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2012 ARVO Explores Microbial Keratitis

This year’s ARVO meeting explores practitioner strategies and treatment options for microbial keratitis.

Each year, eye care practitioners are provided with an opportunity to gain insight on the latest groundbreaking research in vision science. And, this year’s Association for Research in Vision and Ophthalmology (ARVO) annual meeting, held May 6-10 in Ft. Lauderdale, Fla., delivered. Research presented at this annual event helps practitioners formulate best practices through evidence-based science and stimulates researchers to ask, and attempt to answer, additional questions pertinent to clinical practice.

This year’s abstract review topic was microbial keratitis—an important conversation due to the devastating consequences the disease leaves in its wake. The abstracts presented at ARVO were teeming with helpful tools designed to help the practitioner develop new strategies, direct treatment plans and ultimately improve patient outcomes.

Program #6132
Pseudomonas aeruginosa Keratitis: Pathogen Genotype Impacts Clinical Presentation and Outcomes

Researchers from UC San Francisco, UC Berkeley School of Optometry and the Aravind Eye Hospital in Madurai, India assessed how cytotoxicity and invasiveness, two P. aeruginosa virulence factors, affect clinical outcomes and corneal baseline characteristics. Ulcers caused by P. aeruginosa with the invasive genotype presented with better visual acuity, but were associated with less improvement at three months when compared to cytotoxic ulcers. Steroids were associated with better outcomes for invasive P. aeruginosa corneal ulcers but with worse outcomes for cytotoxic ulcers. A tailored treatment approach by genotypic subtype using PCR testing may be advisable for P. aeruginosa keratitis.

Program #6133
Virulence Factors in Pseudomonas aeruginosa Keratitis

Researchers in Liverpool, United Kingdom, identified virulence factors in cases of P. aeruginosa keratitis to be used in personalizing treatments and prognosis. Clinical outcome data showed that clone A, serotype O11 and the presence of exoS were associated with prolonged healing time, larger corneal ulcers and gentamicin resistance. Identification of clonal type and virulence factor exoS is of prognostic significance. When these factors are present in patients with P. aeruginosa keratitis, it may help future therapies and target treatment.

Program #6134
The Role of Dendritic Cells in Flagellin-Induced Protection Against Pseudomonas aeruginosa Keratitis

Researchers at Wayne State University and the Kresge Eye Institute in Michigan studied underlying mechanisms for flagellin-induced dendritic cell (DC) recruitment and/or activation and defined their role in corneal innate defense. Dendritic cells are recruited and/or activated in the cornea’s response to flagellin. Deletion of DCs increased corneal innate susceptibility to P. aeruginosa and abolished flagellin-induced protection in B6 mice. Dendritic cells play a critical role in corneal innate immunity and defining their role opens a new area of investigation.

Program #6139
Genotypic Characterization of Acanthamoeba keratitis

Researchers at the Ehime University Graduate School of Medicine in Toonishi, Japan investigated the genotypic characterization of methicillin-susceptible S. aureus (MSSA) and methicillin-resistant S. aureus (MRSA) isolates from eyes with keratitis and healthy conjunctival sacs. MRSA isolates from eyes with keratitis have genotypic characteristics similar to those of commensal MRSA strains, but certain sequences occur more often in MSSA isolates from eyes with keratitis than in commensal MSSA strains. The results suggest that MSSA lineages with specific genotypic characteristics are more likely to cause keratitis. S. aureus remains a common ocular pathogen with emerging resistance in practice. Additional research looking at the virulence of particular lineages should aid in the management of these common corneal infections.

Program #6140
Molecular Characterization of Virulence Genes Associated with MRSA Keratitis Isolates

Researchers at the Bascom Palmer Eye Institute in Miami identified and characterized the molecular spectrum and frequency of virulence genes associated with MRSA isolates recovered from keratitis. Findings revealed that MRSA isolates recovered from keratitis are predominantly healthcare-related (SCCmec II), PVL negative and harbor the quorum-sensing genotype for vancomycin heteroresistance (agrII). This combination of virulence genes may impact efficacy and selection of antibiotic prophylaxis, and therapeutic management of patients with MRSA keratitis.

Program #6145
Acanthamoeba-Associated Microbial Communities

Researchers at the Bascom Palmer Eye Institute, University of Miami School of Medicine and the University of Washington School of Medicine, used a combination of
metagenomics and next-generation sequencing techniques to document the presence, complexity and diversity of Acanthamoeba-associated microbial communities in isolates recovered from patients with amoebic keratitis. Culture-independent molecular methods reveal complex and diverse Acanthamoeba-associated microbial communities in clinical isolates. Community complexity and diversity may impact clinical severity, course and time to cure. Acanthamoeba may harbor unique microorganisms that might contribute to the severity of the disease.

Program #6149
**Bilateral Herpetic Keratoconjunctivitis in Cancer Patients**
This study, conducted at the University of Texas in Houston, is the first in literature to retrospectively review and describe bilateral HSV and HZV keratoconjunctivitis in 90 cancer patients. It was most frequently observed in patients on systemic steroids and an immune-compromised patient population despite prophylaxis for herpetic disease. Bilateral presentations signal concern for atopy (cited in past research) or an immune-compromised state possibly in occult cancer patients. Future studies are necessary to elucidate predisposing factors for bilateral disease in this population.

Program #6064
**Boston Type 1 Keratoprosthesis: Microbial Colonization and Antibacterial Resistance**
Investigators at the Hospital of the University of Montreal characterized the ocular flora of patients who had the boston keratoprosthesis (KPro) implantation. The KPro implant imparts lifelong risk for keratitis and endophthalmitis. Patients with the KPro were more likely than controls to colonize fluoroquinolone (FO)–resistant Staphylococci (coagulase negative). The researchers blame the chronic use of FO for prophylaxis as the main reason for antibiotic resistance and recommend modifications in prophylaxis in order to prevent emergence of resistant pathogens. One option may be to rotate antibiotics periodically.

Program #4690
**Risk Factors for Contact Lens Related Microbial Keratitis: A Prospective Multicenter Case Control Study**
Scientists at the Strasbourg University Hospital in France conducted a study to identify risk factors and the social burden of contact lens related microbial keratitis. They cite concern with the increasing availability of contact lenses through the Internet or local market highlighting the need for professional supervision and the lack of information about the basics of hygiene and handling. Of interest, daily disposable lenses and two-week replacement options had a slightly higher relative risk for infection when compared to monthly replacement lenses (maybe due to the lack of basic rules of hygiene, such as lack of hand washing).

Presentation #237
**The Roles of Epigenetic Factors in the Pathogenesis of Keratitis**
Researchers at the Henan Eye Institute in China studied the role of histone deacetylation (HDAC) in the pathogenesis of fungal keratitis. They found the aberrant expression of HDAC in fungal infected corneas. The expression of HDACs and the loss of balance between histone acetylation and deacetylation are the major features of fungal keratitis. Inhibitors of HDAC, like Trichostatin, may play a vital role in the therapeutic management of fungal keratitis.

Program #1075
**Treatment of Severe Bacterial Keratitis with Corneal Collagen Crosslinking**
Investigators at the Louisiana State University Department of Ophthalmology in New Orleans looked at characterizing the antibiotic effect and induced histological alterations of corneal crosslinking (CXL) in bacterial keratitis. Thirty minutes after CXL, the experimental cornea was significantly less edematous than the antibiotic treated corneas with severe keratitis. Histological evaluation of the stroma showed a tightly-packed and coherent lamellae.

Colony counts showed statistically significant differences between the CXL eyes and controls at 30 minutes. CXL appears to be a useful adjunct to treat corneal infection and to maintain structural integrity of the cornea in severe bacterial keratitis.

Program #89
**Confocal Microscopy: Interpretation of the Clinical Images in Atypical Keratitis**
Researchers at the Aarhus University Hospital Department of Ophthalmology in Denmark evaluated the utility of in vivo confocal microscopy (IVCM) in patients with atypical keratitis. They cited an increased frequency of identifying fungal keratitis by localizing highly reflective branching structures, but a decreased ability to recognize Acanthamoeba keratitis (AK) infections. In AK, cysts often lack a visible ring making the organism difficult to recognize from inflammatory cells in the cornea. This finding indicates a higher sensitivity and sensitivity in identifying fungal infections by IVCM than AK.

Program #81
**The Association Between History and Culture Isolates from Bacterial Keratitis Cases in Shanghai**
Scientists at the Eye and Ear Hospital of Fudan University in Shanghai studied the microbiologic characteristics of bacterial keratitis cases at their location. They explored the association between history and culture isolates from their patients affected.
Low education levels, ocular surface disease, trauma, cigarette smoking and presence of diabetes were linked to increased odds of gram-positive bacterial keratitis. Contact lens wear was the main risk for gram-negative bacterial infections. They suggest that consideration of risk factors may be useful for choosing empiric antibiotic treatment before pathologic bacteria are identified.

Program #4702
Opinions on Bandage Contact Lens Practice in the UK
Researchers at the Royal Victoria Infirmary, United Kingdom, studied the prescribing practices of bandage contact lenses (BCL) among members of the Bowman Club (UK Cornea Society). They were surveyed for opinions regarding indications and prescribing patterns, concomitant medication for prophylaxis and complications related to BCL use. The most common lens use was for pain relief, followed by promotion of healing epithelial defects, for wound apposition and mechanical protection of the ocular surface. A high incidence of secondary corneal ulcers was reported and topical antibiotic usage was only found to be used in 42.3% of the consultant’s surveyed. A final recommendation includes sterile lens insertion using forceps and the use of topical antibiotics for prophylaxis.

Program #4046
Incidence of MRSA/MRSE and Co-Existing Ophthalmic Drug Resistance in Refractive Surgery Seeking Patients
Scientists at the U.S. Army Refractive Surgery Research Program in Virginia conducted a study to report the incidence of MRSA colonization in refractive surgery seeking patients, and to evaluate co-existing resistance to normally prescribed ophthalmic medications. Positive cultures for MRSA/MRSE were found in 16.6% of patients in a high-risk group who presented for refractive surgery evaluations. It should be noted that ocular cultures won’t identify MRSA/MRSE carriers. Coexisting ophthalmic drug resistance to medications used in refractive surgery (including later-generation FQ) is common.

Program #14
Long-Term Visual Outcomes, Graft Survival and Complications of Deep Anterior Lamellar Keratoplasty in Patients with Herpes Simplex Related Corneal Scarring
This retrospective non-comparative case series study from the United Kingdom investigated long-term visual outcomes, complications and graft survival of patients undergoing deep anterior lamellar keratoplasty (DALK) to treat corneal scarring secondary to herpes simplex virus keratitis. Patients undergoing DALK for HSV corneal scarring have a higher rate of complications following surgery. Graft failure is uncommon with timely and aggressive therapy. There are a large percentage of secondary operations following DALK in this cohort and adequate informed consent is important when counseling these patients.

Hope you enjoy this year’s review. If you are interested in reading through additional abstracts, visit www.arvo.org. For those who have never attended an ARVO meeting, I hope you can do so next year!
ONS Holds Roundtable

Only 18% of baby boomers take supplements to support their eye health, according to a national survey conducted by the Ocular Nutrition Society (ONS). Sponsored by Bausch + Lomb, ONS recently held a roundtable event, featuring experts in the fields of ophthalmology, optometry, diet and nutrition and primary care, to discuss the state of eye health in the baby boomer population. In a post-event statement, ONS cited scientific evidence to support the role of nutrients like zinc, vitamins C and E, lutein, zeaxanthin and long-chain omega-3 fatty acids, to help promote health in the aging eye. The experts gathered discussed the lack of these nutrients in the American diet and the need for baby boomers to take dietary supplements for eye health.

Survey results also showed that more than 60% of respondents were unaware of the role of omega-3 fatty acids, 66% were unaware of the role of lutein and 89% were not aware of the role of zeaxanthin.

For more information, visit www.ocularnutritionsociety.org.

ABB Webinar Series is COPE-Approved

ABB Concise announces that its Practice Partnership webinar series, presented by Patrick Caroline, C.O.T., of Pacific University, has continued COPE approval. Sponsored by Paragon Vision Sciences, the series features topics that support successful treatment options and outcomes with gas-permeable lens fittings. For a $35 fee, a 10-question online exam is available for CE credit. For more information, visit www.abbconcise.com.

GPLI Announces 2012 Symposium

The Gas Permeable Lens Institute (GPLI) will host “GP Lens Practice... Today and Tomorrow,” on June 3, 2012 in Denver. The symposium will allow attendees to select from seven courses in fundamental and advanced GP lens education. Speakers include Ed Bennett, O.D., Ms.Ed., Christine Sindt, O.D., Tom Quinn, O.D., M.S., and Shawna Hill Vanderhoof, O.D., to name a few. The conference will be offer up to seven hours of COPE, NCLE and/or JCAHPO credit. For more information, visit www.gpli.info.

OcuSoft Releases New MGD Emulsion

OcuSoft announces the availability of Retaine MGD ophthalmic emulsion, a new therapy for individuals suffering from dry eye syndrome and meibomian gland dysfunction. Retaine MGD is a preservative-free oil-in-water emulsion that moisturizes, lubricates and protects moderate to severe dry eyes, using Novasorb technology to prolong corneal contact time. The hypotonicity of the emulsion adds moisture by lowering the salt concentration of tears while the lipid component lubricates and protects the eye surface. For more information, visit www.retainebrand.com.
AK: Let’s Shift the Blame

*Acanthamoeba* keratitis is not limited to contact lens wear.

From fungal keratitis to an update on the 2006 *Fusarium* outbreak, we have recently covered several infectious diseases. Now, it is time to revisit another past culprit—*Acanthamoeba* keratitis (AK), a rare and sight-threatening disease caused by free-living protozoans. In 2007, the CDC released several public health warnings regarding an outbreak thought to be associated with the use of Complete MoisturePlus (Abbott Medical Optics) solution. AMO voluntarily recalled the product.

Putting this dangerous pathogen under the public’s microscope was, and continues to be, extremely important. A plethora of literature associating AK with contact lens wear has been published. Much of this literature also details the importance of hygiene and compliance, as well as analyzing solutions to determine their efficacy in killing *Acanthamoeba* cysts.

While AK is most commonly associated with contact lens wear, everyone is potentially at risk for infection. It is important for practitioners to suspect AK when examining contact lens and non-contact lens wearing patients who present with telling symptoms of the disease. Increasing evidence tying *Acanthamoeba* to water sources means that all patients and clinicians should be knowledgeable about this dangerous pathogen.

The Disease

*Acanthamoeba* is one of the most prevalent and abundant protozoa on earth and has been isolated from treated water, seawater, tap water, soil, dust, and air. The species’ life cycle consists of trophozoite and cyst stages, and if AK is not caught and treated early, may have sight-threatening consequences.

The correlation between AK and contact lens use is high: In the United States, 85% of cases occur in contact lens wearers. However, the disease is still quite rare—the incidence of disease is estimated at approximately one to two cases per million contact lens users. Contact lens wearers are frequently touching their eyes, therefore putting themselves at a greater risk for infection; contaminated lenses have been known to act as “vectors” for *Acanthamoeba* species.

Educate Your Patient

It is the practitioner’s responsibility to ensure that patients who wear contact lenses maintain a healthy and safe care regimen. Fostering open communication with your patient, as well as providing key information on compliance, is crucial in the hopes of avoiding infection (see “CL Tips to Reinforce” page 9).

Anyone is at Risk

With the brunt of educational materials focusing on the link between AK and soft contact lens wear, practitioners may be slower to diagnose *Acanthamoeba* in patients with hard or rigid gas-permeable lenses, or in patients without lenses. Similarly, patients who practice appropriate lens care and hygiene practices are not completely immune to AK. However, because of its broad association with contact lens use and similar appearance to other viral, fungal and bacterial infections such as herpes simplex keratitis, AK is easy to misdiagnose. Most often, an accurate diagnosis is made when all treatments fail, or when the parasite is identified through cultures or pathological evaluation.

In a retrospective review of all AK cases diagnosed at Massachusetts Eye and Ear Infirmary between 1990 to 1994, Emil Chynn, M.D., and colleagues sought to identify potential differences in both time to diagnosis and final visual outcome between contact lens and non-contact lens users with AK. Results showed that mean time to diagnosis was significantly longer in non-contact lens wearing patients; 50% of non-contact lens wearing patients had a poor outcome vs. 14% of contact lens patients. The lesson: Practitioners should never rule out the possibility of AK in non-contact lens users.

Treatment of AK starts with early identification and diagnosis. Strongly suspect AK in chronic keratitis that does not respond to standard antiviral or antibacterial
Continued from page 7

therapy within five to seven days, and in those who report pain to a much worse degree than their clinical appearance suggests. The clinical presentation of AK can vary greatly—patients with AK may present with symptoms of unilateral foreign body sensation, photophobia, decreased visual acuity, tearing, and pain or redness in the eye. A ring-like ulceration of the corneal tissue may be appear upon later presentation, as well as limbitis or anterior stromal infiltrates and epithelial defects.7 Treating an AK infection is often difficult, as the cyst form of Acanthamoeba is quite resilient. Current medical treatment usually includes a topical cationic antiseptic agent such as polyhexamethylene biguanide (0.02%) or chlorhexidine (0.02%), with or without a diamidine such as pro-mamide (0.1%) or hexamidine (0.1%), and therapy may last from six months to a year. Steroids are usually avoided, and pain control can be helped by topical cycloplegic solutions and oral non-steroidal medications.8 In some severe cases, the patients may require a therapeutic corneal transplant to prevent the infection from spreading beyond the cornea.

Education is crucial in preventing patients from AK, and equally crucial for the eye care practitioner. We must properly train and inform our patients while maintaining our guard for the signs of all ocular pathogens, no matter how rare they may be.  

References available at www.reviewofcontactlenses.com

CL Tips to Reinforce

• Wash your hands with soap and water every time before handling lenses, and make sure to thoroughly dry them afterwards.
• Because Acanthamoeba isolates have been found in water sources, such as tap water, swimming pools, hot tubs, lakes and ponds, remember to remove your contact lenses before swimming or showering.
• Never top off. Used solution should be disposed of daily, because the disinfecting capability of the solution is short lived. Use fresh solution every time you store your lenses in their case.
• Tap water or saline should never be used as a cleansing solution; they are usually avoided, and pain control can be helped by topical cycloplegic solutions and oral non-steroidal medications.

Advertiser Index

Akon Laboratories................................................................. Cover 2
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We complain about and cite poor compliance as a major risk factor for contact lens infections. Yet, in some of our own practices, we routinely make common compliance mistakes.

The Importance of Hand Washing

Bacteria and viruses are commonly transmitted through the hands of health care workers. Hand washing is the single most important intervention to prevent the spread of disease. Keep in mind, I mean hand washing by all office employees. Numerous infectious outbreaks have been traced to contaminated hands of healthcare workers, including reports of epidemic keratoconjunctivitis.1

In spite of these concerns, compliance with hand washing guidelines remains a problem in most health care settings. Even in controlled study conditions, the hand washing rate usually does not exceed 40%.2 A number of factors are associated with low rates of compliance, including the lack of availability of sinks, skin irritation with repeat exposure, high work volume and low perceived risk.2

Washing hands for 15 seconds achieves a microbial kill of $10^{4.1-1.1}$ and for 30 seconds $10^{3.2-3.8}$.3 Unfortunately, however, many individuals wash their hands for less than 10 seconds, which may not achieve a satisfactory microbial kill rate.

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According to the Centers for Disease Control and Prevention, using solutions that contain 60% to 70% alcohol are most effective on gram-positive, gram-negative and spore-forming bacteria, as well as fungi and viruses.4 Hand disinfectant should be used regularly throughout the practice, but use standard hand washing when handling contact lenses.

Contact Lens Hygiene

It is vital to properly clean and store reusable contact lenses. The American National Standards Institute last updated the criteria for in-office disinfection of contact lenses in October 1999. However, the changing lens material and care product market leaves the practitioner with questions on how to clean, disinfect and store current non-disposable diagnostic lenses.

• Gas-permeable (GP) lenses are fairly easy to clean and disinfect. Start by using a GP-approved cleaner or polish for a wash. Soak in ophthalmic-grade hydrogen peroxide for 10 minutes. Rinse with saline and store dry. Finally, lubricate with conditioning solution prior to insertion.

• For soft lenses, autoclaving is the only 100% effective disinfection method. However, most practitioners use multipurpose solutions to disinfect and store lenses. If a multipurpose solution is used, follow the manufacturer’s recommendations on rubbing, rinsing and solution replacement (usually every 30 days).

The Role of Tap Water

The use of water with contact lenses is significantly linked to microbial keratitis infections, specifically *Acanthamoeba*. During the past decade, the Environmental Protection Agency has downregulated control of *Acanthamoeba* in the U.S. tap water supply. They have cited that the critical point identification for the presentation of *Acanthamoeba* in contact lens wearers is personal hygiene, not drinking water.5 Therefore, regulating *Acanthamoeba* will not reduce health risk for the general population.

However, numerous studies have shown that direct contact with water—including tap water, swimming pools, hot tubs and showers—is the primary point of contamination and subsequent infection with the organism.6-9

The lesson: Hands should be thoroughly dried before handling lenses. When rinsing cleaner from GP lenses, switch to sterile saline or multipurpose solution.

Being ever vigilant about our own compliance habits will ensure patient safety in our own practices. 


Hallmark Signals of Bioincompatibility: Infiltrative Keratitis and OPTI-FREE RepleniSH

Recently, there has been a great deal of discussion in the literature and at conferences regarding an increase in the rate of sterile infiltrative keratitis and its associated risk factors, especially with silicone hydrogel lenses used for daily wear. Contact lens associated infiltrative keratitis (CLAIK) may be a hallmark clinical sign of biocompatibility of lens and care solutions particularly with the increased rates reported with specific lens care solutions.

Through independent studies, infiltrative keratitis has been reported to be associated with several factors including different lens types, smoking, and bacterial biofilm. Notably, infiltrative keratitis has repeatedly been associated with a particular lens care solution, OPTI-FREE RepleniSH, in as many as 71% of cases.

The latest study showing this association is Kern et al. (AOA, June 2011). The researchers presented results of an Alcon-sponsored study investigating the association of symptomatic soft contact lens-related corneal infiltrative events (CIEs) with soft contact lens material, lens care products, and other risk factors.

Cases of symptomatic CIEs were identified at 5 academic eye care centers in this multicenter case-control study. One important outcome in the Kern study was that OPTI-FREE RepleniSH is significantly associated with symptomatic corneal infiltrative events (CIEs). Of the 166 patients with symptomatic CIEs that were analyzed, a univariate analysis of patients using lens care solutions indicated patients using OPTI-FREE RepleniSH are 63% more likely to develop symptomatic corneal infiltrates compared to the other brands. In fact, of the 10 lens care brands used by patients in this study, including renu multi-purpose solutions, only OPTI-FREE RepleniSH had a significant association with symptomatic CIEs.

While selective results of the significant univariate risk factors (Age, increasing CL Power, EW, reusable SCLs, silicone hydrogel and student status) were identified in the published abstract it failed to report that OPTI-FREE RepleniSH was also identified as a significant risk factor amongst these risk factors for daily wear. OPTI-FREE RepleniSH was disclosed as an important univariate risk factor for CIEs, in the poster presented at the AOA 2011 meeting.

The researchers also conducted a multivariate analysis on a selection of factors from the univariate analysis. Although several significant risk factors were identified in the multivariate analysis (age, EW and Reusable SCL), an underpowered statistical design can result in false negatives when differences do exist.

The significance of the association of OPTI-FREE RepleniSH with symptomatic soft contact lens-related corneal infiltrative events should not be ignored or dismissed in this Alcon-sponsored study. In fact, these results support the recent research reported by others. Further investigation is warranted to determine the causality of the infiltrative keratitis events associated with the use of OPTI-FREE RepleniSH.

Additionally, the association of infiltrative keratitis with OPTI-FREE RepleniSH reported by Kern et al is in stark contradiction to the Alcon-sponsored Staining Grid, which implies OPTI-FREE RepleniSH is safe and biocompatible simply because it has lower levels of corneal hyperfluorescence at an arbitrary 2-hour time point. Such a tool may mislead an eye care practitioner to recommend lens care solutions solely based upon an observation that is not a proven predictor of future adverse events. Determining the biocompatibility of lens care solutions is not based on a singular transient ocular sign as suggested by some tools, but rather based on more comprehensive clinical observations, patient symptomatology, and contemporary epidemiological evidence. Eye care practitioners should also review the recent evidence for CIE risk factors as they supersede predictions of compatibility based on limited exposure and should be attentive to the reference of older peer-reviewed publications that have been superseded by newer research.

Bausch + Lomb lens care products have an extensive history of proven biocompatibility with both hydrogel and silicone hydrogel contact lenses.

REFERENCES

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ADVERTORIAL
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The Argument For Daily Disposable Torics
Practitioners should consider the newest technologies when picking the right modality for their patients.

We, as eye care practitioners, are fortunate to practice in a time when there are new technologies, materials and modalities consistently emerging in the contact lens marketplace. There are many more options available for today’s contact lens wearer, especially in the single-use daily disposable category.

Daily disposable contact lenses, and the latest introduction of the toric designs, offer many advantages—starting with convenience. It is important that practitioners discuss the new materials and new modalities available with their patients, starting with the daily disposable option for your astigmatic patients.

Consider making a unified approach to growing this market in your practice. The perception of high costs may appear to be a barrier, but instead focus on the savings your patient would see in contact lens solution purchases throughout the year and the manufacturer rebates available. Many patients appreciate the convenience and the comfort of having a new lens every day. Many practitioners believe this modality is safer than their two-week and one-month counterparts for a variety of reasons, especially a much higher compliance rate.

For the Allergy Sufferer
By utilizing a proactive approach with diligent allergy history questioning, you may be surprised to learn how many allergy sufferers are currently not wearing their contact lenses, not being diagnosed or treated in your practice. A diligent data gathering process will help reveal these potential contact lens dropouts due to allergy-induced comfort issues.

Studies have shown these allergy patients are excellent one-day disposables candidates. Mary Jo Steigemeier, O.D., and Stuart Thomas, O.D., described significant increases in comfort for patients with ocular allergies when they were fit with daily disposable contact lenses. Of often times, patients were self-treating during periods of allergy-induced contact lens discomfort by simply not wearing their lenses at all.

As a modality, the daily disposable contact lenses may be a perfect solution for this patient. They have a new, clean lens placed on their eye every day. There are no cleaning, compliance or depositing issues that need to be considered with this modality. (Tip: Don’t ask about allergy symptoms only while collecting the patient’s history, but continue the questioning while you are looking through the slit lamp at the lower lids.)

The Ideal Candidate
Daily disposable contact lenses offer patients the convenience of a fresh lens each time, without the hassle of cleaning and monitoring a replacement schedule. If a patient is looking for part-time wear, (i.e., while participating in sports, over weekends, while traveling) or simply looking for a more convenient alternative, then daily disposables are probably the best choice. One-day contact lenses are very useful for patients who have had a history of non-compliance, solution or material sensitivity or toxicity. This lens modality may also be the best choice for our less responsible pediatric and teen population. By offering this opportunity to your astigmatic patients, you can potentially add a significant number of contact lens wearers to your office.

The Astigmatic Patient
Our astigmatic patients are typically delayed when it comes to availability of contact lens technologies. In fact, we still occasionally see astigmatic patients who are told they cannot wear lenses due to their astigmatism. In reality, a significant portion of our astigmatic patients wear spherical equivalent contact lenses. This technique is used to mask the uncorrected cylinder, but
often does not provide optimal vision correction for these patients.

There are several one-day disposables options for patients with astigmatic refractive correction: Focus Dailies Toric Contact Lenses for Astigmatism (nelfilcon A, Alcon), ClearSight 1 Day Toric (ocufilcon D, CooperVision), Soflens Daily Disposable Toric (hilafilcon B, Bausch + Lomb) and Acuvue 1Day Moist for Astigmatism (etafilcon A, Vistakon). The limited power availability is the primary restriction with one-day disposable toric lenses (see “Power Availability in Daily Disposables,” above).

A Case Study

Melanie, a 39-year-old white female, lives with her three kids and one dog. She is a new patient in for her annual eye health check, and reported using one-month disposable toric contact lenses. She wanted to renew her contact lens prescription and had no allergy complaints when giving her history.

During the anterior examination, I discovered moderate amounts of papillae on her inferior palpebral conjunctiva in both eyes. When prompted, she revealed intermittent blurred vision and difficulty wearing her contacts during the spring and fall. She said she usually cuts back on her contact lens wear, and instead uses her six-year-old back-up glasses for a period of four to six weeks. This has been consistently happening for the past few years, and she usually treats her symptoms with over-the-counter allergy drops.

She was refit with daily disposable toric contact lenses, along with a prescription for a dual-acting topical antihistamine/mast cell stabilizer.

Keep in mind that new technologies are important to the bottom line of a contact lens practice, and that they are the most profitable early in the product’s life cycle. Early adopters will typically reap larger benefits with respect to contact lens technologies. One-day disposable contact lenses are one of the fastest growing segments in the contact lens marketplace and practices need to consider this lens as an opportunity.

From single-use daily disposable contact lenses to two-week, one-month and the less common quarterly or yearly replacement schedules, today’s contact lens wearers have many options to consider when choosing a lens modality. But ultimately, the eye care practitioner is responsible for selecting a proper contact lens modality, material and solution combination to ensure lens wear success. Consider one-day disposable toric contact lenses next time you see an astigmatic corrective patient in your exam chair.

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<td>8.6</td>
<td>+4.00 to -8.00</td>
<td>(-0.75, -1.50)</td>
<td>020, 180, 160, 070, 090, 110</td>
<td>30 or 90 pack</td>
</tr>
<tr>
<td>ClearSight (or Biomedics) 1 Day Toric (cooperVision, ocufilcon D)</td>
<td>8.7</td>
<td>plano to -7.00 (no + powers)</td>
<td>(-0.75, -1.25)</td>
<td>020, 180, 160, 090</td>
<td>30 pack</td>
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<tr>
<td>Soflens Daily Disposable Toric (Bausch + Lomb, hilafilcon B)</td>
<td>8.6</td>
<td>plano to -9.00 (no + powers)</td>
<td>(-0.75, -1.25, -1.75)</td>
<td>020, 180, 160, 090</td>
<td>90 pack</td>
</tr>
<tr>
<td>Acuvue 1 Day Moist for Astigmatism (Vistakon, etafilcon A)</td>
<td>8.5</td>
<td>+4.00 to -9.00</td>
<td>(-0.75, -1.25, -1.75, -2.25)</td>
<td>010, 020, 060-120 (in 010 steps), 160-180 (in 010 steps)</td>
<td>30 pack</td>
</tr>
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Power Availability in Daily Disposables

What percentage of your patients wear daily disposable contact lenses?

Poll Results:

<table>
<thead>
<tr>
<th>Poll Options</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 5%</td>
<td>31%</td>
</tr>
<tr>
<td>6% to 15%</td>
<td>28%</td>
</tr>
<tr>
<td>16% to 25%</td>
<td>24%</td>
</tr>
<tr>
<td>Over 25%</td>
<td>17%</td>
</tr>
</tbody>
</table>

The Power of Old Wisdom

While the principles of practice building have not changed, it is time to re-evaluate how you implement those old strategies.

I recently met with a practitioner to discuss new strategies in practice management. As I have heard before, this practitioner said he knew it all and that he could summarize practice management in a few words: "Buy smart, hire good staff, be a sharp marketer and focus on customer service." It was the same old rhetoric.

In response, I asked him if he conducted an inventory of his contact lenses. When he looked at me with a blank stare, I repeated the question. He considered the question and then dismissed it, saying that not only did he not inventory his contact lenses, but also that he didn’t see how my question had anything to do with practice management.

My point was simple. There are a lot of new things in practice management and, in fact, what’s old is new again. Just like the principles of optics haven’t changed, the principles of practice building also haven’t changed. It is the mechanisms and tools to execute those principles that have changed. It makes sense for all of us to periodically make sure that the techniques from our past are revisited, recycled and then recalibrated to current market conditions.

Lens Inventory

As an example, let’s look at a practice’s inventory of contact lenses—an interesting notion, because so few of us do this anymore. While it may have been commonplace to keep a stocked inventory in the olden days of vialled lenses, today’s manufacturers and distributors have made it incredibly easy and efficient to order lenses online, and to use their fulfillment systems to do so. For the practitioner, this shifts the need to inventory lenses away from us and onto them. Therefore, in the context of the above discussion, there is room to review contact lens inventories in another way, and like many old practice-building ideas, this too is worth revisiting and recycling.

Revisiting the Old Wisdom

• **Buy smart.** Generally, when you buy an inventory of lenses, your unit pricing drops. While it’s true you will incur costs for carrying inventory, you should move your inventory quickly with good forecasted data. With careful planning and smart buying, you can plan around a 30-day schedule and negate nearly any added expenses.

  Keep in mind that you do not need to inventory every lens. Start with what you consider to be your go-to lenses in the most common powers. Next, create a list of your second-tier lenses and stop there.

• **Hire good staff.** Your staff has to understand the reason why—and be able to articulate that reason to your patients. In this case, your staff should understand the benefits of having an inventory of lenses, how to dispense ideally a year’s supply of lenses on the spot and how this practice can help with patient compliance and pricing.

• **Be a sharp marketer.** Patients should perceive you as the place to get contact lenses, and having their lenses in stock is one way to support that now uncommon marketing position. Having a well-researched, carefully planned inventory might be one of the least expensive marketing tools at your disposal.

• **Focus on customer service.** Think about it, what could be more convenient for a patient than walking out of your office with everything they need in hand—from lenses and solutions to cases and eyeglasses? Being able to have what your customer needs is one of the many hallmarks in great customer service. In our case, serving your patients’ needs when they need them to be served goes along with this mindset.

This article is not specifically about inventorying lenses. Rather, it is about realizing that business-building fundamentals have remained unchanged from essentially the earliest street markets. Offer great products, value and service in a memorable atmosphere and work with an educated staff—and you’re highly likely to succeed.

The key is rethinking and modernizing your strategy. Instead of a billboard on a highway, use social media. Instead of the Yellow Pages, use search engine optimization. A television commercial may be replaced with your own YouTube channel.

While using these new methodologies, stick to the core elements of old-school business building. Don’t get into a rut and think that there is nothing new in practice management. If you get complacent, you’ll find that your practice is the one that suffers.
What’s the Solution

By Steve Lowinger, O.D.

Sponsored by

In today’s society, the phrase “image is everything” rings true. How we present ourselves to our patients is our biggest asset in the marketing of our practice. This presentation encompasses all facets of the practice: the staff who greet the patients as they enter the office, the lenses and lens care decisions the practitioner makes and the instructions the patients receive before they leave our office. What we say and how we educate our patients in the office will shape their visual health and comfort for the upcoming year.

Often times it is the little things we do for our patients that have the biggest results in growing and maintaining our practice. Patients come to us for our expertise, and stay when they can walk away with better vision and comfort.

Our patients have one simple expectation. They wish to see well and be comfortable. Numerous studies cite comfort as the primary reason that patients drop out of contact lens wear.1 Some of these dropouts are vocal, while others simply fade away from our practice. Consider that spending an extra minute with your patients to review their lens care regimen may be the deciding factor in keeping those patients in your practice or losing them entirely. Every contact lens dropout will affect your practice’s bottom line—both in lost revenue and through loss of referrals.

Improve Comfort

The comfort equation has many variables, the most important being the interaction between the contact lenses and the multipurpose solutions which disinfect, create wettability and enhance the comfort of the contact lens. One of the latest advances is the introduction of OPTI-FREE® PureMoist® MPDS and HydraGlyde® Moisture Matrix. HydraGlyde® Moisture Matrix was designed to make the entire contact lens surface hydrophilic and wettable.2

This increased wettability allows a patient to wear their lenses comfortably for a longer period of time, feel more comfortable at the end of the day and achieve clear vision.3 By providing the patient with a product that makes their lenses more wettable, we can achieve a better contact lens experience in comfort.

In an ongoing survey of over 3,000 patients, 88.3% of patients who sampled OPTI-FREE® PureMoist® MPDS experienced all day comfort. In the same survey, 59% of patients reported end-of-day dryness with their habitual contact lens solution vs. only 19% of the users after switching to OPTI-FREE® PureMoist® MPDS.4 What we learned is that a small conversation educating our patients on the benefit of a contact lens system can lead to a 67% improvement in end of day moisture with OPTI-FREE® PureMoist® MPDS.4

Sometimes we need to remember that it is the little things that really make the big difference in our practices. Spending a few extra moments with our patients to educate them on best practices for maintaining good eye health, vision and comfort can make a large difference in both their outcomes and their perception of your practice. This is especially important for the contact lens patient who is always looking around for a better option. Take the time to explain the benefits of why you are recommending a contact lens solution. Keep in mind that this breakthrough in wetting technology, HydraGlyde® Moisture Matrix, can lead to hours of comfort and moisture for your patients, which could keep them coming back to your office and ultimately grow your practice.


Minimize Dropouts: Select OPTI-FREE® PureMoist® MPDS and HydraGlyde® Moisture Matrix
With the advent of the prostaglandin analogues, a paradigm shift in the treatment of glaucoma and ocular hypertension was realized. Finally, a once-daily, well-tolerated, safe and efficacious medication was introduced into the treatment armamentarium for a potentially blinding optic neuropathy. Today, this description of the prostaglandin class continues to hold true for the vast majority of patients for whom we daily prescribe either latanoprost (Xalatan, Pfizer), bimatoprost products (Lumigan, Allergan) or travoprost products (Travatan, Alcon). The relative drawbacks have been local side effects such as hyperemia, iris and periorbital darkening, and eyelash growth, as well as the cost of the medications.1

The New, The Old, The Reformulated

Because the prostaglandin class is indispensable in the treatment of intraocular pressure, the past 15 years have seen various changes in the respective product lines to try to counteract side effects and cost.

Latanoprost

Latanoprost, for example, is now available through multiple generic manufacturers. This substitution opens up access to patients who are self-pay or have high deductibles and/or co-pays for brand name medications. It is important to remember, however, that generic medications for the eye are not required to be tested by the FDA for bioequivalence or therapeutic equivalence, but only require the active ingredient to be identical to the brand.2 Inactive ingredients can alter the pH, the penetration, the viscosity and other characteristics of ophthalmic medications which can change the clinical efficacy and side effect profile of the drug. This fact should be taken into consideration for each individual patient and with each different generic manufacturer.

Bimatoprost

Bimatoprost is generally regarded as the most efficacious of the prostaglandin analogue ophthalmic class.3 Its original 0.03% formulation, however, also demonstrated increased amounts of hyperemia, which discouraged both physicians and patients from using it. In response, Allergan lowered the strength of Lumigan from 0.03% to 0.01% and changed the preservative concentration, with a resultant 65% less moderate to severe hyperemia and equivalent clinical efficacy.4 The 0.01% formulation allows for the known efficacy of brimatoprost with a much better side effect profile.

Travatan

The original Travatan 0.004% was reformulated as Travatan Z as an option to agents containing benzalkonium chloride (BAK) as a preservative. The concentration of travoprost remained at 0.004% and the BAK was removed and replaced with sofzimat (SofZia), an ionic buffered preservative system. One study found that travoprost with SofZia was less toxic to corneal and conjunctival cells than those exposed to BAK-containing travoprost.5 The amount of hyperemia between Travatan and Travatan Z was unchanged at 30% to 50%.

Zioptan

Recently, another prostaglandin analogue was approved that will further entrench this medication class as the first-line treatment of glaucoma and ocular hypertension. The latest agent to be approved is called Zioptan (tafluprost 0.0015%, Merck) and offers the advantage of being completely preservative-free with the same clinical advantages we have come to expect from the prostaglandin class.6 Zioptan is packaged in unit-dose vials similar to Restasis (cyclosporine, Allergan) and other preservative-free ocular preparations and is recommended for once-daily administration at bedtime. The package insert recommends each vial be discarded immediately after opening because sterility cannot be maintained without a preservative. There is sufficient quantity in each vial for both eyes.

Typical of the topical prostaglandins, Zioptan’s most common adverse reaction is conjunctival hyperemia, reported to be between 4% and 20%—which is closer to the hyperemia profile of latanoprost.5,7 Multiple clinical trials with preservative-containing tafluprost have illustrated its efficacy, and at least one study shows the preservative-free formulation to be equivalent in IOP-lowering effect.5,9
Why Choose Preservative-Free?

It is important to remember that the hyperemia associated with the prostaglandin class is unrelated to the presence or type of preservative. In fact, the original Xalatan had the highest amount of BAK than any of the original three prostaglandin brands, but the lowest amount of reported conjunctival redness. Hyperemia is a side effect of the prostaglandin chemical structure.10

The reason prescribers should consider a preservative-free option is to avoid the toxicity and ocular surface disease inherent with the use of preservatives in general, especially when used chronically or in excess. Although true allergic reactions are rare, multiple daily applications of BAK and other preservatives have been shown to be toxic to corneal and conjunctival epithelial cells and could compound various ocular surface conditions such as dry eye syndrome.11 Patients who do not have an ocular surface disease and/or use monotherapy to control their intraocular pressure may not need a preservative-free option.

Various statistics indicate that our glaucoma patients have compliance rates as low as 50%.12 The most common causes of non-compliance include forgetfulness, medication cost, side effect profile and lack of understanding regarding this asymptomatic disease state. The aforementioned adjustments in the new prostaglandins class and the new tafluprost has paved the way for more affordable and/or better-tolerated medication, and will give prescribers the ability to use these agents on an even broader range of patients with glaucoma or ocular hypertension. Along with better education on our part, we hope to increase the ease of usage and the compliance of our patients in order to avoid the devastating effects of this optic neuropathy.

The last several decades have seen the evolution of resistant strains of bacteria and the decline in antibiotic efficacy. As practitioners, it is time to confront the situation.

By J. James Thimons, O.D.

The most noteworthy clinical development of the 21st century is likely the evolution of highly resistant bacteria that are being identified in ocular infections.

Traditionally, the ophthalmic arena has been spared most of the concerns associated with resistance of bacteria and efficacy of therapy due to the simple fact that we have the luxury of applying the therapeutic agent directly to the site. To a large degree, this bypasses the concerns associated with GI absorption and access to remote parts of the body. We are also lucky to have a wide array of potential agents available to meet the specific needs of individual patients.

But all that is changing.

History of Bacterial Infections

Over the last seven years we’ve seen a rapid decline in the efficacy of antibiotics and a slowing of the technology pipeline for new drug development. This creates both a current challenge and future concern for all clinicians. Historically, the most common causes of bacterial infections of the eye have been *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Moraxella*, *Serratia Marcescens* and occasionally, *Enterococcus*. Over the past several decades, these bacteria had shown little change in susceptibility, which has allowed practitioners to manage most topical infections without significant concern. In particular the third- and fourth-generation fluoroquinolones gave us a powerful weapon to address almost any type of infection.

Ophthalmic Infections

A 2008 study by Kara Cavuoto, M.D., looked at bacterial isolates in ophthalmic infections and found an almost three-fold increase in resistance to third-generation fluoroquinolones (ciprofloxacin) relative to *S. aureus* over a 10-year period (from 1994 to 2003), and an emergence of MRSA from 4.4% to 42.9% of all cultures. Additional work by Penny Asbell, M.D., Michael H. Goldstein, M.D., and Fabiana Marangon, M.D., support this concern of increasing resistance in ocular therapy. In 2009, Marguerite McDonald, M.D., identified a remarkable increase in multidrug resistant isolates to ciprofloxacin in relation to MRSA, which showed that 65% of MRSA isolates and 47% of MRSE isolates also showed ciprofloxacin resistance.
There has been a number of identified trends in resistance to agents such as azithromycin, gentamicin and tobramycin. Maria Regina Chalita, M.D., showed a decrease of sensitivity for gentamicin and tobramycin from 88% and 95% respectively, to 50% and 80% over a 15-year period.10,11

**Bacterial Keratitis**

The more significant issue is the growth of resistance in the past decade to organisms involved in sight-threatening infectious keratitis and endophthalmitis. Several studies have identified this pattern of rising resistance related primarily to gram-positive bacteria such as *S. aureus*. Tristan Bourcier, M.D., Ph.D., conducted a study of 291 patients with bacterial keratitis, noting that the predominant culture positive bacteria was gram-positive (83%) with a surprisingly low gram-negative (17%).12 This trend is concerning because the antibiotics used to treat microbial keratitis (MK) are still quite effective against gram-negative bacteria (*Pseudomonas* specifically). However, the loss of efficacy seen in gram-positive coverage has been both rapid and alarming.

MRSA has seen a rapid rise in bacterial isolates, increasing from 29.5% in 2000 to 41.6% in 2005.13 Additionally, the efficacy patterns also underwent significant change: Fourth-generation fluoroquinolones maintained status against methicillin susceptible (MSSA) bacteria, while there was a marked decline in susceptibility against MRSA isolates. This shifting pattern implies significant concerns about the clinical protocols used to manage bacterial keratitis in both contact lens and non-contact lens lesions.

**Ocular Infections**

In a seminal work by Dr. Asbell and colleagues, the Ocular TRUST (Tracking Resistance in U.S. Today) was developed to address these rapid changes in microbial resistance as they relate to ocular infections. The first data report assessed 197 cultures from participating centers and looked at *S. aureus*, *S. pneumoniae* and *H. influenzae* isolates from 2005 to 2006. Antibiotics tested were all the available topical agents used in clinical practice.

The outcomes were both interesting and concerning. Among *S. pneumoniae* isolates, all were susceptible to the fluoroquinolones except five that showed intermediate resistance to ciprofloxacin. The other agents varied from a low of 18.3% with penicillin to a high of 100% with polymixin B. The *H. influenzae* isolates showed overall sensitivity to all agents except trimethoprim. The real concern was with *S. aureus*—agents that showed good efficacy to MSSA, but demonstrated high-level resistance to MRSA. Fourth-generation fluoroquinolones such as moxifloxacin, gatifloxacin and levofloxacin demonstrated 15% sensitivity and over 80% resistance to MRSA isolates.14

A European study also demonstrated the declining efficacy of the fluoroquinolones against MRSA in a review of 582 isolates.15 This has occurred despite initial marketing that indicated that it was nearly impossible for bacteria to evolve resistance because it would require a simultaneous topoisomerase and DNA gyrase mutation. The clinical implications of this information are significant: The agents that have been the backbone of therapy for the last decade are exhibiting an Achilles’ heel that makes treating microbial keratitis a moving target.

**Post-Surgery**

Another area of concern is the changing pattern of microbial isolates following both cataract and refractive surgery. Eric Donnenfeld, M.D., and colleagues presented data at the 2009 American Society of Cataract and Refractive Surgery meeting showing that 77% of positive lid or conjunctival cultures were either *S. epidermidis* or *S. aureus*.16 They also noted that the incidence of colonization of MRSAMRSA was 33% of all patients assessed, which increased with age to 50% at 80 years old. They identified that colonization of the ocular surface is more likely in health care workers (1.25), age (1.27) and glaucoma patients (1.44).16

Darlene Miller, D.H.Sc., M.P.H., and colleagues showed similar patterns of microbialization in the surgical population, and also found that 65% of patients with ciprofloxacin-resistant organisms demonstrated in vitro cross resistance to moxifloxacin and gatifloxacin.17

Treatment protocols also have begun to change as a result of increasing resistance. The European endophthalmitis trials demonstrated a 78% reduction of incidence with an intraoperative injection of ceftoxime in addition to all typical pre- and post-operative regimens.18 LASIK and PRK surgery also have shown significant increases in the rate of MRSA infections with similar patterns of antibiotic sensitivity.19

These resistance changes are consistent with evolving patterns of microbial behavior, both systemic and global.20 There is evidence that the emerging patterns of MRSA resistance are independent of the
traditional hospital-based organisms, and instead represent a trans-species infection pattern that is derived from a separate source.

An October 2007 study reviewed the status of MRSA across the United States and found an occurrence rate of 95,000 cases with a mortality rate of 19,000.\textsuperscript{21} Compare that statistic with 12,500 AIDS-related deaths during the same period.\textsuperscript{21} A subsequent November 2007 study identified the likely source of this outbreak as the use of low-dose fluoroquinolones in the animal husbandry business to promote faster weight gains in farm animals, specifically swine.\textsuperscript{21} There is also evidence that this same mechanism may be producing a ciprofloxacin-resistant S. aureus. The original MRSA is now referred to as HFB-MRSA (hospital-based) and the new strain is called CA-MRSA (community-acquired).

For practitioners, the primary impact of this finding is in the management of patients who present with MK, with or without contact lens wear.

**A Treatment Plan**

I still recommend therapy be initiated with a fourth-generation fluoroquinolone at the appropriate dose rate (qh to q2h) and the patient be seen daily until therapy has demonstrated improvement. If, however, at any time in the first 48 to 72 hours, the patient demonstrates regression or lack of progression of the MK, it is reasonable to assume a fluoroquinolone failure and to initiate additional therapeutic intervention to address the issue.

The first step is to culture the patient and send out for laboratory analysis; this is best done via blood and chocolate agars, thioglycollate broth and Sabourauds media. The material should also be plated for Gram and Giemsa stains.

The next step after culture and stain is initiation of fortified antibiotics. While drugs like Polytrim are effective against MRSA conjunctivitis, they are not indicated for suspected MRSA/MK unless they are used only until vancomycin can be obtained. I recommend fortifying the vancomycin to 25mg/ml and dosing at qh, alternating at qh with the fluoroquinolone that was initially used until culture results are back.

In some contact lens-wearing patients, it is also appropriate to start additional gram-negative coverage with an agent like tobramycin, fortified to 14mg/ml, on the same alternating dose to address the possibility of *Pseudomonas*. In most cases, it is reasonable to simultaneously start doxycycline 100mg p.o. b.i.d. to attempt to delimit the collateral damage from collagenase and the recruitment of cytokines and interleukins. The patient must be seen daily until the culture is reported, and then the clinician can make adjustments based on results.

Due to the aggressive nature of the more resistant bacteria, it is common to have significant tissue damage associated with MK, so consider the use of a steroid after the field has been sterilized with several days of treatment. While each case is unique, the role for the anti-inflammatory properties must be considered but clinicians need to be cautious in implementing it.

**Future Considerations**

Unfortunately, due the aggressive nature of MRSA, the concern regarding the organism mutating against vancomycin is already a reality. Simon R. Bababeygy, M.D., cited two 2009 cases of preseptal cellulites that were vancomycin resistant but responded to rifampin and linezolid therapy.\textsuperscript{27}

The pharmaceutical pipeline to address the rising rate of resistance is not strong at this time. The only new agent recently released is a chloro-fluoroquinolone, Besivance (besifloxacin 0.6%, Bausch + Lomb). It has demonstrated increased sensitivity to MRSA and MRSE in clinical studies in conjunctivitis.\textsuperscript{24-26} Its increased efficacy may be related to the unique structure of the molecule.\textsuperscript{27} While there is little data related to its role in MK management, animal model studies of endophthalmitis compare it to the other fourth-generation agents.

The World Health Organization (WHO) has begun the process of creating guidelines for the worldwide use of antibiotics in an effort to bolster current sensitivities and decrease future resistance development. Recently, WHO issued a guideline for the cessation of antibiotic use in animals, with a complete discontinuation to follow within several years. Given the current issue with trans-species MRSA, this will hopefully begin the process of better balancing our use of antibiotics with our needs.\textsuperscript{28}

Practitioners should periodically review contact lens-related epitheliopathies and their treatment options to provide their patients with the best lens wear experience.

By Mile Brujic, O.D., and Crystal Brimer, O.D.

While advancements in contact lenses and lens care technology have improved the wear experience, several physiological effects of lens wear continue to contribute to secondary epitheliopathies. There is decreased tear exchange under the lens, which can create a pooling effect of carbon dioxide, debris, antigens and bacteria. The quality of the tear film, especially the mucin layer as it relates to infection, can be negatively affected with a reduction in lipid layer integrity and increased tear evaporation. Changes in the tear film can then have a secondary effect on the functionality of the epithelium.1-3

In addition to the concerns of conservative and compliant lens wear, many patients are at even higher risk due to external factors, such as overnight wear, protein and lipid build up, hygiene issues, poorly fit lenses, solution hypersensitivity and lid or ocular surface disease.4,5

In this article, we will explore several epitheliopathies associated with contact lens wear and provide a breakdown of treatment options.

Non-Infectious Infiltrates

Non-infectious infiltrates are an immune-driven response of

Dr. Brujic is a partner of Premier Vision Group, a four-location optometric practice in northwest Ohio. He lectures extensively in the areas of ocular disease management and contact lenses.

Dr. Brimer is a graduate of UNC-Chapel Hill and Southern College of Optometry. She has practiced full-scope optometry in Wilmington, N.C. for 12 years and has special interest in contact lenses and dry eye management. She is also the owner of Crystal Vision Services, an ophthalmic equipment and practice management consulting company.

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Goal Statement: This article will offer a review of contact lens-related epitheliopathies and provide an outline of their treatment options.
Faculty/Instructional Board: Mile Brujic, O.D., and Crystal Brimer, O.D.
Credit Statement: COPE approval for 1 hour of CE credit is pending for this course. Check with your local state licensing board to see if this counts toward your CE requirements for relicensure.
Joint-Sponsorship Statement: This continuing education course is joint-sponsored by the Pennsylvania College of Optometry.
Disclosure Statement: The authors have no financial relationships to disclose.
the cornea to antigens. Corneal insult initiates chemotaxis of leukocytes from the surrounding limbal vasculature into the anterior stroma. An infiltrate presents as a single (or multiple) round epithelial and sub-epithelial lesion that often does not stain with fluorescein, or may demonstrate late-phase staining. Late-phase staining often appears faintly with poorly demarcated borders several minutes after instillation of fluorescein. When an infiltrate stains, it is essential to pay close attention to its pattern in order to help differentiate it from an infectious ulcer.

The inflammatory cascade and subsequent collection of white blood cells can cause overlying epithelial damage. Because the damage is secondary, the overlying epithelial defect and staining pattern will be smaller than the underlying infiltrate. Typically, there is sectoral injection, only trace cells in the anterior chamber (if any), and just moderate pain and photophobia. Non-infectious infiltrates are small in size (under 2mm) and usually are located toward the peripheral cornea, but may be scattered throughout the entire cornea. This inflammatory response is well controlled with a steroid.

And, because any overlying epithelial defect originates from the inflammation, suppressing it with a steroid actually aids the re-epithelialization process. Using a combination antibiotic/steroid will protect the compromised cornea from secondary infection. The recommended dosing is q2h while awake for the first one to two days if needed, then q.i.d. until resolution. Often, practitioners simply will dose the combination agent q.i.d., which seems to resolve most cases.

**Infectious Keratitis**

Infectious keratitis is a completely different entity that requires meticulous care—both in its diagnosis and treatment. It is the direct result of an infectious organism invading the corneal tissue. A recent study showed that contact lens wearers were 9.31 times more likely to experience microbial keratitis than non-contact lens wearers.

Clinically, bacterial ulcers will usually present as a single, more centrally located infiltrate that stains with fluorescein. They are generally larger in size (greater than 2mm). The staining pattern closely outlines the footprint of the infiltrate because an ulcer originates in the epithelium before penetrating into the stroma. There generally is an anterior chamber reaction, stromal edema and significant conjunctival hyperemia. Often, there is much more pain associated with an infectious infiltrate than sterile infiltrates, as well as decreased vision and discharge.

Differentiating infectious from non-infectious infiltrates is critical, because the protocol is substantially different between the two treatment regimens (figure 1). Bacterial ulcers are seen at a considerably lower frequency than sterile infiltrates.

For an infective keratitis, the treatment goal is to eradicate the offending organism and promote corneal healing. This is often done with highly concentrated topical fourth generation fluoroquinolones. Typically, the newer fluoroquinolones—moxifloxacin, gatifloxacin or besifloxacin—are first-line treatments; however, none of these agents currently are approved for use in microbial keratitis.

Depending on the severity of the infection, it is appropriate to initiate treatment at an accelerated frequency over the first several days to rapidly decrease concentrations of offending microorganisms. Additionally, it is reasonable to incorporate Poly-
trim (polymyxin b/trimethoprim, Allergan) due to its efficacy against MRSA.

The standard of care for more aggressive or centrally located ulcers is to culture and treat with the appropriate fortified antibiotics. Some doctors prescribe 30-minute dosing intervals in those cases, alternating fluoroquino-

nolones with the fortified antibi-

otics. However, some research shows equivalent efficacy of fourth-generation fluoroquino-

lones to combination fortified antibiotic treatment.13

If the ulcer responds well after 48 hours, the drops can often be decreased to q2h until re-

epithelialization and then tapered to q.i.d., according to the corneal response. Cycloplegics can help decrease the patient’s pain signifi-

cantly as the infectious infiltrate is healing.

Despite immediate treatment, corneal scarring can threaten the patient’s visual outcome, and concurrent steroid treatment has been questioned as a means to minimize the resultant scarring from these infectious events.

A recent, large-scale study established that there was no benefit to the patient’s best-corrected visual acuity or resultant scar size when steroids were incorporated into the treatment protocol.14 However, patients with central ulcers greater than 4mm or those with the worst entering acuities did experience nearly a two-line improvement in visual acuity with adjunctive steroid treatment.

The study also illustrated the safety of concurrent steroid use after 48 hours of fluoroquino-

lone treatment in culture positive patients and confirmed that there was no delay in re-epitheliali-

zation time in the group using steroids.15

Advancing Wavelike Epitheliopathy

Advancing wavelike epitheliophasis is a rare condition that consists of centripetally advanc-

ing wavelike epithelium that usually extends from the superior limbus towards the visual axis.15 The individual’s visual acuity may be affected, depending on how far the irregular epithelium extends to the visual axis. This can be seen during standard slit lamp examination, but is significantly easier to identify after the instillation of fluorescein dye while viewing the cornea with a cobalt blue light through a Wrat-

ten filter (figure 2). Other signs that may occur include ocular irritation and redness, depending on the severity of the clinical pre-

sentation.

In vivo confocal microscopy is remarkable for the presence of atypical, elongated and cetripe-

tally oriented cells.16 Additionally, these cells are remarkable for relatively large, hyperreflective nuclei and a loss of visible cellular borders in the basal epithelium.16,17

The pathophysiology of advancing wavelike epithelium is poorly understood, but is believed to be multifactorial. Risk factors for its development include topical antiglaucoma medications, contact lens solutions, contact lens wear, previous ocular surgery and atopic derma-

titis.15-17

There have been reports in the literature that describe the effectiveness of an application of 1% silver nitrate to the superior limbus.15-17 Liquid nitrogen also has been documented as an effective treatment for this condition. During the treatment, the corneoscleral limbus and surface corneal epithelium are exposed to liquid nitrogen through a double freeze-

thaw procedure. The technique is to apply liquid nitrogen to the affected area for one to two sec-

onds, wait 30 seconds, and then reapply for another one to two seconds.19

In 2005, Professors Patrick Caroline and Mark Andre reported on a case in which advanc-

ing wavelike epitheliopathy was included in the differential diagnosis. The recommended treat-

ment called for removal of the offending agents while having the patient utilize non-preserved arti-

ficial tears.20

In our office, if visual acuity is not affected, we follow the same treatment plan of removing the suspected offending agent. Initially, we switch contact lens patients who use a multipurpose solution to a hydrogen peroxide system (figure 3). We also look to a daily disposable option, if one is available for their prescription. If the epitheliopathy either is not improving or progressing, it is reasonable to discontinue contact lens wear and have the patient discontinue artifi-

cial tears. If it continues to progress and/ or visual acuity becomes affected, more extreme measures may be warranted.
Neovascularization

Corneal neovascularization is a sign of tissue hypoxia. Normally a transparent, avascular structure, the cornea acquires its nutrients from the aqueous, the tear film and the atmosphere. Deeper vascularization is also possible and signals a more serious condition. Although the sclera and bulbar conjunctiva are continuous with the cornea, the rich vascular supply that typically nourishes these structures usually abruptly stops at the limbus. Under circumstances of low oxygen, the cornea attempts to acquire more oxygen to nourish itself. This will lead to limbal vasculature signaling and subsequent growth of new blood vessels in a centripetal manner to meet the increased oxygen demands.20,21

There still doesn’t seem to be a true consensus on the amount of oxygen required by the cornea under normal, open-eye conditions. Minimum oxygen permeability requirements range from 24 Dk/t to 90 Dk/t.22,23 Clinically, most of the contemporary hydrogel contact lenses utilized in the last two decades seem to avoid significant neovascular changes under daily wear conditions. Concern arises, however, when patients sleep in these lenses for extended periods of time. In the face of such non-compliance, corneal neovascularization is more likely to occur.

High-oxygen permeable contact lenses have alleviated much of the breathability concerns for patients who sleep in their contact lenses. The silicone hydrogel lenses have offered significantly lower rates of corneal neovascularization and are an ideal lens option for those sleeping or suspected of sleeping in their lenses. Be cautious because extended wear will increases the risk for other contact lens complications, such as microbial keratitis.24,27

There are a number of epithelial conditions that can affect our contact lens wearers. Through understanding these conditions and modifying risk factors, along with accurately diagnosing and treating these patients, we can regain healthy corneal physiology and facilitate successful lens wear.28

1. How do non-infectious corneal infiltrates usually present?
   a. With a significant anterior chamber reaction.
   b. As a single lesion that causes notable pain.
   c. As a single or multiple, round sub-epithelial lesions that often do not stain with fluorescein, or may demonstrate late-phase staining.
   d. A dense collection of inflammatory cells with an overlying epithelial defect that mirrors the infiltrate.

2. How do you best protect a compromised cornea from secondary infection?
   a. A steroid.
   b. A bandage contact lens.
   c. An oral antibiotic.
   d. A combination antibiotic/steroid.

3. What is an infectious keratitis?
   a. An inflammatory event.
   b. A direct result of an infectious organism invading the corneal tissue.
   c. A simple break in the epithelium.
   d. Multiple corneal infiltrates.

4. How do bacterial ulcers usually present?
   a. As a single or multiple sub-epithelial infiltrates.
   b. As a single, more centrally located infiltrate that stains with fluorescein.
   c. Usually without an anterior chamber reaction.
   d. With mild pain.

5. Which agents are NOT used to treat corneal infections?
   a. Alternated fluoroquinolones and fortified antibiotics.
   b. Topical mast cell stabilizers.
   c. Fourth-generation fluoroquinolones (e.g., moxifloxacin, gatifloxacin or besifloxacin).
   d. Cycloplegics.

6. What is advancing wavelike epitheliopathy?
   a. An infectious event.
   b. A poorly understood inflammatory condition.
   c. A rare condition that consists of centripetally advancing wavelike epithelium that usually extends from the superior limbus towards the visual axis.
   d. A new corneal dystrophy.

7. What is NOT a sign of advancing wavelike epitheliopathy?
   a. Reduced visual acuity.
   b. Anterior chamber reaction.
   c. Ocular irritation.
   d. Redness.

8. What is a primary risk factor for the development of advancing wavelike epitheliopathy?
   a. Contact lens wear.
   b. Increased age.
   c. Male sex.
   d. Family history.

9. What is the correct technique to apply liquid nitrogen?
   a. Apply five drops, close and rotate eyes for 60 seconds, then rinse.
   b. Apply one drop every 15 minutes for one hour.
   c. Bring it very close, but do not allow it to touch the eye. Hold for one to two seconds, wait 30 seconds and then bring it close again for an additional one to two seconds.
   d. Apply to the affected area for one to two seconds, wait 30 seconds and then reapply for another one to two seconds.

10. What is the cornea’s minimum oxygen permeability requirements?
    a. 12 Dk/t to 76 Dk/t.
    b. 24 Dk/t to 90 Dk/t.
    c. 70 Dk/t to 90 Dk/t.
    d. 90 Dk/t to 140 Dk/t.
Conceptually, orthokeratology has been around for more than half a century now. But, it is the improvements in lens materials, design and fabrication over the last decade that have triggered significant changes in how we provide this treatment. When you consider the data published over that same 10-year span showed a retarding effect on the progression of myopia, it is clear that orthokeratology has never had greater potential to be a significant factor in the realm of vision correction—particularly for children.\(^1\)\(^-\)\(^3\)

In this regard, it is an exciting time to be able to offer orthokeratology to our patients. However, there still is much to study and learn about the long-term effects of orthokeratology on the corneal tissue. Reports of ocular infections with lens wear may cause patients to be nervous about pursuing orthokeratology, particularly when parents consider the procedure for their child. It is therefore important that we do our part to alleviate the concerns by knowing what risk factors exist and what problems may arise.

**Why Ortho-K?**

We can all agree that there are some indisputable benefits of orthokeratology—such as convenience and safety. Keep in mind that you should mention both the pros and cons of ortho-k with your patients.

First and foremost, we cannot underestimate the advantage of experiencing freedom from corrective lenses wear, especially for children. How many times have you had frustrated parents coming in for the fifth time in a month to get their child’s glasses fixed or adjusted? How often do children end up replacing glasses because they are broken or scratched to the point of uselessness? In general, children are harder on eyeglasses than adults—due to their active lifestyles and relative carelessness when it comes to their spectacles. Keep in mind that the long-term cost of orthokeratology vs. glasses is not significantly different when you consider that you are replacing glasses annually, if not more frequently.

Secondly, glasses are awkward to use when playing sports or other physical activities. This is one reason why many parents consider contact lenses in the first place. Many parents, however, are torn between concerns that their child is not ready for contact lenses and the alternative of their child having to wear glasses for athletics.

While not risk free, orthokeratology allows practitioners to offer new treatment options to our young patients.

**By Jason Jedlicka, O.D.**
Orthokeratology is a perfect solution for both of these problems. For children active in athletics, there is no better means of correction at any age than orthokeratology.

Ortho-K vs. Soft Contact Lenses

It could be debated that soft contact lenses can be just as advantageous for active children as orthokeratology, but the arguments fall short. For example, while soft lenses should not be worn when swimming, this is not an issue with orthokeratology. Because soft lenses are worn during the active times of day, any problem with lens drying or stability will affect vision and function during times of visual demand. This is not the case with orthokeratology. Soft lenses are applied at home, but the child then spends the majority of their day away from home and, most likely, away from their care system, case and back-up glasses. This means that any issues that arise while wearing their soft lenses may not be managed optimally. On the other hand, with orthokeratology, children manage their lens use at home never far from assistance and lens care products.

Comparing cumulative costs, there is little monetary difference when you compare orthokeratology vs. soft lens use. Although the initial cost of orthokeratology is higher, the annual cost of soft lenses will usually catch up in the long run.

Myopia Control

One would-be advantage that is currently being researched is the possibility of myopia control through orthokeratology. One theory for why myopia progresses stipulates that the hyperopic defocus on the peripheral retina with standard forms of vision correction leads to further progression of myopia. With orthokeratology, only the central 4mm to 5mm of the visual axis is optimally corrected, while the peripheral retina is left in varying degrees of myopic defocus, as evidenced by looking at the topography of the cornea before and after treatment (figure 1). This myopic defocus leads to less development of myopia to a statistically significant degree.

Evidence certainly is mounting to suggest that there is more to orthokeratology than just the obvious benefits of convenience—it may become increasingly clear that this option should be discussed with the parents of all children who are exhibiting myopia progression. At first, it may be difficult to get into the habit of discussing this treatment option—but, you will soon start to see the benefits of orthokeratology become a reality for your patients.

Minimizing the Risks

If there are significant risks to ocular health with orthokeratology, the benefits may be negated. So, what are these risks? The main short-term concern is ocular infection, leading to loss of best-corrected visual acuity. Long-term risks revolve around morphologic change to the corneal tissue, which affect its function.

Ocular infection is a risk factor of results that compared axial eye elongation in a group of children using orthokeratology lenses with a control group. Their research showed 46% less axial elongation in patients with ortho-k lenses vs. those in the control group.

In 2009, Jeffery Walline, O.D., Ph.D., reported nearly identical findings in a completely different patient population. These results have been followed with additional research in different areas of the world, including two 2011 studies—one by Tetsumiko Kakita, M.D., and colleagues and one by Jacinto Santodomingo, Ph.D., M.Sc., and colleagues—which showed a slowing of axial elongation and vitreous chamber growth.

Other tests are ongoing, including the Retardation of Myopia in Orthokeratology (ROMIO) Study, which is randomizing participants into orthokeratology or single-vision spectacles. Early results show data comparable to the other four previously mentioned studies.

Evidence certainly is mounting to suggest that there is more to orthokeratology than just the obvious benefits of convenience—it may become increasingly clear that this option should be discussed with the parents of all children who are exhibiting myopia progression. At first, it may be difficult to get into the habit of discussing this treatment option—but, you will soon start to see the benefits of orthokeratology become a reality for your patients.
for any type of contact lens wear. Overnight lens wear is associated with a higher risk of ocular infection than daily wear lens use, but gas-permeable (GP) lens wear typically presents a lower risk than soft lenses.6

Additionally, how does the risk for keratitis compare in orthokeratology lens wearers to that of other lens wearers? The problem we face is that the volume of cases is relatively small to make a good estimation. We know that infectious keratitis does indeed occur, as several articles have chronicled these cases.7,8 The American Academy of Ophthalmology last published its stance on the safety of overnight orthokeratology in 2008, suggesting that a better-controlled, level 1 study needed to be completed to fully evaluate the risk and the potential for myopia control.9

What can we do in the meantime to minimize that risk to patients, specifically children? Clearly, good lens care practices are of the utmost importance (figure 2). Use of only approved contact lens care products, along with the elimination of tap water use on lenses, has been recommended to reduce the risk; the highest incidence of infectious keratitis occurs in regions of the world where good care practices are less likely to be followed.3

In addition, provide careful instruction to parents and children about what is to be expected with lens wear, and include comfort upon application, signs and symptoms of problems and after-hours contact information. These steps are vital to minimize the chance of a lens causing serious problems. Written directions and instructions, as well as informed consent, is highly recommended to all orthokeratology lens wearers.

Finally, using only high Dk/t lens materials and FDA-approved designs not only minimizes the risk to patients, but also improves the efficacy of the treatment.10 Requiring the highest level of compliance to accepted practices and the highest quality materials will minimize the risk of short-term complications for patients.

Long-term complications of orthokeratology involve permanent and undesirable changes to corneal shape or function. Some of these changes can be very significant, while others may not necessarily have any impact on ocular function. One study documented residual corneal flattening among a group of 28 patients; the impact of this change is still undetermined.11 Certainly, any change to the corneal tissue is bothersome, but mild flattening of the cornea may or may not create real issues. The aforementioned study evaluated keratometric change two weeks after discontinuation of lens wear vs. pre-treatment levels. It is possible that, with longer time out of lenses, the corneal curvature changes may return to baseline. But, it is also possible that some permanent structural restructuring may occur.12

Reduction in corneal sensation has been documented after three months of overnight orthokeratology lens wear.13 The significance of this finding has not yet been determined, but it is useful to keep this in mind for our patients. Perhaps of more significance are the 2011 findings of Amelia Nieto-Bona, O.D., M.Sc., and colleagues, which examined the corneal tissue of 15 eyes with confocal microscopy. The researchers reported several changes to corneal tissue—some of which returned to baseline after discontinuation of lens wear, and others that showed an increase in endothelial cell polymegathism and a decrease in epithelial layer thickness.14 Again, the significance of these findings is not known, but studies continue to look at the possible long-term morphologic changes to the cornea as a result of orthokeratology and their effects on ocular health.

We all want what is best for our children. Good vision and ocular health are important aspects of our children’s lives. To be able to provide vision correction that is convenient, safe and effective at slowing the deterioration of their vision over time is something most of us would want for our children who require vision correction. Orthokeratology seems to be able to provide all these features. Further research will continue to determine the true short- and long-term safety for those children in orthokeratology lenses, as well as the effects it has on slowing the progression of myopia.15

When treating ocular conditions, topical medications can offer many advantages, including the ability to achieve high tissue concentrations and with limited systemic side effects. However, delivering an effective dose to ocular tissues can be a challenge. The bioavailability of most topical ophthalmic medications is surprisingly limited. The tears and lacrimal system efficiently wash drugs out of the eye before they can be absorbed, and competition with tissues other than intended targets can reduce available drug levels substantially. Even the corneal epithelium itself presents a formidable barrier to drug penetration.

With the high cost and regulatory burdens associated with new drug development rising rapidly, a variety of strategies and technologies have been developed to increase the effectiveness of existing drugs. The use of engineered drug delivery vehicles increases ophthalmic drug bioavailability and typically improves therapeutic effectiveness. For example, the propriety vehicle DuraSite (InSite Vision, Inc.) is used in the drugs AzaSite (azithromycin 1%, Merck) and Besivance (besifloxacin 0.6%, Bausch + Lomb) to prolong drug-ocular surface contact time, which results in enhanced penetration. DuraSite creates a polymeric mucoadhesive matrix depot, which forms a gel upon instillation into the eye. Xanthan gum, used in both TobraDex ST (tobramycin 0.3%/dexamethasone 0.1%, Alcon) and Moxeza (moxifloxacin 0.5%, Alcon), have a similar mechanism of action.

Why Contact Lenses?
Renowned Czech chemist, Otto Wichterle, Ph.D., invented the first hydrogel material. Quickly recognizing the potential for hydrogel materials to be manufactured into contact lenses, Dr. Wichterle produced the first soft lenses in his own kitchen using a spin-casting apparatus that he devised.1

Contact lenses are becoming an increasingly attractive option for drug delivery in our patients with a variety of ocular disorders.

By Art Epstein, O.D.

Dr. Epstein is a popular speaker and well-known author. He serves as an adjunct associate clinical professor at Midwestern University Eye Institute in Phoenix, Ariz. and is the Chief Medical Editor of Optometric Physician.
Soon afterwards—even before the first hydrogel lenses were commercially available—J. Sedlavek, a Czech ophthalmologist, explored the use of hydrogels to deliver drugs.2

The benefit of using soft bandage lenses in managing a variety of ocular diseases and conditions quickly became apparent.3,4 Numerous reports describing bandage lens applications to protect the cornea and facilitate healing were published in the ophthalmologic and optometric literature during the 1970s and 1980s.5 Some clinicians advocated the concurrent use of topical antibiotics with long-term bandage lens use to prevent infection.6 Bandage lenses soon became standard of care, replacing pressure patching in most situations.

Because of the affinity of hydrogel materials for water-soluble topical ophthalmic medications, the use of bandage contact lenses to deliver medications quickly gained favor. Early reports describe the use of soft lenses as depots to dispense glaucoma medications, anti-inflammatories and anti-infective agents.7,8

Conventional hydrogels are a mixture of hydrophobic plastics and water. Their relatively high water content and typically large pore structure make them an effective depot for many drugs. The addition of silicone to conventional hydrogel materials improves permeability and can enhance the delivery of certain medications.9,10

The relatively slow release of drugs from hydrogel and silicone hydrogel lenses increases ocular bioavailability well beyond what can be achieved with conventional eye drops. Drug-releasing contact lenses also prolong residence time, enhance the effectiveness of most pharmaceutical agents and generally aid with patient compliance. Slower drug release rates promote diminished systemic absorption, which limits the potential for associated side effects.11,12

An additional benefit of soft lenses is that most patients can easily apply them to the eye after appropriate training, and the lenses are designed to be comfortable and compatible with ocular tissues. Compared to having patients instill drops several times a day, using lenses to dispense ophthalmic drugs can be more convenient for long-term therapy. More consistent drug levels are also maintained in target tissues, which often equates to greater therapeutic efficacy.

Today’s Drug Delivery Technology

For a contact lens to be successfully used as a drug delivery vehicle, the drug cannot interfere with the essential characteristics of the lens. Added medications should not affect comfort, oxygen permeability, modulus, transparency or surface wettability of the lens. Also, the addition of a drug should not change lens-fitting characteristics or the prescription. Alteration of these critical properties can render the lens unwearable.

Traditionally, lenses were loaded with drugs—either by frequent instillation while the lens was worn or by presoaking the lens in the desired medication.7,4 In the former case, the lens served as a depot, absorbing the instilled medication and releasing it at a much slower rate as the drug sought equilibrium with the tears. Presoaking the lens was more efficient; less drug was lost upon instillation and there was a more even distribution. Results with either technique using commercially available lenses are quite variable, depending on drug chemistry, solubility, lens material, water content and numerous other factors.

A number of novel approaches have been used to optimize and extend drug delivery with contact lenses. Techniques to incorporate pharmaceutical agents directly into lens materials include encapsulation of drug within liposomes; incorporation of drug particles and nanoparticles directly into the lens material; use of polymer and fibrin films; and adding surfactants to control drug release. Additionally, lens-incorporated cyclodextrins contain hydrophobic cavities that can form inclusion complexes that foster slowed drug release. Imprinting of drugs unto contact lenses has also been successfully
accomplished. Further, drugs can be impregnated within lens material matrices through the use of solvents at high temperatures and pressures. Incorporating transport barriers into lenses is another promising approach for controlled elution of drugs. Barrier incorporation can be tuned to provide prolonged therapeutic levels of various drugs.

Clinical Application

- **Microbial keratitis.** Sight-threatening conditions, such as microbial keratitis, require rapid deployment of high levels of medication to the affected tissues. Currently, patients with severe microbial keratitis are hospitalized to ensure continuous delivery of therapeutic levels of antibiotic through round-the-clock dosing. Management of these patients could be dramatically improved through the use of an effective drug delivery system, ensuring continuously high antibiotic levels. Contact lens delivery of antibiotics has been investigated, yielding sustained, high therapeutic levels with potential utility for managing bacterial keratitis.16,17

- **Glaucoma.** Chronic ocular conditions, such as glaucoma, require long-term pharmacologic treatment. Frequent dosing often leads to compliance failures, making this an excellent application for the use of extended-release, drug-eluting contact lenses. A feasibility study investigating efficacy and toxicity of contact lenses that were passively impregnated with timolol maleate and brimonidine tartrate found IOP reductions equivalent to conventional therapy and no toxicity. This means that we can offer prolonged controlled drug delivery. A recent study found that contact lenses increased drug bioavailability and decreased systemic absorption.19

- **Allergy.** Patients with ocular allergy also could benefit from continuous delivery of therapeutic levels of allergy medication. The use of ketotifen-containing contact lenses for the management of ocular allergy has been investigated experimentally, and has also undergone several safety and efficacy clinical trials.20,21

- **Dry eye.** Another promising area for the use of drug-eluting contact lenses is the controlled release of phospholipids. Meibomian gland dysfunction (and dry eye in general) has been associated with a lack of phospholipids in the tear film. Phospholipids are an essential component contained in meibum, which acts to stabilize the tear layer. Phospholipid-eluting contact lenses may provide an effective treatment for some forms of dry eye, and possibly can improve end-of-day dryness in contact lens wearers by stabilizing the tear film and enhancing lens wettability.22 This may be especially helpful in wearers of silicone hydrogel lenses, which sequester lipids due to the hydrophobic nature of their surfaces.23

In addition to the familiar refractive and protective role soft contact lenses have played for the past 50 years, developments in drug delivery technology are likely to propel soft lenses to even greater heights of clinical significance in the future. Contact lenses are uniquely able to provide sustained effective levels of medication to the eye. Breakthroughs in drug delivery are also likely to help eliminate end-of-day dryness in contact lens wearers and offer help to dry eye sufferers. These advances in drug delivery technology are likely to extend the usefulness of contact lenses for the foreseeable future.

Large-diameter rigid gas-permeable lenses are the future of contacts.

By Langis Michaud, O.D., M.Sc.

A few years ago, my esteemed colleague Nathan Efron, Ph.D., D.Sc., made a strong statement about the imminent death of rigid gas-permeable (RGP) contact lenses, which were supposed to be eradicated in the subsequent years. His words created a shockwave. However, obviously this scenario never became a reality. In fact, the marketplace is now saturated with RGP lenses to better serve our patients’ needs.

Based on today’s technology and a better understanding of the dynamics between the new lens designs and the cornea, modern large-diameter RGPs are the lenses of the future. In fact, I estimate that they will double their presence in the market within the next five years, competing to replace soft lenses as the go-to option in many cases. This will happen simultaneously with the launch and development of a new generation of lenses—with large diameters and made from very high-permeable materials.

They will be as comfortable as soft lenses, as easy to fit as soft toric lenses, but with all the benefits of rigid materials, including better visual acuity and less infections or inflammatory events.

Evolution or Revolution?

In the last five years, manufacturers have developed interesting RGP lens designs featuring large diameters that exceed the corneal border. The increased availability of material to produce such large lenses, improved manufacturing processes to customize their design and a better understanding of the conjunctival anatomy helped establish new standards in RGP lens fitting.

Nowadays, large-diameter lenses are available from 14mm to 24mm in spherical, toric, reverse geometry and even multifocal designs. In addition, we now have two new types of lenses: corneo-scleral (<15mm diameter lenses partially supported by the cornea) and mini/true scleral (14.3mm to 16mm diameter lenses supported only by the conjunctiva aimed to vault the cornea). The latter offers better options to restore and protect the ocular surface.

Clinical applications for large-diameter lenses are numerous and exceed the natural niche for RGP lenses (corneal ectasia, irregular corneas, post-surgical correction of ametropia). Modern large-diameter lenses offer a valid option for correcting moderate to high spherical refractive errors, moderate to high astigmatism and presbyopia. This represents not only a true evolution in this category of contact lenses, but a real revolution for the entire profession.

Benefits of Large RGPs

Large-diameter (14.3mm to 18mm) RGP lenses offer many advantages over their small-diameter counterparts. For starters, initial discomfort—the primary reason practitioners are not
fitting small RGP lenses—is no longer an issue because the lenses lie on conjunctiva, a less sensitive tissue. Most of the large-diameter lenses vault the cornea, without touching it. This not only preserves the tissue integrity but alleviates any intolerance or corneal sensation associated with contact lens wear. Once properly fitted, large-diameter lenses are as comfortable as a soft lens.

Also consider that there is no invasion of dust and particulates under the surface of a large-diameter lens. Many RGP wearers complain that, especially in the wind, some debris can remain trapped under their lenses, which creates immediate discomfort that ultimately leads to the lens removal. This cannot happen with large-diameter RGP lenses—once again, offering the same comfort as a soft lens.

Ocular dryness is the leading cause of contact lens dropout. With large-diameter RGP lenses, the cornea is bathing in fluid during all the wearing hours. Primary ocular dryness can be reduced, and contact lens-induced dryness at the end of the day is eliminated. Therefore, large-diameter lenses can provide a solution to address these issues, which is the reason why many corneal specialists look at large-diameter RGP lenses to treat even the most severe dryness conditions.

Keep in mind that RGP lenses provide a crisp and sharp visual acuity that cannot be compared to soft lenses. This is especially true when moderate to significant astigmatism is involved. Because RGP materials do not dehydrate over time, and large lenses do not move a lot and do not rotate, these lenses are the optimal choice to correct astigmatism (up to 4D). They also are preferred for the correction of presbyopia and emerging designs of large-diameter lenses are showing promising results.

As an added bonus, large RGP lenses currently are unavailable for purchase on the Internet. This can give practitioners an upper hand in practice sales, as well as in their ability to effectively control the patient’s eye health.

Additional Considerations

The future success of large-diameter RGPs will become a reality if a significant number of practitioners prescribe and fit these lenses. This evolution is not instantaneous.

We need to begin considering large-diameter lenses as our first option. The potential market for these RGP lenses include toric lens patients who are not completely satisfied with their vision, patients who report end-of-the-day ocular dryness or RGP lens wearers complaining of periodic discomfort.

Learning how to fit large-diameter RGP lenses is relatively easy. The exact learning time will vary, of course, based on experience. Fortunately, the newest lenses in today’s market are user-friendly; the smallest of the large-diameter lenses (14.2mm to 15mm) are as easy to fit as soft lenses. Outside of this range, true scleral lenses remain a challenge due to conjunctival toxicity.

The key is to devote enough time initially to learn the fitting process and to be able to troubleshoot the problems as they occur. You can build your expertise by familiarizing yourself with the lenses through regularly fittings.

Learn to Troubleshoot

Difficulty handling large-diameter lenses is the number one reason why many patients cannot wear this modality. For some, such as our arthritic patients, insertion and removal of the lenses can be a challenging task, especially without help.

Another common complaint is tight lenses, a syndrome that is characterized by the sudden occurrence of a red and painful eye after only a few hours of wear. This happens when the lens becomes tight on the ocular surface and seals off the corneal periphery. The absence of tear exchange (habitually limited, but present) contributes to trapped debris and toxins under the lens surface, which triggers a severe inflammatory reaction. At that time, the fit has to be revisited, allowing for more tear exchange and increased movement of the lens.

Discomfort with the large-diameter lenses is a sign of a bad fit. In theory, lens awareness can be present in the first minutes of wear, but true discomfort is certainly not expected.

Keep in mind that large-diameter lenses take time to be fitted. At minimum, it takes 20 to 30 minutes for the lens to settle. In some conditions, once the optimal lens is found, a practitioner may first prefer to reassess the fit after a few hours of wear before deciding on the modality.

Once stabilized on the eye, a clearance of 125µm to 150µm at the thinnest point is considered optimal for lenses under 15mm. For large lenses, a 200µm clearance is acceptable; although, some practitioners prefer a clearance of 300µm to 400µm. Optical coherence tomography (OCT) can help to evaluate the lens-to-ocular surface relationship, and to accurately define the appropriate modifications needed. Some labs offer custom designs based on the OCT measurements.

Large-diameter RGPs represent a true, modern alternative to other modalities. They can compete with soft lenses in both comfort and convenience. They outperform other lenses for visual acuity and in the treatment of ocular dryness. Contrary to all predictions, RGP lenses are not dead—in fact, I believe they are taking on a whole new life.
Daily Disposables

Proceedings from a live interactive webinar event, attended by several of the industry’s most renowned contact lens practitioners.

Moderated by Brian Chou, O.D.

Kicking off the April event on daily disposables, moderator Brian Chou, O.D., asked the audience if they believe all patients should be put into daily disposables. The results were divided: 36% said yes, 39% said no and 25% said yes with some reservations.

Panelists Jason Miller, O.D., M.B.A., and Mile Brujic, O.D., said the survey results reflected a debate that’s been ongoing between the two of them. “I personally think all patients can be placed in daily disposables, but it’s hard to say yes because we don’t always have available powers to make it the go-to lens for all patients,” said Dr. Miller.

After first acknowledging the benefits of daily disposables from a health perspective, Dr. Brujic summed up the challenge: Is the daily disposable technology as comfortable as two-week or monthly options? Can we create all of the parameters that we currently have available in specialty lenses?

Interestingly, said Dr. Miller, the percentage of eye doctors and optometric staff that wear daily disposables is very high, but these same practitioners are not aggressive in putting their patients in this modality. Dr. Brujic said he thinks it is the preconceived notions, like cost for example, that causes practitioners to fall back to old habits when it comes to fitting patients.

Dr. Chou provided some history: In 1995, when the modality was first introduced to the U.S., the market share hovered around 5% and went up to 15% in 2011.1 Why the change? Several factors were mentioned starting with the reality that, in the past decade, there have been two major solution recalls, which naturally led practitioners to look at alternative options.

The audience also had a lot to add to this event. Attendees submitted several questions throughout the discussion, including one regarding whether daily disposables helped drive referrals to the panelists’ practices. Drs. Miller and Brujic, who were able to answer online in real-time, said they have seen an increase in new patients looking specifically for daily disposables and existing patients asking questions about this modality. In response to another audience question, Dr. Miller said that an added bonus is the aggressive manufacturer rebates that allow practices to set reasonable prices for the lenses, which generally keeps patients from shopping around.

The audience was then polled on whether the cost of daily disposables hinders their ability to use the product. The response: 21% strongly agreed, 54% somewhat agreed, 13% somewhat disagreed and 13% strongly disagreed. Dr. Brujic said this was interesting since while there is an initial higher purchase cost with daily disposables over two-week or monthly counterparts, the expenses even out over the course of the year.

Dr. Miller disagreed slightly, saying that the patient’s perception is that daily disposables are more expensive and their perception is their truth. While it is important to address the expense factor, it is also important not to dwell on the issue. Rather shift the focus onto the ease, convenience and freshness of the daily option.

From the financial breakdown to the health benefits, this month’s talk on daily disposables was highly informative. A special thank you to our active audience who participated throughout the evening. We welcome you to join us at our next live conversation, which will focus on steroids. You can register for upcoming online events at www.reviewofcontactlenses.com.

CONTROVERSIES IN CARE POLL

Are daily disposables as good as their two-week and monthly disposable counterparts?

Poll Results:

<table>
<thead>
<tr>
<th>Yes</th>
<th>84%</th>
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<tr>
<td>No</td>
<td>16%</td>
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Wearers with astigmatism

They need consistently crisp, clear vision.

Bausch + Lomb PureVision®2 HD and PureVision®2 HD For Astigmatism contact lenses are designed to give your patients a consistently crisp, clear vision. Both feature High Definition™ Optics for crisp, clear vision, and significant design advancements for comfort and breathability. Plus, new PureVision®2 HD For Astigmatism lenses include our unique Auto Align Design™ for consistent on-eye stability and fewer visual fluctuations. Add it all up, and you’ve got a family of lenses that give your patients what more of what they are looking for.

What wearers are saying about PureVision®2 lenses:

- **83%** of first-time lens wearers say PureVision®2 HD lenses are the ideal lens for them.
- **87%** of astigmatic wearers rate their vision with PureVision®2 HD For Astigmatism as good to excellent.
- **84%** of eye care professionals say PureVision®2 HD provides crisp, clear vision.

Scan to learn how HD Optics help deliver crisp, clear vision.

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NOW AVAILABLE FOR ASTIGMATISM

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