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Review of Cornea & Contact Lenses

NOVEMBER 2009

THE RESEARCH ISSUE

ALSO INSIDE:

- Top 10 for the Past Five Years
- No-Fee CE: Promoting Healthy Contact Lens Wear
- The Ins and Outs of Corneal Dystrophy
- Genetic Aspects of Keratoconus

Supplement to
REVIEW OF OPTOMETRY
November 2009

By Joseph P. Shovlin, O.D., F.A.A.O.

The Lifeblood for Continued Success

As the pulse of every contact lens practice, advances in research ensure a bright future for lens wearers.

Over the years, contact lens practice has advanced through the research contributions of a relatively small group of researchers and astute clinicians. These pioneers, such as Tuohy, Wichterle and Lim, Sarver, Mandel, Polse and Korb, have provided groundbreaking ideas and novel approaches on ways to improve the experience of contact lens wear.

In an effort to recognize the achievements of contact lens research, our editorial board was asked to submit recommendations for the top 10 research articles over the past five years. From a list of almost 100 articles submitted by the editorial board, ten were chosen and are highlighted in this issue. The papers chosen have significant relevance to contact lens practice, and many set the stage for future research initiatives.

Some of the articles discussed this month use original study designs; others feature descriptive epidemiology and study group recommendations. They answer important questions such as, "How might contact lens clinicians better diagnose and manage dry eye related problems?" "How do biofilms interact in the contact lens tear film milieu?" " What led to the mini-epidemics of *Fusarium* and *Acanthamoeba* ketatitis?"

In the past, contact lens research has opened the door to significant progress and new ideas. Looking toward the future, we must continue to ask thought-provoking questions that will spur researchers on. We must continue seeking novel approaches that advance the field of contact lens practice, rather than simply designing research to prove what we believe is true.

Unfortunately, as the cost of research spirals upward, fewer scientific experiments or clinical trials will be funded by government agencies. In addition, I worry that contact lens research may be viewed as low-priority by those funding government research. Because of these limitations, it is extremely important to cultivate young inquisitive researchers who have an interest in the area of contact lenses.

I hope you enjoy the articles that we have highlighted from the past five years. It might be nice to someday go back and review our research history in more detail by selecting the best research studies of all time. In the meantime, future researchers can search for new ways to make contact lenses comfortable for nearly everyone, reduce infection rates and inflammatory events, and fully correct refractive errors, thus increasing the number of patients who confidently and comfortably wear contact lenses. RCCL

Joseph P. Shovlin, O.D., F.A.A.O., Clinical Editor

Top 10 for the Past Five Years

1. Korb DR, Herman JP, Greiner JV, et al. Lid wiper epitheliopathy and dry eye symptoms. Eye Contact Lens. 2005 Jan;31(1):2-8.
2. Stapleton F, Keay L, Jalbert I, Cole N. The epidemiology of contact lens related infiltrates. Optom Vis Sci. 2007 Apr;84(4):257-72.
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7. Dumbleton K, Woods C, Jones L, et al. Patient and practitioner compliance with silicone hydrogel and daily disposable lens replacement in the United States. Eye Contact Lens. 2009 Jul;35(4):164-71
8. Nichols JJ, Sinnott LT. Tear film, contact lens, and patient related factors associated with contact lens related dry eye. Invest Ophthalmol Vis Sci. 2006 Apr;47(4):1319-28.
9. Szczotka-Flynn LB, Imamura Y, Chandra J, et al. Increased resistance of contact lens related bacterial biofilms to antimicrobial activity of soft contact lens care solutions. 2009 Sep;28(8):918-26.
10. Alfonso EC, Cantu-Dibildox J, Munir WM, et al. Insurgence of *Fusarium* keratitis associated with contact lens wear. Arch Ophthalmol. 2006 Jul;124(7):941-7.

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In The News

• **Unilens Vision Inc**. has launched the new monthly **C-VUE Advanced Toric Multifocal**. This lens will be sold directly to independent eye care practitioners. The C-VUE Advanced Toric Multifocal for astigmatic presbyopes offers made-to-order base curves, diameters, powers and cylinders combined with axes in one-degree steps and the ability to specify the add power and zone size. It is made of hioxifilcon D.

• **SynergEyes, Inc., has received an additional patent** for the company's hybrid contact lens bonding technology and manufacturing processes from the U.S. Patent and Trademark Office. The patent is for a hybrid contact lens with intermediate zones that facilitate chemical bonding between the zones and the methods to manufacture.

• **CA-200**, the new placido-based **corneal analyzer from Topcon Medical Systems, Inc**., can operate as a stand-alone unit independent of an external PC and is equipped with an eight-inch LCD touch screen display as well as WiFi connectivity. This topography system consists of 24 rings on a 43.00D cone with corneal coverage of 0.3mm to 10.5mm and a diopter range from 1.00D to 120.00D. This system automatically selects the best-focused image and determines the diameter of the pupil to provide vital information for contact lens fittings. Optional features include additional software modules for onboard contact lens fitting and Zernike analysis, as well as basic, advanced and network viewer software for external PC connectivity.

AOA Gives Back

Because vision is an important aspect of overall health, well-being and independence, the AOA has established several programs to help consumers. Volunteers In Service In Our Nation (VISION USA), eye care practitioners who donate their time and resources, provide free basic eye health and vision services to working low-income, uninsured individuals and their families.

A survey by the American Optometric Association (AOA) revealed that 36% of Americans say they are limiting their doctor visits because of the recession, with 63% visiting their dentist less often, followed by primary care physician (59%) and eye doctor (52%). Only 8% of participants indicated that they are sticking to their regular health schedule. Also, for the fourth year in a row, the AOA's American Eye-Q survey showed that consumers worry most about losing their vision (43%), over their memory (32%) or even their ability to walk (12%).

Regardless of ethnicity, gender or geographic location, the recession appears to be affecting Americans' health care decisions. More women (38%) than men (32%) said they are limiting doctor visits. In terms of specific doctors, women (53%) are more inclined to cut back on seeing an eye doctor than men (51%). The survey also indicated that more women (52%) wear glasses or contact lenses, than men (48%). Women also tend to be more frequent sufferers of dry eye.

Two-thirds of survey respondents who live in rural areas said that they have cut visits to their eye doctor. Only 50% of urban and suburban respondents said they are changing their regular eye-care schedule.

Optometry's Charity, The AOA Foundation, created InfantSEE, a no-cost public health program developed to provide professional eye care for infants nationwide. Through InfantSEE, practitioners provide a one-time, comprehensive eye assessment to infants between six and 12 months of age, regardless of a parent's ability to pay.

For more information, visit www.aoa.org or call 1-800-766-4466.

The Gift of Vision

Just in time for this holiday season, Optometry Giving Sight introduces an online Gift of Vision catalogue, which offers opportunities to address the needs of the millions of people who are blind or vision impaired simply because they do not have access to an eye exam and a pair of glasses. The Gift of Vision program is the result of a successful trial with optometrists, practice staff and optical companies in the U.S., Canada, the U.K. and Australia.

Those who'd like to give the gift of sight in someone else's name may choose their gift at www.givingsight.org/giftofvision and write a personalized message for the card. Optometry Giving Sight does the rest by sending the card and using the gift contribution to fund programs that deliver sustainable vision care services in the developing world.

For more information, visit www.givingsight.org/giftofvision, email usa@givingsight.org or call 1-888-OGS-GIVE.

Review of Cornea & Contact Lenses

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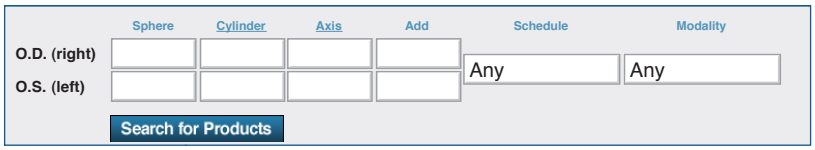
Locate Lenses Online

CooperVision unveiled its LensLocator, an online tool that allows doctors to easily search across the company's portfolio of contact lenses to identify the most appropriate choices. CooperVision will be donating a dollar to New Eyes for the Needy for each unique visitor to LensLocator.com, up to $5,000. Endorsed by the American Academy of Optometry, New Eyes for the Needy is a non-profit volunteer organization that helps improve vision by providing new and recycled eyeglasses to children and adults worldwide.

The LensLocator can be accessed at www.LensLocator.com.



Worst Cities for Allergies

The Allergy Capitals is an annual research project of Asthma and Allergy Foundation of America (AAFA) to identify "the 100 most challenging places to live with allergies" in the spring and fall seasons. This year's cities are: McAllen, Tex.; Wichita, Kans.; Louisville, Ky.; Oklahoma City, Okla.; and Jackson, Miss. To help allergy sufferers better understand and manage the condition this fall, AAFA is offering a free educational brochure titled "Eye Health and Allergies." The brochure, supported by 1 Day Acuvue Moist contact lenses (Johnson & Johnson Vision Care), includes vital allergy season advice for the nation's 40 million contact lens wearers. The brochure, which also includes a Free Trial Pair Certificate for the contact lenses, can be downloaded at www.AllergyCapitals.com.

A New Resource For Practitioners

Center for Patient Insights was initiated in June and designed to deliver news, insights and trends to eye care practitioners. Center ForPatientInsights.com will aggregate this critical information and serve as a point of entry for practitioners.

The web site offers summaries of industry trends, market research on patient attitudes and insights on how these data can be used to improve the practice. Information can be downloaded and printed for future reference. The portal also includes a search function that allows users to easily locate specific information via keywords and categories, including vision conditions, patient outcomes and patient preferences.

Advertiser Index

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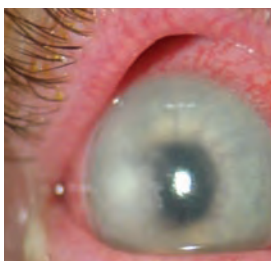
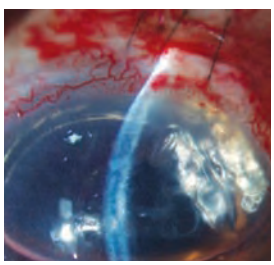
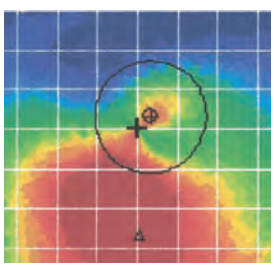






Departments

By Mark B Abelson, M.D., C.M., F.R.C.S.C., and Daniel Dewey-Mattia

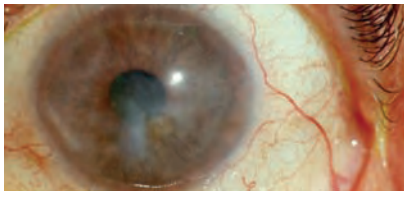
Recognizing Iritis

Shield your patients from the exacerbating effects of anterior uveitis with early detection and appropriate treatment.

Iritis, or anterior uveitis, is an occasional complication of contact lens wear. Its primary causes are infectious corneal ulcers and contact lens-induced hypoxia, which leads to corneal edema. Currently, contact lens-related iritis is less frequent than it was when older-style lenses or hard contact lenses were worn. This condition is still seen occasionally, primarily in extended-wear lens wearers. Its most common symptoms are ocular pain due to corneal changes and the classic circumlimbal flush of dilated ciliary blood vessels.

Hypoxic lens-related iritis must be differentiated from microbial keratitis, particularly when the ulcer is small. In infectious cases, the pain is more severe, the cell and flare in the anterior chamber is greater, the redness beyond the limbal area is deeper and the photosensitivity is increased. Additionally, asymmetric and irregular pupils are generally evident in infectious cases.

The third group of causes, unrelated to contact lens wear, includes rheumatoid arthritis, herpetic infections, blunt or penetrating trauma and certain autoimmune diseases. A surface antigen known as HLA-B27—which is commonly associated with autoimmune disorders (e.g., rheumatoid arthritis), inflammatory arthritis and inflammatory bowel disease—is believed to play a role in the development of many cases. HLA-B27 positive uveitis is more commonly associated with frequent and acute occurrence and a younger age of onset.[1]



Herpes simplex viruses are a common cause of infectious iritis.

Diagnosis

The best way to diagnose iritis is in a dark room with a small slit beam on an angle to both the vertical and horizontal. The number of cells visible within the slit lamp beam should be estimated with flare or the Tyndall effect and graded by density.[2]

Inflammatory white blood cells, including neutrophils, monocytes and lymphocytes, will leave the inflamed iris and be visible floating inside the anterior chamber. But, just as "one swallow does not make a spring," one or two rare cells visible in the anterior chamber do not warrant an iritis diagnosis. Occasionally, stray pigment cells or macrophages may flow through the anterior chamber after exercise, pupil dilation or mild trauma; this occurrence may also be associated with unrelated pathologies. Among the conditions commonly misdiagnosed as iritis is Krukenberg's spindle, a condition that occurs in patients with pigment dispersion syndrome. In these patients, pigment cells accumulate on the corneal endothelium and may be incorrectly identified as inflammatory cells.

Such overdiagnosis sometimes poses problems in the way data is currently collected in contact lens studies. Iritis needs to be appropriately evaluated in the full context of associated signs and symptoms.

Treatment

Contact lens-related hypoxic causes of iritis should be addressed by changing the lens type or the wearing pattern. Or, recommend temporary discontinuation of lens wear and prescribe a prophylactic antibiotic, which should clear up symptoms within 24 to 48 hours. This treatment will differentiate from the second critical cause of iritis, which will only get worse as the pain and redness gets more severe and the cell and flare increases toward hypopyon.

If the condition progresses, culture these patients and refer them for scrapings, followed by intensive antibiotic therapy. Small infiltrates should be treated aggressively if they are associated with the classic triad: miosis, redness and photophobia, as well as purulent discharge and significant redness and pain.

Underneath It All

Proper diagnosis and treatment of iritis is important in order to accurately determine the root cause of the inflammation and to avoid potential complications including cataract, glaucoma, band keratopathy or, in the case of endophthalmitis, loss of the eye. RCCL

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By John M. Rinehart, O.D., F.A.A.O.

When the Lens Fits

Learn how to achieve that perfect fit with each GP lens patient.

Tight Lens	Decrease the sagittal depth by decreasing the OZD and/or flattening the base curve radius.
Loose Lens	Increase the sagittal depth by increasing the OZD and/or steepening the base curve radius.

Regardless of how conscientious we are when fitting GP lenses, sometimes the results are not exactly what we anticipated. Whether the fit was done empirically or with the aid of diagnostic lenses, some fits need to be modified in order to achieve our ultimate goal.

Our goal is reached when the following criteria are met:

- The patient is comfortable.
- The patient has good vision.
- The health of the eye is not compromised.

All potential lens problems can be classified in one of following categories:

- Poor vision.
- Poor lens centration and movement.
- Physiological problems.

Fixing a vision problem is easy—over-refract and order a lens with the power change. But, this assumes all else is perfect. In cases where the patient experiences lens flare, it may be necessary to increase the optical zone diameter (OZD). One solution may be to flatten the base curve by 0.25D for every 0.5mm that the OZD of the lens is increased, in order to maintain the same fitting characteristics.[1]

Poor lens centration is limited to three locations: the lens is too high, too low, or decentered laterally. But, it is not always necessary to modify a lens that does not center perfectly. Many GP lens fitters prefer a lens that centers slightly high and is attached to the upper lid. However, if the lens moves above the superior limbus and does not move on a blink, it needs to be modified. A low-riding lens that moves with the blink and does not cause discomfort to the patient may not need to be changed, but if the lens is fixed low, or the patient experiences lens awareness, the fit should be modified. These modifications will affect the fit of the lens:

- Increasing the sagittal depth of the lens.
- Decreasing the sagittal depth of the lens.
- Increasing or decreasing the lens diameter and optic zone.

A lens that sits low is most likely fit tight, which means that the sagittal depth is too great. This can be remedied in-office by reducing the optical zone diameter.

Conversely, a lens that positions too high is loose, and the solution is to increase the sagittal depth of the lens.

When a lens decenters laterally but can move from limbus to limbus, increase the lens diameter to improve the lateral centration. When the lens decenters laterally and does not move from limbus to limbus, decrease the sagittal depth and increase the lens diameter, or decrease the sagittal depth of the lens alone. The latter will allow the lens to better clear the cornea, which should result in better centration.

It is not possible to increase the sagittal depth of an existing lens; in such cases, a new lens must be ordered. But, the sagittal depth of a lens can be decreased with in-office modification—reducing the OZD will decrease the sagittal depth of the lens.

So, how much must we modify the fit for the outcome to be significantly improved? I was taught not to waste time making a base curve change less than 0.50D or an OZD change less than 0.2mm.

The most common physiological change is three and nine o'clock staining. If the staining is minimal, there is no conjunctival injection and patient comfort is not compromised, no lens change may be necessary. If staining is heavy, if there is conjunctival injection, or if the patient experiences discomfort, lens changes are necessary.

Among the causes of three and nine o'clock staining are excessive edge lift, which does not allow the lid to properly resurface the cornea, and inadequate edge lift, which can cause mechanical rubbing of the cornea.

The remedy here is to decrease or increase the edge lift, respectively. Edge lift can also be increased with in-office modification by widening and/or flattening the intermediate and peripheral curves. Edge lift can be reduced by decreasing the overall lens diameter and by using steeper intermediate and peripheral curves when reordering. RCCL

1. Harris MG, Kubo RJ. The relationship between the contact lens base curve and optic zone diameter for alignment fitting. Am J Optom Arch Am Acad Optom. 1971 Apr;48(4):311-5.

By Gary Gerber, O.D.

Plan Your Comeback

Here are the steps you can take now to ensure that your marketing efforts succeed in the future.

As I write this article, I'm listening to the news and hearing that unemployment is up again to 9.8% and that the amount of home foreclosures last month was the worst ever. Have we hit the bottom of this economic recession?

That question is for greater minds than mine to determine. But, what I can tell you is that now is the perfect time to prepare your marketing program. Perhaps now is not the best time to execute it, but preparing a plan is a good idea. It's time to get ready to spend more than you usually would on your marketing efforts. But, remember, timing is important! You should only do so once the economy shows solid signs of recovery!

Will You Be Ready?

There's no question that consumer spending and confidence has decreased. In fact, many contact lens wearers compartmentalize their lenses as a discretionary expense. For that reason, during this current recession, we have seen an even further decrease in disposable lens compliance and fewer new wearers coming into our offices.

But, it's a safe bet that once the current economic cloud dissipates and patients become more liberal with their spending, savvy marketers who have well-planned campaigns at the ready will beat those who sit on the sidelines and wait things out.

Start Today

To that end, now would be a great time to review previous marketing efforts you've used in the past and freshen them up for an imminent re-launch. Look back on any particular media that worked well previously, such as newsletters, radio ads, postcards, etc.

Once you've determined which media you'll use, update any graphics, and make sure the content is timely. An extreme (but illustrative) example of not paying attention to up-to-date content would be a message that talks about the benefits of using heat sterilization with vialed lenses. A more subtle example: an ad that discusses the benefits of a type of solution your practice now rarely uses since transitioning most of your patients into continuous wear.

You get the idea—proofread your materials carefully and don't send out anachronistic information.

Strategize

As you would do with any marketing, make sure that any needed follow-up messaging or office systems are in place well in advance of the actual campaign. For example, if you are going to send a letter to current two-week daily-wear disposable lens wearers that discusses the benefits of monthly continuous wear, make sure your phone call follow-up strategy is in place before you drop off the letters at the post office.

But, in this economic environment, since you don't yet know the exact date you'll be sending your mailing, use a dynamic calendar that would say, for example, "Ten days after the letters are sent, we will call the first 100 patients over five days."

Iron Out the Details

Early planning will also help you allocate all necessary resources and address all the concerns before they turn into burning questions. In our scenario above, who will make the calls? If it's a staff member from your office, who will cover that staff member's job while he or she is making the calls? Will you be fitting these new continuous lens wearers from stock? Is your inventory adequate to do so? How far in advance do you need to order more lenses to ensure you get the best pricing and delivery? If you plan on a significant promotion, where will the lenses go? Where will the two-week lenses that you will no longer use go? How will you respond to current two-week lens wearers who ask why you no longer fit those lenses?

Just like it's a good idea to use this slow time in your office to work on practice-building projects, take advantage of the current economic lull to get your marketing ducks lined up for when things finally do turn around. RCCL

By Ernie Bowling, O.D., M.S., F.A.A.O., Dipl.

Prophylaxis and Disease Management

Learn about the pros and cons of topical NSAID therapy.

For more than fifty years, topical steroids have been the standard of care for treating ocular inflammation.[1] The development of topical nonsteroidal anti-inflammatory drugs (NSAIDs), devoid of most of the side effects of steroid therapies, was a significant advance in ocular therapeutics. Topical NSAIDs are used in the management and prevention of ocular inflammation and cystoid macular edema after cataract surgery, pain reduction after refractive surgery, corneal abrasions and seasonal allergic conjunctivitis.[2] These drugs act primarily as cyclo-oxygenase inhibitors, reducing the formation of prostaglandins and subsequently decreasing inflammation.[3]

Water-soluble NSAIDs, including Ocufen (flurbiprofen 0.03%, Allegan) and Profenal (suprofen 1%, Alcon) were the first treatments approved by the FDA for intraoperative use to inhibit excessive miosis during cataract surgery.[4] Acular PF (ketorolac tromethamine 0.5%, Allergan) followed soon after and was approved for seasonal allergic conjunctivitis, post-cataract surgery inflammation and post-refractive surgery pain. Acular PF is also the only topical NSAID available in a preservative-free formulation.[3]

Voltaren (diclofenac, Novartis) is indicated for the treatment of inflammation after cataract surgery and for the temporary relief of photophobia and pain in refractive surgery patients. Xibrom (bromfenac 0.09%, ISTA Pharmaceuticals) is the first topical NSAID to receive b.i.d. dosage approval. (Until this point, NSAIDs were generally dosed on a q.i.d. regimen.) Results from one clinical study showed that bromfenac effectively reduced post-cataract surgery inflammation as early as three days post-surgery.[5]

Allergan has added a new formation to its Acular series: Acular LS (ketorolac tromethamine 0.4%). This lower-dose drug is indicated for the reduction of pain and burning, specifically after corneal refractive surgery. Nepafenac (nevanac 0.1%, Alcon) is the first NSAID pro-drug. Studies have shown that it inhibits retinal inflammation and exhibits superior corneal penetration vs. other NSAIDs.[6,7]

Other suggested indications for topical NSAIDs are inflamed pterygia and pingueculae, laser trabeculoplasty, glaucoma and strabismus surgery.[8-11] In contrast to postoperative inflammation, many forms of uveitis require prolonged corticosteroid therapy to control inflammation. At times, the therapeutic effort must be escalated to the use of oral steroids or periorbital steroid injections. In these situations, risk of local toxicity from prolonged steroid use becomes substantial—so, NSAIDs are safer in certain forms of uveitis.[12]

When applied topically, NSAIDs may result in transient burning, stinging, conjunctival hyperemia and corneal anesthesia.[2] Drug absorption through the nasal mucosa results in systemic exposure and also presents the potential for adverse systemic events or complications.[13] Though rare, systemic adverse events include exacerbation of bronchial asthma, gastrointestinal irritation and ulceration, inhibition of platelet function and renal disease.[14,15] Obtain a thorough drug and medical history before initiating treatment to ascertain the potential for any drug-disease interaction.

The decision to prescribe NSAIDs must be guided by the clinical presentation, the diagnosis and the individual risk-to-benefit ratio of each patient. When used properly, NSAIDs can achieve prophylactic and therapeutic goals in a safe and effective manner. RCCL

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By Michael Slusky, O.D.

Not All Multi-Purpose Solutions are Created Equal

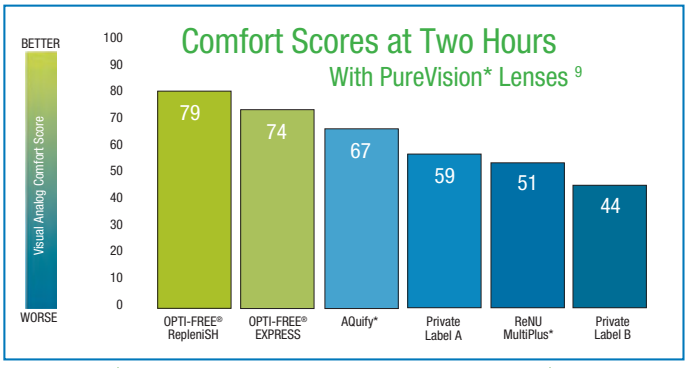
You always prescribe your trusted solution to accommodate each patient's individual demands, but who will influence your patients' contact lens care decisions for the remaining 364 days in the year after they leave your office? Facing an annual dropout rate of 2.7 million contact lens wearers, eye care practitioners must figure out a way to boost the power of their contact lens solution recommendation.[1] Drug stores and supermarkets have capitalized by offering a lower-cost alternative through generics or private label solutions, which comprise more than 30% of the market share.[2]

When packaging displays statements such as "comparable to the national leading brand," patients may be misguided into thinking that all solutions are equal. Store brand multi-purpose solutions typically use PHMB preservatives that are also subject to frequent changes by the retailer.[2] Some PHMB products cause lens/solution interactions that can affect the patient's contact lens wearing experience. Selecting the most biocompatible MPDS is as important as the selection of the contact lens material.

With the industry shifting into silicone hydrogel lenses, we have learned that these lenses attract a higher level of lipids and a lower level of proteins.[3] Unfortunately, the tear proteins demonstrate a much higher rate of denaturation, thus contributing to a greater incidence of contact lens papillary conjunctivitis (formerly known as GPC) and superior limbic keratoconjunctivitis.[4,5] Surface deposition begins within a minute of lens application, and in their denatured state, tear lysozymes lose their anti-microbial properties.[5]

Clinical data supports OPTI-FREE® RepleniSH® MPDS to have superior ability to clean, disinfect and provide added contact lens wearing comfort. Components such as TearGlyde® Reconditioning System retain moisture on the contact lens surface to enhance comfort throughout the day.[6] These deposits become more concerning in patients who are fit with a monthly replacement modality, or longer. Behind the scenes, the POLYQUAD® and ALDOX® disinfecting system of the OPTI-FREE® family maintains the highest level of antimicrobial activity with minimal corneal staining. Significant levels of corneal staining have been found in some PHMB-based solutions due to their ease of preservative uptake during disinfectant soaking and subsequent release into the pre-corneal tear film.[7] It is also believed that PHMB's strong affinity for lipids, such as the phospholipids of bacterial membranes, leads to surface binding with silicone based lenses.[6,8]

These compounding factors may contribute to patients' contact lens discomfort and can increase their chances for complications, inflammations and contact lens intolerance. OPTI-FREE® RepleniSH® MPDS demonstrates the ability to optimize disinfection and contact lens performance to match patients' diverse lifestyles. By taking a moment to educate our patients on the importance of the contact lens solution brand, eye care practitioners have the ability to maintain successful lens wearers and put the prescribing power back in the hands of the professional.



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By Mile Brujic, O.D., and Jason Miller, O.D.

At the Center of the Issue

Help patients with high amounts of astigmatism find their perfect fit.

Most of the time, we can offer soft toric contact lens options that will satisfy patients' visual needs. But, some patients are not able to wear this type of lens successfully. As astigmatism increases, patients become much more sensitive to small amounts of rotation, which can lead to visual instability.

Rigid gas-permeable (RGP) contact lenses are a great alternative for these patients. Here are some RGP pearls to maximize fitting success in this demanding patient population.

Rigid Gas-Permeable Contact Lenses

Spherical RGP contact lenses have the ability to correct low to moderate amounts of corneal astigmatism by creating a tear lens between the back surface of a spherical RGP and a toric cornea *(figure 1)*. But, the situation becomes somewhat more difficult when we attempt to fit corneas with larger amount of astigmatism. One of the challenges we face when fitting a spherical RGP lens on a toric cornea is lens flexure—an RGP lens flexing over the steeper axis of the cornea will diminish the effective tear lens power delivered to the eye.

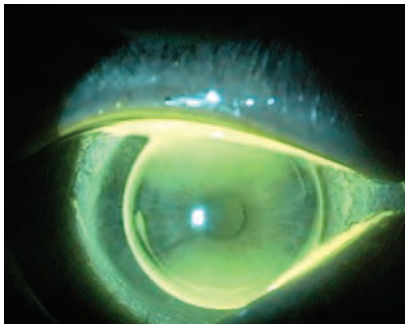
With higher amounts of astigmatism, a toric back surface will add stability and deliver the refractive correction needed. And, the toric back surface of the contact lens will minimize any lens flexure as well.

In some instances, a toric surface may need to be applied to the front of the lens as well to optimize the patient's correction (bitoric design). Practitioners tend to have strong relationships with RGP labs, and although we could calculate the base curves and powers from keratometry readings and refraction, it may be beneficial to speak with the lab directly to design the optimal lens for our patients. This way, the first lens we order will often be the one that is dispensed to the patient. As a helpful resource, consider utilizing the GP Lens Institute (www.gpli.info), which provides lots of useful information on back toric and bitoric designs.

Hybrid Contact Lenses

Increased lens and edge awareness with RGP lenses vs. soft contact lenses is what often sways patients and practitioners away from RGP lenses. Fortunately, there is an option that can deliver the optics of an RGP lens with little edge awareness.

SyergEyes has a hybrid contact lens with a non-ionic 27% water hydrogel skirt that surrounds a 100 Dk RGP center. The diameter of the lens is 14.5mm, and the RGP center is 8.4mm across. CIBA makes a hybrid lens that has an overall diameter of 14.3mm and a 25% water hydrophilic skirt. Just as a spherical RGP corrects corneal astigmatism, so does this lens design. Synergeyes has an enhanced profile design that is less likely to flex because of an increased thickness of the RGP center.



1. The fluorescein pattern typically seen with a spherical RGP on a with-the-rule astigmatic cornea.

The fit of this lens should be assessed using large molecular-weight fluorescein to avoid absorption into the soft skirt. Place the fluorescein into the concave surface of the contact lens before inserting it into the patient's eye. There should be central pooling; this lens is designed to be fit at least 1.50D steeper than flat K. The soft skirt should gently interact with the bulbar conjunctiva. If fluting of the skirt occurs, steepen the curve of the skirt. And, if conjunctival impingement occurs, opt for a flatter soft skirt curve.

A Great Opportunity

Many of our patients require astigmatism correction. We have all had patients who wear their spherical equivalents, and when presented with the astigmatism in their contact lenses, noticed a significant improvement in their vision. Many of them have been told that they cannot wear contact lenses because of the magnitude of their astigmatism, so when you present a viable option, it's a great opportunity for both the patient and the practitioner. RCCL

By Christine W. Sindt, O.D., F.A.A.O.

In-Office Disinfection in a Disposable World

As the market gives way to disposable contact lenses, there are fewer in-office diagnostic lenses to disinfect.

As recently as last year, 10% of materials used for fitting and refitting were gas-permeable, and only 4% of soft lenses were fit on an annual replacement basis.[1] These categories often represent specialty designs with diagnostic lenses that are too expensive to throw away after a single use.

But, with single-use contact lens sales on the rise, it seems that in-office disinfection is now a thing of the past. This is a good thing—both from a safety/disinfection perspective and a staff-labor point of view. But, coupled with a changing contact lens material market and dwindling contact lens care products, this trend places the practitioner in a quandary. How do we clean, disinfect and store current non-disposable diagnostic lenses?

The American National Standards Institute (ANSI) last proposed standards for in-office disinfection of contact lenses in October 1999, and the last peer-reviewed journal article that discussed in-office disinfection systems was published in 1996.[2,3] Since that time, we've seen the introduction of silicone hydrogel lenses, the annihilation of heating devices, the emergence and removal of two care solutions and the soon-to-be-removed standard of care, MiraFlow (CIBA Vision).

Differing Opinions

While some may argue that autoclaving is the only foolproof disinfection method, it is not practical—or even possible—in most practices. Others may say, "Never reuse a lens!" But, this notion carries an expensive burden for the practitioner, the lab and the patient.

There needs to be a balance among practicality, affordability and reasonable disinfection methods. So, I'd like to offer a summary of how my office has handled this challenge. The following ideas have been compiled through literature review, discussions with colleagues and trial and error.

GP Lenses

Prior to handling any contact lens, remember to wash your hands. Clean the lens with a GP-approved cleaner or polish. Soak it in ophthalmic-grade hydrogen peroxide for 10 minutes, and rinse with saline. Store the lens dry, and don't forget to lubricate it with conditioning solution prior to insertion.

Soft Lenses

Rub the lens for 20 seconds with preservative-free, alcohol-based cleaner. Because MiraFlow will no longer be available, the only other product in this category is Sereine Extra Strength Daily Cleaner (Optikem International) According to the 510(K) on safety and effectiveness, submitted on June 13, 2007, this product is "substantially equivalent to MiraFlow."[4] Also, cleaners containing 20% isopropyl alcohol have been shown to effectively reduce microbial organisms, including *Acanthamoeba*.[5,6] There is not a clear consensus on what the next step should be, but most doctors I polled suggest one of two things:

- After cleaning, soak the lens in peroxide for a minimum of two hours in ophthalmic grade peroxide and then neutralize. With sterile tweezers, place the lens in a sterile vial with preservative-free sterile saline and cap it.

Please note—preservative-free saline is only available as Unisol 4 (Alcon), Blairex (Blairex) or in respiratory therapy vials that can be obtained through the pharmacy.

- After cleaning, fill a clean vial with multipurpose solution and cap it. Some of my colleagues suggest re-cleaning monthly (per solution storage guidelines). There is one notable exception: With tinted or prosthetic contact lenses, follow the manufacturers' recommendation. Some multipurpose solutions can purge the tint from the lens or damage the lens surface.

When you're ready to use the lens, remove it from the vial, rub it for 20 seconds with an alcohol-based cleaner, rinse with it preservative free saline and insert.

Working Together

Although it is sorely needed, currently there is no definitive literature on this topic, so I welcome your comments and criticisms. Perhaps by sharing our experiences, we can make lens wear safer for our patients. RCCL

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Top 10 for the Past Five Years

Here's a look at recent research articles that have significantly impacted eye care.

By Joseph P. Shovlin, O.D., F.A.A.O., and Alissa Coyne, B.S.

Dr. Shovlin is a clinical editor for RCCL *and a senior optometrist at the Northeastern Eye Institute in Scranton, Pa. He is past chair of the American Academy of Optometry Section on Cornea, Contact Lenses and Refractive Technologies and of the American Optometric Association's Contact Lens and Cornea Section.*

Ms. Coyne is a fourth-year student at the Pennsylvania College of Optometry at Salus University. She is a 2006 graduate of the Pennsylvania State University.

Deciding which contact lens-related research articles have had (or potentially will have) the biggest impact on clinical practice and future research endeavors is a very difficult task. But, with the aid of *Review of Cornea & Contact Lenses*' Editorial Review Board, suggestions for our "Top 10" list were made. From a list of over 100 excellent papers submitted, only 10 were selected and will be highlighted in this issue. So, let's take a close look at this groundbreaking research and determine the clinical implications of each.

Lid Wiper Epitheliopathy and Dry Eye Symptoms

Patients presenting with dry eye complaints but normal tear breakup time, Schirmer test values and no visible corneal staining present a challenge to eye care practitioners. Donald Korb, O.D., and associates describe lid wiper epitheliopathy as a syndrome that affects the epithelium of marginal conjunctiva of the upper lid in their study, "Lid Wiper Epitheliopathy and Dry Eye Symptoms."[1]

In this 2005 study, 76% of symptomatic patients were found to have positive staining, which indicates lid wiper epitheliopathy, vs. 12% in the asymptomatic group. Symptomatic patients were also eight times more likely to have moderate to severe staining of the lid wiper.

The staining of epithelial changes indicates problems with the lubrication between the lid wiper and the ocular surface. When an inadequate tear film is present, the lid wiper is subjected to constant friction on each blink. These findings are a major discovery in dry eye management—particularly, in cases when patients are symptomatic but show no other ocular finding of dry eye.

This valuable research sets the stage for future clinical trials in contact lens-related dryness. Might this be an objective test with predictive value that can serve as a valuable marker for assessing treatment strategies? For any practitioner who is not familiar with lid wiper epitheliopathy and its clinical value, this article is a good first step in learning about the condition and its management.

The Epidemiology of Contact Lens-Related Infiltrates

Contact lens wearers now exceed 140 million worldwide; therefore, even a small incidence of infection or inflammation affects a large number of people.[2] In "The Epidemiology of Contact Lens-Related Infiltrates," by Fiona Stapleton, Ph.D., M.C.Optom., up to 65% of microbial keratitis infections were associated with contact lens wear.[2] Studies from four different countries concluded that about one in every 2,500 daily wear users and one in

every 500 extended wear (EW) lens users develop microbial keratitis (MK) per year. Regardless of lens material, EW use proved to have an increased risk with infection.

Corneal infiltrates can range from small and asymptomatic to severe and symptomatic. A rise in frequency was evident as soft lens wear became more prevalent. EW resulted in a higher incidence of sterile infiltrates in certain studies that found silicone hydrogel material more likely to result in infiltration than hydrogel.[2] Silicone hydrogel lenses were also associated with an earlier onset of sterile infiltrates during EW use. Regardless of wearing schedule, soft contact lenses had a higher incidence of infiltrates vs. rigid gas-permeable lenses.

Infection and sterile infiltrates have different associations with lens material and wearing schedules. The identified risks associated with these factors allow eye care practitioners to make informed decisions with the patient's well being in mind.

MK continues to plague contact lens wearers, but this valuable incidence study that includes silicone hydrogel lenses parallels other earlier studies evaluating conventional hydrogel materials. Infiltrates, regardless of their etiology, remain a harbinger of serious tissue damage.

Risk Factors for Microbial Keratitis with Contemporary Contact Lenses

MK is a rare yet vision-threatening complication of contact lens wear. With many options available to practitioners, including daily disposables and different brands of silicone hydrogel lenses, a risk analysis is beneficial for the safety of the patient. In "Risk Factors for Microbial Keratitis with Contemporary Contact Lenses," John Dart, M.D., and colleagues concluded that daily disposable lenses show a significant increase in relative risk of contracting MK vs. planned-replacement soft and rigid lenses.[3] But, vision loss as a result of MK and severity of infection are reduced with daily disposable wear.

They also found that silicone hydrogel lenses have essentially no effect on the risk potential or the severity of MK.

In the study, Soflens 66 (Bausch & Lomb) is the least likely to be affected by MK, followed by Acuvue 2 (Vistakon), Biomedics 55 UV (CooperVision), Enhance (Fashion Contact Lenses), and Surevue (Vistakon). Interestingly, no differences were found among the silicone hydrogel products. An extended wear regimen with any brand of lens increased the likelihood of MK five-fold.

The expected reduction of MK with the introduction of daily disposable and silicone hydrogel lenses on the market has yielded a somewhat disappointing outcome. We now know that neither a new wear schedule nor a new material has a major effect in decreasing microbial keratitis in contact lens wearers.

Although this excellent study found no benefit in avoiding infection when wearing daily disposable lenses, the good news is that there were no serious infections found in this group. So, even though the numbers are not reduced, the severity of the disease is. These findings suggest that less modifiable risk factors, such as tear film stagnation and reduced epithelial cell turnover, may play a larger role in microbial infections.

Definition and Classification of Dry Eye Disease

An updated definition of dry eye disease was developed by the Dry Eye WorkShop (DEWS) Definition and Classification Subcommittee.[4] Etiology, mechanisms and severity of the disease make up the foundation of the contemporary definition. A classification scheme for diagnostic criteria was arranged based on the Triple Classification and the Delphi panel report; both methods operate on a severity-based grading system.

The etiopathogenic classification describes the many causes of dry eye disease. The aqueous tear-deficient class includes subclassifications under Sjögren's syndrome and non-Sjögren's-related dry eye. Evaporative dry eye is also described, and intrinsic and extrinsic factors are identified.

The mechanism and cycle of events is illustrated through a common pathway; tear hyperosmolarity and tear film instability are the major factors in the continuous cycle.[4] The final part of the report is based on severity of findings, thereby assisting choices in therapy. The 2007 work of the DEWS Definition and Classification Subcommittee has brought about a new definition and framework of dry eye disease that is helpful in treatment and management in today's practice.

Although this article is not a contact lens-related article, the implications in screening and follow-up of patients who wear contact lenses are abundantly evident. Eye care practitioners can attempt address the cause(s) of lens-related dryness in lens wearers by using this new scheme.

Tear Oxygen Under Hydrogel and Silicone Hydrogel Contact Lenses

Joseph Bonanno, O.D., Ph.D., and associates present the first study that directly measures oxygen flux and corneal oxygen consumption in vivo in humans across a variety of

soft contact lenses, "Tear Oxygen Under Hydrogel and Silicone Hydrogel Contact Lenses in Humans."[5] Phosphorescence decay of BSA-porphine was used to determine a steady-state tear oxygen tension in an open eye for each lens brand. Closed eye estimates were then calculated by measuring the change in tear oxygen tension after shutting the eyes for five minutes. Because the closed eye data was estimated, an alternative method utilizing a pair of goggles to control inflow and outflow over the lens was used. The goggle method showed no significant difference in the tear oxygen tension from the closed eye estimate in lenses with oxygen transmissibility (Dk/t) less than 30.[5]

Results demonstrate that, as the Dk/t of a lens increases, the tear oxygen tension also increases. The data show that silicone hydrogel lenses significantly increase oxygen tension and availability to the cornea when compared to conventional hydrogel lenses. Furthermore, the findings of increased oxygenation of lenses with a Dk/t greater than 140 contradict previous mathematical and in vitro study results and thus illustrate the continued necessity of higher Dk/t lenses.

The quest for higher amounts of oxygen flux may not be over! This novel study sets a new bar for oxygen in lens wearers, especially during continuous wear. This work sets the stage for additional questions and the need for additional studies.

The Association of Contact Lens Solution Use and *Acanthamoeba* Keratitis

The recent outbreak of *Acanthamoeba* keratitis (AK) in contact lens wearers has largely been attributed to the use of a specific contact lens solution. In the retrospective case-controlled study, "The Association of Contact Lens Solution Use and *Acanthamoeba* Keratitis," by Charlotte Joslin, O.D., and associates, 53% of subjects with AK reported Complete MoisturePlus (Abbott Medical Optics) solution use.[6] Multivariate analysis also identified Complete MoisturePlus as a risk factor in AK. Previous studies have shown that these multipurpose solutions have less affinity for *Acanthamoeba* when compared to other multipurpose solutions. Solution reuse, lack of rubbing lenses and showering with lenses showed a hygiene-related positive association with AK.

Complete MoisturePlus has a significant association with AK; however, this multipurpose solution's use cannot account for all cases. Other factors associated with lens hygiene have a weak but statistically positive association noted in subjects with AK.

These results suggest further research in identifying other factors for AK is necessary.

Compliance with Silicone Hydrogel and Daily Disposable Lens Replacement

Planned replacement lenses have decreased the likelihood of complications and other contact lens related problems. But, in "Patient and Practitioner Compliance with Silicone Hydrogel and Daily Disposable Lens Replacement in the United States," authors suggest that individuals are still relatively noncompliant in replacing their lenses—especially when considering manufacturer and/or doctor recommendations.[7]

Comparing daily disposable, two-week and one-month replacement lenses, patients on a two-week replacement schedule are self-reported as the most noncompliant (22%).[7] Ten percent of daily disposable lens users report noncompliance, followed by 2% of one-month replacement lens users. Overall, 40% of subjects reported wearing lenses longer than the manufacturer's recommendation. A significantly higher number of toric lens wearers were also found to be noncompliant.

The subjects gave numerous reasons why lenses were not replaced as recommended. Forgetting the specific day for replacement was the most reported cause, followed by saving money and lack of time.[7]

Interaction and education between doctors and patients can help to increase compliance in contact lens wearers. In this study, subjects' own recommendations was acted as a reminder system in order to promote compliance, especially in the case of those patients wearing two-week replacement lenses.

Factors Associated with Contact Lens-Related Dry Eye

Approximately half of all contact lens wearers report symptoms of dry eye. Previous studies suggest that increased evaporation, inadequate tear production and inflammation play a role in this condition. But, Jason Nichols, O.D., Ph.D., and Kathryn Sinnott, O.D., examined the tear film, contact lenses and other factors related to dry eye in contact lens wear in "Tear Film, Contact Lens, and Patient Related Factors Associated with Contact Lens Related Dry Eye."[8]

Subjects' pre-lens tear film was examined three consecutive times using a thickness-dependent, fringe-imaging interferometer. The refractive index and water content of subjects' hydrogel lenses were also determined. The refractive index was identified in silicone hydrogel lenses; however, measuring the water content of these lenses was not possible due to the lack of a linear relationship. Additionally, tear

meniscus height and tear volume were both measured and meibography was utilized.

In this study, dry eye symptoms were strongly associated with prelens tear film thinning time. In symptomatic patients, lipid layer thickness was reduced and osmolarity was increased. These two findings may be related due to the decreased lipid layer, which results in increased evaporation, thereby affecting osmolarity. High-water content (low-refractive index) lenses were also associated with reported dry eye symptoms.

Dry eye symptoms account for a large number of drop outs each year. Because 100% humidity and an environment with no ambient air is not a possibility, finding novel ways to enhance the lipid layer may serve as a reasonable strategy to improve lens wear comfort by reducing dryness symptoms.

Bacterial Biofilm Resistance to Antimicrobial Activity of Care Solutions

Infection and inflammation that are associated with soft contact lens wear have not decreased since the introduction of silicone hydrogel lenses. The likelihood of biofilm on lens and case surfaces is an important factor in soft lens wear regimen. Biofilms can be described as microbial communities that stick to a surface, contain polymeric substances and are associated with differential expression of genes and proteins.

Adverse events associated with cetrtain lens materials may be associated with biofilms on the contact lens surface. Bacteria within these biofilms are more resistant to antimicrobials and biocides. Six popular contact lens solutions were compared in the study "Increased Resistance of Contact Lens Related Bacterial Biofilms to Antimicrobial Activity of Soft Contact Lens Care Solutions," by Loretta Szczotka-Flynn O.D., M.S., and associates to determine their activity against *Pseudomonas, S. marcescens* and *S. aureus* biofilms. Clear Care (CIBA Vision) hydrogen peroxide solution proved to be the only solution effective against all three types of biofilms. Multipurpose solutions had a disappointing showing, especially when faced with *S. marcescens*.[9]

The presence of biofilms on contact lens surfaces and cases may be the cause of infection in lens wearers, despite good compliance. Findings that demonstrate the resistance of these biofilms—especially to multipurpose solutions—are important in the continued research of keratitis in soft lens wearers.

Incidence of *Fusarium* Keratitis in Contact Lens Wear

Microbial keratitis has long been associated with soft contact lens wear. But, fungal keratitis is becoming more commonplace than previously reported. A 27-month retrospective study by Eduardo Alfonso, M.D., and associates, examined 34 patients with positive cultures of *Fusarium* species and describes the clinical presentation and treatment modalities for this keratomycosis.[10]

In a majority of the cases (91%), patients were first treated with topical antibacterials. Diagnosis of fungal keratitis took an average of 9.1 days from onset of symptoms, which included redness, tearing, pain and impaired vision. Delay of diagnosis or treatment prolonged the length of treatment until cure. Corneal infiltrates, located centrally or peripherally, were observed in 63% and 37% of cases, respectively. *Fusarium* oxysporum was identified in 59% of the cultures.[10]

Eye care practitioners should consider possible *Fusarium* infection or other keratomycosis in the presence of ulcerative keratitis. Nonresponsive ulcerative keratitis patients must be carefully examined with a higher suspicion of fungal keratitis infection.

An outbreak of keratitis in lens wear highlights the need for close monitoring of patients and puts the antimicrobial efficacy of multipurpose solutions under scrutiny. The U.S. Food and Drug Administration has held a pair of summits on solution efficacy and standards in testing for unusual corneal pathogens that will likely impact future approval systems.

The Driving Force

Research remains a vital ingredient in the advancement of contact lens technology. Clinical studies have provided new materials, lens designs and methods to treat and manage various problems in contact lens patients. Manufacturers, clinicians and scientists strive to make lens wear safer, more convenient to use and comfortable. RCCL

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Promoting Healthy Contact Lens Wear

Daily disposable lenses offer practitioners and patients an invaluable modality for optimal ocular health and convenience of wear.

By Gregory W. DeNaeyer, O.D.

The first commercially available soft contact lenses were on the market in 1971. Of course, these lenses were not disposable, and replacement was costly and time consuming. The contact lens paradigm radically shifted when daily disposable soft contact lenses were introduced in 1995, resulting in improved comfort and fewer complications. They offered patients the convenience of not having to bother with solutions or lens care.

According to the International Contact Lens Prescribing report of 2008, 13% of contact lens patients were fit with daily disposable (DD) lenses in the United States from 2002 to 2008.[1] By contrast, during the same time, Denmark had a DD fitting percentage of 64% and Taiwan's percentage was 50%.[1] The general consensus explaining the relatively low trend in the U.S. is that practitioners think that DD lenses are too expensive for the majority of their patients. These lenses are probably only prescribed if patients ask about them or as a last resort when finding a lens for "trouble" patients. But today, availability is becoming less of a barrier—contact lens companies are offering a wider range of powers *(see "Available Daily Disposable Soft Contact Lenses," pg. 20)*. Toric and multifocal DD lenses are already available, and the first silicone hydrogel DD will be available in late 2009. These lenses offer patients many advantages, but let's focus on how eye care practitioners can use DD lenses to promote healthy, uncomplicated contact lens wear to high-need patients.

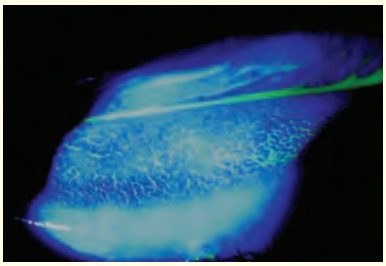
Allergies and Contact Lenses

What role do allergies play in contact lens wear? It has been reported that 55% of the U.S. population tests positive for one or more allergens, and 50% of those people will have symptoms of ocular allergies.[2] Recently, the Asthma and Allergy Foundation of America (AAFA) conducted a survey of 800 online participants; 33% stated that they were current contact lens wearers.[3] Forty-five percent of the participants reported that eye-related allergy problems often prevented them from wearing contact lenses.[2] Finally, 12% of those respondents indicated that they discontinued contact lenses due to allergies.[3]

There are two types of allergens: seasonal and perennial. Seasonal allergens include pollen and are typically present during spring or fall, while perennial allergens, such as pet dander and mold, are present throughout the year. Patients with allergic conjunctivitis often complain of red, itchy and irritated eyes, and for these patients, slit lamp findings can include lid hyperemia, conjunctival injection or chemosis and a follicular reaction of the lower tarsal plates *(figure 1)*. Those with dry eyes and subsequent reduced tear volume may have amplified reactions

because the antigens are more concentrated on the ocular surface. As the AAFA survey points out, contact lens wearers with allergic conjunctivitis have reduced wear time and sometimes have to stop lens wear altogether.[3] It has been shown that soft contact lenses can become coated with a biofilm within minutes of insertion, and allergens are able to firmly attach to these biofilms and cause the lens to become an antigen depot.[4] This subjects the conventional or frequent-replacement soft contact lens patient to high concentrations of allergens, as they build up over the wearing period. All these events can set patients up for contact lens wear failure if they have allergic conjunctivitis. Furthermore, films and deposits can persist even with proper cleaning and enzyme use.

An effective strategy to increase comfort and wear time is to have patients try DD contact lenses. Because these lenses are replaced daily, they are not exposed to the chronic build-up of antigenic material. A three-year prospective study demonstrated that patients who compared DD lenses to planned replacement lenses reported fewer symptoms of foreign body sensation, redness, cloudy vision and grittiness.[5] They also reported



1. Severe lower tarsal plate follicular reaction.

better subjective vision, comfort and overall satisfaction. Clinically, they demonstrated fewer lens surface deposits, complications and tarsal abnormalities.[5]

Another study evaluated DD vs. habitual soft contact lenses wear among a group of allergy suffers and showed that 67% of the patients reported improved comfort with DD lenses and had improved slit lamp findings from baseline data.[6] But, the AAFA survey reported that 74% of patients never received any recommendation from their practitioners to try this modality.[3]

Contact lens-induced papillary conjunctivitis (CLPC), also known as giant papillary conjunctivitis (GPC) is not considered to be a typical allergy. It is an immunologic response to foreign substances that most commonly results from coated and deposited soft contact lenses.[7] Additionally, the coated lens may cause mechanical irritation and the release of inflammatory mediators, which contributes to this type of conjunctivitis.[8-10]

The papillary reaction that develops as a result of CLPC on the upper tarsal plate can interfere with lens wear, making it nearly impossible. A retrospective study of 47 newly fit soft contact lens patients aimed to determine the incidence of CLPC for frequently replaced daily wear contact lenses and showed that the incidence of CLPC was 36% in patients who replaced their lenses at four weeks or longer—but only 4.5% in patients who replaced their lenses at less than four weeks.[11] The study also showed that none of the patients wearing DD lenses or two-week replacement lenses developed CLPC.[11] From this, we can conclude that more frequently replaced lenses will have less deposits and thus expose the patient to less antigens and mechanical trauma.[7-10,12]

Another issue to consider is that patients can sometimes develop late-onset adverse ocular response to chemicals in contact lens solutions. Remember that these can take years of exposure to develop. For these patients, DD lenses are also a great option.

Compliance and Contact Lenses

Compliance with contact lens use and care is one of the most important aspects of preventing

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2. A dirty contact lens case that was presented during a routine visit.

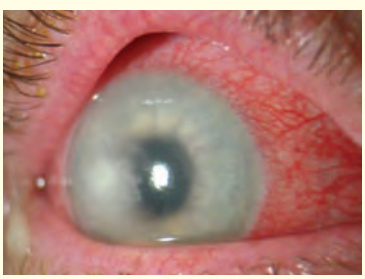
contact lens related problems. Noncompliant contact lens behavior includes hygiene, solution use, appointment attendance, wearing times and replacement schedules.[13] There are estimates that noncompliance in contact lens patients ranges from 40% to 99%.[12-16] In fact, several studies report that patients who stated that they were compliant actually reported a wide variety of noncompliant behaviors.[13,14] One study showed that the poorest level of compliance involved contact lens cases, which were the most frequently contaminated item.[15] Data shows that poor storage case hygiene can put a patient at almost as much risk for microbial keratitis as extended wear *(figure 2)*.[17] Another group of researchers reported that 43% of patients who wore frequent replacement soft contact lenses used one pair of lenses at least one week longer than was prescribed.[18]

Interestingly, strategies such as consistent education using video, booklets, posters, checklists and a health care contract have been shown not to significantly affect compliance levels.[19] Proper compliance with contact lenses requires following a prescribed series of steps. It only stands to reason that the more steps that are involved in this process, the more likely some will be skipped or forgotten. Patients who are noncompliant—whether they realize it or not—are more likely to have their behavior reinforced if they are symptom-free. Targeting known noncompliant patients and fitting them with DD lenses is an easy and straightforward way to simplify the process of lens care. Educate these patients on the benefits and convenience that this modality offers. Most patients will be satisfied that there is an easier path to compliant lens wear. DD lenses eliminate the following noncompliant issues:

- Using non-prescribed contact lens solutions.
- Unwittingly using saline in lieu of multipurpose solution.
- Using dirty contact lens cases.
- Topping off solution.
- Not following the prescribed replacement schedule.
- Case contamination.

Microbial Keratitis

Microbial keratitis (MK) is the most serious complication that can affect a contact lens wearer. MK is rare—affecting approximately five per 10,000 daily wear patients—but when severe, it can be sight threatening.[20-23] MK is an infectious process and most cases are secondary to bacteria; *Pseudomonas* is the culprit in over half the cases.[24] Fungal and protozoan species are also potential pathogens that can cause MK. Patients who present with MK experience pain, redness, photophobia and decreased vision, and their slit lamp findings generally include an area of focal infiltrate with an overlying ulceration *(figure 3)*. In order for an infection of the cornea to occur, the offending organisms must first bind and break through the epithelium to reach the stroma. Lens-induced corneal hypoxia may predispose contact lens wearers to infection associated with compromised corneal epithelial integrity, impaired wound healing and increased bacterial binding.[25-29]



3. Note the infectious infiltrate in this microbial keratitis patient.

For 20 years, we have known that patients who wear hydrogel lenses on an extended-wear basis are at a five-fold increased risk for MK, as opposed to those patients who do not sleep in their contact lenses.[20] So logically, it was hypothesized that the advent of silicone hydrogel lenses with hyper Dk would significantly reduce the risk of MK due to a reduction in hypoxia-related complications. But more recently, two companion studies have helped practitioners to understand the relative risk factors of MK for a variety of lens modalities and materials.[30,31] What we know now from the study by Fiona Stapleton, Ph.D., MC.Optom., and colleagues is that there has been no significant reduction in risk for silicone hydrogel wearers on an extended-wear basis.[30,31] It had also been hypothesized that the advent of DD lenses would reduce the overall risk of MK, as there is no need for hygiene and storage steps that contribute to microbial

Available Daily Disposable Soft Contact Lenses

Bausch & Lomb	SofLens Daily Disposable	hilafilcon B 59%	+6.50D to -9.00D
CIBA Vision	Focus Dailies Aqua Comfort Plus	nelfilcon A 69%	+6.00D to -10.00D
	Focus Dailies with "Aqua Release"	nelfilcon A 69%	+6.00D to -10.00D
	Focus Dailies Progressives	nelfilcon A 69%	+5.00D to -6.00D progressive add up to 3.00D
	Focus Dailies Toric	nelfilcon A 69%	+4.00D to -8.00D Cylinder powers: -0.75D, -1.50D Axis 90° and 180°
Vistakon	1-Day Acuvue	etafilcon A 58%	+6.00D to -12.00D
	1-Day Acuvue Moist	etafilcon A 58%	+6.00D to -12.00D
CooperVision	ProClear 1 Day	omafilcon A 60%	+6.00D to -10.00D
	ClearSight 1 Day	ocufilcon B 52%	+6.00D to -10.00D
	ClearSight 1 Day Toric	ocufilcon B 52%	plano to -7.00D Cylinder powers: -0.75D, -1.25D Axis 180°, 160°, 90°, 20°
Marietta Vision	Day Star 1-Day	methafilcon A 55%	+4.00D to -8.00D
Optical Connection	Definition AC Everyday	methafilcon A 55%	+4.00D to -8.00D
Preferred Vision Group	Preferred Dailies	etafilcon A 58%	-1.00D to -12.00D
Unilens	C-Vue 1 Day ASV	methafilcon A 55%	+4.00D to -8.00D
Ocu-Ease/Optech	Elite Daily Disposable	methafilcon A 55%	+4.00D to -8.00D

contamination.[31-33] But, research conducted by John Dart, D.M., F.C.R.Ophth., found a surprisingly small increased risk for MK for DD lenses vs. planned replacement and a reduced risk of severe MK and vision loss with DD as compared to planned replacement.[31] In this study, no DD lens patients lost vision to a level of 20/40 or worse.

The results from the Stapleton study were similar, with no significant difference in risk of MK between DD and planned replacement lenses, and reduced risk of severe MK with DD.[30] No patients who wore DD lenses in the Stapleton study lost more than two lines of vision. So, why was the risk of mild/moderate MK not reduced with DD as has been hypothesized? A closer look at the Dart study reveals some interesting factors to consider. The study showed that 30% of DD patients were wearing their lenses off-label by occasionally or regularly sleeping in their lenses, which puts the patient at the highest risk for MK.[31] The study also found that the brand of DD lenses made a significant impact on the overall risk of MK. For example, 1-Day Acuvue (Johnson & Johnson) had a lower overall risk of MK as compared to planned replacement.[31]

Obviously, there are additional variables that may put patients at greater risk for MK. For instance, some lenses are more difficult to remove than others.[34] Difficult lens handling may lead to epithelial compromise, putting the patient at greater risk.[31] The tendency to prescribe DD lenses for patients who are already at a higher risk due to hygiene or environmental issues could be another risk factor.[31] Or, severe cases may be avoided with DD wear because lens cases, which can be contaminated with gram-negative bacteria, are not utilized.[30] The causative organism has been shown to be the primary determinant of MK severity.[24] Although DD lenses have not reduced mild/moderate MK as compared to planned replacement lenses, they do reduce the risk of severe MK and vision loss, which are both important considerations.

Besides cosmesis, patients prefer contact lenses because glasses can interfere with athletic or leisure activities. But, as we know, exposure to water can increase

the risk of adverse events, such as MK. Water of all types—tap, swimming pools, rivers and oceans—contains microorganisms. A sampling of swimmers who wore soft contact lenses in a chlorinated pool showed that *Staphylococcus epidermidis* was the most common species identified in the water itself, while small amounts of *Staphylococcus aureus* and *Streptococcus salivarius* were found both in the water and on the lenses of swimmers.[35] And, as can be imagined, the diversity of organisms rises dramatically in the case of streams, rivers and oceans.

The protozoan *Acanthamoeba*—ubiquitously found in water of all types and soil—poses the most serious threat to soft contact lenses patients who are exposed. *Acanthamoeba* are free-living and exist as mobile trophozoites or dormant cysts.[36,37] The active trophozoite form is able to bind to the cornea, especially to areas of abrasion, often associated with contact lens wear. They then produce a cytotoxic serine protease enzyme that destroys corneal integrity, producing a keratitis.[37] *Acanthamoeba* keratitis (AK), which has shown increased incidence in the last decade, usually runs a protracted course that is sight-threatening.[38]

Treatments with antimicrobial agents for six to 12 months are not uncommon. Even after the active infection is no longer present, the cyst may still have the potential to reactivate months later. In cases where corneal transplantation is needed, surgery is ideally delayed until the cyst has resolved. Multiple studies indicate that approximately 30% of all AK cases are associated with patients swimming in their contact lenses.[38-40] To date, *Acanthamoeba* is not included in product approval of disinfection products, but the increased incidence of AK has prompted the FDA to pursue a recertification of care systems that would include testing methodology for this particular protozoan.[37,41]

For all the reasons stated above, it is critical that contact lens patients be educated and take the necessary steps to reduce their risk of *Acanthamoeba* if they are going to wear their soft contact lenses for water-related activities. Instruct patients to wear tight-fitting goggles or masks if they know that they will be submerged or splashed. If the patient's lenses are exposed to water, it seems only reasonable that the safest way to eliminate the risk would be to immediately throw the lenses out when the water activity is over. With this in mind, DD lenses would be the perfect replacement option for these patients, as they would not have to rely on a contact lens care system. Even patients who normally wear frequent-replacement soft lenses could have a set of dailies that they use exclusively for water activities.

Introducing Daily Disposable Wear to Your Patients

With all the benefits of DD wear, why do only 13% of U.S. patients take advantage of this modality? As mentioned earlier, the obvious answer is cost. Unless the patient brings up a specific type of lens or wearing schedule, the practitioner is the one who presents the choices when fitting or refitting patients. Most practitioners are reluctant to even bring up the topic of DD lenses out of fear that the patient will find the increased price unacceptable. But, be careful not to prejudge what a patient is willing to pay for comfortable and safe glasses-free vision. Patients may respond well to your recommendation, and this is especially true for patients who are on the verge of dropping out of lens wear with discomfort as the culprit.

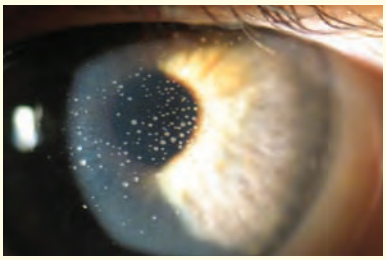
For instance, let's consider a contact lens patient who suffers from severe allergic conjunctivitis. As we know, planned-replacement soft lenses are likely to continually build up environmental allergens on the lens surface, exposing the patient to a greater concentration to antigens. Not to mention that the additional accumulation of protein and lipid deposits provide additional irritation. All of this leads to significantly reduced wearing time or causes the patient to drop out of lens wear all together. Presenting the DD lens modality as an option to this patient could be just what the doctor ordered.

In my practice, a significant percentage of patients who have LASIK consultations cite contact lens discontinuation due to the discomfort of seasonal or perennial allergic conjunctivitis. Yet, many contact lens patients are unaware that DD wear is an option for maintaining healthy and comfortable contact lens wear. The first step to a successful introduction is identifying those patients who would significantly benefit from the DD modality. Besides allergy suffers, other candidates might include patients with a history of poor compliance, athletes and heavy depositors *(figure 4)*. Once you've selected the candidates, the next step is to educate them about DD lenses and how they can immediately impact their soft contact lens wear. Patients must

understand exactly why this lens is more beneficial—otherwise, they won't pay more for something they perceive as providing little additional advantage. Discuss the advantages of this modality—increased comfort, increased wearing time, easier compliance, less risk of severe MK and vision loss. The final step is to let them try the lenses for one to two weeks. In my experience, allergy and CLPC patients immediately find DD lenses more comfortable and appreciate the DD advantages. And, noncompliant patients will enjoy the simplicity of not having to deal with any care regimen. Some may like to stay in their planned-replacement lenses, but use DD lenses for sports related activities or traveling. Again, a trial pack of lenses will best demonstrate the simplicity that DD lenses have to offer.

Health and Convenience

Daily disposable lenses can serve as the turning point that offers allergy suffers a more comfortable way to wear contact lenses. For known noncompliant patients, DD wear eliminates the risk associated with dirty contact lens cases and topping off. For swimmers, they offer the advantage of a more convenient way to discard lenses, especially in the event of water exposure. While these lenses do not reduce the risk of mild to moderate MK, they greatly decrease the risk of severe MK and associated vision loss, which has always been the worst-case scenario for contact lens patients. The development of lens materials that incorporate an antimicrobial surface may further improve the safety profile of DD lenses. With increased parameter and material options, DD wear will continue to provide more patients with healthier contact lens options. RCCL



4. This is a heavily deposited soft lens on a potential candidate for single-use contact lenses.

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Self-Assessment Examination: Promoting Healthy Contact Lens Wear

DIRECTIONS: To obtain 2 hours of continuing education credit, complete the exam by recording the best answer to each self-assessment question on the Examination Answer Sheet on Page 23. Mail the answer sheet to Optometric CE, P.O. Box 488, Canal Street Station, New York, NY 10013. A minimum score of 70 is required to obtain a certificate of completion. There is no fee for this course.

1. Daily disposables were first available in ____?
a. 1990.
b. 1995.
c. 2000.
d. 2003.

2. According to the 2008 International Prescribing Report, what percentage of patients in the U.S. were fit into daily disposable soft contact lenses?
a. 10%.
b. 13%.
c. 20%.
d. 30%.

3. According to a survey by the Asthma and Allergy Foundation of America, what percentage of respondents indicated they discontinued contact lens wear due to allergies?
a. 1%.
b. 12%.
c. 20%.
d. 40%.

4. Patients with allergic conjunctivitis often exhibit which of the following slit lamp findings?
a. Uveitis, meibomian cysts and chemosis.
b. Conjuctival injection and chemosis.
c. Chemosis and pterygia.
d. Lower tarsal plate follicular reaction, conjuctival injection and chemosis.

5. Within minutes of contact lens insertion, contact lenses can become coated with which of the following?
a. Lipids.
b. Proteins.
c. Biofilms.
d. Toxins.

6. GPC or CLPC is an immunological response most commonly secondary to which of the following?
a. Exposed sutures.
b. Contact lens deposits.
c. Ocular prosthetics.
d. Dry Eye Syndrome.

7. In a study by Donshik and Porazinski, what percentage of patients who wore daily disposables developed CLPC?
a. 0%.
b. 5%.
c. 0%.
d. 20%.

8. Which of the following is not associated with contact lens noncompliance?
a. Hygiene.
b. Wearing time.
c. Appointment attendance.
d. Contact lens drop out.

9. The Yung study showed that the poorest level of contact lens noncompliance involved which of the following?
a. Multipurpose solutions.
b. Contact lens cases.
c. Wearing time.
d. Replacement schedule.

10. Daily disposables target all of the following behaviors except_____.
a. Using saline solution for soft contact lens storage.
b. Dirty contact lens cases.
c. Wearing lenses on an extended wear basis.
d. Topping off multipurpose solutions.

11. The rate of MK for daily wear contact lens wearers is approximately:
a. 5/10,000.
b. 500/10,000.
c. 750/10,000.
d. 1/1,000,000.

12. Which of the following pathogens can cause MK?
a. Bacterial, fungal, protozoan.
b. Protozoan and bacterial
c. Prionic and viral.
d. Fungal.

13. Patients who sleep in their soft contact lenses increase their risk for MK by:
a. Five-fold.
b. Three-fold.
c. 15%.
d. 20%.

14. Daily disposables may be beneficial for allergy sufferers because_____.
a. They eliminate the use of contact lens cases.
b. They eliminate chronic build up of antigenic materials.
c. They are able to sleep in their lenses.
d. Daily disposables are coated with antihistamines.

15. According to studies by Drs. Dart and Stapleton, the risk for severe MK and secondary visual loss with daily disposables is_____.
a. Increased.
b. About the same as with other modalities.
c. Reduced significantly.
d. Increased significantly.

16. What puts patients who wear daily disposables at most risk for developing mild or moderate MK?
a. Daily wear use.
b. Replacing lenses every three days.
c. Wearing daily disposables on an intermittent basis.
d. Wearing daily disposables as extended wear basis.

17. Why do daily disposables significantly reduce the risk of severe MK and associated vision loss?
a. Elimination of solution use.
b. Elimination of contact lens cases.
c. Reducing contact lens deposits.
d. Improved patient compliance.

18. *Acanthamoeba* is found in_____?
a. Tap water.
b. Salt water and soil.
c. Streams and rivers, chlorinated pools, tap water and soil.
d. Soil and tap water.

19. Candidates for daily disposables are_____.
a. Those with a history of poor compliance, athletes and heavy depositors.
b. Non-compliant patients.
c. Extended wear patients.
d. Astigmats.

20. A three-year prospective study found that patients reported the best vision, comfort and overall satisfaction with which of the following?
a. Daily disposables.
b. One-month replacement.
c. Two-week replacement.
d. Conventional wear.

Examination Answer Sheet

Valid for credit through November 30, 2010

Promoting Healthy Contact Lens Wear

Directions: Select one answer for each question in the exam and completely darken the appropriate circle. A minimum score of 70% is required to earn credit.

Mail to: Optometric CE, PO Box 488, Canal Street Station, New York, NY 10013

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There is an eight-to-ten week processing time for this exam.

1.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	
2.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	21. The goal statement was achieved:
3.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	◯Very Well ◯Adequately ◯Poorly
4.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	
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6.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	◯Very Useful ◯Useful ◯Not Very Useful
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12.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	◯Greatly ◯Somewhat ◯Hardly
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By submitting this answer sheet, I certify that I have read the lesson in its entirety and completed the self-assessment exam personally based on the material presented. I have not obtained the answers to this exam by any fraudulent or improper means.

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Lesson 106415

RO-RCCL-1109

The Ins And Outs of Corneal Dystrophy

Although early stages of corneal dystrophy may be asymptomatic, practitioners must recognize the signs of this often vision-threatening condition.

By Verinder Nirankari, M.D., and Barry Weiner, O.D.

Dr. Nirankari holds a Clinical Professorship of Ophthalmology at the University of Maryland and is Director of Cornea, Complicated Cataracts and Refractive Surgery at Union Memorial Hospital.

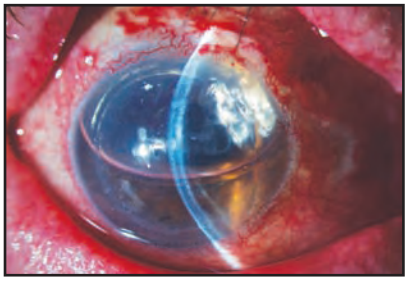
Dr. Weiner has a private practice, specializing in contact lenses in Phoenix, Md. He is an adjunct faculty member at the Wilmer Institute of Johns Hopkins Hospital.

The term "corneal dystrophy" actually encompasses many conditions that affect the cornea, and they range from mildly uncomfortable to outright debilitating and even sight-threatening.

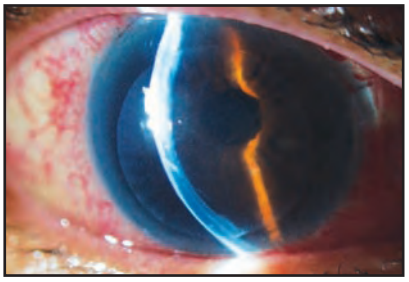
Corneal dystrophic conditions are rare. They are usually genetic, either autosomal-dominant or more rarely, recessive—and the patient typically has a familial history of the condition.

These conditions are usually bilateral and may be present shortly after birth or may begin to manifest later in life. Dystrophies can be epithelial, stromal or endothelial and may cause little visual disturbance or lead to functional blindness. They may be progressive or non-progressive in nature. For this reason, treatment plans are correlated with the severity of the disease. Treatment plans may be passive, consisting of mere observation or aggressive, consisting of full thickness corneal transplants or other invasive treatments. It is necessary to differentiate corneal dystrophy from corneal degeneration. Corneal degenerations are usually late in on-set and may be unilateral. They may result from corneal inflammation or systemic disease.

Informing patients and their families of what to expect with corneal dystrophy is an important step. But first, practitioners must have a working knowledge of the various conditions under the corneal dystrophy umbrella. A thorough understanding of each will aid with disease identification



This one day post-DSEK patient, shows central clear endothelial keratoplasty with a 50% air bubble in the anterior chamber.



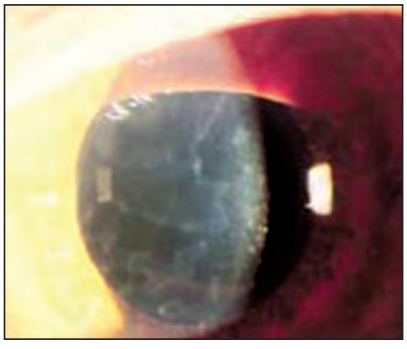
This successful one month post-op DSEK graft demonstrates a clear central endothelial graft.

and the initiation of appropriate treatment.

Epithelial Dystrophy

Meesmann's Dystrophy. This condition was first described by Dr. Alois Meesmann and Dr. F. Wilke in 1939, and it usually occurs at age one or two. The clinical picture: fine, punctate opacities in the epithelium or Bowman's membrane that can best be seen with the slit lamp using trans illumination. The basement membrane also appears thickened.

Meesmann's is usually non-progressive and causes little or no visual disturbance, but it may cause complaints of foreign body sensation at times. Treatment is palliative and consists of using artificial tears to help relieve symptoms if they should occur.



In this patient, a slit lamp evaluation revealed severe basement membrane disease with typical map-dot-fingerprint patterns.

Epithelial Basement Membrane Disease (Map-dot-fingerprint Disease, Cogan's Dystrophy). This is the most common corneal dystrophy. Debate exists: Is it an inherited condition? Should it even be classified as a dystrophy? It is usually non-progressive but will fluctuate in the severity of its symptoms. It is most often bilateral but not in every case, and it usually affects females more than males.[1]

Patients may be asymptomatic but may also complain of blurred vision with ghost images and possible monocular diplopia, flare and glare, photophobia or a foreign body sensation. In these patients, slit lamp evaluation will usually show irregular, geographic, gray-white patches with clear areas (maps) and gray-white round or irregular areas (dots) in the epithelium. Clusters of concentric lines 0.25mm to 4mm in length are also visible (fingerprints).[1]

Irritation can usually be alleviated with artificial tears and ophthalmic ointment at night. Hypertonic salines and ointment are indicated in more advanced cases or following an episode of corneal erosion. Bandage contact lenses can be used to relieve the pain of recurrent erosions and to protect the healing cornea from the shearing effects of the lids. These lenses are usually worn on an extended-wear basis for two to three months, and hypertonic solutions are also used.

Reis-Buckler's Dystrophy. This dystrophy is an autosomal-dominant condition that usually begins in early childhood as a bilateral disease. It may cause decreased visual acuity, photophobia and a foreign body sensation with occasional spontaneous corneal erosion.

Slit lamp evaluation will usually show fine reticular opacities in the epithelium that gradually progress in the second or third decade of life into central or mid-peripheral honeycomb-like opacities. A diffuse anterior stromal haze may also be seen. Palliative treatment with tears may be needed for irritation and a bandage contact lens for any erosion problems.

These patients' visual acuity tends to get progressively worse, and surgical intervention is generally necessary around 50 years of age.

Surgical Treatment For Epithelial Dystrophy

In cases where medical therapy fails, the next step is surgical debridement of the abnormal dystrophic epithelium—specifically, either a localized area or both the central and paracentral epithelium.

Chemical agents are used, such as 4% topical cocaine or alcohol or by debriding the epithelium using the excimer laser, which is a procedure known as phototherapeutic keratectomy (PTK). PTK is usually followed by insertion of a bandage contact lens until re-epithelialization is complete.

If there is an area of localized erosions—secondary to epithelial dystrophy that is not in the

visual axis—it can be treated with a stromal puncture either by mechanical means or by using the excimer laser.

Stromal Dystrophy

Granular Dystrophy. This is a rare autosomal-dominant bilateral condition that results in a deposition of stromal opacities by age 20.[2] Patients report decreased acuity, photophobia and pain associated with recurrent erosions. Corneal erosions can be treated with bandage lenses and hypertonic solutions, much like in other dystrophic situations.

Discrete, white granular deposits are usually located in the anterior stroma with clear areas between them. These central deposits will become larger and increase in quantity with time. Patient with granular dystrophy may eventually need surgical intervention if acuity becomes a problem.

Macular Dystrophy. This is a rare autosomal dominant condition that is usually recognized in the first decade of life and may cause severe visual loss by 20 to 40 years of age. Patients report decreasing visual acuity with photophobia. In rare cases, corneal erosions occur.

Gray-white stromal opacities can be seen extending to the peripheral cornea, unlike granular dystrophy where these opacities are usually central or mid-peripheral. There are usually no clear spaces between the opacities, as is the case with granular dystrophy. Central corneal thickening and corneal guttata may also be noted.

Medical treatment may be needed in cases where recurrent erosions are a problem, and sunglasses are needed for the photophobia.

Lattice Dystrophy. This autosomal dominant condition occurs between two and seven years of age. But, many patients with lattice dystrophy are asymptomatic until their 20s or 30s.

A slit lamp examination will show branching refractile lattice-like lines that are best visualized with retro-illumination. These lines will coalesce with stromal opacities to form an anterior stromal haze and cause decreasing acuity and increasing photophobia. As with other stromal dystrophies, recurrent erosion may occur and is treated accordingly.

Surgical Treatment For Stromal and Subepithelial Dystrophy

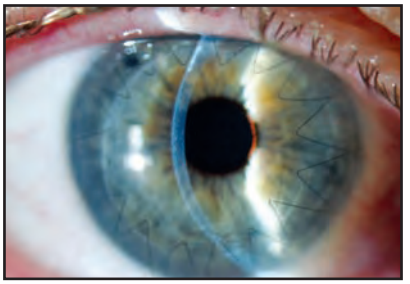
If the condition does not involve the endothelium, the preferred treatment is deep anterior lamellar keratoplasty (DALK). The surgeon can use the manual technique for deep dissection by utilizing the Melles dissector, or he or she may opt to use the "big bubble technique," first popularized by Mohammed Anwar, M.D.

The goal of either procedure is to remove the affected stroma, preferably all the way to Descemet's membrane, and to replace it with healthy stroma. The advantage of DALK is that the host endothelium is preserved with a marked reduction in the incidence of graft rejection.

Endothelial Dystrophy

Fuchs' Endothelial Dystrophy. This autosomal-dominant condition is usually bilateral and progressive. It is more common in females, at a ratio of nearly 3:1, and it most often manifests after the age of 40.[3]

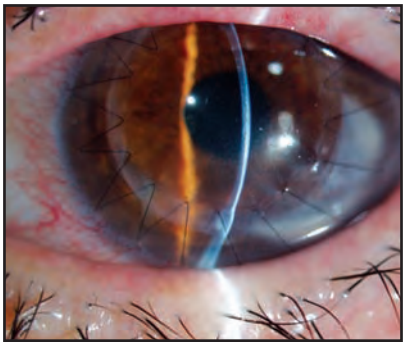
Fuchs' is characterized by a slowly progressing corneal edema and corneal guttata formation.



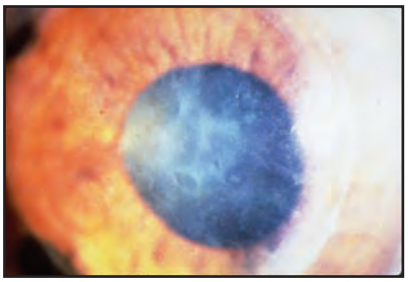
This patient is one year post-full thickness PK with a clear corneal graft and 10-0 running nylon suture.

These lesions form between Descemet's membrane and the endothelium. As the guttata enlarge, the endothelial cells stretch and slough off, and the remaining cells enlarge to cover the gaps. The reduced number of cells causes the endothelial pump mechanism to become stressed, which leads to increased edema.

The early stages of this condition may be asymptomatic, but as it progresses, patients note decreased vision, halos, glare and photophobia. Epithelial microcysts might be noted; these can progress and coalesce to form bullae, which can cause irritation and a foreign body sensation. Or, the bullae may rupture, causing the patient to experience intense pain. Stromal edema is likely and usually begins posteriorly, progressing toward the anterior



This six months post-penetrating keratoplasty patient shows slightly elevated host-donor junction.



Reis-Buckler's epithelial dystrophy may require the use of bandage contact lenses as the disease progresses.

progressing toward the anterior stroma with stromal thickening.

The medical treatment of Fuchs' depends on the patient's symptoms; usually, no intervention is necessary in the early stages of the disease. As it progresses, a regimen of hypertonic solutions four to six times daily and hypertonic ointment nightly will help reduce the edema and lessen the visual symptoms. Also, careful use of a hair dryer to blow warm air across the corneal surface will help reduce the edema that occurs upon awakening. Bandage contact lenses can reduce the pain and may improve the patient's acuity by smoothing out surface irregularities caused by the bullae.

Posterior Polymorphous Dystrophy (PPD). This condition was first described by Leonhard Koeppe, M.D., in 1892. This autosomal-dominant condition is bilateral, but it does not necessarily manifest the same in both eyes. Patients are usually asymptomatic, and the dystrophy may be non-progressive or progress very slowly. Some patients may experience slightly decreased acuity with photophobia and a foreign body sensation.

Slit lamp examination will show vesicles, clustered or individual, on the posterior corneal surface with surrounding halos. Additionally, stromal and/or epithelial edema may be noted in very advanced cases.

Most patients do not require medical intervention, but any care should be based on the reported symptoms. Glaucoma is possible with PPD due to the possibility of angle closure from iridocorneal adhesions. In such cases, the patient is managed with therapeutic drops or surgical treatment, if the pressure lowering medications do not control the IOP adequately.

Congenital Hereditary Endothelial Dystrophy. This inherited, bilateral disorder is characterized by a thickened corneal stroma and a diffuse "ground glass" appearance. There are both autosomal-recessive and autosomal-dominant forms.

The recessive form is more common and is usually present at birth. The dominant form manifests at age one or two. Nystagmus tends to be present in the recessive condition, but not in the dominant one. The recessive form is non-progressive, while the dominant may progress slowly over five to ten years. If opacification is severe, penetrating keratoplasty may be necessary to prevent amblyopia.

Slit lamp examination will show a ground glass appearance, stromal thickening (as much as three times the normal amount) and an "orange peel" effect at Descemet's membrane.

Practitioners should recommend genetic counseling—there is a 25% chance of this condition occurring in a sibling.[3]

Surgical Treatment For Endothelial Dystrophies

The traditional surgical approach for endothelial dystrophies has been penetrating keratoplasty (PK). The central full-thickness cornea is replaced with a healthy cornea from an eye bank. The success rate in low-risk cases is relatively high. But, complications can include delayed healing and visual rehabilitation, unpredictable refractive changes, high astigmatism and decreased corneal sensation resulting in ocular surface problems.

The introduction of endothelial keratoplasty (DSEK, DSAEK, EK) has offered several advantages over traditional PK, including rapid visual recovery and minimal induced astigmatism. In addition, a small DSEK incision does not seriously compromise the structural integrity of the eye. Possible complications of DSEK include a higher central endothelial cell loss, dislocation of the graft (which requires additional surgery) and interface haze. Follow-up care for DSEK patients is the same as for PK patients. Most complications occur immediately post-op or shortly thereafter. However, the advantages far outweigh the possible and potential drawbacks, and DSEK is rapidly becoming the preferred treatment in cases of endothelial failure.

Overcome the Challenge

Corneal dystrophies have a number of similarities, so they can be difficult for practitioners to diagnose and treat. Knowing the precise characteristics of each condition allows us to make a differential diagnosis.

Once the issue is identified, we can inform patients of their condition, their options and their prognosis before initiating prompt and appropriate treatment. RCCL

1. Catania L. Primary Care of the Anterior Segment, Second Edition. Appleton and Lange. Norwalk, CT. 1998. 102-105.
2. Catania L. Primary Care of the Anterior Segment, Second Edition. Appleton and Lange. Norwalk, CT. 1998. 90
3. Catania L. Primary Care of the Anterior Segment, Second Edition. Appleton and 4. Lange. Norwalk, CT. 1998. 91-92.

Genetic Aspects of Keratoconus

Practitioners must stay tuned for answers about the hereditary links of KC.

By Patricia M. Winters, O.D., F.A.A.O.

Dr. Winters is with the Contact Lens Clinic and Vision Rehabilitation Service at the University of Minnesota Department of Ophthalmology in Minneapolis, Minn.

Keratoconus (KC) is a heterogeneous, noninflammatory corneal disease that affects the collagen structure—specifically, its organization and intercellular matrix. Its clinical hallmarks include central corneal thinning with subsequent corneal protrusion and decreased vision.[1,2] Apoptosis and necrosis of keratinocytes lead to changes in the anterior stroma and Bowman's lamina, causing weakness of the corneal tissue. Prevalence of overt KC is 1:2000 in the general population, but there is also an undiagnosed, subclinical population in which prevalence cannot be determined.[3,4] The degenerative process of KC begins during the teenage years with highly variable disease expression and timing of onset. The disease progresses in 20% of cases, leading to the arrest of the condition in the third or fourth decade. KC is a major indication for keratoplasty.[3,4]

Diagnosing KC

Clinical signs of KC include stromal thinning, Vogt's striae, Fleischer's ring and scissoring of the retinoscopic reflex with a fully dilated pupil.

Videokeratography (VKG) produces quantitative indices that are reproducible and that aid in diagnosis and management. Three characteristics noted with VKG include an increased area of central or pericentral corneal power surrounded by concentric areas of decreasing power, inferior-superior power asymmetry (I-S value) and skewing of the steepest radial axes above and below the horizontal meridian (AB/SRAX).[2] Combining clinical signs with VKG results allowed Yaron S. Rabinowitz, M.D., to establish a consistent classification scheme for KC.[2]

A quantitative index (KISA%) has been determined with the minimal VKG criteria and regular astigmatism as demonstrated by K readings to aid in the diagnosis of KC in its earliest stages. This value may also be used to monitor progression of the disease.[2] But, qualitative VKG patterns may appear prior to changes in quantifying indices.[5] Posterior corneal curvatures and elevation maps may be helpful in KC diagnosis. In fact, posterior corneal elevation indices have been used to exclude "normals" from control cohort study populations.[6]

The KC Link

KC has been documented in association with multisystem disorders (e.g., Down or Marfan syndrome), ocular disorders (e.g., aniridia or Leber's congenital amaurosis) and corneal conditions (e.g., atopic keratoconjunctivitis or Axenfeld's anomaly).[2] None of the subjects of the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) study reported systemic conditions often associated with keratoconus in the literature, including

Levels of KC Diagnosis	
KC suspect	No clinical signs; VKG reveals an AB/SRAX pattern.
Early KC	No slit lamp findings; scissoring of retinal reflex with full dilation of pupil; VKG reveals an AB/SRAX pattern.
KC	One or more clinical signs; VKG reveals an AB/SRAX pattern.

Down syndrome, Ehlers-Danlos syndrome, Marfan syndrome, osteogenesis imperfecta, oculodentodigital syndrome, infantile tapetoretinal degeneration or Reiger's anomaly.[7] Although the mechanisms and etiology leading to isolated KC are still not known, there is evidence of a genetic basis for this disease. Most KC cases reported in the literature are sporadic and have a 5% to 10% positive family history when reviewing both autosomal dominant and autosomal recessive case data.[8] Genetic pathogenesis has been discussed as a cause for KC mostly in studies involving twins and familial aggregation. Bilaterality of this disease along with formal genetic testing also supports this etiology.[2,4] (The literature also discusses the complex interaction between genetics and environmental factors for this disease, but this topic will not be explored here.)[2]

Familial Factors

A comparison of the incidence of a disease in monozygotic vs. dizygotic twin studies indicates hereditary vs. nonhereditary etiological factors, and a strong concordance of KC in monozygotic twins has been noted.[2-4] Additionally, eighteen sets of monozygotic twins have been studied with a 54% concordance rate documented in the literature.[8] Keeping in mind that monozygotic twins may not be identical in all tissues, disease in dizygotic twins can be due primarily to genetic factors also, rather than nongenetic factors.[2]

The CLEK Study revealed a 14% positive family history, which supports the theory of familial aggregation.[2] Such transmission in anywhere from 6% to 23.5% of cases has been well described in the literature.[2,3] Prevalence of KC in first-degree relatives of known KC patients participating in the Keratoconus Genetics Research program in 2000 was up to 67 times greater than that in the general population.[2] VKG indices were highly correlated in siblings or parent-child pairs vs. spousal pairs.[2-4] But, autosomal dominant (AD) inheritance of KC is more frequently described in families with incomplete penetrance and variations of expression (e.g., form fruste keratoconus). VKG studies, including the subclinical cases, support the AD inheritance pattern. Autosomal recessive patterns of inheritance have also been documented.[2,4]

Studies Around the World

Molecular studies to identify genes for KC have revealed multiple gene loci that may have roles in the pathogenesis of KC.[2] Most linkage studies for KC have been performed in white families.[9] Ideally, studies of small populations with a common founder that have a higher incidence of KC provide the best hope of reducing heterogeneity to improve result validity.[2] Twenty families in Finland—with an autosomal dominant pattern of KC without evidence of genetic disease—were studied with linkage to chromosome 16q22.3-q23.1.[2] But, further studies at the Cedars-Sinai Medical Center excluded this linkage for KC genetic pathogenesis.[2]

In Tasmania, a familial group with five-times more KC than in its general population was identified with possible linkage to chromosome 20q12.[2] This marker was excluded as a causative gene for KC. Additionally, a large family in Utah with KC and Down syndrome was studied by Dr. Rabinowitz and associates with possible linkage to chromosome 21. Again, no known genes were identified for genetic pathogenesis of KC in this group.[2] But, in a linkage study in 90 KC sibling pairs within a small Hispanic population, two linkage regions were found on chromosomes 7 and 17.[9] More recently, 18 families with autosomal dominant KC were identified in Ecuador. However, genetic sequencing analysis of 12 genes at the chromosome 13q32 KC locus in this study revealed no mutations that were segregated for KC.[6] Linkage mapping of seven possible loci for KC (16q, 15q22.23-q24.2, 3p1-q13, 2p24, 5q14.3-q21.1, 20q12 and 21q) has also been discussed in the literature.[10]

Genetic penetrance much less than 100% in families supports nongenetic risk factors as possible etiology.[10] The genetic heterogeneity of this mapping suggests that related pathways may converge on common targets to reveal the phenotype, but a disease gene has yet to be cloned.[3,10] Review of the Online Mendelian Inheritance In Man Morbid Map lists several chromosomal loci with evidence of linkage to KC, which is listed in the OMIM as 148300.[1]

Identifying the KC Gene

The VSX1 homeobox gene (20p11-q11) has been linked to about 5% of isolated KC cases.[2] A large study with mutations found in KC patients, but not in 277 controls, strongly suggests genetic pathogenesis.[2] VSX1 mRNA has

been detected in the inner nuclear layer of the retina, embryonic craniofacial tissue and in the adult cornea.[2] VSX1, a transcription factor of the retina, is isolated to the cone bipolar cells of the inner nuclear layer and aids in maintenance of the adult retina. It is also expressed during in vitro and in vivo corneal wound healing process when keratocytes become myofibroblasts.[15] But, VSX1 has not been identified in adult corneal tissue or associated with isolated KC without retinal findings in studies by the National Eye Institute.[2] A VSX1 clone has been found in the retina and is listed in some NEIBank human eye cDNA libraries.[10]

Although several DNA variants of VSX1 have been associated with KC patients, significant debate within the ophthalmic research community as to the pathogenic vs. nonpathogenic nature of these variants can be found in the literature. Seven VSX1 sequence variants identified in KC families are also controversial in their pathogenesis role for KC.[3] The D144E mutation in VSX1 was noted to be much higher in patients with KC and their relatives vs. controls.[3]

Investigation of asymptomatic carriers of D144E without pathogenesis has revealed possible relevant clinical pearls for practitioners who may be examining a potential KC patient. A thin pachymetry strip in the corneas of the carriers along with irregular posterior topographical changes and normal VKG supports further diagnostic criteria for KC to include corneal thickness and posterior corneal mapping.[3] Although VSX1 missense mutations and polymorphisms have been recently described in a study of unrelated Korean patients with KC, VSX1 has virtually no role in KC pathogenesis.[7,15] This is supported by the lack of evidence of pathogenic mutations of VSX1, failure of demonstrating corneal expression of this gene and presumed pathogenic mutations in less than 2% of patients with KC.[7]

KC6 was found during the analysis of seven KC corneal host buttons, resulting in 4090 clusters of clones, during gene expression studies at NEIBank.[10] This gene was mapped to 8q12.3 with no evidence found that it encodes a protein. This gene is specific for expression in the cornea and in embryonic stem cells. This study mentions the localization of corneal stem cells to the limbal area but raises the question of whether corneal stem cells are more widely distributed throughout the cornea.[10]

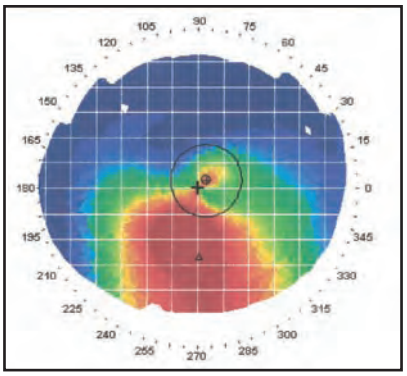
In the same study as the discovery of KC6, aquaporin 5 (chromosome12q13) was unexpectedly absent in the human KC cDNA collection of the KC corneal host buttons. This integral membrane protein functions as a water channel and is expressed in salivary and lacrimal glands, as well as in the corneal epithelium. Such defective water channels may explain the corneal thinning that occurs with KC, but they were also associated with corneal swelling in mice studies.[10] Interestingly, the gene for aquaporin 5 (AQP5) appears normal in KC, but the expression occurs in the latter stages of KC when keratoplasty is indicated. It is difficult to determine whether AQP5 gene suppression contributes to the KC phenotype or if it is a late-stage effect of KC. Further studies on the use of antibodies for AQP5 would be beneficial; the NEIBank study did not find protein levels in normal or keratoconic corneal tissues possibly due to the age of the specimens studied.[10]

On the Cellular Level

Apoptosis—programmed cell death—is increased in keratoconic corneas vs. corneas that are normal or have stromal dystrophy. Sixty-seven apoptosis-related gene transcripts have been identified in a study where cDNA was synthesized and sequenced from seven KC corneal host buttons.[10] While several caspases (cysteine proteases) were described as key executioners in apoptosis for KC, clusterin was noted as a protector from apoptosis.[10] Clusterin prevents reactive oxygen species production and RPE cell death induced by hydrogen peroxide. Specifically, clusterin creates

Cytogenic Map Locations of KC Genes

KTCN (OMIM 605020)	20p11.2	Visual System Homeobox Gene 1.[11]
KTCN2 (OMIM 608932)	16q22.3-q23.1	A genome wide scan on 20 Finnish families with AD KC linking the KC with chromosome 16q22.3-q23.1.[12]
KTCN3 (OMIM 608586)	3p14-q13	Reported in 2004, an Italian family of two generations with AD KC was linked to 3p14-q13.[13]
KTCN4 (OMIM 609271)	2p24	Linkage analysis was performed in 28 families with KC from France, Spain and Guadeloupe. This was a mixed population of Caucasian, Arab and Caribbean-African. Evidence of linkage was found on chromosome 2p24.1.[14]



Please note the AB/SRAX pattern on this VKG axial map. This marks a patient as a KC suspect.

an environment for cellular survival and significantly inhibits caspase-3, whose levels increase with this type of oxidative stress.[16]

One of the five most abundant clones for known corneal markers derived from KC corneal host buttons is transforming growth factor (TGF)-β1 (BIGH3).[10] TFG-β is a cytokine that mediates fibrotic wound repair via myofibroblast differentiation in the corneal wound-healing process.[17,18] Produced and stored in corneal epithelial cells, it diffuses to the stroma with injury to the basement cell membrane and stimulates receptors on keratocytes.[17,18] Activation of these receptors creates a cascade of events that ultimately result in keratocyte-to-myofibroblast transformation. Extensive wound healing via the myofibroblasts can severely reduce corneal transparency, while downregulating this transformation may improve visual outcome after trauma.[17]

Human corneal fibroblasts/myofibroblasts produce α integrin chains in vitro and if treated with TGFβ, even higher concentrations of α integrin chains are found.[15] Integrins are major adhesion receptors that connect cells to the extracellullar matrix. Increased levels of α integrin chains play a significant role in scarring of keratoconic corneas and compromised basement membrane integrity. Likewise, signaling between integrins is important in cell survival, proliferation and differentiation.

Most integrin mutations cause embryonic or perinatal death. The α integrin chain may be involved in the ordered collagen matrix of the cornea, thereby aiding in corneal transparency. Scarring of the cornea includes cell migration, collagen deposition and reorganization. Observation of an α integrin chain in scarred keratoconic corneas—very similar to the patterns of α chains of collagen IV and V—may indicate a role in corneal remodeling.[18] Elevated levels of cyclic-AMP has been shown to inhibit TGFβ-induced fibrosis during the keratocyte-to-myofibroblast transformation in rabbit corneas. Therefore agents to increase cyclic-AMP to reduce a fibrotic response in vivo rather than cytotoxic agents may be an alternative in the future.[17]

Drawing Parallels

In the "web of causation," many etiologies work together to cause a disease process. Relationships are more likely to be believed when many avenues of evidence converge on the same outcome.

Although not enough evidence is available at this time for a genetic screening test for KC, a negative screening test may not be enough to deny a genetic etiology.[5] Both deep anterior lamellar keratoplasty and penetrating keratoplasty are indicated for KC, and each procedure has its own advantages.[19-21]

The ophthalmic research community's zeal for finding better ways of diagnosing KC sooner and more permanent solutions for patients with early disease has not wavered. Continued genetic susceptibility testing for KC will hopefully be more rewarding in the future. As clinicians, with the advent of gene therapy, a molecular basis for KC is more compelling with each KC patient we see in our clinics. RCCL

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