A Supplement to
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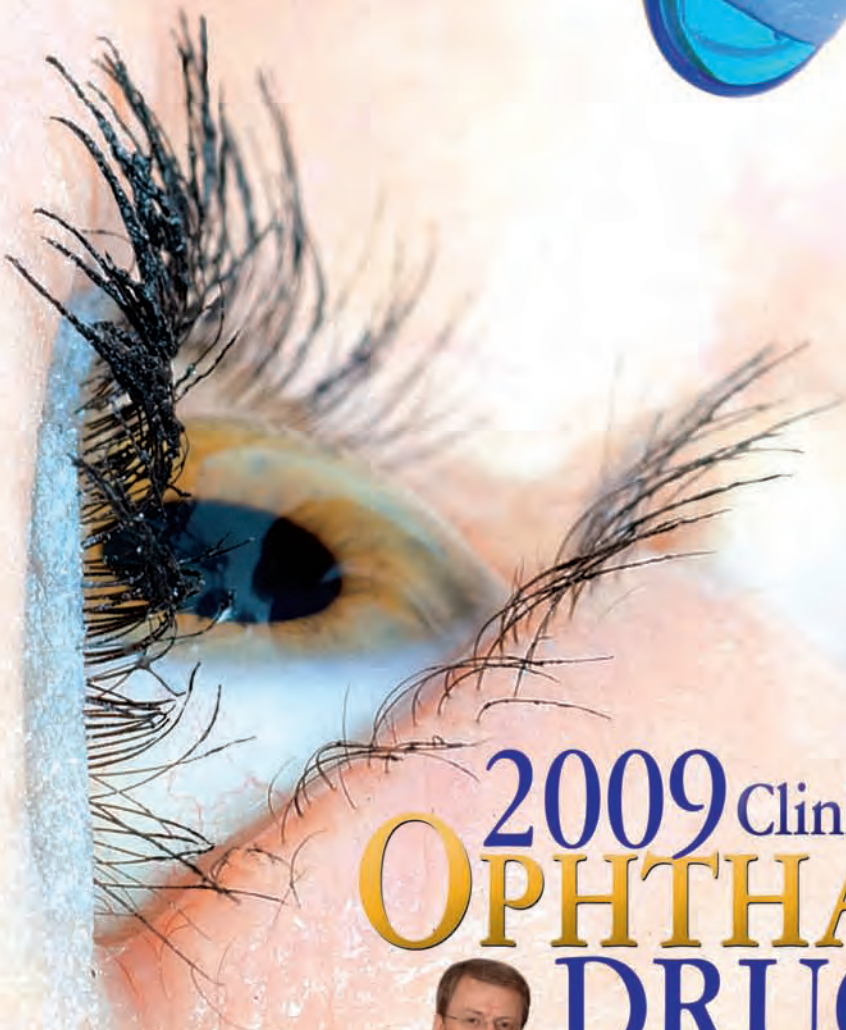

2009 Clinical Guide to OPHTHALMIC DRUGS

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

Supported by an unrestricted grant from
Bausch & Lomb

INTRODUCTION

Dear Friends,

Welcome to the 2009 edition of our "Clinical Guide to Ophthalmic Drugs." On behalf of the optometric profession, we thank *Review of Optometry* as well as Bausch & Lomb for their commitment to consistently publish this annual clinical guide for the ultimate benefit of our patients.

Indeed, there have been some noteworthy milestones to occur over the past year. Cosopt is now generically available, as is TobraDex suspension. Another topical corticosteroid is now available, and a new chloro-fluoroquinolone has been born. A side effect of bimatoprost has been capitalized upon and is now marketed as an eyelash-enhancing medicine.

We continue to be impressed with how doctors of optometry have stepped up to the plate regarding expansion of medical services to their patients. Prescriptions are at an all-time high, and the growth rate is exciting. "Optometrists continue to grow in importance as providers of a wide range of eye and vision care services," reads the February 2, 2009 *AOA News*. Specifically, "growth may be the most striking in the area of eye disease management and medical eyecare services."

We, as a profession, have accomplished much—and yet much achievement still lies ahead. It is our perception that care for glaucoma and dry eye still suffer across the board. We encourage attentive and thoughtful introspection (and obsessive clinical consideration) regarding these two select areas of patient need.

Meanwhile, there is enormous interest in, and discussion of, the industry-doctor relationship. It is still very much in the crescendo phase. We feel it is important for us to share our personal perspectives with our family of optometry.

First and foremost, everything any of us do must be centered on how we treat our patients. We must remember that every human being we are privileged to care for is someone's mother, father, daughter or son. Sometimes, in the hustle-bustle of the business aspects of running an office, the very essence of why we exist can be lost.

Second, we love to teach. Those who read our work or attend our lectures clearly understand this.

Third, we have worked with many optometry-related corporations over the past 20+ years, and have received monetary compensation for our professional services. There are some companies with whom we very much enjoy working; others, we avoid. We can speak enthusiastically about the products for which we know there is clinical value to the patient. We have never, and will never, make a statement about a drug or product that we feel is less than in the best interest of patient care, whether we receive compensation or not. We hope this statement of faithfulness to our patients and to our profession is received in the spirit in which it is intended.

As always, we hope the knowledge, experience, perspectives and insights we share herein allow you to continue to enhance the comprehensiveness and quality of your patient care.

Our very best wishes to each 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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Topical Antibiotics

It's a shame there aren't more bacterial eye infections—it would at least substantiate the high number of prescriptions for topical antibiotics. The truth is, bacterial eye infections are pretty uncommon.

We've often wondered why so many antibiotic eye drops are prescribed. Our best guess is that when clinicians are presented with red eyes, and they're uncertain of the diagnosis, they default to an innocuous therapeutic trial. After all, antibiotics, by and large, are certainly safe, but they render no therapeutic effect unless there are proliferating pathological bacteria on the ocular surface. Thankfully, the natural history of many external eye diseases are rapidly self-limiting, and so there is at least the appearance of a therapeutic effect.

Speaking of placebo power, an article by Marc Abelson, M.D., et al, in the June 2008 American *Journal of Ophthalmology*, found that when comparing topical azithromycin to vehicle, the clinical cure rate for gram-negative bacteria was 91.4% for the drug and 78.6% for the vehicle.[1] Against gram-positive bacteria, the clinical cure rate

Topical Antibiotic Drugs

BRAND NAME	GENERIC NAME	MANUFACTURER	PREPARATION	PEDIATRIC USE	BOTTLE/TUBE
Fluoroquinolones					
Besivance	besifloxacin 0.6%	Bausch & Lomb	suspension	≥ 1 yr.	5ml
Ciloxan, and generic	ciprofloxacin 0.3%	Alcon, and generic	sol./ung.	≥ 1 yr./ ≥ 2 yrs.	2.5ml, 5ml, 10ml/3.5g
Iquix	levofloxacin 1.5%	Vistakon Pharm.	solution	≥ 6 yr.	5ml
Ocuflox, and generic	ofloxacin 0.3%	Allergan, and generic	solution	≥ 1 yr.	5ml, 10ml
Quixin	levofloxacin 0.5%	Vistakon Pharm.	solution	≥ 1 yr.	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

for the drug was 89.4% and 60.6% for the vehicle. Now that's a rather remarkable cure rate for a mere vehicle!

The summary statement from this article succinctly concludes: "Because it [azithromycin] was well tolerated in this population, it may be a viable treatment option for children and adults with bacterial conjunctivitis." We certainly agree. **AzaSite** (azithromycin 1%, Inspire Pharmaceuticals) is formulated with DuraSite (a vehicle owned by InSite Vision, Inc.), a new co-adhesive matrix that holds active drug at the ocular surface for long periods of time (a few hours), thereby yielding good efficacy with much less frequent dosing. Indeed, the recommended dose schedule for AzaSite is one drop twice a day (about eight to twelve hours apart) for two days, then only once daily for five more days. This dosing schedule can be especially helpful when treating young children.

There is considerable discussion of the use of AzaSite in helping control posterior blepharitis/meibomian gland dysfunction. Some advocate the use of a drop of AzaSite at bedtime with gently rubbing of the excess medicine along the eyelid margins. Others advocate the use of a drop on the closed eyelids and then rub the medicine along the eyelid margins. Whether one should do either of these once or twice daily, and for how long, is not yet established. Our thought is to try the former approach twice a day for a week, then just at bedtime for two more weeks. This is completely anecdotal, as no large, prospective, double-blind studies provide any scientific guidance. Furthermore, we wonder if a month or two or oral doxycycline at 50mg per day with or without a two-week course of antibiotic steroid eye drops four times a day would be more, or less, effective. With the best interest of the patient being foremost, we, as a professional community, should try a number of clinical approaches with the hope of establishing a consensus of expert opinion as to the most effective approach for posterior blepharitis.

The big concern in treating bacterial infections is the continuing emergence of resistant bacterial species, particularly methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE). Now this concern plagues the primary care community more than the eye care community, mainly because eye doctors are privileged to treat eye infections with topical eye drops, which are usually able to overpower the most stubborn bacteria. This is because such high concentrations of drug can be achieved on the ocular surface with topical application, as opposed to a small pill diluted in about five liters of blood. It is not a fair fight. We may share more of the burden with the primary care community when it comes to treating eyelid infections, where orally administered antibiotics are employed.

Although the standard in vitro susceptibility testing is important in the management of infectious diseases, MIC values should be interpreted in light of the expected delivery and drug concentration at the site of infection. This point may be especially important for ocular

FDA Approves New B&L Fluoroquinolone

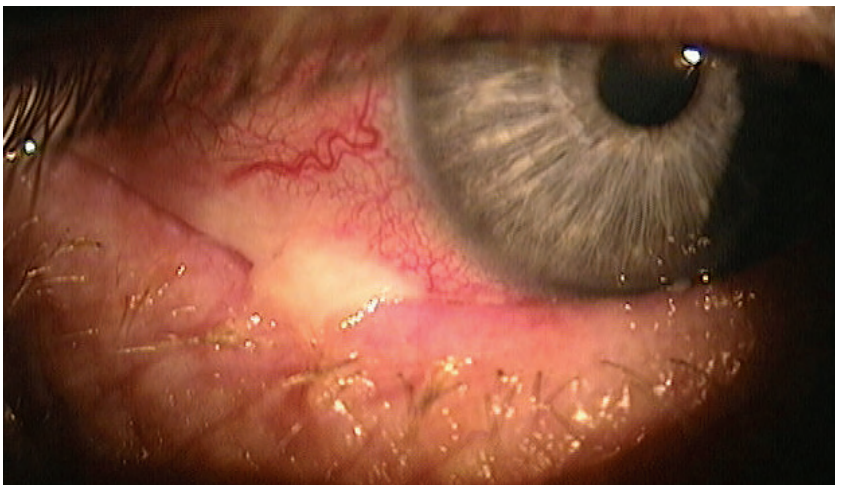
In late May, the FDA approved **Besivance** (besifloxacin 0.6% ophthalmic suspension, Bausch & Lomb) for the treatment of bacterial conjunctivitis. Besivance is a new topical ophthalmic antibacterial that treats a broad range of bacterial ocular pathogens, including the strains that are the most common causes of bacterial conjunctivitis (*Haemophilus influenzae, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae*, and others). Activity was shown both in vitro and in clinical infections.

The FDA's approval of Besivance was based on a series of eight clinical trials designed to test its efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics.[1,2] Its efficacy was evaluated in three multi-center, randomized, double-masked trials involving nearly 2,400 patients with a clinical diagnosis of bacterial conjunctivitis. In clinical trials, investigators found that Besivance treatment resulted in a greater proportion of patients experiencing clinical resolution and microbial eradication when compared to its vehicle.

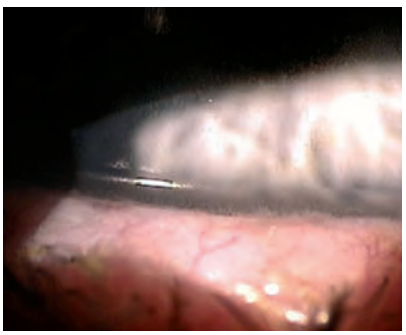
Besivance is formulated with the DuraSite drug delivery system (InSite Vision), which prolongs the ocular surface residency time and likely enhances therapeutic efficacy.

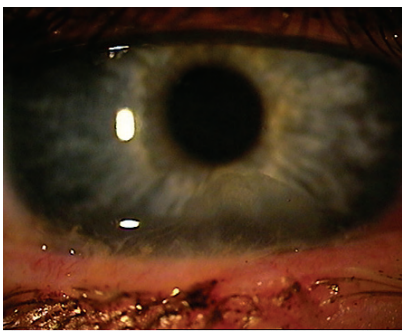
Besivance will be available in the second quarter of 2009, B&L says.

1. Karpecki P, Depaolis M, Hunter JA, et al. Besifloxacin ophthalmic suspension 0.6% in patients with bacterial conjunctivitis: A multicenter, prospective, randomized, double-masked, vehicle-controlled, 5-day efficacy and safety study. Clin Ther. 2009 Mar;31(3):514-26.
2. Tepedino ME, Heller WH, Usner DW, et al. Phase III efficacy and safety study of besifloxacin ophthalmic suspension 0.6% in the treatment of bacterial conjunctivitis. Curr Med Res Opin. 2009 May;25(5):1159-69.



The evident mucopurulent discharge is pathognomic for bacterial conjunctivitis.





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.

infections treated topically, where local concentrations of antibiotic may be much higher than maximum serum levels obtained from systemic dosing.

To give more insight into microbial resistance and antibiotic effectiveness, a nationwide system of study and evaluation of these concerns was established in 1996, the year levofloxacin was brought to market. This system is called "Tracking Resistance in the United States Today," or TRUST. More recently, in 2005 to 2006, Ocular TRUST was established, which looks specifically at ocular bacterial isolates.[2] You'll be rather amazed at what has been discovered. Basically, with regard to MRSA infections, the fluoroquinolones—levofloxacin, moxifloxacin and gatifloxacin—all performed identically and were effective only about 20% of the time. In contrast, trimethoprim was effective against 95% of MRSA isolates. These fluoroquinolones were effective against 80% of methicillin-sensitive *Staphylococcus aureus* (MSSA) isolates, whereas both tobramycin and trimethoprim were approximately 95% effective.

Regarding *Streptococcus pneumoniae*, these three fluoroquinolones were 100% effective. Against *Haemophilus influenzae*, the three fluoroquinolones were 100% effective and trimethoprim was about 85% effective.

Now, from a clinical practical perspective, what does all this mean? To explain, the Ocular TRUST authors state: "Although in vitro activity may be predictive of efficacy, it is not a guarantee because a multitude of factors influence clinical response."[2] Most all of our currently available topical antibiotics, used frequently enough, will eradicate most bacterial infections of the conjunctiva and cornea. If you're not achieving clinical cure with a fluoroquinolone, an aminoglycoside or trimethoprim, then switch or add one of these other classes/drugs. On rare occasions, we add Polysporin or Neosporin ophthalmic ointment at bedtime.

The general principle of treating with antibiotics or a corticosteroid is to have the patient use whichever drug you prescribe frequently (for example, every two hours) for at least a couple of days before dropping down to q.i.d. for four to six more days. It is not particularly the antibiotic chosen, but the frequency of the instillation that determines the clinical efficacy of most drugs.

There are two main subdivisions of antibiotics:

• *Bactericidal and bacteriostatic.* Bactericidal antibiotics are represented by the aminoglycosides, the fluoroquinolones, the penicillins, and the cephalosporins. Conversely, bacteriostatic drugs are sodium sulfacetamide, trimethoprim, and to some degree, erythromycin.

• *Concentration-dependent and time-dependent.* Concentration-dependent drugs are aminoglycosides and fluoroquinolones. Time-dependent drugs are the macrolides (erythromycin, azithromycin, and clarithromycin), and the penicillins.

All ophthalmic antibiotics with widely used oral counterparts will ultimately develop resistance—and yes, that includes the so-called "fourth generation" varieties. It is evident that gram-positive bacterial

pathogens (particularly *Staphylococcus aureus* and *epidermidis*) are the most common causes of ocular infections, but a sizable minority is gram-negative (mostly *Serratia*, *Pseudomonas* and *Moraxella* species). With this in mind, we need to use broad-spectrum drugs.

Fortunately, nearly all topical ophthalmic antibiotics are broad spectrum, and so meet the needs of the marketplace. Face it: a drug having only gram-positive or only gram-negative activity would require definitive culture results in order to enact a rational therapy for moderate to severe infections, which is, in practicality, irrational.

Now, let's take a clinically practical look at each drug:

Bacitracin

Developed in 1943, bacitracin is an excellent gram-positive bactericidal drug. Its mechanism of action is the destruction of the bacterial cell wall. It is only available as an ophthalmic ointment, which severely limits its clinical use, because adults do not like to have highly viscous ointments in their eyes. It has two main uses: infectious blepharitis and for nocturnal supplementation to topical eye drops in the treatment of bacterial corneal ulcer. Bacitracin is generically available.

Bacitracin with Polymyxin B

Polymyxin B is excellently bactericidal against most gram-negative bacterial species. Its mechanism of action is destruction of the bacterial cell membrane. Polymyxin B is not a stand-alone drug, however. It is always found in combination products to provide coverage against gram-negative pathogens. The combination with bacitracin is known as Polysporin ophthalmic ointment, and it is not available in the United States in eye drop form. The ointment formulation is available as a generic product. OTC (non-ophthalmic) Polysporin comes as a 15gm tube, contains the same two drugs, and performs identically.

Bacitracin, Polymyxin B and Neomycin

Neomycin is an aminoglycoside, which, like polymyxin, is not found as a stand-alone drug. It is always found in a combination formulation. Neomycin works to inhibit protein synthesis and is inherently broad spectrum, with the notable exception of *Pseudomonas* species (this is why polymyxin B is commonly combined within neomycin). Neomycin is an excellent drug, but it is mostly known for its potential to cause a Type IV delayed hypersensitivity reaction, which is manifested as a low-grade blepharoconjunctivitis, with variable expression of inflammatory blepharodermatitis. This red, weepy skin reaction can easily be reversed by drug cessation. Such so-called "neomycin reactions" occur in 5 to 10% of treated patients, and is nothing more than an inconvenience.

This triple antibiotic is an excellent, broad-spectrum drug that is available generically in both solution and ointment form. Because of solubility issues, gramicidin replaces bacitracin in the solution form. Gramicidin and bacitracin are clinical equivalents in combating gram-positive bacteria.

Trimethoprim with Polymyxin B

Trimethoprim is an excellent, broad-spectrum bacteriostatic antibiotic. Though it inhibits bacterial folic acid synthesis in a manner similar to the sulfonamides, it is not a sulfa-related drug.

Systemically, trimethoprim combined with sulfamethoxazole, historically marketed as Bactrim (AR Scientific) or Septra (Monarch), is a drug of choice when treating systemic soft tissue infections caused by MRSA pathogens. As can be

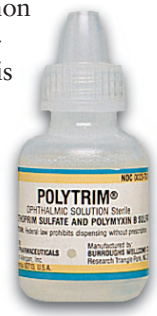
The Enduring Value of Generics

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.

Most ophthalmic generic drugs can be purchased directly through many ophthalmic supply companies for $2 to $4 each. Given the altruistic nature of optometrists, the character of our economy, and decreasing drug sampling, it might be wise to simply purchase a generous supply of some of these medicines to keep in our offices to help our indigent patients, and for after-hours medical emergencies when pharmacies may be closed.

deduced, trimethoprim is not active against some gram-negative bacteria, which is why it is combined with polymyxin B. Because this combination drug is particularly effective against *Streptococcus pneumoniae* and *Haemophilus influenzae*, two common pathogens in the pediatric population, this is the drug of choice in children with bacterial conjunctivitis. Originally known by the brand name **Polytrim** (Allergan), this ophthalmic solution is now available generically.



Erythromycin

The most common use of erythromycin in eye care is as a nocturnal lubricant when a lubricant with antibiotic properties is desired. Erythromycin, topically and systemically, has limited use because of its poor resistance profile. It is hardly ever used to actively treat an infection, but is almost always used in a prophylactic role. Just as with bacitracin, ophthalmic erythromycin is available only as an ointment, which limits its practical application.

Erythromycin is essentially bacteriostatic against many gram-positive and gram-negative bacteria. It exerts its antibacterial action through the interruption of protein synthesis. However, because of its systemic use for decades, resistance (particularly against *Staph*. species) has developed and has limited its clinical usefulness.

Azithromycin

This more modern rendition of a macrolide antibiotic is well known by its original brand name of Zithromax (Pfizer). It is prescribed systemically as a Z-Pak, and is available in a packet of six 250mg capsules; Tri-Pak, which is available in a packet of three 500mg capsules; or as a 1,000mg oral suspension and 2,000mg oral suspension (Zmax).

The ophthalmic formulation of azithromycin, known as **AzaSite** (Inspire Pharmaceuticals), is produced as a high-viscosity eyedrop solution. Since azithromycin has a particularly prolonged intracellular half-life, both in systemic and topical form, it is dosed less frequently than other ophthalmic drugs. For AzaSite, the standard dosage is one drop every eight to 12 hours for the first two days, then one drop daily for five more days.

Its mechanism of action is the inhibition of protein synthesis. Because of its spectrum of activity, it, like trimethoprim (with polymyxin B), has its greatest value in treating pediatric bacterial eye infections.

Its main advantage is its more patient-friendly dosing frequency. Since it is only available by brand name, it is relatively more expensive than generic Polytrim.

AzaSite comes in a white, opaque bottle containing 2.5ml of drug. It has an easy-to-open safety seal very much like that found on the Xalatan bottle.

Chloramphenicol

This drug is a workhorse in combating bacterial conjunctivitis in many countries throughout the world. Its use in the United States is markedly limited because of the remote possibility of causing aplastic anemia. Chloramphenicol is a highly lipophilic drug with excellent corneal penetration and broad-spectrum coverage. Its mechanism of action is inhibiting bacterial protein synthesis. It is generically available in both solution and ointment forms. Because of (probably unfounded) medicolegal concerns and the availability of many excellent antibiotic options, chloramphenicol is rarely prescribed in the U.S.

The Aminoglycosides

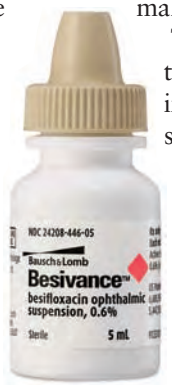
Aminoglycosides are a class represented by gentamicin, tobramycin, and neomycin. The first two are the only members of this class with broad-spectrum antibiotic properties, which allows them to function as standalone drugs. The aminoglycosides are not used systemically (because they can cause ototoxicity) and therefore, they have not had their antibiotic properties compromised by widespread primary care use. They exert their bactericidal action through the inhibition of bacterial protein synthesis.

Both gentamicin and tobramycin perform about the same, except that tobramycin appears to be even less likely than gentamicin to cause any epitheliotoxic response. While all aminoglycosides have the potential to cause ocular surface toxicity, this is not a practical concern when used for a short time, as they would be rationally prescribed in eye care (i.e., seven to 10 days), unless the ocular surface was already compromised prior to the institution of treatment. These drugs are generically available in 5ml bottles.

They are excellent, broad-spectrum antibiotics. Like the fluoroquinolones, their forte is in the gram-negative spectrum, and the highest MICs are for streptococcal pathogens. Also like the fluoroquinolones, these two drugs should be dosed frequently (every one to two hours initially until the infection comes under control), then the dosing frequency can be reduced as appropriate for the amount of time deemed necessary to achieve a clinical cure, usually seven to 10 days.

The Fluoroquinolones

Like erythromycin, the oral fluoroquinolones have enjoyed enormous popularity among primary care physicians. This has begun to cause significant resistance to this class of drugs. Most such "resistance" arises from in vitro studies and can usually be overcome clinically because of the huge relative volume of drug-per-surface area achievable on the ocular surface. While there are newer generations of fluoroquinolone (just like newer generations of oral cephalosporins), they are only marginally superior to older ones in clinical performance. Like the aminoglycosides, the fluoroquinolones are concentration-dependent in their bactericidal properties. Ciprofloxacin (**Ciloxan,** Alcon), ofloxacin (**Ocuflox**, Allergan) and gatifloxacin (**Zymar**, Allergan) are all available as a 0.3% concentration; levofloxacin (**Quixin**, Vistakon Pharmaceuticals) and moxifloxacin (**Vigamox**, Alcon) are available as a 0.5% concentration; the newly FDA-approved besifloxacin (**Besivance**, Bausch & Lomb) is available as a 0.6% ophthalmic suspension; and levofloxacin (**Iquix**, Vistakon Pharmaceuticals) is available as a 1.5% concentration. The 1.5% levofloxacin is FDA approved for bacterial keratitis, and other than ofloxacin and ciprofloxacin, is the only fluoroquinolone specifically FDA approved for this purpose.



So what does all this mean clinically? Not very much. When a fluoroquinolone is deemed the class of choice for a particular infectious condition, it is not particularly the specific drug chosen that matters as much as how frequently the drug is dosed. For example, an article in the September 2007 issue of *Ophthalmology*, compared 1% moxifloxacin, fortified tobramycin/cephazolin, and 0.3% ofloxacin in treating bacterial keratitis.[3] The result: they all performed equally. This is one example—of many—of why it is so important for O.D.s to consistently read the literature.

In summary, the topical antibiotics are grossly overutilized—in optometry, ophthalmology, and general medicine. Make every effort to pinpoint an accurate diagnosis (which, in most cases of acute red eye, is not of bacterial etiology), and then select an appropriate drug or drug class to achieve renormalization of tissues.

The frequency of instillation is almost always more important than the drug selected.

As best as we can determine, the four best drugs to combat acute bacterial infection in adults are: bacitracin/polymyxin B/neomycin; tobramycin; 0.6% besifloxacin; and 1.5% levofloxacin.

In children, we use either generic trimethoprim/polymyxin B or topical azithromycin.

The best, general-purpose ophthalmic ointment is a combination of bacitracin with polymyxin B. Only in advanced ocular surface infection would we use eye drops hourly and an ointment at bedtime; otherwise ointments are largely limited to blepharitis care.

We are fortunate to have such an awesome arsenal of medicines available to treat bacterial infections. Use them wisely, judiciously—and aggressively when indicated. ■

1. Abelson MB, Heller W, Shapiro AM, et al; AzaSite Clinical Study Group. Clinical cure of bacterial conjunctivitis with azithromycin 1%: vehicle-controlled, double-masked clinical trial. Am J Ophthalmol. 2008 Jun;145(6):959-65.
2. Asbell PA, Colby KA, Deng S, et al. Ocular TRUST: nationwide antimicrobial susceptibility patterns in ocular isolates. Am J Ophthalmol. 2008 Jun;145(6):951-958. Epub 2008 Mar 28.
3. Constantinou M, Daniell M, Snibson GR, et al. Clinical efficacy of moxifloxacin in the treatment of bacterial keratitis: a randomized clinical trial. Ophthalmology. 2007 Sep;114(9):1622-9.

Adenoviral Infections: Take Charge of EKC

There is indeed an excellent, highly effective, easily applied and very cost-effective treatment for acute EKC. To maximize therapeutic response in viral infections, initiate therapy early in the disease process.

The following letter perfectly sets the stage for where we are, as a profession, regarding the care of patients afflicted by this acute infectious disease:

Dear Drs. Melton and Thomas,

I am an O.D. in a seven-doctor ophthalmology/optometry practice. The majority of my patients are within the realm of corneal disease, as I work closely with our corneal specialist.

I was intrigued when I read your recent article in the November 2008 issue of Review of Optometry, *regarding the use of 5% Betadine to treat acute EKC. From December 2006 through March 2007, we had an outbreak of a very aggressive strain of EKC among our three offices. While we did see patients who were obviously through our office (we seriously amended our cleaning and disinfecting protocols), we also saw patients new to our office with EKC. All in all, we saw close to 275 patients during that time with EKC. Yet, in my research, I never found anything like your protocol.*

Upon reading the recent article, I decided I would implement treatment on the next acute EKC patients that I saw in the office. I treated four patients the month of January, one of whom was a technician, two confirmed with the RPS test. All had improvement of their symptoms within two days, and resolution within four to five days. None developed infiltrates or membranes.

Development of thick membranes can be seen in more advanced cases of EKC. After instillation of topical anesthetic, these membranes can be peeled off using curve-tipped forceps. Had we seen this patient earlier, such horrendous sequelae could have been prevented with treatment of Betadine 5% along with Lotemax.

I find it curious that most of optometry and ophthalmology have not embraced this treatment. I spoke with a colleague regarding the treatment and he was not impressed. His response was that they will get better in a week any-

way. Most of the doctors (M.D.s) within my practice had never heard of this treatment, including one who recently completed his fellowship in anterior segment. I can tell you in 12 years of practicing, I have never seen true EKC clear up in a week. These patients are miserable, uncomfortable, and unable to work. Perhaps after seeing nearly 200 patients during that outbreak has hyper-sensitized me.

I work closely with a corneal specialist. He shares my opinion that this is not well embraced and that extensive research into some obscure ophthalmology journals is required to even find mention of off-label 5% Betadine use to treat EKC.

As primary care providers, optometry needs to embrace this treatment and put it into practice. All that is required is a careful history and slit lamp biomicroscope, as well as some 5% Betadine.

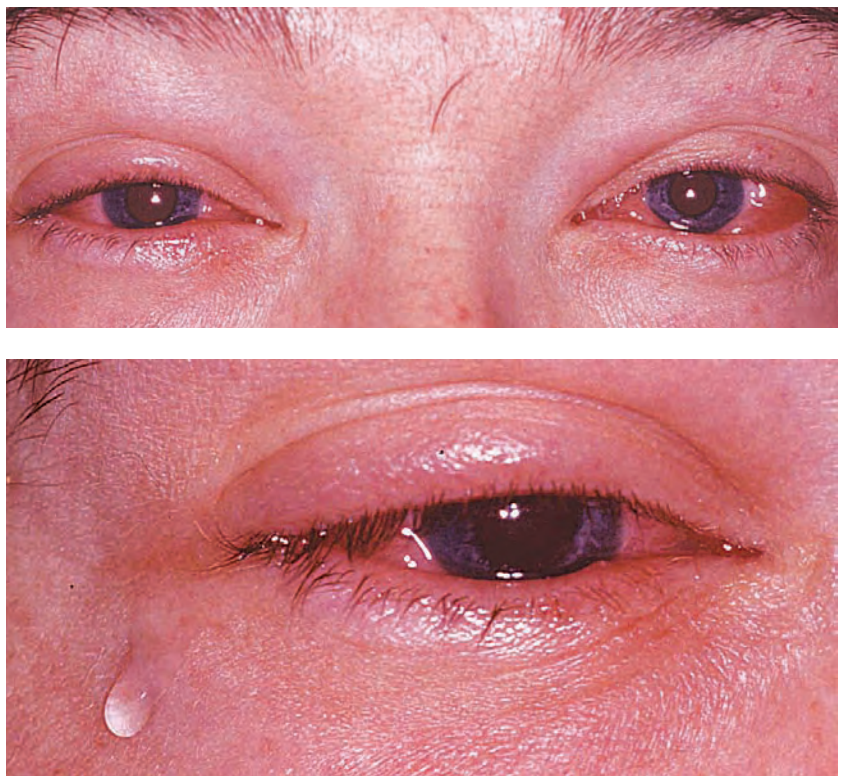
Again, thank you for your time and for the fascinating article.

To further illuminate the dismal awareness of this excellent, off-label, medical treatment, let's look at the following two quotes from the contemporary medical literature:

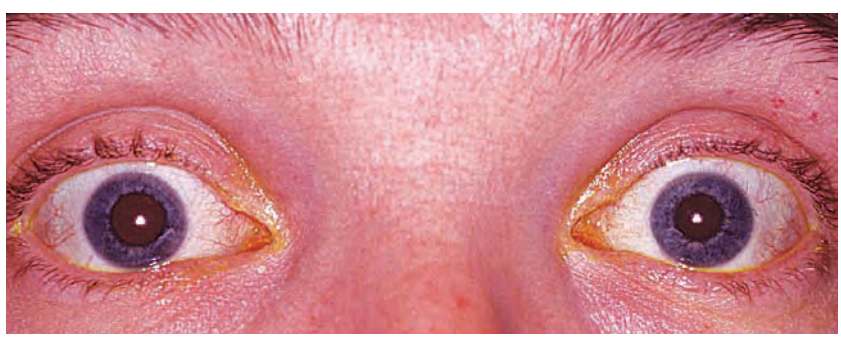
"Unfortunately, no effective treatment has been found for viral conjunctivitis."

— *Ohnsman CM. Study looks at exclusion of students with conjunctivitis from school.* Ocular Surgery News. *2007 April 15;25(8):160-3.*

"Since the initial description of epidemic adenoviral ocular infections in Austria in 1889 until the present day, no effective drug to treat such patients has been found. Today, acute adenoviral ocular infections (epidemic keratoconjunctivitis, follicular conjunctivitis, and pharyngeal conjunctival fever) remain among the most common external ocular viral infections seen clinically worldwide … There are 51 serotypes of adenovirus, of which approximately one-half have been shown to cause ocular disease. The American Academy of Ophthalmology Preferred Practice Pattern proposes symptomatic treatment for these infections and the use of topical steroids to reduce scarring in severe cases of adenoviral keratoconjunctivitis with marked chemosis or lid swelling, epithelial sloughing, or membranous conjunctivitis. Lacking an effective Food and Drug Administration-approved antiviral, clinicians recognize the continuing need to develop a drug to reduce patient morbidity, to reduce the extent of or entirely prevent the formation of vision-altering subepithelial infiltrates, to reduce lost time from



This patient presented with severe EKC. He had the classic signs of acute red eye (top) and watery discharge (above).



Just two days after treatment with our EKC-Betadine protocol, his eyes were white and quiet.

school or work, and to reduce or prevent the transmission of ocular infections within households, communities, and medical facilities."

— *Romanowski EG, Gordon YJ. Update on antiviral treatment of adenoviral ocular infections. Am J* Ophthalmol. *2008 Nov;146(5): 635-7.*

Perspective on 'Off-label' Use of Ophthalmic Medications

"The practice of ophthalmic off-label drug use is neither uncommon nor new," says an editorial in the May 2007 *American Journal of Ophthalmology*. "The prevalence and clinical importance of prescribing drugs for unlabeled uses are substantial … thus the prescribing of drugs for unlabeled use is often necessary for optimum patient care."

The article also quotes an FDA statement on "off-label" usage: "Good medical practice and the best interest of the patient require that physicians use legally available drugs according to their best knowledge and judgment. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the products' use and effects."

In summary, "Treatment with any drug or therapy is based on a consensus between a well informed patient and physician. This is no different in the case of the use of off-label ophthalmic medications. The more scientifically sound the information supporting its use, the more confidently can the physician and patient assess the possible value of the proposed unapproved treatment."

"The Ophthalmic Mutual Insurance Company recognizes that 'off-label' use of approved medications is a legal and necessary part of the practice of medicine."

Parrish R 2nd, Sternberg P Jr. Does "off-label" mean off limits for patient care? Am J Ophthalmol 2007 May;143(5):853-5.

The good news is there *is* indeed an excellent, highly effective, easily applied and incredibly cost-effective treatment therapy for acute EKC. The key to a maximal therapeutic response in viral infections is to initiate therapy early in the course of the disease process.

Let's look at the clinical features of acute EKC. Almost all of these patients present with a history of acute redness starting in one eye, and spreading to the fellow eye in two to three days. A watery discharge is a constant feature. A palpable preauricular node is commonly detected (if one feels for it) on the side of the initially infected eye. In more advanced cases, the bulbar conjunctiva can demonstrate multiple petechial hemorrhages, most commonly seen superiorly. Bacterial conjunctivitis can have variably expressed microvascular injection of the conjunctiva, and evident mucopurulent discharge. Only in "hyperacute" bacterial conjunctivitis is there evident preauricular lymph adenopathy. If diagnostic certainly is elusive, the RPS Adeno Detector (www.rps-tests.com) may be helpful.

Sources for Betadine 5%

We're often asked, "Where or how can I acquire 5% Betadine?"

There are probably many sources. Here are a few:

- OCuSOFT.com
- www.hilco.com
- Eyecareandcure.com
- Sigmapharmaceuticals.com

These companies offer a broad array of ophthalmic products. The 30ml opaque plastic bottle of Betadine 5% sells for approximately $16.

Also, if "sampling" becomes an historic event, one can purchase at minimal cost a wide variety of generic ophthalmic drops from these same sources to keep in the office for altruistic use for indigent patients, or when seeing emergency patients after hours.

If diagnosis of adenoviral disease is elusive, the RPS Adeno Detector may help.

When we encounter a patient with moderate to advanced EKC, we generally treat them via the following "**Melton-Thomas EKC-Betadine Protocol**":

1. By history, rule out any allergy or sensitivity to iodine, the molecular backbone of Betadine.
2. Instill a drop of 0.5% proparacaine, as Betadine (like tropicamide) stings upon instillation.
3. Betadine can cause mild stippling to the corneal epithelium resulting in marked stinging. So instill a drop or two of a topical NSAID.
4. Instill four to five drops of Betadine onto the eye.

5. Ask the patient to gently close the eyes and roll them around to ensure thorough distribution of the Betadine across the ocular surfaces.

6. After one minute, lavage out the Betadine (to avoid any unnecessary toxicity and discoloration of the tissues) with any sterile ophthalmic irrigating solution.

7. Just for good measure, instill another drop or two of the NSAID (or even proparacaine if the patient has any discomfort).

We have now essentially eliminated the adenoviral load; but of course, we've done nothing for the secondarily inflamed conjunctival tissues. To address the inflammatory component, prescribe Lotemax q.i.d. for four days.

Between the two of us, we have used this procedure more than 200 times now and find it enormously helpful for our patients with acute EKC. More importantly, we have queried audiences all across the country, and have yet to find any optometrist who reports anything other than success with use of this protocol.

Antiviral Infections

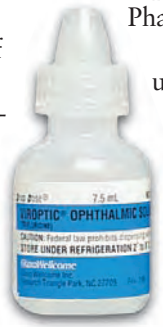
In addition to EKC adenoviral infection, there are two additional viral infections that are clinically important: herpes simplex and varicella zoster.

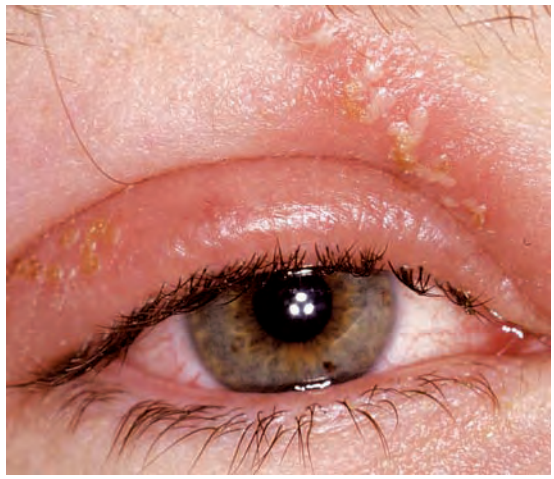
We should be well prepared to diagnose and competently intervene therapeutically on behalf of patients with diseases caused by these viruses.

Herpes Simplex Virus

Herpes simplex viruses (HSV) are responsible for nearly 50,000 new and recurring cases of HSV keratitis each year in the United States.[1] HSV almost exclusively manifests as dendritiform or geographic epithelial keratitis.

Fortunately, we have a tried-and-true, FDA-approved medicine to kill the herpes simplex virus, available both generically as trifluridine 0.1% ophthalmic solution and by its original brand name of **Viroptic** (Monarch Pharmaceuticals). Treatment is usually straightforward: one drop to the affected eye every two hours (while awake) for four to five days, then q.i.d. for four or five more days, depending upon the individual response. Preservative-free artificial tears are the only other eye drops





Herpes simplex blepharitis.

Clinical Pearls for Herpes Simplex Virus

- Be sure to explain to your patient that HSV can be recurrent.
- Unlike some medicines, the generic of Viroptic seems to work as well as the original formulation. Both are expensive (about $100 to $140 per 7.5ml bottle), but the generic is generally $30 less per bottle than the name brand.
- The 7.5ml bottle of Viroptic or its generic equivalent is stored under refrigeration until dispensed to the patient, who can keep it at room temperature. If any medicine remains following treatment, it should be kept in the refrigerator to be used in case of a recurrence before the medicine's expiration date.
- There is rarely—if ever—a need to use both topical and oral antiviral therapy.
- Viroptic is a pyrimidine analog and vidarabine 3% ointment is a purine analog. This chemical distinction prevents cross allergenicity and therefore on those very rare occasions where a patient became allergic to or intolerant of trifluridine, vidarabine ointment could be effectively substituted. While Vira-A is no longer commercially available, it can be obtained via Leiters Pharmacy of San Jose, Calif. (1-800-292-6773; www.leiterrx.com). The cost is approximately $200. However, we almost always prescribe oral acyclovir (incidentally, also a purine analog) if a patient becomes intolerant of trifluridine. The dosage is 400mg five times a day for one week. We concurrently have the patient use a preservative-free artificial tear every couple of hours until the viral keratitis is cleared. Any oral antiviral works as well as acyclovir.
- About 20% of cases ultimately express themselves not as an infectious keratitis, but rather as a stromal immune keratitis, or rarely as herpetic uveitis. While an epithelial infectious keratitis is treated with antiviral medications, these immune (or inflammatory) expressions are treated with potent topical corticosteroids such as Lotemax or Pred Forte. Usually antiviral "cover" is given as trifluridine q.i.d. or oral acyclovir (ACV) 400mg three or four times a day. This antiviral cover is generally prescribed until the steroid drops have been tapered down to b.i.d. The steroid taper is protracted in the setting of stromal immune disease. It generally takes a month to get down to b.i.d. dosing, then perhaps a month or two at b.i.d. before tapering to once daily or every other day indefinitely, depending upon the individual response.

that might be helpful in conjunction with this topical approach.

Then again, many doctors now bypass topical therapy and simply initiate therapy with an oral antiviral, such as 400mg of oral acyclovir five times a day for one week or Valtrex (valacyclovir, GlaxoSmithKline) 500mg t.i.d. for one week.

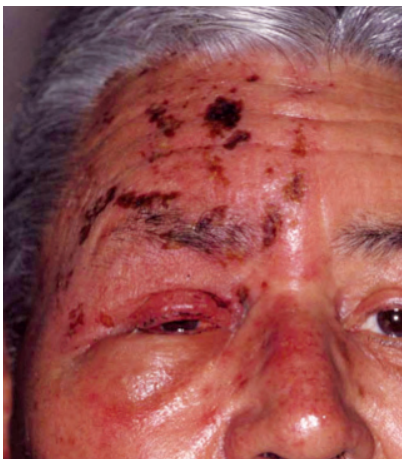
Herpes Zoster (Varicella Zoster) Disease

The head and/or face is the second most common site (after the trunk) for the expression of shingles. More specifically, the ophthalmic (or first) division of the trigeminal nerve is the most common head/face site of expression. Regardless of site, the treatment is uniform: 800mg of acyclovir (ACV) p.o. five times a day for one week.

Patients are commonly sent to eye doctors by internists, dermatologists and family physicians to rule out eye involvement. Sometimes patients with head/face shingles simply present first to an eye doctor for care. In either case, it is essential to assess the global tissues, looking specifically for anterior uveitis and/or an inflammatory keratitis, as these are by far the most common eye manifestations of the VZ virus. The eye itself is involved in approximately half of all ophthalmic division cases.[2] The rest are simply dermatologic cases. If the eye is involved, it is always an expression of inflammation, and is usually quickly controlled with the aggressive use of a potent corticosteroid such as Lotemax or Pred Forte.

Since the herpes viruses are neurotrophic, afferent sensation can be perturbed for many months after successfully treating the initial zoster disease. Such post-herpetic neuralgia is probably best treated by a primary-care physician or dermatologist. Treatment is generally accomplished with a tricyclic antidepressant, such as amitriptyline, and analgesics.

For cases of chicken pox occurring in children over the age of two and generally weighing over 40lbs., the FDA's and CDC's recommended dosage of ACV is up to 800mg q.i.d. for one week, depending upon the weight of the patient. We think this strongly demonstrates the safety of these antivirals.



In adults, the varicella zoster (herpes zoster) virus manifests as shingles. The eye itself is involved in approximately half of all ophthalmic division cases. The rest are simply dermatologic cases.

There are three oral antivirals currently available. Besides acyclovir (Zovirax, GlaxoSmithKline), there is valacyclovir (Valtrex, GlaxoSmithKline) and famciclovir (Famvir, Novartis). Valtrex's zoster dosage is 1,000mg t.i.d. for one week. For herpes simplex, it is dosed at 500mg t.i.d. for one week. Famvir's zoster dosage is 500mg t.i.d. for one week; for herpes simplex, it is dosed at 250mg t.i.d. for one week. All three drugs are minimally biologically active until they are activated via viral thymidine kinase phosphorylation. This wonderfully unique mechanism of viral kinase activation is the mechanism that makes this class of oral antivirals so safe, yet so highly effective.

These medicines are maximally effective when instituted within the first three days of disease manifestation; however, they still render a positive therapeutic effect when used even five, six or seven days into the disease event. Keep this in mind so that patients will not be denied proper medical care.

One area of caution with regard to these oral antivirals is renal disease. Since these drugs are excreted via the kidneys, make sure there is no known kidney disease. If there is kidney function impairment, then call the patient's nephrologist or primary care physician to learn the patient's creatinine clearance value. You should then have a telephone visit with a pharmacist or the patient's physician who, via a quick and simple computer program, will be able to calculate the appropriate antiviral dosage for your patient based upon this value. It's very straightforward.

In summary, there are excellent, safe and highly effective drugs available to treat viral diseases afflicting the human eye: 5% ophthalmic Betadine for EKC, trifluridine (or oral antivirals) for epithelial herpes simplex, and oral antivirals for shingles and/or chicken pox. When properly applied, these drugs bring rapid relief to nearly all patients. ■

1. Liesegang TJ. Herpes simplex virus epidemiology and ocular importance. Cornea 2001 Jan;20(1):1-13. Review.
2. Pavan-Langston D. Herpes zoster ophthalmicus. Neurology 1995 Dec;45(12 Suppl 8):S50-1.

Corticosteroids

Inflammation, either alone or as a component expression, is the most common of ocular conditions, so a masterful knowledge of the corticosteroids is of paramount importance.

Without debate, this class of drug reigns supreme in the treatment of inflammatory eye diseases.

There are two main types of ophthalmic corticosteroids: those that are ketone-based, and one that is ester-based. Almost all the side effects—most notably posterior subcapsular cataracts and increased intraocular pressure—are minimal or absent with the ester-based formulation, and only occasionally problematic even with the ketone formulation. The most commonly prescribed ketone-based steroids are prednisolone and dexamethasone. The only representative of the ester-based class of steroids is loteprednol.

As a reflection of epidemiology, this class of drugs enjoys very widespread use. However, for reasons beyond our understanding, there continues to be perpetuated great fear, caution and reserve in the use of these wonderful drugs. Perhaps it is because of the potential negative effects they can have with long-term use, both topically and orally, or perhaps it reflects a lack of ample clinical experience. Perhaps it is because corticosteroids do have the potential to worsen some conditions if there is misdiagnosis, such as HSV keratitis or fungal keratitis. Whatever the case, when properly used, corticosteroids have the ability to rapidly suppress ocular inflammatory diseases, thus helping to restore health and normalcy to afflicted ocular tissues.

The reality is that almost all acute-onset ocular conditions and diseases are inflammatory in nature. Examples include: noninfectious conjunctivitis; the uveitides;

Difluprednate: A New Steroid

Durezol (difluprednate 0.05% ophthalmic emulsion, Sirion Therapeutics) is the first "emulsion" formulation of corticosteroid to come to the market. Unlike a suspension, an emulsion does not require shaking because emulsions maintain homogenous molecular distribution within the vehicle. It is a difluorinated derivative of prednisolone, and therefore another ketone-based corticosteroid, similar also to dexamethasone. The emulsion vehicle allows for enhanced ocular surface contact time, thereby allowing less frequent instillation, as compared to non-emulsion delivery systems.

Durezol is FDA-approved specifically for the "management of inflammation and pain after intraocular surgery," but we have every reason to believe it could effectively treat any type of eye inflammation. Studies have documented that Durezol is as equally effective as Pred Forte with half the dosing frequency. If this result is corroborated in widespread clinical use, then Durezol could displace Pred Forte as the drug of choice in treating moderate to severe anterior uveitis. We expect this drug to be used mostly in a postoperative manner, but may find a nice niche in uveitis management as well.

Durezol 0.05% ophthalmic emulsion is preserved with a 0.1% sorbic acid, and is available in a 5ml opaque bottle.

DaVanzo RJ. Durezol compared to Pred Forte in the treatment of endogenous anterior uveitis. Poster presented at 2009 Association for Research in Vision and Ophthalmology (ARVO) meeting. May 5, 2009; Fort Lauderdale, FL. Abstract #2697/D1106.

episcleritis; inflamed pingueculae; chemotoxic keratoconjunctivitis; phlyctenular keratoconjunctivitis; contact lens associated red eye (CLARE); allergic conjunctivitis; giant papillary conjunctivitis; blepharitis; corneal infiltrates; rosacea-associated blepharokeratoconjunctivitis; superior limbic keratoconjunctivitis; ocular trauma; recurrent corneal erosions; stromal herpetic keratitis; herpes zoster ophthalmic manifestations; Thygeson's superficial punctate keratitis; glaucomatocyclitic crisis; microcystic edema; and a host of nonspecific inflammatory conditions.

In radical contradistinction, the indication for the use of an antibiotic is evidence of mucopurulent infection, or prophylaxis if there is a true need for such. As can readily be seen, we are much more likely to need to employ a corticosteroid drug compared to an antibiotic.

Since there are so many indications to use corticosteroids, we suggest the best way to gain an understanding of these drugs is to know the three or four occasions when their use *alone* is either absolutely or relatively *contraindicated*. Obviously, the likely therapeutic misadventure is to use a topical steroid in the face of epithelial herpes simplex keratitis. However, any seasoned clinician has had such an event occur.

Here's a classic case: The nursing home called the ophthalmologist's office (this could have been an O.D. office just as easily, but in keeping with the true story, this is how this case played out) explaining that Mrs. Jones has a painful red eye and would he please call in a prescription for an eye drop for her. He prescribed an antibiotic-steroid combination drug to be used q.i.d. After two weeks of this therapy, Mrs. Jones' eye was no better, and in fact was steadily worsening. (It is pitiful that the nursing home waited two weeks to follow back up.) So, in two weeks, Mrs. Jones was brought to the office, where she was found to have an advanced case of HSK with reduced visual acuity.

Here's what was done: the antibiotic-steroid was stopped (not tapered—you only need to consider tapering when treating an intrinsic inflammatory condition), and trifluoridine therapy was started (q2h for four days and then q.i.d. for one week). She recovered normal vision, and did just fine.

Certainly the patient was considerably inconvenienced, but ultimately, no enduring harm was done. This case nicely reveals the reality of this therapeutic misadventure, and note that the eye did not fall out of the orbit!

Here are a few thoughts to consider:

First, you should never call in a prescription for a steroid or steroid-containing eye drop, especially if it is a unilateral red eye.

Second, If the patient has a bacterial, fungal or *Acanthamoeba* infection, use of a steroid would be unwise and counterproductive—and yet this too happens occasionally, even in the best of hands.

Third, if there is a significant epithelial defect (not ordinary SPK) such as a corneal abrasion, corneal ulcer, etc., do not use a steroid alone.

Finally, and this is the relative contraindication: If the diagnosis is unknown, perhaps the steroid would be the best medicine, and perhaps not. We opine that if the diagnosis is clearly not one of the above three conditions, a steroid or combination antibiotic-steroid would probably well serve the patient.

Topical Corticosteroid Drugs

BRAND NAME	GENERIC NAME	MANUFACTURER	PREPARATION	BOTTLE/TUBE
Maximum Strength Steroids				
Durezol	difluprednate 0.05%	Sirion Therapeutics	emulsion	5ml
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
generic	prednisolone sodium phosphate 1%	generic	solution	5ml, 10ml, 15ml
Vexol	rimexolone 1%	Alcon	suspension	5ml, 10ml
Moderate Strength Steroids				
Flarex, and generic	fluorometholone acetate 0.1%	Alcon	suspension	5ml, 10ml
FML, and generic	fluorometholone alcohol 0.1%	Allergan	suspension	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

Now, we must make a couple of significant modifications to the above three conditions when choosing to use a combination antibiotic-steroid rather than a steroid alone:

• With HSV epithelial keratitis, any steroid or combination drug is still absolutely contraindicated.

• Many times, our patients with significant bacterial conjunctivitis have considerable associated conjunctival injection. We typically treat these with a combination drug. With this approach, we eradicate the bacteria and suppress the conjunctival inflammation concurrently, thus bringing rapid relief and cure to the patient. The teaching that steroids exacerbate infectious processes is true *if used alone*, but is of no significance if an effective antibiotic is simultaneously used. We almost always prescribe Zylet (loteprednol/tobramycin, Bausch & Lomb) q2h for two or three days, then just q.i.d. for four or five more days. We have done this many hundreds of times with complete success. Since there are no combination drugs with antifungal or anti-acanthamoeba properties, then both a pure steroid and antibiotic/steroid combination should be avoided in such conditions.

• What about significant epithelial defects? Many such epithelial defects are secondary to anterior stromal leukocytic infiltration, which cause the overlying epithelium to secondarily break down. This is commonly seen with peripheral corneal infiltrates and staphylococcal exotoxin epithelial compromise. These are primarily inflammatory conditions, but since there is significant secondary epithelial compromise, employing a combination drug is probably a

Clinical Perspectives on Corneal Infiltrates

Corneal infiltration is still commonly mistaken for an ulcerative process. For example, this young man (*below*) smokes and sleeps in his over-worn contact lenses AMA (against medical advice). He presented to his optometrist, who had him use an antibiotic eye drop hourly around the clock. After 36 hours of sleep deprivation and no improvement, he sought a second opinion, and his condition was properly diagnosed by another optometrist. Lotemax was added q4h, and the antibiotic drop was reduced to q.i.d. In two days, the cornea (and the patient) were vastly improved.

We marvel that these scenarios continue to occur. Let's look at how to improve patient care in this setting. There are a number of factors to consider in the differential diagnosis between a leukocytic infiltrate and a bacterial corneal ulcer:

• First, pay attention to the epidemiology of these two conditions: infiltrates are very common; ulcers are very rare.

• An anterior chamber reaction (i.e., cells and flare) is most always seen with an ulcerative process. While an anterior chamber reaction is usually absent with an infiltrate, trace cells are sometimes seen, especially if the condition has been ongoing for several days.

• The appearance of the conjunctival injection pattern can also be very helpful. With an infiltrate, sector injection is the rule; in an ulcerative process, the entire bulbar conjunctiva is injected.

• While not highly sensitive nor specific, the degree of pain the patient describes can be helpful. An ulcer tends to evoke much more pain than an infiltrate.

• Location can also be helpful, but not absolute. As a rule, ulcers are solitary and tend to be more central, while infiltrates can be single or multiple and strongly tend to express themselves at or near the corneal limbus.

The fluorescein staining pattern of the lesion is probably one of the characteristics we find most helpful in making a definitive diagnosis. With an ulcer, the size of the fluorescein staining pattern closely mirrors the size of the corneal lesion, whereas the staining pattern of an infiltrate is significantly smaller than the underlying lesion. This is because an ulcer begins in the epithelium, and expands laterally and in depth, creating an epithelial defect closely paralleling its stromal invasion. An infiltrate results from the chemotactic attraction of leukocytes from the paralimbal microvasculature. The accumulation of white blood cells in the anterior stromal tissues results in some secondary compromise to the overlying epithelium, which tends to cause a relatively small defect in the center of the underlying stromal lesion.

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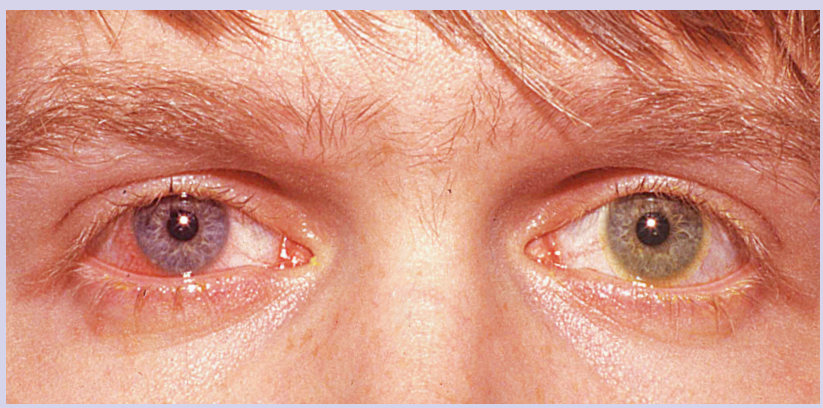


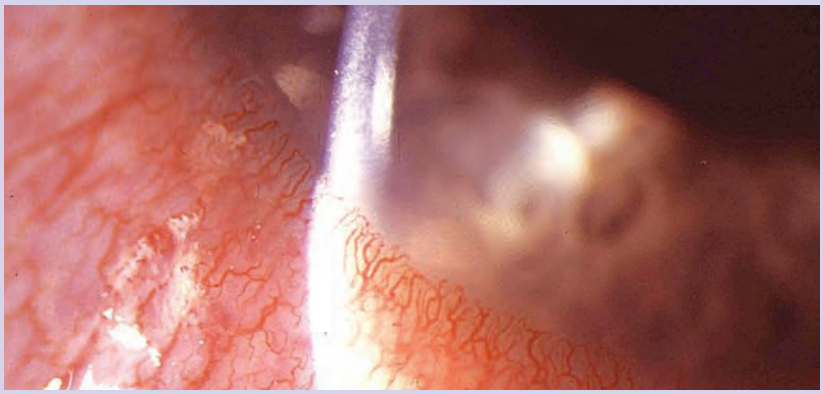
After 36 continuous hours of hourly fluoroquinolone eye drops, this young man's "bacterial corneal ulcer" still showed no improvment.

Clinical Perspectives on Corneal Infiltrates

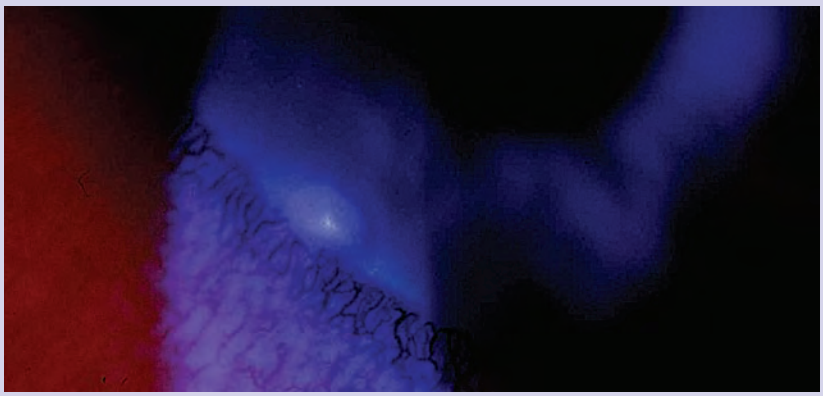
(continued from previous page)

An attentive clinician should, with most all presentations, be able to correctly identify the lesion as either an infiltrate or an infectious ulcer and treat appropriately; however, there are some cases that defy a clear, confident diagnosis. Let's look at diagnostic and therapeutic considerations:

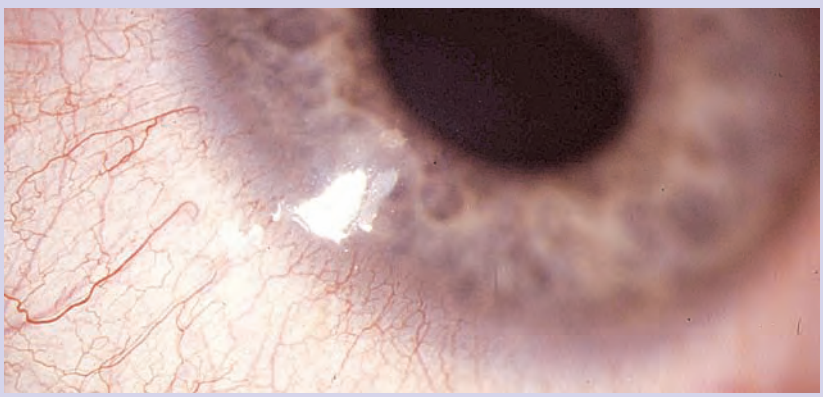
1. If the lesion is clearly infectious, a fluoroquinolone hourly while awake with Polysporin ointment at bedtime may be an excellent initial approach. If there is no response or suboptimal response, add generic Polytrim hourly, because if this ulcer is caused by a MRSA bacterium, the fluoroquinolone may be suboptimal and the trimethoprim should be able to complement eradication of any resistant bacteria.



Is it an ulcer or an infiltrate? Note the peripheral location of the lesion.



The fluorescein dye-to-lesion ratio is invariably indicative of an inflammatory process. This is a sterile leukcytic infiltrate with anterior stromal inflammation caused an small overlying epithelial breakdown.



Two days later—using Lotemax every four hours and reducing the antibiotic drop to q.i.d.—the cornea (and the patient) were vastly improved.

2. If it is clearly an infiltrate, use Zylet q2h for two or three days, and then just q.i.d. for three to more five days.

3. If the diagnosis is problematic, then initiate therapy with a fluoroquinolone hourly for a day or two while the patient is awake. If desired, generic Polysporin ointment at bedtime can be added. If there is little or no improvement, the diagnosis is likely a sterile infiltrate, and Lotemax can be added q.i.d. Reassess progress in a day or two. Always remember that hourly around-the-clock eye drop instillation is brutal to the patient. A highly efficacious ophthalmic ointment such as Polysporin should nicely address the infectious process during the sleep cycle, if indicated.

In closing, consider the following quote from prominent Harvard ophthalmologist Mark B. Abelson, M.D., in the January 2005 *Review of Ophthalmology*. His advice perfectly mirrors our approach as set forth above:

"Left untreated, marginal infiltrates generally disappear within a week or two. Ocular steroids have been the best and only recognized drug therapy for sterile marginal infiltrates, and their application will shorten the course of inflammation, regardless of causative origin. For many patients, a quicker recovery from symptoms such as redness, tearing, and discomfort is important for improving their quality of life. Steroids are often prescribed in conjunction with an antibiotic in order to decrease the chance of developing a secondary infection or corneal ulcer and to protect against misdiagnosis."

wise choice. There are numerous examples in which a steroid (with antibiotic cover) can indeed potentiate re-epithelialization. As previously mentioned, if the diagnosis is uncertain, yet the condition is not representative of one of the above discussed contraindications, then a steroid or combination drug will most likely bring healing.

One example in which this would *not* be true would be chlamydial (adult inclusion) conjunctivitis, in which no topical eye drop is therapeutic. (Oral azithromycin dosed at one single dose of 1,000mg is the treatment of choice. No topical eye drops are indicated at all.)

One final caveat regarding whether to choose a pure steroid or a combination product in the context of corneal disease: If the corneal epithelium is intact, then using a pure steroid is usually appropriate, whereas if there is significant epithelial compromise, a combination drug such as Zylet would probably be wiser, or at least make the prescriber feel more comfortable. ■

Corticosteroids for Chronic Care

The key to a successful clinical outcome lies predominantly in the frequency of instillation. For example, in treating an iritis, one would select a potent steroid, advise the patient to shake the bottle vigorously prior to each instillation, and to use it hourly while awake until the iritis is well suppressed. Then, and not until then, should the tapering process begin. The longer the steroid has been used, the longer the tapering process should be. There is little reason to taper steroids if a clinical condition succumbs in just a few days. Tapering is usually needed only if the condition is severe, and intense therapy is needed for more than a few days.

There are always conditions that fall outside of "typical" and we could use this entire guide to cover all the details of all ocular inflammatory conditions. For example, patients with Thygeson's superficial punctate keratopathy, stromal herpetic keratitis or chronic recurrent uveitis may need to use a drop or two of a steroid daily for months or even years to keep their condition under control. Without exception, loteprednol, an ester-based molecule, is the drug of choice in such a setting because of its vastly enhanced safety profile as compared to ketone steroids such as dexamethasone and prednisolone.

While we once traditionally used Pred Forte to treat all cases of anterior iritis, we have modified this practice. Dr. C. Stephen Foster, M.D., is a world-class uveitis subspecialist whose excellent lectures we were privileged to attend at SECO earlier this year. Following one of his lectures, we asked Dr. Foster for his perspective on using Lotemax to treat uveitis. He quickly responded, "Sure, that's what it's designed for," and clearly stated that he would use Lotemax for uveitis cases of grade 2 or less. As we have done this for many years in our practices, we were pleased to know that such a renowned expert shared our practice patterns.

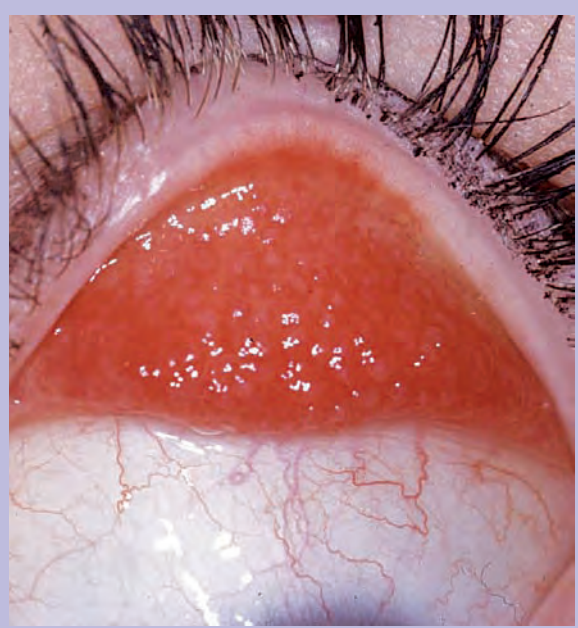
We also treat many of our chronic/recurrent uveitis patients with Lotemax. We try to minimize recurrences by having these patients use Lotemax once or twice daily for months (or years in some cases) at a time. We have never had a problem with this clinical approach, and are very comfortable with the long-term safety profile of Lotemax.

The Melton-Thomas GPC Protocol

If giant papillary conjunctivitis (GPC) is due to overwear of contact lenses (e.g., overnight wear or suboptimal replacement), convert to daily wear, decrease daily wearing time, or replace lenses more often.

- Discontinuation of lens wear for a week is usually necessary to separate the offending device from the irritated tissues, and allow for unbridled medical therapy.
- If GPC is due to inadequate precorneal tear film function, address the dry eye with Soothe XP, and/or Lotemax, and/or punctal plugs, and/or omega-3 supplementation.
- Medical treatment: If there is clinically significant conjunctival injection, then we use Lotemax every two hours for two days, then q.i.d. for five to seven days. This rapidly dampens the conjunctival inflammation and enhances tear film function.
- After one week, we *conservatively* reintroduce the contact lens. We continue the Lotemax b.i.d., once prior to lens insertion and again after lens removal, for one or two more weeks. We also encourage gentle contact lens rubbing along with usual nightly disinfection.

We have used this protocol routinely for many years with excellent success.



The Melton-Thomas Anterior Blepharitis Protocol

Since most anterior blepharitis cases are mixed seborrheic/staphylococcal, we pretty much treat in a generic manner.

We have long abandoned using diluted baby shampoo, and now strongly favor prepackaged commercially prepared lid scrubs. This allows us to do an abbreviated treatment in the office, which helps patients to intimately understand how to accomplish proper and effective eyelid hygienic maneuvers. Also, the commercially available eyelid scrubs certainly appear more professional than diluted hair shampoo.

We then medically treat with Zylet ophthalmic suspension q.i.d. for two weeks, and then b.i.d. for two more weeks. Alternatively, have the patient rub an antibiotic-steroid ointment into the eyelid margins q.h.s. for two weeks. Tobramycin is an excellent medicine against *Staph.* species, and nothing suppresses inflammatory eye disease like a steroid.

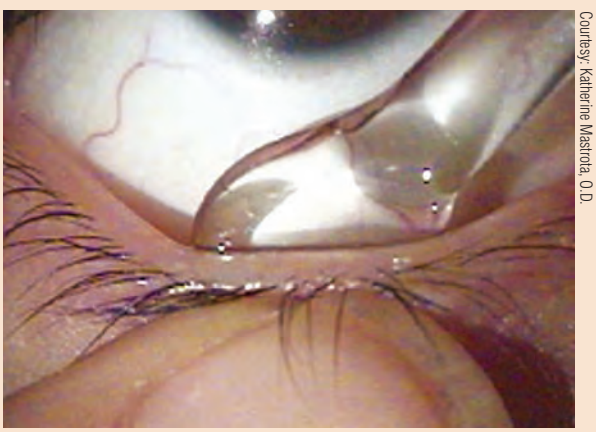
The Melton-Thomas Posterior Blepharitis Protocol

Stagnation/inspissation of the meibomian glands can easily lead to disruption of the tear film lipid layer and thus cripple tear film integrity. Symptomatic dry eye disease commonly follows.

There is a three-step process that we use:

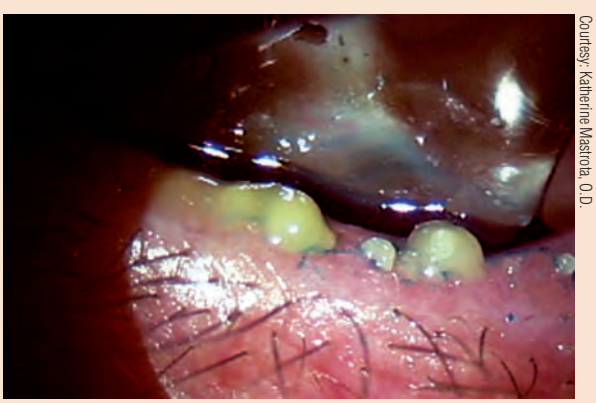
1. Apply warm soaks to soften glandular secretions. Such can be accomplished with a clean washcloth at the lavatory sink, with a moistened washcloth warmed in the microwave oven, with a wrapped, warm baked potato, and any number of other unique approaches that work. OCuSOFT and Advanced Vision Research have novel self-generating, heat-producing "goggles" that may be the best means to accomplish heat application to the eyelids.

2. Express the glands. Now that the sebaceous secretions are relatively loosened, massage/express the previously constipated glands. In your office, this can be accomplished, usually without the need for prior heat application, at the slit lamp. A wonderfully simple device was invented by Katherine Mastrota, O.D., for this "express purpose" (pun intended). Her device is known as the Mastrota paddle, and it is available through OCuSOFT. Trust us; it is cheap, lasts a lifetime, and nicely facilitates the expression of meibomian glands. In the home, patients can perform meibomian gland expression by simply massaging out the glands with their fingers. We recommend that meibomian expression be performed in our office the first time so that we can ensure the patient knows how to effectively accomplish the task. Once the glands have been expressed, the patient can use a cotton swab, clean washcloth, or lid scrub to clean away the expressed debris, whichever they prefer.



Courtesy: Katherine Mastrota, O.D.

3. Medical therapy. Once the mechanical maneuvers have been accomplished, oral doxycycline can be used concurrently to augment the mechanical therapy and, on a more protracted basis, help maintain increased physiologic glandular function. We typically prescribe 50mg per day for three to four months, or longer if needed. The tetracycline class of medicines (of which doxycycline is a member) has other beneficial effects beyond its antibiotic properties. Drugs in the tetracycline class are workhorses in dermatology in that they alter and enhance the quality of sebaceous glandular function. In the setting of meibomian gland disease, the doxycycline rearranges the fatty acid structure within the meibomian glands and helps normalize their function.



Courtesy: Katherine Mastrota, O.D.

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.
- 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.

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

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
FML-S	Allergan	fluorometholone 0.1%	sodium sulfacetamide 10%	suspension	5ml, 10ml
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	5ml, 10ml

PREGNANCY CATEGORY: All drugs listed above are Category C.

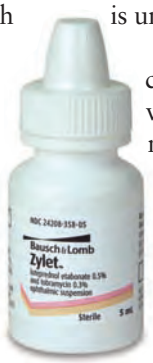
topical steroid.

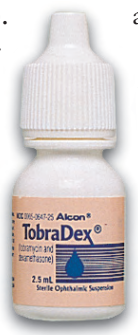
If the accurate diagnosis of bacterial conjunctivitis is made, the decision is whether to prescribe an antibiotic or a combination drug. The prime determinants are twofold:

1) The severity of the infection.

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 nasolacrimal 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 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.

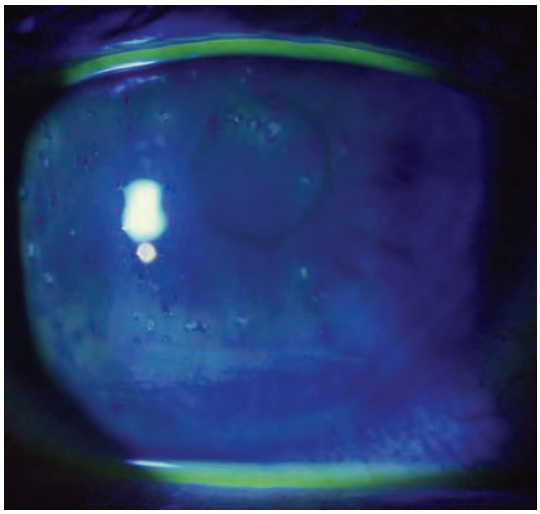
Thygeson's Superficial Punctate Keratopathy (SPK)

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 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



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, then b.i.d. for one to two more weeks), quickly brings resolution in most cases.

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)

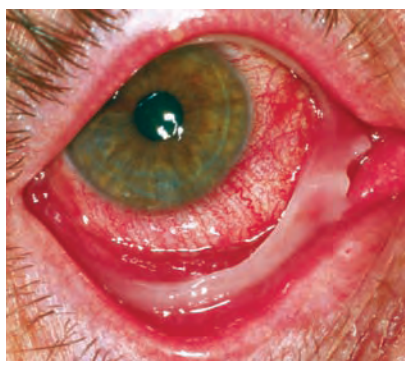
If the EKC is severe, and especially if tarsal conjunctival membranes have formed, there can be epithelial compromise. The key here is to physically peel away these membranes, as they exert toxic and mechanical trauma to the epithelium. Be sure to wear gloves when performing this procedure, as minor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

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 hastens acute symptomatic recovery. Second, since the virus particles residence time has been considerably truncated, the potential for viral



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.

Pearls for Using Combination Drugs

- Any time 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.

antigenic (stromal immune) keratitis is largely pre-empted. *(See also "Adenoviral Infections: Take Charge of EKC," page 10A.)*

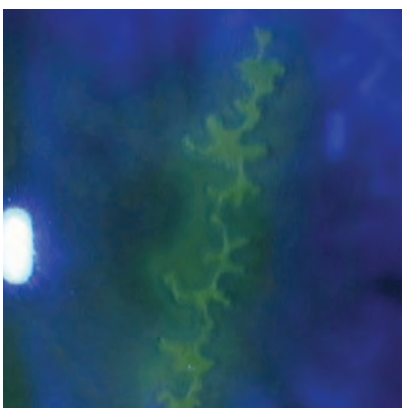
Note: since Betadine stings, always pre-treat the cornea with a drop of proparacaine. Furthermore, to diminish any patient discomfort, we generally instill a drop or two of **Voltaren** (diclofenac sodium, Novartis Ophthalmics) or **Acular LS** (ketorolac tromethamine, Allergan) before, and again after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

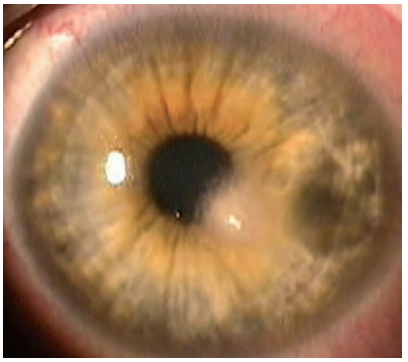
Herpes Simplex Keratitis (HSK)

Here is another condition that commonly demonstrates considerable epithelial compromise.

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



Fungal (*fusarium*) infection with stromal infiltrate.

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

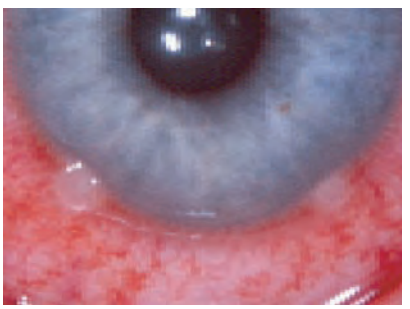
Most such defects heal within a day or two, regardless of any therapeutic maneuvers. To our knowledge, no studies have prospectively followed "no treatment" of abrasions, but it would be interesting to know the absolute need for prophylactic antibiotic use, which is standard practice in these situations. 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.

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)



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

• Slightly raised, dirty-white infiltration
• Satellite lesions
• Partial or complete ring
• Secondary anterior uveitis

For perspective, in our combined 54 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.

While one would think staphylo-

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 "Clinical Perspectives on Corneal Infiltrates," page 17A.*)

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.

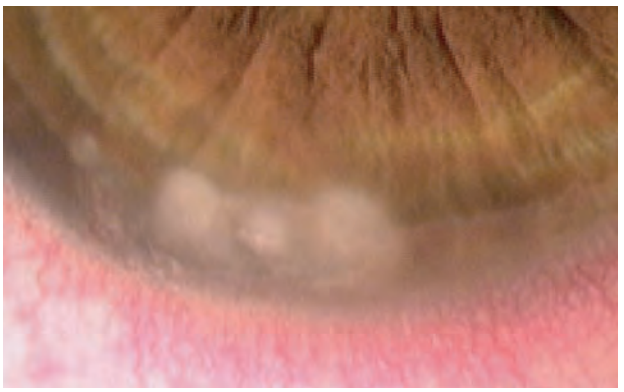
There is a less intensive approach that can be used if you think your patient has a leukocytic infiltrate, but are still concerned about possible infection. Here, use any fluoroquinolone or aminoglycoside hourly until the patient is seen back the next day to assess the clinical course. In either diagnostic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

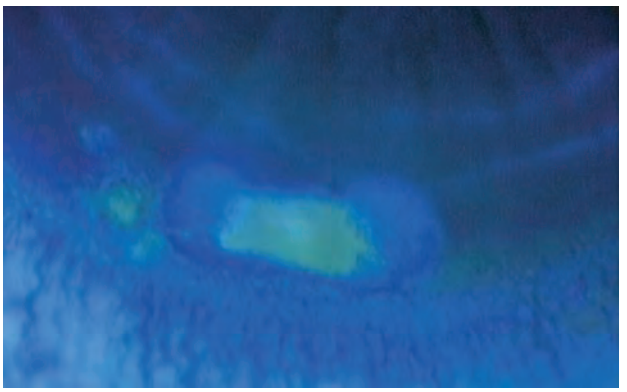
Naïve practitioners who witness such improvement may wrongly deduce that the lesion must have been an infective process, and be glad they used an antibiotic. Once again, infiltrates are very common, and bacterial keratitis is very rare.

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.





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).

coccal 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 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 corticosteroid/antibiotic 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 it would depend on 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! ■

Current Therapy in Ocular Disease

by Drs. Ron Melton and Randall Thomas

Past recipients of the "Glaucoma Educator of the Year" Award by the American Academy of Optometry

Authors of *Review of Optometry's* annual *Clinical Guide to Ophthalmic Drugs*

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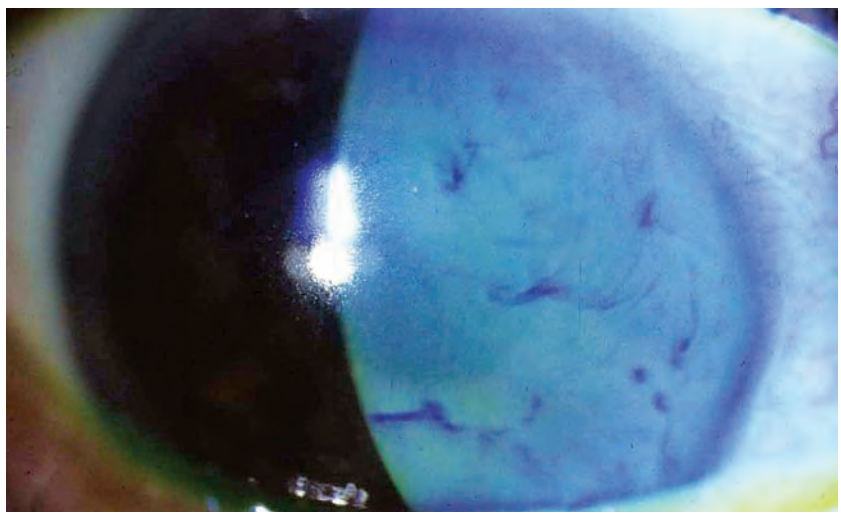
Dry Eye and the Literature

Reducing inflammation is key to treating ocular surface damage. Here's a sound, successful, literature-based protocol for patients with ocular surface dryness.



Dry spots on the corneal surface are associated with a reduced tear break-up time.

There is a lot of marketing spin regarding the medical treatment of dry eye. We propose to set forth a rational, scientifically sound and clinically successful, literature-based protocol for truly helping patients who suffer from ocular surface dryness.

Bear with us as we set the foundation for our clinical approach. Two of the most respected clinicians in this field of study are Michael A. Lemp, M.D., and Gary N. Foulks, M.D. Dr. Lemp is widely regarded as one of the pioneers in dry eye research and has been with the Georgetown University School of Medicine for many years. Dr. Foulks has chaired the cornea service at Duke University and the University of Pittsburgh, and is currently at the University of Louisville, in Kentucky. He is editor-in-chief of the authoritative journal, *The Ocular Surface* (www.theocularsurface.com), a journal we highly recommend to all practicing eye doctors.

Now, let us examine some pertinent quotes from these clinician/scientists from the peer review literature. In the July-August 2007 issue of *Survey of Ophthalmology*, Dr. Foulks states:[1]

- "Increasing the thickness of the tear lipid layer improves the stability of the tear film, suggesting that in selecting a dry eye therapy, an important feature would be the ability of the treatment to mimic the lipid layer of the tears."
- "One drop containing Restoryl, the active ingredient of **Soothe XP** [Bausch & Lomb], more than doubled lipid layer thickness."
- "Restoryl has been shown to replenish the aqueous layer of the tear film. When applied to the eye, Restoryl differentiates into neutral oils (helping to rebuild the lipid layer), interfacial molecules (stabilizing the interface between the lipid and aqueous layers, and supporting the mucin layer), and water (helping to restore the aqueous layer)."
- "Overall, decades of research have shown a strong correlation between dry eye symptoms and the state of the tear film lipid layer, as well as a clear connection between the status of the lipid layer and the osmolarity of the tear film."

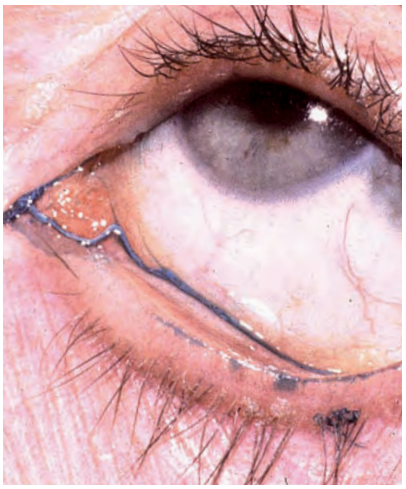
In the September 2008 *American*

Journal of Ophthalmology, Dr. Lemp states: "Tear osmolarity is considered 'the central mechanism causing ocular surface inflammation, damage and symptoms, and the initiation of compensatory events in dry eye'."[2]

We have learned from Dr. Foulks that Soothe XP stabilizes the lipid layer, thus protecting the tear layer from becoming hyperosmotic. Dr. Lemp established the (hyper) osmotic tear film as the prime cause of ocular surface inflammation. We believe these two foundational cornerstones establish Soothe XP as a key element in helping patients with dry eye. Dr. Lemp continues: "Although the exact place of inflammation in the stream of events leading to ocular surface distress is not clear, its role is unmistakable." He goes on to say, "In the use of cyclosporine (Restasis) to modulate immune activity and to suppress inflammation in dry eye, there is increasing evidence that the use of topical corticosteroids as temporary or pulsed therapy can be useful in reducing the damaging effect of inflammation."

Furthermore, the Report of the International Dry Eye WorkShop (DEWS), published in 2007, clearly established that "corticosteroids are an effective anti-inflammatory therapy in dry eye disease."[3]

Now, let's talk about the use of the steroids in ocular surface inflammatory disease. This is very simple and very straightforward. Steroids continue to suffer from the myth that they are dangerous. Cars have the *potential* to be dangerous; in fact, 38,000 people die in them every year. The truth is that Americans love their cars and, while cognizant of this statistic, they confidently get in their beloved vehicles on a routine basis with great confidence they will return home safely. Well, steroids have the potential to cause harm, but many thousands of people are helped by steroids every day. It is so important to keep the enormous beneficial attributes of steroids in focus. As intensely busy clinicians, we have been able to help thousands of patients over the decades, and we cannot recall a single therapeutic



Ropy discharge seen in a patient with moderate dry eye that stains with lissamine green.

Using Lotemax for 'Pulsed Therapy'

Michael Lemp, M.D., in his article "Advances in Understanding and Managing Dry Eye Disease," stated, "there is increasing evidence that the use of topical corticosteroids as temporary or pulsed therapy can be useful in reducing the damaging effect of inflammation." We have discussed that a two to three-month course of Lotemax may well suppress clinically significant ocular surface inflammation, but as we all know, human beings are rarely model patients. Once the initial symptoms subside, many patients suboptimally use their artificial tears and their symptoms rebound.

This would be the point at which we would stress the importance of compliance with their Soothe XP (or other artificial tear) and prescribe a pulsed dose of Lotemax. There is no set way to do this. We generally have our patients pulse the Lotemax at q.i.d. for two weeks and then stop, or q.i.d. for two weeks, and then b.i.d. for two to four weeks, then stop. In our clinical experience, this re-pulsing may need to be done once or twice a year. We have found such pulse therapy to be a safe, cost-effective manner to keep our patients with ocular surface dryness happy and comfortable.

Lemp MA. Advances in understanding and managing dry eye disease. Am J Ophthalmol. 2008 Sep;146(3): 350-356. Epub 2008 Jul 2. Review.

Clinical Insights Into Soothe XP

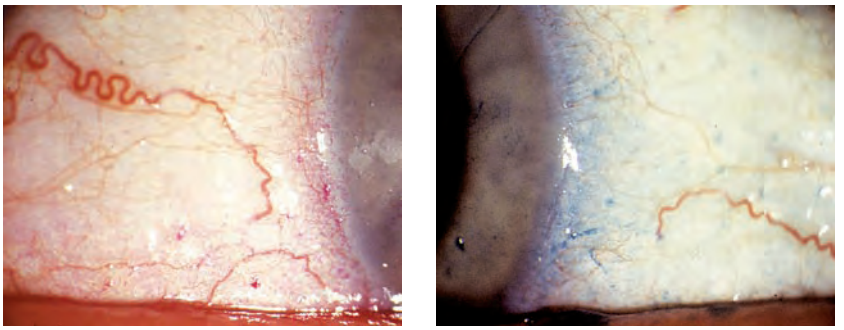
Soothe XP was the yield of decades of research by Donald Korb, O.D., and his research team in Boston. It is an ultrafine mineral oil emulsion, which makes it able to enhance the lipid layer. The downside to this mineral oil emulsion is that it causes considerable blurring for about 30 seconds with each instillation. It is important to advise patients of this event prior to their initial use. Soothe XP is not BAK preserved. Instead, it is preserved with PHMB (polyhexamethylene biguanide), a relatively gentle formulation.

On the side of the box is an inaccurate statement: "remove contact lenses before use." Now, let us remember that this product was designed by one of the most prestigious contact lens researchers in the world, but to test the safety and compatibility of Soothe XP with every FDA-approved contact lens was simply cost prohibitive, thus the default language imposed by the FDA. Yet, because Soothe XP works so well as a rewetting agent, we take the time to explain this to the many patients to whom we recommend this excellent product for this purpose.

Soothe XP comes in a white, opaque, 15 mL bottle. It is available OTC for about $10. *(For a more extensive discussion of Soothe XP, see our* 2008 Clinical Guide to Ophthalmic Drugs*, page 25A.)*

misadventure with corticosteroids.

There are two types of steroid molecules: ketone-based, such as prednisolone and dexamethasone; and one that is ester-based, loteprednol. Human systems do not possess "ketonases," but have an abundance of esterases. It is this reality that sets loteprednol apart as a very safe and very effective molecule. In fact, the loteprednol molecule is nearly identical to the prednisolone molecule except that a ketone moiety is replaced with an ester moiety. So, for 10 years, the world has had extensive experience with loteprednol and it is authoritatively established as a highly effective, yet very safe, anti-inflammatory medicine. Obviously this makes Lotemax the best available choice in the management of ocular surface inflammation.

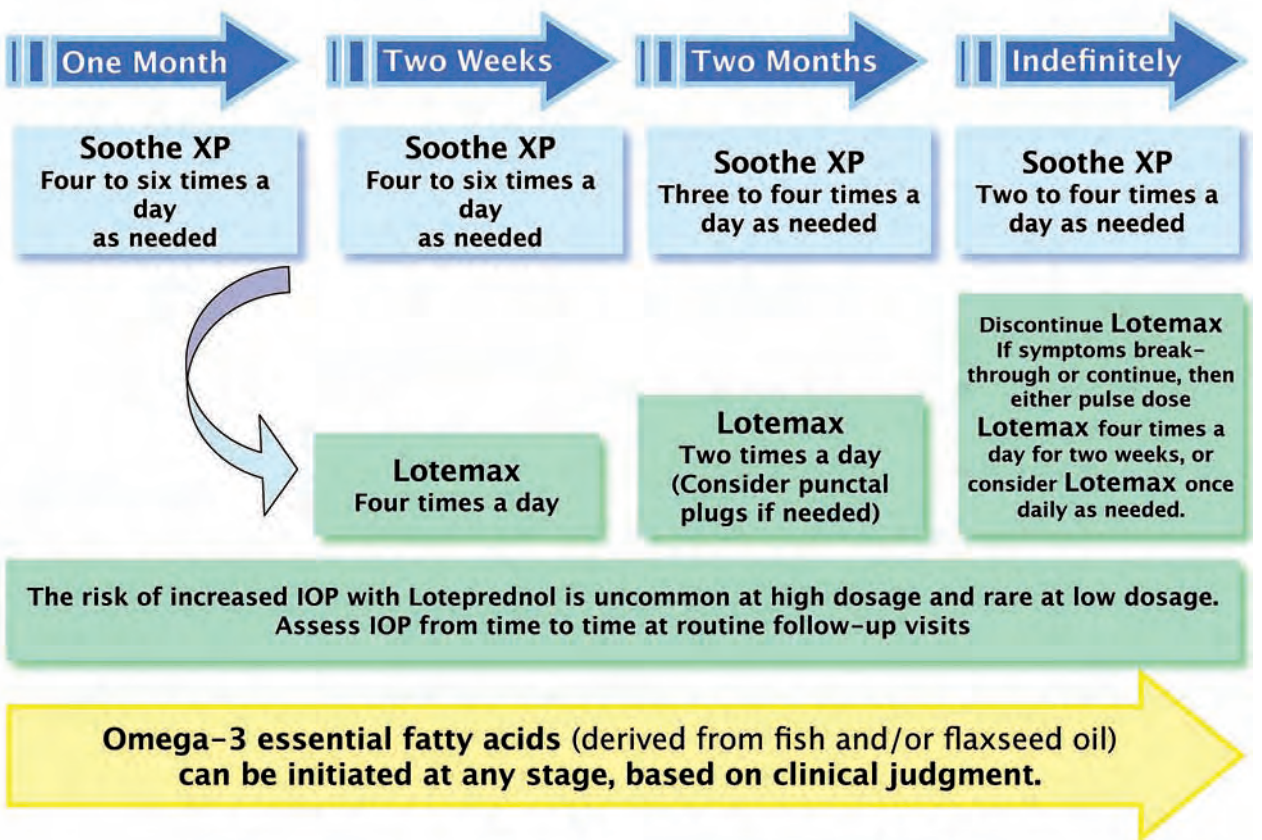


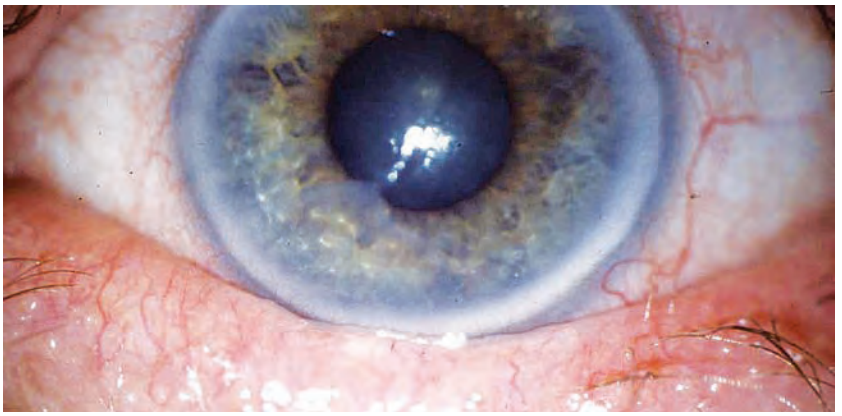
Rose bengal and lissamine green staining of the conjunctiva and cornea in a patient with Sjögren's syndrome.

Now, the stage is set so we can care for our dry eye patients in an enlightened manner. Here is how we have approached these patients since the formulation of Soothe XP came to market a few years ago:

• First, we do a therapeutic trial with Soothe XP for a month. We encourage our patients to use the drops as often as they would like, but at least four times a day. At the one-month follow-up, if they are happy, our goal is met, and the patient is encouraged to continue to consistently use the Soothe XP as needed. We stress here that Soothe XP, being a mineral oil emulsion, is

Melton and Thomas Soothe XP/Lotemax Dry Eye Management Protocol





Telangiectasia of the lid margin in a patient with advanced dry eye. Also note the absence of inferior lacrimal lake height, which is classic in advanced dry eye states.

radically different from other artificial tears and cannot intelligently be grouped as "just another artificial tear" due to its completely different molecular design.

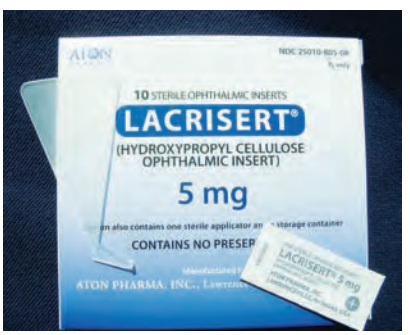
• If the patient is only partially improved, we recommend adding Lotemax q.i.d. for two weeks, being sure to separate the two eye drops by about 30 minutes. We have found that most, but not all patients, achieve relief with this approach. If there is a clinically significant inflammatory component to the patient's dry eye, then it is our opinion that a two-week course of q.i.d. loteprednol is sufficient to suppress the ocular surface inflammation.

• Assuming clinical success, we now decrease the Lotemax to b.i.d. for two more months and allow the patient to try to reduce the frequency of instillation of the Soothe XP.

• At the two-month follow-up (assuming we have a satisfied patient, which is typically the case), we are at another decision tree. By this time, most patients are using Soothe XP two to three times a day, and we can try to stop the Lotemax. Remember that Drs. Lemp and Foulks have showed us that tear osmolarity is "the central mechanism causing ocular surface inflammation." So, via Soothe XP, we have bolstered the lipid layer, thus reducing tear osmolarity, and with Lotemax, we have addressed whatever hyperosmolarity-induced inflammation preexisted. At this juncture, there should be little or no clinically significant ocular surface inflammation.

• Now, back to the decision tree: Following the two to three-month "inflammation suppression" phase, we stress the importance of consistent ocular surface lubrication to help prevent any reestablishment of inflammation, and we generally stop the Lotemax. Keep in mind that we prescribed it q.i.d. for two weeks and b.i.d. for two months, which we think is ample time to suppress any ocular surface inflammation. Now, we are in a "maintenance phase," using only artificial tears. Some doctors continue the Lotemax once daily for a few more months, and while we have no issue with this, we do not feel it is necessary in most cases.

We must now considerably digress. Obviously, one cannot treat every patient with a rigid protocol. It is incumbent upon us to attentively treat every patient on an individual basis, so we offer the following perspectives: it is well established that omega-3 supplementation can be helpful in cardiovascular disease, rheumatologic disease and meibomian gland dysfunction. It may be that most adults



Lacrisert is a once-daily dissolvable hydroxypropyl cellulose micro pellet. This tiny insert is placed in the inferior cul-de-sac and can provide 12 to 24 hours of moistening and lubrication to the eye. While not first-line therapy, it can be helpful in cases of advanced or severe dry eyes.

The Cost of Dry Eye Care

The care of any chronic disease is expensive. For example, a year's supply of a prostaglandin eye drop costs approximately $700 to $800. An article in the February 2009 issue of *Archives of Ophthalmology* reports that Restasis can cost about $1,200 per year. We submit that using Lotemax according to our protocol (only one to two months) with Soothe XP is more cost-effective for our patients. We challenge you to ponder the economic benefits and clinical excellence of this recommended approach to patient care.

Brown MM, Brown GC, Brown HC, et al. Value-based medicine, comparative effectiveness, and cost-effectiveness analysis of topical cyclosporine for the treatment of dry eye syndrome. Arch Ophthalmol. 2009 Feb;127(2):146-52.

would be well served to take such supplementation. Regardless, neither the exact amount nor the ratio of DHA to EPA has been established in prospective clinical trials.

And, even if such data existed, one would still have to treat each patient on an individualized basis. Our approach is generally to suggest supplementation early on in the treatment with the goal of using the least amount of topical eye drops to maintain comfort.

It is our impression that oral doxycycline most potently and more quickly enhances meibomian gland function than the omega-3s, so we often prescribe doxycycline 40mg to 50mg per day for three to four months and then replace the doxycycline with one of the omega-3 products for enduring use. (It may be that 20mg each day of doxycycline would be effective, but we can find no authoritative support for this.) Any antibiotic can cause gastrointestinal upset and, in women, vaginal candidiasis can be problematic, so discuss these issues proactively. Doxycycline can be taken with food, and doing so generally solves the GI issue.

There is some chatter about using azithromycin (either topically or orally) in place of oral doxycycline. Remember, doxycycline is being used at sub-antimicrobial dosages to reduce meibomian gland inflammation and to enhance the fatty acid metabolism within the meibomian glands. We have now consulted several dermatologists and they have unequivocally stated that doxycycline has a vastly more beneficial clinical effect than azithromycin in this setting. We encourage you to have a similar conversation with dermatologists in your community.

Punctal plugs can be very beneficial *once any ocular surface inflammation has been controlled*. To "plug first and steroid later" can actually exacerbate ocular surface inflammation initially. In our opinion, it is senseless to monkey around with dissolvable collagen plugs "to see if the patient is helped temporarily."

We believe the need, or lack thereof, of punctal occlusion should be profoundly evident to a seasoned clinician. "Just do it," if in your judgment the patient can benefit. Whether you choose to plug the more symptomatic eye as a trial (to see how much relief is obtained), or

New Insights Into Punctal Plugs

Have you noticed that many patients who benefitted from punctal occlusion can return after several months and still be doing well, yet the plug(s) has vanished? If punctal occlusion initially helped patient symptoms, then why would the patient not return to baseline symptomatology when the plug(s) was absent?

The answer to this puzzle is found in the December 2008 *American Journal of Ophthalmology*: "Stenosis of the punctum and proximal canaliculus are reported to be a frequent observation after spontaneous loss of punctal plugs … While stenosis is commonly found at the punctum, it is more commonly found within the vertical portion of the canaliculus … The abrasion of the canalicular inner wall caused by the plug is theorized to be the main cause of stenosis."

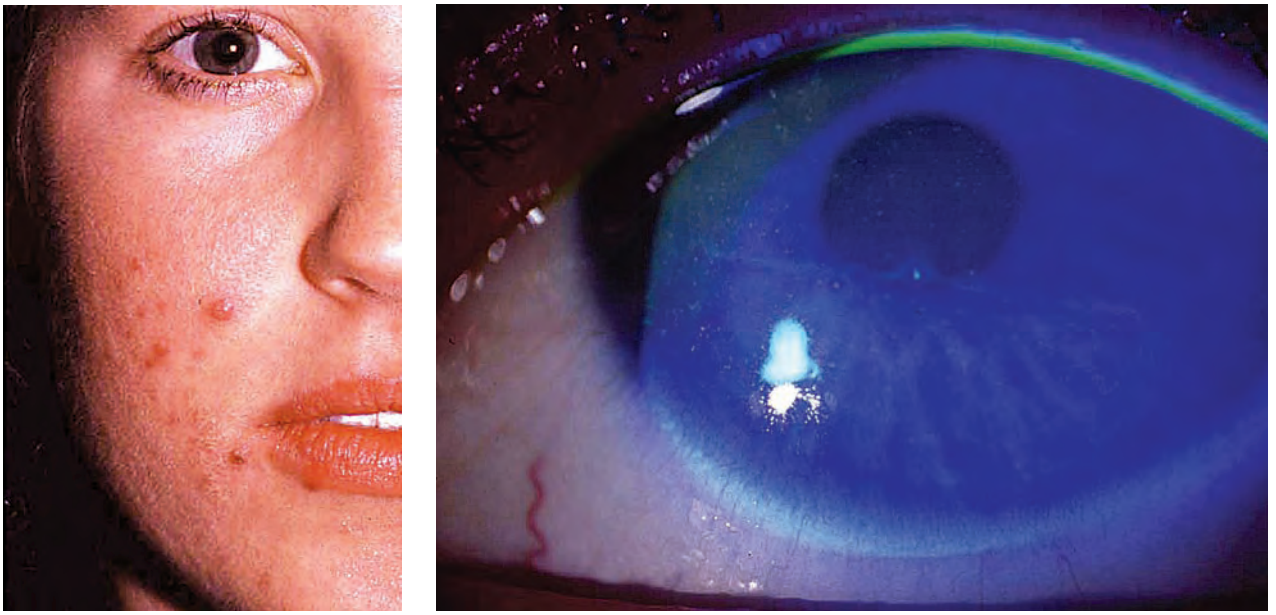
Another theory is that "Mechanical stress on the mucosa might lead to a mild chronic inflammation, causing a stenosis."

The authors add, "It appears that plug size is not a major determinant of stenosis, but larger plugs are thought to be more likely to do so than smaller plugs." One might wonder: how long must the plug reside within the punctocanalicular tissues to evoke such an unplanned iatrogenic stenotic response? Interestingly, such stenosis "seemed to develop independently from the time of insertion. In summary, it seems that the stenosis acts like an occlusion with a punctal plug."

We found this to be a particularly enlightening article that provides a rational anatomic explanation for the enduring relief from dry eye symptoms, even when the plug is long gone.

Punctal plugs are an underutilized modality in the care of patients with insufficient tear volume. Patients may benefit even after the plug is long gone.

Boldin I, Klein A, Haller-Schober EM, Horwath-Winter J. Long-term follow-up of punctal and proximal canalicular stenoses after silicone punctal plug treatment in dry eye patients. Am J Ophthalmol. 2008 Dec;146(6):968-72.e1. Epub 2008 Aug 23.



This patient was being treated with Accutane for cystic acne. Slit lamp exam shows scattered superficial punctate keratitis (SPK).

plug both lower puncta simultaneously, is a judgment call.

We always employ *punctal* plugs, and never use intracanalicular devices. This is mainly so we, and our patients, can monitor whether the plug is still there or not. *(See "New Insights Into Punctal Plugs," page 37A, on why replugging is often unnecessary should the initial plug become extruded and lost.)*

Our experiences have demonstrated to us and our patients that the approach that we have set forth here works well and leaves precious few patients unsatisfied.

We close this discussion with an example of the success of this approach. A very pleasant, 65-year-old white female had been leaving our general area and driving a few hours away every three months for the past five years to a highly prestigious medical center for treatment of her dry eyes. After trying to help her for five years, she was still symptomatic and unhappy, but was told everything that could be done for her had been done. They suggested she find a local ophthalmologist to continue to care for her and save her all these time-consuming and expensive trips.

She found one of us, and here is what our records can document. Yes, she had tried every artificial tear (except Soothe XP); yes, she had properly placed punctal plugs; yes, she was on Restasis; and yes, she was using omega-3 supplementation. Here is what we did to enable this lady after two months to say, "This is the best my eyes have felt in years." We replaced her artificial tears with Soothe XP, we added 50mg of oral doxycycline (and continued her omega-3), and replaced the Restasis with Lotemax, as we described earlier.

As we have clearly set forth, caring for patients with dry eyes is not all that challenging—if we wisely use the good medicines at our disposal. ■

A Few Pearls on Dry Eye Management

• If there is considerable SPK at the initial visit, we may begin artificial tear therapy using preservative-free, unit-dose products such as TheraTears Liquid Gel or Soothe. We typically convert to Soothe XP after about a month. Nowhere can we find any reason to use an antibiotic in the face of dry eye-related SPK. We would simply employ Lotemax as previously set forth if we decide to embark upon a course of corticosteroid therapy.

• Do not forget GenTeal Gel at bedtime. This is an excellent help for those patients who, in your judgment, need nocturnal lubrication. It seems as though patients using a CPAP mask (for sleep apnea) find nocturnal dryness a common challenge.

• It is common to get good relief with lower punctal occlusion; however, our experience with plugging both upper and lower puncta commonly results in complaints of the eye or eyes being too wet, even to the point of epiphora. Problem solved: several companies make a "flow controller" plug, which limits, but does not totally eliminate lacrimal outflow. Such a flow controller seems to provide the optimum balance.

1. Foulks GN. The correlation between the tear film lipid layer and dry eye disease. Surv Ophthalmol. 2007 Jul-Aug; 52(4):369-74. Review.
2. Lemp MA. Advances in understanding and managing dry eye disease. Am J Ophthalmol. 2008 Sep;146(3):350-356. Epub 2008 Jul 2. Review.
3. Management and therapy of dry eye disease: report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop (2007). Ocul Surf 2007 Apr;5(2):171.

Perspective on Systemic Drugs

There are two web sites we recommend to gain perspectives on the prescription rates of FDA-approved medicines: www.drugtopics.modernmedicine.com and www.rxlist.com. Looking at American prescribing by drug class can even provide anthropological and societal insights. To wit, the most prescribed class is the lipid (or anti-cholesterol) regulatory drugs. (Think diet and exercise!)

Analgesics are the second most common class of drugs prescribed. (Hydrocodone/APAP is the most prescribed drug in the U.S.).

Third are the antidepressants. (There may be a direct relationship with 401K profitability!)

Fourth, the ACE (angiotensin-converting enzyme) inhibitors help regulate systemic blood pressure. (Again, think diet and exercise.)

Fifth are the beta-blockers, which have a wide range of clinical uses from heart/blood pressure regulation to migraine prevention.

The sixth most common class of drug prescribed is the proton pump (or hydrogen pump) inhibitors. These have largely displaced the histamine subtype 2 (H-2) antagonists, such as cimetadine (Tagamet), etc., in the treatment of peptic/gastric ulcer disease. (Once more, think diet and exercise, and add smoking).

As you read down through this list of the top six drug classes, we ask you to ponder the impact of our volitional behavior on the burden to our health care delivery system. For added perspective, here are the 10 most prescribed drugs in the U.S. in 2008:

Drug	Number of prescriptions written in 2008
hydrocodone/APAP	124.0 million
lisinopril (ACE inhibitor)	75.5 million
simvastatin (cholesterol reducer)	66.7 million
levothyroxine (thyroid replacement)	61.4 million
Lipitor (cholesterol reducer)	57.9 million
azithromycin	51.1 million
amoxicillin	50.9 million
hydrochlorothiazide, or HCTZ (diuretic)	47.5 million
amlodipine besylate (calcium channel blocker)	44.1 million
furosemide (a loop diuretic)	43.4 million

Iatrogenic Diplopia ... from Statins

The "statins" are formerly known as hydroxymethylglutaryl coenzyme A reductase inhibitors. It is the inhibition of the enzyme HMG-CoA reductase that limits cholesterol synthesis. The prime clinical benefit is lower cholesterol levels. Yet, for all their life-extending benefits, the statins have a dark side beyond potential liver toxicity. While side effects are rare, skeletal muscle myopathy is well documented.

Ophthalmically, such a myopathy could manifest as diplopia, ptosis and/or ophthalmoplegia. In an article by Drs. Fraunfelder and Richards, published in the December 2008 issue of *Ophthalmology*, we learn that the average age of such afflicted patients is 64.5 ±10 years. The ocular adverse events occurred about eight months on average after initiation of therapy, and the side effects are completely reversible upon discontinuation of the medicine.

Fraunfelder FW, Richards AB. Diplopia, blepharoptosis, and ophthalmoplegia and 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitor use. Ophthalmology 2008 Dec;115(12):2282-5.

A New Topical Anesthetic

From Akorn comes Akten, the first new topical ophthalmic anesthetic in a long time. This is of practical clinical relevance if you have a patient who is (or claims to be) allergic to the "-caines." Not all artificial tears are alike. Not all steroids are alike. And, not all antibiotics are alike. Well, neither are the "-caine" drugs.

Most of the "-caine" drugs used in eye care are ester-based—such as cocaine, proparacaine, tetracaine and dorsacaine (benoxinate). In chemical distinction, lidocaine, the most commonly employed non-ocular anesthetic, is an "amide" formulation. The ester-based and amide-based anesthetics do not share cross-allergenicity. Amide-based anesthetics rarely ever cause or develop allergic responses.

If a patient can't use proparacaine, Fluress (benoxinate/fluorescein, Akorn) or tetracaine, then topical anesthesia can be accomplished using lidocaine. Lidocaine tends to give deeper and slightly more prolonged anesthesia than the ester-based anesthetics, so it may be most helpful in removing limbal corneal foreign bodies, removing calcium concretions from the tarsal-conjunctival tissues, forced duction testing, and other procedures in which good anesthesia is required.

Akten is a 3.5% ophthalmic gel drop, and comes in a 5ml bottle. As it is preservative-free, it is approved for a one-time use. We have a feeling most doctors will simply store it under refrigeration, and use it until its expiration date. It is pregnancy Category B.

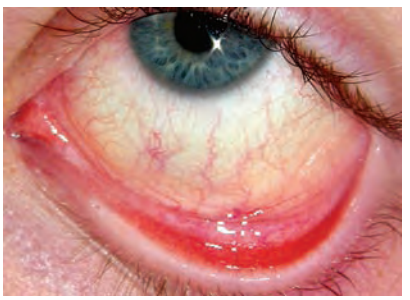
While not a major enhancement to our therapeutic armamentarium, we think Akten 3.5% may be helpful when performing diagnostic and therapeutic procedures in which enhanced anesthesia might be desired; so, it might be wise to keep a bottle on hand to be used as needed.

The Simplicity of Allergy Management

If itching is the primary symptom, determine if it is an isolated symptom or if it is associated with concurrent inflammatory signs.

For the most part, when a patient presents with symptoms of a dry, scratchy, itchy, burning and gritty feeling, this is a patient suffering from "dry eyes." Even though itching is a component of the constellation of presenting symptoms, this subcomponent itching is likely an opportunistic expression resulting from ocular surface tear film dysfunction, i.e., dryness. This "packaged" symptomatic itching is best managed by treating the underlying primary dry eye. This is extensively discussed in the dry eye section (*see page 33A*).

Now, if itching is the predominant symptom, drug selection is dichotomous. If there are minimal associated signs of allergy such as chemosis, conjunctival injection, and/or eyelid edema, then a topical antihistamine/mast cell stabilizer is an excellent clinical approach.



Instruct patients not to rub their itchy eyes. Rubbing causes mast cell degranulation, perpetuating the allergic cycle.

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.
Refresh (OTC)	ketotifen fumarate 0.025%	Allergan	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.

Within this class, there are four drugs:

- azelastine (**Optivar**, MedPointe)
- epinastine (**Elestat**, Allergan)
- ketotifen (**Zaditor** [Novartis], now available generically and OTC)
- olopatadine (**Patanol/Pataday**, Alcon)

Notwithstanding fine differences, all of these antihistamine subtype 1 receptor blockers nicely suppress ocular itching. All are dosed initially b.i.d. (except Pataday, which is dosed once-daily). We recommend after two weeks at b.i.d., try reducing these to once-daily as "maintenance" therapy. In our experience, once symptomatic itching has been brought under control, it takes less pharmacological effort to maintain that control.

Perhaps the best news for the consumer is the loss of patent protection for Zaditor. Now ketotifen is available generically and OTC. In addition to Zaditor, there are several "brand name" OTC ketotifen preparations, such as **Alaway** (Bausch & Lomb) and **Refresh Eye Itch Relief** (Allergan). All come in 5mL bottles (except for Alaway, which comes as a 10mL bottle). Interestingly, our casual observations in a variety of pharmacies reveal that the cost of 10mL Alaway is very near (and occasionally cheaper) than the price of its 5mL counterparts. So, it should be clearly evident that OTC Alaway is the most cost-effective way to suppress ocular itch.

The other side of the dichotomous allergy presentation is represented by the patient who presents with predominant itching along with one or more concurrent signs such as conjunctival redness, chemosis and/or eyelid edema. For this subset of patients, a topical corticosteroid such as Alrex, Lotemax or FML ophthalmic suspension would be more appropriate treatment.

The only other decision tree would involve frequency of instillation, which could be q2h for two days, then q.i.d. for one week, followed by b.i.d. for one more week. Once the inflammatory signs are controlled, then switching the patient to an antihistamine/mast cell stabilizer for ongoing symptom control can be considered.

According to a conversation we had with Mark Abelson, M.D., a world renowned ocular allergist at Harvard Medical School, there is little or no clinical use for pure mast cell stabilizing drugs. He says that the antihistamine/mast cell stabilizer drugs more effectively stabilize the mast cell membranes than stand-alone mast cell stabilizers such as pemirolast (**Alamast**, Vistakon), nedocromil (**Alocril**, Allergan) or cromolyn sodium (generic). Based on this expert opinion, we now use an antihistamine/mast cell stabilizing drug when protracted mast cell stabilization is indicated.

Remember, allergy is a subset of inflammation. Cold compresses can be helpful in most all ocular surface inflammatory diseases. Infectious processes, on the other hand, are commonly helped by the application of warm soaks.

In summary, if itching is not the primary symptom, be sure to consider dry eyes as the foundational condition and treat accordingly. If itching is primarily expressed, determine if it is an isolated symptom or if it is associated with concurrent inflammatory signs. ■

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 10 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.
- Discourage patients from rubbing their itchy eyes. Rubbing causes mast cell degranulation, which perpetuates the allergic cycle.

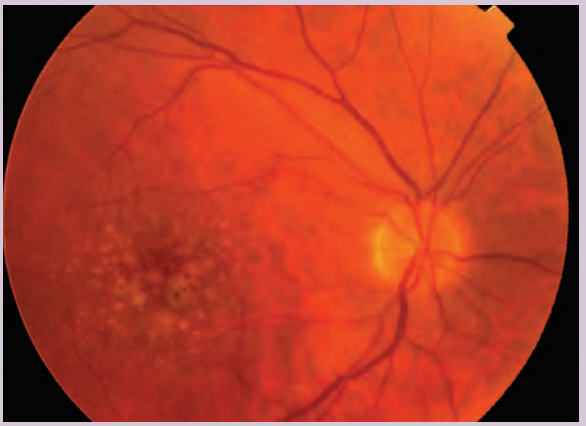
Preventing Macular Degeneration

While the recent spotlight has appropriately been on the inhibition of vascular endothelial growth factor (VEGF) in the treatment of the hemorrhagic form of macular degeneration, we should never neglect the opportunity to prevent progression of the dry/atrophic form of the disease. Just as a reminder, the Age-Related Eye Disease Study (AREDS) documented that a specific formulation of vitamins A, C and E, along with zinc, can slow the rate of progression of the atrophic form of AMD by 25%.[1] Bausch & Lomb's PreserVision is the exact formulation supplied to, and used in, this landmark National Eye Institute study.

The original formulation required taking four tablets each day; however—and fortunately—the current formulation only requires two "soft gel" capsules per day.

Since smoking has been established as an independent risk factor for macular degeneration, it is evident that many AMD sufferers are, or have been, smokers. It is also thought that high dosages of vitamin A, concurrent with smoking, can increase the risk for lung cancer.[2] So, Bausch & Lomb has made available an alternative formula in which lutein is substituted for the vitamin A. This formulation is PreserVision Soft Gels Lutein, and is also dosed twice daily.

Correspondence in the April 2009 issue of *Ophthalmology* revealed that maybe only about half of patients were taking the correct dosage (twice daily) of the AREDS supplement.[3] These two independent writers stressed "the importance of improved education among eye health care professionals and the target patients in order to reduce morbidity from age-related macular degeneration." In response, the authors say that "education of practitioners and patients at risk of age-related macular degeneration progression in the proper use of supplements is critical to achieve the greatest benefits from the conduct of the AREDS."



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

We agree; optometrists need to carefully explain to patients exactly how to properly use these potentially sight-saving supplements.

We tend to start these supplements with any patient (generally over the age of 40 or 50) with a family history of AMD, and any patient at the earliest ophthalmoscopic sign of atrophic macular changes.

1. 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.
2. Goodman GE, Thornquist MD, Balmes J, et al. The Beta-Carotene and Retinol Efficacy Trial: incidence of lung cancer and cardiovascular disease mortality during 6-year follow-up after stopping beta-carotene and retinol supplements. J Natl Cancer Inst. 2004 Dec 1;96(23):1743-50.
3. Ng WT, Goggin M. Vitamin usage patterns. Ophthalmology. 2009 Apr;116(4):819-20; author reply 820.

Drug Information Resources

Our clear first choice for drug information is Drug Facts and Comparisons (www.factsandcomparisons.com).

Another source is called DailyMed, an online service of the National Library of Medicine (www.dailymed.nlm.nih.gov). As a government source, it only discusses medicines that are FDA-approved and does not venture off-label, which can limit some of its clinical usefulness. (When accessing information from this site, we recommend entering the generic name of the drug of interest in the search field.)

www.factsandcomparisons.com

www.dailymed.nlm.nih.gov

Journal Watch—A Unique Way to Keep Up on General Medicine

Each January, the editors and publishers of *Journal Watch* (www.jwatch.org), a bimonthly publication of the Massachusetts Medical Society, highlight the top 10 medical news stories of the past year. As members of the health care team, doctors of optometry need to be knowledgeable of major scientific happenings, and *Journal Watch* is an excellent way to keep abreast of *all* aspects of general medicine. Following are some items we found particularly interesting from this helpful publication:

• **Stem cells.** In the January 1, 2009 issue, one of the "Top Ten" news stories was "Stem Cell Biology Moves Closer to Becoming Stem Cell Medicine." The medical and ethical issues surrounding embryonic stem cell research may soon be (thankfully) moot. Japanese and American researchers have discovered ways to reprogram specialized adult cells into induced pluripotent stem cells (iPS), which have all the potential of embryonic stem cells! This breakthrough is still in the in vivo research stage, but portends enormous advances in human medicine. Follow this closely.

• **Drug adherence.** Another article (July 1, 2008) addressed compliance issues in "Poor Adherence to Once-Daily Antihypertensive Drugs is Common." In this study on the use of drugs to treat systemic hypertension, almost half of patients for whom these medicines were prescribed had stopped treatment altogether at one year out. Episodic missing of doses was seen during the summer months and on weekends. Interestingly, "Morning takers were significantly more likely to execute than evening takers." The authors conclude: "These results suggest that, in patients with insufficiently controlled blood pressure, clinicians should first inquire about, and address, non-adherence before adding another drug to the patient's regimen, which would make adherence only more difficult."

Obviously, such challenges parallel those in our quest to control intraocular pressure via medicines for ocular hypertension. Do note that time of instillation with the prostaglandins minimally affects therapeutic efficacy, so we might want to consider prescribing for morning instillation if some of our prostaglandin users have difficulty adhering to their evening eye drop regimen. For the non-selective beta-blockers, morning instillation is always recommended, so this is a self-solving challenge for many of those patients.

On improving patient adherence: "Morning takers were significantly more likely to execute than evening takers." And, "clinicians should first inquire about, and address, non-adherence before adding another drug to the patient's regimen, which would make adherence only more difficult."

• **New migraine drug.** Regarding treatment of migraine headache, a new class of drug is on the horizon (January 16, 2009). "Migraine headache is commonly treated with triptans (serotonin-receptor agonists), but because these agents are associated with side effects (such as chest discomfort, dizziness, and throat tightness), they are poorly tolerated by some patients, and contraindicated in those with cardiovascular disease. Telcagepant is a new calcitonin gene-related peptide antagonist that lacks the vasoconstrictive effect of triptans … An editorialist suggests that the proof of efficacy of telcagepant—the first of a new class of drug—'marks a new era in migraine therapy.' If this drug is approved by the FDA (the manufacturer plans to file a new drug application in 2009), telcagepant and its future congeners show promise as effective alternatives to triptans."

• **Fishy fatty acids?** The February 15, 2009 issue of *Journal Watch* states that "EPA and DHA each have different properties, and the ideal formulation of EPA and DHA in a fish oil supplement is unclear." Yet we hear and read quite a bit of dogma on this topic. Interesting.

• **Vitamins and cancer.** *Journal Watch*, February 1, 2009: "No basis exists for recommending supplementation with Vitamin C or E, or selenium for preventing prostate cancer." Furthermore, "One after another, published trials have failed to demonstrate that antioxidant vitamin supplements—administered for varying durations during middle age—prevent cancer or cancer deaths. Patients who spend money on antioxidant vitamin supplements should be advised of these findings."

Worldwide Perspective on Glaucoma

Much can be learned from a close and thorough survey of the glaucoma literature. Here are selected excerpts on recent research in the medical therapy of glaucoma.

This year, we take a considerably deeper look at glaucomatous disease. While there have been no major new medicines or breakthroughs in the field of glaucoma over this past year, there is much to learn from a look at insights and perspectives from the worldwide body of glaucoma experts.

As members of the Optometric Glaucoma Society, we receive the journal *International Glaucoma Review* (IGR) every two months. The IGR is the most comprehensive update and review of the professional glaucoma literature around the globe.

From this international journal, we have carefully selected articles and quotes (or in-context paraphrases) germane to medical therapy of the glaucomas, and offer them to you, along with our commentary (indicated in blue).

From *The International Glaucoma Review (IGR)*, Vol. 6-3, March 2005:

CCT and measured IOP response in the Ocular Hypertension Treatment Study[1]

Purpose: To determine whether central corneal thickness (CCT) correlates with measured intraocular pressure (IOP) responses to topical hypotensive medication in the Ocular Hypertension Treatment Study (OHTS).

Conclusions: Individuals with thicker corneas had smaller measured IOP response to ocular hypotensive medication than those with normal or thin corneas.

Once-daily nonpreserved timolol vs. timolol maleate gel-forming solution[2]

Conclusion: This short-term study has demonstrated the equivalence of nonpreserved timolol to timolol maleate gel-forming solution in terms of IOP control.

This was demonstrated to be true a few years ago. There is no reason to prescribe more expensive gel solutions when less expensive, conventional solutions perform just as well.

Once-daily vs. once-weekly latanoprost[3]

We [S. Kurtz, G. Shemesh] evaluated the efficacy and safety of latanoprost eye drops once-weekly, compared to once-daily for improving patient compliance … The difference between post-treatment IOP was insignificant in both groups at each time point. The study group had fewer minor side effects than the control group (1/10 versus 6/10, respectively).

Conclusion: Latanoprost treatment once-weekly was as effective, and bore fewer minor side effects, as once-daily treatment after three months of follow-up.

While we all desire our patients to be consistent with their *use of* prostaglandins, perhaps we do not need to be *overly* concerned when they miss a drop or two from time to time. We know of some doctors who have patients using these meds Mondays, Wednesdays and Fridays *only*. In this economy, this may well be a rational approach, as long as target IOP is maintained.

IGR, Vol. 7-1, June 2005:

Compliance and Persistency[4]

Recent Findings: The primary obstacles to medication compliance appear to be situational/environmental (e.g., being away from home or a change in routine) or related to the medication regimen (e.g., side effects or complexity). Persistency with ocular hypotensive therapies has been found to be poor. Retrospective cohort studies using survival analyses have reported that fewer than 25% of patients are persistent over 12 months.

Summary: Physicians may mistake either medication noncompli-

ance or lack of persistency with poor efficacy. Such errors would likely increase health care costs if they result in unnecessary changes to a patient's therapeutic regimen or in surgery.

IGR, Vol. 7-2, November 2005:

Cooperation with Medical Therapy[5]

Olthoff, et al. reviewed many of the papers on cooperation with medical glaucoma therapy. They conclude that we know the following facts:

- Noncompliance with prescribed therapy is common;
- It may be a cause of worse visual outcomes;
- No patient characteristics accurately identify non-compliers;
- Patients underreport their noncompliance;
- Monitoring ideally should use mechanical devices;
- Pharmacy refill data are probably less accurate predictors of cooperation;
- Educational efforts may be useful in improving compliance;
- Compliance may be better with simpler regimens (fewer drops/day, less complex schedules of medications);
- Patients probably comply better if they make more doctor visits.

The *main* reason we see established glaucoma patients every three to four months is to urge them to comply and persist with their therapy. (We also check their IOP and examine their ONHs.) Unrelenting encouragement plays a powerful role in glaucoma patient care. Also, frequent "no-show" patients, in our experience, are commonly "noncompliant." Be sure to have a system in place in your office to detect glaucoma patient "no-shows." This enhances care and defends against malpractice.

Combining Prostaglandins[6]

In a well powered randomized clinical trial, the addition of topical bimatoprost to latanoprost significantly raises, rather than lowers, IOP. Despite [the trials] not having demonstrated a precise mechanism of why the co-administration of these two individually potent drugs should result in an elevated IOP, the message that latanoprost and bimatoprost should not be used together is still compelling.

It is probably reasonable to assume that none of the prostaglandins should be used together, and that no prostaglandin should be used more than once daily.

IGR, Vol. 8-1, June 2006:

Glaucoma Worldwide[7]

A recent review of the data on prevalence of glaucoma for the coming four to 14 years indicates that the vast majority of angle-closure glaucoma (ACG) patients will be seen in Asia (87%), and half of the predicted blindness is due to ACG.

Results: Women will comprise 55% of OAG (open-angle glaucoma), 70% of ACG, and 59% of all glaucoma in 2010. Asians will represent 47% of those with glaucoma and 67% of those with ACG.

Conclusion: Glaucoma is the second leading cause of blindness, disproportionately affecting women and Asians.

We need to be very attentive to our Asian patients as they tend to be genetically predisposed to narrow angles. It may well be that all Asian patients should undergo gonioscopy (unless they have wide open Van Herick angles).

IOP and Glaucomatous Damage

In his editorial, "Ocular Hypertension and the Lost Suspect," Erik Greve, M.D., Ph.D., states, "we are not so much interested in the absolute level of IOP (unless it is high) as in the relative raised IOP. It is the raised IOP (relative to the original) that is considered a risk factor for the development of glaucomatous damage." He explains,

A Preservative-Free Beta Blocker

For decades, Merck manufactured unit-dose, preservative-free Timoptic. While certainly not a "high need" product, there are undoubtedly glaucoma patients who are intolerant to BAK, yet need a beta-blocker to achieve and/or maintain target IOP.

Now that this product has lost patent protection, it is available generically from Aton Pharma, Inc. (www.atonrx.com). Their market research indicates that more than half of ophthalmologists are unaware that such a product exists, and this number is surely similar to that for optometry (which is an example of why this drug guide is written).

Aton also distributes Lacrisert, a once-daily dissolvable hydroxypropyl cellulose micro pellet. This tiny insert is placed in the inferior cul-de-sac and can provide 12 to 24 hour moistening and lubrication to the eye. While not first-line therapy, it can be helpful in cases of advanced or severe dry eyes.

"An original IOP of 12mm Hg may rise by as much as 50% to 18mm Hg and still be considered normal." Thus, "a good percentage of so-called normal pressure glaucomas are 'simply' raised pressure glaucomas." Greve concludes, "we will have to rely on the detection of the earliest damage, or even better, the earliest change of damage," to identify disease.

A very excellent point. This also emphasizes the value of getting prior patient records as these may provide an indication of IOP behavior over the past few years.

Correlating Structure and Function

Reported at the Glaucoma Society of India Meeting (December 2005):

"Measures of function and structure are synergistic in everyday clinical practice and should be used in combination whenever diagnostic uncertainty exists."

Glaucoma Screening[8]

In The Nottingham Family Glaucoma Screening Study (Sung, et al.), "High frequencies of OAG/suspect OAG in siblings were confirmed." This study found that, "About half of siblings initially diagnosed with OAG had visited optometrists in the previous year, indicating low sensitivity for OAG detection at those visits."

This study indicates optometric care is equally as poor as ophthalmologic care, where roughly 50% of patients with glaucoma were missed or misdiagnosed, regardless of whether seen by an optometrist or ophthalmologist.

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%	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	Aton Pharma, generic	0.25% 0.5%	5ml, 10ml, 15ml 5ml, 10ml, 15ml
Timoptic (preservative-free)	timolol maleate	Aton Pharma	0.25% 0.5%	unit-dose unit-dose
Timoptic-XE, and generic	timolol maleate	Aton Pharma, 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
Combination Glaucoma Medications				
Combigan	brimonidine/timolol	Allergan	0.2%/0.5%	5ml, 10ml
Cosopt	dorzolamide/timolol	Merck	2%/0.5%	5ml, 10ml

***IGR*, Vol. 8-2, September 2006:**

Gonioscopy

• Gonioscopy is indispensable to the diagnosis and management of all forms of glaucoma and is an integral part of the eye examination.

• An essential component of gonioscopy is the determination that iridotrabecular contact is either present or absent. If present, the contact should be judged to be appositional or synechial (permanent). The terms 'iridotrabecular contact' (and number of degrees) and 'primary angle closure suspect' should be substituted for 'occludable', as more accurate. The determination of synechial contact may require indentation of the cornea during gonioscopy, in which case a goniolens with a diameter smaller than the corneal diameter is preferred.

• It is desirable to record gonioscopic findings in clear text. Describing the anatomical structures seen, the angle width, the iris contour and the amount of pigmentation in the angle are all desirable.

While an ideal glaucoma workup includes attentive gonioscopy, studies of clinical practice patterns reveal that less than 50% of doctors perform gonioscopy, thus impeaching the term "indispensable" to characterize this procedure. As we have stated before, in our combined 56 years of caring for patients with glaucoma, gonioscopy has yielded the least valuable diagnostic information from the array of tests and procedures we routinely perform in our glaucoma workup. That being true, it is still wise to include gonioscopy in your glaucoma workup, as there are those uncommon patients for whom these findings can be helpful in managing their disease.

Laser and Medical Treatment of Primary Angle Closure Glaucoma

• Medical treatment should not be used as a substitute for laser peripheral iridotomy (LPI).

• Prostaglandin analogues appear to be the most effective medical agent in lowering IOP following

A New Extension of Bimatoprost

The American entrepreneurial spirit seems best exhibited when an unintended side effect can be marketed to take advantage of that side effect. While 0.03% bimatoprost can effectively reduce IOP, it possesses the potential to cause considerable side effects, some very desirable, some not so much. As reported in *Ophthalmic Plastic and Reconstructive Plastic Surgery*, July/August 2008, a study by Theodoros Filippopoulos, M.D., et al, found, "In eyes treated with bimatoprost 0.03% periorbital fat atrophy, deepening of the upper eyelid sulcus, relative enophthalmos, loss of the lower eyelid fullness, and involution of dermatochalasis was noted compared with the fellow untreated eye." The study concluded: "Physicians and patients should be aware of the potential of bimatoprost 0.03% to produce periorbital changes."

These side effects notwithstanding, the commonly observed enhancement of eyelash appearance is almost universally seen as a benefit (reminiscent of how Viagra, an antihypertensive agent, commonly benefits men with ED). The idea of capitalizing on the eyelash enhancement aspect of 0.03% bimatoprost has led to the marketing of Latisse by Allergan.

So, let's understand how to maximally benefit patients desiring enhanced eyelash appearance. First, there are two phases to lash follicle growth: the growth phase, known as the anagen phase; and the resting phase, known as the telegen phase. Prostaglandins tend to shift eyelash follicles from the resting phase into a growth phase. The relative composition of these phases within scalp follicles does not lend itself to enhanced growth.

The eyelash follicular life cycle is about five months, which means that once maximal lash enhancement occurs—at about four to five months—maintenance dosing is required. The exact

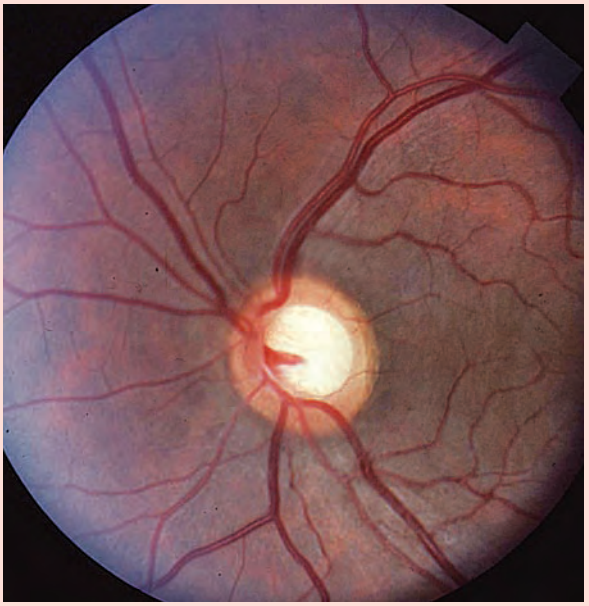
schedule of such maintenance therapy is unknown, but we expect it to be two to three times per week.

Latisse comes in a 3mL bottle and is packaged with 60 single-use brushes (enough for one month), which enable a single drop to be applied along the upper eyelash line at bedtime. Lower eyelid treatment is not needed since sufficient medicine comes in contact with the lower lid from upper lid apposition. The cost is expected to be approximately $120 per month during therapeutic induction and perhaps half this amount during the maintenance phase. Latisse is a prescription medicine, and we anticipate any O.D. will be able write for it if their state law allows for bimatoprost prescribing (although this remains to be seen). Like bimatoprost eye drops, we expect that eye redness and other bimatoprost-associated side effects can occur.

Because Americans are sufficiently endowed with ample vanity to spend billions of dollars annually on cosmetic-type products, we anticipate great financial success with Latisse.

LPI, regardless of the extent of synechial closure.

This latter point is true, but it is important to recognize that beta-blockers and alpha adrenergic agonists, such as brimonidine, are "rapid onset" drugs and therefore are key pharmacotherapeutic players in the quick reduction of IOP. Certainly, the prostaglandins have the potential to ultimately achieve the greatest IOP reduction, but these drugs may take a day or two (at least) to achieve uveoscleral tissue remodeling via enhancement of matrix metalloproteinase activity. Moreover, LPI trumps medical therapy in an acute setting, and so prostaglandin use after LPI would be an excellent treatment choice (as would a once-daily topical beta-blocker).



ISN'T That Something

- Helpful diagnostic observation in ONH evaluation
- Normal neuroretinal rim anatomy follows the ISN'T rule:
  - **I**nferior rim should be thickest
  - **S**uperior rim is slightly less thick
  - **N**asal rim is slightly less thick
  - **T**emporal rim should be the thinnest
- Most ONHs are round or slightly vertically oval
- ISN'T rule may not hold if ONH horizontally oval

Detection of Primary Angle Closure Glaucoma

- Angle closure case detection or opportunistic screening should be performed in all persons 40 years of age and older undergoing an eye examination.
- Given the low specificity of the flashlight test, it is not recommended for use in population-based screening or in the clinic.
- A shallow anterior chamber is strongly associated with angle closure.
- An acute attack of angle-closure is not glaucoma; if the optic nerve and visual field are normal, it is only an acute angle-closure.

We think any patient with Grade II or less Van Herick angles should undergo gonioscopy, particularly when that patient is over 40 years of age. The last bullet is right on the money; an angle-closure attack is just that – it is not glaucoma unless measurable damage occurs to the optic nerve. For instance, most patients with glaucomatocyclitic crisis do not develop glaucoma.

Genetically Regulated CCT and Glaucoma[9]

The recent finding that CCT is among the most heritable aspect of ocular structure, suggesting that CCT is genetically regulated, lends credence to the idea that CCT is linked somehow to glaucoma risk at a fundamental, biological level.

Conflicting findings and approaches as represented by these studies are typical of early work in any new field, as we begin to investigate potential biological links. The story of CCT and glaucoma is just starting to get interesting!

Interesting, indeed! Recently, a woman in her 40s presented in our office and requested a glaucoma evaluation because her father, who lived in another state, had been told he had glaucoma. Our examination found this lady to have CCTs of 640, IOPs of 23, and C/D ratios of 0.2. We'd be willing to bet her father also has thick corneas and actually does not have glaucoma, but rather, "corneal thickness-induced" ocular hypertension. We hope to be able to render a second opinion to this patient's father when he comes down for a visit. We believe many cases of ocular hypertension are errantly called "glaucoma." Remember, it's all about the optic nerve! Study the optic nerve. In glaucoma, all findings revolve around the optic nerve! (Repetition intended.)

Optic Nerve Health

The glaucomatous process is best recognized by the damage it causes to the optic nerve in so-called 'characteristic' ways. Valid determination of the health of the optic nerve is, then, one of the most important and direct methods of evaluating and managing patients with glaucoma.

Because physicians rely so heavily on the presence of 'cupping,' as a sign of a disc damaged by the glaucomatous process, critical consideration of the validity of this sign is appropriate and important. There are fatal flaws in the cup-to-disc ratio system, however, and indeed all systems that use the width of the

cup as a measure of the presence of glaucoma damage. One of those fatal flaws, not recognized until recently, is that the size of the cup is strongly affected by the size of the optic disc.

Not evaluated by this study, but of equal importance, is the recognition that small discs tend to have small cups, and that systems that do not take this into account will also yield misleading results when considering small discs, indicating that discs are normal, when in fact they are acutely pathologic.

These comments are from Jost Jonas, M.D., of Germany, who is arguably the world's foremost expert in the optic nerve. He stresses that optic disc size need not be exactly measured, but rather a, "crude assessment," as to whether the disc is small, normal-sized, or large is all that is necessary. This is an excellent point that pushes us to become even more attentive to the optic nerve.

Ocular Drug Delivery for Glaucoma[10]

Human sclera is more permeable than the cornea to many hydrophilic and hydrophobic drugs. Furthermore, the rate of diffusion is determined by molecular mass and size. While drug diffusion through the cornea is not very efficient, the rate of drug diffusion through the sclera is significantly higher, roughly equal to the cornea denuded of epithelium. Further, the surface area of the sclera (approximately 17cm^2) is a lot bigger than the cornea (approximately 1cm^2). Thus, an effective case was made that perhaps the most compelling location from which to deliver sustained drugs to the eye (either anterior or posterior) may be the scleral surface.

The future for glaucoma therapies is very bright indeed. Opportunities are being developed that aim to deliver drugs in a sustained manner for prolonged periods of time that rely less on individual patient administration.

Provide Written Instructions[11]

B. V. Kharod, et al. reported in the *Journal of Glaucoma* 2006 on their study of the effect of written instructions on accuracy of self-reporting medication regimen in glaucoma patients. At the end of their visits, patients were given a written chart describing their ophthalmic medications, frequency, and dosage.

Conclusion: The education level of the patient and the number of medications showed direct correlation with the patient's ability to report medications accurately. Patients showed improvement in accuracy of reporting medications when given written instructions about their regimen, regardless of their level of education or number of medications.

IGR, Vol. 8-3, December 2006:

Treating Ocular Hypertension to Reduce Glaucoma Risk: When to Treat?

When to treat the patient who presents with ocular hypertension has been a question that has 'stumped' the ophthalmic community for decades. The clinician should consider key factors such as age, thin corneal thickness measurements, large cup-to-disc ratio and mean IOP when determining who should be treated. However, the ultimate decision of when to treat will be determined by other issues such as life expectancy, the general health and the number of risk factors. Clearly, the treatment of only high-risk patients with ocular hypertension should be considered.

This one simple paragraph embodies the essence of clinical decision-making. "When to treat" is the ultimate decision, and can only be made by attentively evaluating each patient as an individual person.

Beta-blockers and Depression[12]

Conclusions: Use of topical beta-blockers by glaucoma patients does not appear to increase the risk of depression in this population.

While the opposite has been taught as true for two decades, it has been clearly shown that there is

Preservatives in Topical Glaucoma Drugs

BRAND NAME	PRESERVATIVE
Beta Blockers	
Betagan	0.005% BAK
Betimol	0.01% BAK
Betoptic-S	0.01% BAK
Istalol	0.005% BAK
Timoptic	0.01% BAK
Timoptic in Ocudose	*preservative-free*
Timoptic-XE	0.012% BDD
Prostaglandin Analogs	
Lumigan	0.005% BAK
Travatan	0.015% BAK
Travatan Z	*sof*Zia *
Xalatan	0.02% BAK
Alpha Agonists	
Alphagan P	0.005% Purite **
Iopidine	0.01% BAK
Carbonic Anhydrase Inhibitors	
Azopt	0.01% BAK
Trusopt	0.0075% BAK
Combination Glaucoma Medications	
Combigan	0.005% BAK
Cosopt	0.0075% BAK

* *sof*Zia: boric acid, propylene glycol, sorbitol, zinc chloride.

** Purite: stabilized oxychloro complex.

no association.

Effects of previous argon laser trabeculoplasty on the ocular hypertensive action of latanoprost[13]
Results: Latanoprost induced a 17.5 ±16.6% decrease in the study group (ALT-treated eyes) and a 25.8 ±17.2% reduction in the control eyes. Conclusions: Latanoprost is less effective in ALT-treated eyes than in eyes with POAG not treated with ALT.

Note the very wide-ranging responses in IOP reduction. We imagine these findings would hold true for any of the prostaglandins.

The cost-effectiveness of bimatoprost, latanoprost and timolol in treatment of primary open-angle

Read Everything, But Don't Believe Everything You Read: A New Perspective on Peer-Reviewed Literature

For two decades now, we've urged, begged and pleaded with our optometric colleagues to consistently peruse several journals each and every month. Until we all begin to immerse ourselves in the literature on a consistent and widespread basis, our profession will not achieve its full potential.

However, new insights and perspectives came to light in the January 2009 *American Journal of Ophthalmology*, which to some degree dampens the validity of our above statements. Wallace L. M. Alward, M.D., the developer of the most advanced teaching tool for gonioscopy (see www.gonioscopy.org), and a consummate medical professional, offered his perspective of industry influence on peer-reviewed professional literature. His remarks are in response to a landmark research article published in the January 2009 *AJO* titled, "Discrepancy Between Results and Abstract Conclusions in Industry- vs. Nonindustry-funded Studies Comparing Topical Prostaglandins," by Tariq Alasbali, M.D., et al.[1]

Read these critical excerpts from Dr. Alward's editorial, "How I Choose a Prostaglandin Analogue":[2]

"The highly profitable prostaglandin analog market has led to fierce competition and has generated intense pressure on ophthalmologists and health plans to choose one manufacturer's PGA over the others. How does one choose between these agents? I have always admonished my residents and fellows to eschew biased information from pharmaceutical representatives and to instead rely on the peer-reviewed literature. I am now not sure that this is sage advice. In this issue of the Journal, Alasbali and associates provide data to support what has long been suspected: that corporate-sponsored studies overwhelmingly show the superiority of the sponsor's own product."

Dr. Alward goes on to say, "While 90% of corporate-sponsored papers had abstract conclusions favoring the sponsor's product, the data presented in the body of the text showed a significant outcome measure only 24% of the time. And, while the abstract conclusion corresponded to the main outcome measure in 100% of non-industry-funded studies, this correspondence was found in only 38% of industry-funded studies … This timely article by Alasbali and associates should serve as a wake-up call for ophthalmology."

Then, Dr. Alward asks, "So, what do I do? And what do I teach my residents and fellows? I read the peer-reviewed literature, but now recognize that, while the body of the manuscript should be fact, the abstract conclusion may be fiction. I use all of the PGAs to develop my own opinion on how well they work and how well they are tolerated. I talk to trusted colleagues about their experience. It is sad that we each need to go through this process and we are not able to confidently rely on the peer-review literature to guide us."

What, then, should an optometrist do? Our recommendations:

1. Read the literature vigorously, and look for consistent underlying messaging from a variety of respected authors. If you have a firm grip of the facts, you won't be misled by any single lecturer or article.

2. As Dr. Alward said, try all the drugs for yourself. You're a smart doctor; it shouldn't take you long to determine clinical reality.

3. Again, as Dr. Alward says, talk to trusted colleagues about their experiences. We agree with Dr. Alward's sentiment that it is a real pity that truth and fact are increasingly difficult to acquire, but this seems to be evident.

4. Finally, there is an abundance of discussion about "evidence-based medicine," a laudable mode of practice; however, if in the establishment of such "evidence" many "tainted" peer-reviewed articles are used, the very foundation of this noble concept is corrupted.

We hold strong to the belief that insufficient numbers of optometrists subscribe to the ophthalmological literature. We both personally subscribe to *Ophthalmology*, the *American Journal of Ophthalmology* and *Survey of Ophthalmology* via the web site Ophsource.com. We wholeheartedly urge all of our colleagues to join us each month as we peruse together these highly valuable educational resources. Only through such monthly self-study can we all reach our potential to maximally care for our patients.

1. Alasbali T, Smith M, Geffen N, et al. Discrepancy between results and abstract conclusions in industry- vs nonindustry-funded studies comparing topical prostaglandins. Am J Ophthalmol. 2009 Jan;147(1):33-38.e2.
2. Alward WL. How I choose a prostaglandin analogue. Am J Ophthalmol. 2009 Jan;147(1):1-2.

glaucoma in five European countries[14]

Conclusion: First-line treatment of latanoprost is dominated in all countries. In four out of five countries, the timolol first-line therapy with add-on latanoprost is also dominated. Based on this pharmacoeconomic analysis, the most cost-effective strategy seems to be timolol first line with add-on latanoprost if target is not met after three months.

IGR: Vol. 9-1, June 2007:

Target IOP

From the WGA Consensus Meeting on Intraocular Pressure, May 2007: The determination of a target IOP is based upon consideration of the amount of glaucoma damage, the IOP at which the damage has occurred, the life expectancy of the patient, and other factors including status of the fellow eye and family history of severe glaucoma. At present, the target IOP cannot be determined with any certainty in any patient.

Common Findings in Myopic Eyes[15]

Optic nerve head findings of tilted discs and peripapillary atrophy are common features found in myopic eyes. Corresponding visual field defects may or may not be present. As a result, establishment of glaucomatous damage and progression monitoring becomes more difficult bringing about uncertainties in glaucoma diagnosis and management. In one study of mostly myopes with optic disc cupping and visual field abnormalities suggestive of glaucoma, their condition was found to be stable during seven years follow-up. This is not surprising, considering the fact that the subjects on the average belong to the young and middle aged group. It is also worth mentioning that 56% of the subjects received treatment (IOP lowering medications). This opens the question whether the threshold for instituting treatment should be lowered or raised. For this particular group, withholding treatment is a good option.

We often encounter patients being treated for a disease they do not have. Remember, glaucoma is a *progressive* optic neuropathy. We might be wise to definitively determine progression prior to the institution of therapy!

Effects of Marijuana on IOP[16]

Marijuana lowers IOP for only two to three hours, making it highly impractical in most patients, and furthermore in the majority of patients the IOP lowering effect is lost in continued dosing.

IGR: Vol. 9-3, December 2007:

Glaucoma Screening and Prevention

Pregnancy and Glaucoma

From *The International Glaucoma Reivew*, Vol. 9-1, June 2007:

"A survey by Viadeanu and Fraser underscores the lack of consensus among consultant ophthalmologists with regard to treatment of glaucoma during pregnancy. In this study, 605 questionnaires were sent out, with 208 (47%) returned. Of the respondents, only 26% had previously treated a pregnant patient with glaucoma. When asked what they had done in this setting, of those who had dealt with this previously, 71% continued the pre-pregnancy management, and when all respondents were asked what they would do in this clinical situation, a full 31% responded that they were unsure. These figures suggest that the majority of clinicians have little expertise in this circumstance, and that there is no widely accepted algorithm to consult when the situation arises. Despite the fact that all of the current IOP lowering drugs are pregnancy category C with the exception of brimonidine, it is interesting that a full 71% of respondents who had treated pregnant patients continued with their pre-pregnancy medication management. Also, when the respondents who stated what treatments they would use if they needed to lower IOP, 45% stated they would use a beta blocker, 33% would use a prostaglandin, and 22% would start with some other medication. These widely varying treatment plans highlight our current lack of a strategy with demonstrated safety and efficacy in this patient population."

The September 2007 issue of *Focal Points*, by the American Academy of Ophthalmology, is called "Drugs and Pregnancy." The following quotes are from this excellent source:

- "When an eye doctor is faced with the treatment of glaucoma in the woman who is pregnant or might become pregnant, no published guidelines exist to aid in the decision-making process."
- "The American Academy of Pediatrics listed timolol as a 'maternal medication usually compatible with breast feeding.'" Beta-blockers are Category C.
- "Brimonidine tartrate is the only commonly used glaucoma medication categorized as pregnancy Category B."
- "It is unknown whether brimonidine is excreted in human milk."
- "Brimonidine can have significant systemic side effects in neonates and infants, including CNS depression, somnolence, and apnea, thereby raising the concern for these side effects if it is indeed secreted in human breast milk." All prostaglandins are Category C.
- "Given their potential effects on uterine muscle contractility, [prostaglandins] should be avoided in women who are pregnant and in those who desire to become pregnant."

Vaideanu D, Fraser S. Glaucoma management in pregnancy: a questionnaire survey. Eye. 2007 Mar;21(3):341-3. Epub 2005 Nov 25.

• With 90% of glaucoma undiagnosed worldwide, methods to bring more cases in for care may be considered theoretically worthwhile. Since patients, siblings, and children of OAG cases are five to ten times more likely to develop OAG, one approach is to bring in family members.

• High rates of undiagnosed glaucoma exceeding 50% are reported from various population studies in developed and developing countries, while current screening methods outside the clinical office have been proven to be non-cost effective.

We all need to more aggressively reach out to family members of glaucoma suspects to maximize prevention of glaucomatous vision compromise.

IGR, Vol. 9-4, March 2008:

Angle Assessment: Gonioscopy and Illumination

• Sadly, ophthalmologists perform gonioscopy less frequently than they should. Moreover, when gonioscopy is performed the technique might not be ideal. Too often, gonioscopy is performed in a brightly lit room employing a diffuse bright beam of light. It has long been felt that excessive illumination could artificially open the iridocorneal angle, making the examiner miss people at risk for pupillary block angle-closure glaucoma.

• Ophthalmologists who perform gonioscopy in a bright room or with a slit lamp entering the pupil risk failing to identify occludable iridocorneal angles.

Obviously, these statements hold equal truth for optometrists.

CAIs and Corneal Effects

• Carbonic anhydrase (CA) isoenzymes II and IV play an important role in the pump function of the endothelium, keeping the cornea in a relatively steady state of dehydration.

• Dorzolamide is a potent inhibitor of CA II. In normal eyes, both original regulatory safety data and in subsequent studies, dorzolamide exhibited little in the way of corneal toxicity. There are, however, numerous anecdotal and published reports of irreversible corneal decompensation during dorzolamide therapy in some patients.

• Data suggests that patients with preexisting endothelial disease are more susceptible to the adverse corneal effects of topical carbonic anhydrase inhibitors (CAIs).

• The glaucoma clinician should pay more attention to the corneal endothelium, and in patients with compromised endothelia (i.e., Fuchs' dystrophy, bullous keratopathy, penetrating keratoplasty), consider other drugs before topical CAIs.

IGR, Vol. 10-1 (and its supplement), July 2008:

Diabetes and Glaucoma[17]

There is no clear evidence to support a relationship between diabetes and glaucoma … IOP level is usually slightly higher in diabetic patients … [however] this slight increase is currently thought to be caused by a higher central corneal thickness (CCT) in these patients. As reported in the OHTS, central corneal thickness (CCT) was higher in diabetic compared with non-diabetic subjects, and this increase in CCT may be responsible for an overestimation of IOP.

We stress that newer studies do NOT support a direct relationship between diabetes and glaucoma!

Sleep Apnea Syndrome and Circadian IOP[18]

Obstructive sleep apnea (OSA) is more prevalent in subjects with primary open-angle glaucoma (POAG) than in the general public and POAG is more prevalent in subjects with OSA than in the general public. OSA is often treated by nocturnal administration of continuous positive airway pressure (CPAP). CPAP is known to raise intraocular pressure (IOP).

In a study to determine the impact of CPAP on circadian IOP, it was noted that IOP dropped signifi-

A New Prostaglandin Side Effect

After a decade of prostaglandin use, we are surprised that yet another potential side effect has been highlighted. Obviously, such a side effect would be rare. However, when patients using prostaglandins complain of (or, if after reading this you begin to inquire regarding the presence of) gastrointestinal distress, it could be an iatrogenic result of the prostaglandin.

Actually, travoprost lists gastrointestinal distress as a possible side effect in its package insert, but it is high probably that such can occur with any of the prostaglandins. These gastrointestinal responses usually occur within minutes to hours after instillation. The proposed mechanism of action is unknown; however, the current thought is that these effects are secondary to stimulation of the smooth muscle of the intestinal tract. So, when a patient returns for follow-up after initiation of a therapeutic trial of any of the prostaglandins and has a complaint of gastrointestinal problems, it may very well be drug related.

We doubt GI doctors are aware of this, so sharing this knowledge with your GI colleagues may solve some GI mysteries for them and their patients. The prostaglandin-related GI problems usually resolve quickly once the drop is discontinued.

Papachristou GC, Ritch R, Liebmann JM. Gastrointestinal adverse effects of prostaglandin analogues. Arch Ophthalmol 2008 May;126(5):732-3.

cantly within 30 minutes of stopping CPAP in the morning. By raising intra-thoracic pressure, thus venous pressure, thus episcleral venous pressure, CPAP likely raises IOP by reducing aqueous outflow. CPAP-induced IOP elevation may explain the increased prevalence of POAG in subjects with OSA, and these subjects may warrant ongoing glaucoma screening. When established glaucoma patients require CPAP therapy, the clinician should be aware that the resulting IOP changes may not be detectable during office hours, and that these patients may be at risk for disease progression despite apparently well-controlled IOP as measured in the diurnal period.

IGR, Vol. 10-2 (and its supplement), September 2008:

Caffeine is Not a Risk Factor for Glaucoma[19]

In a rigorous cohort study with nearly thirty years of follow-up, the authors found no increased risk of glaucoma with increasing amounts of caffeine (even though) the large sample size of the study increases the risk of finding a statistically significant result that is not clinically significant. When our patients ask us about caffeine intake and glaucoma, we should tell them that caffeine was not found to be associated with glaucoma.

SWAP or Double?

A symposium on visual fields was held at the Second World Glaucoma Congress, where four timely questions were asked. These questions are set forth below, and then followed by expert consensus answers. We hope you will find the revelations pertinent to your clinical practice.

Q: Should SWAP and FDT be used to monitor glaucoma suspects with normal SAP?

A: The experts concluded that in the present state of understanding, there is no compelling evidence that either SWAP of FDT should be used, rather than SAP, to monitor glaucoma suspects having no known visual field defects.

Q: Should FDT be used for routine screening for glaucoma?

A: The panel agreed that although under well-controlled conditions FDT may be suitable of early detection of glaucomatous damage, in 'real-world conditions' it is likely to pick up functional defects due to other diseases as well. On the other hand, as screening campaigns are usually not designed to detect glaucoma alone but eye disease in general, FDT may have its place in mass screening, with other tests establishing the final diagnosis.

Q: Is FDT better than SWAP for the detection of early glaucoma?

A: The experts agreed that all evidence on this question is relatively thin and that the single study on which it was based, although carefully designed, needs to be complemented by further studies exploring the mechanisms underlying SWAP and FDT.

Q: Does selective testing with SWAP and FDT make them good for monitoring disease progression?

A: The panel agreed that there is no clear answer yet to this question, as there is no 'Gold Standard' to ascertain progression and as there are many uncharted areas that need to be explored by additional work before the ability of each method to detect change is established. With the evidence that is currently available, there seems to be no clear advantage to using either SWAP or FDT in place of standard automated perimetry to monitor glaucoma progression.

IGR, Vol. 10-3, December 2008:

Imaging Technology in Glaucoma[20]

Today we have several instruments that provide objective and quantitative measurements that are highly reproducible and show very good agreement with clinical estimates of optic disc and visual function. Yet, many clinicians continue to wonder how to use these in their clinical practice and clinical trials. Now, more than ever, it seems to be an appropriate time to assess the use of imaging in clinical practice.

Optic nerve head photography, particularly stereoscopic, provides a permanent record, but generally is not used because it is impractical and cameras generally are not available. Moreover, the differences

The 'Economy' of Glaucoma Therapy

There are plenty of anecdotal reports of glaucoma patients no longer filling their prescriptions as a result of the current economic downturn. These circumstances can cause both patients and physicians to ponder solutions for such challenges.

Within the context of glaucoma patient care, we must be aware that compliance is the weak link. Cost is a major determinant of compliance. There are two maneuvers that can be considered, regardless of the economy, to help our patients succeed in maintaining IOP control. These are:

- Use a non-selective beta-blocker only once daily, with morning instillation. A 5mL bottle of generic timolol is readily available at about $4 at many pharmacies. Beta-blocker use in this manner is without a doubt the most cost effective of the available medicines.
- Consider the use of a prostaglandin only Mondays, Wednesdays and Fridays. Numerous studies clearly demonstrate that this class of medicines reduces IOP for at least two or three days, and perhaps up to a week, with a single drop.

among clinicians in their interpretation of photographs, either for diagnosis or progression, is remarkably large.

Given the substantial advances in glaucoma imaging, it is important to remind clinicians that current glaucoma diagnosis cannot be solely instrument-based. Rather, the imaging information should be considered as being complementary to other clinical measures. Nevertheless, given the variability of drawings and subjective photographic interpretation, imaging may elevate the assessment of the optic nerve by the general clinician, perhaps to the level of a fellowship-trained glaucoma specialist. Moreover, imaging enables the clinician to objectively evaluate the parapapillary RNFL [retina nerve fiber layer] that changes early in the course of the disease, which cannot be readily measured by clinical examination. Finally, imaging enables a practical comparison of a patient with a population of age-matched normals, facilitating the ability to identify abnormal structural features … Thus, clinicians should not make clinical decisions based solely on the results of one single test or technology.

This is wonderfully stated, and should be earnestly taken to heart by all clinicians!

You have just read a selection of information from glaucoma experts around the world. We hope the knowledge these experts provide enables you to offer enhanced, expert care to your patients with glaucoma.

We thank Murray Fingeret, O.D., for his precedent-setting vision in formally ushering our profession onto the world stage via the establishment of The Optometric Glaucoma Society, a member of the World Glaucoma Association. ■

Glaucoma

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