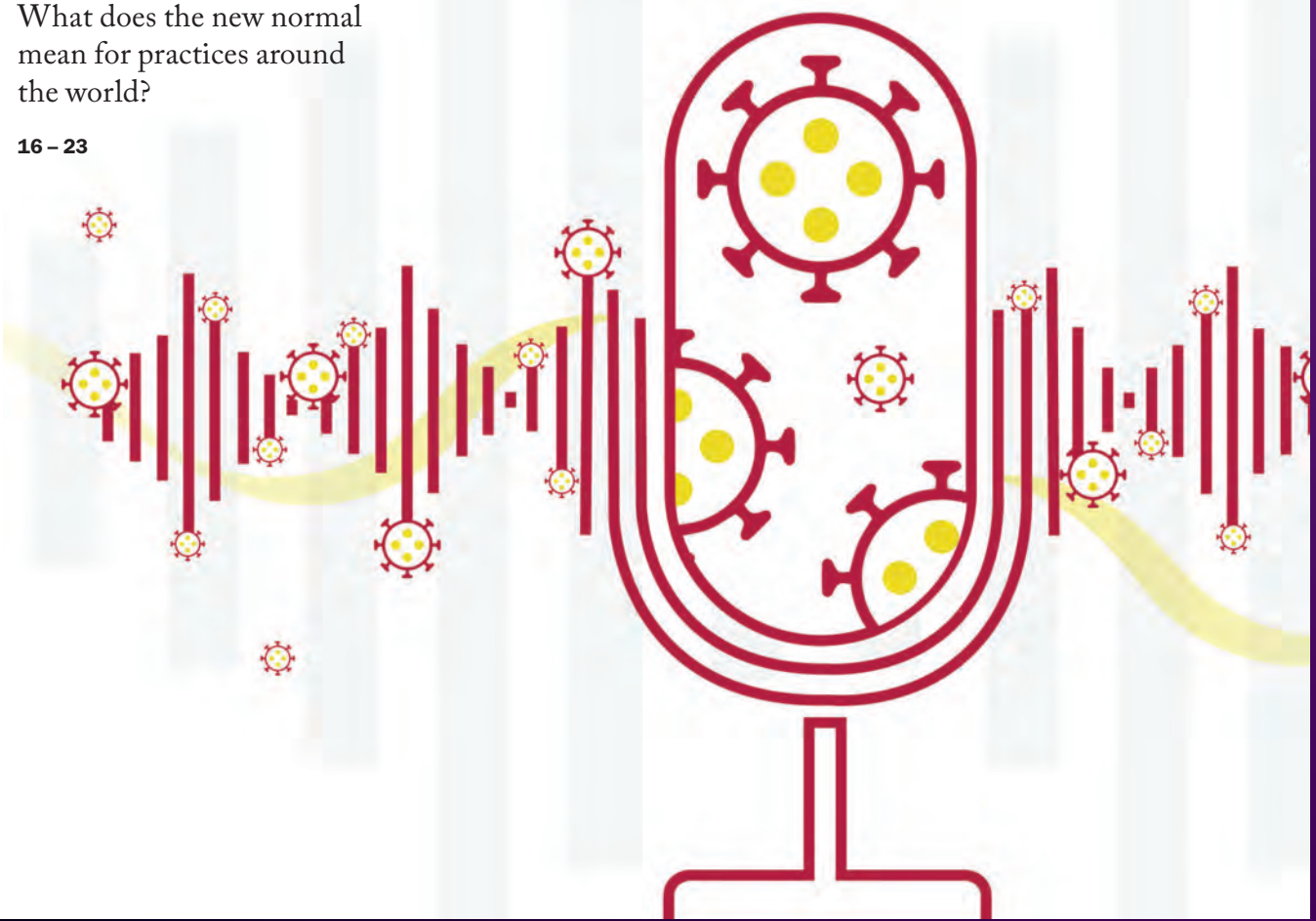
OCTOBER 2020 # 48

the Ophthalmologist™

Refractive Recovery and COVID-19

What does the new normal mean for practices around the world?



DEXYCU®
(dexamethasone intraocular suspension) 9%

Ready to support you and your patients

The future may seem like it's filled with questions, but EyePoint Pharmaceuticals wants to help provide answers. You and your patients need certainty, and there may be concerns about what your practice may experience.

You may be considering ways to help:

Ease patient concerns about exposure

Minimize patients touching their faces

Reduce office and pharmacy visits for patients and caregivers

To learn more about how DEXYCU® (dexamethasone intraocular suspension) 9% can help, visit DEXYCU.com or call 1-833-EYEPOINT (1-833-393-7646).

INDICATION AND USAGE

DEXYCU® (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Increase in Intraocular Pressure

- Prolonged use of corticosteroids, including DEXYCU, may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision
- Steroids should be used with caution in the presence of glaucoma

Delayed Healing

- The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation
- In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of corticosteroids

Exacerbation of Infection

- The use of DEXYCU, as with other ophthalmic corticosteroids, is not recommended in the presence of most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures

WARNINGS AND PRECAUTIONS (cont'd)

Exacerbation of Infection (cont'd)

- Use of a corticosteroid in the treatment of patients with a history of herpes simplex requires caution and may prolong the course and may exacerbate the severity of many viral infections
- Fungal infections of the cornea are particularly prone to coincidentally develop with long-term local steroid application and must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection

Cataract Progression

- The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts

ADVERSE REACTIONS

- The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema and iritis

Please see brief summary of full Prescribing Information on adjacent page.

EyePoint PHARMACEUTICALS

07/2020
US-DEX-2000098

DEXYCU (dexamethasone intraocular suspension) 9%,
for intraocular administration
Initial U.S. Approval: 1958

BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE

DEXYCU (dexamethasone intraocular suspension) 9% is indicated for the treatment of postoperative inflammation.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Increase in Intraocular Pressure

Prolonged use of corticosteroids including DEXYCU may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma.

5.2 Delayed Healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of corticosteroids.

5.3 Exacerbation of Infection

The use of DEXYCU, as with other ophthalmic corticosteroids, is not recommended in the presence of most active viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal disease of ocular structures.

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex). Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection.

5.4 Cataract Progression

The use of corticosteroids in phakic individuals may promote the development of posterior subcapsular cataracts.

6 ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Increase in Intraocular Pressure *[see Warnings and Precautions (5.1)]*
- Delayed Healing *[see Warnings and Precautions (5.2)]*
- Infection Exacerbation *[see Warnings and Precautions (5.3)]*
- Cataract Progression *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

The following adverse events rates are derived from three clinical trials in which 339 patients received the 517 microgram dose of DEXYCU. The most commonly reported adverse reactions occurred in 5-15% of subjects and included increases in intraocular pressure, corneal edema and iritis. Other ocular adverse reactions occurring in 1-5% of subjects included, corneal endothelial cell loss, blepharitis, eye pain, cystoid macular edema, dry eye, ocular inflammation, posterior capsule opacification, blurred vision, reduced visual acuity, vitreous floaters, foreign body sensation, photophobia, and vitreous detachment.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of DEXYCU (dexamethasone intraocular suspension) in pregnant women. Topical ocular administration of dexamethasone in mice and rabbits during the period of organogenesis produced cleft palate and embryofetal death in mice and malformations of abdominal wall/intestines and kidneys in rabbits at doses 7 and 5 times higher than the injected recommended human ophthalmic dose (RHOD) of DEXYCU (517 micrograms dexamethasone), respectively *[see Data in the full prescribing information].*

In the US general population the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

8.2 Lactation

Risk Summary

Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. There is no information regarding the presence of injected DEXYCU in human milk, the effects on breastfed infants, or the effects on milk production to inform risk of DEXYCU to an infant during lactation. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for DEXYCU and any potential adverse effects on the breastfed child from DEXYCU.

8.4 Pediatric Use

Safety and effectiveness of DEXYCU in pediatric patients have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between older and younger patients.

Manufactured for: EyePoint Pharmaceuticals US, Inc. Watertown, MA 02472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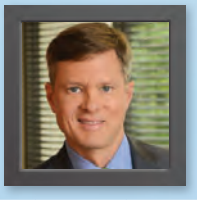
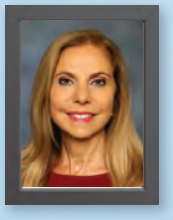
Eric Donnenfeld


John Hovanesian


Mitch Jackson


Richard Lindstrom


James Loden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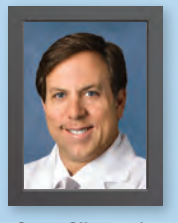
Steve Silverstein


Inder Paul Singh


Denise Visco


Keith Walter

Your name here

These cataract surgeons use OMIDRIA® (phenylephrine and ketorolac intraocular solution) 1% / 0.3% for **less stress, pure success** in their O.R. day[1]

What about you?

OMIDRIA helps your cataract surgery by inhibiting prostaglandin release to block inflammation and maintain iris tone, preventing miosis and reducing postoperative pain for your patients.[2,3] Experience less stress in your O.R. day with OMIDRIA.[1]

INDICATIONS AND USAGE

OMIDRIA® (phenylephrine and ketorolac intraocular solution) 1% / 0.3% is added to ophthalmic irrigating solution used during cataract surgery or intraocular lens replacement and is indicated for maintaining pupil size by preventing intraoperative miosis and reducing postoperative ocular pain.

IMPORTANT SAFETY INFORMATION

OMIDRIA must be added to irrigating solution prior to intraocular use.

OMIDRIA is contraindicated in patients with a known hypersensitivity to any of its ingredients.

Systemic exposure of phenylephrine may cause elevations in blood pressure.

Use OMIDRIA with caution in individuals who have previously exhibited sensitivities to acetylsalicylic acid, phenylacetic acid derivatives, and other nonsteroidal anti-inflammatory drugs (NSAIDs), or have a past medical history of asthma.

The most commonly reported adverse reactions at ≥2% are eye irritation, posterior capsule opacification, increased intraocular pressure, and anterior chamber inflammation.

Please see the Full Prescribing Information for OMIDRIA at www.omidria.com/prescribinginformation.

You are encouraged to report Suspected Adverse Reactions to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

References: 1. Omeros survey data on file. **2.** OMIDRIA [package insert]. Seattle, WA: Omeros Corporation; 2017. **3.** Al-Hashimi S, Donaldson K, Davidson R, et al; for ASCRS Refractive Cataract Surgery Subcommittee. Medical and surgical management of the small pupil during cataract surgery. *J Cataract Refract Surg.* 2018;44:1032-1041.

The healthcare professionals portrayed in this advertisement are consultants of Omeros Corporation.

OMEROS

OMIDRIA®
(phenylephrine and ketorolac intraocular solution)
1% / 0.3%

The Other Virus

Do we have any ammunition that can shoot down misleading and dangerous claims?

I doubt there is a person reading these words who has not, at times, felt stressed and anxious over the past few months. Supposed to be The Year of the Ophthalmologist and a celebration of eye care, the year 2020 had other plans – and made us cancel most of ours. Unfortunately, as Viren Swami and colleagues have shown, stress is a predictor of believing conspiracy theories and misinformation (1).

The widespread use of social media – where anyone can post an opinion (whatever their qualifications) – and the current political discourse have been blamed for false claims and misleading stories being shared en masse. And the pandemic has really added fuel to the fire.

As Timothy Melley wrote in "Empire of Conspiracy," when people feel they are losing control over their lives, they may develop "agency panic" – a belief that they are not being told the truth about the reality they're living in; they may feel that their autonomy is being taken away (2). Faced with an invisible enemy, tangible effects of the climate emergency in the form of fires devastating Australia and the USA, and worldwide protests, some choose to "prove" their free agency by believing and spreading misinformation – and lots of it (3).

Sheraz Daya, in a fascinating discussion among leading refractive experts (see page 16), says that all patients who enter his practice abide by the mask-wearing rule, but it is not unusual to meet people who question control measures, transmission routes, and mortality figures. Have you come across them in your practice? Do you engage with them? Do you feel like you know how to debunk the myths?

Misinformation can be reduced if we get ahead of the game. We must aim to actively present scientific evidence before people come across misrepresentations, frequently correct false claims, and offer actual or more probable alternative explanations (4, 5). Easy-t0-understand information that is repeated often tends to stick with people. Creating a safe environment, putting the patient in control as much as possible, and using humor to increase positive emotions can reduce belief in conspiracy theories (6).

There are no easy solutions, but active engagement and the ability to carefully listen can slowly break down the wall of misinformation. Dialog matters now more than ever.

Aleksandra Jones
Editor

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1. *V Swami et al., "Putting the stress on conspiracy theories: examining associations between psychological stress, anxiety, and belief in conspiracy theories," Pers Individ Dif, 99, 72 (2016).*
2. *T Melley, Empire of Conspiracy: The Culture of Paranoia in Postwar America, Cornell University Press: 2000.*
3. *MS Islam et al., "COVID-19-related infodemic and its impact on public health: a global social media analysis," Am J Top Med Hyg, [Epub ahead of print] (2020). PMID: 32783794.*
4. *JWW van Prooijen, KM Douglas, "Belief in conspiracy theories: basic principles of an emerging research domain, Eur J Soc Psychol, 48, 897 (2018). PMID: 30555188.*
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Upfront

Research
Innovation
Trends

Harvard Medical School. Photographic postcard, ca. 1928. Credit: Wellcome Collection.

Ready, Steady, Graft

A new stem cell technique offers hope for chemical burn victims

The first cultivated autologous limbal epithelial cell transplantation (CALEC) has been performed in the US. The technique, developed in 2018 by researchers at Harvard Medical School (HMS), Massachusetts Eye and Ear, Boston Children's Hospital, and Dana-Farber Cancer Institute, was used to treat four patients with chemically induced corneal injuries. CALEC uses a patient's limbal stem cells – found at the outer border of the cornea – to create an ocular graft. The process is carried out in a clean room environment to maintain maximum sterility and takes approximately three weeks, at which point the graft is ready for transplantation. Ula Jurkunas, Associate Professor of Ophthalmology at HMS and Associate Scientist at the Schepens Eye Research Institute, has been working on the technique for more than a decade.

"Using the patient's own stem cells is a big step for regenerative medicine," said Jurkunas (1). "With this clinical trial, we hope to pave the way for better care for patients with corneal blindness." The only treatment options currently available are corneal transplantation – which carries risk of infection and the development of glaucoma – or conjunctival limbal autograft, which involves transplanting a portion of healthy corneal cells directly onto the affected area. Jurkunas considers CALEC to be an ideal alternative because it carries no risk of rejection and does not require patients to take steroids or immunosuppressive medications. The patients who received the CALEC graft reported no pain, confirming the technique's feasibility and allowing researchers to begin the second phase of the trial, which will continue through 2021.

Reference

1. *Harvard Medical School (2020). Available at: https://bit.ly/3hDJ6mw.*

INFOGRAPHIC

The Kids Are (Not) All Right

With 75 million children to serve, America's pediatric ophthalmologists face a tough task in the wake of COVID-19

PEDIATRIC SPECIALISTS are struggling to keep their **PRACTICES VIABLE** since the shutdown (1).

3%

of practices have closed permanently

BUSINESS IN BRIEF

The latest industry news, appointments, and acquisitions

- Oculis SA has appointed Sylvia Cheung as Chief Financial Officer. Cheung will be based in the newly established Oculis US office, succeeding Páll Ragnar Jóhannesson, who is now Chief Strategy Officer. This is the second significant hiring in recent months, following Grace Chang's appointment as Chief Medical Officer in August.
- Oxurion has enrolled the first patient in its Phase 2 study evaluating THR-149 for the treatment of DME. THR-149 is a potent plasma kallikrein inhibitor for those who respond suboptimally to anti-VEGF therapy. Patrik De Haes, Oxurion CEO, said, "The start of this trial is a major step in our plans to build a DME franchise for specific, complementary target patient groups."
- Two sight-saving charities are set to merge on January 1, 2021. Clearly and the International Agency for the Prevention of Blindness will combine to form a network of over 150 members working in international eye health and leading global advocacy for the sight sector. The organizations say the move marks the "next exciting phase in the battle to deliver vision for everyone."
- Israeli AI and eye-tracking technology start-up NovaSight closes US$8 million Series A financing in a quest to combat vision disorders worldwide. The new funds will be used to develop future eye care products and advance clinical trials for the company's amblyopia treatment device, supporting its path to FDA clearance.

- Michael Chiang has been selected as the new director of the prestigious National Eye Institute. Chiang currently holds the position of Knowles Professor of Ophthalmology and Medical Informatics and Clinical Epidemiology at Oregon Health and Science University, where he also serves as associate director of the OHSU Casey Eye Institute.

Erin Scott. Credit: Texas A&M University.

Spicing up Uveitis Treatment

Can a common cooking ingredient help treat ocular inflammation?

The team at Texas A&M University in the USA have used turmeric – specifically, its compound called curcumin – to develop a therapeutic that decreased ocular inflammation in canines suffering from uveitis. The novel formulation of curcumin has been shown to successfully bypass intestinal and ocular barriers, resulting in improved absorption of the medication. Unlike current uveitis treatments, which have multiple unwanted side effects, such as stomach ulcers, affecting kidney and liver function and increasing diabetic patients' glucose levels, curcumin has no known side effects. According to Erin Scott, Assistant Professor at the Texas A&M University College of Veterinary Medicine & Biomedical Sciences, the new therapeutic has great potential for treating uveitis in humans, aiding cataract treatment.

Reference

1. *R Ganugula et al., Science Advances 6, 35 (2020).*

5.4%

have declared bankruptcy or are considering the idea

2%

feel their practice viability remains "DAY-TO-DAY" with BANKRUPTCY as a possible outcome

51 PERCENT

continue to operate with REDUCED STAFF compared with PRE-COVID-19 LEVELS

Reference

1. *AAPOS. Available at: https://bit.ly/3hiEOAV.*

New Virus, Old Story

Why are patients with AMD at greater risk of developing severe COVID-19?

A recent paper in Nature has found a connection between the severity of COVID-19 (and the risk of dying from the disease) and mutations in genes responsible for complement and coagulation (1).

Complement, one of the oldest parts of the immune system, enhances the way antibodies deal with pathogens and damaged cells, removing them from the body and stimulating inflammation. Patients with AMD, which is caused by overactive complement, may develop more serious complications of COVID-19, resulting in more hospitalizations and deaths in this patient group.

How does SARS-CoV-2 affect complement and coagulation? Sagi Shapira, Assistant Professor of Systems Biology at Columbia University Vagelos College of Physicians and Surgeons and one of the lead investigators of the study, explained, "Viruses have proteins that can mimic certain host proteins to trick the host's cells into aiding the virus with completing its life cycle. The new coronavirus – by mimicking complement or coagulation proteins – might drive both systems into a hyperactive state" (2).

As part of the study, researchers looked at patients with AMD who were admitted to Columbia University Irving Medical Center with suspected COVID-19. They determined that over 25 percent of AMD patients died, compared with an average mortality rate for admitted patients of 8.5 percent – a difference not explained by the patients' age or sex. Patients with other conditions where complement also plays an active role – such as obesity or diabetes – also have a higher risk of needing intubation or dying as a result of SARS-CoV-2 infection.

Analysis of data from the UK Biobank, which contains the genetic information of half a million people, confirmed that variants of many genes associated with severe forms of COVID-19 also influence complement and coagulation activity.

This might not be good news for AMD patients; however, it may also mean that medications designed to inhibit the complement system could be used to treat patients with severe COVID-19.

References

1. *V Ramlall et al., Nature Medicine (2020). PMID: 32511494.*
2. *Columbia University Irving Medical Center (2020). Available at: https://bit.ly/3kBX5et.*

The Trouble with Triage

What risk do asymptomatic COVID-19 patients pose to ophthalmologists during elective examinations?

Because of COVID-19's threat to healthcare professionals, it is now common for clinics to screen patients before elective examinations – but how effective is triage when many carry the virus asymptomatically? Researchers at the İzmir Tepecik Training and Research Hospital, Turkey, decided to find out by studying an examination room visited by patients who had passed triage. Samples were taken from five circular zones within a one-meter diameter of the patient – including slit lamp breath shield, phoropter surfaces, tonometer and door handles – and analyzed for viral material. The bad news? SARS-CoV-2 was found in two of seven post-examination samples. The (potentially) good news? The study could only detect viral material – not infectivity, virulence, viability, or viral load. Further research is needed to assess the potential infection risk of asymptomatic patients during routine eye exams.

Reference

1. *H Aytoğan et al., "Detection of coronavirus disease 2019 viral material on environmental surfaces of an ophthalmology examination room," JAMA Ophthalmol [Epub ahead of print] (2020). PMID: 32761201.*

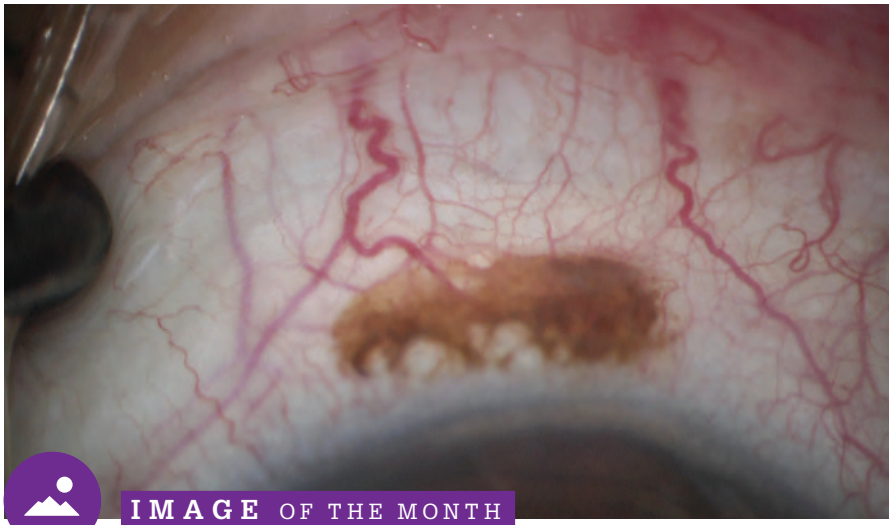


IMAGE OF THE MONTH

Clash of the Titans

"Sometimes something artistic comes from unexpected places and slaps you in the face," says Richard Koplin, Co-Director of the Cataract Service at the New York Eye and Ear Infirmary of Mt. Sinai, NY, USA. it, "I was adjusting the operating microscope in preparation of initiating a routine cataract procedure, when I was stopped in my tracks by the odd presentation of the conjunctival melanosis at the limbus in this case. It took very little imagination to conjure up two large and formidable animals butting heads."

Credit: Richard Koplin

Would you like your photo featured in Image of the Month?
Send it to edit@theophthalmologist.com

QUOTE OF THE MONTH

Commenting on the IIRSI Intrascleral Haptic Fixation webinar line-up:

"This all-star ophthalmology program needs to do better. Manels = all male panels do not reflect the diversity of colleagues dedicated to protecting sight. Thought leaders need to police themselves."

Ravi Goel, Ophthalmic Surgeon, Wills Eye Hospital, USA
Twitter, *https://bit.ly/32Re72t*

Tube Talk

Researchers discover a communication structure that is essential for fully functional retinal cells

A new mechanism of blood redistribution has been uncovered by researchers at the University of Montreal Hospital Research Centre (CRCHUM). The in vivo study found that activated retinal areas received more blood than non-activated ones via a unique regulation system operated by pericytes. These cells have the ability to control the amount of blood passing through a single capillary simply by squeezing and releasing it. "Using a microscopy technique, we showed that pericytes project very thin tubes, called inter-pericyte tunneling nanotubes, to communicate with other pericytes located in distant capillaries," said Luis Alarcon-Martinez, a postdoctoral fellow at CRCHUM and one of the lead authors of the study. "Through these nanotubes, the pericytes can talk to each other to deliver blood where it is most needed." When capillaries lose their ability to shuttle blood where it is required – following an ischemic stroke, for example – cells begin to die. The findings suggest that microvascular deficits observed in neurodegenerative diseases, such as glaucoma and Alzheimer's disease, could be the result of impaired blood distribution.

Reference

1. *L Alarcon-Martinez et al., "Inter-pericyte tunnelling nanotubes regulate neurovascular coupling," Nature, [Epub ahead of print] (2020). PMID: 32788726.*

In My View

Experts from across the world share a single strongly held opinion or key idea.

Ticking Timebombs

Following the recall of the Raindrop corneal inlay, efforts must be made to notify all remaining affected patients

By Harvey Carter, refractive and cataract surgery specialist at Carter Eye Center, Dallas, Texas, USA

As some of you may know, the original maker of the Raindrop corneal inlay, Revision Optics (RVO), abruptly closed its doors on January 30, 2018. On October 22, 2018, the US Food and Drug Administration issued an FDA Safety Communication – a recall of the Raindrop corneal inlay (1). This FDA recall followed the FDA's premarket approval of the Raindrop corneal inlay on June 29, 2016 (2).

I was an FDA investigator in the original clinical trial. The best estimate of the number of Raindrop corneal inlays implanted during the period of commercial implantation is between 2,000 and 3,000. The initial reason for the FDA recall was the development of corneal haze that could affect clear vision – but this did not address the other, more significant issues associated with untreated corneal haze, including impending corneal melt, corneal melt, and corneal melt with extrusion of inlay.

I have now removed all of the inlays I implanted as part of the FDA trial, but I have recently seen a cluster of patients with the known late complications of the Raindrop corneal inlay. These patients were implanted in other settings; they are now presenting with severe haze and impending corneal melt.

Since October 2018, efforts have been made to contact every patient implanted with the Raindrop to notify them of the recall and offer them appropriate treatment options, ranging from inlay explantation to more frequent follow-up examinations. However, some patients have clearly not responded to the notifications and others have chosen to continue with the inlay despite the known risk. There was clearly a corneal haze complication "honeymoon" period noted in the FDA trial; this was extended during commercial implantation by burying the inlay deeper in the cornea and using mitomycin C to delay the development of corneal haze. The original honeymoon period in the FDA trial lasted for about a year and a half after implantation, so the cluster of cases I have just seen coincides with what was shown in the trial.

I strongly suggest that every surgeon who implanted a Raindrop corneal inlay

"The most recent patients I have seen were implanted in other settings; these patients are now presenting with impending corneal melts."

should contact every remaining inlay patient and advise them of the need for continuing follow-up appointments until the inlay is explanted. It should also be noted that there are known cases of haze-related problems occurring six months after explantation of the device. Although we do not know the magnitude of the problem, we do know that there are still Raindrop corneal inlays in eyes out there – and that they are potential ticking timebombs.

Go to top.txp.to/ticking-timebombs to see the images of affected eyes.

References

1. *US FDA, "Increased risk of corneal haze associated with the raindrop near vision inlay: FDA safety communication" (2018). Available at: https://bit.ly/3hyxmBG.*
2. *US FDA, "Premarket Approval (PMA)" (2016). Available at: https://bit.ly/3hxPEDl.*

Ever the Optimist

The highs and lows of residency during a pandemic

By Anesu Madikane, Fourth Year Resident at Steve Biko Academic Hospital, University of Pretoria, South Africa

Medicine tends to have a rigid hierarchical structure. At the top are professors – those who have reached the peak of their careers – deities you have no access to. Everyone else is beneath them. At least, that was the case until very recently – the pandemic has shaken this structure, providing a small silver lining to this time of global upheaval.

The COVID-19 pandemic seems to have brought with it a wave of openness, with people becoming more forthcoming and generous with information they are willing to share – there has been a lot of free, easily accessible online content available to junior ophthalmologists over the last few months. It has been wonderful to see that a lot of recent webinars have been open access, whereas traditionally many top professors would use exclusive private platforms for sharing their knowledge with their peers. Even at congresses, there are often certain meetings that are paid access or invitation only.

It has been really good to see some of those traditional hierarchical systems in medicine being broken down, with open access to information through the use of technology and webinars. But there is only so much a webinar can teach. You can watch 100 videos of the best surgeons in the world, but unless you get the opportunity to perform a surgery with a mentor by your side, you will not achieve the surgical proficiency that makes you an excellent surgeon. Nothing beats hands-on experience.

As a final-year registrar, nearing the end of my training, the focus of my residency would usually have been on refining skills – by now, I should have all the basic competencies. "Perfecting" is an important phase of training – and it is the one that has taken perhaps the biggest knock this year.

I have lost around six months of surgical time. While I've continued to do emergency cases and glaucoma drainage device surgery or trabeculectomies here and there, I haven't even got close to the volume that I was used to.

While I am anxious about the time lost due to the pandemic, this year has taught me that often the things that we believe to be pressing matters are not as urgent as we might think they are. I remain optimistic and grateful for the lessons I've learned during the pandemic. I have a lifetime as an ophthalmologist ahead of me – more than enough time to make up for those lost surgical cases!

"You can watch 100 videos of the best surgeons in the world, but unless you get the opportunity to perform a surgery with a mentor by your side, you will not achieve the surgical proficiency that makes you an excellent surgeon."

The SCOPE of Things to Come

Dry AMD is no longer a disease without hope. It is your responsibility to encourage patients to seek help – and the SCOPE study is a good place to start.

By Paulo Eduardo Stanga, Retina Service Lead, Consultant Ophthalmologist and Vitreoretinal Surgeon at the London Vision Clinic, UK

Dry AMD is the most common cause of blindness among the elderly, affecting between 36 and 40 million people globally, according to the 2010 Access Economics Report. Right now, there are no approved treatments. The SCOPE study run by Gyroscope Therapeutics is a global natural history study enrolling participants at approximately 60 sites globally, including centers throughout the UK, including the London Vision Clinic (1). It is a prospective, observational protocol designed to evaluate the natural progression of anatomical and functional visual parameters in genetically defined patients with Geographic Atrophy (GA). We plan to genotype 2,000 people – preferably more – at our network of centers throughout the country, with the goal of identifying patients with mutations in their Complement Factor I (CFI) gene. The study will allow the characterization of patient phenotype, including disease progression. It is, in a word, groundbreaking.

As far as I know, a genotyping study of this size has never been attempted before for dry AMD. We have compelling evidence that complement factors play a significant role in the condition. Now, we need to better understand the pathophysiology of GA to find a treatment for it. By genotyping such a significant number of patients, we will generate a hugely valuable dataset. We have reason to believe that we will find one dry AMD patient with a rare variant in every 30 we screen and – we might even find other variants and associations as we go. Either way, the information we get from SCOPE will be critical in guiding the current Phase 1 interventional study FOCUS, and also guide future Phase 2 studies and beyond.

As part of the SCOPE study, patients with GA are screened for eligibility and genotyped via saliva sample. Patients who are found to have a rare variant are then observed for 96 weeks, with any eligible patients offered the opportunity to participate in FOCUS (or another interventional study). The primary objective of FOCUS is to evaluate the safety of three doses of GT005 – Gyroscope's investigational, one-time gene therapy, designed to restore balance to an overactive complement system by increasing production of the CFI protein. We have reason to believe a subset of GA patients with low CFI serum and rare variants may be best suited to treatment with GT005. We are using an adeno-associated virus type 2 vector method of CFI gene transfer (essentially, what GT005 is) to ensure sustained expression of CFI. The idea is that patients will not need to have periodic injections of CFI because their eyes will be able to rebalance the complement cascade on their own, nudging the body to produce its own therapy. This is exciting – but it will only be possible with your help.

We need as many patients as possible to join the study. Though I know some are understandably reluctant to return to clinical settings, it is crucial that we encourage our older patients with significant visual impairment to take part in this research. Our clinic takes safety very seriously and is safeguarding against every possible precaution, even offering free door-to-door transport for anyone taking part in our studies. So, what are we looking for? Specifically, patients with significant GA – preferably confirmed by autofluorescence, with best corrected visual acuity of 34 letters or more – in late-stage disease. The reason for this is simple: we need precise diagnosis to reduce noise in data analysis. It is very possible that we will find new gene variations which will, in turn, allow us to develop new therapies.

Patients who participate in these research activities do so for their own benefit and for those to come after them. For years, patients with dry AMD have been told there was nothing that could be done – some are still being told that. It is vital that patients – and doctors – know that there is hope. I encourage you to refer patients with GA to the centers that are providing care throughout the care. We can only beat dry AMD by working together.

Information on enrolment can be found at https://www.gyroscopetx.com/patients-families/ or by calling the freephone number +44 1438 532142

Reference

1. *Clinical Trials, "First in human study to evaluate the safety and efficacy of GT005 administered in subjects with dry AMD" (2020). Available at: https://bit.ly/2E7h3yd.*

The Power of the Personal Touch

The good, the bad, and the new normal – how the pandemic has changed things for young ophthalmologists

By Henal Javeri, Third Year Resident at Sri Sankaradeva Nethralaya Hospital, Guwahati, Assam, India

Young ophthalmologists have played – and continue to play – an important role in the pandemic. We have acted as frontline workers, shielding senior consultants who are at much higher risk of developing a more severe form of COVID-19 due to their age. The experience had an added benefit of allowing us to see a patient, assess their condition and come up with a plan of action for managing their condition – all on our own. In a strange way, the pandemic has given us independence and the confidence to reach our own conclusions – but with the comfort of having our mentors by our side.

But it has not all been good. There are certain aspects of the doctor-patient relationships that have suffered over the last few months. There is only a certain amount of connection that you're going to be able to build with a patient behind a face mask. As a doctor, what you really want to do is comfort the patient before the examination even begins. It might be as simple as patting the patient on the back or shaking their hand – the personal touch cannot be replaced by a virtual medium. This is particularly true of pediatric patients who are so apprehensive before an examination, it can be difficult to get them to sit in one place and let you examine them. In that sense, I feel this will new way of working will take some getting used to. But perhaps we should just think of it as a different form of communication, and a different form of doctor/patient relationship. It is something that we're going to have to build on, but I'm hopeful that in time we will form connections again – just in a new way.

REFRACTIVE RECOVERY *and* COVID-19

Five refractive leaders discuss how the world has changed for them – and the profession – since the pandemic hit

Sat around our **VIRTUAL TABLE** *are:*

Chair and moderator:
ARTHUR CUMMINGS,
Medical Director of the Wellington Eye Clinic in Dublin, Ireland

SHERAZ DAYA,
Medical Director and Chairman of Centre for Sight in London, UK

BEN LAHOOD,
refractive, cataract and laser vision correction surgeon in private practice in Auckland, New Zealand

MARIA SCOTT,
Chief Medical Officer of Vision Innovation Partners, Founding Partner and Medical Director of Chesapeake Eye Care and Laser Center, and Chesapeake Eye Surgery Center, and Medical Director at TLC Laser Eye Center in Annapolis, USA

DENISE VISCO,
ocular surgeon and Medical Director and Founder of Eyes of York in Pennsylvania, USA

WHAT IMPACT HAS COVID-19 HAD ON YOUR PRACTICE – AND WHAT DID RE-OPENING YOUR PRACTICE LOOK LIKE?

Denise Visco: I work at a small (two-surgeon) practice. We are based in central Pennsylvania, USA, and we employ three supporting optometrists. We closed around March 16, but we were able to reopen on May 2. Although we are fully open at this point, our guidelines for seeing patients have definitely changed. Our goal was to try to get back up to 100 percent of the throughput we had prior to COVID-19, and we were able to reach that target around the end of June, but with very different processes in place.

Following the changing curve of COVID-19 cases and working out new safety guidelines has been a challenge for me as the main decision maker.

Maria Scott: It has been a very interesting time for my practice, and it has really made us much more innovative. Vision Innovation Partners in Maryland, USA, closed down its offices on March 16. We have 23 offices, 13 practices and employ around 70 ophthalmologists and optometrists. We started gradually reopening our practices around May 18, and since late June we have fully opened all of our centers.

Sheraz Daya: We were instructed to lock down on March 23, but we had a few transplants that we didn't want to lose, so we continued surgery with full precautions, locked down on March 25, and saw only emergencies every week throughout the lockdown period. Retinal surgeons in our setting were still operating on retinal detachment patients, and dealt with a couple of vitreous hemorrhages, ensuring there were no holes and tears that would need attention later. We re-started on June 1, but we started very slowly to ensure we got used to the "new normal:" enhanced cleaning, making sure our staff understood the processes of checking patients' temperature and getting specific questionnaires filled out, and so on. All this preparation made patients a little more vigilant, which can only be a good thing under current circumstances. It's amazing how quickly you get up to speed – we are now ready to see all our patients back, and our schedules are back to normal volumes.

Ben LaHood: In New Zealand, we have done pretty well with containing the virus. We initially had a lockdown period for a month, when we weren't doing anything except taking care of emergencies. Then we gradually moved from serious restrictions over a few weeks to having very vague guidelines about when it would be safe to return to refractive surgery and elective cataracts. And that's why we got together as a group of ophthalmologists across the country; together, we decided that it was safe for us to carry on with procedures. We got back to practically 100 percent of elective cataract surgery and laser surgery.

DID YOU MAKE USE OF TELEMEDICINE DURING THE LOCKDOWN PERIOD, AND ARE THERE ANY ELEMENTS OF IT YOU'RE KEEN TO RETAIN?

Maria: In some locations, such as our Annapolis center, our retina surgeons continued to deal with emergencies and carry out injections – that was one area where telemedicine would obviously not work. Our oculoplastics specialist was easily able to switch to telemedicine, and other specialists used it a little in their practices. I used it for all the surgical patients I had already scheduled to make sure nothing had changed. For those patients, it was a wonderful way of making them feel like we were still connected.

In the US, you are required to have an eye exam at least 90 days ahead of surgery, so the telemedicine visit served that purpose – we didn't have to bring the patients in another day. We're continuing to do telemedicine now: we have our optometrists rotating on a weekly basis using telemedicine. They're doing a lot of triage, so the sub-conjunctival hemorrhage, conjunctivitis, and sty patients can be seen remotely. Our one-week post-op second eye visits are also being conducted through telemedicine.

Sheraz: We did indeed try telemedicine. In my experience, it took a lot of time trying to get our elderly patients to understand how to use it, so we got them to use our portal for uploads instead. We gave them clear instructions on how to take photographs, put them on their computer screen and measure the distance to check their vision. We quickly abandoned it. We didn't have to see any emergencies as a result of telemedicine

> *"In the US, you are required to have an eye exam at least 90 days before the surgery, so the telemedicine visit served that purpose, meaning that we didn't have to bring the patients in another day."*

consultations. Usually in the triage process we knew which patients had to be seen in person and we just brought them into the office. They were, without fail, all true emergencies.

I think telemedicine works great for oculoplastics, but I'm not sure it's a good solution for refractive surgery. And yet, colleagues around the world are talking about doing their consultations online! I don't know how they can do that, without obtaining a diagnosis in person first. I find it very hard to be convincing and reassuring to a surgery candidate without important, solid data in front of you. I have also found that it takes longer to see a patient using telemedicine, so I didn't think it was very efficient. Given my recent experience, I'd describe it as quirky and gimmicky.

Arthur Cummings: I've always been very optimistic about telemedicine, and have been keen to try it out based on the experience of colleagues of mine, notably the Zaldivars in South America. I have used a system that allows me to examine the eye on a slit lamp. We started using telemedicine mostly for emergencies. I have found that it was possible to build a rapport with a patient using telemedicine, which has been reassuring. Some of those patients came into the clinic afterwards, and we felt like we had met each other in person already.

When COVID-19 is no longer active, my colleagues and I want to look back and think we never played any part in spreading the virus – and that's why we're trying to make our clinic consultations as short as possible. Patients come in for their scans and for a refraction, and for the part of the examination that has to be done in person, but we have also introduced a process using telemedicine, where nurses or technicians go through an online form with the patient around four days before the visit. They check the patient's preferences, hobbies, and they create a relationship that is important when the patient comes into the clinic in person. When they arrive, they've already thought about different options, so the conversation I have with them is much more focused. Before the lockdown, our conversion rate after the visit was around 55 percent; now, if a patient is suitable, they simply make a plan to go ahead with the surgery. They are less likely to shop around – once they've made up their mind about the procedure, they just want to get on with it.

"I think telemedicine works great for oculoplastics, but I'm not sure it's a good solution for refractive surgery."

WHAT PROTECTIVE MEASURES HAVE YOU USED TO ENSURE STAFF AND PATIENT SAFETY?

Maria: Keeping patients safe has been our priority from the very beginning of the pandemic. The safety of our staff has also been paramount: they all have families that they want and need to protect. There is also a financial aspect to it: if one of your surgeons or other specialists cannot work for eight or 10 weeks, it has serious financial implications. We've done most of the things that the AAO recommended. Everyone is given the option of wearing an N95 or a surgical mask, but we try to stress that technicians and doctors should wear N95s because of their close contact with patients. We developed our own slit lamp shields.

When I'm dressing for work, I look like I'm going into battle: I wear goggles, a surgical cap, scrubs, an ENVO N95 mask, and a surgical mask on top of that. I also have protective shields in front of my desk. As we don't have any family members coming with patients, it feels much more intimate. Patients come in and very soon they're ready to leave. My schedule is much more reasonable now; I'm happier and I cherish the fact that I can spend much more time with my cataract consults.

Sheraz: We wear N95 masks, patients are given a mask if they don't come in wearing one. I think the mask is now a fashion accessory, so we have found that all patients come in with masks on. We don't allow relatives in unless they come with elderly patients or they act as an interpreter. We schedule elderly and vulnerable patients earlier. We measure patients' temperature; we have a COVID-19 checklist with a consent form. We physically distance within the clinic. One thing I have found difficult was wearing goggles, so I started using a pair of clear glasses to shield instead.

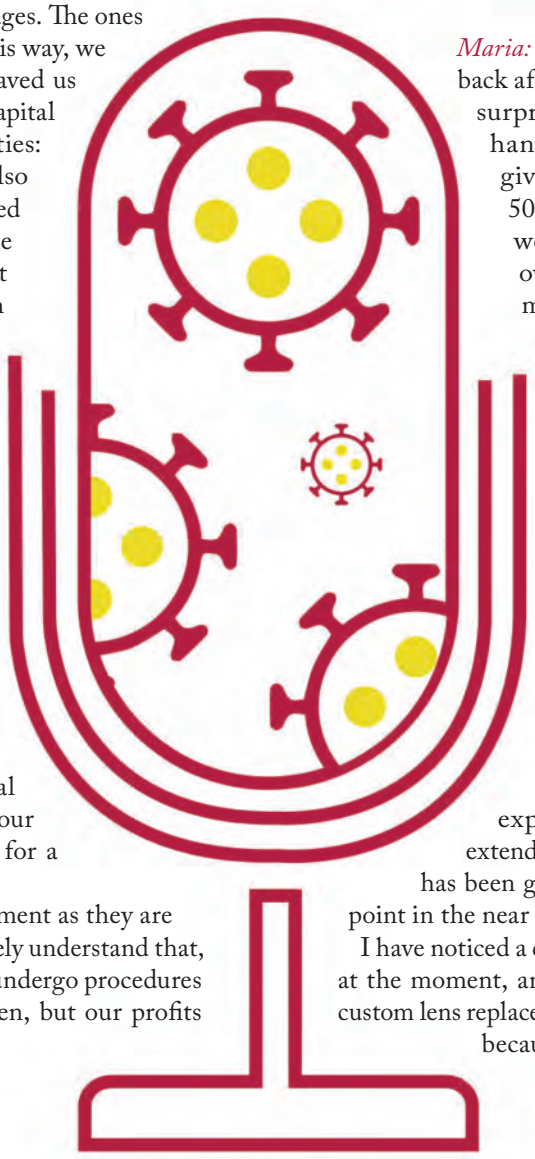
"My schedule is much more reasonable now, I'm happier and I cherish the fact that I can spend much more time with my cataract consults."

HOW HAVE YOU MANAGED TO GET THROUGH THIS PERIOD FINANCIALLY?

Sheraz: Half of our staff were furloughed, with the UK government paying 80 percent of their wages. The ones that stayed on were a skeleton crew. In this way, we cut down our salary bill, but that only saved us a small amount. We managed to get a capital break on the mortgages on our properties: we paid interest, but not capital. We also managed to defer equipment loans, to mixed reactions from our vendors. I think some of them genuinely wanted to help, but it wasn't always easy to agree terms with them, so I basically told them I would pay the bills when I had cash coming in again, which is what is happening now. Thankfully, we have been able to keep all of our staff.

We have taken out an interest-free loan from the government, around £50,000 (~$65,000). I'm really worried about a second shutdown, and in anticipation of that I'm going to preserve as much cash as possible. Even if we're profitable, we're going to learn the lessons of being lean and mean, and will keep it that way for a long while to come. There won't be any major capital expenditures – I'm not going to upgrade our equipment until we're on an even keel for a good period of time.

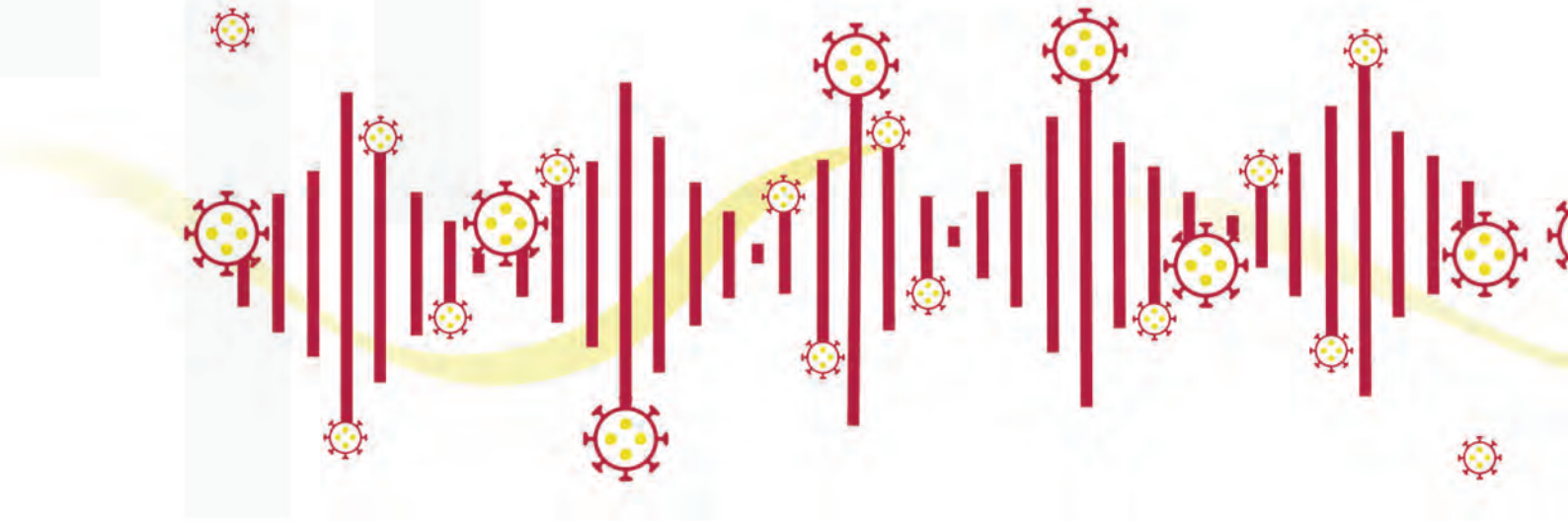
Some patients are deferring their treatment as they are worried about COVID-19, and I completely understand that, but there are also those who are ready to undergo procedures now. I expect we are going to break even, but our profits will suffer.



Maria: We brought almost all of our staff back after the lockdown. I was pleasantly surprised with how the government handled the situation in the US, giving businesses with fewer than 500 employees loans and grants. We were not eligible because we have over 500 employees, but many of my ophthalmology friends who had slightly smaller practices managed to secure help. The payment we received from the Centers for Medicare & Medicaid Services was a wonderful surprise. American Express deferred their bills for two months, and almost all of our rentals and mortgages were deferred. It was great to see how everyone worked together in this crisis. However, I am worried about what is coming in the autumn; I don't think this story is over, by any means.

Arthur: We have had very similar experience: we also deferred or extended loans and even tax bills, which has been great, but it does mean that at one point in the near future we're in for a big hit.

I have noticed a demand for laser refractive surgery at the moment, and for refractive lens exchange or custom lens replacement. And that helps us quite a lot because these patients are self-payers,



so we don't have to wait for the insurer to pay, and they are also mostly younger and less fearful of COVID-19. And it has resulted in us bringing younger patients in quicker; patients aged 75+ are very happy to wait another three months. Not only is it safer, but it has also helped us with the cash flow.

Maria: I was concerned that the economy wasn't going to be doing as well and patients would go for basic options, but it seems that patients have reassessed their financial priorities and have decided that their eyesight is important for their lifestyle, so many of them are actually choosing multifocals. Some have money available that would otherwise be spent on holidays, for example.

In terms of spending, we have a big reception and waiting room area, which is not being used right now, so we might think about changing it in six months or so, to make better use of the space.

Sheraz: One of my recent patients, when asked why they wanted surgery now, replied, "Life is short." This pandemic is certainly giving people a new perspective: they want to enjoy their lives because you never know what's around the corner. For our patients, this might make the decision about surgery a lot easier.

Arthur: Yes, there's an element of "Seize the day" in patients' decisions now. And, as Maria said, there's not so much for people to spend their disposable income on (assuming they have any).

Denise: We have been very diligent about planning for when COVID-19 strikes again, so that we can continue to see patients. Having those plans in place, making sure that the surgery center doesn't run out of PPE, and putting systems in place for potential employee sickness are how we have tried to protect ourselves. Barring the government telling us that we can't perform elective procedures or routine examinations again, we should be able to sustain our practice.

We have used the post-lockdown period as an opportunity to differentiate ourselves from our competition. As our patients are younger, and have busy schedules, we bring them in for a slit lamp exam with an optometrist when it suits them, and record it for the surgeon, who can then arrange a telehealth visit with the patient at a suitable time – sometimes in the evening – to go over appropriate laser vision correction options. Patients really appreciate this "higher level of service" – we make it easier for them to fit the surgery into their busy lifestyles, with extras, such as prescriptions delivered to their house, for example. And it has made a difference; we have seen numbers of LASIK, SMILE and PRK up this year compared with the same time last year.

Ben: Everyone at our practice decided to take a pay cut so that we could retain staff. We have seen a big demand for surgery, but I can't tell whether it will continue, so we have been making sure we communicate clearly that it is safe for patients to come and see us – we use social media, clips on

Facebook, and let people know we are using the correct PPE and have updated our procedures. We will have to focus more on encouraging the Chinese community to come back; they are usually a big part of my practice, but the numbers of those patients have dropped significantly.

HOW WILL THE WORLD LOOK IN A YEAR'S TIME?

Maria: COVID-19 will be with us for longer, and with the upcoming election in the US, there is a lot of uncertainty. By 2021, we will be living a much more normal life, but it will be different from what we have been used to. I can't see another longer lockdown happening in the USA.

Sheraz: Human beings are amazingly resilient. In the last two centuries there have been major wars, the GDP has shrunk considerably, and we had the 1918 pandemic. But people fight back and change things for the better. Having said that, with a huge loss of GDP, many people are going to lose their jobs and livelihoods. We all live in one community and we are all part of one society, so we need to work together and help each other. Our businesses might sometimes take a hit, but it's OK to have less money in your pocket – the most important thing is to avoid civil unrest and suffering. We all need to be in this together.

Arthur: Ophthalmologists have always looked forward to the year 2020 for all the obvious reasons, and it's been a damp squib so far. Nevertheless, 2020 has made us see the world differently. I think we'll look back and say that it was the year we started seeing things for what they really are. I've always known I had an amazing, independent team, but they have never worked the way they are now. You're right, Sheraz, there's a strong, palpable energy and vigor at work.

Denise: I am an optimist, and I do feel that healthcare in general, and ophthalmology in particular, will come out stronger, as people focus more on their well-being. Not having your glasses fog up or being able to see first thing in the morning may sound like a trivial thing, but for us, who fix these issues for a living, it's definitely not trivial, and it won't be for our patients. I believe what we give to our patients will have greater value than before COVID-19.

Ben: New Zealand is a country that does team up together well – we talk a lot about being a team of 5 million people. We are getting through this, but my concern is that, with a lot of financial boosts (like six-month mortgage holidays), we have simply shifted all our worries into the future. We rely a lot on overseas travel, imports and exports, and I think that once we get through this period of widespread support, there will be a downturn that will affect the whole economy, including ophthalmology. Nevertheless, I believe that the team mentality will get us through this and next year.

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In Practice

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Ever Evolving, Always Improving

MIGS has revolutionized glaucoma surgery, but there's still room for improvement. Let's talk XEN…

By Daniel Lee

The introduction of minimally invasive glaucoma surgery (MIGS) – the first generation iStent – back in 2008 signaled a big change in the way that we practiced glaucoma surgery and in the outcomes we were witnessing in patient safety and visual recovery. Since then, the MIGS philosophy has become pervasive; devices have been developed for every known target tissue in the aqueous fluid pathway and it feels like we hear about a novel device or new technique every year.

The initial MIGS buzz surrounded internal drainage devices, which allowed us to augment the natural outflow pathways of the eye. Today, surgeons are implanting the second-generation trabecular bypass devices (iStent inject and Hydrus), which have been shown to incrementally improve efficacy while maintaining an excellent safety profile.1

The supraciliary pathway has garnered a lot of interest, too, but without enjoying the same level of success; several ab-externo devices have failed to progress beyond the clinical trial stage. The recent voluntary recall of Cypass also did this approach no favors. It continues to be a target of interest, though, especially right now with the anticipated release the iStent Supra.

And finally, targeting subconjunctival flow has also generated some excitement, in particular with the release of the XEN gel stent. I will focus the attention of my article on this device, along with some of our recent results using an adaptation of the implantation technique.

More art than science

For more than a century, subconjunctival drainage procedures have remained the cornerstone of glaucoma surgery. Since the introduction of the first guarded filtering procedure in 1968, trabeculectomy has reigned as the time-tested, gold-standard glaucoma surgery. During the ensuing decades, a number of key modifications to the original technique were introduced which further optimized the procedure. For example, adjunctive antimetabolites, such as 5-fluorouracil and mitomycin-C, have improved long-term efficacy, while releasable and laser lysis of sutures improved safety. However, consistent outcomes and the elimination of serious adverse effects have remained elusive, thanks to the complex interplay of patient and surgical factors. Even after the wealth of clinical experience gained during the half-century of performing trabeculectomies, most glaucoma surgeons would agree that it is more an art than a science.

In my opinion, the XEN45 stent brought science to the art of glaucoma surgery by applying the principles of fluid dynamics to its design. A 6-mm long hydrophilic gelatin tube with a 45 µm internal diameter (designed using the Hagen-Poiseuille equation), the stent serves as a channel to drain aqueous fluid from the anterior chamber to the subconjunctival space. Under physiologic conditions, the implant confers a steady state resistance of 6 to 8 mmHg, significantly reducing the risk of hypotony.2 It's implanted with an ab-interno approach using a preloaded 27-gauge injector system; the absence of conjunctival incisions and sutures virtually eliminates the risk of wound leaks and induced astigmatism. These unique design and delivery characteristics address the common drawbacks

"Early on, this was modified to a 1-2-3 placement with the goal of traversing the injector further through Tenon's layer to achieve a more superficial placement."

associated with trabeculectomy; however, they expose certain vulnerabilities, too.

Design drawback

The length and internal diameter of the stent confer a standardized flow resistance, making early postoperative pressure outcomes highly predictable; however, these outcomes tend to diverge after a few weeks when fibrosis begins to set in during the proliferative phase of healing. Fibrosis is a well-known risk factor for surgical failure in all bleb forming subconjunctival drainage procedures. It turns out the very features that confer the good safety profile of the XEN45 potentially leave it vulnerable to obstruction; it is easier to obstruct a 45 µm opening compared with the filtering perimeter of a trabeculectomy flap. This issue is further magnified when the distal end of the stent becomes entangled in Tenon's layer. In practice, this is manifested with the significantly high proportion of patients requiring needling after XEN45 and a slight reduction in efficacy compared with trabeculectomy.3

Trying something different

The surgical technique has evolved extensively though, with the majority of modifications placing the distal tip of the stent more superficially to reduce Tenon's entanglement and subsequent obstruction. In its original conception, a 2-2-2 placement of the XEN45 stent was recommended – meaning the anterior chamber, intrascleral, and subconjunctival portion were to be equally distributed at 2 mm. Early on, this was modified to a 1-2-3 placement with the goal of traversing the injector further through Tenon's layer to achieve a more superficial placement. Along the same lines, others have described the "Air XEN" technique4, where air is injected to create a dissection plane separating the conjunctiva from the underlying Tenon's; the XEN45 is delivered into the "supra-Tenon's" pocket to ensure a superficial placement.

More recently, a growing number of surgeons have taken to implanting the stent using an ab-externo approach, which has several potential benefits over the traditional ab-interno approach. First, it frees the surgeon from the ergonomic limitations of working through a corneal incision. The outside-in approach expands the option for stent location from superonasal quadrant to the entire superior hemisphere, which is particularly useful if the superonasal tissue has unfavorable conditions, such as pre-existing fibrosis or scleromalacia. Second, an external approach eliminates the requirement for viscoelastic and consequently the possibility of retained viscoelastic occluding the stent in the early postoperative period. Finally, it potentially positions the distal portion of the stent more superficially thereby decreasing the likelihood of the distal stent becoming embedded in the Tenon's layer.

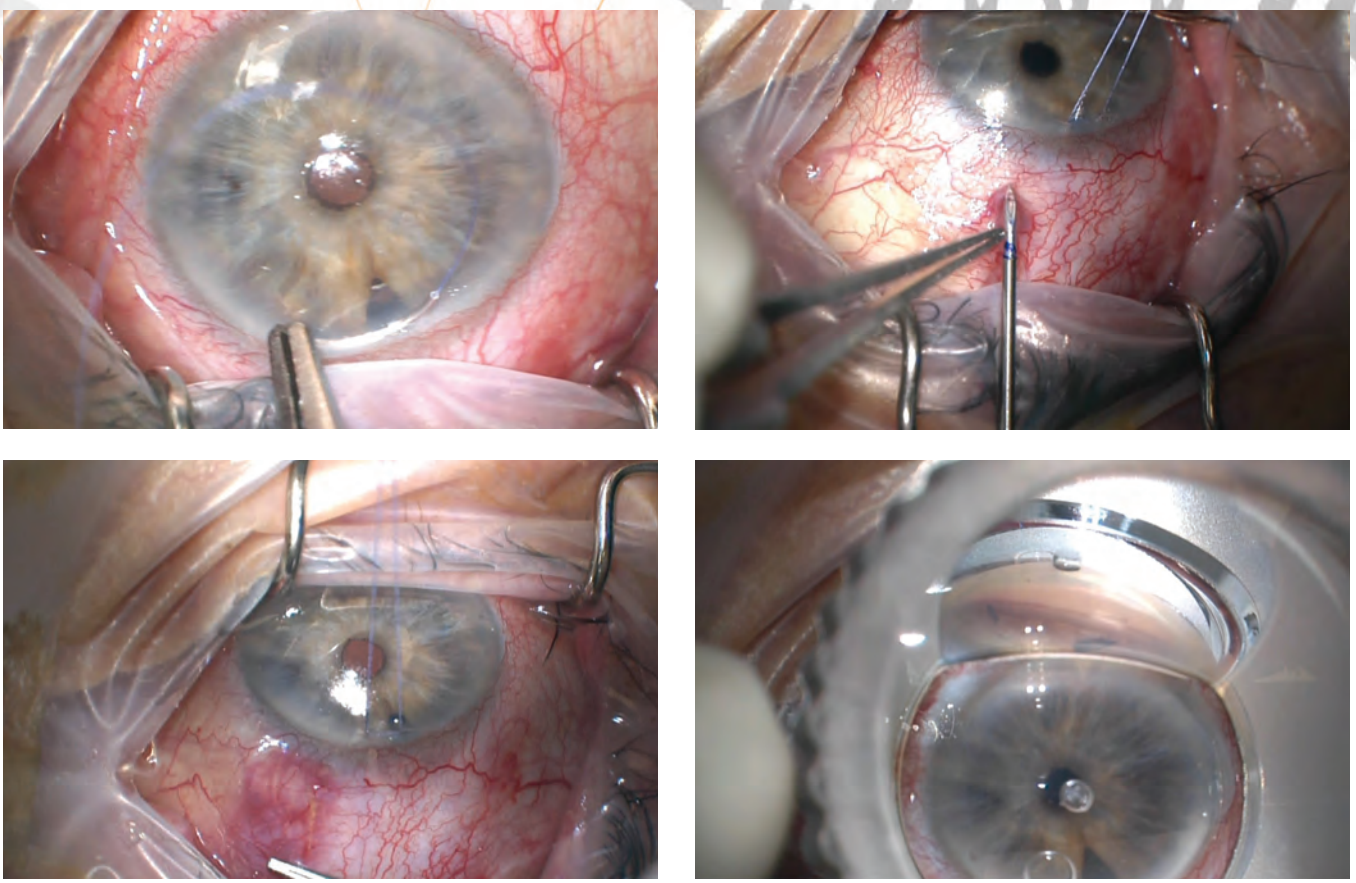

Figure 1. Ab externo implantation technique. (A)A traction suture is placed to aid in exposure. After the tip of the XEN45 stent is visualized, marked and retracted into the injector tip, (B) The injector enters the subconjunctival space and engages the sclera approximately 2mm posterior to the limbus. (C) The XEN45 stent is deployed and visualized in the subconjunctival space. (D) A mirrored gonioscopic lens is used to confirm proper positioning of the stent.

How do we do it?

Sebastian Gagne has been credited as first describing this technique and several variations have been made since.4 At Wills, we perform ab-externo implantation under topical anesthesia. My preference is to place a corneal traction suture to aid in exposure and counter traction throughout the case. Here's how I go about it.

Prior to beginning the case, the injector is prepared and the blue slider is advanced to confirm the presence of the implant. Once the implant is visualized, a marking pen is used to highlight the tip of the XEN45 and the conjunctiva is entered at least 7 mm posterior to the limbus. The injector needle is carefully progressed anteriorly through the subconjunctival space taking care to avoid blood vessels to prevent subconjunctival bleeding. The needle enters the sclera approximately 2 mm posterior to the limbus and is tunneled into the anterior chamber. The needle is securely anchored in the sclera, at which point a mirrored gonio lens may be used to confirm proper needle entry. The blue slider is advanced until the previously marked stent tip is visualized in the anterior chamber.

As the injector was designed specifically for ab-interno delivery, the stent will tend to implant longer in the anterior chamber. To avoid this, a blunt tipped forcep may be used to gently grab the implant through the conjunctiva to adjust stent position. An alternative option is to partially deploy the stent until the tip reaches the desired length and then manually retract the needle from the scleral tunnel. Mitomycin-C is injected following stent placement with care being taken to direct the wheel away from the limbus to prevent reflux of antimetabolite into the eye.

Prior to concluding the case, the final stent placement should be assessed as it could significantly impact outcomes. A posterior placed stent may become occluded by the iris or rub and liberate

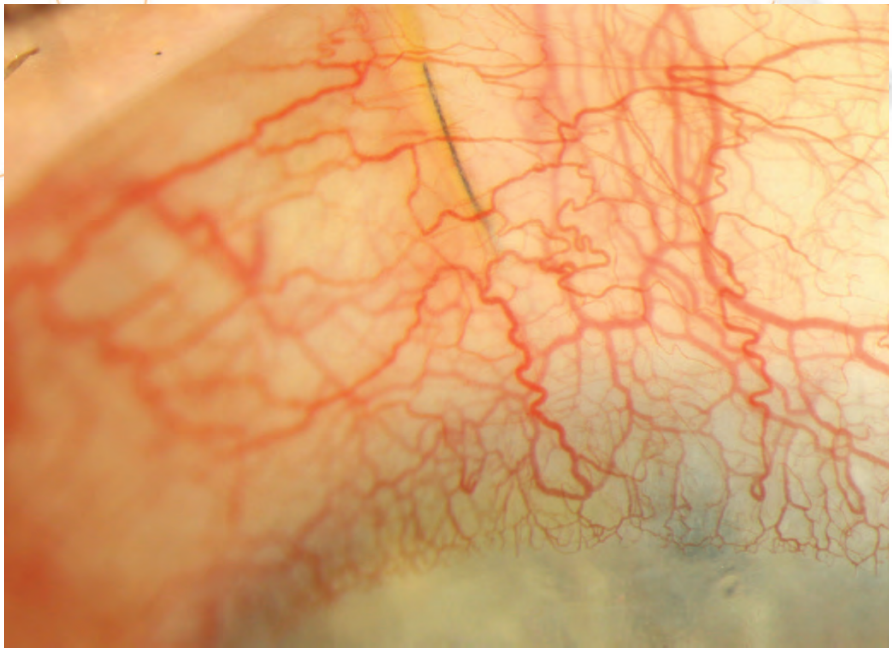

Figure 2. Image courtesy of M. Reza Razeghinejad, Wills Eye Hospital.

"If positioning is in question, the XEN45 should be retrieved (typically ab-interno) and re-implanted."

pigment granules which could occlude the internal lumen (see Figure 2). Therefore, we discourage intraoperative iris manipulation or postoperative laser as iris debris may compromise the stent. Conversely, an anteriorly placed stent carries a theoretical risk of progressive endothelial cell loss. If positioning is in question, the XEN45 should be retrieved (typically ab-interno) and re-implanted.

And the results say…

We recently reported our 12-month, single-surgeon outcomes at the 2020 American Glaucoma Society annual meeting. All surgeries were performed by Jonathan S. Myers with 38 and 23 eyes, respectively, having undergone XEN45 ab-interno and ab-externo implantation.5 Our study demonstrated that, although both approaches had a similar clinical efficacy and safety with no significant difference in IOP, number of medications, or complications, there was a significantly greater need for at least one bleb needling procedure in the ab-interno group compared with the ab-externo group (55 percent vs 13 percent, $p < 0.001$). This four-fold reduction in postoperative needling supports the claim that ab-externo implantation leads to a more ideal stent position, reducing the need for postoperative manipulation. We now look forward to expanding our analysis to include the remaining members of Wills' Glaucoma Service.

To be continued

The mastery of subconjunctival glaucoma surgery requires perfect control of both aqueous flow and postoperative fibrosis. I feel that the introduction of the XEN45 was a revolutionary step toward achieving this ideal. In the short few years since it was released, the surgical technique and postoperative management have undergone tremendous evolution, and inventive approaches are continuously being described. Ultimately, a similar leap in fibrosis control is necessary and whether it be sustained release technology or an entirely novel approach, we eagerly await the next revolution.

Daniel Lee is a member of the Glaucoma Service at Wills Eye Hospital and a clinical instructor of ophthalmology at Sidney Kimmel Medical College, Philadelphia, USA.

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Caution: Surgeons at Risk

Understanding all routes of viral spread during surgery should mitigate the risk of COVID-19 transmission from patient to doctor

By John Liu, Irfan Nizarali Kherani, Iqbal Ike K. Ahmed

The sudden cancellation of millions of elective surgeries globally as a result of the COVID-19 pandemic (1) has created a substantial backlog of cataract procedures for ophthalmologists – and plenty of hurdles to overcome before we can get anywhere close to "practice as usual."

As surgical centers begin to clear this unenviable backlog, it is more important than ever to understand and minimize all possible routes of infection during surgery. Although various infection control and personal protective equipment (PPE) measures recently recommended for ophthalmologists have shown decreased transmission rates during clinic visits (2) (3), they have not specifically taken the OR into account. Nonetheless, we must make sure we're protected.

We are exposed

Increased COVID-19 transmission is related to extended exposure time; although the exact infectious dose remains unclear, it has been estimated that infection could be possible after roughly five minutes speaking with an infected person (4). Ophthalmologists spend prolonged periods of time in close proximity to a patient's mucosal membranes when performing surgery, so it stands to reason that this could increase the risk of contracting COVID-19.

Movement in, out, and around the OR can also be problematic. Have you ever felt the need to apply caution when unfolding PPE, such as a surgical gown or drape? Research reveals that, even when appropriate PPE is used to standard protocols, the unfolding process could generate a large number of potentially infectious airborne particles (5). OR staff turnover is also considered risky; surgical site infection rates have been shown to decrease in hospitals with lower turnover (5). Ophthalmology is a surgical specialty with a very high case turnover rate, resulting in increased foot traffic and drape or gown movement throughout the day – and an even greater risk of viral transmission.

Finally, it's possible that ophthalmologists will work even longer hours in a bid to clear the strenuous, pandemic-induced backlogs of cataract surgeries. Health authorities may even increase the volume of surgeries conducted, for instance by allowing OR time during weekends. So, it's essential for us to examine all possible infection risks in the OR and make every effort to mitigate them.

Condensation capped

At the time of writing, TLC Laser Eye Centers in Oakville, Ontario, had performed over 80 routine phacoemulsification and intraocular lens (IOL) implantation surgeries since a return from the COVID-19 hiatus.

During surgery, we observed condensation appearing on the IOL when it was placed 1 cm above the patient's eye just prior to insertion, in sync with the patient's breathing (Figure 1). After seeing the same scenario play out in many cases, we realized that the condensation was an indicator of air leakage from underneath the surgical drape seal around the patient's eye, so we began to test the integrity of the seal.

Why was it important to do that? Leakage of a patient's breath could increase the infection risk of COVID-19 from patient to ophthalmologist, especially if that patient were to sneeze or cough, as demonstrated in a simulated ophthalmology OR setting (6).

How did we mitigate that risk? We began to

tape patients' face masks along the top brim onto the midface prior to surgery (Figure 2). In so doing, we noted a significant reduction in condensation appearing on the IOL. This small, but important change has now become a standard practice at TLC Laser Eye Centers.

A simple solution

Although it is unclear whether containing air leakage from under a drape prevents any significant harm, we must protect ourselves from any factors that could potentially increase our risk of infection. Our use of IOL condensation as a marker of ophthalmic drape integrity and therefore infection transmission risk is quick, convenient, and comes at no cost. We encourage any ophthalmologist who performs IOL insertion surgery to assess the integrity of the drape seal using this technique, even if infection risk appears low. A simple adjustment to a patient's face mask, or to your own PPE, could prevent infection.

From our experience, we suggest taping facemasks onto the patient's midface prior to all ophthalmic surgeries as a solution to reduce air leakage; however, individual ophthalmologists may find other PPE enhancements that work more effectively or are better suited to their setting.

Our finding also highlights the importance of carefully and intentionally applying a complete seal when draping around the eye. To ensure a complete

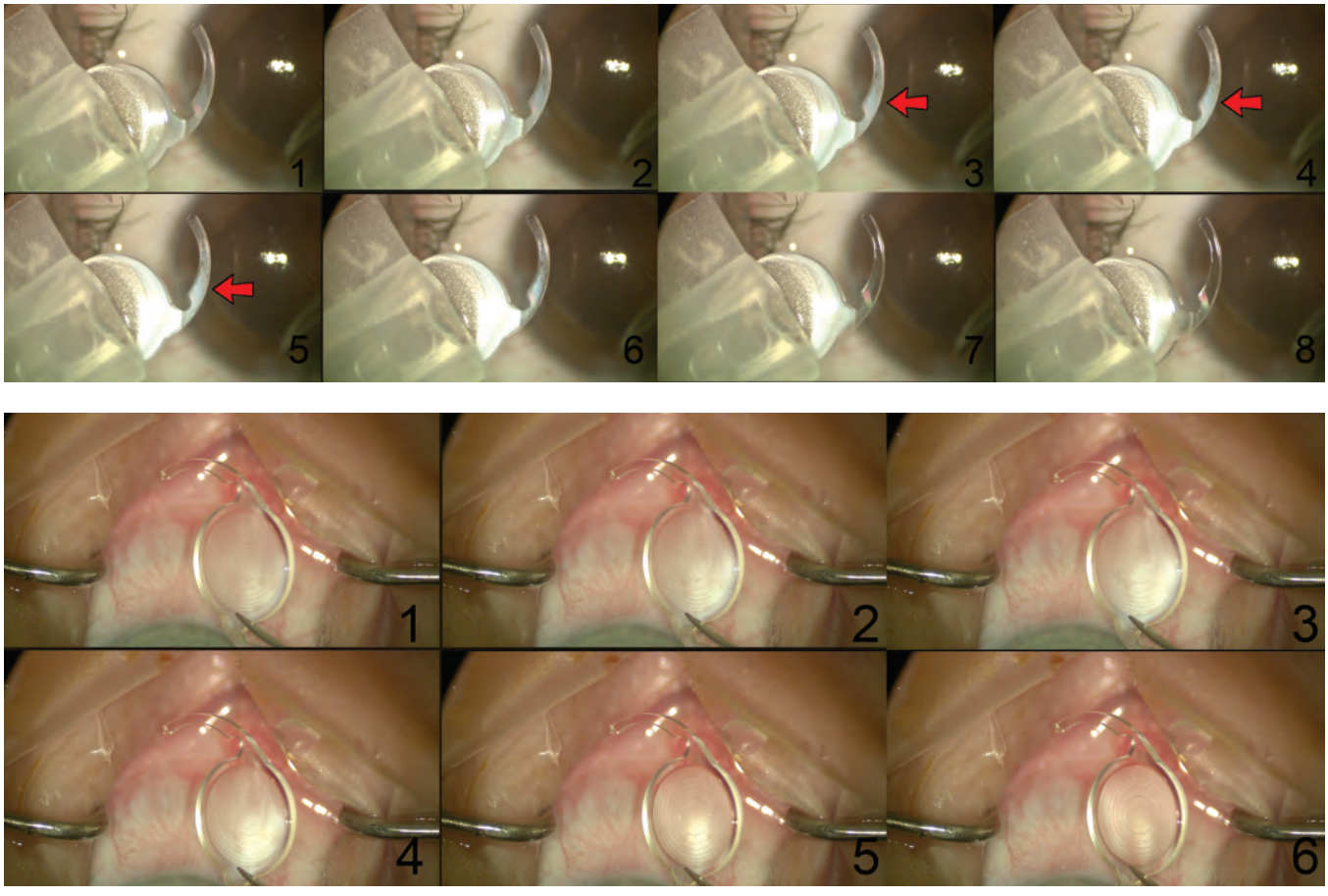

Figure 1. Video frames demonstrating condensation on an intraocular lens, noted particularly in frames 3–5 along the haptic.

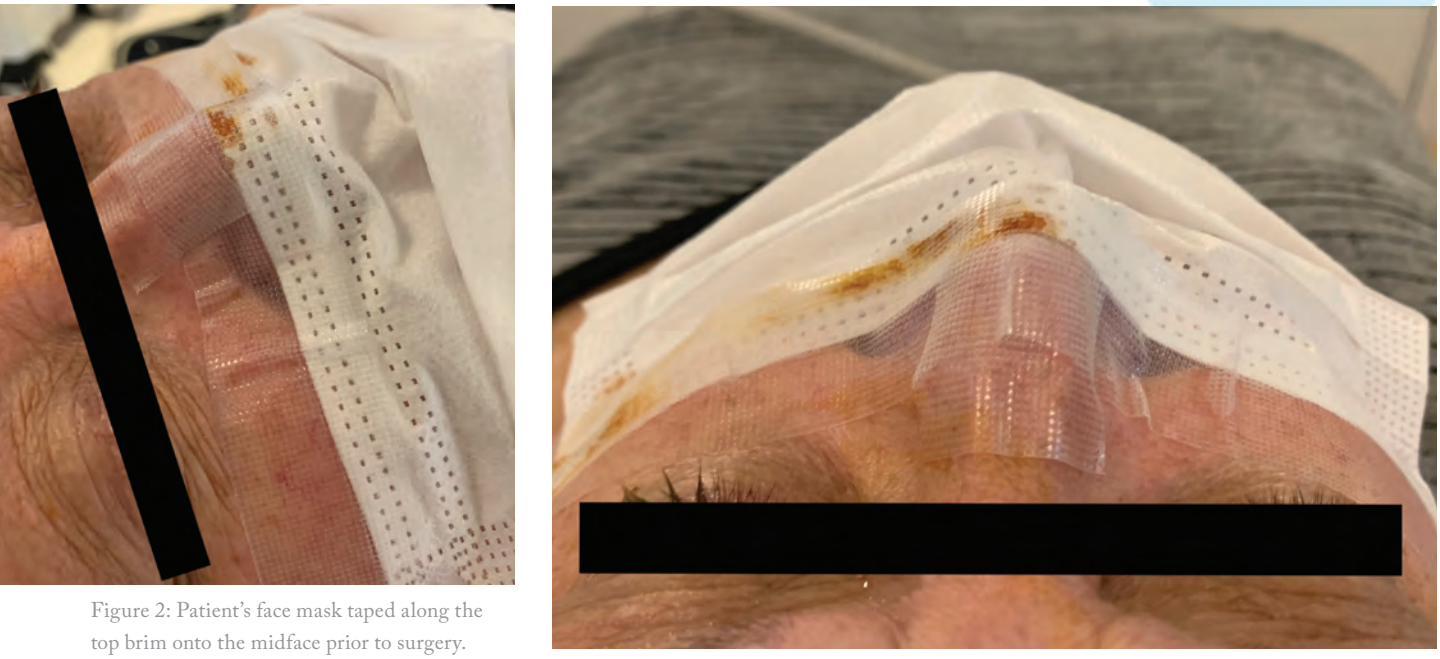

Figure 2: Patient's face mask taped along the top brim onto the midface prior to surgery.

seal, we recommend taking the following steps: i) dry the patient's skin around the eye thoroughly from any antiseptic preparation solution; ii) press firmly down on the patient's eye for a longer duration when applying the adhesive; and iii) hold one hand down on the drape adhesive attached to the eye while using the other hand to toss the remaining portion of the drape toward the patient's waist. Evidence has shown that a complete seal with adhesive tape around the surgical field, along with a taped facemask, can prevent the spread of respiratory droplets in cough simulation (6), so it is especially important to ensure the seal's integrity.

We think it is vital to consider implementing these very simple steps during any IOL insertion surgery for the foreseeable future, in particular while the risk of contracting COVID-19 still exists.

Let's not rest on laurels

With a backlog of elective surgeries, ophthalmologists may face increased pressure to complete more surgeries fast. But, considering the worldwide health and economic impacts of COVID-19, it is prudent to identify and aggressively adhere to safety precautions. Here, we have suggested a method to improve infection control measures in the OR, but concerns for future waves of infection persist. The need for vigilance in the OR is not just a personal, but also a public safety concern – so we encourage further investigation into infection control and safety measures.

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Go to top.txp.to/surgeons-at-risk to find the full list of disclosures.

Longer-Lasting Benefits

Are sustained-release drugs the answer to ophthalmology's topical drop problem?

By Alice T. Epitropoulos

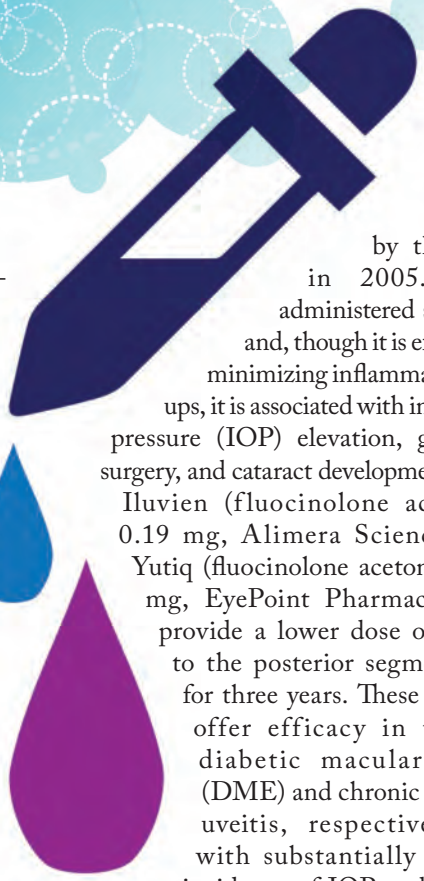
Ocular drugs are only as good as their delivery. The ideal delivery system is designed to enhance bioavailability, permeate ocular barriers, and provide controlled and sustained drug release – where the therapeutic is needed. Strides have been made in achieving these goals in both the anterior and posterior segments in recent years, and additional advances are being achieved with each new approval. Topical drops remain widely used, but these standard treatments can be challenging for many of our patients. Adherence to topical drop regimens, either for chronic treatment or in the postoperative setting, is known to be poor. Some of our patients have a real fear of putting drops in their eyes, while others may have physical limitations, such as poor dexterity or a tremor, that makes it difficult to properly instill the drops, particularly for post-surgical patients who may have limited experience with their use.

Indeed, a study by Jella An and colleagues demonstrated that more than 90 percent of post-cataract patients administer their eye drops incorrectly (1). Intraocular injections, on the other hand, are invasive, carry a risk of infection, and often require that patients return faithfully to the retina specialist's office, month after month (2). In addition to adherence issues associated with complex eye drop regimens, there are important cost concerns that can be mitigated by reduced dependence on drops. As the cost of drops continues to increase (driven by higher co-pays and increasingly limited formularies), we often take this into consideration when we prescribe them. Sometimes the decision is taken out of the physician's hands; for example, when branded drops are substituted with generics at the pharmacy.

Inherent treatment challenges

Suboptimal drug bioavailability with topical drops further reinforces adherence and cost issues and results from multiple barriers to drug entry, including nasolacrimal drainage, epithelial transport barriers, and clearance from the vasculature in the conjunctiva. Estimates suggest that less than 5 percent of a topical ophthalmic drug reaches target tissues (3). The challenge when it comes to treating disease, whether at the front or the back of the eye, is achieving effective drug concentrations for prolonged periods of time while minimizing side effects (and overcoming adherence challenges).

Developments in the treatment of retinal disease have ushered in implantable pharmacotherapies that allow controlled release of the drug to specific targets in the eye. And we continue to see interesting research and development into sustained-release intraocular alternatives to traditional topical and systemic ocular therapies. Sustained-release delivery platforms have grown in popularity throughout medicine and are well suited in ophthalmology – particularly for chronic diseases. Whether the regimen includes topical drops or injections, the need for consistent dosing day after day, month after month, can take a significant toll. Sustained-release medications can help ease the burden on both patients and physicians.



Platforms and products

An early entrant into the sustained-release ophthalmic drug category is Lacrisert (hydroxypropyl cellulose insert, Bausch + Lomb), a once-daily self-administered lubricating insert for patients with dry eye disease (DED). Though it does not directly address the inflammatory aspect of DED, Lacrisert can be especially helpful to patients who are using artificial tears multiple times a day. It is indicated for moderate-to-severe DED and, because it is preservative free, it can work well in contact lens wearers (4). Once inserted, the implant softens and slowly dissolves to help stabilize the tear film. Lacrisert can be administered before bed at night, which is beneficial for patients who experience blurred vision or foreign body sensation.

Historically, the posterior segment has seen relatively more development in sustained-release implants. Retisert (fluocinolone acetonide 0.59 mg, Bausch + Lomb), a three-year intraocular implant indicated for chronic noninfectious posterior uveitis, was approved by the FDA in 2005. It is administered surgically and, though it is effective in minimizing inflammatory flare ups, it is associated with intraocular pressure (IOP) elevation, glaucoma surgery, and cataract development (5).

Iluvien (fluocinolone acetonide 0.19 mg, Alimera Sciences) and Yutiq (fluocinolone acetonide 0.18 mg, EyePoint Pharmaceuticals) provide a lower dose of steroid to the posterior segment, also for three years. These implants offer efficacy in treating diabetic macular edema (DME) and chronic posterior uveitis, respectively, but with substantially reduced incidence of IOP and cataract complications (6, 7). A shorter-duration, bioerodible intravitreal implant, Ozurdex (dexamethasone 0.7 mg, Allergan) is used to treat macular edema secondary to branch or central retinal vein occlusion (RVO), DME, and posterior uveitis (8). Iluvien, Yutiq, and Ozurdex, notably, are administered via in-office intravitreal injection.

Sustained-release approaches to the delivery of anti-VEGF agents are also of great interest; the closest to approval is perhaps the ranibizumab port delivery system (PDS; Genentech). Challenges in formulating anti-VEGF molecules for sustained delivery in a way that preserves their structure can be overcome by the PDS, which is a refillable reservoir implanted via a surgical procedure, or by nanoformulations, hydrogels, and other encapsulation techniques in development (9).

"Historically, the posterior segment has seen relatively more sustained-release implants."

Post-op pain and inflammation

More recently, the anterior segment has seen the welcome introduction of sustained-release corticosteroid options to minimize the need for patient administration of postoperative drops. Dexycu (dexamethasone intraocular suspension 9%, EyePoint Pharmaceuticals) is the first FDA-approved intraocular corticosteroid administered as a single injection to treat postoperative inflammation. Its approval was followed by Dextenza (dexamethasone ophthalmic insert 0.4 mg, Ocular Therapeutix), an intracanalicular insert indicated for the treatment of ocular inflammation and pain after ophthalmic surgery.

Dexycu is formulated using proprietary Verisome sustained-release technology – a cohesive, bioerodible liquid steroid depot that is injected into the ciliary sulcus at the end of ocular surgery, where it delivers a tapering dose of dexamethasone for about 21 days. In controlled clinical studies, Dexycu provided a significant anti-inflammatory effect (comparable to QID topical prednisolone drops) that began early and was sustained throughout the postoperative period (10, 11). The Verisome technology enables Dexycu to immediately deliver and maintain a therapeutic concentration of the steroid at the target site. The steroid is released at its highest concentration in the first two weeks, with a naturally decreasing concentration over – and after – that period. Such tapering is similar to how we traditionally use our topical steroids, but it eliminates the need for patients to understand or remember the schedule. Although the pivotal trials for Dexycu were conducted in cataract surgery, it is approved for any ocular surgery and has been used for post-op inflammation control in MIGS procedures and even vitreoretinal surgeries (12).

Dextenza is inserted into the lower

lid canaliculus at the end of ocular surgery and is currently being investigated for the treatment of allergic conjunctivitis (13). Dextenza uses a resorbable hydrogel vehicle to deliver a tapering dose of medication to the ocular surface for 30 days, as it gradually resorbs (14). The product is preservative-free and conjugated with a small amount of fluorescein that enables visualization. It also provides occlusion of the punctum, which may be helpful for patients with DED. If there is a pressure spike, the implant can be irrigated or expressed out. Ophthalmic surgeons and consultants at my practice participated in clinical trials for Dextenza and have used both Dextenza and Dexycu in practice, and found them to be safe and effective with minimal postoperative pressure spikes or breakthrough inflammation. These new drug delivery platforms are a major step forward, extending our armamentarium so that we can better tailor therapy to meet individual patients' needs.

Glaucoma paradigm shift

The most recent entrant into the sustained-release ophthalmic drug arena to receive FDA approval is Durysta (bimatoprost 10 µg implant, Allergan). This is the first intracameral, biodegradable sustained-release implant indicated to reduce IOP in patients with open-angle glaucoma (OAG) or ocular hypertension (OHT). FDA approval was based on results from two phase 3 studies of 1,122 patients with OAG or OHT that evaluated the safety and efficacy of Durysta compared to twice-daily topical timolol drops (15). Bimatoprost SR reduced IOP by 30 percent during a 12-week period, demonstrating noninferiority to timolol with a single administration. In real-world practice, it is expected that Durysta will be administered quarterly, making it a true paradigm shift in the medical treatment of glaucoma.

What's ahead?

Extraocular rings, drug-secreting contact lenses, nanoparticles, modified molecules, hydrogels, photo cross-linked biodegradable technologies, and stem cells are among the innovative vehicles that we will undoubtedly see move from the developmental pipeline into the clinic and OR. Now that cataract, retina and even glaucoma patients are benefiting from sustained-release drug technology, my hope for the not-too-distant future is for dry eye and allergy patients to access the same levels of convenience, cost savings, and precision.

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Relevant disclosures: Allergan, OTX, EyePoint, and Bausch + Lomb.

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Patient Safety Without Borders

The importance of accreditation in delivering eye care to all patients, regardless of location

By Hunter Cherwek and Noelle Whitestone

The definition of accreditation: the official recognition of someone having a particular status or being qualified to perform a particular activity.

For eye care centers around the world, accreditation demonstrates a strong commitment to excellence and continuous improvement in patient care, efficient facility operations, minimized organizational risk, disaster/security preparedness, and continuing medical education.

To Orbis, it's especially important; we deliver training, support, and care services via teams from around the world to oft-forgotten global communities where, sometimes, even the most basic healthcare is scarcely available. The "good enough" model of charitable healthcare is not, in our opinion, good enough; each patient should receive the highest level of clinical and surgical care, no matter where in the world they live.

To that end, we sought accreditation from AAAASF (American Association for Accreditation of Ambulatory Surgery Facilities), which has since proven invaluable.

Why accredit?

The Orbis Flying Eye Hospital is the world's only ophthalmic teaching hospital on board an MD-10 aircraft. We travel around the world to deliver skills and enhancement programs, training, education, and clinical resources to low- and middle-income countries through a network of volunteers that includes some of today's leading ophthalmologists, anesthesiologists, nurses, and biomedical engineers.

Why did we seek AAAASF accreditation (see "Accreditation Advantages")? In short, achieving the same standard of high-quality care for patients in our partner hospitals is a top priority and instituting accredited processes is paramount to that goal.

Closing the gaps in healthcare standards

The risks associated with not implementing proper clinical and surgical safety standards are equivalent regardless of geography – patient safety has no borders.

Today, there is significant variability among eye healthcare practices across non-accredited facilities. Utilizing a third party to benchmark, review, and supply accreditation is the best way forward to ensure adherence to evidence-based, global-standard protocols.

And, despite the diverse locations of our staff, volunteers, and partner hospitals, we have been able to deliver education and training with the help of technology. The Flying Eye Hospital has a state-of-the-art onboard operating theater as well as multichannel programs and mobile platform technology to deliver education and training and to demonstrate accreditation practices.

Mindset, modeling, monitoring

Having a third-party assessor, like AAAASF, review and accredit our clinical and surgical programs gives us the confidence that Orbis teams can replicate critical tasks when we work with our host-country partners.

When a partner enrolls in an accreditation program, we initially focus our efforts on three core areas. The first is mindset: we emphasize the value of following uniform processes and the importance of understanding how staff, equipment, and standards inform quality and patient safety. This is particularly important for care teams; when staff members adhere to the same high-quality standards for each task, it creates a consistency that breeds quality and accountability and reduces the risk to patient safety. Team training is critical in supporting the proper mindset.

"We emphasize the value of following uniform processes and the importance of understanding how staff, equipment, and standards inform quality and patient safety."

Second, role-modeling proper processes when working directly with our in-country host partners is critical for Orbis training programs. Accreditation drives consistency and focuses on quality and, importantly, standardization helps overcome assumptions and potential miscommunications among our staff and between our volunteer faculty and host-country partners.

Finally, it is important for partners to understand the value of documentation, benchmarking, and tracking. Surgical logs, instrument sterilization logs, consumable tracking, and so on, leave a trail of data that can be easily referenced in the event


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Accreditation Advantages

- *A system-wide, high-level standardization of clinically relevant operations*
- *Consistency and continuity in patient care and safety standards*
  Orbis employs staff from around the world who come from different backgrounds and medical training. While all clinical staff are licensed and well-qualified, practicing one universal system of procedures is vitally important to streamline best practices in surgical and clinical care and safety standards, and crucially, it ensures practice continuity and closes any gaps that could jeopardize patient care.
- *Standardized operational and organizational processes, documentation, and tracking*
- *Protection against potential medical malpractice lawsuits*
- *Appropriate licensing for surgeons and clinicians in low- to middle-income host countries*
- *Benchmarking*
  In its ongoing effort to assess, benchmark, and improve patient care, AAAASF developed a quality assurance program that involves both traditional peer review and online patient safety data reporting to analyze surgical outcomes for all facilities it accredits. For the Flying Eye Hospital, this requires that we regularly submit mandatory clinical and surgical process reports, including case reviews of surgeries conducted onboard the aircraft. The AAAASF data set includes millions of patient procedures dating back to 2001, and contributes to patient safety research, journal articles, and standards revisions.
- *Objectivity and independence*
- *In-person inspections and customized support*
  Orbis regularly invites surveyors from AAAASF to join our programs and work directly with Orbis staff and partners on the major areas of concern for that particular partner hospital, or ministry of health-level facility. This includes hospital walkthroughs with key personnel to review their systems and infrastructure in a non-confrontational, non-judgmental, and educational tone that yields the trust and understanding needed to implement accredited clinical and surgical standards. In many cases, adjustments needed to address gaps are no-to-low cost to implement. Sometimes it is the simplest of ideas that can greatly improve safety in a hospital setting, particularly in low- to mid-income countries.

questions arise about a particular case, or in the unfortunate event of an infection or other unanticipated outcomes. For example, robust documentation proves which instruments were used during a surgical case, how it was used, and the movement of that particular instrument before the surgery. Tracking the supply chain and documenting information on when medical consumables were received, when they expire, how they are stored, whether appropriate temperatures are maintained, and when they are used helps maintain clinical and surgical excellence and reduces patient risk. This level of detail can also help identify other patients who may have been exposed to a potential risk factor.

Emphasis on education

One major component of accreditation focuses on the ongoing training of staff and we're now working closely with AAAASF on the next phase of our e-Learning offering; Cybersight (www.cybersight.org) – Orbis' proprietary online educational portal (1).

Accreditation focuses on job-specific training, equipment use, and emergency preparedness roles, which ensures that a facility's staff is equipped not only to treat but also to respond to an emergency and to perform their other operational functions, such as instrument processing. Given the vast geographies that we support and the diverse locations of our partner facilities, creating on-demand materials that can be accessed by the staff of a partner hospital is vitally important for us. This is the next step for us: creating lectures, forms, and standardized checklists, which will all form part of the distance learning curriculum that Orbis aims to introduce with AAAASF in the future.

How important is it?

Not everyone is convinced of the value of accreditation, though. Is it important that the same processes and procedures are in place all over the world to protect patients? Would a universal system of standards benefit eye healthcare if all facilities used the same processes? In our opinion, absolutely! The result would be streamlined, high-level protocols and

practices focused not only on individual patients but also on community care. We must encourage a continuous pursuit of clinical and surgical safety to ensure the highest possible standard of care. Most importantly, safety has to be reproducible and facility data should be collected, analyzed, and studied to ensure quality. This can only be done if we follow standardized protocols.

Overcoming country hurdles…

We are not naïve; we fully understand that conformity with accreditation protocols takes buy-in, time, money, and resources, some of which are in scarce supply for our partner hospitals. And there is the political landscape to navigate in host countries, too, such as lack of government or institutional mandates on a country's healthcare system, a challenging national infrastructure, and the idea that instituting these practices will not offer an immediate return on investment when facilities are already considering budget-cutting measures.

In some parts of the world, difficult fiduciary decisions must be made to meet the demand of current health situations. Furthermore, accreditation requires institutions to review their processes with a critical eye. Annual chart reviews, surveys, and documented training programs may strain the demand for human resources. Unfortunately, this is a level of commitment that many

"Would a universal system of standards benefit eye healthcare if all facilities used the same processes? In our opinion, absolutely!"

eye health centers are simply unable or unwilling to make. However, interim advances can still be made, and all Orbis partners institute long-term action plans to integrate a high-level standard of practice mandated by accreditation.

…one step at a time

Setting goals and long-term planning in cooperation with our country partners is key, and taking a step-by-step approach is often the best way to achieve this, especially when faced with country-specific barriers. This is why it is important, even if the institution is not yet seeking formal accreditation, to begin implementing accreditation-defined processes immediately.

We understand that many of our partners do not have the resources to achieve (or potentially afford) a formal accreditation, which is one reason that Orbis' programs are so impactful. We do not overwhelm our partners with an entire accreditation structure (or process) at one time. We introduce the most critical and practical components that can be reasonably adopted. In time, we can build upon previously met goals, creating a lifelong pathway of continuing medical education, quality assurance, and safety that supports evolving systems of clinical excellence.

Hunter Cherwek is the Vice President of Clinical Services for Orbis International. He oversees the organization's flagship Flying Eye Hospital and the Cybersight telemedicine initiative.

Noelle Whitestone is a Project Consultant for Orbis International. Noelle led the successful launch of the third generation Flying Eye Hospital – an MD-10 aircraft.

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The Forgotten Crisis

For those living in Zaatari, the largest Syrian refugee camp in Jordan, the privilege of eye care is far from guaranteed. Meet the volunteer program hoping to change that.

By Natalie Weil

The Syrian civil war officially began on March 15, 2011. Since then, hundreds of thousands of people have been killed in the brutal conflict and more have fled to neighboring countries. Now in its 10th year, the Syrian refugee crisis is the largest displacement of the modern age. Around 5.6 million Syrians are refugees, and another 6.2 million are displaced within Syria. At least half of those affected are children (1).

Today, Syrian refugees account for over 10 percent of Jordan's population, placing immense pressure on the country's already overstretched medical system during one of the most difficult economic periods in its history. Although most refugees live in host communities, others find themselves in Zaatari, the world's largest Syrian refugee camp outside of Syria. Zaatari opened in 2012 less than 10 miles from the Syrian border and has since become Jordan's fourth-largest city (albeit unofficial).

With few ophthalmologists on site, refugees rely on medical interventions provided by NGOs and volunteers, like myself, for eyecare. In 2017, anterior segment and cornea specialist, Soroosh Behshad, my colleague and cataract surgeon at the Emory Eye Center, took part in a surgical mission with the Syrian American Medical Society with the goal to treat as many people as possible. He worked his way through the adult population – but noticed a large number of children with eye problems and no one to treat them. When he returned, he asked if I would be interested in helping. Six months later, I found myself in Zaatari.

Life in the camp

Our work was split with two different focuses: screening children and surgical intervention. Upon arriving to Zaatari on my first trip, I did not know what to expect. So, my personal goal was to screen as many children (from birth to 18) as possible over a seven-day period. I knew I would need the help of technology

COVID-19 in the camp

Over the last few months, life has changed a lot for all of us, and especially for refugees. The COVID-19 pandemic has resulted in regulations preventing doctors from traveling, and limiting access to the refugee camp.

Jordan has handled the pandemic very well and had very few cases. Within the country there were very strict lockdown guidelines forbidding residents to leave their home, even for essentials, during a period of time. Children began homeschooling, and for those living in the refugee camp this was through television programming, but the camp only has a limited supply of electricity per day. According to the United Nations High Commissioner for Refugees, the residents of Zaatari were under lockdown, not allowed to leave their shelters within the camp during the height of the pandemic. Shops were closed and people were instructed to shelter in place, except for emergencies. There have been a few reported cases of COVID-19 among refugees outside the camp.

There is much concern for preventive medicine during this time and, unfortunately, this is the first time in four years we've missed a trip to see our patients in Zaatari. I look forward to the lifting of regulations and getting back to helping refugee children through building a vision screening program for the children of Zaatari.

"Surgery presented its own challenges because many of the patients were not allowed to leave the camp without permission from the government, so it required a formal paperwork process to allow a patients a day's leave and access to the hospital with an operating room."

in order to be efficient. With the help of trained volunteers, we combined two technologies, Plus Optics and Gocheck Kids (photo screeners that help identify risk factors for amblyopia) and PEEK (a free app designed by the London School of Hygiene and Tropical Medicine that combines smartphone-based vision tests, eye health service analytics, and RAAB eye health surveys). I worked alongside Soroosh Behshad and retina specialist Aref Rifai from the Retina Center of Pensacola in Florida, US, who provided injections and photocoagulation for untreated diabetic patients. Over the course of the week, we gave out hundreds of pairs of glasses and identified countless candidates for surgery. Surgery presented its own challenges because many of the patients were not allowed to leave the camp without permission from the government, so it required a formal paperwork process to allow a patients a day's leave and access to the hospital with an operating room. Some of our patients had not been outside the camp in seven years; others had only ever lived within its walls.

In addition, we worked with local medical students and residents to provide education and exposure to ophthalmology. In the past, we tried to find Jordanian ophthalmologists willing to perform the surgeries for free, but this was difficult as Jordan's medical system was already under extreme stress. For a time, the government offered discounted surgeries to refugees, but this did not last long. Currently, most surgeries are paid for by the patient. By offering our services to the local population as well as to refugees, we increased access to care for poor Jordanians – and earned the government's favor. Today, around 30 percent of our patients are Jordanian.

Ophthalmology in Jordan

We are working to create stronger relationships with the Jordanian Ophthalmology Society and various NGOs who also work in Jordan. Although Jordanians generally have a very advanced medical system, there is a shortage of subspecialists. For example, Amman, the capital, has eight glaucoma specialists for a population of more than four million. The dearth of subspecialists is partly because ophthalmologists in Jordan are required to travel for fellowships, often to Europe or the USA. Our goal is to help eliminate the need for travel, and provide local physicians with the face-to-face subspecialty training by bringing experts in the field to Amman. There are many volunteers interested in training Jordanian ophthalmologists in subspecialty care, so we hope to bring this idea to fruition soon. We hope it will not only help the refugee population, but local Jordanians as well.

Our ultimate goal is to create a permanent, self-sufficient clinic in the camp that can continue screenings by the local Zaatari camp residents. Since January 2018, we have created partnerships with various organizations, including the incredible Two Billion Eyes – an organization that brings all the equipment needed to build an optical lab and provides training to grind lenses and make glasses. Only by creating sustainable programs that can function for as long as they are needed can we have long-term change. Orbis has also been a big help in the search for funding. We have a guaranteed amount for the next two years – but, because it does not cover the number of surgical interventions the camp needs, we are applying for funding from a number of other sources.

Boots on the ground

When we travel to the Zaatari camp, we partner with the Arab Medical Relief Clinic, one of the few spaces within the camp that has ophthalmology

equipment. We are also joined by a local ophthalmologist Ala' Shalabi who visits Zaatari for half a day every two weeks to deliver eye care to many refugees. Aside from NGOs that come and go, he is the sole provider of eye care in the camp – and he works for free.

Numbers fluctuate, but there are roughly 79,000 people living in Zaatari (2). To properly serve a population of that size, we need a team of dedicated ophthalmologists, each offering subspecialty care: glaucoma, retina, oculoplastics, and pediatrics. However, that's not feasible at this point. A more realistic goal is to have a single ophthalmologist and a few vision screeners on site every week. Behshad, Rifai and I have been trying to create a system whereby subspecialists provide surgeries to anyone who needs them via NGOs. At this stage, it is more achievable to arrange surgical trips with a volunteer every two months (followed by postoperative follow-up care) than to outsource our care – but we are getting closer to achieving our goal. Every six months, we meet with our partners on the ground, and we are finally close to hiring a full-time program coordinator and a physician, which is promising.

Prevention is better than cure

Like most volunteers, I have a full-time job in addition to my work at Zaatari. We have all dedicated a significant amount of our personal time to building this program, but it is a slow process. We haven't received any substantial equipment donations for the clinic – so far, the only items we received from industry partners are lenses – so we rely heavily on grants. Fortunately, the medical community's interest in refugees has increased over the last few years. As a collective, we are realizing how problematic it is that large swathes of the population have no access to medical care. Our focus is beginning to shift from acute care to preventative care. Prevention is especially important for children as their vision is in a fundamental developmental stage. A child with severe refractive error, who never receives glasses, can become legally blind for the rest of their life – but, if we intervene at a young age, they can have a normal, productive life.

We recently performed an IRB-approved vision screening study looking at 100 patients within Zaatari camp and found very high failure rates in comparison to the general population. A lot of groups work exclusively with adult cataracts, but we have identified a real need in children, too. Bringing attention to the pediatric population is a key part of our work. We are working to create a vision screening program, run by ophthalmologists, at the approximately 25 schools within the camp. We hope to create a model that we can apply to other populations in crises around the world.

The right place, the right time

People ask me why I chose this cause. I have always been interested in global ophthalmology and I'm fortunate to work at Emory Eye Center, which has one of the few training programs in the USA with a dedicated global ophthalmology initiative. The program director in 2015 was Danny Haddad, now a director at Orbis. Danny acted as my mentor, showing me how I could help on a global level. It was around this time that I became more aware of the refugee crisis. I remember sitting on my sofa, watching the news, knowing I had everything and these people had nothing. I thought, "What can I do to make an impact?" When Soroosh Behshad asked me to help, it honestly felt like my calling.

I only truly understood the scale of the problem once I got involved. Each trip, I made a list of everyone who needed surgery next time. I told them, "I will see you in six months," and I stayed true to my word. I have been treating patients for years at six-month intervals despite living halfway around the world, and I look forward to treating them for many years to come.

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References

1. *World Vision, "Syrian refugee crisis: Facts, FAQs, and how to help" (2020). Available at: https://bit.ly/31ThXYN.*
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The Eyes of Youth

Sitting Down With… Lisa Park,
Associate Professor of Ophthalmology, Columbia College of Physicians & Surgeons, New York, USA

Why ophthalmology?

As a medical student at Yale, I was required to submit a research paper ahead of my graduation, so the summer after my first year I started looking for an interesting project. I saw a flyer from the ophthalmology department and visited its lab, where I met a group of enthusiastic people who clearly enjoyed what they were doing. It looked like so much fun that I decided that was what I wanted to do.

My second choice was pediatric cardiology – the fellows at Yale were awe-inspiring giants who were saving the lives of tiny babies. However, I realized that I'd have to complete a pediatrics residency, so I chose ophthalmology instead. Nevertheless, I completed a transitional internship, spending a month on a pediatric ward. I remember the chairman bursting into our morning conference one day, asking who had done a lumbar puncture on a newborn the day before. Apparently, no other resident had ever obtained a sample containing no red blood cells, so I suppose I could have also been successful in that field!

Who did you look up to during your training?

I first trained at the Manhattan Eye, Ear & Throat Hospital (MEETH) and was a part of the last group of residents to enter those historic halls as a MEETH resident. My mentors included Jack Dodick, Larry Yannuzzi, Renee Richards, Norman Medow, Richard Lisman, Albert Hornblass, and the inimitable Abe Schlossman. I also spent a little time with Charlie Kelman and heard him give Grand Rounds more than once about his incredible journey and the invention of phacoemulsification. I was very honored to be sitting with his closest friends when he received the American Academy of Ophthalmology's first lifetime achievement award. To see thousands of ophthalmologists rise as one body to acknowledge his contribution to our field was a truly unforgettable experience.

What's the biggest change you've seen in your subspecialty?

I didn't truly appreciate it at the time, but I began my training in 1998, which was the time period just after phacoemulsification became widely adopted by most surgeons as the standard of care for cataracts. My surgical training was on the Bausch + Lomb Millennium, and we talked a lot about the Venturi versus peristaltic pump systems. Since that time, we have seen many technological advances with more efficient machines and advanced fluidics, which have made surgery much safer and easier – even for the novice surgeon.

I have noticed this progress most in my surgical teaching. When we first started using torsional phaco, a resident called me about a case I had just supervised, and reported that on post-op day one the cornea was clear. I scoffed and went to examine the patient myself; despite the long phaco time, it was as he described! And that's when I knew that the new generation of machines was making a big difference.

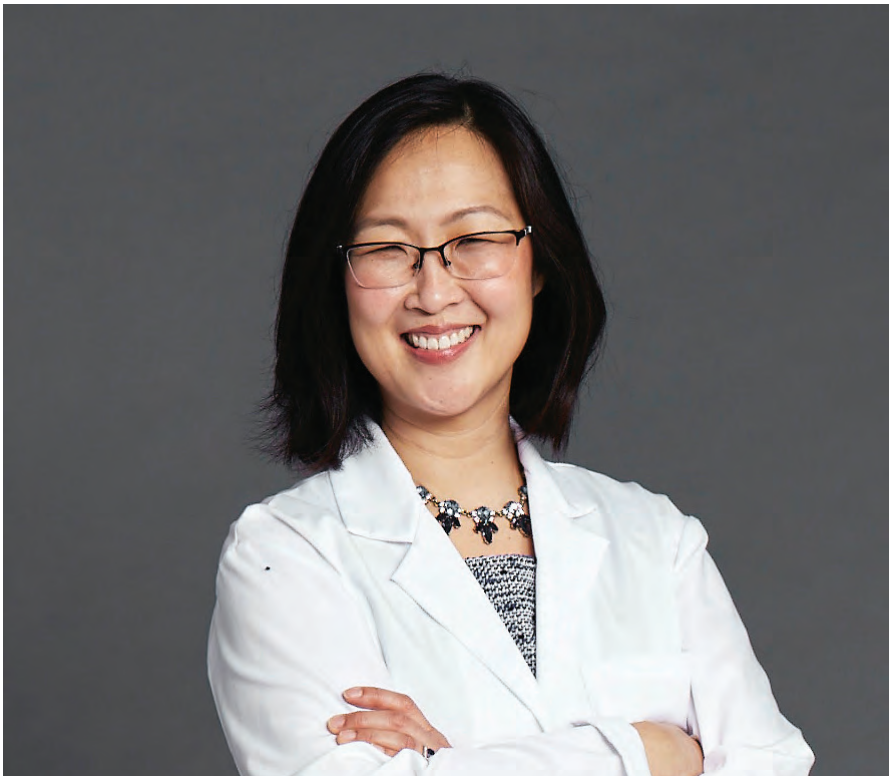
What's your proudest achievement?

I spent nearly a dozen years as the Chief of Ophthalmology at Bellevue Hospital, the flagship city hospital in New York City. In this type of setting it is a constant battle for limited resources, and I'd often sit at a table surrounded by chiefs from every other surgical subspecialty – such as orthopedics, neurosurgery, and urology – and they would brush aside our department as being non-essential. I thought: "Hopefully, I will never need their expertise in the future but, as a cataract surgeon, I am sure every single one of them will end up needing mine!" Over the course of my tenure, I managed to convince my colleagues and the hospital administration that sight is an essential aspect of health. We were allocated a marked increase in resources and raised the standard of care to a high level. I am very proud of that achievement.

"I believe that the impact of poor vision has been greatly underappreciated in our own neighborhoods."

Please tell us about your humanitarian work...

My main humanitarian activities are with the international NGO, Vision Care USA. I have been traveling and performing surgery in east Africa, mostly Ethiopia, since 2013. Through happenstance there are a number of organizations focused on the same region, each with their own area of expertise – the ASCRS Sinskey Eye Institute, the Himalayan Cataract Project, ORBIS/Cybersight, and Sightsavers, among others. All of us share the objective of supporting the development of sustainable eye care systems in this part of the developing world. Vision Care's niche is the ability to set up and perform portable phaco surgery in addition to MSICS in any part of the world with electricity and clean water. In Ethiopia, we have a partnership with a city hospital in Addis Ababa, and we have been running a Phacoemulsification Training Course (PTC) in collaboration with the Ophthalmological Society of Ethiopia for the last 10 years. I am proud that we have now trained 20 percent of the country's eye surgeons in modern surgery techniques.



"The use of artificial intelligence to more efficiently triage our patients is an area of untapped potential."

Perhaps even more importantly, we have been able to work collaboratively with many global humanitarian groups, and we've seen a synergy and a rise in the fundamental approach to eye care. Global healthcare – and dollars spent on it – usually focus on other needs, such as infectious diseases or maternal and fetal health, but I believe that putting the spotlight on curing world blindness has an exponential impact on global health.

What long-term eye care goals have you been focusing on?

As a faculty member at Columbia University Medical Center, I am serving on a task force to address social determinants of health and the impact of structural racism. The disparity in the delivery of healthcare in the USA needs to be addressed. I believe that the impact of poor vision has been greatly underappreciated in our own neighborhoods. As our population continues to age, ophthalmology will gain an even greater importance in overall healthcare.

What is your ultimate dream for the field?

As a refractive cataract surgeon, curing presbyopia is the holy grail. Though we already have many good tools at our disposal, none of them truly simulates accommodation. There are a few exciting innovations in the pipeline, but my ultimate dream would be a fundamentally radical approach able to reproduce or maintain the eyes of youth.

What advice do you share with your students?

I always begin the academic year by saying: "Remember that what you learn from me now is the cutting edge in terms of surgical technique today, but it is not how you will practice in 20 years. The most important thing is to understand and master the fundamentals – know what the eye is capable of and understand what our current limitations are, so that you will pursue, recognize and adopt future innovations that are worthwhile." The other piece of advice I give is that, no matter how advanced the technology is, it is not useful if you do not hear and understand a patient's vision needs and expectations. Listen carefully, and tailor your approach to the individual.

How has the pandemic affected your activities?

We've all had to make the shift to telemedicine in the last few months, and I believe this could be a gamechanger for ophthalmology. Even though our department has resumed "normal" clinical activities, I am continuing to work on innovative ways to integrate telemedicine into our clinical practice. One example is asynchronous telemedicine, which has great potential to maximize efficiency in reaching our patients. The use of artificial intelligence to more efficiently triage our patients is also an area of untapped potential; I dream it will, one day, be integrated into our clinical practice.

Because Vision Care's teams are unable to travel overseas, we are busy converting our Phaco Training Course to a virtual platform. Fortunately, the local doctors we have already trained in Ethiopia will serve as our hands-on trainers, with our remote supervision. We look forward to this innovation in surgical teaching and eagerly await the day we can visit again.

XIIDRA® (lifitegrast ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 2016

BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

4 CONTRAINDICATIONS

Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation *[see Adverse Reactions (6.2)]*.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Hypersensitivity *[see Contraindications (4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In five clinical trials of DED conducted with lifitegrast ophthalmic solution, 1401 patients received at least one dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had less than or equal to 3 months of treatment exposure. One hundred-seventy patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5%-25% of patients were instillation-site irritation, dysgeusia, and reduced visual acuity.

Other adverse reactions reported in 1%-5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus, and sinusitis.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Xiidra. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Rare serious cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, urticaria, allergic conjunctivitis, dyspnea, angioedema, and allergic dermatitis have been reported. Eye swelling and rash have also been reported *[see Contraindications (4)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Xiidra use in pregnant women to inform any drug-associated risks. Intravenous (IV) administration of lifitegrast to pregnant rats, from premating through gestation day 17, did not produce teratogenicity at clinically relevant systemic exposures. Intravenous administration of lifitegrast to pregnant rabbits during organogenesis produced an increased incidence of omphalocele at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD], based on the area under the curve [AUC] level). Since human systemic exposure to lifitegrast following ocular administration of Xiidra at the RHOD is low, the applicability of animal findings to the risk of Xiidra use in humans during pregnancy is unclear *[see Clinical Pharmacology (12.3) in the full prescribing information]*.

Data

Animal Data

Lifitegrast administered daily by IV injection to rats, from premating through gestation day 17, caused an increase in mean pre-implantation loss and an increased incidence of several minor skeletal anomalies at 30 mg/kg/day, representing 5,400-fold the human plasma exposure at the RHOD of Xiidra, based on AUC. No teratogenicity was observed in the rat at 10 mg/kg/day (460-fold the human plasma exposure at the RHOD, based on AUC). In the rabbit, an increased incidence of omphalocele was observed at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the RHOD, based on AUC), when administered by IV injection daily from gestation days 7 through 19. A fetal no observed adverse effect level (NOAEL) was not identified in the rabbit.

8.2 Lactation

Risk Summary

There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocular administration is low *[see Clinical Pharmacology (12.3) in the full prescribing information]*. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

8.4 Pediatric Use

Safety and efficacy in pediatric patients below the age of 17 years have not been established.

8.5 Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.

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*In some patients with continued daily use. One drop in each eye, twice daily (approximately 12 hours apart).[3]

†Xiidra is an LFA-1 antagonist for the treatment of dry eye disease. **Pivotal trial data:** The safety and efficacy of Xiidra were assessed in four 12-week, randomized, multicenter, double-masked, vehicle-controlled studies (N=2133). Patients were dosed twice daily. **Use of artificial tears was not allowed during the studies.** The study endpoints included assessment of signs (based on Inferior fluorescein Corneal Staining Score [ICSS] on a scale of 0 to 4) and symptoms (based on patient-reported Eye Dryness Score [EDS] on a visual analogue scale of 0 to 100).[3]

A larger reduction in EDS favoring Xiidra was observed in all studies at day 42 and day 84. Xiidra reduced symptoms of eye dryness at 2 weeks (based on EDS) compared to vehicle in 2 out of 4 clinical trials. Effects on signs of dry eye disease: ICSS (on a scale from 0-4; 0=no staining; 4=coalescent) was recorded at each study visit. At day 84, a larger reduction in inferior corneal staining favoring Xiidra was observed in 3 of the 4 studies.[3]

Indication

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of signs and symptoms of dry eye disease (DED).

Important Safety Information

- Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients.
- In clinical trials, the most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.
- To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.
- Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.
- Safety and efficacy in pediatric patients below the age of 17 years have not been established.

For additional safety information about XIIDRA®, please refer to the brief summary of Full Prescribing Information on adjacent page.

References: 1. US Food and Drug Administration. Code of Federal Regulations, Title 21, Volume 5 (21CFR349). Accessed April 17, 2020. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=349&showFR=1 **2.** Jones L, Downie LE, Korb D, et al. TFOS DEWS II Management and Therapy Report. *Ocul Surf.* 2017;15(3):575-628. **3.** Xiidra [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp; June 2020.

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