage and the development of optic neuropathy. However, scientifically, the relationship between the two is, "probably causal." The role of the optometrist is "advisor and educator" to cardiologists regarding the potential for amiodarone-associated optic neuropathy. The key is to educate cardiologists to seek optometric consultation for their patients on amiodarone who develop vision problems.

• **Drugs to treat diaphoresis (excessive sweating) are commonly anticholinergics.** Recently, we had an emmetropic 15-year-old white female present with recent onset accommodative difficulty. We questioned her about the time of onset, and reviewed her medical history. As it turned out, her focusing problem began around the same time she had started on an antidiaphoretic drug. A quick look in the reference text, *Drug-Induced Ocular Side Effects* (5th ed., Butterworth Heinemann, 2000), clearly states that accommodative difficulty, especially in younger people, is seen with use of cyclobenzaprine (Flexeril, McNeil). Use of temporary reading glasses and a nice letter of explanation to her physician were the key components of her care.

The pearl here is threefold: Be an attentive investigator; have good reference texts readily available; and communicate with your patients' physicians.

• **Regarding drug side effects, "clusters of case reports suggesting an adverse ocular reaction are frequently the first and only signal that such a problem could be occurring."**[5]

It is important, then, that when you encounter what you deem a reportable drug side effect, that you contact both of the following agencies: FDA MedWatch (www.fda.gov/medwatch/index.html), and the National Registry of Drug Induced Ocular Side-Effects (www.eyedrugregistry.com or http://piodr.sterling.net).

• **In multiple sclerosis patients, "the earlier the [beta-interferon] treatment is started, the better the outcome appears to be,"** according to the November/December 2006 issue of *EyeNet*. In some cases the, "apparent disconnect between MRI findings and physical disability may be just a matter of time lag." The currently available beta-interferons (Avonex, Betaseron and Rebif), "can't reverse the damage already caused by the disease, but they can help reduce the frequency of attacks and slow the rate of future disability."

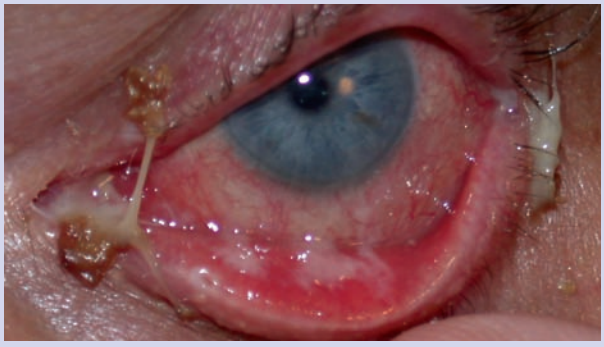
Our overview: When a patient presents with optic neuritis, an MRI should be accomplished within one to three days, and a neurological consult should scheduled for a day or two after the MRI is done. If the MRI is positive for demyelinating disease, the patient and neurologist should have a thorough discussion regarding immediate treatment with IV methylprednisolone and subsequent long-term treatment with a systemic anti-MS agent. The O.D. can, and should, play an intimate role in facilitating the above maneuvers through the healthcare system. For more information, see our web site, www.eyeupdate.com. ■

Giant Fornix Syndrome: A 'New' Clinical Entity

It is hard to imagine in this highly enlightened age that a new ophthalmic diagnostic entity would be "discovered," for surely giant fornix syndrome has existed for decades, or even centuries. But, such appears to be the case, and we experienced it firsthand.

Diagnostic Data

When a 76-year-old white male presented with a left red eye and severe purulent discharge of five days duration, we presumed that removing the discharge (which took 10 cotton swabs!) followed by a few days of Vigamox (moxifloxacin, Alcon) would cure it. *Wrong!* When the patient returned three days later, he looked very much the same as he had initially (*see image*).



It took 10 cotton swabs to remove all the purulent discharge for this patient with 'giant fornix syndrome.'

Diagnosis

Very fortuitously for both patient and doctor, the August 2004 issue of Ophthalmology had arrived and contained an article that depicted this patient's symptoms with near-divine intonation. The article, by G.E. Rose, described twelve patients who had giant fornix syndrome. From this article, we learned these patients demonstrated "copious amount of thick, purulent debris and a yellow coagulum lodged in the depths of the upper fornix—this debris universally culturing *Staphylococcus aureus*." Dr. Rose found that, "the condition settled rapidly on appropriate systemic antibiotics [ciprofloxacin or ofloxacin], intensive topical antibiotics, and high-dose potent steroids."

Management

In light of the above study, we started this gentleman on Augmentin (amoxicillin/clavulanate potassium, GlaxoSmithKline) 875mg b.i.d., continued him on Vigamox hourly, added Lotemax (loteprednol 0.5%, Bausch & Lomb) q2 hours, and urged him to continue his use of warm soaks. In three days, the patient's condition showed considerable improvement, and he had complete resolution five days later. We stressed to the patient the need for meticulous eyelid hygiene, and instructed him to return immediately should he experience any recurrence of symptoms.

Giant fornix syndrome is a unique clinical entity that requires a unique clinical approach. Patients with this condition are typically over age 75, and are likely to have excessively large recesses to their superior cul-de-sacs. This allows sequestration of a thick coagulum-harboring staph reservoir. Initially, this condition may require daily follow-up or every-other-day follow-up so that the superior fornix can be swept. We use sterile cotton swabs coated with TobraDex (tobramycin/dexamethasone, Alcon) ointment to accomplish this. Should the patient have a history of penicillin allergy, we prescribe Levaquin (levofloxacin, Ortho-McNeil) 500mg once daily for one to two weeks; otherwise, we prefer Augmentin 875mg b.i.d. for the same length of time. TobraDex ointment is instilled at bedtime for the first week, then the patient may use just GenTeal Gel (Novartis) for two more weeks, depending upon the presence or expression of toxic epithelial keratitis.

In more recalcitrant or recurring cases, daily use of an antibiotic/steroid such as Zylet (loteprednol/tobramycin, Bausch & Lomb) b.i.d. to q.i.d. for a month or two may be required. Instruct the patient to meticulously clean the eyelids using one of the newer lid scrub products, such as SteriLid eyelid cleaner (Advanced Vision Research). It is a good idea to demonstrate the technique in the office for the patient and/or the caregiver.

When encountering an older patient with copious, cream-colored, purulent discharge, consider the diagnosis of giant fornix syndrome, particularly if the condition responds poorly to conventional topical antibiotic therapy.

Rose GE. The giant fornix syndrome: an unrecognized cause of chronic, relapsing, grossly purulent conjunctivitis. Ophthalmology 2004 Aug;111(8):1539-45.

1. Cetinkaya A, Akova YA. Pediatric ocular acne rosacea: long-term treatment with systemic antibiotics. Am J Ophthalmol 2006 Nov;142(5):816-21.
2. Jonas JB, Papastathopoulos K. Ophthalmoscopic measurement of the optic disc. Ophthalmology 1995 Jul;102(7):1102-6.
3. Melo GB, Libera RD, Barbosa AS, et al. Comparison of optic disk and retinal nerve fiber layer thickness in nonglaucomatous and glaucomatous patients with high myopia. Am J Ophthalmol 2006 Nov;142(5):858-60.
4. Budde WM. Glaucoma or myopia? Glaucoma Today 2006 Sep/Oct;5:23-6.
5. Fraunfelder FW, Fraunfelder FT. Scientific challenges in postmarketing surveillance of ocular adverse drug reactions. Am J Ophthalmol 2007 Jan;143(1):145-149.

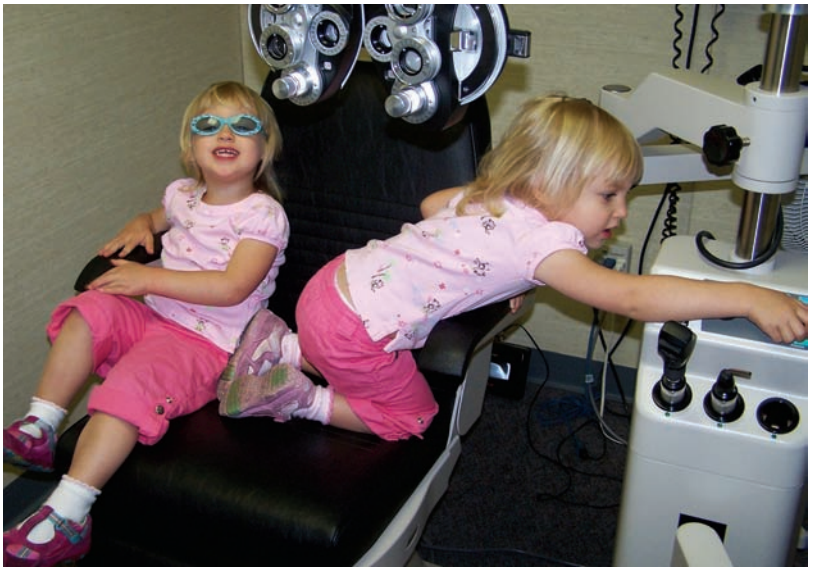
CALL FOR CLINICAL CONUNDRUMS

Got a problematic patient? Having difficulty determining a diagnosis? Can't come to a conclusion on course of therapy? Send your clinical conundrums to Drs. Melton & Thomas at DrugGuide@jobson.com. They'll publish your question—and their answer—in next year's *Clinical Guide to Ophthalmic Drugs*.

PEDIATRIC PEARLS

Here, an expert pediatric ophthalmologist provides some very practical, down-to-earth clinical pearls on how to handle both pediatric patients and their parents.

Our good friend and colleague, Sandra M. Brown, M.D., is an outstanding pediatric ophthalmologist who offers the following insights regarding pediatric eye care. It is always a breath of fresh air to glean wisdom from expert, "in-the-trenches," subspecialists. We thank Dr. Brown for her willingness to share these very helpful clinical insights with us and you.



Pediatric pearl #9: Sit squirmy children in the parent's lap.
Pediatric pearl #9a: One squirmy child at a time!

• **Treating blunt trauma (without serious eyelid edema) in an upset child.** First, forget the slit lamp. Use the direct ophthalmoscope as a side illumination source; it gives broader and more even illumination than a muscle light, without bright Purkinje reflexes. You can see hyphemas and pupil irregularities easily. You can treat traumatic iritis empirically; although in children, this improves rapidly and spontaneously without treatment. Check for a red reflex since you've got the ophthalmoscope in your hand.

Have the parent hold the child in a "soothing" position in the exam chair. Let the child do his or her own eye opening; don't touch the child's face. Be reasonable about a dilated exam. If you think it is essential, do what you are compelled to do; otherwise, skip it.

• **Treating the child with a suspected corneal abrasion.** When you suspect a corneal abrasion, put the anesthetic in the eye first. This can turn a screaming, thrashing kid into a both-eyes-open, whimpering one. However, if the child already has the eye open, don't put anything in the eye until you have completed your assessment, or you will quickly be regarded as THE ENEMY.

• **Treating blunt trauma with serious eyelid edema.** Put on gloves to get a good grip on the eyelids. Place the child flat on his or her back (chair laid back), and have your technician/office assistant (NOT a parent) hold the child's head. For toddlers, keep the child on the parent's lap and lean them both back; put the parent in charge of the arms, torso and legs. Skip the anesthetic. You may get just a glimpse of a rolling eyeball, but this should allow you to answer the most critical question: open globe—yes or no?

• **Children with elevated IOP.** Children can tolerate moderately elevated IOP for weeks, so it is better to presume the IOP is not dangerously elevated than get into a major battle with the child in order to measure it. When the child is upset, the IOP will be spuriously elevated, anyway.

• **Keeping the child with an eye injury quiet.** Have the parent sedate the child with any safe preparation on hand at home that is known to make him or her sleepy. Children's cold and cough medications often work well, particularly Benadryl, if it is available. Have the parent dose per the medication's instructions, according to the child's body weight.

Older kids are often content to lie on the couch and watch TV or DVDs. Video games and hand-held game devices should not be allowed because they encourage jerky eye movements. Be specific that the child is not to play outdoors at all, nor to roughhouse indoors with siblings or friends. Younger children find being still for a lengthy period of time is very difficult. Better to let them play gently on the floor than to force them to stay in bed. Hospitalization is required for truly uncontrollable children with hyphemas. More often this decision is reached the next day when the parents report an inability to comply with activity limitation at home.

• **Tips for managing the parent(s) of an upset child.** If both parents are present, and one parent is crying or anxious, even a mildly injured child may react frenetically or even hysterically in response to that parent. Address both parents and say something like, "I know this is frightening and upsetting to you. We will do everything we can to take care of Joey, but to do so, we absolutely must look at his eye. Children quickly pick up on the vibes their parents send, and of course you are very worried. It might help if you (addressing the upset parent) step out of the room for just a minute." This will cause one of two things to happen: the upset parent will leave the room (rarely); or (more often) the upset parent will get it together, and (usually) the child will become calmer, as well. Regardless of the parents' reactions, it is important to validate their emotions as "reasonable under the circumstances."

If only one parent is present, this parent MUST be present with the child at all times to prevent any claims of battery. Note that torso bruising related to the original incident may precipitate a report of battery if the parent is not allowed to remain with the child, hears blood-curdling shrieks from the exam room, and presumes the bruising was caused by the staff handling the child too roughly.

If the child is particularly tough to control, you can motivate the parent to help more by saying, "keep him still or he may rebleed and possibly go blind," or, "he'll have to be in the hospital for three or four days." Sometimes drastic situations call for dramatic threats!

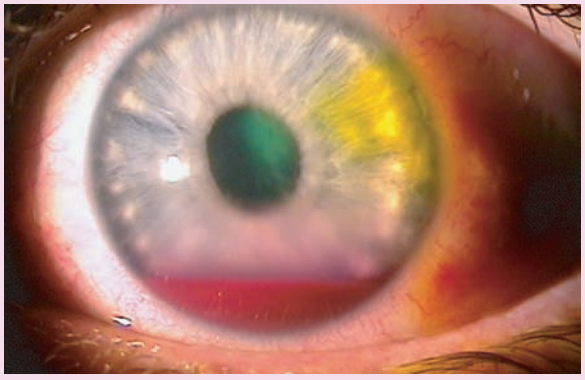
Except in cases in which the condition/injury is very mild, the child is older and more cooperative, and the parents are quite reliable, it is a good idea to schedule a one-day follow-up examination to see how the behavior management is going.

• **Hyphema management.** To quiet the eye and decrease the risk of bleeding, have a potent steroid, such as Pred Forte, instilled six to eight times a day. Prescribe at a higher frequency if you think Mom or Dad is likely to miss a dose or two, or will have trouble instilling the drops in a squirmy child's eye.

Prescribe a long-acting cycloplegic drop such as atropine, scopolamine or 5% homatropine for use once daily at bedtime.

Stress to the parent that only Tylenol (or generic acetaminophen) should be given for pain. No NSAIDs (naprosyn, ibuprofen or aspirin, etc.) should be used because any of these could potentiate bleeding.

If the child is of African, Mediterranean or Middle Eastern descent, have labs drawn to rule out sickle cell trait. These children can have greater problems with rebleeding, are more likely to have an elevated IOP with a small hyphema, and cannot tolerate elevated IOP as it causes intravascular RBC sludging and ocular ischemia. Sickle trait is widely distributed and a negative family history for hemoglobinopathies is not sufficient evidence. If the child is positive for sickle trait, the need for accurate serial IOP measurements is greatly increased; in the worst-case scenario this may mean sequential brief general anesthesias. Topical or oral carbonic anhydrase inhibitors are contraindicated in cases of sickle cell.



A hyphema is typically treated with cycloplegia and a topical steroid, such as Lotemax.

• **Getting oral medications "down the hatch."** Some medications, such as prednisone, taste quite nasty in liquid form. Try to order concentrated solutions so that the volume is small, and tell the parent(s) to mix the medication with straight Hershey's Chocolate Syrup in a larger spoon.

• **Mulch attacks.** As mulch has become an increasingly frequent playground material, more kids are getting ocular surface abrasions from falling or getting mulch thrown in their eyes. Mulch tends to stick, so look hard and deep in the inferior fornix, and be sure to flip the upper lid(s). Particularly if you note fine vertical abrasion lines, assume there is mulch under the

upper lid(s) until proven otherwise. Fortunately, the dark brown color of the mulch is easy to see. Often, parents won't know of a particular mulch injury, but they may report the child came home from school or daycare, "with a red eye." If you specifically ask, you may learn there is mulch in the play areas.

I don't know why mulch gets thrown more often than sand; it just does. Perhaps it is because most parents have had lots of occasions to instruct their children not to throw sand, but since mulch is relatively new on the scene, they may not have had as many occasions to specifically instruct their children not to throw mulch!

• **Here is another pediatric pearl we've gleaned: Herpes simplex keratitis (HSK) in children is bilateral in about 25% of cases,** according to a small retrospective study.[1] As in adults, recurrence was seen in about half of these patients, and these recurrent episodes tended to occur within two years of the initial episode. No eye with epithelial keratitis alone developed stromal keratitis, but half of those with combined epithelial and stromal keratitis at presentation later developed stromal keratitis. Lastly, about half of these children developed a residual corneal opacity.

The study found oral acyclovir to be useful during acute therapy. Our recommended dosage would be 200mg to 400mg (based on the child's weight) five times daily for one week. A liquid formulation of acyclovir is also available as an oral suspension in a concentration of 200mg/5ml (i.e., one teaspoon). ■

1. Chong EM, Wilhelmus KR, Matoba AY, et al. Herpes simplex virus keratitis in children. Am J Ophthalmol 2004 Sep;138(3):474-5.

In-Office Adenoviral Test

Adenoviral conjunctivitis, especially epidemic keratoconjunctivitis (EKC), can cause significant discomfort and inconvenience to patients. While the diagnosis of EKC is most usually a very straightforward clinical diagnosis, there are patients whose presentation poses a diagnostic dilemma.

The RPS Adeno Detector (Rapid Pathogen Screening, Inc.) is a simple, in-office, non-invasive device/procedure that can provide highly sensitive and specific results in about 10 minutes. The optometrist simply purchases one or more kits at the cost of about $25, and can then provide hospital laboratory-quality diagnostic services conveniently in the office. For more information, consult their web site: www.rps-tests.com.

CALL FOR CLINICAL CONUNDRUMS

Got a problematic patient? Having difficulty determining a diagnosis? Can't come to a conclusion on course of therapy? Send your clinical conundrums to Drs. Melton & Thomas at: DrugGuide@jobson.com. They'll publish your question—and their answer—in next year's *Clinical Guide to Ophthalmic Drugs*.

When the Pharmacy is Out of the Prescribed Medication

We have, from time to time, encountered patients with herpetic eye disease, acute uveitis, keratitis, and other severe (or potentially severe) eye conditions for which the patients' pharmacies were either out of, or did not stock, the medicines we prescribed.

Frequently, the pharmacist will tell the patient he can order the drug and have it for the patient in a day or two. This may not be compatible with optimum care—in fact, it usually is not.

Therefore, we provide the patient with proactive instructions to accompany the prescription(s) in these special conditions. You can simply print several of these adjunctive instruction notices on plain paper, cut them into prescription pad-sized squares, and staple them directly to the prescription as needed. In many cases, this "extra mile" measure significantly enhances patient care.

Here is a sample of the notice we use:

> **THIS MEDICATION IS URGENTLY NEEDED!**
>
> If your pharmacy does not have this drug available, please help direct the patient to a pharmacy that can provide it to them so that therapy can begin right away.
>
> – Thank you