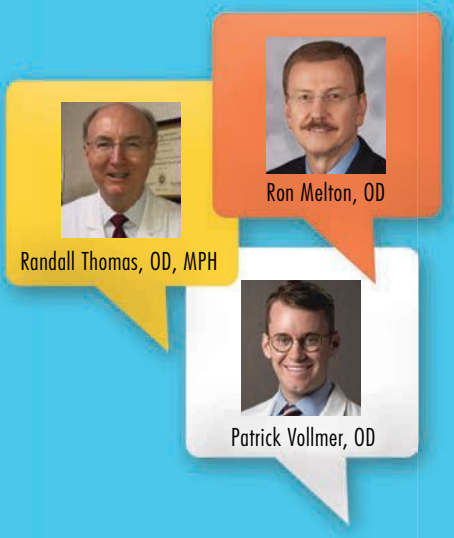
CLINICAL PERSPECTIVES ON PATIENT CARE

25th Edition

Answers You Need From Experts You Trust

INSIDE:

*Practical guidance on more than **100 questions** about clinical care.*



A supplement to

REVIEW of OPTOMETRY

Supported by an unrestricted grant from Bausch + Lomb

Your Questions—Answered

Last year, you spoke up about eyecare issues that matter to you most. We listened, and address your most pressing questions in this year's installment.

Welcome to the 25th edition of what is colloquially known as "The Drug Guide," even though it no longer bears a name limited to drug therapy. The big change in the 2020 edition was the expansion into other clinical areas beyond drugs and a change of name to reflect that.

The cancelling or postponment of live meetings that began in March 2020 severely truncated our personal appearances over the past year, and we had to default to doing most of our educational programs virtually. While we found this to be much less dynamic and enjoyable, the silver lining was your numerous questions, which were captured electronically.

So this year, in large part, we are answering your verbatim questions across the spectrum of clinical patient care. It is a time-honored reality that when one attendee asks a question, it's highly likely that many others had the same question in mind. Thus, in that spirit, we are answering those questions for the benefit of all optometrists.

Prior to this outpouring of electronic questions, we had to assume that we understood your needs, and so we wrote from that perspective. Now that we know with certainty the questions that you have, we can be more exacting in answering your clinically related quandaries.

One interesting development occurred last year, validating what we have been saying all along about dry eye. Since 1998, when loteprednol came to market as Lotemax, the notion that "inflammation" was foundational in the care of patients with dry eye disease had not yet been realized. Finally, in 2020, the FDA acknowledged the role of loteprednol in dry eye disease treatment by approving a 0.25% rendition with that specific indication.

This governmental formal recognition in no way modifies our clinical care, but it does underscore what we have known for about 20 years: corticosteroid suppression of ocular surface inflammation is indeed foundational to caring for patients with dry eye disease. 'Bout time!

Last year, we comprehensively discussed the impact of hydroxychloroquine on retinal tissues; in like manner, this year we discuss giant cell arteritis—a condition never to be missed—among other topics pertinent to high-quality patient care.

We hope you enjoy our responses to your many questions and that this knowledge will serve to further enhance your patient care. Remember, treat your patients in the manner in which *you* would like to be treated.

With our best wishes,
Drs. Melton, Thomas and Vollmer

Disclosure: Drs. Melton and Thomas are consultants to, but have no financial interests in the following companies: Bausch + Lomb and Icare. Dr. Vollmer has no financial interests in any company.

Note: The authors present unapproved and "off-label" uses of specific drugs in this publication.

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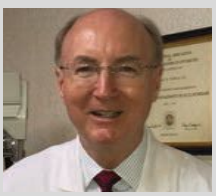
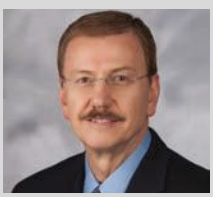


Randall K. Thomas, OD, MPH, FAAO



Ron Melton, OD, FAAO

Patrick M. Vollmer, OD, FAAO

A PEER-REVIEWED SUPPLEMENT

Your First Five Years

Practicing in your formative years is exhilarating, exhausting, but most of all—rewarding.

By Patrick Vollmer, OD

Almost five years ago, I graduated from my residency program in Columbia, SC. Several months later I purchased a private, one-doctor practice... in a small town I'd never heard of until days before I started, and with business knowledge I thought I needed but didn't have. Looking back, I think I was able to "succeed" through sheer ignorance about the fact that I may have not succeeded! In my experience, if you own a private practice, committing to a high level of patient care will make up for your lack of business knowledge in the interim.

KNOW YOUR MEDICAL COMMUNITY

I think new graduates should all strongly consider private practice. When you own your own clinic, you can build your vision from the ground up. I made up for my lack of business experience with a relentless work ethic and an understanding that things take time to fall into place. However, there are ways to make these things fall into place faster. One of the best decisions that I made early on in my career was to integrate with the medical community at large. I went to every medical office in my community many times over to introduce, then reintroduce myself. Almost every physician has my personal cell phone number or knows how to get in touch with me immediately through our after-hours line.

Hanging an "open" sign on your door and waiting for patients to come to you is not helpful and undermines your self-worth. This goes double for medical and emergent cases. In year five, I don't think there is one physician, PA, NP or RN in my community that doesn't know exactly what I can do for their patients. This realization can only come through a high-level commitment to integrating yourself into the medical community.

DON'T REFER OUT NON-SURGICAL CASES

Your referrals from local medical professionals will be short-lived if you refer all of these cases to ophthalmology. Barring extreme cases, there is no reason to refer out any case that does not need to have surgical care—ever. Additionally, patients will not be pleased when, after you take their co-pay, you tell them that you cannot be any assistance to their case. In a small town, you have a handful of chances to make a lasting impression, which will endure for better or worse.

DO YOUR OWN THINKING

Medical professionals will often refer their patients with ocular emergencies to your clinics with a presumptive diagnosis already in hand. I have found that these "diagnoses" are oftentimes incorrect. However, it is crucial that you do your own thinking and not let external opinions influence your management decisions. Ultimately, you are responsible for the patient in your chair. The same holds true for patients coming to you who have pre-diagnosed their condition. Don't be thrown off by an outside diagnosis.

PRESCRIBE (LOTS AND LOTS OF) CORTICOSTEROIDS

Corticosteroids are the greatest drug we have access to in our armamentarium. I prescribe oral or topical steroids every day in my clinic, multiple times a day. Once you have identified that your patient's condition is inflammatory (it almost always is), it is critical to dose them appropriately with corticosteroids. For example, I will dose marginal corneal infiltrates Q1H for one day, Q2H for one day and QID for four days. I will treat mild cases of iritis in a similar manner. The point is, don't dose hesitantly with topical or oral steroids. Rid the patient of inflammation, and dose early and often.

REFUSE TO FAIL

The first few years in practice is a strange time. Initially, patients can't always tell if you are the doctor, the tech or the intern. One "positive" aspect of being young is that patients assume that you must know everything since you just graduated! This is likely true, despite your inexperience. Don't

REFRACTIONIST OR DOCTOR?

- **A new world of vision testing and eye wear sales is dawning now that refractions and prescription fulfillment are being offered online.**
  - » Visibly
  - » EyeNetra
  - » My Vision POD
  - » My Eyelab
  - » Smart Vision Labs
  - » Vmax Vision
  - » Warby Parker
  - » Digital Optometrics
- **These developments may not be a negative for ophthalmology practices and patients.**
- **ODs: expand your scope of patient care services to protect your future!**
- **The AOA is aggressively fighting for optometry: Join the AOA!**

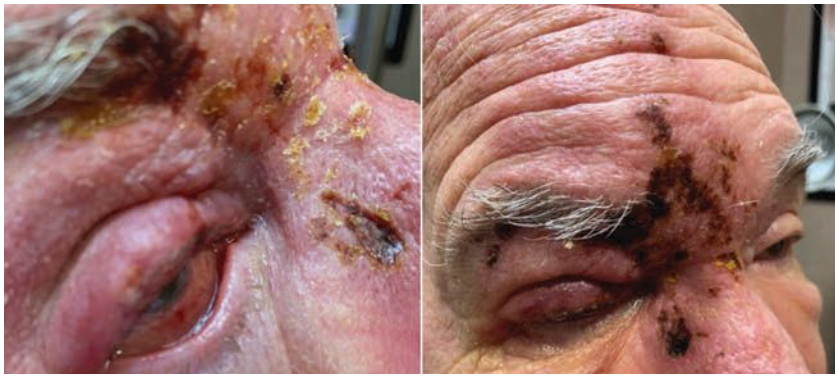


Fig. 1. Herpes zoster ophthalmicus.

be afraid to take on the hard cases: the treatments are almost always straightforward. Connect with your patients on a deeper level and make sure that they know you are there for them. My emergency colleagues have my direct cell phone number, and no one has ever abused this privilege during my time at my clinic. If you don't feel comfortable with this, make sure they have a method to reach you after hours.

On the days you are not busy (and there will be those days), refuse to sit idle and wait for more patients to come in. You must get out in your community and connect if you want patients to walk in your door.

DON'T LET YOUR PATIENTS GO TO AN ER!

Last year, we begged our colleagues to let your patients know to call your office if they developed a "medical eye emergency," and there is a ton of good will and resultant practice growth in doing so. A new study further defines the need for eye patients to see an eye doctor. Check out these quotes:

- "Most ocular conditions that present in emergency departments aren't urgent, and can be treated in an outpatient facility. Even if patients were to seek treatment in an ER, new research reports that the personnel in these facilities are not usually equipped to measure important ocular vital signs, including visual acuity (VA) and intraocular pressure (IOP)."
- "Most common ocular diagnoses that presented emergently involved the cornea or conjunctiva. They included uveitis, corneal abrasion, corneal ulcer, meibomian gland dysfunction, dry eye, blepharitis, punctate epithelial erosion and conjunctivitis or epidemic keratoconjunctivitis."
- "ER doctors measured VA and IOP in about 41% and 17% of patients, respectively."
- "VA measurement agreement between ER personnel and ophthalmologists was just under 12%. The agreement between IOP testing was worse, with the two groups coming to the same conclusion less than 1% of the time. Diagnosis agreement occurred in about half the cases."
- "In terms of symptoms, patients present eye pain, irritation, foreign body sensation, dryness, light sensitivity or a combination of these signs. It's critical that the standard workup of ocular cases include an accurate assessment of VA and IOP."

If we truly care for the people who entrust us with their eye care, we need to let them know to never seek eye care at an ER; rather, "call our office, and we can help you." This is so reassuring to our patients, and these types of situations are rare.

1. Tang VD, Safi M, Mahavongtrakul A, et al. Ocular anterior segment pathology in the emergency department: a five-year study. Eye Contact Lens. 2021;47(4):203-7.

2. Cole J. ERs Unequipped to manage ocular conditions. Review of optometry. 2020:157(12):5.

The first week I was in practice, we saw 33 patients total. I typically will now see 25 to 35 a day and about one-third of all of these patients are emergency patients. Don't let discouragement get the best of you and don't fall prey to worthless measurements like "gross revenue per patient." If you concern yourself with providing extraordinarily high-level care, your numbers will take care of themselves and your patients will honor and respect your clinical prowess. One day you'll appreciate these early years and the undeniable struggle that accompanies your initial startup efforts. Be the best doctor you can be and let the rest fall in place.

What now follows are several interesting cases I'd like to share.

Case 1. Herpes Zoster Ophthalmicus: All ODs should be able to rattle off the three antiviral schedules to treat shingles:

- Acyclovir: 800mg 5x a day for 10 to 14 days
- Valacyclovir: 1000mg TID for 10 to 14 days
- Famciclovir: 500mg TID for 10 to 14 days

Make sure to ask about adequate kidney function every time before starting patients on any of the above antivirals. Compromised kidney function will alter dosing schedules. Check with their nephrologist prior to starting treatment.

Treatment: This patient was started on valacyclovir 1000mg TID for 14 days and oral prednisone 30mg for one week, then 20mg for one week (*Figure 1*). Keep in mind, this patient was not diabetic. With HZO, I like to use Maxitrol ointment to the facial lesions QID and Pred Forte 1% QID if the globe is involved. If there is a concomitant inflammatory iritis, a cycloplegic will have to be initiated as well. Don't forget that these cases will often "get worse" before they get better—a key point that you and your patient will want to understand. Viruses run their course.

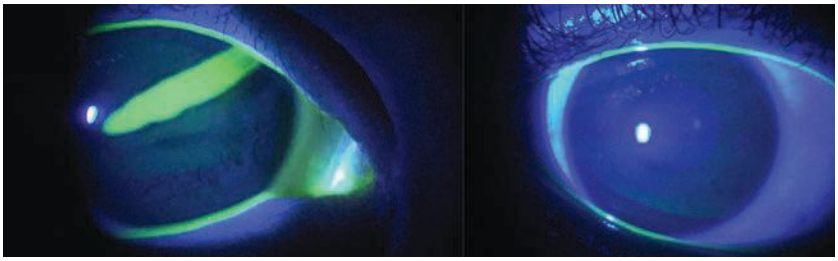


Fig. 2A. A four-year-old child was hit in the eye with a metal coat hanger (left). Five days later, there was complete resolution (right).

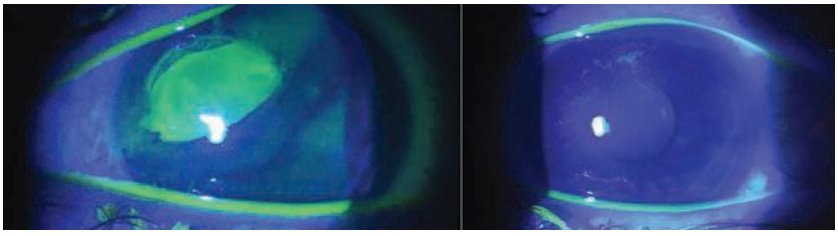


Fig. 2B. A 20-year-old female was scratched in the eye by a dog (left). A week later, she was 90% improved.

Case 2. Lesions: These cases (*Figures 2A and B*) are always fun because the treatment is so straightforward, and I've never had a case that didn't resolve completely. Don't let dramatic appearances throw you off and don't even consider referring these cases.

Treatment: Once I identify the extent of the lesion and make sure the eye is void of foreign bodies in the upper and lower lids, I immediately start therapy. For me, I cycloplege these patients every time. You can guarantee that there will be a traumatic iritis. I keep atropine in my clinic and always place a drop into the affected eye.

At this point, I will use an antibiotic ointment and firmly tape the patient's eye tightly shut. In some instances, I prescribe an oral antibiotic for coverage. The important thing to know is that I will not see these patients back in the next 48 hours. They will have my direct cell phone number to reach me with any complications, but I have found it to be superior to keep the eye taped closed. The patient will not be instilling any drops on their own. They simply leave their eye alone.

Case 3. Subconjunctival Hemorrhages: In almost every case, subconjunctival hemorrhages are benign and idiopathic. We call them "Halloween eyes" in my clinic: they look scary to our patients, but they always self-resolve. This case (*Figure 3*) highlights the importance of knowing our patients' current medications. In this case, warfarin was the antagonist. Patients on warfarin should have an INR between 2 and 3. Lower than 2, and they are at risk for stroke and venous thromboembolism. Above 3, and their risk of bleeding rises considerably.

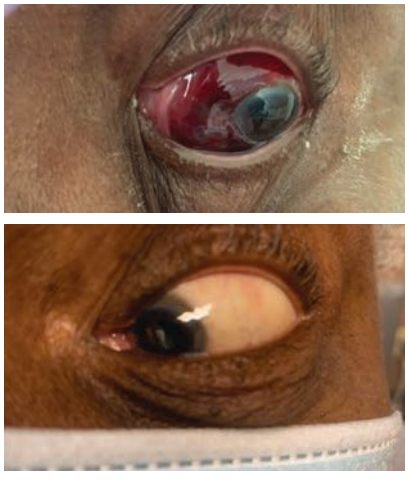


Fig. 3. A 73-year-old male on warfarin presented with a dramatic subconjunctival hemorrhage (top). His international normalized ratio (INR) was over 6! Three weeks later, the hemorrhages resolved (bottom).

Treatment: This patient was taking too much warfarin, causing an elevated INR. Their posterior segment was unremarkable on dilation. We comanaged with their primary care physician to ensure the patient was properly dosed, and the hemorrhages resolved less than a month later.

Case 4. Ocular Allergy: These cases can manifest with various presentations from mild to dramatic (*Figure 4*). They present with little to no pain at all and itching can be a hallmark.

Treatment: I treat almost all of these cases with oral and topical steroids. The poison ivy case (*Figure 4D*) was treated with 20mg oral prednisone for one week, Lotemax SM QID ophthalmic drops to the affected eye, children's Benadryl as directed

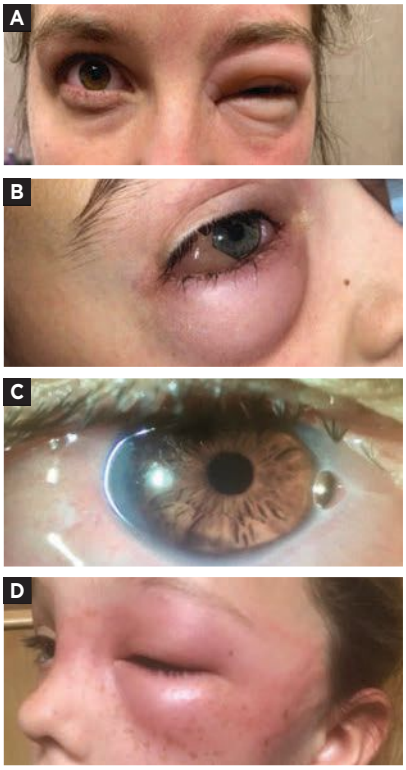


Fig. 4. Examples of ocular allergy. Not to be confused with preseptal cellulitis, these presentations had an explosive and painless onset. In the bottom photo, attention is drawn to the periocular area (poison ivy).

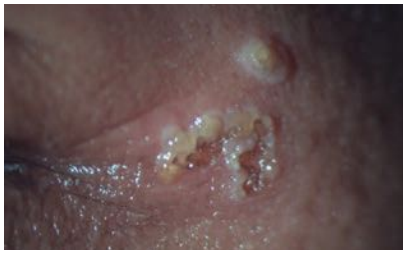


Fig. 5. Herpes simplex (blister lesions). The case had no corneal involvement.

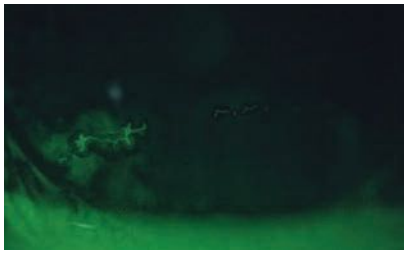


Fig. 6. Herpetic dendrite discovered with topical steroids in a period of eight hours.

and ice packs. The other cases were treated in an identical manner aside from the children's Benadryl—I used the adult dose in those cases. As with any presenting inflammatory case, it's critical to hammer the inflammation early and often.

Case 5. Herpes Simplex: Herpes simplex remains one of my favorite pathologies to treat. These cases should never be referred out and rarely comanaged with primary care. Simplex can often present as 'blister like' lesions in the periocular area. Don't confuse these lesions for bacteria! The treatments are identical to zoster, with the dosages halved:

- Acyclovir: 400mg five times a day for 10 to 14 days
- Valacyclovir: 500mg TID for 10 to 14 days
- Famciclovir: 250mg TID for 10 to 14 days

Treatment: Two of these cases were treated with valacyclovir for 10 days and went to resolution quickly. *Figure 5* was interesting in that the affected eye was one of my patients who is a nurse practitioner. In the morning she presented a unilateral red eye. Initially, the lesion looked like a small abrasion, but she could not remember trauma or previous trauma in the past. At the time, her cornea did not have a staining pattern obvious for herpes simplex keratitis (HSK). I let her know we were going to place her on a steroid Q2H and to come back in the evening for a second look.

HSK cases are worsened by topical steroids. Sure enough, a small dendrite was present at her evening follow-up just eight hours later. Steroids were discontinued, and the patient was started on valacyclovir. Three days later, the cornea was void of dendrites. This case illustrates the importance of occasional ambiguity and vital follow-up care.

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THE DIAGNOSTIC CHALLENGES OF THE SOLO PRACTITIONER

It is a fact that "failure to diagnose" is by far the most common reason that optometrists are successfully sued. Solo practitioners in general have about a 20% misdiagnosis rate. "We found that groups of all sizes outperformed individual subspecialists on cases in their own subspecialty." We find this shocking. The old saying, "two heads are better than one," appears to be scientifically sound. "We found that collective diagnosis by groups was associated with improved accuracy over individual diagnosis. Given the few proven strategies to address the high prevalence of misdiagnosis, these results suggest that collective intelligence merits further study in a real-world clinical setting."

This article states the obvious: "Diagnostic accuracy is largely a function of knowledge and experience. A growing literature suggests that diagnostic error is common and can lead, not unexpectedly, to harm."

"The diagnostic accuracy of aggregated opinion, which they refer to as 'collective intelligence', improved as the number of contributors increased, although the rate of accuracy began to plateau at two to three contributors. Group diagnoses also appeared to be more accurate than those of individual specialists solving cases within their specialty."

A summary statement might read like this: "Attention, solo practitioners—seek to bring on and partner with another colleague. The science is clear that collaborative assessments enhance patient care. The optometric profession is becoming more and more medically oriented day by day. As the public learns they can seek optometric care for all sorts of diverse conditions, our collective duty is to become increasingly astute diagnosticians. For example (and this could just as easily apply to optometric care), "A well-appearing 14-month-old girl was referred for the evaluation of recurrent left subconjunctival hemorrhage with increasing frequency since seven months of age. Multiple prior office visits with referring ophthalmologists during which eyes were dilated showed normal results."

"This patient presented to several outside ophthalmologists with recurrent subconjunctival hemorrhage, but the possibility of an orbital mass was not considered because of a lack of proptosis or other ocular abnormalities." My goodness, such a history is just not normal, and a high index of suspicion should have prompted deeper diagnostic intervention. When something is plainly out of the ordinary, extraordinary investigation is merited!

None of us have all the answers, but putting two heads together may very well enhance patient care!

1. Barnett ML, Boddupalli D, Nundy S, et al. Comparative accuracy of diagnosis by collective intelligence of multiple physicians vs individual physicians. JAMA. 2019;2(3):e190096.

2. Harrie RP, Levin AM, Owen L. Recurrent subconjunctival hemorrhage in a child with an orbital mass. JAMA Ophthalmol. 2021;139(1):125-6.

Prescribing for Eye Disease: An Expert Q&A

Settle in as we tackle 75 (!) clinical questions from the trenches in this section alone.

Q Is it still best to use non-generic Pred Forte to treat iritis? I had a pharmacist who recently changed my prescription to a generic and they said it was the exact same thing.

A The literature has been consistent and clear for many years that the generic versions are not as clinically effective as the original Pred Forte. However, this is not terribly critical since even the generics, when properly shaken and properly used, perform reasonably well.

The good news is that there are coupons available that allow patients under age 65 with a commercial drug plan to get the "real deal" for $50, which is a fair price. Just Google "Pred Forte coupons." Now, if the iritis is marked, we would go straight to difluprednate (Durezol) and not even risk pharmacy modification. Coupons are also available for Durezol. The way we practice is to use Durezol for severe iritis and episcleritis, and we use loteprednol for everything else.

Q For eyelid dermatitis, when would you use oral vs. topical steroids?

A If the erythematous, scratchy, dry, scaly area of dermatitis is superficial and localized, our choice is 0.1% triamcinolone cream. However, if a patient has a broader or more erythematous expression, such as with a poison ivy encounter, then we would generally prescribe 40mg of oral prednisone for about three days.

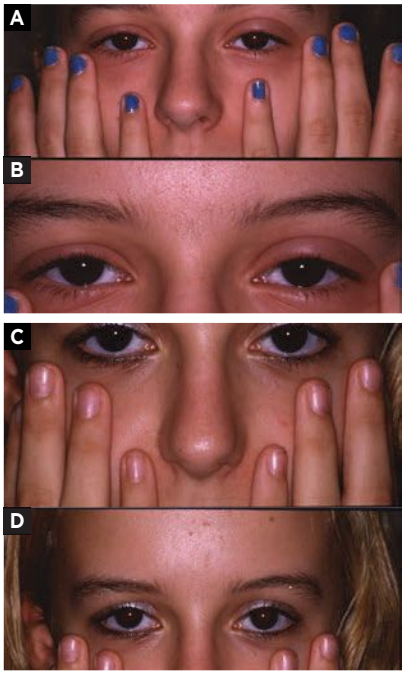


Fig. 1. Photos A and B are before treatment for eyelid dermatitis. Photos C and D are after.

Q Is it safe if triamcinolone cream gets into the eye?

A Yes. Kenalog is a brand name for triamcinolone. It is routinely injected into the eye by retina specialists to help resolve inflammatory diseases. We've never had a single issue from the triamcinolone cream getting onto the ocular surface.

Fig. 2. This is a case of contact blepharodermatitis where we would prescribe 0.1% triamcinolone cream.

LOW-DOSE ATROPINE AND OCULAR BIOMETRICS

"Low-concentrations of atropine (0.05%, 0.025% and 0.01%) have no clinical effect on corneal or lens power. Antimyopic effects of low-concentration atropine act mainly on reducing axial length elongation, and therefore could reduce the risk of subsequent myopia complications."

Li FF, Kam KW, Zhang Y, et al. Differential effects on ocular biometrics by 0.05%, 0.025%, and 0.01% atropine: low-concentration atropine for myopia progression study. Ophthalmology. 2020 Dec;127(12):1603-1611.

SUNSHINE: THE ENEMY OF MYOPIA

Time spent outdoors is correlated with a decreased risk of myopia onset. "If a child has two parents with myopia, the hereditary genetic effects increase the child's chances of developing myopia to approximately 60% if time spent outdoors is low. More time spent outdoors, approximately fourteen hours per week (or two hours per school day), can nearly neutralize that genetic risk for the child to approximately 20%, the same chance as a child without any parents with myopia." It is thought that "the protective effect relates primarily to myopia onset while questions remain about a similar effect on myopia progression." It is odd that simply getting away from the gravity of "the screen," to go outside and play can have so many positive benefits.

This is a teenager who appeared to be considerably myopic by the appearance of his eyeglasses. Is there a connection? Highly probable!

Zadnik K. Myopia prevention: here comes the sun. Ophthalmology. 2020 Nov;127(11):1470-1.

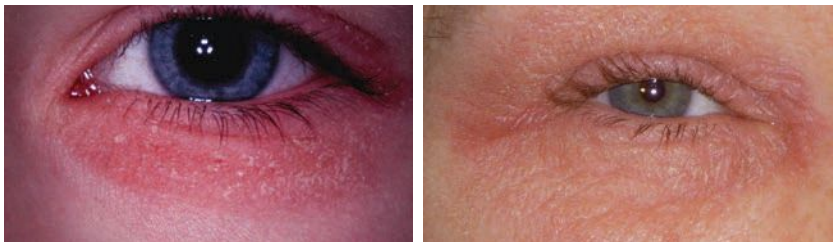


Fig. 3. These are two more presentations of periocular contact dermatitis.

NON-OPHTHALMIC STEROID OINTMENT/CREAM/LOTION

- **Triamcinolone, a moderate potency steroid**
- **Available in cream, ointment and lotion (0.5%, 0.1%, 0.025%)**
- **Our favorite: the 0.1% cream**

Source: Drug Facts and Comparisons

Q Any opinion on OTC 1% hydrocortisone cream for contact dermatitis rather than triamcinolone?

A Yes. Inflammation can be undertreated, but is rarely over-treated. We always hit it hard to do our best to quell the inflammatory process, thus limiting tissue damage to the fullest extent possible. While OTC 1% hydrocortisone cream can indeed work on some mild cases, we would rather prescribe our tried-and-true, highly effective triamcinolone.

PEDIATRIC EYE INJURY FROM HAND SANITIZERS

COVID can cause bodily injury in a wide variety of ways. One of the (relatively) least important assaults comes in the form of children's eyes. Of course, to eye doctors these types of injuries are (relatively) very important. We are all aware in one way or another that the Goldmann tonometer "tattoo" can result from not fully drying the alcohol off the tonometer prism tip before applanating the cornea!

Alcohol-based hand sanitizers (ABHS) have always been around, but COVID precautions brought them front and center just over a year ago. In fact, such reported exposures went from 1.3% in 2019 to 10% in 2020. Most cases were of no clinical significance, but there are a few reported serious corneal and conjunctival injuries. Most such encounters occurred in stores or malls where these dispensers tend to be at children's eye level. Immediate rinsing/dilution with water is appropriate first aid. Most of the ABHS solutions contain 80% ethanol or 75% isopropanol. Keep in mind that ethanol is widely used in corneal and refractive surgeries to facilitate epithelial debridement, but these are 20% concentrations and are applied for up to 30 seconds. Note, however, that there is no permanent scarring to these alcohol toxicities.

We treat most such ABHS encounters with a preservative-free artificial tear, but if there was any significant microtrauma to the tissues, we would prescribe an antibiotic/steroid, such as Zylet (Bausch + Lomb) or generic Maxitrol QID for four days.

Colby K. Unintended consequences of hand sanitizer use in the coronavirus disease 2019 pandemic. JAMA Ophthalmol. 2021;139(3):352.

Q With contact dermatitis cases, do you usually ascertain what the antigen is? What recommendations do you provide to reduce recurrences? What if there is no discernible/known trigger found?

A We try to. Most of the time the offending agent/substance can be determined via a good history. Exposure to poison ivy or other potentially noxious vegetable matter is common. Various cosmetics, especially fingernail polish, are another common cause. If a specific trigger cannot be identified, just ask the patient to be keenly attentive should there be another episode.

Q Can Lotemax ointment be used on periocular skin tissues similar to triamcinolone?

A Certainly, but Lotemax ointment is just much more expensive. Any time nocturnal suppression of inflammation of the globe is needed, Lotemax 0.5% preservative-free ointment is the prime choice. In situations where dry eye disease patients would prefer not having to deal with eye drops by day, we use this ointment at bedtime Monday, Wednesday and Friday for two weeks, then just Monday and Friday for two more weeks. On rare occasions, such ointment supplementation may be needed for stubborn cases of anterior uveitis and in some cases of recurrent corneal erosion.

Q Instead of triamcinolone, can Protopic be used?

A The patient in *Figure 4* teaches two facts: fingernail polish is a very common cause of contact dermatitis, and the patient made the mistake of seeing a doctor who obviously had the same thought you had. The tacrolimus 0.1% (Protopic) did not work, and once she was placed on our beloved 0.1% triamcinolone cream, she was restored to normal in three days. You have just got to cherish the wonderful benefits

Fig. 4. This patient first sought care for her eyelid contact dermatitis from a dermatologist. Note that she would not have sought a second opinion if the initial treatment had worked! We still have no idea why doctors are reluctant to prescribe steroids—it's frustrating. Once we had the patient using our tried, true and trusted 0.1% triamcinolone cream, she was almost back to normal in three days.

But there is more to this story: be attentive to her fingernail polish, a highly common cause of contact dermatitis to the eyelids (which was news to her). We educated the patient to try a more hypoallergenic brand of polish. Attentive, effective healthcare is what we all seek.

of corticosteroid suppression of inflammation. The patient was advised to either stop using fingernail polish, or perhaps try another brand.

Q Why use Lotemax gel and not drops, when gel produces blurry vision in some patients?

A There may be some confusion here with nomenclature. The Lotemax eye drops—Lotemax gel and Lotemax SM—are indeed viscous liquids (gel drops) that lose their viscosity after several blinks over a couple of minutes. The Lotemax ointment, like all ointments, will severely blur vision for minutes.

Q What is your steroid of choice for recurrent episcleritis, and after how many recurrences do you go to a low-dose maintenance steroid like Alrex?

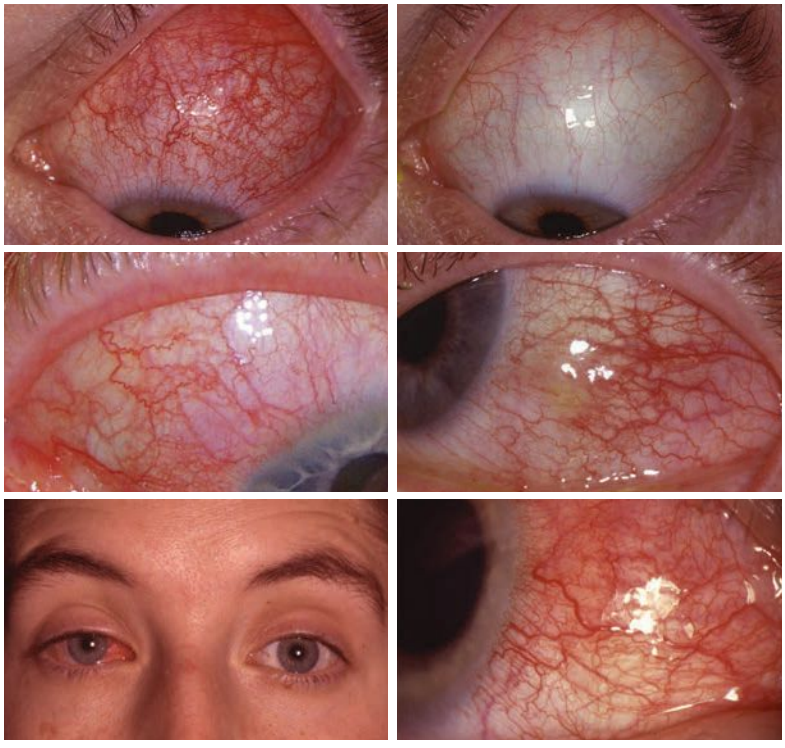
A In our experience, when treated authoritatively, episcleritis uncommonly becomes recurrent. At the first recurrence, we would send a note to the patient's primary care provider and give them specific guidance as to what conditions may be associated with episcleritis, such as rheumatoid arthritis, systemic lupus erythematosus, Wegener's granulomatosis, syphilis and gout. We could order testing for these conditions ourselves, but involving the PCP is more appropriate in our opinion; they do need our professional guidance as to these commonly associated conditions, however. Keep in mind that most all cases of episcleritis are idiopathic. We do still ask the patient about the presence of any current medical conditions at the initial presentation, but we rarely pursue a diagnostic workup then.

Q Are topical steroids more effective in treating episcleritis than oral NSAIDs? Or could they be used as an alternative?

A Topical steroids are key in treating episcleritis. For advanced cases, we use Durezol; for

EPISCLERITIS UP CLOSE

- Inflammation of the superficial sclera
- Usually sectoral, benign, idiopathic
- Occurs mostly in young adults
- Two types: simple and nodular
- Chief complaint is eye redness; mild discomfort is the rule
- Recurrence is common
- Systemic associations: RA, SLE, Wegener's granulomatosis, syphilis, gout
- Tx: artificial tears, cold compresses, topical decongestants, topical steroids



Here are several images of episcleritis; the top two show before and after corticosteroid suppression.

mild to moderate cases, we use Lotemax SM. Using NSAIDs is like using a squirt gun on a house fire in the setting of acute, prominent ocular inflammation. Oral NSAIDs are useful in scleritis but are way underpowered in suppressing episcleral inflammatory disease. There is no alternative to a steroid; only clinical efficacy gives us choices—FML or Alrex vs. Durezol, as an example.

Q Do you hesitate to use steroids in a pregnant patient presenting with inflammatory eye disease (*e.g.*, episcleritis, dry eye)?

A When oral prednisone is indicated for severe inflammatory diseases, we always consult the patient's obstetrician. Working together collegially best serves patient care. For topical eye drops, we typically do not consult; we do what is prudent to diminish systemic absorption. We direct the patient to do gentle eyelid closure for three minutes, or we use punctal plugs, or we prescribe an ointment formulation since ointments are known to have very minimal systemic absorption.

Q If my patient is allergic to sulfa, can I prescribe Maxitrol?

A Maxitrol contains neomycin, polymyxin b sulfate and dexamethasone. Sulfa-based medicines do not share a cross-allergenicity with sulfates, so yes is the answer.

Q Do these drops under development for presbyopia reverse early presbyopia already in progress?

A This is a topic of keen importance. Research is ongoing. Based on limited knowledge, we would theorize that perhaps starting when the patient first presents with presbyopic complaints would be the optimum time to consider such a therapeutic intervention. As the lenticular nucleus becomes more sclerotic, we would think that any such drug would be less effective. Only one investigational drug works to reduce sclerosis. For those presbyopic drugs that work via a quasi-pinhole effect, patient age might not be as critical. You will definitely hear much more about these medical interventions in the next year or two.

Q What is your opinion, given COVID-19 concerns, regarding reuse of conventional bottles for administering diagnostic drops in the exam room? For example, mydriatics or cycloplegics.

A The question might be rephrased as to whether the preservatives in these bottles would inactivate the COVID-19 virus. We have seen no studies addressing this. As always, we would be vigilant to not contact the patient with the dropper tip, and if we did, then we would discard the bottle (in a known, active COVID patient). Probably a good and sufficiently hygienic technique would be sufficiently cautionary.

Q Is there much risk for clostridium difficile infection when using doxycycline as a primary treatment for MGD?

A *Clostridium difficile* superinfection is rarely seen with doxycycline! We personally have never

FACTS ABOUT "SULFUR" ALLERGY

Here's something we all need to know regarding the concept of sulfur allergy. "The term 'sulfur allergy' is misleading and dangerous, and should not be used. An allergy to a sulfonamide antibiotic may imply cross-reactivity with other sulfonamide antibiotics, but does not imply cross-reactivity with non-antibiotic sulfonamides or other drugs containing sulfhydryl or sulfate groups. Allergy to sulfonamides also does not imply cross-reactivity with sulfite preservatives, sulfates or elemental sulfur."

"The term 'sulfonamide' applies to a sulfone group connected to amine group. All antibiotics sulfonamides are arylamines. A review of all available relevant studies concluded that the dogma of cross-reactivity between sulfonyl arylamines and other sulfonamide drugs cannot be supported by the evidence. In patients who have had an allergic reaction to one drug or allergic reactions to other drugs—even if entirely unrelated—occur more commonly."

"Sulfur is a natural element and it exists in many forms. There are many substances which have names stemming from 'sulfur' such as sulfites (preservatives in food and drugs) and sulfates (common compounds found in drugs, soaps and cosmetics). Some patients who have suffered from hypersensitivity reactions to a sulfonamide antibiotics are unfortunately labeled 'sulfa allergic.'

This term creates confusion for the patient and often for health professionals. Many patients believe that having been 'sulfa allergic' means they are also at risk for adverse reactions or allergies from sulfites, sulfates and even elemental sulfur, and they attempt to avoid them."

So, such medicines as polymyxin B sulfate or trimethoprim sulfate are perfectly fine to use in patients who claim to be allergic to sulfa drugs. The carbonic anhydrase inhibitors also have a sulfa moiety, but they do not share a cross-allergenicity with sulfa drugs.

"The commonly used canister type of metered dose inhalers do not contain sulfites, but several do contain sulfate salts and some patients need to be reassured that sulfates are inactive and do not cross-react with sulfites."

1. Smith WB, Katelaris CH. 'Sulfur allergy' label is misleading. Australian Prescriber, 2008;31:8-10.
2. Annals of Allergy, September 1987.

experienced this in any of our patients. Most antibiotics hold the potential to set the stage for *C. diff.* infection, though this is an uncommon event. Clindamycin is an excellent alternative for those rare individuals who truly have an allergy to penicillin, but it does carry an increased risk of *C. diff*. Interestingly, and as an aside, fecal transplantation has been shown to be highly effective in treating some of these complicated cases.

Q For varicella zoster viral (VZV) keratitis, would Maxitrol and oral antiviral work?

A The keratitis (or keratouveitis) as a concurrent or secondary expression of herpes zoster (shingles) is one exclusively of inflammation, therefore there is no need to incorporate an antibiotic/steroid combination. The oral antiviral nicely eliminates the active virus, and a topical steroid nicely suppresses the associated inflammation.

RISK OF UVEITIS RECURRENCE

- **Acute uveitis = less than three months**
- **Chronic uveitis = more than three months**
- **Risk factors for recurrence of chronic anterior uveitis are:**
  - **Longer duration of inflammation**
  - **Younger age**
  - **Bilateral uveitis**
  - **Prior cataract or glaucoma surgery**
  - **Juvenile idiopathic arthritis**
  - **Spondyloarthropathy (ankylosing spondylitis, psoriatic arthritis or reactive arthritis)**
  - **Presence of keratic precipitates and synechiae**
- **"Patients with these factors should be managed taking into account the higher probability of a longer disease course."**

Sobrin L, Pistilli M, Dreger K, et al. Systemic immunosuppressive therapy for eye diseases Cohort Study Research Group. Factors predictive of remission of chronic anterior uveitis. Ophthalmology. 2020; 127(6):826-34.

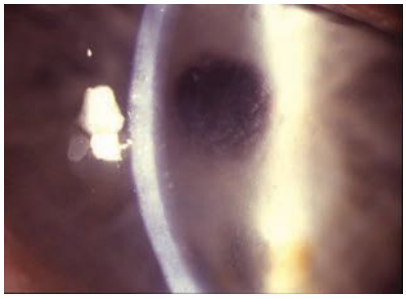


Fig. 5. Similar to glaucomatocyclitic crisis, this post-herpetic keratouveitis with elevated IOP was quieted with a topical steroid (and with oral valacyclovir 500mg daily for a month). Note the pancorneal leukocytic infiltration.

Q What is your go-to in-office "cocktail" for breaking posterior synechiae? Is it extremely important to break them sooner rather than later?

A Synechial formation in some cases of iridocyclitis can be problematic. Sometimes synechia can be broken ("unglued") in the office, sometimes only after a few days of intensive topical corticosteroid therapy, and, depending upon severity and length of time it has gone on, they may never be completely broken. We often prescribe 1% atropine to be used QID and 2.5% or 10% phenylephrine BID. This is done concurrently with hourly (while awake) instillation of Durezol (which, because it is an emulsion does not have to be shaken). We see these patients back about every three days, then less often as the condition improves.

Q Can a patient with multiple episodes of uveitis have a low-grade AC reaction?

A Absolutely. These are common patients, and in spite of the best of care, some uveitis cases cannot be 100% suppressed. These are those "steroid for life" patients (similar to those with corneal transplant and stromal herpetic disease) who may need to use a drop of steroid a day indefinitely. There are also some mild, "smoldering" cases that do not require long-term steroids. Every case is individualized.

GARDENING AS A CAUSE OF CORNEAL EDEMA

- **Acute onset corneal edema and blurred vision**
- **Most usually unilateral—rubbing face and eyes**
- **History is critical to making the diagnosis of isolated corneal edema**
- **Milkweed contains cardiac glycosides, which can alter endothelial enzymes, largely sparing epithelial tissues!**
- **Onset of symptoms after exposure: 12 to 24 hours**
- **Tx is topical steroid therapy—QID for four days, then BID for two days**

Venkateswaran N, Tonk RS, Berrocal A. Corneal edema in a gardener. JAMA Ophthalmol. 2020;138(9):998-99.

Q Is there any reason you would need to taper oral prednisone for an ocular acute inflammatory response? Or is it fine to stop the 40 mg daily dose after four days?

A Many such cases can be successfully stopped after a few days, and some may take months of a slow taper. As with any medical treatment, the goal is to treat effectively and then try to stop the medicine as soon as possible. So, if after a week to ten days of acute treatment the medicine is stopped or tapered, and if the condition returns, that is a clear indication a more protracted course of therapy is required. It's all (to some degree) trial and error. It is the "art" of practicing medicine!

Q With conjunctivitis, I was taught that mucopurulent discharge inactivates Polytrim. True or false?

A Bacteria synthesize folic acid from para-aminobenzoic acid and are a component of mucopurulent discharge, but not to any clinically significant degree. Recall that both sodium sulfacetamide and trimethoprim work along the metabolic pathway inhibiting the production of folic acid, but trimethoprim is not a sulfa-based drug. So, false.

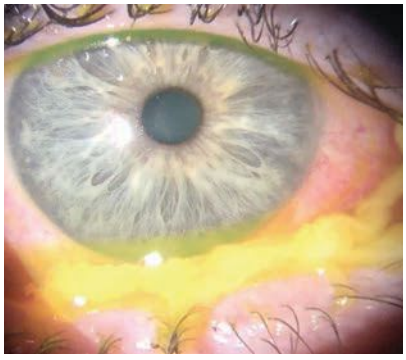


Fig. 6. Copious mucopurulent discharge with mildly injected eye.

Q How long do you use a topical steroid with the systemic antiviral for stromal herpetic disease?

A This is a largely unanswerable question because the length of treatment can vary wildly from patient to patient. A common scenario might look something like this: valacyclovir 500mg once daily for a couple of months. At the same time, we would use Lotemax SM QID for one to two weeks, then BID for two months, then every day for six months, then every other day for another six months, but this gives a flavor for the long-term suppression of this secondary inflammation that can be associated with herpetic eye disease.

INR: INTERNATIONAL NORMALIZED RATIO

- A universally accepted measure of "coagulability"(clotting) behavior of blood in patients taking Coumadin (warfarin).
- An INR of 1 is a normal, physiological clotting behavior.
- Target anticoaguable profile is an INR generally between 2 and 3.
- The higher the INR > 3, the thinner the blood, thus increasing risk of bleeding and hemorrhagic stroke.

QUOTABLE

While the Xa inhibitors Xarelto (rivaroxaban) and Eliquis (apixaban) are steadily replacing Coumadin (warfarin), there are still plenty of patients on warfarin, so it is incumbent upon us to be cognizant of the INR, which is the blood-derived laboratory measure of coagulative status.

Q Please review when you would not want to use steroids during inflammation/infection situations or when you would delay the steroids.

A The prime contraindication for using steroids is the evidence of acute epithelial herpetic simplex disease. Always consider any unilateral red eye as possibly herpetic in origin. Otherwise, that's about it. Here is the key to therapeutic patient care: if you are just not sure exactly what is going on, treat with a combination antibiotic/steroid and then call the patient a few days later to check on them. If the condition were to ultimately turn out to be herpetic, it's no problem at all. Just discontinue the initial medicine and start the more appropriate medicine; it is truly that simple. We have medically treated thousands of patients over the decades, and have only had to modify our treatment a handful of times. We tell every patient we medically treat something like this: "This medicine should have you improving in just in a couple of days; however, we are not perfect, and should your eye worsen, please give us a call." This statement is also documented in our medical record.

Q What is the cost of new anticoagulant drugs as compared with warfarin?

A These new anticoagulants are indeed considerably more expensive than warfarin, but this has to be viewed in two distinct ways. If the patient has good insurance, cost of the newer drugs is likely not to be an issue. With warfarin, there are the requisite monthly laboratory checks to monitor the patient's international normalized ratio (INR). Once the time and lab expenses are calculated, the cost of the newer medicines is not all that different. Eliquis (apixaban) and Xarelto (rivaroxaban) are far more effective and convenient in that there is less side effect potential with other drugs and there are no dietary restrictions. These newer drugs (known as Xa factor inhibitors) interfere with the blood coagulation cascade and do not affect platelet function. Just a reminder: aspirin works on platelet function, but is not an anticoagulant per se.

Q For foreign body sensation, instead of sweeping the superior cul-de-sac, have you tried one of the instruments to double-evert the lid?

A You can know we have done this many, many times, but the fulcrum "flip" is at the top of the

ASPIRIN FOR PRIMARY PREVENTION: NOT SO GREAT

"Aspirin confers an 11% relative reduction in cardiovascular disease risk and a relative 43% increase in the risk for major bleeding, and only patients with very high cardiovascular disease risk and low bleeding risk would gain a net benefit for aspirin therapy."

"This study confirms that most patients do not benefit from primary preventive aspirin."

"Even among patients with favorable benefit/harm balance, the probability of benefit is tiny, about four per 1,000."

As we try to keep current with all common aspects of human medicine, we pass these findings on to our optometric physician colleagues.

Annals of Internal Medicine, October 2019 (as reported in NEJM Journal Watch, October 2019).

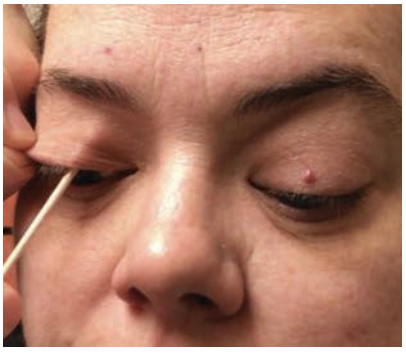


Fig. 7. After instilling proparacaine, moisten the tip of the cotton swab with an ointment for lubrication. Have the patient look down and insert the cotton swab. Gently sweep the entire cul-de-sac back and forth two to three times.

tarsal plate, yet the recesses on up to the cul-de-sac remain blinded. Only a sweep of the cul-de-sac can remove foreign material remotely located in the cul-de-sac (see *Figure 7*).

Q I saw a patient who had a bungee cord accident in one eye. Her vision was good, but she had a vitreous hemorrhage and acute iritis but no RD. I put her on Pred Forte, and cyclopleged and referred her to a retina specialist, who didn't do anything except monitor her. Would you have managed the patient differently?

A Yes, we would have kept the patient in our care, and we would have monitored her ourselves! Our profession needs to develop the confidence to manage more and more of these types of situations. Your care was just perfect.

Q Is oral prednisone an appropriate treatment for a chalazion?

A No. A chalazion is a ball of granulomatous scar tissue most commonly resulting from a previously untreated or undertreated bacterial infection of a single (or multiple) meibomian gland. Intralesional steroid injection can be helpful in some of these cases, but in-office excision and curettage is still a commonly needed intervention. It is just difficult to get a high enough concentration of the steroid via the oral route.

Q A contact lens wearer had some dust blow in his eyes. He slept in his contact lenses that night, and the next day he had a bacterial conjunctivitis in both eyes. His lids were so swollen that his eyes were barely visible. What is the best way to treat the lid edema? The lids were not painful. Homatropine TID? Oral prednisone?

A Cold compresses and 40mg of PO prednisone for two days is what we would typically advise. There is no need for cycloplegia since there is no intraocular inflammation. Use an antibiotic/steroid combination every two hours for a couple of days, then QID for four days. Threaten the patient with severe trauma if he ever sleeps in his contact lenses again!

AMOXICILLIN/CLAVULANIC ACID (AUGMENTIN)

- Clavulanic acid enables amoxicillin to be bactericidal against common gram positive pathogens
- Useful in treating soft tissue infections
- Cannot use if patient is allergic to penicillin
- Tx: 250, 500 and 875 (generic) or 1000mg (branded only) tablet q12 hours for seven to 10 days
- Can be taken with meals

KEFLEX (CEPHALEXIN)

- Children >2 months
- For skin and soft tissue infections, may be given every 12 hours

Weight (lbs)	Dose (250 mg/5ml)
11	¼ tsp
22	½ tsp
33	¾ tsp
44	1 tsp (250mg cap)
66	1 ½ tsp
88+	2 tsp (500mg cap)

OVERVIEW OF PENICILLIN "ALLERGY"

- "Severe anaphylactic reactions to oral amoxicillin are rare."
- "IgE-mediated penicillin allergy (the real deal) wanes over time, with 80% of patients becoming tolerant after a decade. Cross-reactivity between penicillin and cephalosporin drugs occurs in about 2% of cases."
- "Many patients report they are allergic to penicillin but few have clinically significant reactions."

Blumenthal KG, Shenoy ES. Am I allergic to penicillin? JAMA. 2019; 321(2):216.

ALLERGIC REACTIONS TO CEPHALOSPORINS

- **19 of "more than a million" patients experienced allergic reactions.**
- **"Almost 66,000 patients who received cephalosporins had previously documented allergies to penicillin and 3,300 had previous reports of cephalosporin allergies."**
- **"Cross reactivity between cephalosporins and penicillin has long been a concern; however, in recent studies, almost all penicillin-allergic patients have received cephalosporins safely."**

J. Allergy and Clinical Immunology. March 2015 (as reported by NEJM JournalWatch).

Q Can you describe your gonioscopic criterion for when photoiridotomy is indicated prior to dilation?

A If the angle is so narrow that there is some appositional iridocorneal contact, then there are two options: go ahead and do routine dilation (usually with 1% tropicamide and 2.5% phenylephrine) or perform the laser photoiridotomy. Regarding the diagnostic challenge of pupillary dilation, it is best to do this in the morning so that if angle-closure does occur, timely and unhurried LPI could be done (or arranged for) in the afternoon.

Q Can you go over when you might modify your oral dosing for children, very heavy-set patients or 90-pound elderly patients? Do you have any pearls for weight adjustment?

A Generally speaking, small bodies need less medicine and large bodies may need more. For example, Augmentin (amoxicillin with clavulanic acid) is an excellent antibiotic with its forte being in the gram-positive arena. It comes as 250mg, 500mg tablets, 875mg and 1,000mg tablets. This gives one many options. For example, one could prescribe 250mg for children; 500mg for small adults; 875mg for most adults and 1,000mg for a large person. Augmentin is to be taken twice daily and is best taken with a meal to minimize the potential for stomach upset.

Q A 70-year-old male presented with an inferior corneal ulcer secondary to poor lower lid coverage. I prescribed Vigamox, but the insurance company denied it as: "This drug is not approved for this diagnosis." The pharmacist at least called, but substituted tobramycin.

A Ah, the joy of working with a pathologically over-bureaucratized healthcare system! How does the pharmacy even know what the diagnosis is? At any rate, prescribing "off-label" is totally routine, and is done thousands of times each day. You are the doctor and you have the position of authority (and responsibility) to write for any medication within your state's prescriptive authority. Tobramycin is a good drug, as is Vigamox; we would have written for non-substitutable besifloxacin based on scientific research (*see ARMOR study data below*).

Q What contraindications to oral prednisone do we need to be aware of? With its 40mg a day dosage, do you prescribe 10mg QID? We would prescribe to take four 10mg tabs at one time with breakfast.

A "Contraindications" should probably be substituted with the term "concerns." There are four circumstances where we would be particularly attentive, and those would be with patients with diabetes, peptic ulcer disease, possible tuberculosis and pregnancy. In all four such

2020 ARMOR SURVEILLANCE DATA: MIC_{90} COMPARISONS FOR STUDY ISOLATES

	S. aureus		MRSA		CoNS		MRCoNS	
	2015 (n=1169)	2020 (n=2189)	2015 (n=493)	2020 (n=765)	2015 (n=992)	2020 (n=1765)	2015 (n=493)	2020 (n=871)
Besifloxacin*	0.25	1	2	2	0.25	2	4	4
Vancomycin	1	1	1	1	2	2	2	2
Trimethoprim*	2	4	2	2	32	>128	>128	>256
Moxifloxacin*	1	4	1	16	1	16	32	32
Gatifloxacin	2	4	16	16	2	16	32	32
Ofloxacin	8	>8	>8	16	8	>8	>8	32
Ciprofloxacin	8	128	256	256	8	64	64	64
Tobramycin*	1	128	>265	256	4	16	16	32
Azithromycin	>512	>512	>512	>512	>512	>512	>512	>512

* Denotes the four antibiotics we use most routinely, given their proven efficacy and relatively low resistance profile.

As a reminder, the lower the MIC_{90}, the more potent the anticipated efficacy.

CoNS = coagulase-negative *Staph.* species, of which the majority are *Staph. epidermidis*.

Sources: Asbell PA, et al. JAMA Ophthalmol. 2015;133(12):1445-1454.
Asbell PA, et al. JAMA Ophthalmol. Published Online April 9, 2020.

While these ARMOR data are *in vitro*, we can still glean some clinical guidance. It is well understood that fortified vancomycin (which has to be compounded) is the gold standard when treating suspected gram-positive corneal infection. Note that these comparisons are based on MIC (minimum inhibitory concentration) at which 90% of the bacteria are eradicated. Based on these comparative data, besifloxacin shows very similar performance to vancomycin, which is why we prescribe this unique suspension when treating severe conjunctivitis or keratitis.

A NOVEL FLUOROQUINOLONE: BESIFLOXACIN

- A unique bi-halogenated quinolone
- New chemical entity: an 8-chloro-fluoroquinolone
- Not used systemically; relatively resistance-proof
- FDA-approved medication: bacterial conjunctivitis
- FDA-approved treatment protocol: TID for seven days
- Pediatric approval: ages one and older
- Preserved with 0.01% BAK (Durasite vehicle)
- Marketed as Besivance 0.6% ophthalmic suspension by Bausch + Lomb

cases, we would call the physician relevant to our specific concern, and chat about our need to use oral prednisone.

What we have learned from the specialty physicians: regarding diabetes mellitus, patients with type 1 diabetes know how to administer their insulin on a "sliding scale," so they should be able to easily adjust their dosing. For patients with type 2 or adult-onset diabetes, we have been told that these patients are out of control from time to time anyway, so having transient hyperglycemia for a few days is not a major concern. For peptic ulcer disease, our gastroenterology friends advise us to have the patient purchase over-the-counter Pepcid or Prilosec (20mg tablets of omeprazole), and to take that medicine once daily while taking the oral prednisone. If the patient has been in an environment where tuberculosis is common, such as third world countries or some nursing homes, then the possibility of TB must be considered, and that is why we would chat with the patient's primary care physician first. If the patient is pregnant, certainly we would do as we always do—call and have a conversation with her obstetrician. For all of these patients, we put our heads together with the proper physician to come up with the best formulation to maximally and safely provide patient care.

Q Can you explain prescribing oral steroids again? What size tablets and how many times per day?

A There are two common ways to prescribe oral prednisone. First is with a variety of dose packs:

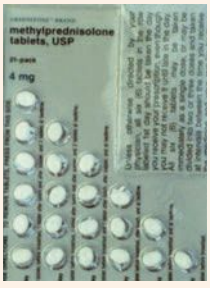
- 4mg dose-pack (starting with six tablets (24mg) on day one, and then follow with five, four, three, two and one tablet on day six).
- 5mg dose-pack (starting with six tablets [30mg total] and tapering as above).
- 10mg dose-pack (starting with six tablets [60mg total] on day one, and then tapering at 10mg per day as above).

Or simply prescribe 10mg tablets (with customized dosing)

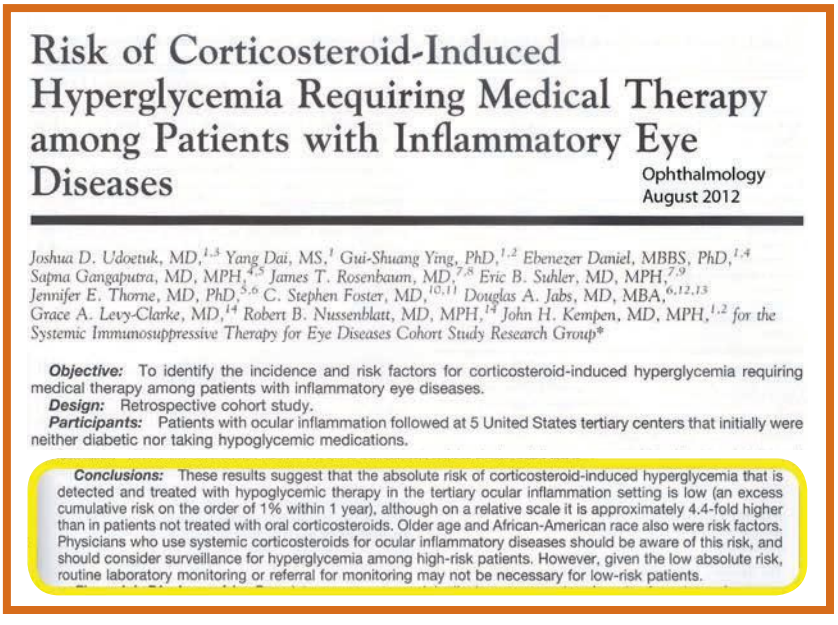
- For example, take four tablets per day for four days or take four tablets for three days, and then two tablets for three more days.

PREDNISONE POINTERS

- Most commonly Rx'd systemic corticosteroid
- Common initial dosage: 40mg to 60mg
- Available generically in both tablets and DosePaks
- Questions to ask before prescribing:
  - » Diabetic?
  - » Peptic ulcer disease?
  - » Tuberculosis?
  - » Pregnant?



This is the classic 4mg Medrol dose-pack. Note that the initial starting dose is only 24mg, and such a slow taper over six days is rarely—if ever—warranted. We typically write for 10mg tablets (easy math!) and, for example, have the patient take four tablets for four days. We have them take all four tablets at one time with breakfast. There is no need to taper if oral prednisone is used for less than one week.



Risk of Corticosteroid-Induced Hyperglycemia Requiring Medical Therapy among Patients with Inflammatory Eye Diseases

Ophthalmology August 2012

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Objective: To identify the incidence and risk factors for corticosteroid-induced hyperglycemia requiring medical therapy among patients with inflammatory eye diseases.

Design: Retrospective cohort study.

Participants: Patients with ocular inflammation followed at 5 United States tertiary centers that initially were neither diabetic nor taking hypoglycemic medications.

Conclusions: These results suggest that the absolute risk of corticosteroid-induced hyperglycemia that is detected and treated with hypoglycemic therapy in the tertiary ocular inflammation setting is low (an excess cumulative risk on the order of 1% within 1 year), although on a relative scale it is approximately 4.4-fold higher than in patients not treated with oral corticosteroids. Older age and African-American race also were risk factors. Physicians who use systemic corticosteroids for ocular inflammatory diseases should be aware of this risk, and should consider surveillance for hyperglycemia among high-risk patients. However, given the low absolute risk, routine laboratory monitoring or referral for monitoring may not be necessary for low-risk patients.

40mg for four to seven days is the most common dosage we prescribe; but, as with all prescribing, every patient's condition is unique and therefore individualization of care is the order of the day.

At 60mg or 80mg per day dosing, we generally divide the medicine in half. For example, for 60mg per day, our *sig* would be #3, 10mg tablets with breakfast and #3, 10mg tablets with lunch. Obviously, with 80mg per day, the number of 10mg tablets would be #4 tablets BID, preferably with breakfast and lunch. A few people get some jitters or have difficulty sleeping with higher doses of prednisone, so we typically try to avoid "after-lunchtime" dosing. Having prescribed this medicine well over 200 times, we have not had any significant issues, so take heart.

Q Are we managing the "high" dose oral prednisone with taper ourselves, or referring to the PCP?

A Our prescribing style varies. Sometimes we prescribe ourselves; sometimes we ask the patient's PCP or specialist to do so. Our job is to make the right diagnosis, initiate the right therapy and then pass the patient (along with a succinct letter detailing the situation and diagnosis) onto the PCP, internist or rheumatologist, depending upon the unique situation. We often do initial tapering (within the first week or two), but if long-term tapering is needed, we generally ask the medical providers to handle this.

Q Is the dosage of oral antiviral the same for kids?

A Dosing is different and needs to be weight-adjusted. *Table 1* on the next page nicely provides guidance. Keep in mind that of the three oral antivirals, only acyclovir comes as a liquid at 200mg/cc (or per tsp).

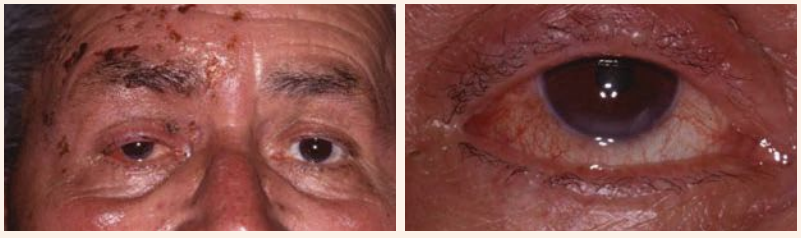
PAIN MANAGEMENT IN THE SETTING OF SHINGLES

Pain is a common accompaniment to acute shingles. Oral antivirals and oral prednisone are very helpful in reducing viral replication and reducing secondary inflammation (and its resultant pain) respectively.

Occasionally, oral opioids are needed for only a few days. Studies have shown that alternating oral ibuprofen and oral acetaminophen QID can be roughly equivalent to hydrocodone/acetaminophen (Vicodin/Lortab). Sometimes doctors prescribe gabapentin or pregabalin (Lyrica) for acute pain relief, but such use has shown to be unhelpful. To wit, these drugs are only approved for the management of post-herpetic neuralgia: "Both gabapentin and pregabalin are approved for managing post-herpetic neuralgia, but both are used often for acute zoster pain, for which studies have shown no benefit."

Most shingles patients do not require supplemental oral prednisone or supplemental analgesia (other than acetaminophen); however, for patients with more advanced disease—particularly older patients— 40mg to 60mg of oral prednisone for a week may well be in order. Keep in mind that early intervention with an oral antiviral quickly subdues the disease process such that oral prednisone and/or oral analgesics may not be needed at all.

JAMA Internal Medicine, March 2019 (as presented in NEJM Journal Watch, April 2019).



This gentleman presented acutely with a one-day history of redness in his right eye. This is a typical case of first (ophthalmic) division shingles. He has a concurrent/secondary mostly temporal episcleritis, but minimal discomfort. He was treated with oral famciclovir 500mg TID for a week along with Durezol Q2hours for two days, then QID one time a week.

Q Should we consider using trifluridine ophthalmic solution for treating ocular herpes? Or [should] the oral treatment always be the first instance? In which cases should the drops be used?

A It should be stressed that only in a severe case (which we have yet to see) would oral and topical treatments concurrently be indicated. We cannot think of a case in which we would use topical therapy; perhaps in a patient with dysphasia (difficulty swallowing).

Q What dosage of antivirals do you use for HSV?

A We almost always use valacyclovir 500mg TID for one week.

Q How do you treat secondary iritis with HSV disease?

A Just treating the primary infection is hugely helpful in improving iritis signs and symptoms, and good cycloplegia such as with cyclopentolate 1% QID or atropine 1% BID should be all that is needed.

Q Does Shingrix reduce the risk of herpes simplex keratitis?

A Since herpes simplex and herpes zoster are cousins of sorts, one would think this would be the case. However, Shingrix vaccine only actively intercedes against herpes zoster (shingles). It's a two-dose vaccine, as are most of the COVID vaccines.

TABLE 1. TREATMENT AND PROPHYLACTIC DOSAGES FOR ACYCLOVIR IN CHILDREN

Age	Treatment Dose Thrice Daily	Prophylactic Dose Twice Daily
Infants (up to 18 months)	100mg (2.5 ml)	100mg (2.5 ml)
Toddlers (18 months to three years)	200mg (5 ml)	200mg (5 ml)
Young children (three to five years)	300mg (7.5 ml)	300mg (7.5 ml)
Older children (six years and older)	400mg (10 ml)	400mg (10 ml)

Source: Ophthalmology, October 2012

This chart nicely guides proper dosing of the oral suspension of acyclovir.

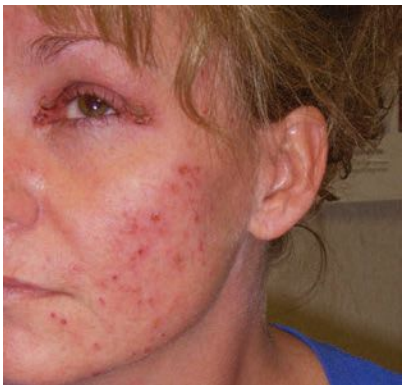


Fig. 8. This case of shingles is more disseminated than the common isolated dermatome in that it appears that both first and second dermatomes are afflicted. Also, the patient exhibited more lesions just below her neck. She did well with only oral antiviral therapy.

Q What are the oral treatment options for shingles?

A While shingles expression can range from mild to severe, the antiviral dosage is the same for most all cases. We usually prescribe valacyclovir at 1000mg TID for one week, but sometimes for 10 days. Practical dosing is breakfast, mid-afternoon and at bedtime. The more challenging question would be: when do we concurrently prescribe oral prednisone along with the oral antiviral? Generally speaking, if the patient is over age 60 and the presentation is moderate to severe (or if there is considerable pain), then we would prescribe 40mg or 60mg oral prednisone per day for a week. When we use prednisone for less than that, there is no requirement to taper.

If cost is of the antiviral is critical, acyclovir is always less expensive, but it has to be used five times a day, so the dosing is a bit burdensome (about every three and a half hours).

If the patient is over 65, we generally use generic famciclovir, as it seems to be better tolerated in this population than acyclovir or valacyclovir. The usual dosage is 500mg TID for seven to 10 days.

STAMP OUT SHINGLES

This painful, debilitating experience can have serious consequences for the cornea in particular, but also the skin around the eyelids. Newer vaccines in use now will lessen the incidence some years hence, but for now it remains an ongoing risk to many.

Incidence: Herpes Zoster Ophthalmicus

- Shingles occurs in one-third of adults.
- Of these, about 15% involve the ophthalmic division; of these about half will afflict the globe.
- Rate is increasing in ages 35 to 55.
- "Given the shift in HZO burden toward middle-aged individuals, it is crucial for clinicians to support vaccination efforts for individuals 50 years of age and older."
- "Varicella (chicken pox) vaccination (Varivax) of children began in 1996 and became more effective after the two-dose regimen started in 2006."

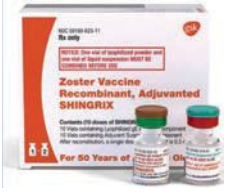
Kong CL, Thompson RR, Porco TC, et al. Incidence rate of herpes zoster ophthalmicus: a retrospective cohort study from 1994 through 2018. Ophthalmology. 2020 Mar; 127(3):324-30.

The Latest on Shingles

- Mean age of event: 52.
- Patients who have had HZO should be examined "within several weeks before and after vaccination against herpes zoster" because they may be at risk for recurrent eye disease.
- We should "recommend strongly" that patients over 50 get Shingrix.
- Our advocacy could "play an important role in increasing vaccination rates."
- About 10% of people have a reaction to Shingrix, more after the second dose.

Policy Statement. Recommendations for Herpes Zoster Vaccine for Patients 50 Years of Age and Older Ophthalmology. Nov. 2018

Shingrix Replaces Zostavax



- Shingrix is the second vaccine to be FDA-approved to help prevent shingles.
- Approved for people ages 50 and older.
- A non-live vaccine (Zostavax is live, attenuated).
- Administered in 2 IM doses (initially then two to six months later).
- About 90% effective and maintained over four years.
- If the last Zostavax vaccine was at least five years ago, can have Shingrix.
- Marketed by GlaxoSmithKline.

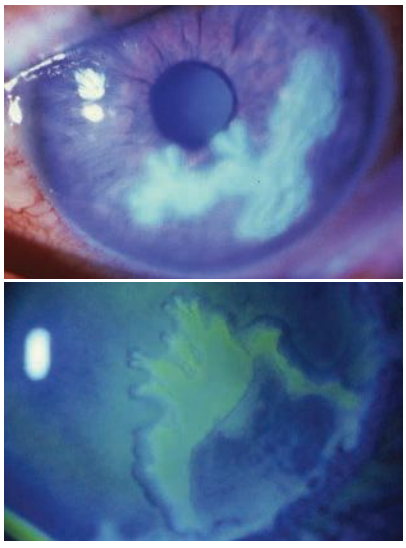


Fig. 9. Examples of HSV epithelial keratitis.

Q Do topical antivirals have a role in herpes simplex disease any more?

A Certainly, but only minimally. The oral antivirals are equally effective, less toxic and less expensive than topical therapies.

Q For chemical burns of the cornea and/or conjunctiva, does Lotemax ointment work even during the day? If the cornea is still intact, is it true that the burn won't be as bad as when the corneal epithelium is off?

A Yes, you are correct, although we would be more inclined to use the less expensive Maxitrol ophthalmic ointment. Toxic chemicals are also bactericidal, but having an antibiotic drug along with the steroid might be a better course of action, even during the day—as well as at bedtime. Your second observation is generally correct, because this would be a mild chemical burn if the epithelium is still intact.

Q What type of lens would you use to view the fundus with the slit lamp instead of binocular indirect ophthalmoscopy with scleral depression?

A Any of the "90-D" type lenses are excellent for retinal viewing. We generally prefer the Volk Super 66, but any of these similar lenses perform well. We continue to rely heavily on the binocular indirect ophthalmoscope (BIO), as we feel we can get to the peripheral retina more effectively with that instrumentation.

Q Is scleral depression standard of care? Years ago, I remember a lecturer saying it must be performed and documented as a "CYA." I would love to hear it is not considered necessary. Thanks!

A Retina subspecialists are the masters of scleral depression and are most likely the ones doing the lion's share of these procedures. A study in IOVS from 2013 offers an updated perspective that we greatly appreciate.

- "An examination using a 28 diopter lens with scleral depression did not provide any additional benefit to an examination without depression during indirect ophthalmoscopy."
- "In many areas around the world ophthalmologists have progressively shifted from indirect ophthalmoscopy with 28 diopter-type lenses to new fundus lenses at the slit lamp to improve the comfort of the patient without scleral depression."

Q How do you handle an associate OD who isn't comfortable with medical optometry and typically refers most glaucoma patients and other conditions within our scope?

A This is more in the realm of practice management, but since you asked, we'll take a crack at it. First of all, this topic should have come up in the interview and initial office visits. After four years of intense clinical training, how could an optometrist not be comfortable with these conditions? There is ample continuing education readily available to help address such concerns. Last, good, honest, forthright communication (a face-to-face discussion) is critical. At the very least, the "associate" should keep these patients "in-house" so that they can be internally referred to you or another optometric colleague.

Q Orbital inflammatory pseudotumor: how do you know you are not dealing with an inflammatory malignancy without at least doing blood work to rule out lymphomas?

A See the slide below regarding a diagnosis of this disorder. Note that orbital inflammatory disease occurs over a few days. Malignancies take weeks or months to manifest themselves.

Q Regarding idiopathic orbital inflammatory disease, is your first line for a definitive diagnosis like that a CT scan? Would you ever try using steroid eye drops beforehand?

A The diagnosis is usually very straightforward, but an urgent CT scan can quickly seal the diagnosis. Since we are going to make the diagnosis before starting treatment, no eyedrops are needed—only oral prednisone.

IDIOPATHIC ORBITAL INFLAMMATORY DISEASE (ORBITAL PSEUDOTUMOR)

- Usually acute onset, unilateral, red eye
- Chemosis, lid edema and erythema
- Proptosis, EOM dysfunction and diplopia are possible
- Systemic association rare if unilateral
- VA, exophthalmometry, IOP, CT or MRI
- Treatment is oral prednisone, high dose (1mg/kg/d initially) with taper

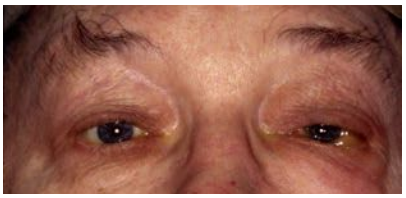


Fig. 10. Idiopathic orbital inflammatory disease. Note hemorrhagic chemosis—no itching—and has been there about four days. CT scan did show orbital inflammation. A consult was done with the primary care practitioner because of the need to treat with 60mg of oral prednisone over one week.

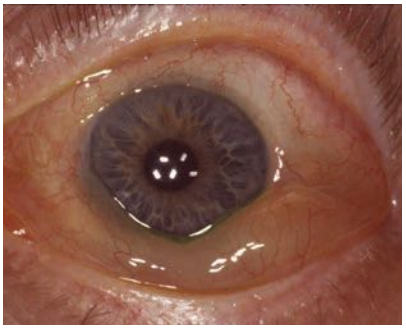


Fig. 11. Non-itching, acute "hemorrhagic" chemosis indicative of orbital inflammation.

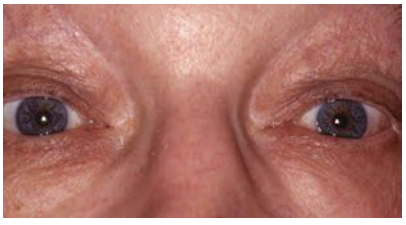


Fig. 12. Photo shows complete restoration to normal one week later.

Q Treating these inflammatory periorbital tumors scares me a little. How can I be more comfortable treating with a steroid first-line vs. an oral antibiotic?

A The "key of keys" in medicine is making the proper diagnosis. Review the teaching slide, do a good "Review of Systems" and get an urgent CT scan. Radiologists can be immensely helpful in these types of cases. Once you have a solid diagnosis, you can then be more confident with the proper therapy.

Q When using the pulse-style dosing of Lotemax for dry eye, what does the literature say about cataract formation?

A To our knowledge, there is not a single case report of cataract formation associated with the use of loteprednol. This is because intrinsic ocular esterases preclude the accumulation of sufficient and prolonged steroid concentration. Even with the ketone-based steroids like prednisolone, dexamethasone and difluprednate, such occurrences are rare.

Q Is it understood why the aqueous-based preservative-free artificial tears did nothing to alleviate symptoms?

A We assume it is because the preponderance of dry eye results from deficiencies in the lipid layer—at least that would make sense.

Q Do you use meibomian gland treatments that warm and express the glands? What are your thoughts?

A We are just now getting into that technology, but our results are quite promising—our preliminary data look really good. Studies to date show that such technology performs considerably better than warm soaks or warming masks.

Q How often do you come across dry eye patients who respond poorly to loteprednol?

A No contact lens manufactured works for every patient, and no medicine performs ideally for every patient. Our success rate is about 80 to 85%. One must bear in mind that no single approach can meet the needs of *all* patients. We guide our patients to use a top-quality, lipid-based artificial tear such as Soothe XP (Bausch + Lomb) or Systane Complete (Alcon), plus warm soaks, blinking exercises and so on, in addition to anti-inflammatory eyedrops to address their condition. While glaucoma management is pretty much straight eyedrop dependent, DED (dry eye disease) is much more complex and most always involves a multifaceted approach. It has been our experience that if a steroid fails to suppress ocular surface inflammation, any and all other non-steroidal medicines will also fail, and that just makes common pharmacologic sense.

Q What are your thoughts on Lotemax compared to IPL or LipiFlow?

A There are no studies of which we are aware that have researched this. IPL, LipiFlow, TearCare, iLux and other similar devices do get more to the primary problem of meibomian gland dysfunction, so *if* these were able to restore a more robust lipid layer, then there would be no more hyperosmolarity and therefore minimal opportunity for secondary inflammation to occur. Lotemax SM very effectively and safely suppresses ocular surface inflammation, so a study of this nature would really be comparing apples to oranges.

Q Are you using autologous serum for dry eye?

A We've had only moderate success with autologous serum eyedrops over the years. With the advent of Regener-Eyes, we have found this drop to work better than autologous serum tears. Since it is commercially available, it is much more convenient for patients.

Q Do you ever use Restasis or Xiidra, or just loteprednol?

A Reports in the literature and our vast clinical experiences have found neither Restasis (Allergan) nor Xiidra (Novartis) to be all that effective in the care of patients with dry eye. There are multiple peer-reviewed articles that fully support the use of loteprednol for suppressing the attendant inflammation in DED. Why make medical eye care expensive—and

relatively ineffective—when rock solid efficacious approaches are readily available? As we have said until we are blue in the face, if we all read the prestigious eye journals monthly, none of this would be surprising!

While there is no universally applicable algorithm to properly treat dry eye disease, loteprednol is the approach we most commonly use, and if this did not work, we would not be doing it.

Q What is the difference between Inveltys and Lotemax SM?

A Actually, an update to your question might be, "What is the difference between Inveltys, Eysuvis (both Kala Pharmaceuticals), and Lotemax SM (Bausch + Lomb)?" These are all different, yet similar formulations of loteprednol, which came to market as Lotemax 0.5% suspension in 1998. Loteprednol is the only ester-based ophthalmic corticosteroid, which provides a greatly enhanced safety profile while maintaining good therapeutic efficacy. As is often said, imitation is the highest form of flattery, so the loteprednol molecule is meritorious of imitation!

Now, let's try to put this increasingly complicated array of loteprednol products into perspective. The original product was Lotemax ophthalmic suspension. Because of the unique chemistry of this suspension, the bottle does not state "shake well" but rather "shake vigorously." As a "runny" liquid, an improved formulation was sought to make it less runny, to have a longer ocular surface residency time, and to eliminate the need to be shaken. Thus was born Lotemax gel 0.5% drops. Further enhancement of the formulation resulted in a smaller particle size to enhance clinical performance. This also allowed for actually decreasing the concentration from 0.5% to 0.38%. Neither the Lotemax gel drop nor the Lotemax SM require shaking before use—other than once to make sure the medicine actually gets positioned up into the dropper tip.

Back to the beginning: Bausch + Lomb also made available its 0.2% formulation of loteprednol, known as Alrex. This is also a suspension, very much like the Lotemax 0.5%. Alrex's forte is in treating allergic conjunctivitis, but it can be used off-label, like all loteprednol formulations, in a wide range of inflammatory conditions.

Because of the high chemo-technical challenges of getting loteprednol into liquid form, Bausch + Lomb was able to maintain brand name exclusivity for over 20 years. Now that other companies have been able to manufacture loteprednol formulations, we have three other renditions of loteprednol available: generic 0.5% suspension; Inveltys, a 1% concentration product; and Eysuvis, which is a 0.25% product. While there is some bureaucratic uniqueness to each of these products, such as FDA-approved indications (which have zero bearing on our clinical practice), these products all perform very similarly because they are all loteprednol!

Inveltys is approved for twice-daily administration with an indication for postoperative care. It requires minimal shaking before instillation. Eysuvis is a 0.2% ophthalmic suspension and uniquely indicated for up to two weeks of QID treatment for DED. Like Inveltys, Eysuvis requires very minimal shaking.

Since these products are all loteprednol etabonate, we just marvel at the various "indications" that are granted them by the FDA. Our vast experience clearly shows that all of these products can be used in any clinical situation when suppression of ocular surface tissue inflammation is needed. Hopefully, as learned doctors, this just makes common sense. Focus on providing your patients the ultimate in clinical care and don't let a federal bureaucracy alter your sound clinical judgment.

Q What are you using in place of homatropine for pain management with abrasions? We keep atropine on the shelf to treat iritis, since pharmacies do not have homatropine, but we are undecided in our practice about its use for pain management. My partner wants to have the local pharmacy stock scopolamine. What are your thoughts?

A You are correct regarding the pain relief from therapeutic cycloplegia. As best we can determine, 5% homatropine and scopolamine are no longer manufactured. However, even 1% cyclopentolate or atropine performs similarly to homatropine. We commonly instill a couple of drops of one of these cycloplegic

ANTIBIOTIC USE IN URGENT CARE CENTERS

- **"Patients with viral upper respiratory infections were treated with unnecessary antibiotics almost half the time."**
- **"Despite proven harms of unnecessary antibiotic use, the battle to limit unnecessary prescriptions rages on."**
- **"Likelihood of antibiotic prescription use was uniformly higher in urgent care centers than in hospital-associated emergency departments (25%) or medical offices (17%)."**
- **"The booming market in urgent care centers has opened another gigantic front in the antibiotic wars."**

JAMA Int Med, July 2018 (as reported in NEJM Journal Watch, July 2018).

JAMA INTERNAL MEDICINE ON RESTASIS

Restasis has never been approved in the EU, Australia or New Zealand "due to insufficient evidence of efficacy."

Schwartz LM, Woloshin S. A Clear-eyed view of restasis and chronic dry eye disease. JAMA Intern Med. 2018 Feb 1;178(2):181-2.

THE TETRACYCLINES

- Tetracycline, doxycycline, minocycline
- Doxycycline most commonly used
- Advantages over tetracycline:
- Maintenance dose 20mg to 100mg daily
- Can be taken without meals
- Contraindicated in pregnancy, nursing mothers, under age eight; photosensitivity warning
- Indications in primary eye care
- Meibomianitis (chronic inspissated glands)
- Adult inclusion conjunctivitis (chlamydia)
- Recurrent corneal erosion

agents while the patient is in the office, since it may take a day or two to get the prescription. Thankfully, you keep atropine in your office, and like the cyclopentolate, you can instill a drop or two in the office depending upon the severity of the condition. Also, topical NSAIDs can be of some help in dampening ocular surface pain (such as your referenced abrasion), so while instilling a drop or two of an NSAID can help, applying a bandage contact lens does a world of good for pain amelioration.

Q When prescribing higher dosages of oral steroids (60mg to 80mg or more per day), what do you recommend for an H2 blocker, since Zantac has been removed from the market due to a contaminant linked to cancer?

A Zantac (ranitidine) has indeed been removed from the market. However, H2 blockers such as Tagamet (cimetadine) 200mg per day and Pepcid (famotidine) 20mg, or a proton pump inhibitor such as OTC Prilosec (omeprazole), Prevacid (lansoprazole) or Nexium (esomeprazole)—which is available as 20mg capsules over-the-counter and as 40mg capsules by prescription—nicely suppresses gastric acid secretion. Either an H2 receptor blocker or a PPI can protect the stomach mucosal lining from the potentially toxic effects of high-dose prednisone. Only very rarely have we found it necessary to co-administer one of these "GI protective" medicines, because of the short duration of their use. We do, however, prescribe prednisone to be taken with breakfast. Further, with these higher dosages, we divide the dosing such that half is taken with breakfast and the other half with lunch. When appropriate, verbal consultation with the patient's primary care provider is initiated.

Q If my patient has moderate meibomian gland dysfunction associated with rosacea, would you start with 20mg of Periostat (doxycycline hyclate) twice daily or 50mg once daily, and for how long?

A Because of the expense of Periostat, we typically prescribe 50mg doxycycline once daily (preferably taken with breakfast) for three to six months for such patients. Periostat is a 20mg BID version of doxycycline, so both of these two approaches are clinically sound. We prefer once-daily vs. BID dosing. Doxycycline comes in both hyclate and monohydrate forms. While not a major deciding factor, we prefer the monohydrate form because it tends to be a bit more GI-friendly. But cost is always a concern and often steers our prescribing. Of course, knowing cost before prescribing is always a challenge.

Q Any problem using doxycycline with concurrent calcium supplements or milk?

A Here is the wisdom stated in *Drug Facts and Comparisons*:

"Food decreases absorption of tetracyclines, except doxycycline and minocycline; these two agents may be taken without regard to food."

"Doxycycline has a low affinity for calcium binding. Gastrointestinal absorption of minocycline and doxycycline is not significantly affected by food or dairy products."

Q For treating recurrent corneal erosions, do you start with doxycycline 100mg orally and Lotemax four times daily for one month and then continue to use ointments at night during this month? Then, can these be stopped without recurrence?

A We tend to use doxycycline 50mg once daily for a month, along with Lotemax SM QID daily for two weeks, then BID for two more weeks, along with GenTeal gel (Alcon) at bedtime for two months. Our hope for the patient is that this regimen is curative. We have about 80% to 90% success with this medical approach. Anterior stromal micropuncture is yet another very viable approach.

Q If a patient has severe dry eye secondary to both meibomian gland dysfunction and decreased tear film with corneal punctate staining, can I still use Lotemax with the doxycycline?

A Yes, indeed! We would use doxycycline 50mg for two months, LotemaxSM QID for two weeks, then BID for one month. Use a lipid-based artificial tear in between use of the Lotemax as often as practical (two to four times a day).

Q I live in a very sunny location. Is a 50mg once-daily doxycycline prescription going to cause photosensitivity?

A Although uncommon, some patients may experience some photosensitivity, especially those with fair complexions. Therefore, we would advise such patients to be aware of this possibility and advise them to wear a hat or long-sleeve shirts during this active treatment.

Getting Adenovirus Under Control

The topic of Betadine gets the prize for generating the most questions.

Unsurprisingly, there was keen interest in the treatment of COVID-19 viral conjunctivitis. Let us not lose perspective that most all ocular infections are indeed adenoviral, and the literature tells us that corona viral conjunctivitis is uncommon. Keep in mind the horse vs. zebra dichotomy.

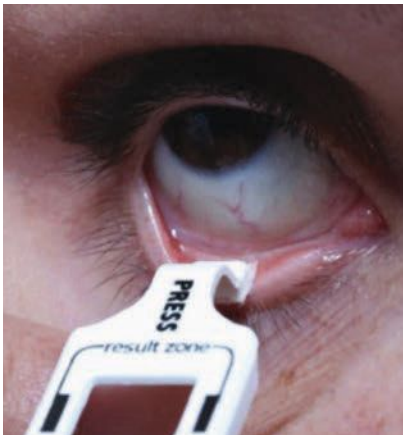
Q Is treatment for pink eye related to COVID-19?

A From all indications, we would use the exact same protocol as we do for adenoviral (EKC) infections. See *"Povidone-Iodine 5% Ophthalmic Solution"* on adjacent page.

Q Do you foresee an increase in the proportion of doctors using Betadine with red eyes of suspected viral nature in their practice in a "post-COVID world" with concern that some of the infections could in fact be from COVID-19?

A This is certainly a prudent approach, since the COVID-19 virus can cause a clinical conjunctivitis identical to adenovirus. Of course, a careful history of smell/taste loss, fever or other constitutional problems will help identify a more specific cause. People with adenoviral conjunctivitis pretty much only have an isolated eye infection. We do know that Betadine is effective against both viruses.

The QuickVue (formerly RPS Adeno Detector) adenoviral in-office test by Quidel only detects adenovirus, not COVID. (Go to quideleyehealth.com for more information.) So, a negative test only tells you that the red eye is probably not adenoviral, because these tests are not as sensitive as would be ideal; the red eye could be from any number of causes.



This shows how simple it is to collect a tear sample using the Quidel QuickVue Adenoviral test when supplemental info is needed. No anesthesia is necessary.

Q The Betadine wash is amazing! When I was in the Army, I used to use it all the time on the basic trainees who would spread it like wildfire. They were miserable right after I did it, but then within the next two days they were thanking me.

A There is no question that what you say is true. We do not know your exact protocol, but we do use proparacaine before instilling the 5% Betadine and also instill a drop of an NSAID, which can dampen ocular surface pain. These approaches do indeed help with the comfort (or less irritation).

BETADINE AND COVID-19

We have long appreciated the many virtues of povidone iodine in the care of our patients with viral epidemic keratoconjunctivitis. Now with the new, uninvited guest of COVID in our midst, it has been discovered that Betadine is even effective against this menace.

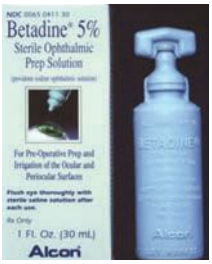
Here are two quotes from an article, titled "Povidone Iodine Mouthwash, Gargle, and Nasal Spray to Reduce Nasopharyngeal Viral Load in Patients With COVID-19: A Randomized Clinical Trial," that will bring you up to speed regarding the many virtues of dilute povidone iodine:

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is primarily transmitted person-to-person through the aerosolization of droplets containing contaminated nasopharyngeal secretions. Povidone iodine (PI) solutions with concentrations as low as 0.5% rapidly inactivate SARS-CoV-2 *in vitro* with contact times as short as 15 seconds. We investigated whether nasopharyngeal application of PI could reduce the viral load in patients with nonsevere coronavirus disease 2019 (COVID-19) symptoms."

"Discussion: Nasopharyngeal decolonization may reduce the carriage of infectious SARS-CoV-2 in adults with mild to moderate COVID-19. Thyroid dysfunction occurred in 42% of the patients exposed to PI, with spontaneous resolution upon treatment discontinuation, as previously reported. Strengths of this study include assessment of viral titer to determine whether the virus was viable and, thus, potentially transmissible. Limitations include the small number of patients in the single-centered design. These data call for a larger clinical trial to confirm the benefit of PI in limiting the excretion and resulting human-to-human transmission of SARS-CoV-2, using lower PI concentrations to minimize adverse effects."

Guenezan J, Garcia M, Strasters D, et al. Povidone iodine mouthwash, gargle, and nasal spray to reduce nasopharyngeal viral load in patients with COVID-19: a randomized clinical trial. JAMA Otolaryngol Head Neck Surg. 2021 Apr 1; 147(4):400-1.

INSIGHTS FROM LITERATURE



By now, we as a profession know Betadine pretty well, given its breadth of use. Still, there are always new revelations from journal articles and clinical practice.

Povidone-Iodine 5% Ophthalmic Solution

- Broad spectrum microbicide.
- Indicated for "irrigation of the ocular surface."
- "Off label" use: Tx adenoviral keratoconjunctivitis.
- No reports in clinical trials of adverse reactions.
- Marketed as Betadine 5% ophthalmic prep solution (30ml opaque bottle) by Alcon.

Our Clinical Protocol

- Anesthetize with proparacaine.
- Instill one or two drops of NSAID.
- Instill several drops Betadine 5% in eye(s); close eye(s).
- Swab or rub excess over lid margin.
- After 60 to 90 seconds, irrigate with sterile saline.
- Instill one or two drops of NSAID.
- Rx steroid QID for four days.

Insights Into Betadine Use

- 5% Betadine works well on the ocular surface.
- Betadine is a broad spectrum antimicrobicide.
- "Brief application of povidone iodine (PI), 5 to 10%, to the ocular surface is commonly used world wide since the '80s."
- Toxicity is concentration and duration dependent.
- It is preoperative standard-of-care.
- Effectively kills bacteria that are resistant to topical antibiotics.
- "Dilute PI solution is widely available, easy to make, inexpensive and has been studied extensively."

Koerner JC, George MJ, Meyer DR, et al. Povidone-iodine concentration and dosing in cataract surgery. Surv Ophthalmol. 2018 Nov-Dec;63(6):862-8.

Preventing Eye Infections (Intravitreal Injections)

- Kill time for Betadine (povidone iodine) 15 to 120 seconds—at any concentration!
- Anaphylaxis to iodine does not exist!
- "Topical moxifloxacin .5% had no additional effect on reducing conjunctival bacterial counts beyond the effect of 5% povidone iodine alone."
- "Preinjection antibiotics either before the day of injection or immediately prior to injection are not generally recommended."
- Gentamicin was vastly more effective than fluoroquinolones.

Wykoff CC, Flynn HW Jr, Rosenfeld PJ. Prophylaxis for endophthalmitis following intravitreal injection: antisepsis and antibiotics. Am J Ophthalmol. 2011 Nov; 152(5):717-9.e2.

Antibiotic Use and Intravitreal Injections

- Preoperative and postoperative antibiotics might have a negative impact on the safety of the procedure because, with repeated injections, patients develop ocular surface bacteria that are antibiotic-resistant.
- Topical antibiotics before the day of injection did not reduce conjunctival bacterial counts more than the immediate pre-injection use of povidone-iodine.
- In spite of this knowledgae, 27% of surveyed retina specialists continue to use pre-injection antibiotics and 63% use post-injection antibiotics.

Brucker AJ. Antibiotic prophylaxis may have negative effect on safety of intravitreal injections. Ocular Surgery News. 2013 June 25.

Betadine and Iodine Allergy

- Seafood allergy is caused by various protein allergens. Thus, an allergy to seafood is not a contra-indication to the use of betadine.
- Allergy to iodinated contrast media is not related to the iodine, but to other intrinsic chemicals.
- "Current literature suggests that iodine itself is not an allergen; it is required for thyroid function and other normal biological processes and does not have the complexity necessary for antigenicity."
- There are currently no reports of anaphylaxis secondary to topical ophthalmic use of P-I.

J Cataract Refract Surg. 2020; 46(5):795-96.

Intranasal Betadine and COVID-19

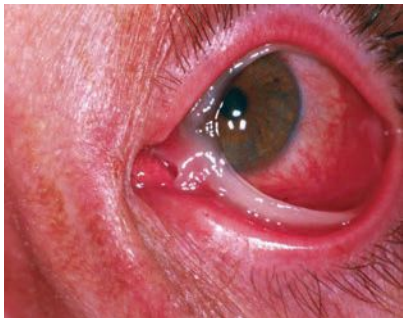
- "P-I nasal antiseptic solutions at concentrations as low as 0.5% rapidly inactivate SARS-CoV-2 at contact times as short as 15 seconds."
- Virus transmission pathway: "Infection of ciliated cells of the upper airway within the nose as the dominant site of infection, followed by subsequent aspiration and seeding of the lungs."
- Perhaps betadine has another role in addition to its effect on adenoviral ocular infection.

Frank S, Brown SM, Capriotti JA, et al. In vitro efficacy of a povidone-iodine nasal antiseptic for rapid inactivation of SARS-CoV-2. JAMA Otolaryngol Head Neck Surg. 2020 Sep 17; 146(11):1-5.

Betadine for Ophthalmia Neonatorum Prophylaxis

- "A controlled clinical trial comparing erythromycin 0.5% povidone-iodine 2.5% and silver nitrate 1% demonstrated that povidone-iodine was more effective than the other agents for preventing infectious conjunctivitis, including chlamydial conjunctivitis."
- "We believe povidone-iodine would be a suitable and perhaps preferable alternative to azithromycin for ophthalmia neonatorum prophylaxis."

Keenan J et al. Research Letters. Archives of Ophthalmology. January 2010



Here is a patient who waited too long to present; what you now see is purely inflammatory membrane formation. The infectious window is closed and all that can or needs to be done is hammer the eye with topical steroids, e.g., every two hours for two days, then QID for a week, then BID for another week or two.

Q Can you use Betadine for EKC treatment after the patient has developed subepithelial infiltrates?

A No. Once the infectious phase is over, all that's left is the subsequent inflammation (*see above photo*). At this stage, if the infiltrates are visually problematic, then we typically prescribe Lotemax SM to be used QID for two to four weeks, then TID for two to four weeks, then BID for two to four weeks, then Q day for two to four weeks, blindly trying to use the least amount of drug to neutralize the antigen antibody reaction which is causing the subepithelial infiltrates. Do remember that these are indeed *sub*epithelial, so there should be no epithelial fluorescein staining. If the subepithelial infiltrates are not visually bothersome, do nothing; they will go away with time. The intensity and duration of problematic SEIs are variable.

Q Do we have to be careful with Betadine treatment if the patient has existing ocular surface disease?

A In the setting of a miserable human being, the baseline ocular surface is relatively irrelevant. That can be addressed once the viral beast has been cleared.

Q How quickly do I need to start Betadine after a red eye develops to be most effective?

A Just like in treating shingles with oral antivirals, you want to catch the patient as early in the active (replicative) phase as possible. If a shingles or EKC patient comes in seven to 10 days or so after the condition began, the effectiveness—if any—of these interventions will be minimal. After all, your body's intrinsic healing responses are kicking in trying to help the body heal itself.

Q What is your take on using steroids to treat infiltrates in EKC? Would you say the use of steroids is controversial in the available literature?

A The first part of your question is answered in the next Q&A. The second part—if it is controversial—we could not explain it. Having prescribed a steroid in this setting numerous times, we know it performs beautifully.

Q What steroid do you use for EKC after Betadine wash?

A The cheapest one you can get. You are only going to use it QID for about four days. Once the active viruses are killed via the Betadine, the secondary inflammation subsides quickly with the steroid.

Q Why has Betadine not become a standard treatment for antibiotic-resistant bacterial ulcers and other vision-threatening corneal infections? Antibiotics, when effective, certainly have fewer adverse reactions, but would a simple in-office Betadine treatment not be an effective in-office cure at presentation?

A Your point is well taken (and appreciated). We are not sure, but there may be an issue with corneal penetration. It certainly would seem meritorious to debulk any necrotic superficial ulcerative debris and then perform a Betadine treatment prior to starting intensive topical antibiotics.

Q How do you prepare (clean and sterilize) your Fluress bottles for the Betadine?

A Rinse thoroughly with tap water, allow these bottles to air-dry then pour in the desired amount of the leftover Betadine once the 30ml bottle has been opened. Think about this: do you have to be concerned with contamination or sterility?!

Q For adenoviral infection, if patient is allergic to iodine, would treatment just be the steroid?

A See *"The Latest on Betadine and Iodine Allergy"* in the box on the previous page.

Q For children with pharyngoconjunctival fever (PCF) or adenovirus, do you have parents keep them home from school?

A If we don't, the school will! Since PCF is caused by less virulent serotypes of adenovirus, we just treat the patient with Alrex QID for about four days. The body heals these less virulent serotypes quickly.

Q Up to what age group are you treating patients with Betadine?

A From birth to 100-plus. See *"Betadine for Ophthalmia Neonatorum Prophylaxis"* in the box on the previous page.

Q What are your thoughts about using hypochlorous acid in the eye for EKC vs. Betadine?

A Academically, this would be a better choice, but our success with hypochlorous acid has been less than ideal. For now, we are devoted to our tried-and-true Betadine.

Smartphone Use in Eye Care

Like all technologies, there is improvement over time. For now, the usefulness of smartphones is limited in developed countries, but can be relatively more helpful in developing countries via telemedicine use.

Google Play has nearly 300 ophthalmic-based apps and the Apple App Store has about 170.

"iPhone add-ons such as the Cell Scope, EyeGo, D-Eye and PEEK are examples of devices that, in conjunction with the high-resolution camera of a smartphone, are capable of taking high-quality images of the anterior and posterior segments of the eye, even in inexperienced hands."

Since compliance and adherence issues with eyedrop applications plague the care of glaucoma, smartphone "reminder systems" could be beneficial to forgetful patients.

"Currently, most smartphone apps do not have the evidence to claim scientific validation for integration into clinical practice; however, the Peek Acuity and the D-Eye apps both have research suggesting that they may be useful clinical adjuncts moving forward. Indeed, the D-Eye app can serve as an excellent replacement of direct ophthalmoscopy on the inpatient wards, given its high accessibility and ease of use when compared to the direct ophthalmoscope, which has had ongoing issues with user proficiency."

Having had the honor of training family medicine residents during their ophthalmology rotations, not a single one possessed clinical competence in direct ophthalmoscopy until this rotation midway through their residencies. (Opinion: this should be a part of core training during medical school!)

"A clinician will find looking for a suitable and validated app very difficult. App store rating systems have low user uptake and are inherently biased and unregulated."

There is no doubt that smartphone apps have the potential to augment some portions of our clinical care going forward. The extent of such will only be known in the years ahead. We have no doubt that "refraction" will be one aspect of these advances.

Hogarty DT, Hogarty JP, Hewitt AW. Smartphone use in ophthalmology: What is their place in clinical practice? Surv Ophthalmol. 2020 Mar-Apr; 65(2):250-62.

FACTS ON FEMTO

While there is a lot of hype and discussion regarding the "benefits" (and increased revenue) from femtosecond-assisted cataract surgery, the consensus of the literature opines that such extra expense to the patient does not meet the clinical return on investment. Knowledge gleaned from the literature is so enlightening. These four studies all corroborate each other.

Femto vs. Traditional Phaco: Virtually Identical

- The results of this large study "found that phaco is as good as femto in terms of vision, patient-reported health and safety outcomes at three months."
- These findings have been consistent with other similar studies.
- *Our take:* the costs associated with femto rarely justify its use.

Day AC, Burr JM, Bennett K, et al; FACT group. Femtosecond laser-assisted cataract surgery versus phacoemulsification cataract surgery (FACT): A Randomized Noninferiority Trial. Ophthalmology. 2020 Aug; 127(8):1012-9.

Femto Not a Factor for Patients

- "There were no statistically significant differences between femtosecond laser assisted cataract surgery and manual cataract surgery in terms of patient-important visual and refractive outcomes and overall complications."[1]
- "Femtosecond laser-assisted cataract surgery did not yield better visual or refractive outcomes than conventional phacoemulsification cataract surgery. Intraoperative complications were similar and low in both groups. Postoperative complications were lower in conventional phacoemulsification cataract surgery."[2]
- Femtosecond laser-assisted cataract surgery did not yield better visual or refractive outcomes than conventional phacoemulsification cataract surgery.
- Intraoperative complications were similar and low in both groups.
- Postoperative complications were lower in conventional phacoemulsification cataract surgery.

1. Popovic M, Campos-Möller X, Schlenker MB, et al. Efficacy and safety of femtosecond laser-assisted cataract surgery compared with manual cataract surgery: a meta-analysis of 14,567 eyes. Ophthalmology. 2016 Oct; 123(10):2113-26.

2. Manning S, Barry P, Henry Y, et al. Femtosecond laser-assisted cataract surgery versus standard phacoemulsification cataract surgery. J Cataract Refract Surg. 2016 Dec; 42(12):1779-90.

Femto's Only Difference: Higher Cost

- "Postoperatively, there was no statistically significant difference found between eyes undergoing femto and eyes undergoing standard extraction with respect to refractive and visual outcomes."
- To us, this is an unnecessary "techno-interruption" that only serves to increase cost to our patients.

Berk TA, Schlenker MB, Campos-Möller X, et al. Visual and refractive outcomes in manual versus femtosecond laser-assisted cataract surgery: a single-center retrospective cohort analysis of 1838 eyes. Ophthalmology. 2018 Aug; 125(8):1172-80.

Are Topical Antibiotics Needed After Oculofacial Surgery?

This question is especially relevant for doctors who comanage such patients. Here are key findings from a recent study:

• "This study of 400 patients found that topical antibiotic ointment application following oculofacial plastic surgery procedures barely outperformed non-antibacterial OTC lubricating ointment. The vast majority of oculoplastic surgeons do indeed prescribe antibacterial ointments, although postoperative infections are exceedingly rare, even with non-antibacterial ointments."

• "Many topical antibiotics are associated with drug allergies, and patch testing has identified neomycin allergy in 11.6% and bacitracin allergy in 9.1% of the population. Notably, the rate of clinically significant allergic contact dermatitis in the periocular area has been reported to be lower, and a large meta-analysis was unable to conclude the relative effect of topical antibiotic vs. non-antibiotic ointment on this complication. In the present study, this complication was encountered rarely in both the placebo and the antibiotic cohorts."

• "A cost analysis was performed antibiotic versus bland petrolatum therapy and found that the healthcare system could save $8 to $10 million annually if all dermatologists switched to bland ointment after surgery."

An invited commentary candidly shared how most of us likely behave:

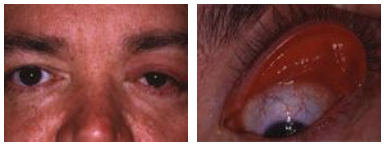
• "Admittedly, I often dress abrasions of my own body with antibiotic ointment and prescribe it for postoperative use, but these decisions are not based on sound evidence, if any."

• In summary, "Patients with periocular wound infections generally improve and experience minimal sequelae. […] Such infections are not only rare, but also when they do occur, they are easy to treat, unlike intraocular or intracranial infections by comparison."

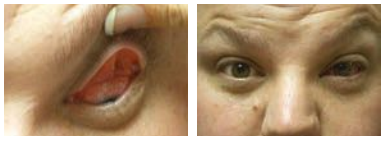
Our take on these findings is that in spite of clinical evidence, human beings are creatures of habit, and new evidence minimally alters clinical behavior. Sound familiar?

Ashraf DC, Idowu OO, Wang Q, et al The role of topical antibiotic prophylaxis in oculofacial plastic surgery: a randomized controlled study. Ophthalmology. 2020 Dec; 127(12):1747-54.

FLOPPY EYELID SYNDROME

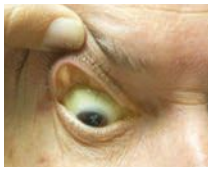


Notice the unilateral ptosis of the left eye, and the classic red, velvety appearance of the palpebral conjunctiva upon simply raising the left upper lid.



An example of a floppy eyelid.

Eyelash ptosis can often be seen prior to the clinical development of floppy eyelid syndrome.



Top photo: Simply raising the right upper lid resulted in spontaneous eversion, which is pathognomonic for floppy lid syndrome.

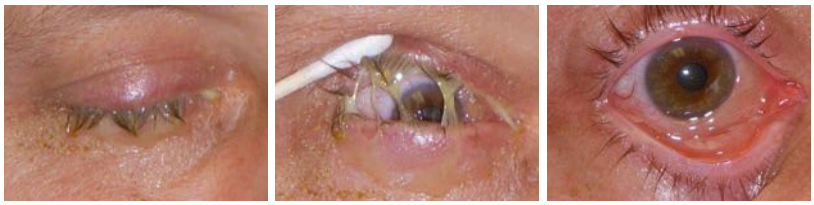
Bottom photo: Note the eyelid and eyelash ptosis in this patient with floppy lid syndrome.

HELP FOR PATIENTS WITH COLOR VISION DEFICIENCY

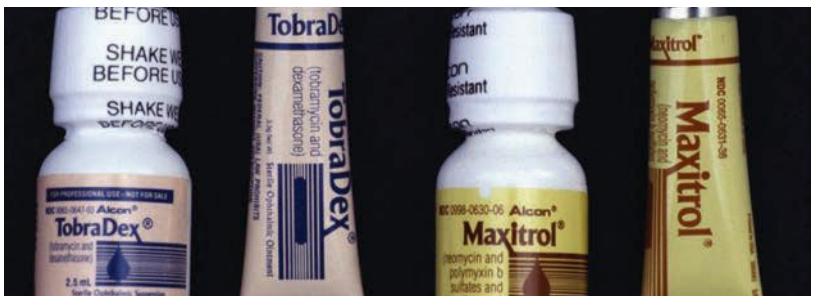
While there are no major breakthroughs for genetically programmed photoreceptor deficiencies, there are contrast-enhancing eyeglass lenses. These do not represent miraculous interventions, but many patients do find subjective benefit, and therefore, these lenses are meritorious of our investigation. These technologies have recently come to our attention, and we feel that they could be helpful to the subset of patients who are afflicted with the challenges of compromised color vision function. For information on these spectacle lenses, we encourage you to examine the website: www.glassesforthecolorblind.com

Historically, X-Chrome and other color-enhancing contact lenses have been helpful for those with color vision deficiencies; however, these "Color My World" lenses appear to be more beneficial.

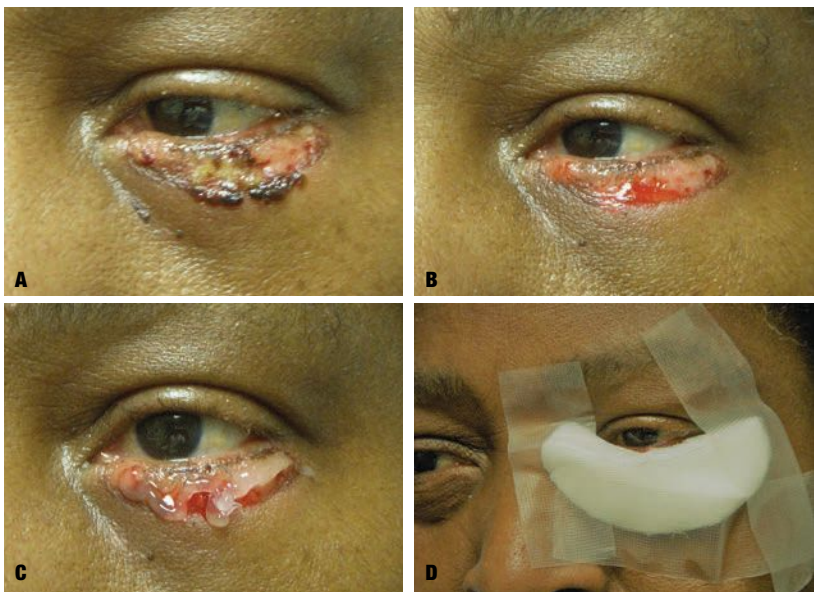
Clinical Cases



Insect in the eye: This bicyclist was struck in the eye by an unknown "bug." The heavy, ropy, mucoid discharge is more compatible with an acute allergic response. Note the inferior chemosis. After removing the "goop," we prescribed an antibiotic-steroid, such as Zylet or generic Maxitrol, QID for four days.

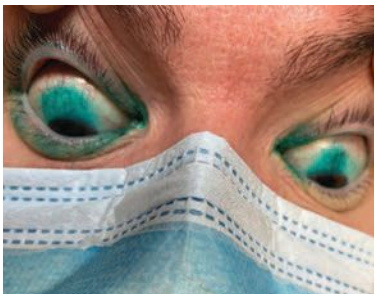


The reason Maxitrol was replaced by TobraDex was patent expiration. If TobraDex were as cost-effective as Maxitrol, we would embrace TobraDex, but the difference in price often is greater than $100 and these two medicines perform identically. Obviously, we would prefer tobramycin over a combination of neomycin and polymyxin-B but, again, cost is typically a major concern for the patient.



Unusual skin infection: (A) This lady presented with an unusual skin infection to her left lower lid. A pledget of proparacaine was applied for 30 seconds, and then necrotic tissues were debrided. (B) Maxitrol ointment was applied. (C,D) The eye was patched.

The patient did fine via a telephone call three days later because she no-showed for her pre-appointed follow-up visit. Taking care of and managing patients is an enduring challenge.



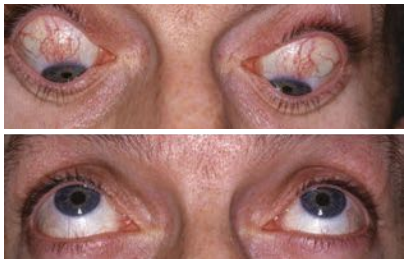
Steroid responder: This 34-year-old gentleman had seen a community optometrist who properly diagnosed superior limbic keratopathy, but rather than take the time and effort to have formulated 0.5% silver nitrate ($AgNO_3$) ophthalmic solution, he was prescribed two different ketone-based corticosteroids respectively.

Still miserable, he sought a third opinion. His entering IOPs were 54mm Hg and 56mm Hg, and as can be easily seen, his superior bulbar conjunctivae stained heavily with lissamine green vital dye. The corticosteroids were discontinued, and he was prescribed 0.5% timolol (he had already spent over $200 for the steroids). A compounding pharmacy was found, and he brought the bottle in four days later when it was applied.

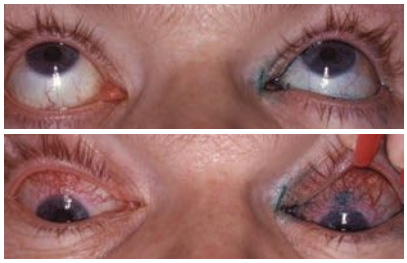
Upon return in one week, as can be seen, the staining was completely gone and IOPs were 15mm Hg and 16mm Hg. The individual was advised that he was a "steroid responder" and should never ever use steroids again. He was told to use a lipid-based artificial tear QID for a month and then return for the second application (since he had already purchased the bottle).

He continues to do well and to use the artificial tears at least BID. This man will become a patient for life because he knows where to come for attentive, competent and compassionate care.

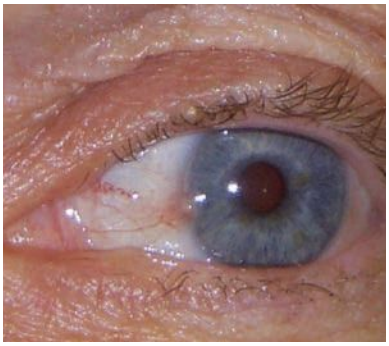
Clinical Cases



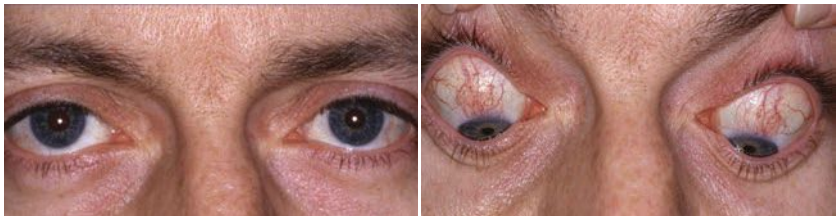
A classic case of superior limbic keratoconjunctivitis. While lissamine green dye can certainly more quantitatively assess the condition, at least in this case it is not required to seal the diagnosis.



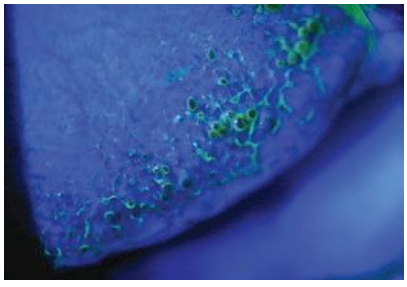
Note that the inferior bulbar conjunctiva is completely normal, but downgaze reveals classic superior limbic keratoconjunctivitis and the lissamine green uptake in the left eye.



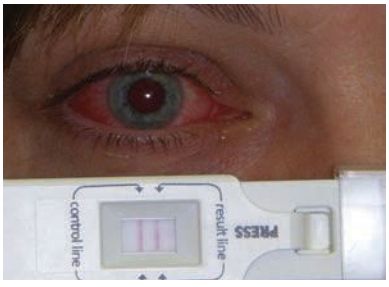
Nonspecific limbal inflammation could be a phlyctenule. Regardless of the exact diagnosis, it is clearly inflammatory and merits the use of a topical corticosteroid.



Eyes in primary gaze appear healthy. Upon downgaze, the diagnosis of SLK is obvious, thus emphasizing the necessity of lifting the eyelids to search for the cause of his presenting symptoms.



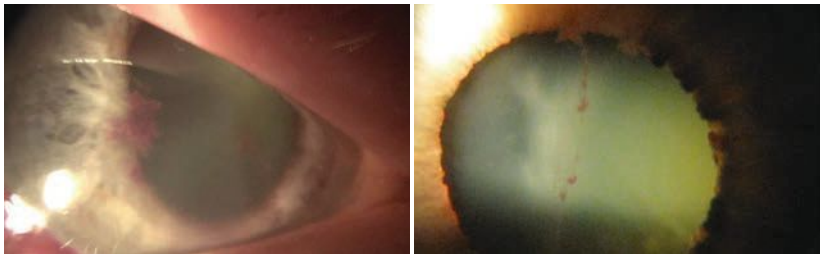
These eroding calcific bodies caused this patient's foreign body sensation.



EKC presents as a unilateral or bilateral inferior palpebral follicular conjunctivitis with epithelial and subepithelial keratitis.

FACTS ABOUT SUPERIOR LIMBIC KERATOCONJUNCTIVITIS

- Both sexes affected, women more than men
- Main symptoms: distressingly irritated eyes
- Dry eyes common companion finding
- Symptoms disproportionate to clinical findings
- Spontaneous exacerbations and remissions
- 25% to 40% have some thyroid dysfunction
- Treatment can be difficult. Several options: 0.5% $AgNO_3$, optimum lubrication, pressure patching, therapeutic soft lenses, surgical resection, cryotherapy



Capillary microhemangiomas can develop over time and can bleed spontaneously. These present no threat to vision, but patients can see this blood in their eye. The diagnosis is made, the patient is reassured and Lotemax SM is prescribed QID for four days. In our experience, this is all it takes.

Practical Pearls for Managing Dry Eye Disease

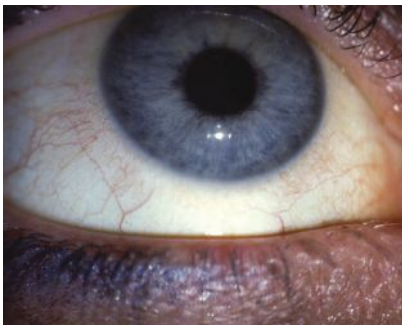
Control the inflammation and you'll fast-forward symptomatic control.

Dry eye has got to be the most common condition we encounter in practice. Because there are so many patients, some clinicians overthink their approach. Here are some of our best tips, suitable for most patients.

• Diagnosis is heavily symptom-guided.

• Only history, a slit lamp examination of the ocular surface with a vital dye, assessing the tear meniscus height and the tear film breakup time are needed for diagnosis. All other assessments are superfluous. Keep it simple—it is!

• Since the vast majority of dry eye disease results from lipid deficiency, always try a standard bottle of a lipid-based artificial tear first. If there is a clinically significant amount of punctate epithelial erosion, then perhaps a preservative-free formulation could be used initially along with something like GenTeal Gel (Alcon) lubricant at bedtime. Follow back up with your patient in about a month to assess progress and to modify the treatment plan as needed.



As can be readily seen, this dry eye patient has a scant lacrimal lake.

• If none of your rational therapeutic interventions alter the symptoms, then consider "neuropathic pain" as the etiology. No eye doctor can successfully "treat" this somatosensory neurological disease. These are relatively rare patients, but they are out there, so be attentive to these recalcitrant patients. A second opinion may be in order.

• The focus of managing dry eye disease is attending to foundational meibomian gland dysfunction. While meibography is optional, practically speaking, it is desirable; however, keep in mind that there is a high probability of meibomian gland disease accompanying and/or causing dry eye.

We recommend starting with this approach: use your golf club spud to scrape back and forth three or four times along the top of the eyelids where the orifices of the meibomian glands are. No anesthesia is required for this maneuver. Of note, there is no CPT for it either. Then, guide the patient to use very warm compresses for at least five minutes, and then to perform gentle to moderate eyelid massage. The LipiFlow device

HOW BEST TO HANDLE DED INFLAMMATION?

Recent reports of Novartis's withdrawal of Xiidra from the drug approval process in Europe for a dry eye indication highlight the importance of matching a medication with the disease process at hand:[1,2]

> **"The European Medicines Agency (EMA) disclosed on June 16, 2020, that Novartis has withdrawn its marketing application seeking approval of Xiidra (lifitegrast) to treat moderate to severe DED in adults who have had an inadequate response to treatment with artificial tears."**
>
> **"Based on a review of the data, the agency stated that its provisional opinion was that Xiidra could not have been authorized for the dry eye indication Novartis was seeking, as the drug's benefit did not outweigh its risks."**
>
> **"The EMA said the effectiveness of Xiidra had not been demonstrated across different symptoms of dry eye disease. Specifically, the Agency noted that while some effect was seen with Xiidra in terms of reducing eye dryness, the benefit was not clinically significant."**

In detailed research from the Dartmouth School of Medicine, such similar observations were found regarding Restasis.

Both Xiidra and Restasis are touted as having anti-inflammatory properties, and such is true. Nonsteroidal anti-inflammatory drugs (NSAIDs) also have anti-inflammatory properties, but why don't we use any of these to treat iritis, episcleritis and countless others? The answer is because we believe they don't possess sufficient anti-inflammatory activity to be clinically helpful.

This same reasoning could be applied to the treatment of DED. There are numerous and consistent peer-reviewed articles fully supporting the virtues of using topical corticosteroids to address the suppression of dry eye disease-associated inflammation, at least short-term. Nothing compares to a topical steroid when inflammation suppression is the goal. Obviously, we think an ester-based corticosteroid such as loteprednol would be the wisest choice in the comprehensive care of DED.

1. Novartis pulls dry eye drug Xiidra's bid for approval in Europe. Reuters, June 27, 2020.

2. Novartis pulls EU filing seeking approval of Xiidra for dry-eye disease. FirstWord Pharma, June 26, 2020.

PERSPECTIVE ON SERUM TEARS IN THE MANAGEMENT OF DRY EYE DISEASE

From time to time the American Academy of Ophthalmology conducts "ophthalmic technology assessment" exhaustive reviews on a wide number of ophthalmically associated technologies. A recent such review discussed "autologous serum-based eyedrops for the treatment of ocular surface disease." Herein, we share the key findings of their research:

- Such therapy can cost several hundred dollars for a two- to three-month supply.
- "There were no randomized controlled studies found in the peer-reviewed literature."
- "The available evidence supports the effectiveness of topical autologous serum eyedrops."
- They "suggest that this treatment is a reasonable option in refractory cases of dry eyes or nonhealing epithelial defects."

We certainly concur with these studious observations. With absolutely no scientific substantiation, it is our opinion that such patients might benefit from a trial of the commercialized biologic eyedrop, Regener-Eyes, prior to embarking on the more complex and expensive approach of blood-derived serum tears. (It should not have to be said, but we have zero direct or indirect financial relationship with the manufacturer of Regener-Eyes.)

It has been our experience that these eye drops work similarly to autologous serum and can play a very beneficial role in treating dry eye disease. We encourage you to visit their website mydryeyes.org to become more familiar with this "biologic" agent.

The company recently began an incentive program that provides additional bottles based on your volume prescribed or stocked.

Regener-Eyes for DED

- First in class "biologic" eye drop
- Contains numerous anti-inflammatory cytokines and growth factors from placental-derived tissue
- Hyaluronic acid for lubrication
- Enhances the lipid layer
- Helps the body to regenerate itself
- Available in a 2.5ml sterile bottle
- See mydryeyes.org

(Johnson & Johnson Vision Care), TearCare (SightSciences) and iLux (Alcon) are technologies to perform such in-office procedures.

• It is well understood that "inflammation" of the ocular surface is commonly present in the setting of dry eye disease. So, the next question is fundamental: which drug class best addresses the "inflammatory" component? It should be profoundly obvious that the answer is a topical corticosteroid. Objectively, the "pick of the litter" is loteprednol because of its efficacy, enhanced safety profile and lower cost.

Just as in glaucoma patient care, cost is a major deterrent to patient compliance. The cost of prescription drugs such as Restasis (Allergan) and Xiidra (Novartis), and even OTC artificial tears, can put an undue burden on the patient. Now, let's put this into clinically relevant, patient-centric perspective. The vast majority of dry eye patients develop symptoms before the age of 65, *i.e.*, while of working age. Lotemax SM (Bausch + Lomb) can be purchased (with a coupon) for $25 to $35. In our experience, nothing out there to treat dry eye symptoms is more efficacious and less expensive. Studies have shown that after one month of corticosteroid suppression, the inflammation is subdued.[1] Once this major pathological component is conquered, there is no reason to use suboptimal, highly expensive topical medicines twice daily for years. So, for less than $70, treatment of the inflammatory aspect of dry eye disease is done—so simple, so patient-centric, so scientifically sound!

However, no single approach works effectively for all patients, and sometimes deviation from our approach is needed to achieve and to maintain patient comfort. We do have several patients who require once-daily loteprednol, as that is the least anti-inflammatory effect that keeps them comfortable.

We have never had a patient develop ocular hypertension at this dosing schedule. For perspective, many patients are using once-daily prednisolone acetate chronically for stromal herpetic disease, corneal transplant rejection suppression or chronic anterior uveitis. This approach to inflammation control is time-honored. Think about this. Which is safer, loteprednol or prednisolone? Such chronic low-dose inflammatory suppression may be required for a subset of patients in a very safe and cost-effective manner.

• Cyclosporine 2.0 is upon us. Authoritative journal articles have questioned the patient benefit of Restasis.[2] It is now well recognized that the vast majority of patients with dry eye disease have some degree of meibomian gland dysfunction, and patient-centric interventions include aggressive use of warm soaks (compresses), mechanical debridement of the meibomian gland orifices and mechanical expression. Note that all renditions of cyclosporine are indicated to "increase tear

production." Without a physiological lipid layer, the addition of tears is minimally effective.

With Restasis (0.05% cyclosporine) now being generically available, there's a market opportunity for a newer brand-name cyclosporine, Cequa, a 0.09% solution, available from Sun Ophthalmics, a division of Sun Pharma. It is thought that its nanomicellar formulation might be an improvement over its predecessor. The data show modest gains. The FDA trials found vehicle-increased Schirmer results of 10mm or more in 9.2% of patients, whereas the 0.09% concentration did this in 16.6% of patients. As with the 0.05% formulation, about 25% of patients using the 0.09% drop experienced instillation-site pain vs. 4.3% with vehicle.[3]

As we have asserted for over 20 years, if the goal is to reduce ocular surface inflammation, a month-long course of loteprednol is optimally effective and vastly less expensive than other brand-name products.

The Medical Letter is a highly prestigious publication and is similar to *Consumer Reports* in its exhaustive and objective analysis. The December 2, 2019 issue of *The Medical Letter* stated that Cequa "appears to be similar in efficacy" to Restasis.[4] It says further the "addition of topical corticosteroids in the first month [of treatment] may be helpful." In our opinion, that is because our experience and the peer-reviewed literature have confirmed that a one-month course of loteprednol suppresses the ocular surface inflammation![1]

We all need to practice based on science and medical literature, not commercial marketing; it is really

USING STEROIDS FOR DRY EYE AND BEYOND

The scientific literature and FDA approvals are finally catching up with the approach we have used for over 20 years!

Loteprednol Approved for Dry Eye

- October 2020 marked the first FDA-approved steroid treatment for DED. Though a 0.25% ophthalmic suspension formulation, only two or three shakes are necessary.
- Unique mucus-penetrating nanoparticle formulation enhances tear film residency time.
- Approved for up to two weeks of QID therapy.
- Can be "re-pulsed" as needed over time.
- "Adverse events and IOP increases were comparable to those seen with vehicle" in clinical trials.
- Marketed by Kala Pharmaceuticals as Eysuvis.
- Eysuvis studies show that "results indicate that LE 0.25% suspension is a rapid-acting, safe and effective anti-inflammatory therapy."[1]
- The study used the loteprednol QID for two weeks, and (unsurprisingly) none of the hundreds of patients experienced an IOP increase greater than 5mm Hg.[1]

1. Guttman Krader C. Investigational topical corticosteroid demonstrates efficacy for dry eye. Ophthalmology Times. May 18, 2020.

Loteprednol's Effect on Dry Eye Disease and Inflammation

- Using 0.5% loteprednol QID for one month was sufficient to control ocular surface inflammation.
- "No cases showing a significant increase of IOP were detected."
- "Pflugfelder and associates reported no clinically significant changes in IOP in any patient who received topical loteprednol four times daily for one month."
- Summary: Loteprednol can provide greater anti-inflammatory effects and clinical benefits through reduction of ocular surface inflammation without serious adverse events.
- Compared with eyelid scrubs with warm compresses alone, additional application of topical 0.5% loteprednol significantly decreased inflammation. There was noticeably improved TBUT, corneal and conjunctival fluorescein staining, lid margin abnormality, meibum quality, expressibility, ocular irritation symptoms and MGD stage.

Lee H, Chung B, Kim KS, Seo KY, Choi BJ, Kim TI. Effects of topical loteprednol etabonate on tear cytokines and clinical outcomes in moderate and severe meibomian gland dysfunction: randomized clinical trial. Am J Ophthalmol. 2014 Dec;158(6):1172-83.

Corticosteroids for Dry Eye Disease

- This study compared PF Refresh Optive to PF 0.1% dexamethasone—each used QID.
- There was no difference in untreated and AT-treated at the two-week mark.
- After two weeks of steroid treatment, signs and symptoms "significantly" improved.
- "Our study shows that corticosteroids can mitigate the adverse effects of low-humidity environmental stress on the ocular surface in individuals with DED."
- "This suggests that the increased irritation and ocular surface epithelial disease that develops following a desiccating environmental challenge is attributable to inflammation that can be modulated by a corticosteroid."

Moore QL, De Paiva CS, Pflugfelder SC. Effects of dry eye therapies on environmentally induced ocular surface disease. Am J Ophthalmol. 2015 Jul;160(1):135-42.e1.

pretty evident, but one has to read in order to be able to separate knowledge from salesmanship.

• Although there is controversy over the impact of omega-3 essential fatty acids in the care of patients with dry eye disease, the vast majority of optometrists (as surveyed in our lecture audiences) subscribe to their benefit, and so do we. We start all of our patients on fish oil at about 2000mg/day. By the way, this dosing is well below the levels that affect blood coagulation based on conversations we have had with cardiologists.

• On the following page, we have laid out a rational, cost-effective, patient-centric and literature-supported approach to diagnosing and managing patients with dry eye disease. Beware of industry-driven "education," and adhere to time-honored, scientifically sound patient care. It is very straightforward.

• A recent literature review comes to the following conclusions:[5]

–"Recognition of the role of inflammation in dry eye has been a crucial factor in facilitating dry eye treatment. Inflammation plays a significant role in dry eye, promoting ocular surface disruption and symptoms of irritation."

–"Pretreatment with Lotemax induction two weeks before the initiation of cyclosporine-A can provide more rapid relief of dry eye signs and symptoms and greater efficacy than cyclosporine-A and artificial tears alone."

–"The inflammatory nature of dry eye has been widely accepted; thus, the direction for treatment research

JAMA INTERNAL MEDICINE ON RESTASIS

- **A fundamental question: "Does Restasis work?"**
- **Restasis has never been approved in the EU, Australia or New Zealand "due to insufficient evidence of efficacy."**
- **"Although Canada approved Restasis, its National Technology Assessment Unit, unconvinced of meaningful benefit, recommended Canada not pay for it."**
- **"Clinicians typically do not learn about new products from regulatory documents; they learn from commercially-sponsored, promotional efforts, such as detailing visits and events where food and beverages are provided."**
- **It is so challenging to separate science from spin; these regulatory documents greatly illuminate reality and truth.**

Schwartz LM, Woloshin S. A clear-eyed view of restasis and chronic dry eye disease. JAMA Intern Med. 2018 Feb 1;178(2):181-2.

MITIGATING SIDE EFFECTS OF RESTASIS AND XIIDRA

- **It is well established that these two drugs can have numerous side effects.**
- **"A short tapering course of Lotemax Gel is helpful in initiating therapy with either Xiidra or Restasis. The steroid gives extremely fast (same day) relief from dry eye symptoms and usually masks the stinging that can accompany the initiation of therapy with either agent. I usually give Lotemax four times a day for two weeks, then twice a day for two weeks."**

McDonald MB, Fumuso PW. Counseling our dry eye patients: How to enhance compliance with lifitegrast or cyclosporine. Ocular Surgery News. 2018 May 31. 2018.

DRY EYE DISEASE: IT'S ALL ABOUT THE SYMPTOMS

Patients suffering from dry eye consistently tell us—in day-to-day practice and in what they report to researchers—that what matters most is how they feel.

Patient Priorities

- "The three most important questions pertained to effectiveness of patient education, environmental modifications and topical anti-inflammatory eye drops."
- Patient interest on "education was top ranked by all subgroups."
- "The three most important outcomes were ocular burning and stinging, ocular discomfort and ocular pain."
- There was little interest in "signs," as patient-centric outcomes (symptoms) were deemed the most relevant to patients.

Saldanha IJ, Petris R, Han G, et al. Research questions and outcomes prioritized by patients with dry eye. JAMA Ophthalmol. 2018 Oct 1;136(10):1170-19.

Keep it Simple

- "The most important metric when treating DED is patient symptoms." *(Our take:* We have been stressing this in our collective lectures for over a decade.)
- "Your patient is not really interested in corneal clearance or the slope of tear osmolarity decline. All they know is how they feel and how well they see."
- "Symptoms direct treatment. Ultimately, symptoms determine the success of our interventions."

White DE. It is still the symptoms: patients care about how they see and feel. Ocular Surgery News, April 25, 2020.

is geared toward the reduction of inflammatory cytokines."

Our take: Let's take a moment here to engage logical thought. When treating inflammatory eye conditions, we never use an NSAID, cyclosporine or lifitegrast; we use a steroid! Studies have shown that loteprednol QID for four weeks eliminates this inflammatory component, so *any* eyedrop following this course of therapy will do just fine, because the targeted inflammation has been conquered.

So, the intelligent, cost-effective, scientifically sound approach is to prescribe Lotemax SM (with a coupon) QID for two weeks, then BID for two more weeks (or a similar approach). Now consider punctal plugs and continuing a lipid-based artificial tear. We start all patients on a premium-quality fish oil at 2000mg per day from the outset. For the most part, treating dry eye disease is straightforward; don't make complex what is simple.

• Regener-Eyes may have a role as an additive therapy in patients recalcitrant to steroid therapy. We have some early and limited experience with this nonmedical (biologic) eyedrop. It is in the same universe as autologous serum tears, but contains numerous biological cytokines and growth factors. We have seen no conclusive studies, but anecdotally at this time, we feel Regener-Eyes may have merit. It is very expensive (about $200 a bottle), but there are patients out there for which you have tried everything without success. This new product may be helpful to some of these more severely afflicted patients. For now, we simply suggest you explore the Regener-Eyes website (mydryeyes.com) and then use your best judgment. By next year, we will have a much more definitive understanding of its role in patient care.

1. Lee H, Chung B, Kim KS, et al. Effects of topical loteprednol etabonate on tear cytokines and clinical outcomes in moderate and severe meibomian gland dysfunction: randomized clinical trial. Am J Ophthalmol. 2014 Dec;158(6):1172-83.e1.

2. Seitzman GD, Lietman TM. Dry Eye Research—Still Regressing? Ophthalmology. 2019;126(2):192-94.

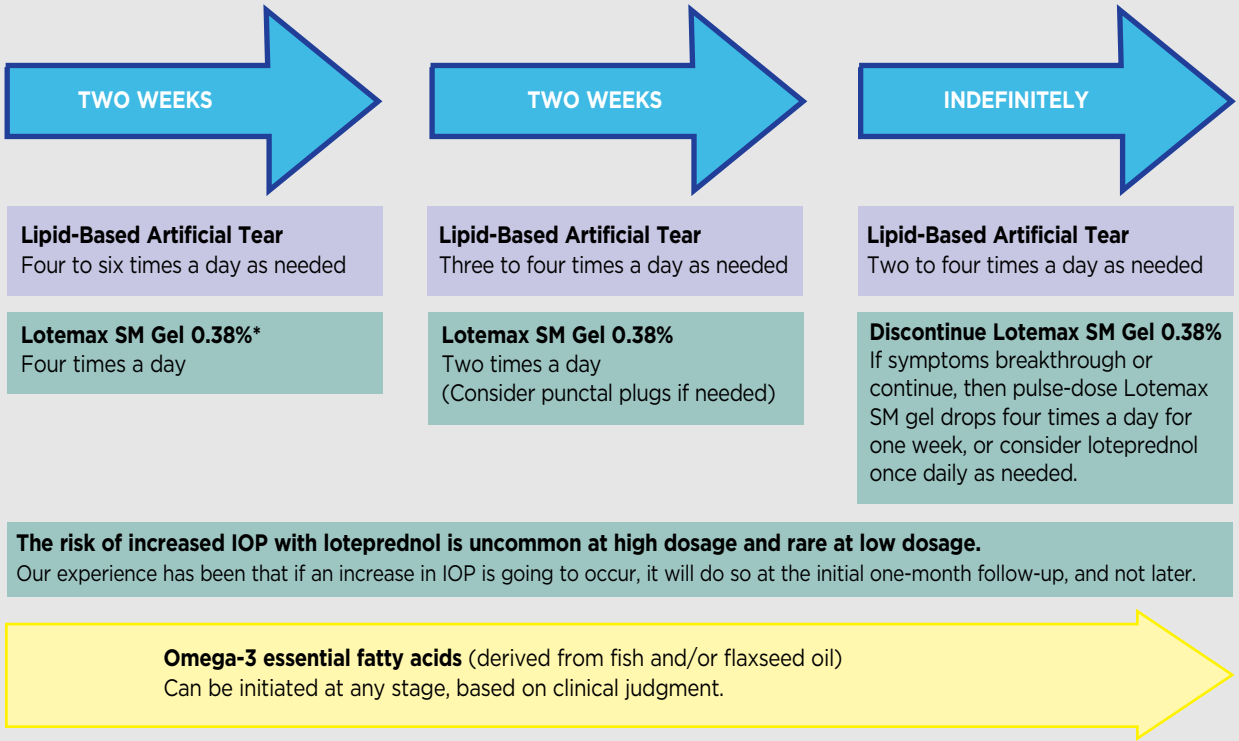
3. Goldberg DF, Malhotra RP, Schechter BA, et al. A Phase 3, randomized, double-masked study of OTX-101 ophthalmic solution 0.09% in the treatment of dry eye disease. Ophthalmology. 2019;126(9):1230-37.

4. Drugs for common eye disorders. Med Lett Drugs Ther. 2019;1586.

5. Hessen M. Cyclosporine Shoot-out: How Do They Match Up? Rev Optom. 2019 May 15;156(5):58-65. 42-9.

OUR DRY EYE MANAGEMENT ALGORITHM

All therapy—dry eye included—should be individualized to the patient. That said, here is our usual approach to symptomatic dry eye management.



*Alternatively, instill loteprednol ointment daily at bedtime for two weeks, then M-W-F for two weeks.
Loteprednol therapy for inflammation due to DED is considered an "off-label" use.

While there is no algorithm for treating DED, this approach is the one we most commonly use (because it is relatively inexpensive and it works about 80% of the time). We all should be attentive to the great benefit of punctal plugs (but only after suppressing the ocular surface inflammation first).

BEWARE POTENTIAL HAZARDS OF FISH OIL!

- **In the setting of heart disease, there is either no benefit or potential harm.**
- **"Not all fish oils are created equal, and most OTC fish oils should be avoided."**
- **"These findings suggest a lack of fish oil effect on cardiovascular benefits. The study's higher incidence of atrial fibrillation among fish oil users [...] warrants caution and further exploration. Given their lack of clinical benefit and possible risk for harm, fish oils should not be recommended."**

1. Curfman G. Do omega-3 fatty acids benefit health? JAMA. 2020 8;324(22):2280-1.

2. Kalstad AA, Myhre PL, Laake K, et al; OMEMI Investigators. Effects of n-3 Fatty acid supplements in elderly patients after myocardial infarction: a randomized, controlled trial. Circulation. 2021 Feb 9;143(6):528-39.

DOXYCYCLINE'S ROLE IN OSD

This tetracycline agent exhibits multiple anti-inflammatory properties that can aid management of dry eye:

- **Inhibits T-cell activation and chemotaxis.**
- **Downregulates pro-inflammatory cytokines, including tissue necrosis factor alpha and interleukin 1 beta.**
- **Inhibits matrix metalloproteinases that have been pathologically activated.**
- **May kill fibroblasts responsible for scar tissue development.**

Batra R, Tailor R, Mohamed S. Ocular surface disease exacerbated glaucoma: optimizing the ocular surface improves intraocular pressure control. J Glaucoma. 2014 Jan;23(1):56-60.

DIAGNOSTIC PRIORITIES

New technology often is vital to diagnostic assessment in eye care—just look at OCT. However, some tools only add incrementally to our understanding or may even unnecessarily complicate matters.

Be Wary of Managing DED by the Numbers

- There is so much marketing push for point-of-care devices, one can be lured into thinking they are critical to the DED diagnostic evaluation.
- Here's a reality check: "Substantial differences in characteristics and physical properties of the tear film, such as levels of inflammation, pH, osmolarity, volume and stability, also exist between night (sleeping) and day (waking), and over the course of the day itself."

Guillon M, Shah S. Rationale for 24-hour management of dry eye disease: A review. Cont Lens Anterior Eye. 2019 Apr;42(2):147-54.

An Enlightened Perspective on Dry Eye Disease

- "First, we are better equipped than ever to manage dry eye. Second, there is the potential for more confusion than ever. Does every patient need every diagnostic test? How should we interpret conflicting test results? Ultimately, how do we arrive at the best treatment, [...] one that is efficient, value-based and effective. We know the more complex the treatment protocol, the greater the likelihood for noncompliance.
- "Arguably, the most plausible approach is a return to the basics. I think most would agree that a good history, a little fluorescein and a careful biomicroscopic evaluation is all we really need."

DePaolis MD. Get back to the basics with dry eye. Primary Care Optometry News, May 2017.

DED Testing to Dye For

- "Of all the available dry eye tests, corneal fluorescein staining is reportedly the most commonly performed and the conjunctival lissamine green is the least commonly used test."
- "This could be due to ease/difficulty of access to these dyes or perhaps lack of knowledge or awareness regarding the significance of each."
- "The degree of baseline conjunctival staining was a significant predictor of the worsening in corneal staining after sustained reading."
- "Subjective symptoms showed the strongest correlation with baseline conjunctival staining of all the dry eye parameters. Conjunctival staining needs particular attention when evaluating patients for dry eye."
- ***Our take:*** This further supports our perspective that DED diagnosis is very straightforward without the need for superfluous ancillary tests. We all need to appreciate the usefulness of lissamine green dye in our DED evaluations.

Karakus S, Agrawal D, Hindman HB, et al. Effects of Prolonged Reading on Dry Eye. Ophthalmology. 2018 Oct;125(10):1500-05.

Rose Bengal or Lissamine Green?

- "Lissamine green may be considered the most underappreciated of the diagnostic dyes. Considering that rose bengal burns and stings, it's surprising that more practitioners haven't already turned to lissamine green as a standard diagnostic tool."

Abelson, M, Ingerman, A. The dye-namics of dry-eye diagnosis. Review of Ophthalmology, November 2005.

ODs KEEP IT SIMPLE WHEN IT COMES TO DIAGNOSTIC TESTS FOR DRY EYE EVALUATION

In January 2021, *Review of Optometry* reported, in an article titled "Dry Eye in Optometry: Trends, Habits and Hang-ups," some of the results of a reader survey.

A total of 215 optometrists in the United States shared their impressions of DED prevalence, diagnostic testing, treatment habits and challenges they encounter managing the condition.

Interestingly, the survey found most ODs primarily rely on simple diagnostic tests and familiar treatments, as financial pressures keep them from advancing their care.

Although there is no shortage of ways to assess prospective dry eye patients, the most popular choices were cost-effective and simple ones, which might come as a surprise to some.

In fact, the No. 1 testing method in the survey was fluorescein staining, with about 37% of individuals reporting this was always their first choice in their dry eye diagnostic toolbox.

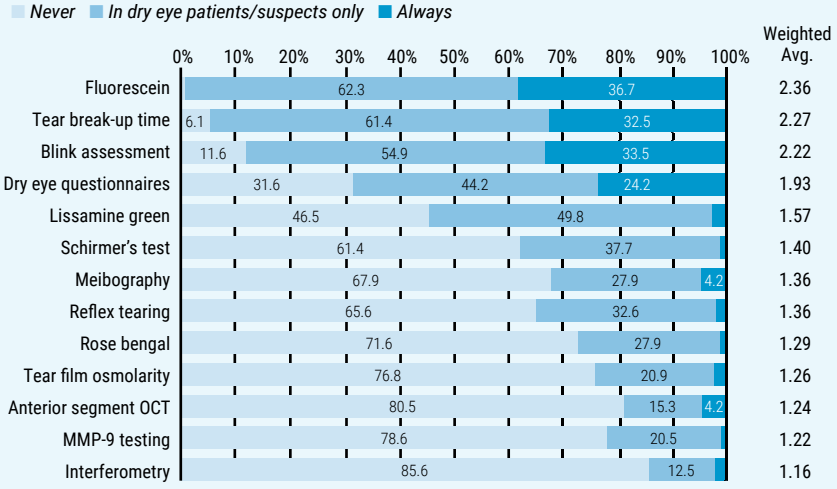
Furthermore, no high-tech tools were in the top five. Meibography ranked No. 7 in popularity, and tear osmolarity came in at No. 10.

These findings echo what we have been telling clinicians for years: there is no reason in the world to complicate dry eye diagnosis for you and your patients. Keep diagnosis simple and cost-effective.

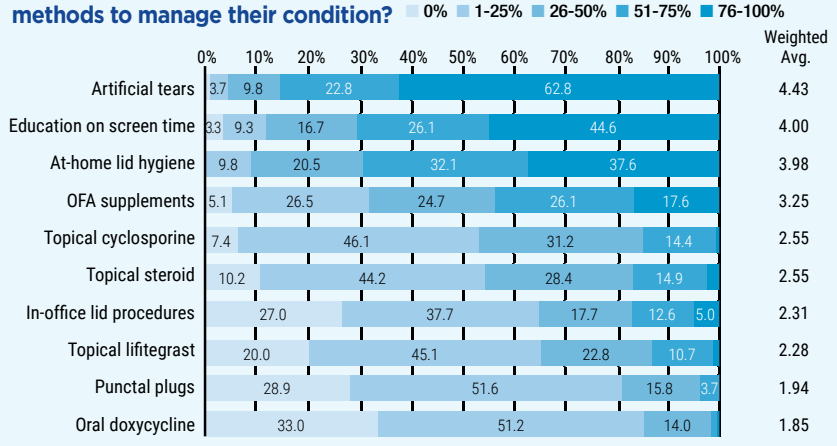
The figures to the right represent some of the findings from the reader survey. Take a look and see for yourself what your colleagues reported to *Review of Optometry*.

The results speak for themselves. Enough said.

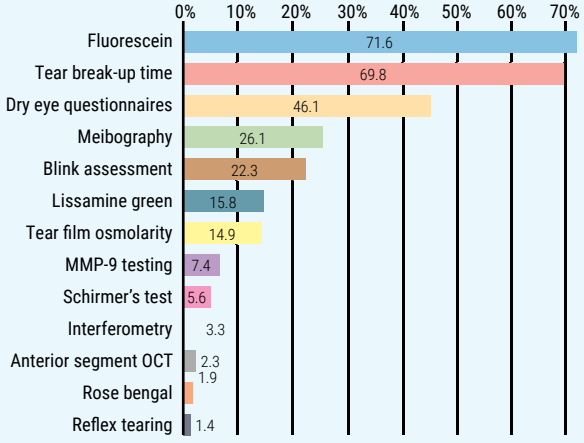
Which of these diagnostic tests do you use?



In what percentage of your dry eye patients do you use each of the following methods to manage their condition?



Which diagnostic tests do you consider the most clinically valuable?



Meibomian Glands and the Golf Club Spud

Help improve patient comfort while they're in your chair.

It is well established that meibomian gland orifice stenosis or occlusion is a focal pathology interfering with meibum secretion, which in turn diminishes the quality and quantity of the oily layer of the tear film.

Years ago, we learned from the legendary Donald Korb, OD, that simply scraping along the top of the eyelid margins can physically/mechanically open these orifices, thus enhancing the lipid layer of the tear film. This is an incredibly helpful maneuver, yet it was either omitted from the therapeutic options, or not done often enough to merit mention. This is just plain sad. In our opinion, this should be at the very top of the list. There is no CPT code because this maneuver is such a "nothing" procedure. It requires no anesthesia, is simple and is extremely helpful. We suppose it is just not as "sexy" as so many other, more expensive procedures that generate revenue.

We want to take this opportunity to once again highlight the great benefit of decapitating the meibomian gland orifices. For all patients with dry eye disease, this should be done or at least considered at every office visit. It takes 10 to 15 seconds per eyelid to do, and patients feel better right away—sort of like an eyelid massage.

Here are a few more pearls that can help your dry eye patients:

- Flush the rose bengal and begin using lissamine green. These two dyes do the exact same thing, but the lissamine green is much more gentle on the ocular surface tissues.
- Always try a lipid-based artificial tear, as opposed to an aqueous-based artificial tear. Remember, the focal dysfunction of the precorneal tear film is centered upon the functionality of the lipid layer.
- Discuss with your patient the importance of deliberate blinking and/or blinking exercises. We recommend a forced closure for five seconds, which is to be repeated several times over the span of one minute. Doing this one-minute exercise from time to time throughout the day can be very helpful.
- Take full advantage of the slit lamp by generally assessing the height/volume of the lacrimal lake. Conduct a tear film breakup time test, as this metric is uniformly endorsed as critical to qualifying and quantifying assessment of dry eye disease.
- Forget all questionnaires: simply ask the patient, on a scale of one to 10, how their eyes feel. Then, at the first month's follow-up visit, ask the question again. This ever-so-simple approach quickly lets you know how your therapeutic approaches are working.

No device that generates a numeric value significantly contributes to the diagnostic assessment. Keep what is simple, simple. Above and beyond the basic steps and interventions aforementioned, a therapeutic trial of loteprednol QID for two weeks is critical to suppressing the inflammation that is known to accompany clinically significant dry eye disease. All other prescription eyedrops pale in comparison to the therapeutic efficacy of corticosteroid suppression, and loteprednol is much less expensive, particularly if coupons are used.

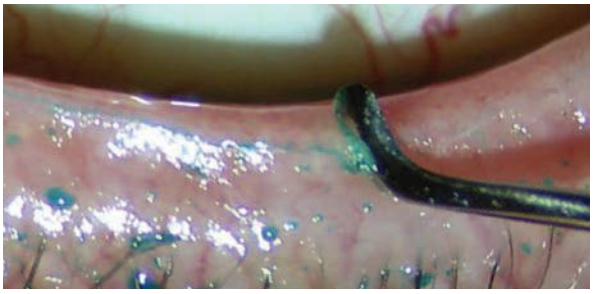
Following a two-week course of corticosteroid suppression therapy, permanent punctal occlusion should be strongly considered, using the plug of your preference.

Dry eye is a chronic medical condition that is not helped by our societal requirement to face all sorts of screens for multiple hours daily. People need to look away and do blinking exercises multiple times throughout the day. Only with unrelenting disciplined "personal hygiene" of blinking, artificial tear use, a humidified sleeping environment and other sensible protective measures can we hope to properly manage dry eye disease.

MG SCRAPING IN TREATING DRY EYE

"In the future, the health and maintenance of the MCJ [mucocutaneous junction] and keratinized lid margin may be considered integral to routine eye care. This shift in our culture will involve improvements in our observation skills and also the willingness to incorporate novel techniques such as debridement-scaling of the MCJ and keratinized lid margin in our clinical practice."

Korb DR, Blackie CA. Debridement-scaling: a new procedure that increases meibomian gland function and reduces dry eye symptoms. Cornea. 2013 Dec;32(12):1554-7.



A "One-Two" Attack on MGD

You and your patient each have duties to perform to ensure optimum results.

In dental care, the standard behavior is to see a hygienist every six months for an in-office procedure, but then the patient is to brush and floss regularly to maintain dental and gingival hygiene. In a similar manner, many people have in-office meibomian gland treatments such as TearCare or other similar interventions to heat and express the meibomian glands.

However, as with dental hygiene, these MGD patients need to maintain glandular hygiene. Self-administered treatments have historically been "warm soaks," but these and all sorts of masks have been suboptimal. EverTears is a highly sophisticated new technology that rapidly heats the meibomian glands to an optimum temperature and maintains this level of heat such that easy five-minute per eyelid home treatments help maintain meibomian gland function.

Not everyone is able to afford these in-office procedures, yet these same people can be benefitted by self-treatments at home with the EverTears technology. In practical reality, some help is better than no help.

DRY EYE AND MEIBOMIAN GLAND DYSFUNCTION

One of the basic fundamental maneuvers in dry eye care is addressing meibomian gland dysfunction. This is done through proper moist heat application followed by massage and cleansing of the meibomian gland orifices. There are three main technologies for in-office procedures: TearCare, LipiFlow and iLux.

Current in-home, self-treatments with warm soaks are suboptimal for addressing meibomian gland dysfunction; however, a new technology, EverTears (www.thermamedx.com), can be effectively used by the patient at home. It is a high temperature, soft/moist applicator that rapidly heats the eyelids to the optimum temperature levels and after only two minutes of heating the eyelids can be massaged and cleansed by the patient him/herself using this simple handheld device. EverTears stands in stark contrast to all other at-home, self-administered approaches, which typically require longer application times. It is always gratifying when new technologies raise the level of patient care. It is our impression that the new EverTears applicators do just this.

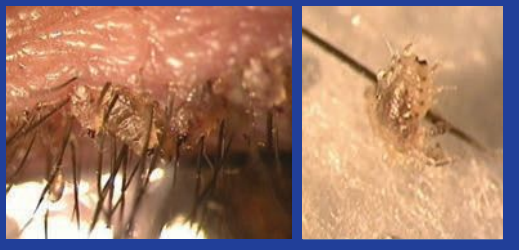
The challenge of rejuvenating meibomian gland function seems unrelenting in our quest to conquer dry eye disease. These two technologies are available to help us in this therapeutic endeavor. We encourage you to research these to see if they could play a role in your untiring efforts to help your dry eye patients.

One last pearl: prior to performing any of the various in-office MGD treatments to warm and express the glands, always use your golf club spud to gently scrap along the tops of the lids to mechanically open the meibomian gland orifices; such a simple maneuver can enhance the efficacy of heat treatments.

CRAB LICE INFECTION

- **Phthirus pubis (crab louse) eyelid infestation**
- **Uncommon form of blepharitis**
- **Symptoms: intense itching (pruritus)**
- **Signs: nits (louse egg cases) and reddish sanguinofecal debris at base of eyelashes classic slit lamp findings**
- **Treatment:**
  - **Forceps to remove lice at slit lamp**

  - **Standard lid scrubs and aggressive ointment to lid margins BID for seven days**
- **Consult with primary care physician**



Crab lice: four are seen in this image (there were 11 total). Note the sanguino-fecal discharge at the posterior aspect of these lice.

Sparse Evidence for Need of "Blue-Blockers"

Last year, we shared an article documenting the lack of benefit of "yellow-tinted lenses." There are now numerous articles shattering the myth of benefit of blue-blocking spectacle lenses. An excellent review article by Drs. Morrison and Yuhas in the January 15, 2021 issue of *Review of Optometry* succinctly documents the lack of significant benefit of blue-blocking light:

- "Unfortunately, marketing and soft science have muddied our conversations about screen time and blue light exposure."
- "Unlike even higher energy ultraviolet light, visible blue light can pass through the cornea and crystalline lens to reach the retina."
- "The preponderance of evidence suggests that sunlight exposure is not a risk factor for AMD."
- "If sunlight exposure is not clearly linked to AMD, then light emitted from screens is not likely to damage the retina either. The reason is that light emitted from personal electronic devices is substantially dimmer than sunlight."
- "Simply put, the light emitted from screens of personal electronic devices is not bright enough to damage the retina. A recent publication investigating the theoretical blue light hazard of using screens concluded that light from screens poses a minimal risk to damage the retina because they are so dim." (O'Hagan JB, et al. Eye [Lond]. 2016.)
- "Some doctors may be inclined to manage the negative effects of screens by eliminating blue light. There is little evidence, however, that blocking blue light with spectacles, especially ones with antireflective coatings designed for that purpose, provides much benefit to the patient. A recent study found that eliminating blue light from a computer screen does no more to reduce strain and fatigue than simply dimming the screen."

This further underscores how worthless "blue-blocker" lenses are. Yet, the desire to "sell" is not abated by scientific knowledge. One study found the following: "Blue-blocking lenses did not alter signs or symptoms of eye strain with computer use relative to standard clear lenses. Clinician advocacy type had no bearing on clinical outcomes."[1]

Our summary: Unnecessary screen time can set the stage for myopia, asthenopia, obesity and ocular surface drying, but blocking blue light is the very least of these concerns. Let's focus on guiding patients to look away for 20 seconds every 20 minutes and to blink more often, not selling them an "add-on" with minimal to no benefit.

1. Singh S, Downie LE, Anderson AJ. Do blue-blocking lenses reduce eye strain from extended screen time? A double-masked, randomized controlled trial. Am J Ophthalmol. 2021 Feb 12;226:243-51.

Here are just two examples of messages our patients are receiving in which retail interests promote "protective" technology in the absence of scientific support.

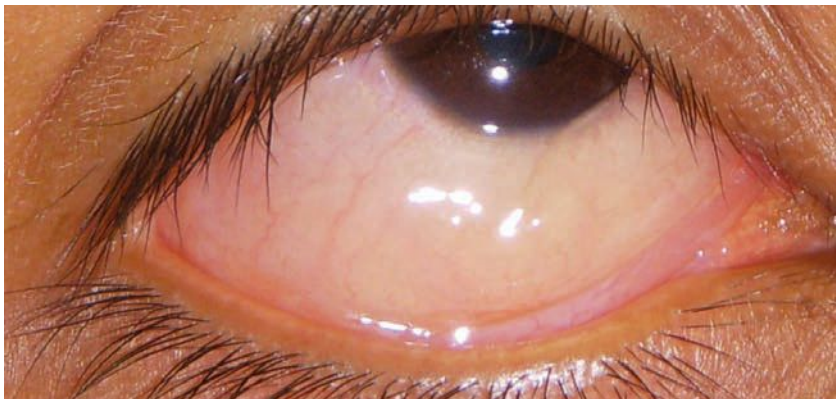
FUNCTION OVER FASHION

Often-forgotten, these "moisture-retaining," side-shield eyeglasses can be a real help in recalcitrant DED. They will not win any fashion contests, but are very practical for select patients.

Don't Overcomplicate Allergy Management

Allergy is so simple. We use a topical antihistamine/mast cell stabilizer once daily (twice daily as needed) if there is symptomatic itching and the conjunctival tissues are quiet. If there is conjunctival injection/eyelid edema/excessive mucoid discharge, go straight to 0.38% loteprednol (Lotemax SM), 0.2% loteprednol (Alrex), 0.25% loteprednol (Eysuvis) or 1% loteprednol (Inveltys).

We would use any of the loteprednol formulations QID for three days, then BID for one week. If itching persists beyond this initial treatment, then we prescribe an antihistamine/mast cell stabilizer as above. If the allergic reaction is acute and severe, then use aggressive cold compresses along with one of the loteprednols. There is obviously more to the expression of allergy, but these simple, straightforward interventions will almost always carry the day.



Classic ocular allergy with chemosis and moderate bulbar conjunctival injection.

Regarding pregnancy, a recent study notes that "the use of topical ophthalmic corticosteroids in pregnant women with allergic conjunctivitis was not associated with any increase in congenital abnormalities, preterm birth or low birth weight."[1] The steroids studied were conducted during the first trimester, and only with ketone steroids. It is our opinion that the ester-based loteprednol would be even safer. The authors of this article state: "Information for the safety of ophthalmic corticosteroids in pregnant women may help reduce anxiety regarding their use in those with allergic conjunctivitis."

1. Hashimoto Y, Michihata N, Yamana H, et al. Ophthalmic corticosteroids in pregnant women with allergic conjunctivitis and adverse neonatal outcomes: propensity score analyses. Am J Ophthalmol. 2020 Dec;220:91-101.

Thoughts on "Sulfur Allergy" Concerns

Here's something we all need to know regarding the concept of sulfur allergy, from the pharmacology literature.[1]

• "The term 'sulfur allergy' is misleading and dangerous, and should not be used. An allergy to a sulfonamide antibiotic may imply cross-reactivity with other sulfonamide antibiotics, but does not imply cross-reactivity with non-antibiotic sulfonamides or other drugs containing sulfhydryl or sulfate groups. Allergy to sulfonamides also does not imply cross-reactivity with sulfite preservatives, sulfates or elemental sulfur."

• "The term 'sulfonamide' applies to a sulfone group connected to an amine group. All antibiotic sulfonamides are arylamines. A review of all available relevant studies concluded that the dogma of cross-reactivity between sulfonyl arylamines and other sulfonamide drugs cannot be supported by the evidence. In patients who have had an allergic reaction to one drug, allergic reactions to other drugs—even if entirely unrelated—occur more commonly."

• "Sulfur is a natural element and it exists in many forms. There are many substances which have names stemming from 'sulfur' such as sulfites (preservatives in food and drugs) and sulfates (common compounds found in drugs, soaps and cosmetics). Some patients who have suffered from hypersensitivity reactions to a sulfonamide antibiotic are unfortunately labeled 'sulfa allergic.'"

This term creates confusion for the patient and often for health professionals. Many patients believe that having been 'sulfa allergic' means they are also at risk for adverse reactions or allergies from sulfites, sulfates and even elemental sulfur, and they attempt to avoid them."

So, such medicines as polymyxin B sulfate or trimethoprim sulfate are perfectly fine to use in patients who claim to be allergic to sulfa drugs. The carbonic anhydrase inhibitors also have a sulfa moiety, but they do not share a cross-allergenicity with sulfa drugs.

• "The commonly used canister type of metered dose inhalers do not contain sulfites, but several do contain sulfate salts and some patients need to be reassured that sulfates are inactive and do not cross-react with sulfites."

1. Smith WB, Katelaris CH. 'Sulfur allergy' label is misleading. Aust Prescr 2008;31:8-10

Acute White Lesions in the Peripheral Cornea: Infectious or Inflammatory?

Don't let unfounded fears about steroids make it harder than it should be.

The answer to this question is, "almost always inflammatory." There are many triggers of leukocytic chemotaxis into the peripheral cornea. If these cumulative concentrations of leukocytic infiltrates remain in the anterior stroma for a few days, a small, retrograde epithelial breakdown can occur that will stain minimally with vital dyes, whereas an infectious corneal ulcer will have a staining defect roughly the same size of the underlying stromal infiltrate.

Any time a round or oval whitish lesion can be seen at or near the limbus, it is almost invariably a sterile, leukocytic infiltrate that merits suppression with a topical steroid. This strategy rapidly enables the corneal epithelium to repopulate or the epithelial defect would endure for many days until innate resolution occurred. We have consistently observed that round or oval defects at or near the limbus are part of inflammatory processes due to the anatomic proximity of abundant humeral immunity (antibodies) and cellular immunity (leukocytes) at the highly vascularized limbus.

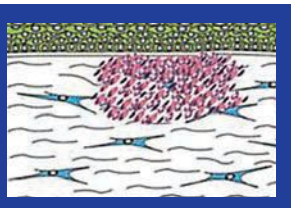
Since there's s a sliver of a chance of secondary opportunistic bacterial infection, we always prescribe an antibiotic-steroid combo drug, such as Zylet (tobramycin 3% with 0.5% loteprednol, Bausch + Lomb), generic Maxitrol (neomycin, polymyxin-B, 0.1% dexamethasone) or generic TobraDex (tobramycin 0.3% with 0.1% dexamethasone). For clinical, practical perspective, recall that generic Maxitrol is the least expensive, followed by Zylet at around $35 (with a coupon). The most expensive agent is generic TobraDex, which costs about $80 to $90. All of these drugs are clinical equivalents and perform identically.

We know of two cases in which such peripheral corneal lesions were mistakenly identified as "corneal ulcers," were treated with topical antibiotics and did not improve—because leukocytic infiltrates do not respond to any antibiotic! In each case, the patient sought out another doctor (which was one of us). We added a topical steroid and the cornea cleared within two to three days.

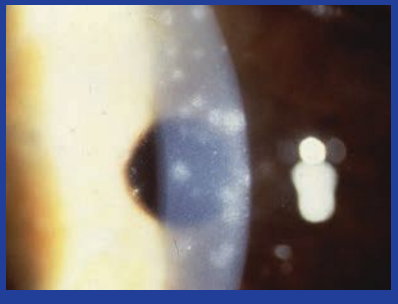
Also, given the highly remote chance that herpes simplex keratitis could manifest as a peripheral marginal ulcer, we always follow-up with the patient in a couple of days.

It is critically important that we collectively understand the difference between inflammation and infection, and realize that, almost without exception, steroid suppression is crucial to achieve enhanced patient care.

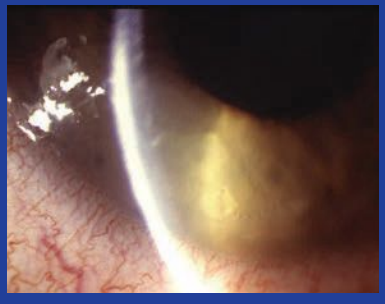
CORNEAL INFILTRATES



- **Chemotactically attracted leukocytes migrate into the subepithelial tissues.**
- **If they are numerous enough or present long enough, epithelial compromise can occur, which will manifest as a relatively small fluorescein staining defect.**
- **At the stage depicted in this rendering (to the right), the bulbar conjunctiva is usually mildly injected.**
- **A topical antibiotic/steroid combination drug used QID for one week is the appropriate treatment.**



Classic subepithelial corneal infiltrates from an untreated case of EKC. These do not stain with a vital dye because they are subepithelial. If vision is significantly compromised, then one could rationally consider loteprednol QID for one month, until "time" decreases the viral antigenic load to below a symptomatic threshold.

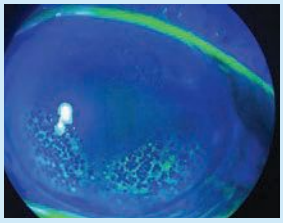


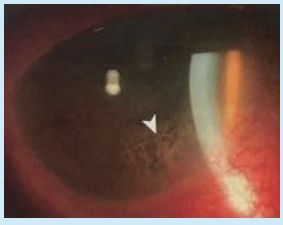
Carefully observe the dense anterior stromal infiltration that occupies about one-third of the stroma and goes up about halfway. This is always evidence of a sterile leukocytic infiltrate, and a combination antibiotic/steroid such as Zylet or generic Maxitrol is ideal. Use the medicine about every two hours for one or two days, then QID for four or five more days. If there is any associated blepharitis, then address that.

MANAGING MICROCYSTIC CORNEAL EDEMA

This condition is generally seen in two circumstances: with acute intraocular pressure rises—usually above 50mm Hg—and as a response to marked corneal inflammation such as with herpes zoster ophthalmicus. The former is treated with IOP-lowering medicines of timolol and/or brimonidine (or in the combination Combigan). Note that prostaglandins are not nearly as fast-acting as are timolol and brimonidine. The latter condition is treated with a topical corticosteroid to suppress the epithelial tissue inflammation.

Glaucoma Drugs that Can Cause Corneal Edema





- Both CAIs and netarsudil (Rhopressa) can alter endothelial function resulting in corneal microcystic "reticular" epithelial edema, particularly after endothelial surgical procedures.
- Not all cases of corneal edema have endothelial dysfunction.
- It may take days to a few months after therapy initiation for corneal edema to manifest.
- Such iatrogenic edema is rare, but be attentive to the possibility should corneal edema be a presentation.

Chen TC, Jurkunas U, Chodosh J. A Patient with glaucoma with corneal edema. JAMA Ophthalmol. 2020 Aug 1;138(8):917-8.

Milkweed and Endotheliopathy

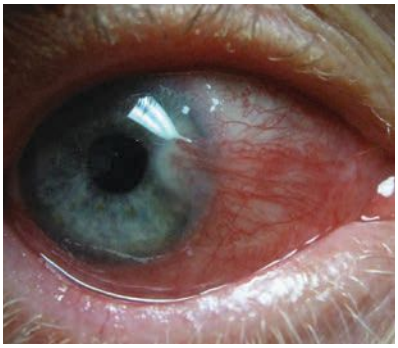
- Exposure to milkweed sap can cause endothelial toxicity in a white eye with no epithelial damage.
- This cardenolide can penetrate the epithelium. When reaching the endothelium, it interferes with ATPase (sodium-potassium pump) resulting in corneal edema.
- Treatment is a topical steroid for four to six days.
- "The value of a through history cannot be overstated."

Rostami B, Lalezary M. The Horticulturist With Blurry Vision. Eyenet, August 2019.

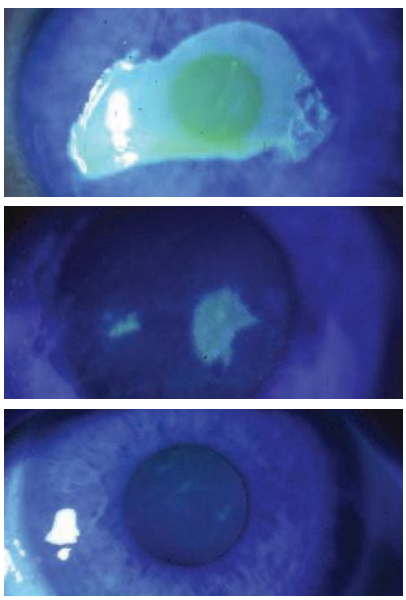
Gardening as a Cause of Corneal Edema

- Acute onset corneal edema and blurred vision.
- Most usually unilateral—rubbing face and eyes.
- History is critical to making the diagnosis of isolated corneal edema.
- Milkweed plants contain cardiac glycosides which can alter endothelial enzymes, largely sparing epithelial tissues!
- Onset of symptoms after exposure: 12 to 24 hours.
- Tx is topical steroid therapy, QID for four days, then BID for two days.

Venkateswaran N, Tonk RS, Berrocal A. Corneal edema in a gardener. JAMA Ophthalmol. 2020; 138(9):998-9.



For pterygia, we initiate treatment with Lotemax SM QID for a week, and then BID for two more weeks. At the start of the second week, we ask the patient to use a lipid-based artificial tear QID and to continue the artificial tear at least BID indefinitely. If there is a significant dry eye component, then we would also consider a punctal plug to the ipsilateral lower eyelid.

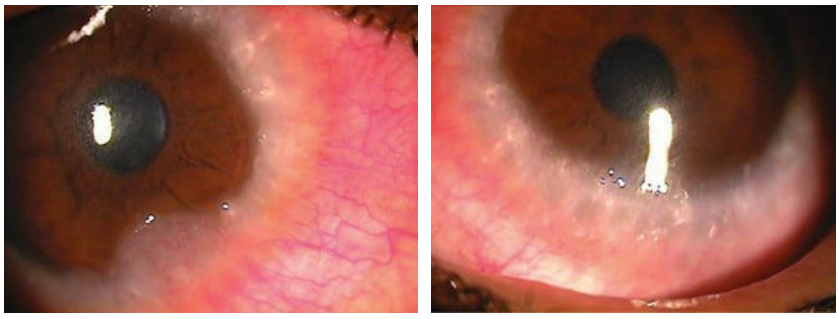


In the images above, a child's fingernail scraped across dad's cornea, resulting in a clear-cut abrasion. Note the roughened, abraded tissues at 3 o'clock. These need to be debrided to ensure clear, neat margins to maximize healing. This was not done, and in the bottom image, healing was retarded. Also in that image, note the ghosting of the subepithelial tissues as well as in the middle image. Here, we would prescribe any steroid or combination antibiotic-steroid for four to six days to reduce any subtle scarring. The patient fully recovered crisp 20/20 vision in just a few days.

The Telltale Signs of Vernal Conjunctivitis

While puberty often ushers in a plethora of challenges, it is commonly the cure for the aggravating disease of vernal conjunctivitis. This clinical entity is largely a disease of children, especially—but not exclusively—black males. There is itching and redness to the eyes with this condition, but the distinguishing feature is the "gelatinization" of portions of the corneal limbus. Within these gelatinized tissues will be seen the classic Horner-Trantas dots, especially when aided with fluorescein dye. There is usually a copious, stringy/ropy mucoid discharge present as well. This is not to be confused with the mucopurulent discharge that is seen with bacterial infections. Patients are also likely to complain of photophobia.

Left untreated, or in more severe cases, there can be an immune-mediated "shield" ulcer. These rare complications are treated with an antibiotic-steroid combination eye drop. However, only a straight steroid like Lotemax SM (Bausch + Lomb) is needed for initial suppression of these relatively uncommon presentations of ocular allergy. Many of these patients also have atopy, so they may be under the care of an allergist as well.



Limbal "gelatinization" and Horner-Trantas dots are classic signs of VKC.

Our usual approach in treating cases of vernal conjunctivitis is to prescribe Lotemax SM to be used Q2hrs for two to three days, then QID for one week, then BID for two weeks. It is our hope at that point to be able to switch the patient to an antihistamine/mast-cell stabilizer BID for several weeks to several months as needed.

FAST FACTS ON VERNAL DISEASE

- **Common in young African and Asian males in hot, dry climates.**
- **Like Thygeson's SPK and SLK, it can be chronic with episodes of acute exacerbations.**
- **Characterized by ropy mucoid discharge, itching and redness; papillary hyperplasia of superior tarsus and limbus. "Shield" corneal ulcers can occur in untreated cases.**
- **History of asthma, eczema and hay fever seen in half of patients**
- **Tx: Loteprednol for two to three weeks, then convert to antihistamine BID PRN long-term. Also, lipid-based artificial tears PRN.**

—Survey Ophthalmol. May/June 2019

The 2020 ARMOR Update

This long-running study of bacterial susceptibility to antibiotics helps us understand which agents are most formidable and which are weakest.

The Antibiotic Resistance Monitoring in Ocular Microorganisms (ARMOR) study—a massive and ongoing effort regarding antibiotic resistance—was recently updated in the May 2020 issue of *JAMA Ophthalmology*.

The researchers tested more than 6,000 isolates of *Staphylococcus aureus*, coagulase-negative staphylococci (CoNS), *Streptococcus pneumoniae*, *Pseudomonas aeruginosa* and *Haemophilus influenzae* collected between 2009 and 2018.

Here are the latest findings:

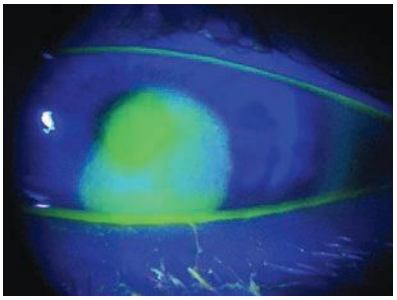
• Vancomycin remained robust for all gram-positive species.

• Besifloxacin was roughly equivalent to vancomycin—a constant finding within the study.

• When the researchers calculated the lowest drug concentrations that inhibited the growth of 90% of indicated isolates, they found that tobramycin, ciprofloxacin, moxifloxacin, gatifloxacin and trimethoprim showed slightly diminished effectiveness against gram-positive species.

• Ciprofloxacin remains the most effective drug against *Pseudomonas*.

• About 30% of *Staph. aureus* isolates and half of *Staph. epidermidis* isolates were methicillin-resistant,



This *Pseudomonas* ulcer was treated with Besivance and cycloplegics.

and this was especially observed in patients older than 80.

- Older patients were more likely to have resistance than children. However, even pediatric patients did show notable levels of antibiotic resistance.
- Of the methicillin-resistant isolates, 75% demonstrated multi-drug resistance.
- Azithromycin was, by far, the least effective of the antibiotics tested.

2020 ARMOR SURVEILLANCE DATA: MIC_{90} COMPARISONS FOR STUDY ISOLATES

	S. aureus		MRSA		CoNS		MRCoNS	
	2015 (n=1169)	2020 (n=2189)	2015 (n=493)	2020 (n=765)	2015 (n=992)	2020 (n=1765)	2015 (n=493)	2020 (n=871)
Besifloxacin*	0.25	1	2	2	0.25	2	4	4
Vancomycin	1	1	1	1	2	2	2	2
Trimethoprim*	2	4	2	2	32	>128	>128	>256
Moxifloxacin*	1	4	1	16	1	16	32	32
Gatifloxacin	2	4	16	16	2	16	32	32
Ofloxacin	8	>8	>8	16	8	>8	>8	32
Ciprofloxacin	8	128	256	256	8	64	64	64
Tobramycin*	1	128	>265	256	4	16	16	32
Azithromycin	>512	>512	>512	>512	>512	>512	>512	>512

*Denotes the four antibiotics we use most routinely, given their proven efficacy and relatively low resistance profile.

As a reminder, the lower the MIC_{90}, the more potent the anticipated efficacy.

CoNS = coagulase-negative *Staph.* species, of which the majority are *Staph. epidermidis*.

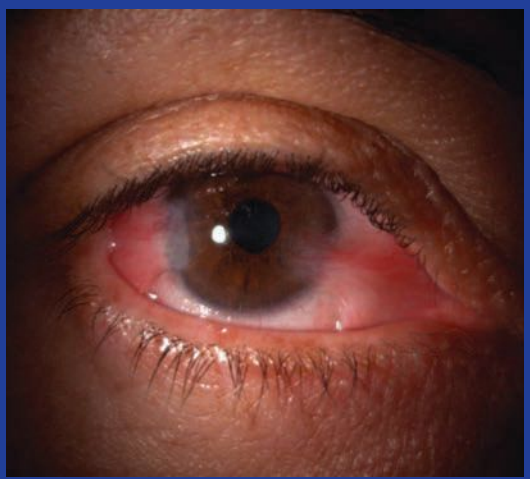
Sources: Asbell PA, et al. JAMA Ophthalmol. 2015;133(12):1445-54.
Asbell PA, et al. JAMA Ophthalmol. Published Online April 9, 2020.

- Both *P. aeruginosa* and *H. influenzae* isolates were found to have low levels of resistance.

Overall, there was little deviation from the data published in 2015. Keep in mind this is an *in vitro* study and thus may not perfectly reflect the clinical efficacy of these drugs.

ORAL DOXYCYCLINE AND PTERYGIAL ANGIOGENESIS

- **UV light is a known trigger for pterygenesis and progression.**
- **Doxycycline (and corticosteroids) can inhibit neovascularization.**
- **Perhaps pterygium management can be augmented with 50mg P.O. doxycycline daily for many weeks or many months after (or concurrent with) topical loteprednol QID for one month, the BID for two months.**



Di Girolamo N, Wakefield D, Coroneo MT. Doxycycline's and ocular angiogenesis. Ophthalmology. 2011 Apr;118(4):789-90; author reply 790-1.

Di Girolamo N, Chui J, Coroneo MT, et al. Pathogenesis of pterygia: role of cytokines, growth factors, and matrix metalloproteinases. Prog Retin Eye Res. 2004 Mar;23(2):195-228.

FACTS ABOUT CEPHALEXIN (KEFLEX)

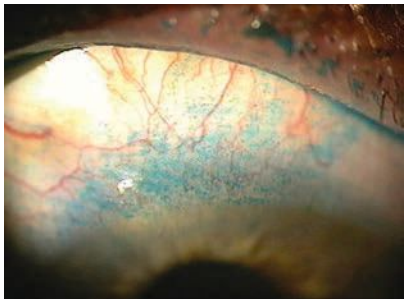
- **Cephalexin—a first-generation cephalosporin**
- **Effective against most gram-positive pathogens**
- **Some earlier-generation cephalosporins share less than 1% cross-allergenicity to PCN**
- **Usual dosage: 500mg BID once a week**
- **Useful in soft tissue *Staph.* infections, such as internal hordeola, preseptal cellulitis and others**

Merits of the "Look Up, Look Down" Manuever

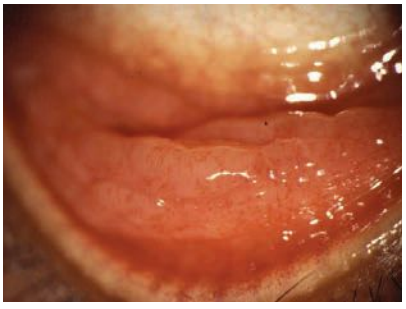
Use this method to evaluate the symptomatic red eye.

There are times when asking the patient to look down (while you hold the eyelid up) can reveal the often missed or misdiagnosed superior limbic keratoconjunctivitis (SLK). Conversely, having the patient look up while you hold down the lower eyelid can reveal the giant follicles indicative of chlamydial infection, which is another often missed or misdiagnosed condition.

The treatment of chlamydial infection is 1000mg of oral azithromycin taken all at once. A brief letter to the patient's primary care provider is most appropriate so that a genital examination can be performed, and to facilitate medical examination of sexual partners. Such cases often involve tedious (and sometimes awkward) conversations, but we must "man up" or "woman up" and be the doctors we are! There are times when having these hard conversations is just part of our responsibility in providing good patient care.



Classic presentation of SLK. Lissamine dye nicely highlights the keratinized epithelial tissues of the superior bulbar conjunctiva.



In upgaze, with the lower eyelid being pulled down, the pathognomonic expression of "giant" follicles is easily appreciated.

A MEDICAL APPROACH TO RECURRENT EROSION

Two studies shed light on the appropriate use of doxycycline in conjunction with other therapies to manage RCE:

- 100mg doxycycline per day for one month and Lotemax QID for one month.
- Curative in most cases.
- Combination therapy with oral doxycycline (50mg two times a day) for two months along with a topical corticosteroid three times a day for two to three weeks produced rapid resolution of cases of recalcitrant recurrent corneal erosion.[1]
- Therapy with a combination of medications that inhibit metalloproteinase-9 prevented further recurrence of RCE cases that were unresponsive to conventional therapies. No recurrence was observed during an average follow-up period.[1]
- Pain resolved and epithelial defects healed within two to 10 days after initiation of therapy.[1]
- Treatment may avoid the risks of scarring or astigmatism as seen in ASP, or induced refractive error as seen in PK.[2]
- At least a 70% short-term relapse-free rate, as well as a subjective improvement in symptoms and decrease in number of recurrences in the majority of patients.[2]
- Long-term follow-up needed to confirm treatment efficacy.[2]

1. Dursun D, Kim MC, Solomon A, Pflugfelder SC, Treatment of recalcitrant recurrent corneal erosions with inhibitors of matrix metalloproteinase-9, doxycycline and corticosteroids. Am J Ophthalmol. 2001;132(1):8-13.

2. Wang L, Tsang H, Coroneo M. Treatment of recurrent corneal erosion syndrome using the combination of oral doxycycline and topical corticosteroid. Clin Exp Ophthalmol. 2008;36(1):8-12.

ANTIMICROBIAL RESISTANCE

- ***Staph. Epi.* most common pathogen**
- **97% of all isolates were sensitive to gentamicin**
- **Fluoroquinolone resistance ranged from 32% to 40%**
- **"The high prevalence of fluoroquinolone-resistant organisms among ocular and nasal flora in our patient population raises concern with regards to the usefulness of topical fluoroquinolones as the best first-line agent in the setting of ophthalmic prophylaxis and for empiric use in acute ophthalmic infectious processes."**

Alabiad CR, Miller D, Schiffman JC, et al. Antimicrobial resistance profiles of ocular and nasal flora in patients undergoing intravitreal injections. Am J Ophthalmol. 2011 Dec;152(6):999-1004.e2.

NEWER FLUOROQUINOLONE: BESIFLOXACIN

- **New chemical entity: an 8-chloro-fluoroquinolone**
- ***Not* used systemically; relatively resistance-proof**

QUESTIONS COLLEAGUES ASK...

Q ***"Do you recommend a specific probiotic when you prescribe doxycycline? I know it has a low risk profile, but a few patients of mine have developed Clostridium difficile (C. Diff infection).***

A As usual, we consulted authoritative literature to gain an answer: "Comparison of findings from the American College of Gastroenterology, the association for professionals in infection control and epidemiology, and the European Society of Clinical Microbiology and Infectious Diseases does not recommend probiotic prophylaxis when antibiotics are prescribed, citing insufficient evidence."[1]

Our take: Rarely have we ever recommended concurrent use of a probiotic with any oral antibiotic. For patients with a history of *Clostridium difficile* infection, we would consult with their primary care practitioner prior to prescribing any antibiotic.

Q ***"What pain regimen do you employ when patients have significant post-herpetic neuralgia?***

A From a lecture we attended on opioid medicines, we learned from an esteemed pain management expert that alternating ibuprofen 400mg QID with 500mg of acetaminophen QID is slightly more effective than the standard 5mg hydrocodone/acetaminophen drugs, so we have heeded this instruction. However, most of the time we direct these patients to a neurologist or a pain management clinic.

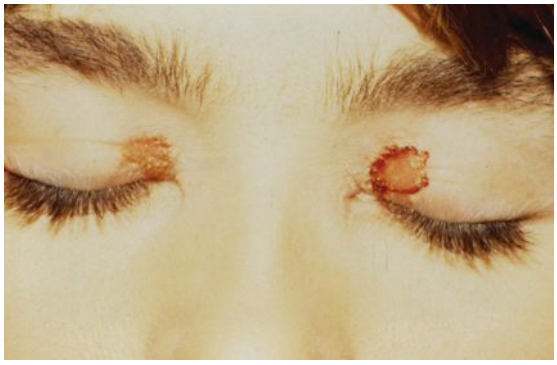
1. Goldenberg JZ, Mertz D, Johnston BC. Probiotics to prevent Clostridium Difficile infection in patients receiving antibiotics. JAMA. 2018;320(5):499-500.

OXYMETAZOLINE 0.1% AND PTOSIS

- **Afrin nasal spray = 0.05% oxymetazoline**
- **To help with acquired ptosis**
- **Alpha agonist to stimulate muller muscle**
- **Used once daily as needed**
- **Provides about 0.5mm to 0.7mm of lid rise**
- **Approved down to age 13**
- **Duration of effect is not yet known**
- **Marked as Upneeq (single-use vial) by RVL Pharmaceuticals**
- **Only available via RVL Pharmacy (www.upneeq.com)**

Upneeq™ (oxymetazoline hydrochloride ophthalmic solution) 0.1%

Slonim CB, Foster S, Jaros M, et al. Association of oxymetazoline hydrochloride, 0.1%, solution administration with visual field in acquired ptosis: a pooled analysis of 2 randomized clinical trials. JAMA Ophthalmol. 2020 Nov 1;138(11):1168-75.



Here is a young woman who sustained severe itching to her eyes and eyelids. She rubbed her eyelids to the point she created a contusion/abrasion. Cold compresses and an antibiotic/steroid ointment were prescribed. She did not return for follow-up.

ADDITIONAL WARNINGS REGARDING ORAL FLUOROQUINOLONES

Although these have been in common use for many years now, their full clinical profile continues to change. Here's the latest from the CDC:

• "During the past 10 years, the FDA has issued several warnings about potentially disabling adverse effects associated with their use, beginning with tendinopathy and tendon rupture. In July, 2018, the FDA strengthened its warning that fluoroquinolones can affect glucose homeostasis adversely, particularly in elders and patients with diabetes who take oral hypoglycemic agents."

• "Now, in its most recent update, the FDA has highlighted another recognized, much less common yet more serious adverse effect of fluoroquinolones—aortic rupture and tearing. Fluoroquinolones up-regulate cellular matrix metalloproteinases, resulting in fewer collagen fibrils of types I and III collagen, which comprise the majority of collagen in both Achilles tendons and the aorta, serving as a likely mechanism for those adverse events. Recently published studies demonstrated similar excess risks for aortic dissection and Achilles tendon rupture with fluoroquinolones, at about 2.5- to 3-fold compared with controlled populations." (About half of these aortic ruptures occurred within the first three weeks of fluoroquinolone therapy.)

U.S. Food and Drug Administration. Drug Safety Communication: FDA warns about increased risk of ruptures or tears in the aorta blood vessel with fluoroquinolone antibiotics in certain patients. www.fda.gove/DrugSafety/ucm628753.htm. December 20, 2018.

Glaucoma Care: Take the Pressure off

Novices and seasoned pros alike have many questions about how to proceed. Here's our time-honored advice.

Q Do we factor nocturnal coverage of IOP-lowering meds (given the known nocturnal IOP spike) in our decision making about prescribing?

A Yes, we do, but in a somewhat conditional manner. Only the prostaglandins express a theorized benefit during the nocturnal period; however, the impact during sleep is reduced at night compared to diurnal efficacy. Given this reality, such consideration is weighted for those patients whom we deem to have a high risk for glaucoma progression. All other glaucoma medicines bring little or no clinically significant reduction to nocturnal IOP.

Q Do you start to worry about vein occlusion at some point with IOP above 30?

A First of all, "worry" might better be replaced with "concern"—and no, we do not. While there is an association with increased IOP and retinal vein occlusion, there is no evidence of a "causal" relationship. We would be much more interested in the IOP-glaucomatous optic neuropathy relationship.

NOCTURNAL EFFICACY

- **"Alpha agonists and beta-blockers have reduced, or even lack, IOP lowering during the nocturnal period."**
- **All prostaglandins reduce nocturnal IOP, but with a "reduced magnitude" as compared to diurnal efficacy.**
- **CAIs might reduce IOP about 15% around the clock, but BID dorzolamide "failed to reduce IOP versus baseline at any of the nighttime measurements."**

Mansouri K, Tanna AP, De Moraes CG, et al. Review of the measurement and management of 24-hour intraocular pressure in patients with glaucoma. Surv Ophthalmol. 2020 Mar-Apr;65(2):171-186.

A similar question amplifies the above query:

Q In a patient with small discs and IOP of 32mm Hg, is there any consideration or concern about vascular occlusion? If the patient had systemic hypertension, would that influence your decision to treat?

A Blood pressure is rarely a deciding factor in our decision making, with the exception of low diastolic BP. Let us digress for a moment: there is sort of a dynamic tug-o-war taking place; high IOP presses against the optic nerve head and its vascular supply. If the BP is low and the IOP relatively high, then there can be suboptimal vascular supply (known as the ocular perfusion pressure) to the optic nerve head. More infrequently, if there is low cerebrospinal pressure, then the effect of the IOP is somewhat exaggerated.

Once cerebrospinal fluid pressure can be noninvasively measured, we

THE BP/IOP CONNECTION

IOP is influenced by many things, including two other fluid forces: blood pressure and cerebrospinal fluid pressure. Since BP is far more accessible to doctors and patients, let's focus on that with a look at three important studies:

Nocturnal Dip in Blood Pressure

- The role of BP in glaucoma pathogenesis is critical.
- Extreme dipping (~20% of people) portends higher risk for glaucoma, especially in normotensive patients.
- Antihypertensive medications need morning administration!
- The relationship between IOP and POAG is weak with lower levels of intraocular pressure.

Melgarejo JD, Lee JH, Petitto M, et al. Glaucomatous optic neuropathy associated with nocturnal dip in blood pressure: findings from the Maracaibo Aging Study. Ophthalmology. 2018 Jun;125(6):807-814.

Blood Pressure and Glaucoma

- Low blood pressure is associated with the incidence and progression of glaucoma.
- "Calcium channel blockers can cause sudden and extreme reduction in blood flow."
- "Nocturnal diastolic blood pressure dip may have a greater impact on VF progression in NTG eyes than nocturnal systolic blood pressure dip. Spontaneous or drug-induced excessive nocturnal DBP dip should be avoided."

Kwon J, Jo YH, Jeong D, et al. Baseline systolic versus diastolic blood pressure dip and subsequent visual field progression in normal-tension glaucoma. Ophthalmology. 2019 Jul;126(7):967-79.

Diastolic BP, Ocular Perfusion Pressure and Glaucoma

- OPP = diastolic BP – IOP
- Theory: OPP <50mm Hg is a risk factor for glaucoma and glaucoma progression.

Examples:

- DBP of 65 and IOP of 15mm Hg.
- DBP of 85 and IOP of 35mm Hg.
- These two patients may be at equal risk because they have the same theorized OPP of 50mm Hg.
- **Take-home message:** begin to check BP on your glaucoma and glaucoma suspect patients, especially those with lower IOPs.

Quaid P, Simpson T, Freddo T. Relationship between diastolic perfusion pressure and progressive optic neuropathy as determined by Heidelberg retinal tomography topographic change analysis. Invest Ophthalmol Vis Sci. 2013 Jan 28;54(1):789-98.

FACTS ABOUT FIELDS

Your choice of testing protocol can change the results you get. While it's important to know the differences, all have great clinical value regardless.

24-2 vs. 10-2

- 50% of all ganglion cells are within 8º of fixation.
- 90% of the visual cortex involves 10° of central VF.
- 24-2 does not sufficiently sample the central VF.
- Using only 24-2 "may underestimate the extent, location, and implication of VF loss."
- Macular damage can occur early in glaucoma.
- "Macular glaucoma as measured by the 10-2 VF is a strong, frequently unmeasured, explanatory variable in vision-related QOL."

Blumberg DM, De Moraes CG, Prager AJ, et al. Association between undetected 10-2 visual field damage and vision-related quality of life in patients with glaucoma. JAMA Ophthalmol. 2017 1;135(7):742-7.

Assessing Glaucoma with 10-2 Visual Fields

- Central VF loss can also occur in early disease.
- 30% of all RGCs serve the central 8º.
- 24-2 has only four central test points.
- 10-2 has 44 central test points.
- Routine 10-2 testing isn't practical.
- Do a 10-2 only when one or two central defects are seen on the 24-2.

We recommend suppressing the urge to micromanage visual field testing. Along with our subspecialty colleagues, we continue to do a 24-2 SITA Fast for most of our primary glaucoma assessments.

However, we would consider doing a 10-2 when one or more of the central 24-2 test spots are defective. We would only do such additional testing in the context of the comprehensive glaucoma evaluation. Remember, observation and study of the optic nerve head is the only component of this evaluation that we *would* "micromanage"!

anticipate that this metric will become a part of the comprehensive glaucoma workup. Most doctors will prescribe for patients with IOP over 30mm Hg, but careful monitoring of a trustworthy patient is also a rational option.

Q Which visual field test is your preferred one at initial testing: 24-2 or 10-2?

A While there is a fair amount of discussion regarding macular ganglion cell complex attenuation as an early sign of glaucoma, we (and the vast majority of glaucoma subspecialists) still perform a SITA Fast Humphrey 24-2 test as our gold standard. If there were considerable paracentral scotomas on the 24-2, we would consider performing a 10-2.

Do keep in mind our strong admonition to not micromanage any individual component of the multifaceted, comprehensive glaucoma evaluation; visual field testing is only one component. Rather, look at the overall "big picture," and do not obsess over a single aspect of the workup.

Q Is there a procedure to tell patients how to instill drops?

A We do not "tell" patients how to instill drops; we show them! We keep a sample bottle of an artificial tear in our lab coat pockets. We slide our chair up beside the patient and raise their chair high enough to give them a bird's eye view. We then tilt our head back, and with our face looking up at the ceiling, we pull down our lower eyelid and bring the bottle to about an inch above our eye and gently squeeze the bottle. We hear so much chatter about how patients are so poor at instilling eyedrops, but we think this weak link

ODs WELL-POSITIONED TO TACKLE PATIENT NON-ADHERENCE

Even the best medication in the world is worthless if the patient won't take it. Glaucoma patients especially need careful instruction and frequent "pep talks." From a public health perspective, this is why optometry should play a much larger role in glaucoma patient care. We can and do spend more time with our patients!

Challenges of Glaucoma Drop Adherence

- "Approximately half of patients with glaucoma do not take their medicines as prescribed."
- There are significant projected shortages in the ophthalmologist workforce and expected increases in the number of people with glaucoma.
- "In one short study of 279 video-recorded patient visits in which a new medication was prescribed, less than one third of patients received any education or counseling about their glaucoma or treatment."

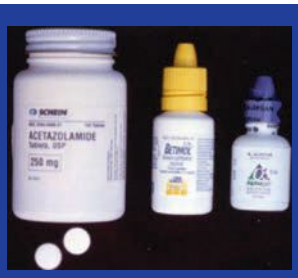
Newman-Casey PA, Salman M, Lee PP, et al. Cost-Utility Analysis of Glaucoma Medication Adherence. Ophthalmology. 2020 May;127(5):589-98.

Physician Communication and Glaucoma Adherence

- "The issue of nonadherence is multifactorial and includes inadequate communication between doctors and patients, resulting in significant costs associated with enhanced disease progression."
- "Surprisingly, a very few studies on glaucoma medication or surgery addressed the concept of adherence. However, adherence is discussed in studies which consider psychological aspects of patients or communication issues between doctors and patients."

Meier-Gibbons F, Berlin MS, Töteberg-Harms M. Influence of new treatment modalities on adherence in glaucoma. Curr Opin Ophthalmol. 2019 Mar;30(2):104-9.

ANGLE CLOSURE MANAGEMENT OPTIONS



- 500mg of acetazolamide in tablet form.
- Brimonidine, q15min x 2 doses.
- A beta-blocker, q15min x 2 doses.
- Pilocarpine 2% once above steps completed.
- Potent steroid q1h with associated inflammation.
- YAG photoiridotomy once control achieved.

RISK OF DEVELOPING PIGMENTARY GLAUCOMA

"The risk of developing pigmentary glaucoma from pigment dispersion syndrome was 10% at five years and 15% at 15 years. Young, myopic men were most likely [affected]. An IOP greater than 21mm Hg at initial exam was associated with an increased risk of conversion."

Siddiqui Y, Ten Hulzen RD, Cameron JD, Hodge DO, Johnson DH. What is the risk of developing pigmentary glaucoma from pigment dispersion syndrome? Am J Ophthalmol. 2003 Jun;135(6):794-9.

PIGMENT DISPERSION SYNDROME (PIGMENTARY GLAUCOMA)

- Predominately affects young, myopic men.
- About 50% of cases progress to pigmentary glaucoma.
- Concave iris rubs zonules causing release of pigmentation particles.
- Pigmented debris can overwhelm trabecular meshwork.
- Gonioscopy reveals dense trabecular pigment band.
- Iris retroillumination defects are hallmark finding.
- Laser photoiridotomy is helpful with PDS, but plays little or no role once pigmentary glaucoma has occurred.

in the glaucoma chain of care could be greatly strengthened if only doctors would take the 30 seconds to demonstrate proper instillation technique.

Q How do you determine target IOP?

A There are a number of ways to go about this, and a number of factors go into this decision-making gymnastic act. Such factors include the health and age of the patient, the degree of glaucomatous damage, and the baseline IOP. So, in one sense this is an unanswerable question. However, shooting from the hip, for moderate glaucoma, aim for IOP of less than 18mm Hg, and for more advanced glaucoma, aim for less than 14 to 15mm Hg. Remember that individualization of patient care is a requirement, and as doctors, we are constantly required to *think*.

Q If a glaucoma suspect is on an oral beta blocker, how effective is it in controlling IOP?

A We have seen no studies directly addressing this topic, but it is our opinion that there would be some IOP reduction. This is why we advise our glaucoma or glaucoma suspect patients who are taking an oral beta

SEEING THE LIGHT

The merits of selective laser trabeculoplasty (SLT) continue to be revealed by research, as well as clinical practice. Still, it should be viewed as just one piece of a comprehensive, lifelong glaucoma management program.

LiGHT Study

- Three-year study on laser treatment in glaucoma and OHT.
- 16% of patients were on a calcium channel blocker.
- SLT was initial Tx in "treatment-naïve" patients.
- 75% of patients drop-free at three years.
- 75% only required one treatment.
- Further treatment was initiated when IOP exceeded 4mm Hg above target.

Gazzard G, Konstantakopoulou E, Garway-Heath D, et al LiGHT Trial Study Group. Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. Lancet. 2019 Apr 13;393(10180):1505-1516.

Follow-up on LIGHT

- At 18 months, only 25% of initially treated patients required a second laser treatment.
- Initial IOP was on average 3.4mm Hg higher than the IOP at the time of the second treatment.
- Repeat SLT can have a longer duration of effect than the initial one.
- "Additional SLT maintained drop-free IOP control in 67% of eyes 18 months later."

Garg A, Vickerstaff V, Nathwani N, et al. Laser in Glaucoma and Ocular Hypertension Trial Study Group. Efficacy of Repeat Selective Laser Trabeculoplasty in Medication-Naive Open-Angle Glaucoma and Ocular Hypertension during the LiGHT Trial. Ophthalmology. 2020 Apr;127(4):467-46.

"Real World" Effectiveness of SLT

- "Most patients initially respond to SLT, but the majority failed within one year."
- Treatment success was 70%, 45% and 27% at six, 12 and 24 months post-SLT.
- Success was best in patients with higher baseline IOPs.
- Mean initial decrease in IOP was 3 to 4mm Hg.

Khawaja AP, Campbell JH, Kirby N, et al. UK Glaucoma Real-World Data Consortium. Real-world outcomes of selective laser trabeculoplasty in the United Kingdom. Ophthalmology. 2020 Jun;127(6):748-57.

blocker to allow us to re-measure their IOP if they ever stop these medicines. Think about this: a drop of beta blocker in one eye can cause a much reduced but measurable effect in the non-treated fellow eye. That being true, it certainly stands to pharmacological reasoning that an oral beta blocker would also have some measurable effect on IOP.

Q Why wouldn't an optic nerve head hemorrhage in someone you thought you had treated correctly and had managed, alert you to probable spike/IOP fluctuation that needed tighter control?

QUOTABLE

"Glaucoma clinics are currently under colossal strain, partly due to aging populations, but mainly because they're increasingly being sent people who have been referred 'just in case' but who in truth have healthy eyes and don't need to be there."

Jones PR, Lindfield D, Crabb DP. Doing what comes naturally. The Ophthalmologist. 2019. 34(6):15-8.

A What's known is that nerve head hemorrhages are indeed common in patients with glaucoma, and these hemorrhages simply come and go (via hemolysis). Remember that bruises (subcutaneous vascular ecchymosis) and subconjunctival hemorrhages generally last about a week or two, and then are resorbed. It could just be that many/most of our glaucoma patients have these, just not when we are seeing them.

OPTIC DISC ASSESSMENT PRINCIPLES AND PEARLS

Technologies like OCT have done wonders for the glaucoma evaluation, but that doesn't free us from our duty to fully understand what the optic nerve head is telling us.

Optic Disc Size and Glaucoma

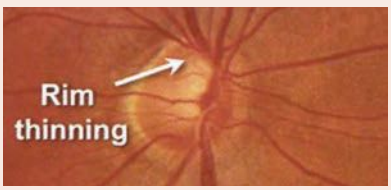
It's been 45 years since Bengtsson articulated some basic principles of disc size in a seminal 1976 paper:[1]

- Normal small discs have small cups.
- Normal large discs have large cups.
- Average disc diameter is 1.5mm.

	Disc Diameter	Mean C/D	Upper Limit
Small	1.0mm to 1.3mm	0.35	0.55
Medium	1.4mm to 1.7mm	0.45	0.65
Large	1.8mm to 2.0mm	0.55	0.75

Implications for glaucoma diagnosis and management:

- A high ratio may not be pathologic.
- C/Ds for large discs change by a smaller amount.
- C/D changes caused by glaucoma occur more slowly in large discs than in small discs (baseline photos of large discs especially important.
- C/D asymmetry is not always pathological.



Two other key principles came out of another important study:[2]

- There is poor agreement between slit-lamp ophthalmoscopy, HRT and OCT in classifying disk size as small, average or large.
- Jonas proposed that in routine practice, the clinician conduct "a quick, crude estimate of whether the disk in question is average-sized (medium), smaller-than-average, or larger-than-average."

1. Bengtsson B. The variation and covariation of cup and disc diameters. Acta Ophthalmol 1976; 54:804-818.

2. Barkana Y, Harizman N, Gerber et al. Measurements of optic disk size with HRT II, Stratus OCT, and funduscopy are not interchangeable. Am J Ophthalmol. 2006 Sep;142(3):375-80.

Optic Disc Cup Association with Retinal Vein Occlusion

- "Persons with incident RVO were more likely to be older, have higher IOP and have had definite or probable glaucoma at baseline."
- "Persons with larger optic cups and higher C/D ratios at baseline were more likely to develop RVO."
- "In multivariate models, IOP was not related to vein occlusion."
- "We found glaucoma, higher blood pressure and diabetes to be associated with risk of RVO."

Klein BE, Meuer SM, Knudtson MD, et al. The relationship of optic disk cupping to retinal vein occlusion: the Beaver Dam Eye Study. Am J Ophthalmol. 2006 May;141(5):859-62.

Perspectives on Disc Hemorrhages

"Patients show structural glaucomatous progression before and after the event of a disc hemorrhage without significant differences. This suggests that a disc hemorrhage is an on-going structural progression in glaucoma and may not be a discrete event that leads to subsequent progression."

Chung E, Demetriades AM, Christos PJ, et al. Structural glaucomatous progression before and after occurrence of an optic disc haemorrhage. Br J Ophthalmol. 2015 Jan;99(1):21-5.

Once thought rare, optic disc hemorrhages occur in most glaucoma patients. It has been proposed that IOP fluctuations represent a key risk factor for glaucoma progression; however, there is no clear evidence to support this concept.

International Glaucoma Review of the World Glaucoma Association. 2008. Vol. 10.

While a variety of opinions regarding disc hemorrhages exist, we believe the latter article squares with most of the literature and our observation over the decades.

IOP OVER 24-HOUR CYCLE

- **"Measuring IOP over a 24-hour period has shown nearly two-thirds of patients experienced peak IOP outside of regular clinic hours, with peak IOP most frequently occurring at night."**
- **"A combination of hydrostatic changes in the body and an elevation of episcleral venous pressure when the body is in a horizontal position contributes to a consistent IOP elevation in this position."**
- **"Two-thirds of patients experienced peak IOP outside of regular clinic hours, with peak IOP most frequently occurring at night."**
- **"We recommend obtaining multiple IOP pressure measurements outside of office hours."**
- **The Icare Home device allows for self-measurement of IOP, and your contact lens technician can easily teach most patients how to perform this technique.**

Mansouri K, Tanna AP, De Moraes CG, et al. Review of the measurement and management of 24-hour intraocular pressure in patients with glaucoma. Surv Ophthalmol.2020;Mar-Apr;65(2)::171-86.

Q Would it be so bad to add a topical antihistamine once to three times daily to help the reaction to brimonidine?

A The brimonidine "allergy" is more of a toxic/inflammatory response than a histamine-mediated process. Therefore, the only current "treatment" is to simply stop the brimonidine and move to another class of drugs.

Q Would you use a prostaglandin in a patient with active rheumatoid arthritis without a history of iritis?

A Prostaglandins rarely evoke iritis or cystoid macular edema in patients who have never had these disease processes before, but we would comfortably try a prostaglandin if such was clinically indicated.

Q To treat acute angle closure, after starting two 250mg tablets of acetazolamide, do you start to treat with drugs in the office, or is the patient using drops after leaving the office?

A It's vital to keep samples of acetazolamide in your office, along with 0.5% timolol and 0.2% brimonidine, since these two eyedrops cause the most rapid reduction in IOP. We instill each of these drops every 15 minutes for two doses. After about 30 to 60 minutes, we put in a couple of drops of 2% pilocarpine, which mechanically opens the angle.

We typically give the patient the balance of the pilocarpine bottle to use about four times a day (while awake) until laser photoiridotomy can be performed in a day or two.

Q Why do you do monocular treatment? Why not start both eyes?

A IOP is dynamic, and there are diurnal fluctuations. So by performing a monocular trial, we are not faked out by physiologic IOP reduction, thinking the reduction was caused by the drug. In some cases, we do in fact treat both eyes; for example when IOP is above 40mm Hg.

Q In low-tension glaucoma, if you get minimal IOP decrease from glaucoma drops, do you prescribe anyway? Which one?

A As the IOP is normal or low to begin with, one would expect a

OFF TO A GOOD START

Initiating glaucoma therapy doesn't have to be nerve-wracking for you or your patient. Here's our approach.

Treatment Goals For POAG

- Establish a target IOP below which optic nerve damage is unlikely to occur.
- Maintain IOP at or below this target with appropriate therapy.
- Monitor VFs and ONH appearance to refine the adequacy of the target IOP.
- Optimally balance the benefits of therapy with any side effects.
- Educate and engage patients in the management of their disease.

Our Glaucoma Medication Flow

- First Tier: prostaglandin (generic latanoprost or Vyzulta) or timolol.
- Second Tier: topical CAI, brimonidine or Rhopressa.
- Third Tier: Combigan, Cosopt, Simbrinza or Rocklatan.
- Fourth Tier: Pilocarpine oral CAI (preferably methazolamide).

The Merits of Mono

"The monocular trial of therapy is effective in accurately predicting the response of an untreated eye to monotherapy with a prostaglandin analogue at all daytime time points measured. There is no requirement for patients to be seen at the same time of day after treatment has commenced. The effect in the first eye predicts both the likelihood and magnitude of an effect in the second eye at all time points during office hours and negates the requirement for an additional visit to check the therapeutic effect when commencing therapy in the second eye."

King AJ, Rotchford AP. Validity of the monocular trial of intraocular pressure-lowering at different time points in patients starting topical glaucoma medication. JAMA Ophthalmol. 2016 Jul 1;134(7):742-7.

relatively muted effect from any eyedrop. That being said, we would first try Vyzulta to see if that achieved target-range IOP. If further reduction is needed, then we would consider adding timolol, and if even further reduction is needed (assuming measurable effectiveness with both of these medicines), we would generally substitute the timolol for a combination medicine such as Combigan, or Cosopt (generically). In most all cases, IOP can be adequately controlled.

Q How is laser photoiridotomy helpful with pigment dispersion syndrome if the patient has diffuse peripheral iris transillumination defects? Why wouldn't a prostaglandin be indicated in pigmentary glaucoma, as it would increase uveoscleral outflow since pigment is blocking the meshwork?

A The posterior iris epithelial chafing is a progressive event. Ideally, if laser photoiridotomy can be accomplished early in the process, the posterior chamber/anterior chamber pressures can be equalized, thus allowing the iris to move anteriorly and halting further chafing. If, however, so much trabecular debris has already accumulated, causing increased IOP, laser photoiridotomy is relatively ineffective and ALT/SLT now becomes the laser procedure of choice. A prostaglandin would indeed be a reasonable initial choice for the reason you nicely pointed out.

Q If a patient has been on Topamax for a while, can they still be at risk for ciliary body effusion? Should we worry about this in patients who have been on Topamax for a while?

A The risk of an iatrogenic event (myopic shift, increased IOP) with topiramate most often occurs within days or weeks of initiating therapy or increasing the dose. You could casually share with your patient that there's a remote chance of such a side effect, but we tell every single one that we are real eye doctors and that, if they ever have any kind of medical eye emergency, to call our office and we (or another OD) will get back to them. This is very comforting and reassuring, and it radically builds practices.

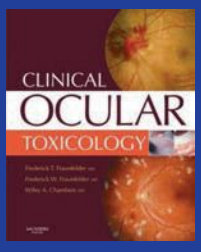
Q When rechecking IOP, is it best to do it the same time of day, and is serial tonometry still beneficial?

A There is a fair amount of discussion regarding the necessity of checking IOP at the same time each day. At the risk of slipping into counterproductive micromanagement, this concern is not a major one to us. Serial tonometry is done less and less now that we know the highest IOP for most patients is during the sleep cycle. There may be some wisdom in checking IOP at different times of the day just to screen for peak diurnal IOP. While your question has a sound rationale, there is probably not a need to check IOP near the same time of day.

ALERT ON TOPIRAMATE (TOPAMAX)

- **Approved in 1996 for seizure disorders.**
- **Mechanism of action is unknown.**
- **Because of a topiramate-associated risk for oral clefts, the FDA has now designated topiramate as a pregnancy category D drug.**
- **Numerous reported cases of acute, bilateral, simultaneous angle-closure glaucoma.**
- **Onset usually within first two weeks of therapy.**
- **Most common presenting symptom: blurred vision.**
- **Exact mechanism of increased IOP is unknown.**
- **Tx: Stat consult with prescribing physician to begin to reduce topiramate dosage; then aqueous suppressants, oral CAI, cycloplegia (retracts ciliary body); no miotics.**
- **IOP normalizes in one to four days, no laser treatment indicated.**

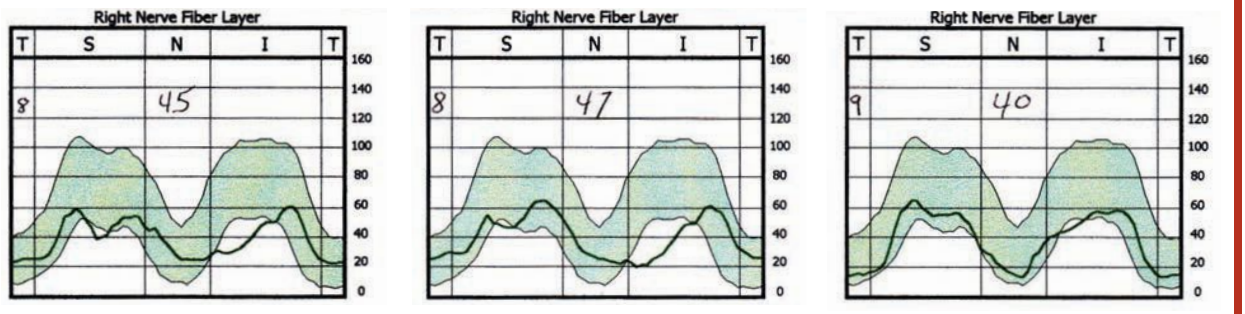
Insights from:



TOPAMAX AND VISION

- **Uses: anticonvulsant, migraine prevention, bipolar disorder, obesity, OCD, IIH, neuropathic pain, essential tremor, post-herpetic neuralgia.**
- **Topiramate is a sulfa derivative (like CAIs).**
- **Idiosyncratic ciliochoroidal effusion is the most common ocular side effect and most always results in a myopic shift with or without increased IOP.**
- **This rare event usually occurs within two weeks of initiation (or doubling) of dosing.**
- **First described in 2001; 70% of patients are female**
- **Tx: D/C the medicine; use PRN beta-blocker, brimonidine, or in refractory case, oral prednisone or IV methylprednisolone. Also, instill cycloplegic agent and do not use pilocarpine.**

Abtahi MA, Abtahi SH, Fazel F, et al. Topiramate and the vision: a systematic review. Clin Ophthalmol. 2012;6:117-31.



Note the very thin inferior retinal nerve fiber layer on the first two annual scans. Yet, at year three, the very obvious thinning is now markedly less thin. The quality scores are eight and nine, attesting to high-quality scans. This shows two important concepts: first, the so-called "objective" scanning devices are only relatively objective (compared with the highly subjective visual field test); and second, this is an excellent example of why one should never micromanage such scans.

Q Cupping may be suspicious, but what about the disc size? Shouldn't this be part of the equation/documentation?

A Yes, your detailed characterization of the disc anatomy is crucial. Small discs tend to have small cups, and large discs tend to have large cups. Keep in mind that cups generally concentric to the disc margins are physiologic. Be especially attentive to superotemporal and inferotemporal erosions of the disc rim. Regarding disc size, for goodness sake do not attempt to measure this with a reticule! Just note in your chart if the disc happens to be larger than normal or smaller than normal. Be attentive, but keep it simple.

Q Which tonometer do you rely on for best IOP accuracy?

A Different studies show varied results. Professor Goldmann's design remains the gold standard, but more and more doctors are beginning to use the Icare tonometer. The notion of single-use disposable probes as with the Icare tonometer was especially popular as a result of the COVID pandemic (which we hope is quickly becoming a bad memory by the time you read this).

Q Are CPAP machines useful for POAG patients?

A Having sleep apnea is a potentially life-threatening condition, and it highly correlates with floppy eyelid syndrome, but it's less concerning in glaucoma care. That is, we do not find the use of continuous positive airway pressure (CPAP) machines a significant factor in our overall care of glaucoma patients. These devices can be a significant contributing factor in dry eye disease, however.

Q Do you consult a glaucoma patient or suspect's PCP if they're on amlodipine to suggest changing their medicine?

A Absolutely. Our succinct letter professionally explains the effect of amlodipine (a calcium channel blocker) on suppressed nocturnal diastolic blood pressure and its detrimental effect on intraocular pressure control. We ask for the doctor's consideration of either morning administration or switching to a non-calcium channel blocker class of drug. It is probably best that all blood pressure medications be taken with breakfast in caring for our patients with glaucoma.

SYSTEMIC MEDICATIONS AND GLAUCOMA

- SSRIs: selective serotonin reuptake inhibitors.
- SNRIs: serotonin-norepinephrine reuptake inhibitors.
- SSRIs (Prozac, Zoloft, Paxil and Lexapro) and SNRIs (Effexor, Cymbalta) showed a 30% protective effect.
- Beta-blockers (mainly metoprolol) offered 20% protection.
- Calcium channel blockers, mainly amlodipine (Norvasc), have a strong harmful association with glaucoma.
- Eye physicians need to be aware of these positive and negative influences on their patients with advancing and advanced glaucoma.

Zheng W, Dryja TP, Wei Z, et al. Systemic medication associations with presumed advanced or uncontrolled primary open-angle glaucoma. Ophthalmology. 2018 Jul;125(7):984-93.

- Participants taking systemic beta-blockers had lower IOPs. (If a glaucoma patient or glaucoma suspect stops their beta-blocker, reassessment of their IOP needs to be done.)
- Multiple longitudinal studies show no increased risk of POAG for individuals with diabetes.
- IOP alone is a poor tool for identifying whether an individual has glaucoma.
- Glaucoma diagnosis requires a careful assessment of all relevant risk factors, an expert examination of the optic disk and an assessment of the visual field.

Foster PJ, Khawaja AP. The association of systemic medication and disease with intraocular pressure. JAMA Ophthalmol. 2017 Mar 1; 135(3):203-04.

Q Does the patient need to be taking bimatoprost drops first to see its effect before considering the Durysta intraocular implant?

A It would certainly seem necessary, and it would make sense, so yes.

Q What is the proper interval for repeating OCT for patients with large/very large discs with cupping with normal imaging and no loss of retinal nerve fiber layer thickness?

A The answer would depend on central corneal thickness, intraocular pressure and baseline appearance of the optic nerve head. However, annual testing is standard for most patients most of the time.

Q Is there any reason to not use anterior segment OCT measurement for central corneal thickness (CCT)?

A No. Remember that CCT measurements are not exact to the millimeter. Just like with optic disc size, note that the cornea is thin (<500µm), normal (500µm to 570µm) or thick (>575µm). Do not get into micromanaging this parameter. Regarding the numeric ranges, we made them up, but they are scientifically sound generalizations.

Q What do you consider a clinically relevant change in RNFL thickness when monitoring a glaucoma suspect with clear visual fields, borderline high IOPs (18 to 21mm Hg) and good RNFL profile? How much RNFL thinning/change would you tolerate before recommending treatment?

A We *never* make any clinical judgments based solely on this one parameter. Depending upon several factors, some doctors wait until the first repeatable visual field defect occurs before starting treatment. To make a therapeutic decision based solely on OCT findings would be naïve. That being said, generally speaking, a 5µm reduction in RNFL thickness is regarded as clinically significant.

Q Have you used ocular perfusion pressure (OPP) as a factor in determining the target IOP?

A Only on rare occasions would we need to get this detailed since there are so many other more impactful parameters we would assess first. That being said, blood pressure should be taken on all glaucoma patients, especially those with normal-tension glaucoma, since low blood pressure can less effectively perfuse the blood supply to the optic nerve.

Q What is the incidence of macular edema with prostaglandin treatment?

A It is exceedingly rare, and even then, most always the patient has a history of cystoid macular edema.

Q When you get a patient with parental family history of glaucoma, large optic nerve cups but normal fields, IOP and RNFL, do you start to wonder if that is really just a family history of large cups and the patient was misdiagnosed?

A Absolutely! Try to see other family members to authenticate your logical suspicions; this can be very reassuring to the patient. It is most important to evaluate siblings if possible. There are many people being treated for a disease that they do not have!

Q With a 34-year-old patient, would you potentially have them on glaucoma medicines for 50-plus years? Would an initial treatment with laser be indicated without starting drops?

A Recent studies have shown that initial laser treatment can push the need for topical medications down the road for a few years. Of course, laser treatment can be considered anywhere along the disease continuum. Surely, new techniques and new medicines will be invented over these decades.

Q When initiating monocular treatment, how much later do you see the patient for an IOP check? Then, when you start the second eye, how much later would you see them after that?

A For prostaglandins, we wait a full three weeks to assess efficacy. For all other topical medications, we re-check in two weeks.

DIAGNOSTIC ACCURACY OF INSTRUMENTS

- **"Differentiating between glaucoma suspects and normal subjects presents a significant clinical challenge because there is substantial overlap of clinical characteristics between the groups."**

- **The best approach to determining the status of a glaucoma or glaucoma suspect patient is to comprehensively examine every single aspect of the glaucoma work-up.**

- **Further, do not micromanage or obsess over any single parameter of the comprehensive evaluation, except when assessing the optic nerve head.**

Dabasia PL, Fidalgo BR, Edgar DF, et al. Diagnostic accuracy of technologies for glaucoma case-finding in a community setting. Ophthalmology. 2015 Dec;122(12):2407-15.

Prostaglandins take longer to achieve their full therapeutic potential. If a good response occurs, we would then treat both eyes and see the patient back in about three months.

Q When do you think is the best time to send a glaucoma patient for a consult for laser procedures? Do you suggest treating first with medications and then sending the patient to the specialist to see if they would benefit, or have them assessed by the specialist first?

A The laser procedures SLT and ALT are temporizing interventions. Although the effectiveness is highly variable, most patients achieve and maintain target IOP for two to five years.

We hold that most people can be properly trained to instill eyedrops (very much like contact lenses). We also hold that if a doctor takes the time to attentively discuss the disease process, most patients can and will be adherent to their eyedrop therapy. It is imperative that patients truly understand the importance of their self-care.

Who can do this better—a doctor seeing 40 to 80 patients per day, or one seeing 25 to 30 per day? This is yet another reason why doctors of optometry should be providing the majority of glaucoma patient care.

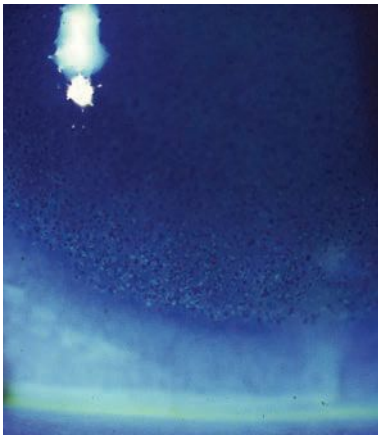
Q What is the proper interval of repeating OCT for individuals who have large and very large discs with cupping on normal imaging and no loss of RNFL?

A Here we are teetering on "micromanagement!" Without more of a comprehensive understanding of the patient, a well-focused answer cannot be given. How old is the patient? Is there a positive family history? What are the intraocular pressure readings? What is the central corneal thickness? So, we now provide a poorly focused answer: annually.

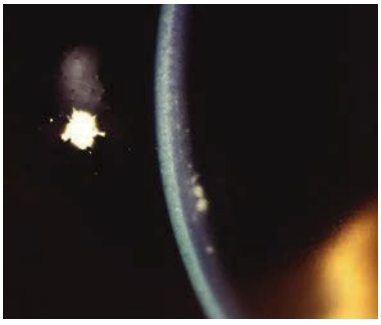
GLAUCOMATOCYCLITIC CRISIS: CASE EXAMPLE

- BVA: 20/20; 20/50
- Pupils normal; no APD
- Conjunctiva quiet OS
- Cornea: 2+ peripheral epithelial edema OS
- Endothelium shows mild KP
- A/C: Grade 1 cell, trace flare
- 4-mirror gonio: open without synechiae
- IOPs: 18, 56
- ONHs: 0.25 OU; healthy rims

This is a straightforward case of glaucomatocyclitic crisis.



Note the inferior microcystic edema. This is because the intraocular pressure went from the upper teens to the mid-50s in just a day or two.



Slit lamp exam shows some keratic precipitates on the endothelium as well as prominent and pan-corneal sterile (leukocytic) infiltration of the anterior half of the cornea.

Treatment was Durezol q2h for two days, then QID for one week, then BID for one week. Suppressing this idiopathic iridocyclokeratitis is essential to quiet the anterior segment tissues, thus enabling the tissues to renormalize, hastening the renormalization of the intraocular pressure.

We also gave the patient a sample of Combigan to use BID for three days to facilitate the IOP drop secondary to steroid suppression of the inflamed tissues.

The ptotic eye is almost always the problematic eye.

BRIMONIDINE TARTRATE

- **Alpha-2 adrenergic agonist; TID FDA approval.**
- **Acts by reducing aqueous production with some enhancement of uveoscleral outflow.**
- **Reduces IOP similarly to timolol 0.5% BID.**
- **Side effects: fatigue and dry mouth are the most common; uveitis has been reported; it may reduce systolic BP by 10mm Hg; causes less tachyphylaxis or allergy than apraclonidine.**
- **Neuroprotective potential speculated but not confirmed.**
- **Alphagan (0.2%, Allergan) and generic, Alphagan P (0.15%, Allergan and generic) and Alphagan P (0.1%, Allergan)**

Don't Miss Giant Cell (Cranial) Arteritis

Largely a disease of the elderly, giant cell arteritis (GCA) can present in numerous ways. Most common is as an anterior ischemic optic neuropathy, but it's also possible for GCA to present with diplopia or retinal microvascular occlusive disease, such as central or branch retinal artery occlusion. Sometimes, patients can present with a history of transient, monocular vision loss.

As GCA can cause blindness, it is imperative that we be experts in this disease process. The following section will enable you to expertly assess and manage the ocular manifestations of this idiopathic vasculitis.

OUR GUIDE TO EVALUATING GCA SUSPECTS

This is essentially a three-step process:

(1) History. Classic symptoms of GCA include: new-onset headache in a person over age 50 (the older the person, the higher the risk); a history of jaw claudication (virtually pathognomonic for GCA); scalp tenderness; diplopia; general malaise; weight loss; and a history of polymyalgia rheumatica. Women are more at risk than men. Race is minimally helpful, with white patients perhaps at some greater risk than others.

(2) General physical examination (which is limited). Palpate the temporal arteries, hoping for a palpable pulse, and perform dilated ophthalmoscopy to look for anterior ischemic optic neuropathy, or branch retinal artery occlusion or central retinal artery occlusion.

(3) Order laboratory (blood) studies. If equipment is available, perform temporal artery ultrasound. Bloodwork suggestive of GCA includes C-reactive protein (CRP) >2.45 and erythrocyte sedimentation rate (ESR) >60.[1] In both of these studies, the higher the result, the greater the likelihood of GCA. Also, order a complete blood count (CBC) to look specifically at the thrombocyte (platelet) count. Thrombocytosis > 400 is commonly seen in the setting of GCA.

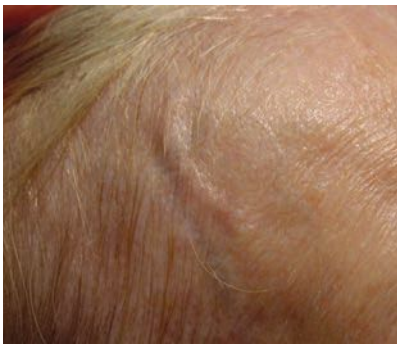


Photo: Michael Trottini, OD

A large, palpable, firm temporal artery is a good indicator of possible GCA.

"In GCA, temporal artery biopsy may not be required with typical disease features accompanied by characteristic ultrasound or MRI findings (of the temporal arteries)," one study noted.[2]

In summary, since GCA has the potential to be a blinding disease, as doctors it is critical that we are keenly attentive to any person who presents with symptoms that could be compatible with cranial arteritis. As optometrists whose primary purpose is to enhance vision, interceding in this idiopathic arterial inflammatory disease in a timely manner can indeed preserve vision.

POLYMYALGIA RHEUMATICA (PMR) AND GCA

These two idiopathic inflammatory vasculopathic disorders are thought to be related in some as yet not fully understood manner. These diseases may even manifest across an inexact spectrum.

PMR typically presents in patients over age 50. These patients commonly present acutely with bilateral upper extremity pain, more exactly as shoulder pain and stiffness, most commonly upon awakening in the morning. These patients often have constitutional symptoms such as fatigue, weight loss, night sweats, depression and low-grade fever.

Just as with GCA, elevated CRP and ESR are most always seen. About half of patients diagnosed with GCA have PMR, and about 20% of those patients afflicted with PMR go on to develop GCA. PMR occurs much more frequently than GCA.

So, in working up patients suspected of having GCA, always ask about a history of PMR—specifically morning shoulder pain and stiffness.

In the setting of suspected GCA, it's also important to begin replacing temporal artery biopsy (TAB) with ultrasound (US) studies of the temporal artery.[3]

While the TAB conditionally endures as the gold standard with suspicion of GCA, its diagnostic dominance is being appropriately challenged with noninvasive vascular US. Keep a few things in mind: patients with arteritic AION may have a history of episodes of transient vision loss, whereas this is not seen in the much more common nonarteritic (vascular) form of AION. Also note that if this same demographic has a history of transient monocular vision loss, these patients may have carotid atheromatous disease. If that is the case, an urgent carotid ultrasound study needs to be accomplished within a day or two.

US evaluation of the cranial arteries should be done within a day or two of the initiation of high-dose steroids. Of course, a combined history (*e.g.*, new-onset headache, malaise, jaw claudication, scalp tenderness) and blood studies (CRP, ESR and CBC) would guide one's presumptive initiation of high-dose oral prednisone. Such corticosteroid vascular inflammation suppression does not negate the validity of a TAB for a few days. When performed properly in a timely manner, US is more sensitive and specific than biopsy.

Given that ultrasounds studies are less expensive, less time-consuming and noninvasive, we anticipate the diagnostic pendulum will steadily swing from TAB to US in the near future.

THERAPY INTERVENTION IN THE SETTING OF GCA

Since high-dose oral prednisone is the primary therapeutic intervention in the setting of suspected or confirmed GCA, we need to have a quick chat with the primary care provider of such patients to ascertain any contraindications to the use of high-dose prednisone. This is just one scenario in which good doctor-to-doctor communication enhances patient care.

There is no firm rule as to what dosage is best: we generally initiate with 80mg per day, but if the patient is small or large, we may reduce/increase the initial dosage accordingly. Once we have the laboratory and/or radiological results (which will further confirm or refute our initial clinical suspicion), we pass these patients on to a rheumatologist or internist for ongoing management. Then we see these patients only to monitor any visual deficits, especially if the patient presented with AION, diplopia or arterial occlusion.

The urgency of intervention is more acute if a patient presents with unilateral vision loss resulting from AION or arterial occlusion. Keep in mind that most cases of AION are indeed nonarteritic and result from systemic hypertension, diabetic vasculopathy or simply age-related vascular disease. But we must always assume the etiology to be giant cell arteritis until appropriate blood studies are done.

Further, always check the blood pressure of all these patients. If the blood pressure is, for example, 210/100, the cause of the AION is heavily weighted toward hypertensive vasculopathy and not GCA; yet, we must always rule out GCA. Keep in mind that visual compromise, diplopia and retinal vascular occlusive disease are ophthalmic manifestations of systemic disease. Our duty is to assess the patient, perform a timely state-of-the-art workup, initiate therapy if indicated, and then get the patient to a specialist for ongoing care.

Comanagement of arteritic AION with a neurologist is essential in GCA patients and suspects. Early steroid treatment is critical and may be required for several years in severe cases to avoid permanent vision loss.

From a medicolegal perspective, we can never miss this diagnosis! For the most part, keeping an attentive ear and a high index of suspicion will guide the clinician to perform an appropriate workup.

THE MEDICOLEGAL ASPECT OF GCA

The Ophthalmic Mutual Insurance Company is a major insurer of ophthalmologists. They published an article titled "Giant Cell Arteritis Claims are Costly and Difficult to Defend" in their *Ophthalmic Risk Management Digest* that shares some interesting cases and insights.[4] Following, we share some paraphrased content from this article that we feel have merit for all eye doctors. While this specific article exclusively addresses ophthalmological care, these cases could just have easily been optometric scenarios!

First, we all need to be mindful that varied and nonspecific constitutional symptoms such as fatigue, malaise and a history of weight loss need to be addressed along with the classic ocular-related symptoms and signs. "The ophthalmologist failed to elicit the non-vision-related symptoms in ten of the fifteen patients who were having them. Defense experts opined that this inadequate history contributed to the delay and diagnosis and was below the standard of care."

A 79-year-old patient presented with amaurosis fugax. A sed rate was ordered, which was 6, and so a second sed rate was obtained, which was also 6. Six days later, the patient had another episode of transient visual loss, developed an afferent pupillary defect and a visual field defect.

Our take: Our perception is that another key consideration would be carotid atheromatous disease, so a carotid ultrasound should have been ordered. The sed rate alone was insufficient. The doctor also should have obtained a C-reactive protein, and a CBC to look for thrombocytosis. The low sed rate finding of 6 partially caused the doctor to let his guard down. Don't let that happen to you!

Two other cases where vision change was the only symptom were settled when OMIC could not find supportive defense experts.

Our take: That is because these cases were so poorly handled that there was no plausible defense.

Another case: The ophthalmologist noted papilledema in an 81-year-old who presented with sudden vision loss, but the doctor did not work up the cause.

"Ophthalmologists examining older patients, especially those with vision changes and headache, need to take a more active role in obtaining the history."

All of us need to "document the encounter and your decision-making process in the medical record."

Just to close out this brief section, the median payment for missing GCA was $335,000. The bottom line is: be attentive, obtain a proper history, conduct a thorough physical examination, order proper laboratory tests, and if indicated, start the patient on high-dose prednisone (around 80mg per day) after consulting with the patient's PCP. Importantly, document all of these steps in your medical record.

1. Buttgereit F, Matteson EL, Dejaco C. Polymyalgia rheumatica and giant cell arteritis. JAMA. 2020 Sep 8;324(10):993-94.

2. Ching J, Smith SM, Dasgupta B, et al. The role of vascular ultrasound in managing giant cell arteritis in ophthalmology. Surv Ophthalmol. 2020 Mar-Apr;65(2):218-26.

3. Pelton RW. Giant cell arteritis claims are costly and difficult to defend. Ophthalmic Risk Management Digest. 2015;25(3).

Dural Arteriovenous Malformations

Keep alert for the "other" red eye.

Not all red eyes are infectious or inflammatory! In the photos to the right, take a careful look at the pattern of the conjunctival injection. Such presentations can herald congestion within the cavernous sinus, thus altering hemodynamics. Note there is also unilateral retinal vasculature tortuosity on the ipsilateral side. These patients need to be sent from the OD's office to radiology in a non-emergent manner for definitive evaluation. No eyedrops are needed.

A case reported in the January 2021 *JAMA Ophthalmology* exhibited ocular manifestation of a systemic (neuro-ophthalmic) disease.[1] A 68-year-old woman presented to the emergency eye clinic with a three-week history of progressive left-eye redness and discomfort unresponsive to topical antibiotics or lubricants, as prescribed by her optometrist. The IOP was raised (26mm Hg) and was treated with a topical beta-blocker. Otherwise, her condition was managed conservatively for presumed viral conjunctivitis.

"She self-presented six days later with intermittent visual blurring, mild eyelid swelling and conjunctival chemosis. The IOP remained raised at 24mm Hg. An inflammatory or allergic etiology was suspected; therefore topical corticosteroids and a prostaglandin analog were also prescribed."

"One week later, at planned follow-up, the patient had dilated and tortuous bulbar blood vessels. Further interrogation of the history revealed a left-sided, nonspecific dull headache, constant for the previous two months, and an annoying 'whooshing' noise in the patient's left ear."

While this case was obviously different because it is a different patient than the one shown here, the clinical presentation looked very similar to the images in these photos. No comment was made on the retinal microvasculature.

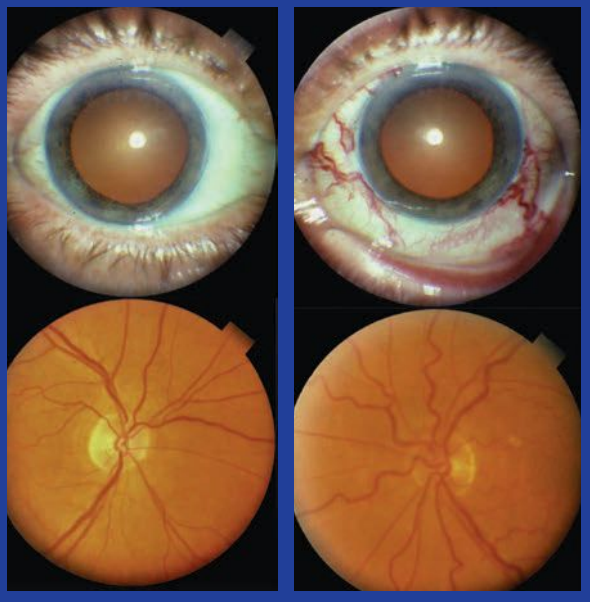
There are several points to be seen here: (1) it is critically important to take a good history and to make an accurate diagnosis; (2) if you do not adequately address the situation, the patient will seek a second opinion elsewhere; and (3) the pattern of the conjunctival blood vessels in no way appears to be similar to that seen in typical infectious conjunctivitis.

Further, there was no palpable node on that left side and no discharge from the eye. So, always keep in mind that infectious processes have a discharge. Last, a much more intensive history in this case would have prompted all of the patient's doctors to arrive at the cavernous sinus foci much earlier. Thankfully, this patient did undergo neuroradiological intervention and had a fully successful outcome.

The moral to this story is: give deep thought to the diagnosis and do your very best to make an accurate assessment.

DURAL AVM FACTS AND CLINICAL FEATURES

- Usually US women ages 50 or older, often with HTN
- Classic syndrome:
  - » mild to moderate proptosis
  - » dilation (tortuosity) of conjunctival vessels
  - » mild to moderate conjunctival chemosis
  - » abducens nerve paresis
  - » venous stasis retinopathy



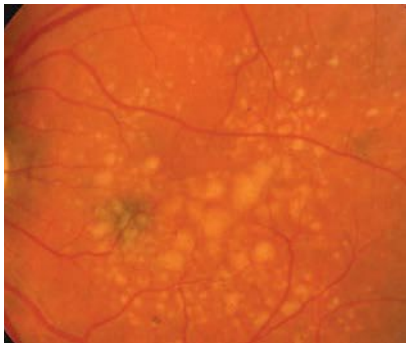
- DDx: Conjunctivitis, dysthyroid orbitopathy, orbital pseudotumor, true orbital mass
- Almost always spontaneous (not trauma associated)
- Workup: comprehensive eye exam, MRI / MRA
- Natural history
  - » rarely affect mortality rates
  - » rarely bleeding
  - » rarely extraocular signs/symptoms
  - » often close spontaneously
- Patient is at risk for infrequent CRVO, rarely glaucoma

Role of Vitamin D and Omega-3 Fatty Acid Supplementation in AMD

While AREDS and AREDS2 supplementation have a significant positive impact on the progression of AMD, it is certainly desirable to further augment their efficacy. A recent trial of physiologic doses of vitamin D (2000 IU/day) and one gram/day of omega-3 fatty acids failed to provide any enhancement to the effects of AREDS or AREDS2 supplementation. Some key findings:

• "These negative results of a large, well-designed and well-conducted clinical trial, performed by highly experienced investigators, are discouraging. This is especially the case because the prior successes of AREDS and AREDS2 have led to considerable optimism that at least one and possibly other common and highly disabling eye diseases can be substantially reduced in severity, or even prevented, by large but safe doses of commonly used and inexpensive vitamins and dietary supplements."

• "In conclusion, in this large randomized trial of initially healthy men and women, supplementation with vitamin D3 and marine omega-3 fatty acids for a median 5.3 years had no significant overall effect on AMD incidence or progression."



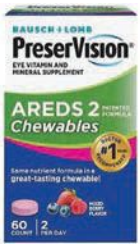
Advanced, soft, large, confluent macular drusen.

So, until some other interventions are discovered, we press on urging our patients who smoke to try their best to quit, and to continue to take their AREDS2 supplements daily. Surely, additional help will be forthcoming.

Christen WG, Cook NR, Manson JE, et al; VITAL Research Group. Effect of vitamin D and ω-3 fatty acid supplementation on risk of age-related macular degeneration: an ancillary study of the VITAL randomized clinical trial. JAMA Ophthalmol. 2020 Dec 1;138(12):1280-9.

LUTEIN-ZEAXANTHIN CONTENT OF FRUITS AND VEGETABLES

Since a good number of our patients are at risk for—or have—clinically significant macular degeneration and do not eat sufficient amounts of these foods, we recommend that they augment their diet with the AREDS2 vitamin/mineral supplement. Preventive care is an optimal approach to good health, and we want to do all we can to preserve and protect vision.



In addition to the more common capsules are these "chewables." Always keep in mind that a sizable minority of patients do have difficulty swallowing large tablets and capsules.

Fruit/Vegetable	Micrograms/100g
Kale	21,900
Collard greens	16,300
Spinach (cooked)	12,600
Spinach (raw)	10,200
Parsley (not dried)	10,200
Mustard greens	9,900
Dill (not dried)	6,700
Celery	3,600
Scallions (raw)	2,100
Leeks (raw)	1,900
Broccoli (raw)	1,900
Broccoli (cooked)	1,800

Mangles R, Holden JM, Beecher GR, et al. Carotenid content of fruits and vegetables: an evaluation of analytic data." J Am Diet Assoc. 1993;93:284-96.

RED REFLEX IN INFANTS IS A CRITICAL OBSERVATION

During the course of routine practice, there are many times a parent is holding a "lap baby" while the doctor is examining an older child (or parent). Our practice has always been to take a few seconds to retinoscope or to use the direct ophthalmoscope to screen these infants and children with a quick assessment of their red reflex. The yield of a positive finding is tiny, but so is the time expended!

One case that comes quickly to mind is the one-year-old who had a unilateral, dulled reflex. It turned out that the child was emmetropic in the red reflex eye and a +5.00D in the dulled reflex eye. Amblyogenic anisometropia was detected and early, and appropriate treatment was initiated, hopefully preventing permanent vision loss. Of course, other causes of a dulled/absent reflex can be a congenital cataract, retinoblastoma, chorioretinal coloboma, vitreous mass or other congenital abnormalities.

As a recent study puts it:

• "Large refractive errors may be observed as changes in red reflex because the passing of light through the eye depends on the bending (refraction) of light by the optical media."

• "Retinal changes that are restricted to the peripheral retina and do not affect the central part that reflects the light will not be detected."

• "Pupil size can be increased by performing the test in a dark room or slightly deviating the angle of illumination may improve visualization of the red reflex if the infant focuses directly on the light source."

• "Not performing red reflex screening will have a detrimental effect on ocular health and visual outcomes."

• "Red reflex testing is not entirely accurate, but it is a good enough, cost-effective, simple screening tool."

Checking the red reflex is just another quick and simple public health service for our patients that shows just how much we really care.

Adams GGW. The enduring value of newborn Red Reflex Testing as a Screening Tool. JAMA Ophthalmol. 2021 Jan 1;139(1):40-41.

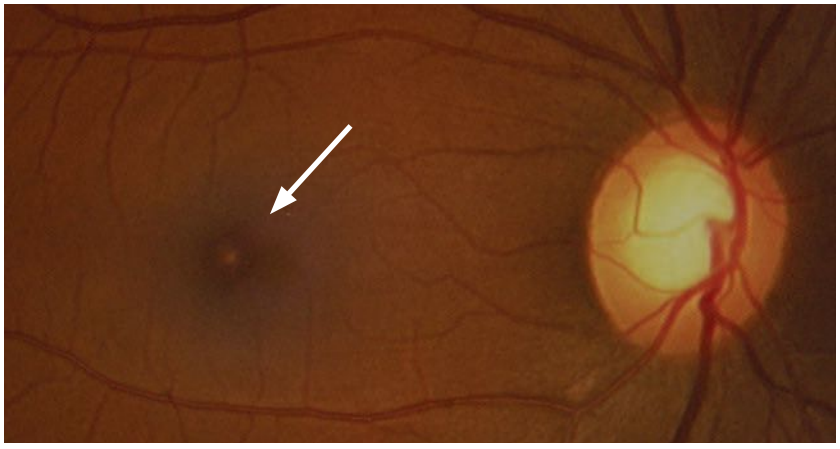
Retinal Injury from Handheld Lasers

Like most technology, the two-edged sword metaphor holds true for handheld lasers. An excellent, comprehensive review on this topic was published in *Survey of Ophthalmology* March/April 2021, from which we share the following clinically relevant information.

First things first: If you ever encounter a male patient roughly between the ages of eight and 28 with unexplained unilateral decreased vision, do an attorney cross examination–like history and obtain an SD-OCT. Approximately half of these young males will deny any laser-associated activities; thus, the need for a penetrating history! Most certainly, both sexes can be involved, the age brackets can be expanded and there can be bilateral vision loss, but we are speaking of the most common scenarios. Vision loss is generally mild, but in severe bilateral cases be mindful of possible underlying psychiatric illness. Now, the details:

• "When exposures occurred in children and young adults (age ≤ to 18 years), they were frequently associated with play behavior (96.1%). Children who sustained retinal injury were typically exposed to lasers by their peers (81.0%). These presentations result in 'unnecessary testing and misdiagnoses in these patients.'"

• "Ninety-eight (98)% of patients' imaged by SD-OCT revealed outer segment macular abnormalities at the initial presentation."



Laser-induced retinal lesion. Note the small, focal, yellowish foveal lesion. Note the focal defect from the laser injury.

• "The large majority of lasers were purchased through the Internet directly by children, indicative of the strong influence of online advertising specifically designed to target the child consumer."

• "Medical professionals, including ophthalmologists, psychiatrists, and primary care doctors need education and awareness of this entity to properly diagnose and prevent further vision loss in patients with laser injuries."

Our take: We continue to be amazed at how optometrists—the primary eye/vision gatekeepers—are ignored. This shows profound ignorance of our critical role as primary providers, or a political attack against our profession; either way, such exclusion is an egregious breach of professional integrity.

• "Unfortunately, some patients are mistakenly diagnosed with macular dystrophies or posterior uveitis. Diagnosis of retinal laser injury is often challenging due to lack of forthcoming history of laser use, requiring evaluating physicians to recognize the clinical and imaging findings indicative of laser injury."

• "Nonspecific foveal retinal pigment epithelial changes and distinctive yellow or gray lesions corresponding to outer retinal phototoxic damage on clinical examination was found in nearly half of all cases and should raise suspicion for handheld laser maculopathy. Visual acuity in patients with these more common macular findings was generally good."

In summary, handheld lasers can be a source of retinal injury. It is the mindful, judicious and attentive clinician with a high index of suspicion who can arrive at an accurate diagnosis. There is no effective treatment, but thankfully most all patients exhibit only minimal visual compromise.

Bhavsar KV, Michel Z, Greenwald M, Cunningham ET Jr,, Freund KB. Retinal injury from handheld lasers: a review. Surv Ophthalmol. 2021 Mar-Apr;66(2):231-60.

FOLLOW-UP AFTER INITIAL PVD EVENT

- **In a recent study, about 2% of patients with normal findings developed a subsequent retinal tear.**
- **45% of retinal breaks "were found more than six weeks after presentation."**
- **At the Wills Eye Hospital Retina Service, "60% of patients in our study had at least a four to six week follow-up. Most physicians in our practice do not routinely follow up patients beyond this timeframe."**
- **Only about half of these subsequent events were symptomatic; therefore, there may be a need to reevaluate acute PVD patients more frequently than is currently common practice.**

Uhr JH, Obeid A, Wibbelsman TD, et al. Delayed Retinal breaks and detachments after acute posterior vitreous detachment. Ophthalmology. 2020 Apr;127(4):516-22.