CONTINUING EDUCATION

A Decision Tree: Proper Antibiotic Selection and Use

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Doing the Keratoconus Two-Step

Keratoconus patients might have better refractive outcomes if they undergo a new two-step surgical approach, Medscape reports. According to a small study presented last month at the American Society of Cataract & Refractive Surgery annual meeting, a protocol that pairs small-incision lenticule extraction (SMILE) with collagen crosslinking stabilized irregular corneas for an average of nine months. And, significantly, mean uncorrected visual acuity in the seven study eyes improved from a baseline of 20/400 to 20/25 at nine months postoperatively. The work was done at the Instituto de Oftalmología Conde de Valenciana in Mexico City.

“The crosslinking is very good for halting progression, but refractively, it doesn’t bring much to the patient,” coauthor Gabriela Pagano, MD, told Medscape Medical News. With the combination procedure, “we’re bringing patients the possibility of spectacle independence.” The work was selected as Best Paper of the 2013 Refractive Surgery Session.

The SMILE procedure for keratoconus uses a femtosecond laser to cut a lenticule of tissue from the stroma, which is removed through a self-sealing incision. The pocket created is then infused with riboflavin and the crosslinking procedure proceeds.

Because the combined procedure preserves the integrity of Bowman’s layer—one of the major contributors to corneal strength—“this should be better than other corneal refractive procedures,” Dr. Pagano told Medscape. Pain is minimal and the risk for infection is lower by keeping the corneal epithelium intact, she added.


In The News

• The World Council of Optometry (WCO) presented to Brien Holden, PhD its highest honor, the Distinguished Service Award, which recognizes optometrists who have made an outstanding contribution to the achievement of WCO’s mission to create a world where high quality eye health and vision care is accessible to all.

Dr. Holden is the founder of the Brien Holden Vision Institute, a worldwide multidisciplinary research center and public health organization focused on developing breakthroughs in eye care that can improve the quality of vision for people who suffer from ocular disease. Through Dr. Holden’s efforts, the Institute has invested more than $450 million in the delivery of eye care to people in need over the last 20 years.

• In a paper presented at ARVO 2013, the Mayo Clinic’s Sanjay Patel, MD, and colleagues compared changes in the corneal endothelium after three different keratoplasty techniques. Studying outcomes after penetrating keratoplasty, deep lamellar endothelial keratoplasty and Descemet-stripping endothelial keratoplasty, they found that, after three years, cell loss was less with the Descemet-stripping procedure.

• GP Specialists rebranded its entire custom made-to-order soft contact lens product line with the name iSight. This includes the designs acquired through its purchase of American BioCurve in 2011. The company says it now offers “one of the largest portfolios of made-to-order products in the industry.”

• TrueVision 3D Surgical and i-Optics announced a collaboration that will integrate the latter’s Cassini corneal diagnostic device with the former’s Refractive Cataract Toolset surgical guidance system. Removing a step in the presurgical cataract work-up can enhance speed and efficiency, they say, and blending the technologies will help to optimize patient workflow.

Lens Wear So Comfortable Patients Don’t Even Notice

In a 74-subject study of patients newly fit with 1-Day Acuvue TruEye (narafilocan A) lenses, contact lens wear was found to have no clinically significant effect on the ocular surface as compared to non-lens wearers across five of six contact lens-related measures associated with eye health, Vistakon research shows. The lens was also shown to provide high levels of comfort from morning to night, comparable to wearing no lenses at all, according to the company. The findings were published recently in Contact Lens & Anterior Eye.

Comfort scores assessed at the six study visits were equivalent for contact lens wearers and patients who had not previously worn contact lenses and remained with spectacle wear for 12 months.

After a full year of wear, there were no clinically significant differences between contact lens and spectacle wearers for bulbar conjunctival hyperemia, limbal hyperemia, corneal staining, neovascularization and papillary conjunctivitis. There was more low-grade “trace” conjunctival staining for contact lens wearers than spectacle wearers.
Encouraging Data on Myopia Control

A new contact lens design shows noteworthy potential for decreasing myopic progression, based on animal study results published in *Investigative Ophthalmology & Visual Science*.

The purpose of the randomized, masked study was to determine the effect of wearing a new lens with a unique optical design on the development and progression of defocus-induced myopia in newly hatched chickens. According to the study, the lens caused a significant reduction in the development of defocus-induced myopia over a 14-day wearing period, compared to a control lens identical in every aspect except optical design. There was also a significant axial length difference, with the control group showing increased ocular axial growth as compared to the test design groups.

The lens is being developed by Visioneering Technologies of Alpharetta, Ga. Research was conducted by the Centre for Contact Lens Research at the University of Waterloo’s School of Optometry & Vision Science in Canada.

This study is the first to report “nearly complete inhibition of defocus-induced myopia in chickens compared to control lenses,” said lead author Jill Woods, MCOptom. The lack of significant axial length increase seen “indicates that these lens designs reduced defocused-induced myopia progression through the inhibition of axial elongation.” Although further work is needed to determine the exact mechanisms by which the lens decreases myopia development, the potential was significant, she added.

Visioneering Technologies says its contact lens technology has multiple applications, including control of myopic progression as well as multifocal vision correction for presbyopia. The company expects to introduce a contact lens for presbyopia incorporating its unique technology in early 2014. An intraocular lens using the company’s technology for presbyopia is also under development.


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**An Early Look at the Performance of a New Lens**

While the US launch of Alcon’s new Dailies Total 1 daily disposable is anticipated later this year, research on the deflecilcon A material’s performance is starting to appear. A meta-analysis of clinical data presented at ARVO 2013 documented an association between lubricity profile, measured by coefficient of friction, and subjective reports of comfort in three assessments: upon initial insertion, overall comfort and end-of-day comfort. Each of the three outcomes showed a highly significant association between the respective comfort measure and coefficient of friction, according to the ARVO abstract (494/B0131).

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Fitting Multifocal Contact Lenses in Patients with Presbyopia

Why so challenging?

The challenge of fitting multifocal contact lenses for our patients with presbyopia lies in being able to give them distinct near, intermediate and distance vision, essentially on demand. All of the current multifocal lenses use a simultaneous vision design in which the power for near, the power for intermediate, and the power for distance vision are each present all the time. The brain has to sort it out and pay attention to the power it wants. Unfortunately, knowing who is going to do well in a multifocal lens and who is not right now seems unpredictable. Is it just simultaneous vision that causes the unpredictability or is it something else?

We’re all familiar with the clinical situation in which one patient needs a particular add power, and we chose a particular brand and that patient does great. But later the same day we can have another patient with the same add power need using the same brand. What is different about these two patients? Their add power need is the same but their distance correction is different: one might be a -2.00 D and the other might be a -6.00 D. You would think that these patients would have a similar result but they often don’t.

What is the cause of this varied success when fitting multifocal contact lenses? The answer may lie within the consistency of the design of the multifocal contact lens and information obtained from power profile measurements that chart the power change from the center to the periphery of the lens help us to understand why. Ideally, the power profile of a lens will be exactly the same for all lens powers across the available prescription range. This consistency of the power profile within each lens affects not only the performance of the distance vision of the lens, it also affects the performance of the addition power of the lens.¹

Power profile consistency across the power range helps ensure that, regardless of which power is fit on-eye, the practitioner can expect a more predictable fitting experience. Many currently marketed multifocal designs contain inconsistencies across the power range and the add power.¹ So a medium or high add may not perform as I think it should as a result of not knowing what the actual lens add power is, or how that add power transitions to distance power. I generally expect a high add to have more plus than a medium add, but that is not always the case. Hence, multifocal contact lenses have the potential to provide variable visual outcomes to patients, in addition to potentially causing an inconsistent fitting experience or an inability to predict how a lens will perform on-eye from one power to the next. This can lead to frustration for patients and practitioners alike.

The good news is that the opportunity exists to enhance patient satisfaction and the predictability of lens fitting by improving the power consistency of multifocal contact lenses.

REFERENCES:
2013 ARVO Explores Lens-related Inflammation and Corneal Infection
Researchers explore strategies to minimize risk and prevent corneal morbidity in contact lens wearers.

Each year, world-renowned eye care scientists share their research at the Association for Research in Vision and Ophthalmology annual conference. Valuable information gleaned from the many studies at this year’s meeting (held May 5-9 in Seattle) can aid clinicians in developing best-practice guidelines while raising important questions that will direct future research efforts.

It’s always difficult sifting through hundreds of abstracts to identify the most useful ones that can translate into immediate clinical practice. This year’s highlights include risk factors related to lens wear, how to prevent infection stemming from lens and storage case contamination, disinfection efficacy and treatment options when disaster strikes.

As no single study is likely to provide the definitive answer to a research question, the findings below should be viewed with a perspective that acknowledges our full body of literature. Nevertheless, this year’s crop of abstracts provides many thought-provoking new ideas that will help us move forward.

New Information on Risk Factors and Prevention
Inherent in any lens wear is a full range of risks that hopefully can be minimized by addressing identifiable factors responsible for getting an infection. How might we best minimize these inherent risks? Several abstracts address these topics. Important to any discussion or investigation of infection are geographic differences in pathogens encountered, risks to travelers, lens storage case contamination and antimicrobial efficacy of disinfecting solutions.

■ Risk Factors for Contact Lens-related Microbial Keratitis in Singapore (Abstract ID: 509/B0146)
Elevated risk of microbial keratitis was associated with showering while wearing lenses (a three-fold higher risk), while washing and drying hands prior to handling lenses lowered the risk eight-fold. Chinese ethnicity also lowered risk seven-fold in this study, possibly due to socioeconomic factors. Behavioral and innate factors should be investigated further.

■ Traveler’s Contact Lens Associated Keratitis (TCLAK): Establishing Preventive and Treatment Guidelines to Close a Gap in Ophthalmic Care (Poster: 511/B0148)
Though the incidence of lens-associated keratitis is low, an increasing number of new cases are identified in travelers due to greater lens use, long duration of wear and travel outside the US. There appears to be higher morbidity risk due to decreased access to ophthalmic care abroad.

The lack of specific recommendations regarding precautions to take while traveling internationally is an obvious patient education gap that requires attention. The authors designed guidelines that include strict adherence to proper hygiene and care, seeking immediate attention if the eye gets red, irritated or experiences vision loss, and advises patients to not overwear lenses while traveling.

■ Quorum-sensing Molecules in the Preferential Selection of Pseudomonas aeruginosa From Contaminated Contact Lens Cases (Abstract ID: 513/B0150)
“Quorum-sensing” proteins/genes were studied to document and correlate their role in the selection of Pseudomonas aeruginosa as a preferential corneal pathogen from contaminated contact lens cases, according to Bascom Palmer researchers. In 76.9% of studied lens cases, Pseudomonas emerged as the corneal pathogen of all matched control/cornea cultures. No proteins recovered correlated with Acanthamoeba species, Klebsiella oxytoca or Mycobacterium chelonae.

The researchers concluded that the production and expression of quorum-sensing genes and signaling molecules in contact lens case ecosystems may allow for the preferential selection of P. aeruginosa as a corneal pathogen. Understanding this mechanism in more detail may lead to the development of new solutions to reduce or neutralize this advantage.

■ An Examination of the Effects of Evaporation on Antimicrobial Efficacy of Contact Lens Care Solutions (Abstract ID: 5480/A0179)
Partial evaporation of multipurpose solutions (MPS) by failing to cap solutions properly may result in loss of antimicrobial efficacy of the solution, leading to contact lens-related infections. In this study from Abbott Medical Optics, evaporation was induced in four MPS products, which were then challenged with P. aeruginosa, Serratia marcescens, S. aureus, Candida albicans and Fusarium solani. Test solutions were compared at four hours to the non-evaporated solutions.
This study demonstrated that with partial evaporation up to 4x (simulating the action of not capping a lens case properly), MPS solutions can lose significant disinfection ability. More pronounced loss was shown in solutions that failed to meet criteria when non-evaporated. Only one MPS tested (an investigational solution) showed full efficacy of disinfection when evaporated at the 4x level.

New FDA guidelines could involve evaporation testing and any loss of efficacy, to attempt to reflect real-world conditions.

■ The Evaluation of the Biocidal Efficacy of Multipurpose Solutions Against Mixed Cultures of Pseudomonas aeruginosa With a Variety of Individual Organisms (Abstract ID: 521/B0158)

This study by investigators at Bausch + Lomb investigated biocidal activity to better simulate polymicrobial contamination of contact lens cases. The organisms used were not the standard five organisms, but rather six separate mixtures of organisms that included *P. aeruginosa* and one of the following: *Candida albicans*, *Candida tropicalis*, *Fusarium solani*, *Fusarium oxysporum*, *Aspergillus brasiliensis* and *Aspergillus fumigatus*. Ten percent organic soil was added for an additional challenge. The mixed inoculum was then used to challenge the MPS. Four- and six-hour time points were evaluated. Results were recorded using log reductions.

Results varied according to the MPS used. Fungi were recovered more than *P. aeruginosa*. Recovery for the four-hour time point ranged from 0.0 log reduction to >0.2 log reduction, and fungal recovery for the four-hour time point ranged from 0.2 log reduction to >4.6 log reductions.

This study demonstrated that MPS have a broad range of in vitro antimicrobial activity against *P. aeruginosa* and fungal mixtures. These results could demonstrate actual use conditions because environmental contaminants are frequently mixtures of organisms.

■ Antimicrobial Activity of Melamine or Cathelicidin Bound Contact Lenses (Abstract ID: 507/B0144)

The development of an antimicrobial contact lens would have the ability to reduce the rate of contact lens-related adverse events. This study, conducted by Allergan, Brien Holden Vision Institute and Bausch + Lomb, evaluated two cationic peptides coated on contact lenses for their activity against *P. aeruginosa* and *S. aureus*. Minimal inhibitory concentration of two peptides, melamine (a synthetic peptide) and cathelicidin (LL37), were measured against strains of *P. aeruginosa* and *S. aureus*.

Increasing concentrations of peptides were bound covalently to contact lenses. Cell death of the bacteria was used to measure the antimicrobial activity compared to the control lenses with no melamine or LL37. Covalently bound LL37 was not active against *S. aureus*; melamine on contact lenses had activity against both bacterial types. This suggests differing mechanisms of action against gram-negative or gram-positive bacteria by these two cationic peptides.

■ Risk Factors for Microbial Bioburden During Daily Wear of Silicone Hydrogel Contact Lenses (Abstract ID: 5479/A0178)

This study from Case Western Reserve University, University Hospitals Eye Institute-Case Medical Center and Alcon Labs assessed risk factors associated with substantial microbial bioburden of lids, cases and silicone hydrogel lenses with daily wear.

A total of 218 patients were fit with lotrafilcon A lenses, randomized to use either a preserved MPS or a peroxide care system, and followed for one year. Lenses, lids, cases and transport saline were cultured at selected visits.

Univariate analysis showed that current or past smokers, clerical occupations and solution type were associated with greater risk of microbial bioburden on lenses, cases or both. Gender, age, healthcare occupations, solution type and other demographic factors were associated with lid bioburden or saline contamination. Multivariate analysis also showed clerical occupations at significantly greater risk of microbial contamination on lenses and cases.

Solution type was associated with microbial bioburden in cases, but not lids, lenses or transport saline. Hydrogen peroxide solution was associated with increased lens case bioburden, but not with bioburden of lids, lenses and transport saline. Case contamination was not a risk factor for corneal inflammatory events in this study.

■ Selenium Covalently Incorporated into the Polymer of Contact Lens Material Inhibits Bacterial Biofilm Formation (Abstract ID: 497/B0134)

Silver has been used as an antimicrobial agent in contact lens cases, but has drawbacks (allergy risk, variable antimicrobial effect, cost, reliance on the agent leaching out of the case). Selenium is a good alternative to silver: it does not have to leach out of the case to be active because it kills by catalytic formation of superoxide radicals, and is much less expensive.

This study investigated the ability of selenium covalently incorporated into the polypropylene polymer of injection-molded contact lens case material to inhibit biofilm formation by different bacteria. Polypropylene containing selenium showed over 7 logs (complete) inhibition against...
S. aureus, S. maltophilia and P. aeruginosa, and was fully active after soaking in PBS for the equivalent of eight weeks.

**Updates on Pathogens in Lens-related Infections**

Surveillance has identified antibiotic resistance of ocular pathogens. These “bugs” have relevance to lens wearers due to different vectors of exposure. It’s important to identify emerging resistance patterns that vary greatly depending on where you practice.

Believe it or not, we’re still talking about *Acanthamoeba* keratitis. Protozoan infection rates have not dropped as expected. We must remain vigilant in looking for ways to minimize even the rare, nonbacterial infections experienced by lens wearers. Microbiologic profiles in younger lens wearers are valuable and shared below.

### ■ Antibiotic Resistance Surveillance of Ocular Pathogens—Four Years of ARMOR Study Results (Abstract ID: 2904/B0273)

The ARMOR surveillance study reported Year-4 data on 456 isolates of *Streptococcus aureus*, coagulase-negative staphlococci (CoNS), *P. aeruginosa* and *H. influenzae* from 25 sites that were subjected to susceptibility testing. Drug resistance among *H. influenzae* isolates was not observed.

Non-susceptibility rates were similar to those of the previous three years. Overall resistance rates did not show substantial changes over the four-year study. A number of isolates showed resistance to commonly used ophthalmic antibiotics. Among MRSA and MRCoNS isolates, multidrug resistance was especially prevalent.

Specific findings include:

- *P. aeruginosa* isolates were nonsusceptible for ciprofloxacin (9.1%), imipenem (11.4%), tobramycin (4.5%) and polymyxin B (4.5%).
- *S. pneumoniae* isolates were non-susceptible to imipenem (13.1%), penicillin (4.9%), chloramphenicol (3.3%) and azithromycin (41.0%).
- *S. aureus* and CoNS isolates were non-susceptible to oxacillin/methicillin (37.3-41.9%), ciprofloxacin (33.8-36.6%), clindamycin (18.3-31.3%), azithromycin (58.8-60.1%) and other antibiotics.
- More than 33% of *S. aureus* and CoNS isolates were resistant to three or more antibiotics.
- Methicillin-resistant isolates of *S. aureus* (MRSA) and CoNS (MRCoNS) were predominantly drug resistant (>73%).

### ■ Risk Factors of Severe *Acanthamoeba* Keratitis (Abstract ID: 5435/A0134)

Japanese researchers studied risk factors for severe *Acanthamoeba* keratitis by comparing severe cases to mild ones (i.e., those with a good prognosis) in a nine-case series.

A history of topical steroid use was found in four eyes in the severe group and three in the mild group. Mean number of corneal scrapings was 13.8 in the severe group and 5.6 in the mild group. Kerato-precipitates were present in all eyes in the severe group. Also in the severe group, *S. aureus* was found in one case by palpebral conjunctive culture, which was resistant to topical antibiotics.

They concluded that the use of corticosteroids and the presence of kerato-precipitates are possible risk factors for severe *Acanthamoeba* keratitis. Attention is also required in patients with comorbidities such as diabetes mellitus and bacterial co-infection.

### ■ Infectious Keratitis in Mexico—10-Year Experience in Corneal Scrapes (Poster Board: #B0091)

Another retrospective study conducted in Mexico City reported the distribution, microbiologic trends and antibiotic sensitivity patterns of infectious keratitis cases from January 2002 to December 2011. In all, 1,638 corneal scrapings were taken. A pathogen was recovered in 616 samples (38%). Bacterial keratitis accounted for 544 of the positive cultures (88%).

Results showed a non-significant increase in recovered gram-positive and gram-negative micro-organisms over time. An increase in resistance to methicillin in almost half the MSRA and MRCoNS isolates was observed. In the last five years of the study, ceftazidime-resistant *P. aeruginosa* increased to nearly 90%.

Vancomycin-resistant micro-organisms accounted for 9.9% of all gram-positive isolates while 13.3% of all bacterial isolates were resistant to quinolones. For now, the authors conclude that this justifies quinolones as monotherapy broad-spectrum treatment for bacterial keratitis.
Editorial

The Proctor Experience With Acanthamoeba Keratitis From 1996-2012 (Poster: #B0105)

This retrospective study described the presentation, management and outcomes of Acanthamoeba keratitis (AK) patients in the Bay Area before and after an AK epidemic beginning in 2004-2005.

Forty-one patients (42 eyes) demonstrated culture-proven AK. From 1996-2004, there were zero to three AK cases. From 2005-2011, there were three to six cases. From 2005-2011, there were three to six cases. The number of microbiology-positive AK cases has increased since 2005 and has not diminished. The duration of symptoms in 1996-2004 is not statistically different from 2005-2012. Visual acuity at presentation was not significantly different from pre-2005 and 2005 to present.

The number of culture-proven AK cases has not decreased to pre-epidemic levels in the Bay Area. Before and after 2005, a median time of four weeks of symptoms prior to diagnosis was endured, and patients presented with visual acuity morbidity. Even with increased awareness, diagnosing AK does not appear to be happening any earlier in its course.

**Advances in Treatment**

New therapies are always exciting to share with readers. This year’s abstracts look at preclinical evaluations of several new therapies for corneal infections including rare, nonbacterial keratitis. Ongoing research should help identify new strategies in treating these morbid corneal conditions.

Clinical Outcomes and Prognostic Factors Associated With Acanthamoeba Keratitis Treated With Pentamidine Isethionate (Poster Board: #B0103)

This retrospective Japanese study described the clinical characteristics, time of presentation, treatment, outcomes and prognostic factors on a series of 24 patients and 26 eyes with Acanthamoeba keratitis (AK) treated with pentamidine isethionate.

A review of all patients was performed, including age, gender, time to diagnosis, use of corticosteroid before diagnosis, combination of bacterial of fungal infections, diagnostic method, initial visual acuity, duration of pentamidine isethionate treatment, side effects and final visual acuity. Treatment failure was defined as AK recurrence or needing a therapeutic deep anterior lamellar keratoplasty.

The onset of symptoms was greatest in September. AK was diagnosed either by typical clinical presentation or by culture. Forty-two percent of eyes were diagnosed previously with herpetic keratitis; 58% were treated with corticosteroid eye drops. Fifty eyes had combined bacterial or fungal infections. Twenty-two eyes were contact lens wearers. Hospital time averaged 26.9±21.7 days. Visual acuity improved from 1.41logMAR±1.00logMAR to 0.19logMAR±0.34logMAR. Soft contact lens wearers tended to have a higher risk of infection and failure is likely to be associated with stromal involvement.

Predictors of Outcome in Fungal Keratitis Using Data From the Mycotic Ulcer Treatment Trial (Abstract ID: 2900/B0269)

The purpose of this study was to determine baseline factors predictive of outcomes in fungal keratitis among the Mycotic Ulcer Treatment Trial (MUTT I) Group.

MUTT I was a multicenter, randomized, double-masked, NEI-funded clinical trial that compared outcomes in 323 patients with fungal keratitis receiving 5% topical natamycin or 1% topical voriconazole.

Significant predictors of worse three-month visual acuity were worse baseline acuity, larger epithelial defect size at presentation and randomization to voriconazole instead of natamycin in the trial. For three-month infiltrate/scar size, significant predictors include larger infiltrate and epithelial defect size, worse presenting visual acuity and use of topical antifungals prior to trial enrollment. Predictors of corneal perforation were worse presentation visual acuity, older age and randomization to voriconazole instead of natamycin. The predictors for longer time to epithelialize were epithelial defect size and presentation ulcer depth.

Study findings suggest that it is difficult to change the course of an ulcer even with proper treatment — ulcer severity at presentation is highly predictive of worse outcomes — but a better understanding of predictive factors may help guide future treatment decisions and management.

Conclusions

Clinically relevant information is not always apparent in high-level research abstracts, but ARVO posters and papers are teeming with valuable information that can be applied to clinical practice. Knowing how to reduce risk and prevent morbidity in lens wearers is extremely useful information. Knowing how to identify in a timely fashion and better treat rare, devastating infections in lens wear is crucial. ARVO has helped us do so year after year.

I hope that you have found this year’s review helpful. For more information and all the abstracts, please visit www.arvo.org/abstracts.
A 32-year-old male with surgically induced Horner’s syndrome in his right eye presented with mild hyperemia and irritation. He reported that his symptoms have persisted for several years. Additionally, a previous eye care provider “diagnosed” contact lens overwear, although that is a rather nonspecific term.

The patient reported dosing his right eye with Visine LR (McNeil-PPC) at least 20 times per day on top of his contact lens for the last decade to help control his Horner-induced ptosis. Upon examination of the right eye, we documented numerous deep-stromal opacities located across the entire cornea, as well as diffuse superficial punctate epithelial erosions. Remarkably, he had minimal hyperemia.

We diagnosed him with medicamentosa secondary to chronic topical dosing. We instructed him to discontinue Visine LR use. Additionally, to treat the underlying ptosis, we recommended either surgical intervention or use of a compounded, preservative-free formulation of oxymetazoline.

What is Medicamentosa?
Medicamentosa is a chemical irritation or a delayed, cell-mediated hypersensitivity response of the ocular tissues to topically applied drugs or preservatives. It may take weeks, months or years for the symptoms of medicamentosa to appear. And, to further complicate the diagnosis, any documented symptoms may, in fact, be caused by unrelated complications—especially in the case of contact lens wearers, where there are other ocular surface irritants.

While there may be improvement of the underlying condition (e.g., ptosis), ancillary symptoms may develop over time, including irritation, grittiness, stinging, burning, photophobia, conjunctival hyperemia, lid swelling and blurred vision. Clinically apparent signs of medicamentosa include corneal or conjunctival staining, corneal edema, pseudodendrites and stromal infiltrates.

The differential diagnoses of medicamentosa include contact lens-related staining, viral keratoconjunctivitis, dry eye and rosacea. Typically, medicamentosa is attributed to the preservative agent in an ophthalmic solution. However, in some instances the drug itself may cause unwanted effects on the eye that worsen with increased dosing.

In our patient’s case, Visine LR contains oxymetazoline (an alpha-1 and partial alpha-2 agonist, which serves as a vascular decongestant and facilitates ptosis relief) and is preserved with benzalkonium chloride (BAK)––a known ocular irritant that causes corneal staining (see “Too much of a good thing?” January 2011). In addition, however, oxymetazoline yields several side effects.

The entire class of topical vasoparconstrictors (including oxymetazoline, naphazoline and tetrahydrozoline) has been shown to cause rebound hyperemia after discontinuation. Also, while commonly used by dry eye patients, these drugs can yield a significant decrease in tear volume and flow.1 There is at least one published study of corneal opacity development secondary to chronic vasoconstrictor dosing.2 In this report, the opacities partially resolved with drop discontinuation.

When medicamentosa is suspected, instruct the patient to discontinue the offending medication or switch to a preservative-free formulation. Keep in mind, however, that treatment of the underlying condition is still necessary.

**Agents Frequently Associated With Medicamentosa**
- Benzalkonium chloride
- Brimonidine
- Atropine
- Neomycin
- Acyclovir
- Prostaglandin analogs

**Medicamentosa**

This patient developed medicamentosa from chronic, long-term oxymetazoline use. How should he be managed?
The concerns over preservatives, in particular benzalkonium chloride (BAK), used in ophthalmic solutions have been well documented.1-7 BAK generally is well tolerated with short-term topical therapies (e.g., an antibiotic for bacterial conjunctivitis or a steroid for episcleritis), but glaucoma patients face long-term challenges. These patients can be maintained on glaucoma medications for several decades and their treatment plan often involves concurrent use of multiple BAK-containing drops. In the end, this translates to significant, cumulative exposure to BAK. What are the implications?

The Research
While most published studies outline the harmful effects of BAK on the ocular surface, some findings are less conclusive and perhaps even contradictory.8 Since much of the data available is lab-based or preclinical and uses non-human models, making the application to clinical practice can be challenging.

In 2010, Robert Noecker, MD, and Kimberly Miller, MD, published a summary of the BAK literature and its effects on the ocular surface—in particular as it pertains to glaucoma medications. They found the majority of the literature says BAK has an adverse effect on the ocular surface and recommended that practitioners should consider non–BAK-containing glaucoma medications to avoid these potential reactions.9

It has been noted that one shortcoming in many past clinical evaluations is the failure to include a control group. Sudipta Ghosh, DO, and colleagues recently compared the prevalence of symptoms and signs of ocular surface disease (OSD) in glaucoma patients vs. a control group. Symptoms of OSD were found to be common in both populations. However, signs of ocular surface disease, including fluorescein staining of the conjunctiva and cornea, were more prevalent in the glaucoma group (70.3% vs. 33%).10 Reduced tear film break-up time and the presence of ocular surface staining were more likely with each additional glaucoma medication used.

While 94.2% of the study used drops containing preservatives, the authors did not compare the effects of different preservatives.10 However, approximately 78% of ophthalmic pharmaceuticals contain BAK, leading to the conclusion that this preservative could be implicated as a contributing factor to the signs of OSD in the above study.11

In a meta-analysis of seven prospective clinical trials, Stefan Trocme, MD, and colleagues failed to demonstrate significant ocular toxicity in patients treated with latanoprost or timolol, both containing BAK. They concluded that when BAK is used in the concentration available in glaucoma medications (0.004% to 0.02%), patients do not experience corneal toxicity.12

Charles Tressler, MD, Richard Beatty, MD, and Michael Lemp, MD, determined that dilution of BAK occurs quickly from a normal tear film; despite a BAK concentration of 0.02% (the highest concentration currently available in a glaucoma medication) upon instillation, it is reduced to 0.0025% in 30 seconds and to 0.0005% in three minutes.12 Therefore, corneal exposure time to any clinically significant concentration of BAK is very short-lived. It should be noted that the dilution would be less rapid in patients with dry eye, a common coexisting condition in glaucoma patients.13

Glaucoma patients who are also contact lens wearers face an additional challenge: The residence time the ophthalmic drop is in contact with the ocular surface increases. If BAK is irritating, the effects will be exacerbated in contact lens wearers who opt to instill their medications while wearing their lenses, despite warnings from eye care practitioners.

Therapeutic Options
• BAK-free options are now available in all classes of contemporary glaucoma medications (see Table 1), except the topical carbonic anhydrase inhibitors that include Trusopt (dorzolamide 2%, Merck) and Azopt (brinzolamide 1%, Alcon)—preserved with 0.0075% and 0.01% BAK, respectively. It should be noted that pilocarpine and Pilopine gel (pilocarpine hydrochloride, Alcon) contain BAK as well.
• Beta-blockers, although not typically used as initial treatment, still play a significant role in glaucoma management due to their reasonable cost and 20% to 25%
efficacy in reducing IOP. Timoptic XE (timolol maleate, Valeant Pharmaceuticals) is formulated as a gel-forming solution; as such, it has a longer residence time than a solution in a once-daily drop. Both the branded and the generic (Timolol GFS, Falcon Pharmaceuticals) are preserved with benzododecinium bromide (BDD), which provides a multiuse container of a non-BAK containing beta-blocker. However, BDD and BAK are both quaternary ammonium surfactants and may have properties too similar to make BDD a feasible alternative for patients intolerant to BAK.

- Timoptic in Ocudose (timolol maleate, Aton Pharma) is available in 0.25% or 0.5% concentrations and is preservative-free. Available in prepackaged individual unit doses contained within a foil pack, the 60 vials are meant to last for one month with BID dosing and the vials are to be used within one month of opening the foil pack.

- Brimonidine, an alpha-agonist, is a well-tolerated medication that is typically prescribed twice daily when used as additive therapy. The branded drug, Alphagan P (brimonidine tartrate ophthalmic solution 0.1% or 0.15%, Allergan) is preserved with Purite, which is an oxychloro complex classified as a “disappearing preservation” that dissociates to water, and sodium and chloride ions once exposed to light. Note that the generic solutions contain either 0.15% of 0.2% of brimonidine and are preserved with BAK.

- Due to a significant incidence of allergic reactions and tachyphylaxis, lopidine (apraclonidine, Alcon) is typically used only for in-office application. The 1% concentration is packaged only in single-unit vials of 0.1ml each, which contain 0.01% BAK.

- When monotherapy fails to sufficiently lower IOP, combinations are often attractive options. Cosopt (Merck) contains 0.5% timolol maleate and 2% dorzolamide; it is available in a preservative-free formulation. Typically used twice a day, this medication is available in a package of 60 single-unit vials. Each foil pack contains 15 vials. Per the manufacturer, once a foil pack is opened, unused

### Table 1. Commercially Available BAK-Free Topical Ocular Hypertensive Medications

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Active Ingredient</th>
<th>Preservative</th>
<th>Contact Lens Wear (Per Drug Labeling)</th>
<th>Packaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alphagan P</td>
<td>Brimonidine</td>
<td>Purite</td>
<td>Not addressed</td>
<td>5, 10, or 15 mL</td>
</tr>
<tr>
<td>Cosopt PF</td>
<td>Timolol maleate 0.5% / Dorzolamide 2%</td>
<td>None</td>
<td>Not addressed</td>
<td>60 SUV (in foil packs) One pack = 15 SUV (0.2 mL each)</td>
</tr>
<tr>
<td>Timoptic in Ocudose</td>
<td>Timolol maleate 0.25% or 0.5%</td>
<td>None</td>
<td>Not addressed</td>
<td>60 SUV One pack = 60 SUV (0.2 mL each)</td>
</tr>
<tr>
<td>Timolol GFS</td>
<td>Timolol maleate 0.25% or 0.5%</td>
<td>Benzododecinium bromide</td>
<td>“Has not been studied in patients wearing contact lenses”</td>
<td>2.5 or 5 mL</td>
</tr>
<tr>
<td>Timoptic XE</td>
<td>Timolol maleate 0.25% or 0.5%</td>
<td>Benzododecinium bromide</td>
<td>“Has not been studied in patients wearing contact lenses”</td>
<td>5 mL</td>
</tr>
<tr>
<td>Travatan Z</td>
<td>Travoprost 0.004%</td>
<td>sofZia</td>
<td>Remove lens before instilling; wait 15 minutes before reinserting lens</td>
<td>2.5 or 5 mL bottle</td>
</tr>
<tr>
<td>Zioptan</td>
<td>Tafluprost 0.0015%</td>
<td>None</td>
<td>Not addressed</td>
<td>30 or 90 SUV (in foil packs) One pack = 10 SUV (0.3 mL each)</td>
</tr>
</tbody>
</table>

SUV = single unit vial
single-unit vials should be discarded within 15 days.

- Due to excellent efficacy and tolerability, prostaglandins are often included in the management of patients with glaucoma and ocular hypertension. Travatan Z (travoprost 0.004%, Alcon) contains sofZia, an ionic-buffered system containing boric acid, propylene glycol, sorbitol and zinc chloride. These compounds break up into nontoxic ingredients when exposed to the ocular surface.

Zioptan (tafluprost 0.0015%, Merck) was approved in February 2012 and is the first preservative-free prostaglandin available in the US. The foil pouches contain 10 single-use vials, used once daily, with labeling that indicates the need to discard any vials within an opened foil pouch after 28 days. Cartons of 30- or 90-unit vials are available.

Should additional preservative-free medications be required, or if a patient needs a specific therapeutic agent not commercially available in a BAK-free formulation, consider a compounding pharmacy.

Remember that not all patients require BAK-free options. However, when patients use multiple drops, they are increasing their daily concentration of BAK—so, for contact lens wearers, patients with existing OSD or those with a known BAK sensitivity, consider avoiding the preservative. Fortunately, within the past year, there have been several new drug approvals to give us many BAK-free glaucoma options to help manage our glaucoma patients.


Make the Most of Everybody’s Time

GP lab consultations are a valuable resource for practitioners. Here are some ways to maximize the value of these appointments.

Whether it is getting started with a new fit or trying to improve a current one, GP lab consultants are an invaluable part of fitting GP lenses successfully. Many of us, however, do not take advantage of these consultation options as often or as effectively as we could. In this month’s column, I spoke with Dan Bell, president and lead consultant of Corneal Design Corporation in Gaithersburg, Md., to discuss how consultants view their interactions with contact lens fitters and to ask for suggestions on how to maximize the time and effectiveness of this communication.

Consultation Etiquette

• **Do not have a staff member fill your shoes.** First, and perhaps most importantly, Mr. Bell made it clear that consultations should involve the individual doing the fitting, not a staff person. When the individual who is calling into a consultation is not the one who has first-hand knowledge of the patient (e.g., seen the lens fit, discussed complications and knows the lens fit history), you do not get the most out of a consultant’s time.

  I had incorrectly assumed that, in most cases, the fitter was the one asking for a consultation. But Mr. Bell said that in almost half the cases, it is a staff person who calls to order the lens through consultation on behalf of the practitioner responsible for the fitting. Instead, ask your office staff only to order lenses that do not require consultation through customer service. Do not ask someone in consultation to work with a staff member who may not be prepared to answer questions based on patient interaction and as such, provide the information needed to optimize the fit.

• **Be thorough in your assessment.** If you anticipate the need for consultation, be sure to collect all data that may be crucial to consultation, including keratometry, over-refraction or fluorescein evaluations of the lens fit. When looking at a lens, Mr. Bell suggested not only to look at the fluorescein pattern but also to take note of how the lid interacts with the lens and what it looks like as the patient blinks and moves his or her eye.

• **Come prepared.** Mr. Bell said to collect all paperwork, including your patient’s chart, and complete the necessary testing prior to scheduling a consultation. Also be sure to inform your lab consultant about any potential complication(s) with the lens fit. Dry eye, thyroid disease, pregnancy, estrogen use and systemic medication use for conditions like high blood pressure or allergies are all important factors when trying to determine why a patient is struggling with lens wear or noticing changes in vision.

  Similarly, images of diagnostic tests (e.g., corneal topography) or photos of patients’ eyes with or without lenses can be very useful to consultants. Make sure that the images are high resolution and in color, so they can be accurately interpreted. Also, be sure to scan and email topographies rather than sending a fax.

• **Plan your schedule accordingly.** Block out an appropriate amount of time when you schedule your call with the lab consultant. Take the time to learn the specifications, materials and design of the lens you are discussing; how the consultant is planning to alter the parameters; and why these changes may improve the patient’s experience. The more you understand about how lab technicians can change a lens and why they are doing so, the less likely you are to need future consultations—and the more likely you are to take better advantage of the service.

Fitting guides are wonderful tools, and experience is priceless. But your lab consultant is also a crucial component of the GP lens fitting process. He or she is there to help make lens fittings easier and more predictable. Whether it is recommending the best design for a particular patient’s needs, helping to improve a fit that is not working as well as it could, or giving you the latest information on a lens design’s intricacies, your lab consultant should be a resource that you call on routinely.
Capitalize on the Astigmatic Presbyope

The newer multifocal designs can help give you an advantage in the presbyopic community.

As eye care practitioners, there are some facts we always know to be true. These include the trifecta: First, new fits generate revenue. Second, specialized contact lens fittings can improve loyalty and set your services apart from the competition. And third, the contact lens industry has developed new and innovative products—e.g., multifocal lenses—which help us offer our patients greater visual freedom by minimizing dependence on glasses.

While there are several ways to help define a practice, consider your strength in delivering new technology and become the local expert on a particular specialization. For example, astigmatic presbyopes are patients who likely have been told that they cannot wear contact lenses and/or only have been offered monovision prescriptions. We know that monovision lenses can be successful in some situations. But in comparison, the newer multifocal lenses improve both vision and depth perception.

By fitting specialized contact lenses, your practice will become synonymous with cutting-edge expertise, and you will likely see better patient retention and an increase in word-of-mouth patient referrals. And, despite worries about excessive chair time, specialty contact lens fitting typically yields higher gross margins, too.

The Patient Response

A decade ago, a Review of Optometry survey found a nearly even split between eye care professionals who fit monovision vs. multifocal contact lenses. Since then, significant improvements in multifocal technology have resulted in a noticeable shift in presbyopic fitting trends.

In a May 2006 study, 76% of patients reported that they preferred multifocal over monovision lenses. In July 2007, another study replicated those results and found a 3:1 ratio of patient preference for multifocal over monovision lenses. The researchers also further demonstrated the added advantage of multifocal contact lenses in the improvement of various visual measurements, including contrast sensitivity and depth perception. When successfully fit with multifocals, patients can enjoy improved binocular vision vs. monovision and improved peripheral vision vs. spectacles.

The technological advances in multifocal designs make the adjustment period relatively quick and easy. Patients also gain the ability to have an intermediate focus, which is particularly important for those with a high add. Keep in mind, however, that there are some patients who will be unsuccessful in multifocal designs and may be better served by monovision.

Office Visits

Take the time to identify your patients’ occupations, hobbies and daily visual requirements. This information will help you properly identify their visual needs and discuss reasonable expectations in advance of the fitting. By taking a few extra steps to customize the multifocal lens fitting to the individual patient’s daily visual tasks, you likely will derail contact lens dropouts and inevitably gain the respect of presbyopic patients—who will, in turn, serve as ambassadors for your practice.

Keep in mind that presbyopic patients tend to command more time and energy—including increased chair, staff...
and doctor time. Therefore, it is important to understand how to properly bill and code for these patients. Develop your protocol ahead of time so everyone is on board when these patients come in for their visit. For example, do you need a corneal topography at every follow-up appointment for a particular specialty fit? Which fitting sets are most important to keep in the office? By planning ahead, you will be appropriately compensated for your time and expertise.

Understand the Technology

• **Soft multifocals.** The soft multifocal toric market is the newest area of growth. These lenses combine the toric technology used to correct astigmatism with the most advanced soft multifocal lenses. This fitting process is two-fold. First, fit the toric correction and adjust for any rotation or instability. Second, customize the multifocal to the patient’s specific visual demands.

  Remember to discuss appropriate visual expectations, the associated fees and the importance of follow-up care. Review how these lenses can provide clear distance and near vision for a vast majority of visual tasks. Try not to bog down the conversation by going into too much detail on the technical aspects of the lens, such as design. Instead, focus on the expected timeline.

  **Note:** One of the major keys to success in fitting presbyopes with soft multifocal lenses is correcting the underlying low astigmatism. We know that uncorrected astigmatism results in distorted or blurred vision, as well as decreased “crispness” in visual acuity. It can cause headaches and eye fatigue. We also know that there is some loss of visual clarity with soft multifocal contact lenses. If we try to mask that cylinder, the overall loss adds up and the success rates decrease. We can help eliminate some of that by first correcting even low amounts of astigmatism. If there is any doubt, demonstrate the cylinder in the phoropter and listen to the response.

• **RGP multifocals.** For presbyopes, RGPs often can provide a greater range of clear vision, which enables the eye care professional to maximize both distance and near vision for their patients. RGPs also have the unique ability to mask irregularities of a compromised or irregular corneal surface.

  For some patients, RGPs are the only effective way to achieve the best visual function. Patients will most often have difficulties when excessive movement exists, so monitor the fit closely.

• **Hybrids.** The hybrid platform is an excellent example of how material science can help even those with unique visual needs wear contact lenses successfully. The only commercially available hybrid lens for this use is the SynergEyes lens, which provides increased oxygen delivery to the cornea through the soft and rigid gas-permeable portions of the lens. There were no previous high-Dk hybrid lenses on the market due to the difficulty in bonding hydrophilic skirts to this materials.

  Certainly, we will always have patients who are intolerant of any lens design. But, for patients who would benefit from the optics that an RGP delivers and cannot wear the lenses because of issues of discomfort, hybrid lens technologies should be considered. The soft skirt surrounding the RGP will lessen the lens awareness.

  Be comfortable and proficient as you work to satisfy the needs of your presbyopic patients. The newer multifocal designs provide good optics and comfort. Take advantage of this opportunity and grow your practice through your expertise.

Lessons Learned from Past Headlines

Man is a junkie for news. Most of us absorb knowledge so quickly—by scanning web pages and blogs—that we rarely, if ever, stop and listen to a remarkable story. When the world of optometry, as we knew it, was altered in 2006 and 2007, suddenly our peers were being interviewed by big media about Acanthamoeba and fungal keratitis.

We were concerned by the realization that although patients were presenting without classic symptomaticology, they were ultimately being diagnosed with sight-threatening pathologies due to the use of certain contact lens multipurpose solutions (MPS) and non-compliance. Reports of poor compliance behaviors and hygiene gave us great concern.1-4 We instructed patients to use specific products for contact lens disinfection. Before long, the issue subsided—as did our universal drive for emphasizing lens care.

Six years later, we are still caring for the same patient base with very complex ocular surface needs. But today we now have new information. As a result, the FDA conducted independent research studies and has recently published their findings.5

FDA Findings

The goal was to examine disinfection efficacy of a PHMB and POLYQUAD®/ALDOX® preserved solution in the presence of a contact lens. The FDA specifically questioned what the soft contact lens itself does to alter disinfection of commonly used products during storage in the lens case.

PHMB is a commonly used preservative in MPS brand-name products and many generic formulations. A single PHMB formulation was challenged with Staphylococcus aureus and Fusarium solani. Six silicone hydrogels and two conventional hydrogel lenses were added to the solution and subsequently challenged with the microbes during a six-, 12-, 24-, 72- or 168-hour soak.6

The FDA found that over time some lens materials can significantly reduce the PHMB concentration and the MPS microbial activity against Staph.6 In the F. solani study, seven of the eight lens materials significantly reduced the MPS’s ability to kill this microorganism and failed to consistently obtain a one-log reduction of F. solani after only a six-hour soak.7 In fact, three of the lens materials induced more than a 50% reduction of PHMB concentrations after only six hours of soaking.7 After a soak of 24 hours or more, three had lost all or almost all fungicidal activity.7 Several authors have indicated that MPS formulations have diminished antimicrobial activity after soaking with lenses.8 9 10

With the aforementioned approach, the FDA conducted a study challenging an MPS containing polyquaternium-1 0.001% (POLYQUAD® disinfectant) and myristamidopropyl dimethylamine 0.005% (ALDOX®) in its activity against Staph., after being used to store seven different soft contact lenses.8 Unlike the PHMB solution tested, the POLYQUAD®/ALDOX® disinfectant concentration in the lens cases was reduced only very slightly over time.8 The presence of the lenses did not adversely affect the biocidal activity of the solution and, in some cases, the efficacy was significantly better.8

Manufacturers introduced one-step MPS to afford our patients fewer procedures to follow and thereby enhance compliance.9 The FDA results highlight the need to carefully evaluate all MPS for their disinfectant potential in the presence of different contact lens materials.8

The FDA and others have reminded us that solution/lens interactions can have an impact on a contact lens wearer’s experience.

This news is worthy of our attention and our immediate response.

References


Because antibiotics are one of the more frequently used medication classes in any office, clinicians sometimes rely on well-established prescribing patterns without full consideration of alternative approaches or special considerations. Prudent prescribing requires knowledge of indications and contraindications for use, side effects and formulary or price comparisons. All of this information helps you select the appropriate antibiotic for your patient.

Remember that individual choices for antibiotic therapy and any additional medications will depend on the particular patient, severity of the condition and each practitioner’s overall management strategy. A patient’s systemic allergy profile and current medications may also limit antibiotic selection.

Specific actions and side effects of each antibiotic can be found in the individual drug’s package insert, Physician’s Desk Reference, various textbooks or through a consultation with the pharmacist.1-3

This article will present a decision tree for therapy guidance, including general directions and caveats concerning therapeutic choices for antibiotics.

Prescribing Antibiotics
There are a few overarching principles to guide a practitioner in starting antibiotic therapy. First, you should give the antibiotic at sufficient dosing to eradicate the particular insulting microbe. Low dosing or insufficient concentrations (minimum inhibitory concentration, \( \text{MIC}_{50} \) and \( \text{MIC}_{90} \)) of an antibiotic can be one of the causes of resistant strains of microbes.4-6

This is typically only advisable when a drug is being used for its anti-inflammatory profile, rather than its antimicrobial effect.7

Tailoring the chosen antibiotic to the suspected microbe’s sensitivity profile is another principle that is

**A Decision Tree: Proper Antibiotic Selection and Use**

When prescribing antibiotics, there are several factors you need to consider. Here is a guide to help you get started.

By William Miller, OD, MS, PhD

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often forgotten. As we have learned from resistance data, treatment should be sufficient to the task (hit it hard) for the minimum duration to cure the infection.

Lastly, in cases of microbe-derived inflammation, you should start with the most conservative treatment regimen necessary to accomplish the task of eradicating the microbe.

Eyelid Disease

Treating and managing blepharitis and meibomian gland dysfunction (MGD) is typically initiated after or during the application of conservative therapies, such as warm compresses and eyelid hygiene. When first-line, conservative therapy is insufficient or the blepharitis or MGD is recalcitrant, consider antibiotic therapy. Inadequate treatment is based on the continued presence of signs and symptoms of the eyelid disease.

For antimicrobial intervention, the go-to choice is topical ointment. Favorite antibiotic ointments include erythromycin and bacitracin, prescribed every night at bedtime for up to a month, after which the patient is re-evaluated for possible continuation, maintenance dosing or effective control using lid hygiene.

However, with the evolution of novel, more viscous carriers, at least one other medication may be appropriate at this stage of therapy—the macrolide antibiotic Azasite (azithromycin 1%, Inspire Pharmaceuticals). Although used off-label for this purpose, the effectiveness of Azasite in the treatment of eyelid disease can be traced to its viscous carrier, Durasite (polycarbophil), which increases the medication’s retention time and allows for more contact on the eyelid margin.

How does it work? Upon contact with a mucosal surface, a gel is formed that is released in a sustained fashion, providing a unique delivery model for use in blepharitis and MGD. As compared to other antibiotic ointments, Azasite provides minimal obscuration of vision, has anti-inflammatory properties that serve as an adjunctive therapy, and is relatively easy to apply. Remember to counsel your patient on out-of-pocket costs and third-party plan coverage.

Azasite is administered BID for two to three days, then QID for the remainder of the month. The patient should apply the drop to a closed eyelid and massage the medication into the base of the eyelashes. Azasite can be used in patients age one or older, while erythromycin is approved for patients as young as two months of age.

Finally, MGD has also been treated orally with low-dose tetracycline drugs, such as doxycline and minocycline. Usual therapy would consist of prescribing either 50mg to 100mg per day for several weeks, followed by titrating the dosage down for maintenance therapy. Be sure to warn patients about sun exposure, and do not prescribe low-dose tetracycline to pregnant women and children under the age of eight.

Bacterial Conjunctivitis

Most current topical ophthalmic antibiotics are explicitly FDA approved for bacterial conjunctivitis. Because most therapy is started empirically, it is sensible to use a broad-spectrum antibiotic. Considering the disease process is mostly self-limited and has a low visual morbidity, there may be no need to prescribe newer-generation antibiotics as a first-line treatment. They can be warranted as a second-line treatment strategy for recalcitrant cases or hyperacute situations.

Commonly used antibiotics for bacterial conjunctivitis include:
- Polytrim (polymyxin B/triamcinolone, Allergan) QID for seven to 10 days.
- Tobrex (tobramycin, Alcon) QID for seven to 10 days.
- Vigamox (moxifloxacin 0.5%, Alcon) TID for four to seven days.
- Zymar (gatifloxacin, Allergan) Q2H for two days and QID for day three to seven.
- Besivance (besifloxacin, Bausch + Lomb) TID for seven days.
- Azasite BID for two days and QD for five days.

Besivance and Azasite, the newest antibiotics on the market, offer certain unique attributes. As an ophthalmic-only medication, Besivance does not have a systemic counterpart to increase the possibility of resistance. And Azasite, through the Durasite carrier, increases the retention time on the ocular surface. In a five-day study Azasite showed a significant improvement in clinical resolution and bacterial eradication vs. placebo. In another trial, Azasite was found to be as effective as tobramycin, with rapid symptomatic resolution.

In cases of bacterial conjunctivitis, having the preservative-free option—Vigamox and Moxeza (moxifloxacin 0.5%, Alcon)—would control untoward effects on the cornea by preservatives. Other
Corneal Abrasion

In most cases, the selection of a topical antibiotic is not as critical, because the application is meant to provide prophylaxis against bacterial infection. However, if suspicion is heightened, select a more potent topical antibiotic. Increased suspicion may relate to the health or immune status of the patient. Concomitant ocular infection, such as blepharitis or MGD, could predispose the patient to an increased risk of corneal infection in a compromised corneal barrier.

Short-term use (fewer than two days) is generally sufficient, given that most abrasions will heal in that period of time. If healing is prolonged, the patient should continue to instill antibiotic drops. Dosing may vary, from four times a day to once an hour, depending on the size and depth of the abrasion. You may need to choose an antibiotic that can be used concurrently with contact lens wear, in which case a QD or BID dosing may be more convenient for the patient to avoid preservative uptake into the contact lens.

Because we are talking about short-term use, there is less of a concern over resistance. Remember to select an antibiotic that is least toxic to the newly regenerating corneal epithelium. Therapeutic recommendations include Polytrim or any of the fluoroquinolones (except the newest generation). The antibiotic may need to be altered or the treatment period extended if suspicions arise concerning likelihood of infection. There may be occasions when an antibiotic/steroid medication needs to be added to address the overall pathogenesis of the disease process. In these cases, remember to take all normal precautions regarding topical steroid use, including monitoring intraocular pressure and keeping the treatment protocol within a brief timeframe.

Microbial Keratitis

The most commonly associated risk factor for microbial keratitis is contact lens wear, followed by ocular surface disease, ocular trauma and ocular surgery. Pseudomonas aeruginosa is the most commonly isolated organism, followed by the Staphylococcus species and other gram positive microbes.

Iquix (1.5% levofloxacin, Vistakon), is the only FDA-approved antibiotic with a label indication for microbial keratitis. However, standard of care and sufficient peer-reviewed research suggests that you have other options as well, including the entire class of fluoroquinolones. Moderate to severe cases may respond to fourth-generation fluoroquinolones, which have been shown to have equivalent clinical activity. Dosing regimens depend on disease severity.

Because many mild cases of marginal keratitis are due to staphylococci, they can be treated using topical fluoroquinolones—Polytrim, tobramycin or gentamicin. Typical dosing should follow a QID regimen, even when the condition is mild. More aggressive therapy can be initiated when the condition is not responding to therapy or begins to worsen. For marginal keratitis, most practitioners may also opt for a topical steroid or antibiotic/steroid in cases that are immune-mediated and not likely infectious.

Cases of frank bacterial keratitis often are initially managed empirically with resultant cultures performed when the keratitis appears recalcitrant or is located centrally or paracentrally. Other factors that may indicate the need for culturing include corneal depth and or thinning, presence of satellite lesions, interaction with vegetative material, feather/rough infiltrative borders and recent care in a hospital environment. A typical treatment regimen includes instillation of a fluoroquinolone every 15 to 30 minutes for six to eight hours, then every hour until the patient begins to show improvement. Dosing is then titrated based on signs and symptoms until the offending bacterial organism is removed.

Severe central and paracentral cases of bacterial keratitis can be treated quite successfully with the new generation of fluoroquinolones—Moxeza and Zymaxid. Also consider fortified antibiotics such as vancomycin (25mg/ml to 50mg/ml), which can be combined with tobramycin/gentamicin (9mg/ml to 14mg/ml) or ceftazidime (50mg/ml). No published studies have investigated the effectiveness of Moxeza and Zymaxid in bacterial keratitis.
treatment. At least one study found Moxeza to have a greater conjunctival tissue concentration than Vigamox, which might shed light on its enhanced penetration into ocular tissue.24

Umost care and judicious prescribing as well as prudent follow-up care are necessary to prevent ocular morbidity. In some cases, you may want to consult with a corneal specialist, depending upon the practitioner’s experience and training on severe forms of bacterial keratitis.

Prophylaxis and Postoperative Refractive Surgery
As in corneal abrasion treatment, the goal in postoperative refractive surgery is to prevent the onset of bacterial infection. Therefore, a broad-spectrum antibiotic that is nontoxic to the healing cornea is preferred. The patient will likely be administered the antibiotic short-term and other topical drops, such as corticosteroids, will accompany the treatment.

Refractive surgeons will make individual recommendations and those will most likely include fluoroquinolone choices, such as Vigamox QID for one week and Bescivin TID for seven days.27,28 Although not approved for postoperative refractive surgery patients, some surgeons are also opting for Zydamox or Moxeza BID or QID for six to seven days.

Keep in mind that a recent ASCRS alert advised against the use of Bescivin, Moxeza and azithromycin among other medications pre- or intraoperatively in refractive surgery, because the drugs contain vehicles to enhance retention on the ocular surface and can potentially be sequestered beneath a LASIK flap or bandage contact lens, such as in the case of photorefractive keratectomy (PRK). This could lead to flap displacement or diffuse lamellar keratitis in LASIK cases and decreased epithelial healing in PRK.27 The alert also mentioned select topical steroids and tear supplements that contain similar vehicles to enhance retention time.

Individual antibiotic choices vary based on the prescribing doctor, and the above is meant to serve as a guide to aid in decision-making. Note: In cases of suspected MRSA or MRSE, the Ocular TRUST study found that likely the best choices are trimethoprim with polymyxin B, gentamicin, tobramycin and vancomycin.30


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CE TEST

1. Which fundamental principle should guide a practitioner’s use of topical antibiotic for ocular surface infections?
   a. Use medication with the lowest efficacy.
   b. Intermittent use is preferable.
   c. Sufficient concentration (MIC₉₀) should be used.
   d. None of the above.

2. Which agent has been used as a vehicle to increase the retention time of Azasite?
   a. Polycarbophil.
   b. Polyvinyl alcohol.
   c. Petrolatum.
   d. Carboxymethylcellulose.

3. When treating blepharitis with Azasite, what is the indicated dosing frequency?
   a. QD.
   b. BID.
   c. TID.
   d. QID.

4. Which topical antibiotic does NOT have a systemic equivalent?
   a. Vigamox.
   b. Ciloxan.
   c. Besivance.
   d. Azasite.

5. What is the most common organism found in an otherwise healthy patient with microbial keratitis?
   a. *Streptococcus*.
   b. *Listeria*.
   c. *Pseudomonas aeruginosa*.
   d. Methicillin-resistant *Staphylococcus aureus*.

6. Which agent is FDA-approved for the treatment of microbial keratitis?
   a. Iquix.
   b. Ciloxan.
   c. Besivance.
   d. Zymaxid.

7. An indication for corneal culturing includes:
   a. Marginal infiltrate placement.
   b. Pinpoint ulceration.
   c. Satellite lesions.
   d. Infiltrates with intact overlying epithelium.

8. Contemporary topical antibiotics with specialized vehicles in post-LASIK patients may cause:
   a. Epithelial ingrowth.
   b. Diffuse lamellar keratitis.
   c. Transient light sensitivity syndrome.
   d. Central islands.

9. Which topical antibiotic contains a vehicle that increases drug retention time on the ocular surface?
   a. Vigamox.
   b. Ciloxan.
   c. Iquix.
   d. Moxeza.

10. According to results from the Ocular TRUST study, which topical antibiotic might be the best choice to combat MRSA?
    a. Tobramycin.
    b. Ciloxan.
    c. Iquix.
    d. Ocuflox.
A Checklist for Steroid Use in the Compromised Cornea

If you can rule out contraindications, aggressive steroid therapy may help minimize the risk of future complications.

By Paul M. Karpecki, OD

Have you noticed corneal disease patients who present with a rise in intraocular pressure, developing cataracts and secondary infections? As you may have guessed, these are all potential adverse effects of corticosteroid use in the treatment and management of corneal disease. However, in my experience, I more frequently see complications due to the withholding of a corticosteroid in corneal disease when it should have been prescribed. Such undue caution can result in corneal neovascularization, prolonged infiltrative keratitis, uncontrolled uveitis, persistent patient symptoms and even corneal scarring. In a number of these cases, the patient was left with only one option—corneal transplant. That said, I add the caveat that practitioners must always be cautious in the use of corticosteroids, and instruct patients to use them appropriately so as to minimize any risks.

Aside from prescriptions related to surgical care, optometry writes more prescriptions for certain steroids, such as Lotemax (loteprednol 0.5%, Bausch + Lomb) than any other medical profession. So, while we are comfortable with the use of corticosteroids, it can be helpful to have a refresher course on the do’s and don’ts of proper use.

Corticosteroids

When incorporating steroids into your treatment plan, there are three potential concerns: IOP elevation (which could lead to glaucoma), secondary infections due to the immunosuppressive nature of corticosteroids and the formation of posterior subcapsular cataracts.

Newer versions of these agents—ester-based steroids—have significantly reduced complication rates. One recent multicenter study comparing dexamethasone to ketone-free loteprednol found half as many cases...
of significant IOP elevation with loteprednol. These findings were comparable to previous analyses. Ketones can form a Schiff base, which is a precursor to cataract development; the absence of a ketone in loteprednol precludes this from occurring. However, decreasing the risk of IOP elevation with an ester-based steroid does not eliminate the risk of significant IOP elevation—especially with long-term use.

Don’ts

• Don’t write refills. This is perhaps more of a personal preference, but I strongly recommend that you do not allow refills—especially on the first prescription for a corticosteroid. Often, the comfort perceived by a patient using topical steroids can lead them to continue the therapy long-term.

  If a patient is prescribed multiple refills, they may no longer experience any symptoms and choose not to return to the office, without awareness that their intraocular pressure may be elevated. If you do not write a refill, the patient is forced to return to your office for an IOP check before he or she can receive another prescription.

  Similarly, a compromised cornea might preclude the use of corticosteroids, such as in the presence of an abrasion. Once the epithelium is breached, there is an increased risk of potential infection. Suppressing the immune system with corticosteroids in an already present trauma situation, where the epithelium has been debrided, could lead to a potential secondary infection.

• Don’t mix steroids and contact lenses. There is some debate as to whether a corticosteroid should be applied on top of a contact lens. I believe that the absorption of medication into a contact lens can alter the effects of the drug on the cornea, due to increased contact time (because the lens acts as a drug reservoir). This could lead to prolonged steroid exposure and potentially increase the individual’s risk of complications.

  In the giant papillary conjunctivitis trials, patients were administered loteprednol drops on top of a contact lens. Even though there

  Don’t forget the well-known infectious keratitis contraindications. This includes the presence of epithelial herpes simplex keratitis (whether it be dendritic, geographic, marginal ulcer or any epithelial form). Simply put, patients diagnosed with HSV keratitis in the presence of corneal staining should not be prescribed corticosteroids. Other infectious conditions that could worsen under the presence of a corticosteroid include fungal keratitis, mycobacterium and even bacterial keratitis (especially in the early stages).

  The Steroids for Corneal Ulcers Trial (SCUT) found that use of corticosteroids in addition to antibiotics for the treatment of bacterial keratitis did not help or hinder healing or complication rates. In fact, more severe bacterial keratitis patients in the SCUT appeared to have a better outcome if corticosteroids were used after the second day and throughout the long-term follow-up.

  It is best to avoid steroids during the early acute phase of a bacterial keratitis; typically, this would mean the first two days for gram-positive bacterial infection and possibly 72 hours for gram-negative rods, such as Pseudomonas aeruginosa.

  I would also advise against using corticosteroids when treating a bacterial corneal ulcer, unless a 48- to 72-hour window (depending on the cultured pathogen) has passed and improvement is noted in the clinical picture. Positive signs include significant epithelialization progress and a pathogen identified via culture that is shown to be susceptible to the drugs being applied. If all of these are met, corticosteroids could indeed decrease the level of inflammation and prevent corneal scarring in a bacterial keratitis.

  • Don’t forget to take a detailed patient history. Avoid corticosteroid use on a compromised cornea in patients with uncontrolled systemic diseases (such as arthritis or lupus) when either an infiltrate or corneal thinning is noted. Unless the systemic disease control is well noted, a corticosteroid could lead to increased breakdown of the epithelium because the patient’s systemic disease is causing further corneal damage.

  In other words, a corticosteroid might be contraindicated in a patient presenting with rheumatoid arthritis and a corneal melt, which is an indication of poorly controlled rheumatoid arthritis. A better choice of treatment would be systemic immunosuppression via a rheumatologist.

  • Don’t mix steroids and contact lenses. There is some debate as to whether a corticosteroid should be applied on top of a contact lens. I believe that the absorption of medication into a contact lens can alter the effects of the drug on the cornea, due to increased contact time (because the lens acts as a drug reservoir). This could lead to prolonged steroid exposure and potentially increase the individual’s risk of complications.

  In the giant papillary conjunctivitis trials, patients were administered loteprednol drops on top of a contact lens. Even though there
were no corneal complications (e.g., infection), the results showed that these patients had a significantly higher incidence of IOP rise vs. studies where a contact lens was not involved. Therefore, it can be assumed that the safety related to IOP rise of even an ester-based corticosteroid is somewhat lost if the drug resides within the contact lens throughout the day. It should also be mentioned that there were no secondary infections reported in any of the patients who received corticosteroid drops directly on the contact lens during clinical trial.\(^7\)

**Dos**

- **Do use corticosteroids in a timely manner.** When a corticosteroid is warranted, withholding it could lead to even greater complications, such as scarring or neovascularization. We have few medications on the market that are angiotensive—i.e., can prevent corneal neovascularization as well as give comprehensive inflammation suppression. For that reason, if corneal neovascularization is present and encroaching the visual axis, it is critical that aggressive corticosteroid therapy be used.

Likewise, infiltrative or inflammatory corneal events require the use of aggressive corticosteroids. However, if a contact lens peripheral infiltrate is noted because the cornea is compromised, it would be more prudent for a practitioner to use a steroid/antibiotic combination agent as opposed to simply pure corticosteroids. Inflammatory conditions tend to be closer to the limbus and often have epithelial defects or staining that is much smaller than the actual infiltrate's size.

- **Do look for critical signs.** Always be cautious of the potential signs of an infectious keratitis in the presence of an infiltrate. This typically can be found in patients with significant symptoms, such as acute onset pain and photophobia, a very red eye \(360^\circ\) in the conjunctiva, decreased vision and the presence of discharge.

  The critical signs of a bacterial keratitis include lid edema, an epithelial defect over an infiltrate with significant staining and an anterior chamber reaction. If the signs are more indicative of a chronic inflammatory event, use steroids readily and aggressively via a combination steroid/antibiotic drop to help the patient with pain and inflammation.

- **Do pick the right delivery method.** Because we have so many options and delivery forms of corticosteroids, ranging from suspensions to emulsions to gels and ointments, it is wise to become familiar with all of the different options and how to use them when the appropriate patient presents.

  For example, the addition of an overnight steroid ungl to daily drops can dramatically improve the level of inflammation when treating iritis. An overnight corticosteroid ointment can also help patients with morning symptoms and/or significant meibomian gland dysfunction.

Since resuspension requires 20-30 bottle shakes, try to select medications that do not require resuspension. Three corticosteroid formulations on the market today—Lotemax gel, Lotemax ointment and Durezol (difluprednate 0.05%, Alcon)—report complete uniformity in each drop. This is critical when treating significant inflammation where an inappropriate amount of drug can result in iritis, uveitis or non-infectious infiltrative keratitis.

Prescribing steroids is essential to successful clinical practice and good patient outcomes. When a patient with a compromised cornea presents, doctors must use caution to determine if corticosteroids could cause harm. Clinicians must look for key signs—everything from infectious keratitis to epithelial defects and even active systemic disease—to determine if a corticosteroid is contraindicated. If not contraindicated, aggressive steroid therapy is warranted and may prevent serious complications.\(^{1-8}\)

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1. Chen M, Gong L, Sun X. A multicenter, randomized, parallel-group, clinical trial comparing the safety and efficacy of loteprednol etabonate 0.5%/tobramycin 0.3% with dexamethasone 0.1%/tobramycin 0.3% in the treatment of Chinese patients with blepharokeratoconjunctivitis. Curr Med Res Opin. 2012 Mar;28(3):385-94.
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Imagine a world where the physical characteristics of a material change as it becomes smaller, or where submicroscopic surgical instruments can be used to repair damaged nerves. This may sound like a scene out of a science fiction movie, but it is our reality today. More so, this technology provides an excellent opportunity to diagnose and treat disease at the molecular level. What are we talking about? It is the world of nanoscience, nanotechnology, and nanomedicine.

A Nano Approach

Let’s start by defining the key players:

- **Nanoscience** refers to the “fundamental study of phenomena and the manipulation of matter at the atomic, molecular, and supramolecular level, where properties differ significantly from those at a larger scale.”

- **Nanotechnology** denotes “the design, characterization, production, and application of structures, devices, and systems that have novel physical, chemical, and biological properties by controlling shape and size at the nanometer scale.”

- **Nanomedicine** encompasses a broad range of technologies. It is defined as, “the science and technology of diagnosing, treating and preventing disease and traumatic injury; of relieving pain and of preserving and improving human health; and using nanoscale structured materials, biotechnology, genetic engineering, and eventually complex machine systems and nanorobots.”

Derived from the Greek word *nano*, or dwarf, a nanometer is one billionth (10⁻⁹) of a meter. Conceptualizing something that minute can be challenging, so contemplate this: A nanometer is proportional to a meter in the same way that a marble is comparative to the earth. To further put that into perspective, the diameter of a double strand of DNA is around 2nm.

Using nanotechnology, we can now manufacture particles no larger than a viral particle or bacterium. Nanoparticles typically are defined as clusters of atoms that range in size from 1nm to 100nm (some objects up to 200nm may still fall under this definition). The properties of a material in nanoscale may differ dramatically from the properties it exhibits as larger particles. For example, in both the “conventional” scale (e.g., a can) or in the “micro” scale (e.g., powder), aluminum possesses the same basic qualities. However, as a nanoparticle aluminum can spontaneously burst into flames.

Implications for the Eye

Nanotechnology offers great promise in health care. The particles are roughly the same size—or, in some
cases, smaller than—the infectious agents that cause disease. For example, a virus is roughly 100nm in diameter, while bacteria are about 10 times as large. Nanoparticles are also similar in size to basic physiologic molecules found in nature: A glucose molecule is approximately 1nm in diameter and an antibody is roughly 10nm in size.

The eye, in particular, may be a very viable site for nanotherapy. The lipophilic corneal epithelium, hydrophilic stroma of the cornea and sclera, conjunctival lymphatics, and blood-eye barrier often make it difficult for molecules to be absorbed into the eye. Topical administration is usually the preferred means of delivering a medication to the eye but, because of the factors previously mentioned, it may be an inconsistent or inefficient means of conveying molecules into the eye. Typically, less than 5% of a topically applied dose reaches the anterior ocular tissues. Incorporating a therapeutic molecule into a nanoparticle may allow better targeting of specific tissues or organs using a significantly lower concentration of drug.

Medications successfully formulated from nanoparticles theoretically would have the potential to deliver adequate intraocular concentrations of a drug to the anterior and posterior eye at lower surface concentrations. This is partially due their small size and the type of structures they form.

**Drug Delivery**

Our understanding of glaucoma has increased exponentially over the past two decades. Still, the reduction of intraocular pressure continues to be the primary method of treating this condition. Unfortunately, current therapy is not free of complications or side effects, which can negatively impact a patient’s quality of life. Treatment itself also may be unsuccessful, especially when you consider that patients may forget to take their medications and/or not be able to pay for the costly doses. In addition, preservatives in glaucoma medications can negatively affect the ocular surface to the point of surgical intervention.

Consider the benefits of incorporating nanomolecules into ocular tension-lowering medications. Jayaganesh Natarajan, PhD, and colleagues fabricated latanoprost-loaded egg-phosphatidylcholine (EggPC) liposomes, each with an approximate diameter of 109nm. Following a single subconjunctival injection of the liposome formulation vs. the eyes treated daily with topical latanoprost solution.

- **Liposomes** are nanoscale spherical vesicles that can be produced from natural phospholipids and cholesterol (see figure 1). Their structure forms when phospholipids are combined with water; the immediate result is a bilayered sphere. One end of each molecule is water soluble, while the opposite end is water insoluble. This configuration allows for delivery of both lipophilic drug molecules incorporated into the bilayer and water-soluble drugs that are trapped inside the liposomal cavity.

- **Micelles** are lipid molecules arranged in a spherical form in aqueous solutions (see figure 2). Their configuration resembles that of liposomes and results from the amphipathic nature of fatty acids (e.g., they contain both a hydrophobic and hydrophilic [polar] end groups). In water, the polar end faces toward the outer surface of the micelle. Micelles offer distinct advantages over conventional delivery because of their small size, reduced toxicity, ability to solubilize drugs and targetability.

Several studies have evaluated the feasibility of micelles as carriers for ophthalmic medications. When applied topically onto the eye, cyclosporin A (CsA) physically entrapped into micelles displayed a prolonged residence time. Topical ketorolac physically entrapped into micelles was compared to the administration of the conventional aqueous preparation; corneal penetration of the micelle preparation was significantly higher than the conventional aqueous suspension and demonstrated higher inflammatory activity. These studies suggest that micelles also may prove to be an excellent alternative...
to conventional ophthalmic preparations.

Severe uveitis is a potentially blinding disease that is often treated with triamcinolone acetonide (TA). Because TA is a water-insoluble corticosteroid, it is typically delivered by subtenon, subconjunctival or intravitreal injection. Intravitreal steroid injection may cause complications, including cataract formation, retinal detachment, hemorrhage and intraocular pressure elevation. In a study using a rabbit model of uveitis, María Rodríguez-Blanco and colleagues compared intravitreal TA suspension to topical TA in nanospheres (TA-NP) and topical prednisolone acetate (PA) suspension.16

While this is an animal-based study, it demonstrates that topical NP provides a pharmaceutical benefit comparable to intravitreal injections of the conventional form of the drug.

**Antimicrobial Efficiency**

The recent increase in antibiotic-resistant bacteria is an issue of great concern to health care providers. This phenomenon has been attributed to several factors, including overprescribing of antibiotics. One plausible means of circumventing this problem is through the use of nanoparticle carriers of antibiotics. By modifying materials at the atomic level, nano-sized organic and inorganic particles can be generated for eventual use in health care. The capability of nanoparticles to kill bacteria largely is a simple matter of size. Bacterial cell size is in the micrometric range (500nm to 5000nm). Bacterial outer cellular membranes have pores in the nanometer range (5nm to 50nm). Because nanoparticles can be smaller in size than bacterial pores, they can actually cross cell membranes. One example of this is the use of nano-sized molecules containing metal oxides.19

Ameer Azam, PhD, and colleagues evaluated the antimicrobial efficacy of nano-sized particles of zinc oxide 18nm (ZnO), copper oxide 22nm (CuO) and ferrous oxide 28nm (FeO). The nanoparticles were synthesized by gel-combustion method and their antibacterial activities were tested against two gram-positive bacterial strains (S. aureus and Bacillus subtilis) and two gram-negative bacterial strains (Pseudomonas aeruginosa and E. coli). The results revealed that ZnO and CuO nanoparticles had excellent antibacterial activity against both gram-positive and gram-negative bacteria. The evidence generally indicates that the smaller the size of the nanoparticle, the more active it is against bacteria. For example, ZnO was 75% more effective than FeO, and 28% more effective than CuO against E. coli.20

Justin T. Seil, PhD, and Thomas J. Webster, PhD, confirmed the significant antibacterial effect of ZnO. They reported that, after just eight hours of exposure to ZnO nanoparticles, there was in excess of a four-log reduction in Staphylococcus aureus. When they added ultrasound to the nanoparticle regimen, they noted an additional 76% reduction in the number of viable colony-forming units.

The size and unique attributes of the eye make it an excellent subject for nanotechnology. The applications discussed in this article represent just a small fraction of the research and technology already completed and under development. We are learning that the potential applications of nanotechnology within eye care are almost limitless and nanotechnology may eradicate some of the conditions and illnesses that steal our vision, shorten our lives or reduce our quality of life.
These days, practitioners constantly hear and see the word “biocompatibility.” Whether related to a new contact lens or solution, it is certainly the buzzword among researchers and manufacturers. This article will review the literature on clinical testing to better understand the concepts as they relate to lens materials.

**Defining the Terms**

Biocompatibility is traditionally defined as a medical device free of toxic or injurious effects on biological systems, or the extent to which a foreign material fails to elicit an immune or other response in the recipient. Eye care practitioners may want to take this a step further to include the concept of mimicking a part of the body (e.g., the ocular surface), where a device such as a contact lens is placed. That is to say, a biocompatible product would have some property, whether inherent in the contact lens polymer or added to the lens after polymerization, that is similar to the cornea or components of the tear film.

**Omafilcon A**

While many lenses might be described as biocompatible, omafilcon A (Proclear, CooperVision) was one of the first polymers touted to mimic the ocular surface. Omafilcon A is a 62% water content material composed of 2-hydroxyethylmethacrylate (HEMA) and 2-methacryloyloxyethyl phosphorylcholine (PC) polymers crosslinked with ethylene-glycol dimethacrylate. PC is similar to phospholipids (e.g., phosphatidylcholine), which are molecules found naturally in human cell membranes (figures 1a and 1b).

Due to their zwitterionic nature (e.g., they contain both positive and negative charges), these molecules
can bond hydrogen with water. Therefore, they attract and surround themselves with water molecules. This property is why daily disposable manufacturers claim that omafilcon A lenses stay “moist and comfortable, even after 12 hours of wear.”

According to the manufacturer, omafilcon A lenses are the only contact lenses cleared by the FDA to “provide improved comfort for contact lens wearers who experience mild discomfort or symptoms relating to dryness during lens wear.” Studies have shown a reduced likelihood of omafilcon A lenses to dehydrate on-eye. Despite increased tear film evaporation rates and decreased tear film break-up times (TFBUTs), omafilcon A lenses have been shown to be relatively sparing of the pre-lens tear film lipid layer structure. Omafilcon A lenses show improved symptoms of dryness and discomfort—compared to habitual lenses in some studies, (although others conflict). Studies have shown a reduced likelihood of omafilcon A lenses to dehydrate on-eye. Despite increased tear film evaporation rates and decreased tear film break-up times (TFBUTs), omafilcon A lenses have been shown to be relatively sparing of the pre-lens tear film lipid layer structure. Omafilcon A lenses show improved symptoms of dryness and discomfort—compared to habitual lenses in some studies, (although others conflict). Delefilcon A lens material containing phosphatidylcholine is the newest technology on the market. The delefilcon A lens (Alcon) is a silicone-containing hydrogel described as possessing a water gradient—from 33% water at core to >80% water at surface, which is only 6µm thick. The manufacturer claims that the 80% water content closely mimics that of the cornea. In addition, this lens is packaged in phosphate-buffered saline solution containing approximately 0.3% of polymeric wetting agents—copolymers of polyamidoamine and poly(acrylamide-acrylic acid). The material is sold for single use daily disposable lens wear.

The published literature on the new delefilcon A material is limited, but research is beginning to show an association between its lubricity profile and subjective reports of comfort. It is known to have a low contact angle hysteresis, which implies better surface wettability (at least in the laboratory). Other physicochemical and biochemical factors beyond wettability also influence ocular response to lens wear and will require study. It will be interesting to see if the reports of good clinical performance of the omafilcon A lens, which contains phosphorylcholine—chemically similar to the phosphatidylcholine in delefilcon A—are replicated for this lens type.

Nelfilcon A

Another lens material described as biocompatible is nelfilcon A (Alcon), a polymer of polyvinyl alcohol partially acetalized with N-formylmethyl acrylamide and with a 69% water content. The packaging contains the moisturizing agents hydroxypropyl methylcellulose (HPMC), polyethylene glycol (PEG) and polyvinyl alcohol (PVA). The manufacturer calls PVA (figure 2) a comfort enhancer that gives the lens “outstanding” hydrophilic properties, such as a very low contact angle (which provides better moisture coverage). PVA is also described an agent that helps to stabilize the tear film and that works in synergy with the other agents to continuously lubricate the lens for improved comfort. HPMC is claimed to optimize the viscosity of the packaging solution to provide superior comfort upon insertion. The manufacturer states that the eye’s natural blinking action releases PVA from the lens, and it and the other moisturizing agents are gradually released over a 20-hour period. Furthermore, this release is associated with “built-in, single-day compliance.”

Prior to the release of this lens, PVA was used in ocular drops and shown to improve TFBUT. If used at a concentration of 1.4% (w/v) PVA improved...
polynvinyl pyrrolidone (PVP) have been used in many different lenses over the years, such as senofilcon A (which uses PVP) or vifilcon A (containing NVP). However, whether the improvements in symptoms or clinical performance with senofilcon A lenses is due to the presence of the vinyl pyrrolidone or other factors such as lens design is not known. Recent evidence suggests that the presence of PVP in narafilcon A lenses is not associated with improved clinical performance in terms of dryness and corneal staining.

Contact lenses generally are biocompatible with the ocular surface, in the sense that they are not toxic and are generally well tolerated by the ocular tissue. The development of materials that are attempting to mimic specific aspects of the ocular surface—be that the water content of the cornea or a structuring of the tear film or the lipid layer of the tear film—is exciting. It seems the days are gone when it was thought that to be biocompatible, the lens should have no interactions with the eye. It will be interesting to see whether the claims of lenses with surface water content similar to the cornea translate into improved clinical performance and biocompatibility with the cornea.

Past experience with high water HEMA-based lenses showed equivocal results for dryness symptoms during wear, and dryness symptoms in relation to lens dehydration. Perhaps the new generation of high water content lenses, or high water content lens surfaces, do not dehydrate as much or as rapidly on-eye? I eagerly await results of clinical trials with these new lenses.

How Will Unemployment Impact You?

Even in a weak economy, there are ways every practice can build and grow.

We rarely hear the argument that high unemployment (or a weak economy) is good for your practice’s bottom line. After all, reason suggests that if your patients don’t have a job, they will likely either avoid coming to your practice entirely or be especially thrifty when they do. But have you considered how unemployment affects your current staff and how that, in turn, impacts your practice?

The rate of unemployment is improving, but at a snail’s pace. Updates about the status of our economy still headline the daily news, and the lingering impact remains at the forefront of our minds. Regardless of whether your staffing situation is good, bad or neutral, the constant reminder of the large number of unemployed in our country can be a help or hindrance to your practice. Let’s look at both sides of the equation.

The Positives

High unemployment rates can mean, at least theoretically, that more people are out of work and looking for jobs. If your current satisfaction with your staff is less than ideal, now might be a good time to try to improve your team. With more people in the job applicant pool, you should have more qualified candidates and increased opportunities to find the best fit for your practice. Be selective and take your time ensuring your next hire is a great fit.

Some positions we need to fill require highly skilled employees, but I would suggest that you focus on filling the vacancies that do not require specialization. Keep in mind that someone who has been out of work for a while may accept lower pay and/or a lesser skilled job. When the economy turns or they find a better-suited position, there’s a chance they will move on. However, because nobody can predict such timelines or other extenuating factors, I’d consider that a risk worth taking.

The Negatives

On the other side of the equation, if a current employee is not happy with his or her position, they might hesitate to leave for fear of not finding another job. Someone who isn’t enthusiastic about their position, or is perhaps burned out due to a hectic schedule, is a drain on your practice’s productivity and profits.

On a related note, it’s typical for marginally happy staff members to begin looking around for other opportunities while working for you. This may lead to subpar job performance. While personal web surfing on the clock should never be permitted, if you do see this happening, be on the lookout for an unhappy employee and be prepared to replace him or her as needed.

Remember that staff training should be routine, regardless of the economy and unemployment numbers. A well-trained staff increases employee loyalty to your practice and reduces subpar performance that may lead you to turnover.

Note: Staff members frequently report that they left a practice because they were never properly trained and, as a result, the expectations of the owner were never clearly communicated.

While high unemployment rates certainly aren’t something to celebrate, there is a silver lining. From a patient-spending perspective, high unemployment may be bad for your practice’s finances. But use this opportunity to strengthen your team and even this economy can be a boon to your practice.
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