

## **Ocular Surface Insight**

Issue 11

The Therapeutic Contact Lens in Ophthalmology A woman surgeon in the time of COVID

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Linkler, IRA, Fittas, TR, Wilson, DA et al. (Robet prevence of trypps and high myops and temporal trends from 2000 through 2050. Ophthamology, 20%; 12:E1036–42; Available From det OOI: 10:00%/lopititie.20%:01006



# Ocular Surface Insight



"It is health that is the real wealth, and not pieces of gold and silver."

Mahatma Gandhi

### Welcome to the spring 2021 issue of **OSI**.

Welcome to the OSI Magazine!

In this issue of the OSI magazine we examine ocular surface symptoms and treatments from a number of different angles.

We have the second instalment of the 'The top five tools I cannot live without when diagnosing Ocular Surface Disease' article. In this edition Brian Tompkins and Dr Keyur Patel examine the slit lamp and digital add-ons to get the best image views of the ocular surface.

We have a second article from Seema Nanda with her insights from across the pond in the USA. She focuses her article on Neurotrophic Keratitis.

Nancy Al Raqqad gives a very personal account of living and working in Jordan as an ophthalmologist through Covid-19 times, and its impact on day-to-day life.

The section on 'The diary of a cornea that didn't like plastic' discusses a particular case of Keratoconus over an 18-month period. There are many other articles with comprehensive and informed perspectives for you to enjoy.

I am pleased to announce that the OSI team have launched our first Middle East edition, and we are excited to grow our readership in that region.

Finally, the whole editorial board of OSI are really keen to invite trainees to submit case studies for publication, we would like to feature at least one in every issue.

Please get in touch via our website or email address.

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Samer Hamada

Samer Hamada, MD, MSc, DO (hons), FRCSEd, FRCOphth

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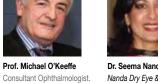
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## What's in the news?

## Evaluation of the effect of topical tacrolimus 0.03% versus cyclosporine 0.05% in the treatment of dry eye secondary to Sjogren syndrome

The purpose of this abstract was to compare the effect of topical application of tacrolimus 0.03% eyedrops versus cyclosporine 0.05% in Sjogren syndrome subjects with severe dry eyes. It was a prospective single-blinded simply randomized controlled study.

60 Sjogren patients were randomized into Group A: 30 patients were instructed to put tacrolimus 0.03% eyedrops in one eye for 6 months and placebo eyedrops in the other eye, (N= 30, 44.9  $\pm$  12.58 years). Group B: 30 patients were instructed to put cyclosporine 0.05% eyedrops in one eye for 6 months and placebo eyedrops in the other eye (N = 30, 49.4  $\pm$  12.92 years).

The main outcome measures: Patients were evaluated at day 0, 90, and 180 for Ocular Surface Disease Index Questionnaire (OSDI), frequency of use of artificial tears, average fluorescein tear break up time (TBUT), ocular surface staining scores, Schirmer I test, meibum quality, and expressibility scores.

Upon comparing both eyedrops, the mean value of OSDI decrease was 38.25 ± 18.29% versus 31.69 ± 18.57% (p-value 0.09), SICCA score decrease was 2.97 ± 1.92 versus 2.27 ± 2.02 (p-value 0.124) the decrease in artificial tear substitute use was  $3.90 \pm 2.22$  versus  $3.63 \pm 1.92$ (p-value 0.616), increase in Schirmer I values were 4.10  $\pm$  4.21 and 4.26  $\pm$  2.00 (p-value 0.590) in eyes treated with tacrolimus and cyclosporine respectively. Neither of them affected meibum quality or expressibility scores.



The conclusion was that both tacrolimus and cyclosporine significantly improved patient symptoms, frequency of artificial tears use and ocular surface staining compared to placebo-controlled eyes. However, no significant difference regarding the efficacy of both eyedrops at the end of 6 months treatment of severe dry eyes of Sjögren syndrome patients.

Eur J Ophthalmol. 2021 Feb 2;1120672121992680.doi: 10.1177 Authors: Pavly Moawad, Rehab Shamma, Dina Hassanein , Gaafar Ragab, Omar El Zawahry

### The treatment of glaucoma using topical preservative-free agents: an evaluation of safety and tolerability

Preservative-free (PF) medications represent a valuable treatment strategy in the lifelong management of glaucoma. By removing preservative toxicity, PF formulations provide tangible clinical benefits to glaucoma patients worldwide. They improve tolerability and adherence, leading to a positive impact in long-term intraocular pressure (IOP) control.

A critical review of the subject is provided, including selected evidence on the safety and tolerability of currently available topical PF formulations. Cumulative evidence confirms that topical PF medications are at least equally efficacious to their preserved equivalents. There is convincing short-term evidence for superior tolerability and safety of PF formulations compared to preserved medications. The long-term benefits and success of PF therapy require further elucidation.

The expert panel concluded that successful stepwise administration of medical therapy for glaucoma remains



elusive. There is a greater risk for ocular toxicity and therapy failure with preserved topical glaucoma therapy. Currently available and emerging PF therapy options potentially optimize lifelong stepwise glaucoma therapy and may enhance outcome. To avert complications from preservatives leading to poor adherence, ideally, future antiglaucoma therapy should become 100% PF. There are still key aspects of PF therapy that warrant further investigation.

Expert Opin Drug Saf. 2021 Jan 21;1-14. doi: 10.1080/14740338.2021.1873947.

Authors: : Anastasios G Konstas, Antoine Labbé, Andreas Katsanos, Frances Meier-Gibbons, Murat Irkec, Konstadinos G Boboridis, Gábor Holló, Julián García-Feijoo, Gordon N Dutton, Christophe Baudouin



Innovative formulation for once-daily dosing

# Break the vicious circle

Take a closer look at dry eye disease with severe keratitis. Ikervis breaks the vicious circle of inflammation in dry eye disease, significantly reducing corneal damage.<sup>1-3</sup>

#### When artificial tears are not enough, prescribe Ikervis



ikervis 1mg/mL

Please refer to the product Summary of Product Characteristics for full details.

Product Name: IKERVIS® 1 mg/ml, eye drops, emulsion. Composition: One ml of emulsion contains 1 mg of ciclosporin and 0.05mg cetalkonium chloride as an excipient. Please refer to the Summary of Product Characteristics (SmPC) for a full list of excipients. Indication: Treatment of severe keratitis in adult patients with dry eye disease, which has not improved despite treatment with tear substitutes. Dosage and administration: IKERVIS treatment must be initiated by an ophthalmologist or a healthcare professional qualified in ophthalmology. The recommended dose is one drop of IKERVIS once daily to be applied to the affected eye(s) at bedtime. Response to treatment should be reassessed at least every 6 months. To reduce systemic absorption, advise patients to use nasolacrimal occlusion and to close the eyelids for 2 minutes after instillation. If more than one topical ophthalmic product is used, 15 minutes should separate their administration. IKERVIS should be administered last. Contraindications: Hypersensitivity to any of the ingredients. Ocular or peri-ocular malignancies or premalignant conditions. Active or suspected ocular or peri-ocular infection. Warnings and Precautions: Use with caution in patients with a history of ocular herpes. Contact lenses: Patients wearing contact lenses have not been studied. Monitor carefully in patients with severe keratitis. Contact lenses should be removed before instillation of the eye drops at bedtime and may be reinserted at wake-up time. Concomitant therapy: Use with caution in patients with glaucoma, aspecially in those receiving concomitant beta- blockers which are known to decrease tear secretion. Caution should be exercised with the co-administration of corticosteroids and IKERVIS since the concomitant use of corticosteroids may potentiate the effects of IKERVIS on the immune system. Immune system effects: Ophthalmic medicinal products which affect the immune system, including ciclosporin, may affect host defences against local infections and malignancies. Regular examination of the eye(s) is recommended at least every 6 months, when IKERVIS is used for years. Contains cetalkonium chloride which may cause eye irritation. Interactions with other medicinal products: Co-administration with eye-drops containing corticosteroids may potentiate effects on the immune system. Pregnancy and Breast Feeding: Not recommended in women of childbearing potential not using effective contraception or during pregnancy unless the potential benefit to the mother outweighs the potential risk to the foetus. Benefits of treatment must be weighed against the benefits of breast feeding. Driving and using machines: Moderate influence on the ability to drive and use machines. It blurred vision occurs on instillation, the patient should be advised to not drive or use machines until their vision has cleared. Undesirable Effects: Consult SmPC for full details. The most common adverse reactions in clinical studies were eye pain, eye irritation, lacrimation, ocular hyperaemia and eyelid erythema. Other common adverse reactions observed were vision blurred, eyelid oedems, conjunctival hyperaemia, and instillation site pain, initation, erythema, lacrimation. Patients receiving immunosuppressive

therapies including ciclosponin, are at increased risk of infections, Special Precautions for Storage: Do not freeze. After opening of the aturninum pouches, the single-dose containers should be kept in the pouches in order to protect from light and avoid evaporation. Discard any opened individual single-dose container with any remaining emulsion immediately after use. Package quantities and basic NHS cost: 30 x 0.3ml single-dose containers £72.00, Marketing Authorisation Holder: Santen Oy, Nittyhsankatu 20, 33720 Tampere, Finland (EU/116/990/0018.002) Legal Category: POM IKERIVS® is a registered trudemark of Santen Pharmaceutical Co., Ltd. Job code: NP-IKERWI-UK-0047

Date of last revision of Prescribing Information: 17/07/2019,

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- 2. Craig J et al. Ocul Surf 2017;15(4):802 812
- Leonardi A et al. Eur J Ophthalmol 2016;26(4):287 296.

Date of preparation: July 2019 Job code: PP-IKERVI-UK-0208

<sup>1.</sup> Baudouin C et al. Br J Ophthalmol 2014;98:1168 - 1176

# What's in the news?

## latrogenic corneal diseases or conditions

Any prescribed or self-administered therapy carries inherent risks of secondary adverse events. While the volume of treatments being administered through healthcare systems has been increasing, scientific advancements in our understanding of the mechanisms of pharmaceutical side effects and complications from procedures now allow us to reduce the risk of non-intentional damage to ocular health.

This review summarizes the most common and leading causes of iatrogenic visual impairment, corneal diseases, and conditions that present in a general ophthalmologic practice, including a comprehensive analysis of their pathophysiology and recommendations for management and prophylaxis. latrogenic corneal diseases and conditions can arise from topical drugs, contact lens use, eye surgeries and procedures, systemic drugs, non-ophthalmological events, and cosmetic procedures.

Topical and systemic drugs may disturb tear film homeostasis or result in ocular surface deposits. The use of ill-fitted contact lenses can trigger eye discomfort and poor hygiene conditions that can predispose to severe infections. Procedures to the eye may result in a variety of anatomical and functional complications that ophthalmologists



should be aware of how to avoid or at least be prepared to manage if they occur. Even non-ophthalmological events such as non-invasive ventilation, radiation therapies and, immune-based conditions, or cosmetic procedures such as eyelash growth and fillers, can result in unwanted damage to the ocular surface.

Exp Eye Res. 2021 Feb;203:108376.doi: 10.1016/j.exer.2020.108376.

Authors: José Álvaro Pereira Gomes, José Arthur Pinto Milhomens Filho

# What's in the news?

## Ocular pathogens and antibiotic resistance in microbial keratitis over three years in Harbin, Northeast China

Understanding the spectrum of ocular pathogens in a given geographic region is important for devising appropriate practical treatment. Therefore, the authors examined the pathogen spectrum and antibiotic resistance of microbial keratitis in northeast China.

In this retrospective observational study, they reviewed the microbiology laboratory records of patients diagnosed with microbial keratitis in a tertiary eye hospital in Harbin, northeast China, between 2017 and 2019, and analysed the pathogen spectrum and antibiotic susceptibility.

462 specimens were collected, of which 282 exhibited positive cultures. Among these cultures, 257 were bacterial and

25 were fungal. Of the 257 bacterial isolates, 214 (83.27%) were gram positive whereas 43 (16.73%) were gram negative. The most prevalent gram-positive pathogen was coagulase-negative staphylococcus (CoNS; 58.37%), followed by Staphylococcus aureus (S. aureus; 20.62%) and Streptococcus pneumoniae (2.33%). Of the gram-negative bacterial isolates, 10 were Pseudomonas aeruginosa (3.89%).



The most frequently detected ocular pathogens from fungal isolates were Fusarium species (40%). They also found more culture-positive cases of bacterial keratitis in summer. Overall, 16.98% S. aureus and 64.00% CoNS isolates were methicillin resistant. These methicillin-resistant bacteria were also more likely to be resistant to other antibiotics, with multidrug resistance found in 77.78% methicillinresistant CoNS. However, all gram-positive isolates were sensitive to vancomycin and linezolid.

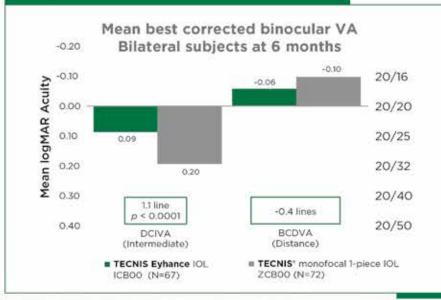
Coagulase-negative staphylococcus are the most common ocular pathogens in northeast China. It also shows the prevalence of methicillin resistance and concurrent multidrug resistance among staphylococcal isolates. Monitoring the patterns of antimicrobial resistance could help in the management selection.

Acta Ophthalmol. 2021 Feb 10. doi: 10.1111/aos.14789.

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- 20/20 distance vision"

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#### Reference

 Date on File, Johnson & Johnson Surgical Vision. Inc. Sep 2018. DOF2018CT4015. "Based on a clinical study, N≅134 achieved mean 20/20 monocular pooled distance BCDVA.

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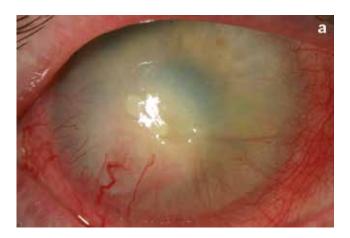
TECNIS Eyhance IOL

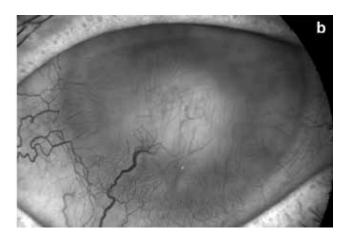
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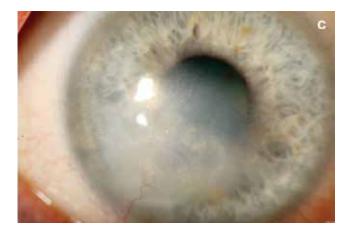


# Successful use of Photodynamic Therapy combined with Subconjunctival Aflibercept to address severe Corneal Vascularisation

By Magdalena Edington FRCOphth & David Lockington FRCOphth PhD







Corneal neovascularisation occurs when the balance between anti-angiogenic and angiogenic factors is disrupted, often due to inflammatory stimuli.1 The resulting vessels are of poor quality, leak inflammatory proteins/lipids and serve as a nidus for further inflammation, leading to corneal opacification and visually significant scarring. The Collaborative Corneal Transplantation Study showed that the incidence of graft rejection increases due to loss of immunological privilege related to number of vascularised quadrants and total number of vessels crossing the graft/donor junction. Conventional treatments include removal of stimulus (including drop toxicity), corticosteroid and non-steroid anti-inflammatory agents, laser photocoagulation, and fine needle diathermy. However, these treatments have limited effectiveness if the vessels are established. We present a challenging case in which severe florid corneal vascularisation was successfully addressed using a single session of photodynamic therapy and simultaneous subconjunctival aflibercept.

#### Case

A 41-year-old patient was referred to our tertiary corneal service for further management. He had been unsuccessfully managed for three months for presumed infective keratitis (treatments had included topical ofloxacin, cefuroxime, gentamicin, polyhexanide, hexamidine, and oral voriconazole). There was no history of contact lens wear. Two separate corneal scrapes and a corneal biopsy did not identify any organisms. Presenting visual acuity was hand movements right eye (6/5 left). His deteriorating clinical picture included reduced corneal sensation, central corneal infiltrates, persistent epithelial defect, and nine clock hours of extensive superficial and deep corneal vascularisation, with painful scleritis. [See Figure 1a]

Initial management included minimizing drop toxicity by stopping all topical antibiotics and starting Cacicol (regenerating matrix therapy agent; Thea, France) and lubricants. By 2 weeks, vision improved to 6/24 with epithelialisation, and his scleritic symptoms resolved following 1g intravenous Methylprednisolone and a tapering course of topical preservative-free steroid. Visual rehabilitation with keratoplasty was discussed, but concern was expressed regarding the high rejection risk associated with extensive deep and superficial corneal vascularisation. [See Figure 1b] To address these florid vessels, we obtained permission for unlicensed use of photodynamic therapy with verteporfin (6mg/m2) combined with a single subconjunctival injection of aflibercept (2mg/0.05ml). Topical dexamethasone was tapered over 1 month. Six weeks later, refracted visual acuity was 6/4 eccentrically, with dramatic reduction of the corneal vessels and less corneal opacification. [See Figure 1c] These vessels remained regressed with a stable corneal appearance at 1 year follow up.

#### Discussion

Anti-vascular endothelial growth factor (VEGF) agents are effective in the management of retinal vascular diseases. Topical and subconjunctival bevacizumab have been used widely to manage corneal neovascularisation, but their effect can be short-lived and require repeat injections.<sup>1</sup> Additionally, anti-VEGF agents only regress active corneal neovascularisation; they do not address established vessels. Photodynamic therapy (PDT) with verteporfin is safe and effective to treat established corneal neovascularisation, by causing microvascular thrombosis resulting in direct closure of vessels, while sparing surrounding healthy tissue.3-5 Rebound inflammation and enhanced VEGF production has been reported following PDT treatment so simultaneous use of an anti-VEGF agent is recommended. Studies using this combination demonstrated vascular occlusion in the majority of eyes and a greater decrease in surface area of corneal neovascularisation than either treatment alone.3-5 Combination therapy is more effective because it targets vessels of various caliber, location and chronicity. Aflibercept is at least as effective as bevacizumab in reducing corneal vascularisation in animal models and has high affinity to all isoforms of VEGF-A, VEGF-B and placental growth factor.6 Aflibercept is commercially licenced for ocular use, and easily accessible, so was our drug of choice. There are no other reports of this treatment modality in the literature. We recommend clinicians consider the combination of subconjunctival aflibercept and PDT to treat florid corneal vascularisation, as it resulted in vessel regression, significant visual improvement, and avoided high-risk corneal transplantation in our case.

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#### Legend

Figure 1: A. Colour photograph of right eye at presentation to corneal services showing dense central infiltrates and 9 clock hours of deep and superficial corneal vessels. B. Red free photograph detailing extent and location of corneal vessels prior to PDT/aflibercept treatment. C. Corneal photograph demonstrating significant reduction in corneal vascularization and haze 1 month after combined PDT/aflibercept treatment.

## What's in the news?

# Efficacy of bandage contact lens for the management of dry eye disease after cataract surgery

The group of authors aimed to evaluate the efficacy of bandage contact lens (BCL) for the management of dry eye disease (DED) after cataract surgery.

A total of 120 patients (140 eyes) with age-related cataract and DED were enrolled in this study. Patients underwent standard micro-incision phacoemulsification surgeries and were divided into control or BCL groups. Using slit-lamp biomicroscopic examination, Ocular Surface Disease Index, keratograph analysis and Schirmer I test were executed, and the levels of tear inflammatory molecules were detected.

The results in the control group, the NIAvg-BUT and Schirmer I test scores were significantly decreased at 1 week post-operation compared with baseline levels (P = 0.035 and P = 0.009, respectively). In the BCL group, the

NIF-BUT and Schemer I test scores were significantly improved at 1 month after operation compared with the control group (P = 0.012 and P < 0.001, respectively).

Levels of IL-6, IL-8 and ICAM-1 were significantly increased in the control group at 1 month after the operation (P = 0.005, P = 0.038 and P = 0.022, respectively), while there was no difference in the BCL group. The increase in the IL-6 level in the control group was significantly higher compared with that in the BCL group (P = 0.047). In DED patients, there were significant correlations between ocular surface parameters and inflammatory molecules.

From the study the authors concluded that cataract surgery could lead to the development or worsening of DED. The application of BCLs after cataract



surgery could stabilize the ocular surface and tear film, improve the corneal healing and reduce the inflammation. Collectively, their findings suggested that proper use of BCLs after cataract surgery played an effective role in the management of DED.

## The diary of a cornea that didn't like plastic

By Dr. Artemis Matsou

The management of keratoconus has seen a tremendous shift over the last decades from "replacing" the diseased tissue (with full i.e penetrating keratoplasty PKP or partial thickness corneal transplantation i.e Deep Anterior Lamellar Keratoplasty DALK) to "remodelling" the ectatic cornea with the use of corneal collagen cross-linking (CXL) and/or implantation of intracorneal ring segments (ICRS). The last two additions in the armamentarium of non-tissue-replacing options for keratoconus have been welcomed with much enthusiasm by the corneal community, while ongoing evolution and refinement of the relevant techniques have been keeping them in the spotlight of research and scientific talks.

ICRS are small devices made of synthetic material which are implanted deep in the corneal stroma at about 70% to 80% depth, in order to reduce the corneal curvature and regularise the front corneal surface, while improving the refractive power and maintaining the existing biomechanics status of the cornea. Several published articles have reported the benefits of ICRS in corneal ectatic disorder like keratoconus<sup>1-2</sup>. Despite improved outcomes with the use of femtosecond lasers for tunnel creation and the mastery of nomograms allowing for customised treatments, there is an associated risk with implanting a synthetic substance within the cornea. Complication rates can be as high as 30% in some case series making some surgeons sceptical about the long-term compatibility of the artificial ring segments with the corneal collagen, despite the good topographical and visual outcomes<sup>3-6</sup>.

With that in mind, the main question remains: Cornea surgeons like the effect of ICRS implantation in the cornea... but does the cornea like plastics?

Here we present a case of a cornea that ultimately rejected an intracorneal ring segment

#### At presentation



FERRARA RING



K1 47.2 Axis 23.7 K2 55.4 Axis 113.7 Q -1.13

PACHYMETRY

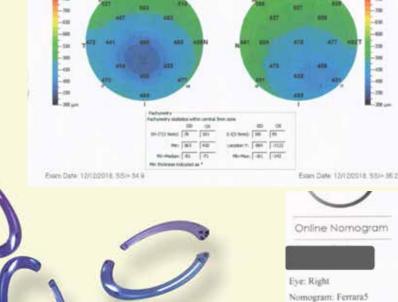
At steepest axis 500 Thinnest in rings track 383

#### RINGS

One Segment 210 degress/200um

#### INCISION

Incision at 120° Incision depth 400um (80% of corneal thickness at the stoepest axis) Laser (FEMTO) Please contact your laser manufacturer



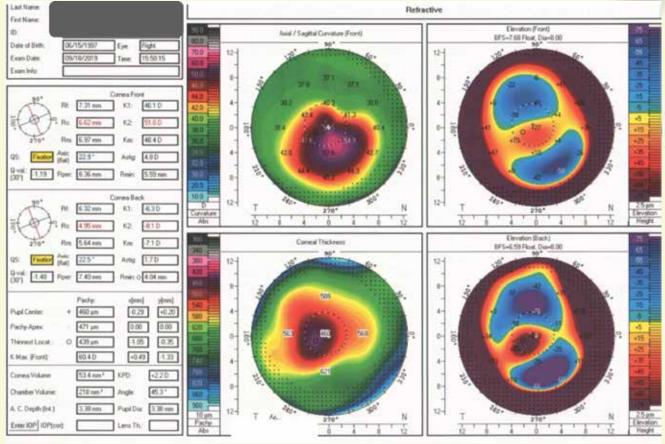
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A 23 year-old male with progressive keratoconus and floppy eyelid syndrome was referred to our department for further assessment and management. His right eye (RE) uncorrected visual acuity (UCVA) was 6/60, best corrected (BCVA) 6/12, and refraction -16.25 sph / -7.00 x 470 cyl. He underwent corneal collagen cross linking (CXL) as a first step, followed by implantation of a 2100 Ferrara-5 intracorneal ring segment (Ferrara Ophthalmics, Belo Horizonte, Brazil) due to contact lens intolerance. His corneal topography prior to ICRS treatment showed an inferior cone with K1 47.2D/ K2 55.4D/ Km 52.0D/ Kmax 66.1D, keratometric astigmatism 8.2D and a Q value of -1.52. The procedure was uneventful. The ring tunnels were created with a femtosecond laser (Ziemer FEMTO LDV Z8, Ziemer Ophthalmic Systems AG, Port, Switzerland) at a 400microns incision depth (80% depth) guided by pachymetric analysis and corneal topography.



#### 6 months later



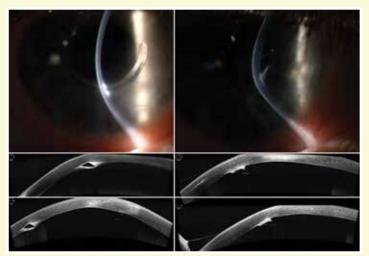
6 months follow-up confirmed a positive effect on refraction (-8.25 sph/-3.25x160 cyl) with a 10 diopter reduction in spherical equivalent and impressive improvement of topographical values with 6D reduction in Kmax, Km improvement from 51.0D to 48.4D, an improvement of 3.4D of keratometric astigmatism and a less negative Q value (Pre-op -1.52 to post-op -1.19). Despite the favourable impact on topographic indices, the patient's UCVA and BCVA remained similar to pre-op, although subjectively quality of vision was better.



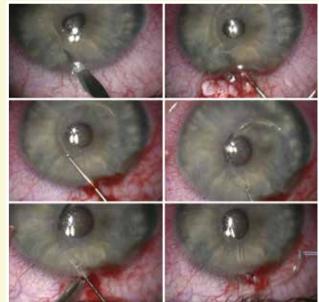
#### The COVID era

Due to the COVID-19 pandemic and compulsory interruption of non-urgent ophthalmic activity, the patient's appointments were postponed and substituted with virtual consultations in line with the new policies. When contacted, the patient did not report any issues.

#### 18 months after ICRS implantation



When COVID restrictions were lifted and the patient was able to attend at 18 months after implantation, he reported a gradual reduction of RE vision of recent onset with redness and discomfort. Slit lamp examination revealed migration of the distal end of ICRS inferiorly into the tunnel with Descemet's membrane/ endothelial perforation and presence of approximately 40% of the segment body into the anterior chamber causing a low grade anterior chamber inflammation and localised corneal oedema. There were no signs of corneal infection nor damage to intraocular structures. There was no history of trauma. The patient denied eye rubbing, however floppy eyelid syndrome was clinically noticeable. An anterior chamber approach was then employed. A corneal incision was constructed, the anterior chamber was filled with viscoelastic offering a protective coating in case the ICRS fell into the anterior chamber and then with a reverse Sinskey hook the ring was eventually successfully removed in one piece. The manoeuvres were slow and careful so not to cause any further damage to the endothelium. The proximal end was still in the tunnel which allowed for controlled pulling of the ring.



#### Next steps



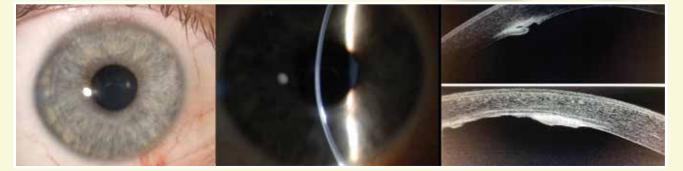
Urgent surgical explantation of the ring segment was arranged. This was initially attempted through the original corneal incision that was femtosecond laser created to insert the ring segment. A reverse Sinskey hook was used to grasp the segment through the positioning hole of the proximal end. However the ring appeared to be slipping further inside the anterior chamber with every move.

After a few attempts to grab the ring segment in that manner, the proximal edge broke off...which meant that there was nowhere to hold the ring from and so this approach needed to be abandoned.





#### 3 weeks after ICRS explantation



At three weeks follow-up the posterior cornea had healed well with no signs of leakage from the anterior chamber, while inflammation had completely settled. Some scarring along the previous ring tunnel was evident. The patient was pleased and relieved with the removal of the ring segment. Surprisingly his UCVA was improved to 6/30, while the corneal topography resembled more the post-ICRS insertion one with a Kmax of 60D and topographic astigmatism of 5.7D, rather than the topography before the procedure.

#### What does this case tell us?

Femtosecond assisted ICRS implantation is generally considered a safe procedure thanks to more precise and predictable size and depth of ICRS implantation. However, despite the evolution that has taken place in ICRS insertion, the question of whether the cornea tolerates synthetic materials still stands<sup>1-3</sup>. In our practice where we treat a large volume of keratoconic patients and have been using ICRS for many years, we do see cases where the cornea sooner or later "reacts" to the ring segment despite a thorough pre-operative assessment to ensure suitability of treatment and formulation of a customised surgical plan. Our approach to insertion of corneal ring segments is consistent in terms of indication, criteria, surgical procedure, and post-operative monitoring.

Amongst the reported complications of the standard synthetic ICRSs are extrusion, intrusion or migration, neovascularisation, corneal melt, corneal necrosis, epithelial ingrowth, and infection. There is also a number of reports in the literature of reactive "sterile infiltrates" around the rings or sterile anterior chamber hypopyon indicating that the cornea is not as compatible as we think with synthetic material after all. The risk of ring segment complication in particular the chance of failure and ring removal should be an important element in the pre-operative discussion and contenting procedure. We have example of patients who were disappointed to have the rings removed especially when there is not many minimally invasive options or alternative to correct their vision.

It is along these lines that the concept of Corneal allogenic intrastromal ring segment (CAIRS) was born, in an effort to reduce complications related to the insertion and presence of a synthetic plastic material in the cornea especially when these types of implant produce similar benefits to patients. Dr Soosan Jacob was the first to introduce this idea, with the reported outcomes so far showing excellent biocompatibility, with follow-up ranging up to nearly three years7. This enhanced tolerance is considered to result from host keratocytes quickly repopulating the small amount of donor stroma, as happens in deep anterior lamellar keratoplasty (DALK) buttons, but quicker due to the much lower volume of tissue transplanted as well as the intrastromal placement. High tolerance also makes CAIRS more flexible than their synthetic counterparts, and allow for implantation at more superficial level of 50% of depth which increases their efficacy in reshaping the cornea<sup>8-9</sup>.

As word spreads, it seems that more cornea surgeons are becoming keen on the idea of using allogenic substance over synthetic plastics. So will cornea surgery follow the "Say No to Plastics" direction?



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# The Therapeutic Contact Lens in Ophthalmology

By Mr Kunal Ajit Gadhvi & Mr Hosam Abdalla

During the recent lockdowns, ophthalmologists have been increasingly reaching for soft hydrogel therapeutic bandage contact lens (BCL) to manage patients in intractable pain from bullous corneal disorders and recurrent corneal erosion syndrome. This simple intervention has been a godsend for many of the patients for whom more definitive management has been difficult to access with elective surgical restrictions. In this short article we will cover the broad use of therapeutic lenses.

Therapeutic lenses are used for various indications, including:

- 1) Managing pain
- 2) Aiding corneal epithelial healing
- 3) Protecting the ocular surface and hydration
- 4) In the context of corneal perforation

Therapeutic contact lenses have varying oxygen permeability, depending on the lens thickness and material. This is reflected in the lenses' DK value: the higher the value, the greater the oxygen permeability. Higher DK lenses reduce the risk of corneal hypoxia, neovascularisation and enable extended wear of these lenses. Other lens variables include rigidity (hard or soft), whether they are reusable or disposable, water content (in hydrogels), the base curve, edge profile and lens diameter. The ideal choice of lens depends on the pathology, the expected period the lens is to be worn and the shape of the eye and cornea.

# 1) Management of corneal pain

The cornea contains 300-600 more sensory nerve endings than the skin and as a consequence, it is not unexpected that following epithelial breakdown, the stimulation of these nerves by the environment and the shearing forces of the lids results in pain. A good fitting soft therapeutic BCL can be valuable in the control of pain by providing a barrier for the exposed nerve terminals from the pain stimulus. A BCL with a high oxygen permeability is often kept in place for a week or until epithelial healing is complete after surgery such as corneal cross-linking (CXL) or PRK. This can greatly enhance the patient experience of the procedure and aids compliance with post-operative treatment. Following a recurrent corneal erosion, a BCL may be placed for up to 4 weeks, with the practice repeated for 2-3 months to aid reattachment of the epithelium to the basement membrane whilst preventing recurrence of erosions and pain.<sup>1</sup>

The practice of BCL in pain management, however, may be associated with a higher risk of microbial keratitis with many centres discarding the use of BCL after CXL in light of this.<sup>2</sup> As a consequence of these infection risks it is common to provide concurrent cover with a topical antibiotic such as a 4th generation fluoroquinolone twice daily and advise patients to avoid swimming.

# 2) Aiding corneal epithelial healing

Whilst therapeutic lenses can help with pain management in patients with persistent epithelial defects (PEDs), it has also been suggested that lenses may aid healing by preventing the fragile epithelium from sloughing off during blinking.<sup>3</sup>

However, lenses should be used cautiously in such scenarios, and combined with anti-microbial cover to reduce the risk of microbial keratitis. Additionally, preservative-free lubricants (hyaluronate based) are recommended to prevent the lens from sticking to the ocular surface and to promote epithelial healing. Ointments should be avoided.

Other options for management of PEDs includes sutured or non-sutured amniotic membrane grafts (AMG) combined with a bandage contact lens to protect the membrane from blinking and degradation. The recently introduced Omnilenz allows for AMG application under a bandage contact lens in the outpatient setting, although where possible many surgeons have continued to rehydrate and suture the dried AMG.

The use of the BCL, plus or minus AMG in PED management, is often more palatable to many patients compared to alternatives such as tarsorrhaphy or levator botulinum toxin, even if BCL-use may be associated with a greater infection risk. The indications for soft BCL-use in the context of PED must be considered carefully however, as it is usually only a short-term solution and may be compounded by the underlying pathology. PEDs in anaesthetic corneas and neurotrophic corneal ulcers are likely to undergo recurrent breakdown of the corneal epithelium and a BCL is unlikely to be a long-term treatment option. Additionally microbial keratitis within this patient group may present late, as such patients do not necessarily develop painful symptoms with keratitis.

#### Protection of the ocular surface and hydration

In conditions such as entropion, lid margin keratinisation, trichiasis and neurotrophic corneas, the protection provided by a contact lens may prevent breakdown of the corneal epithelium and prevent chronic irritation and inflammation of the ocular surface. Where cicatrizing disease presents with concurrent dry eye disease and lid malposition, for example in patients with chronic Steven Johnson syndrome or Graft Versus Host Disease (GVHD). a well-fitting scleral lens may provide adequate support until surgery may be safely performed.<sup>4</sup> The additional high Dk value of these lenses and retention of fluid within the scleral lens reservoir maintains ocular surface hydration in these patients, and therefore also provides a long-term solution to the dry eye disease component. This forms the basis of the Prosthetic Replacement of the Ocular Surface micro-Environment treatment (PROSE).<sup>5</sup> However, scleral contact lens fitting is not readily available in many settings and temporary soft lenses are sometimes used, although soft lenses can exacerbate the pre-existing dry eye disease.

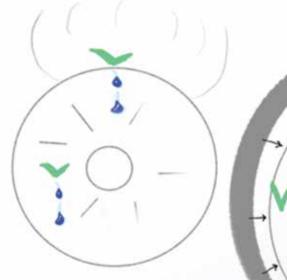
The mechanical protection provided by a large-diameter soft contact lens may also be a valuable adjunct for treating conditions like superior limbic keratitis where mechanical rubbing of the eyelid is believed to potentiate inflammation of the superior limbic region. Previous studies have demonstrated that such lenses can provide dramatic symptomatic relief and facilitate healing of punctate epitheliopathy.<sup>6</sup>

#### 4) Corneal perforation

A soft BCL can also be used in cases with a small. full-thickness corneal laceration where there is adequate apposition of the wound edges and a formed anterior chamber. A BCL in this situation may be sufficient to support the healing of the wound and re-epithelialisation without the need for corneal wound suturing or application of tissue glue. A large diameter soft contact lens may similarly be used following glaucoma filtration surgery to manage early bleb leaks in a case series reporting the use of a 14mm soft lens to successfully stem limbal leaks following trabeculectomy surgery.7 (figure 1).

BCLs can also be used following application of tissue glue in corneal perforations to provide comfort and protect the glue patch from dislodging when the patient blinks.<sup>8</sup>

As the discussion in this article has demonstrated, therapeutic lenses are useful in a host of challenging conditions that may be encountered in clinics and emergency departments. Future developments in contact lens technology such as utilising them as depot drug delivery systems may make the practice even more useful in the management of corneal infections and other diseases, and continue to support the ophthalmologists' armamentarium in the treatment of the ocular surface.



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#### Figure 1:

Compression from a well fitted soft therapeutic lens may be sufficient to stem leakage from these small seidal positive wounds allowing time for re-epithelialisation and healing of the wound without surgery or gluing.

#### ADVERTORIAL

# The intrinsic value of anterior segment imaging

By Ben David AOS General Manager

Regular assessment of the anterior segment is part of everyday life for anyone working in eye health. However, is imaging and objective grading included in these everyday assessments? And without accurate grading and imaging is it possible to deliver the eye health experience, both in and out of practice, that patients want and demand?

It is now standard practice to record findings by use of one of the recognised grading systems and the benefits to the ECP and patient of a grading system are manifold; consistent clinical record keeping, effective monitoring of ongoing eye health conditions, improved patient adherence to treatment pathways to name but a few.

One of the main concerns with grading, however, is the level of subjectivity which can lead to inaccuracy and inter clinician variability. Studies have shown reliability and accuracy between clinicians to be as low as 47%<sup>\*</sup>. This figure suggests an accurate, objective alternative would bring about substantial change for the better.

Digital imaging of the posterior segment has been incorporated into every posterior assessment for years and the benefits of doing so are unquestionable. Retinal photography and optical coherence tomography are routinely used in practice to aid examinations and educate patients on their eye health. If digital imaging has become part and parcel of posterior examinations, then why is this not the case for many anterior assessments?

Visually showing the patient corneal edema, punctuate staining or an epithelial defect has the same benefits as diabetic retinopathy from a fundus image, or wet AMD from an OCT image – namely, significantly improved understanding of their condition compared to a verbal explanation and also for measurements and tracking over time.

Imaging carries the added benefit of not being restricted to an in-practice assessment. The prevalence of smart phones and their photographic capabilities means that a powerful imaging tool is in the hands of almost every patient. Incorporating out of practice patient imaging results in new levels of understanding and, crucially, the opportunity to improve the patient experience, refine existing workflows and maximise 'chair' value.

For ECPs that see the value in anterior imaging and objective grading and want to become a truly patient centric business, Advanced Ophthalmic Systems (AOS) software is the technology that makes this possible. AOS was built firmly with the patient experience in mind, to enable ECPs to use digital imaging to provide the service their patients demand and expect. This revolutionary anterior imaging and grading software allows images of the anterior eye to be analysed in a variety of ways that can then be more easily interpreted and recorded. In so doing it removes the subjective error that might otherwise risk misinterpretation and mismanagement of any individual presentation.

AOS is a device agnostic software designed to automate ocular surface analysis of any digital image of the eye and automate the grading of bulbar redness, lid redness and corneal staining. There are a host of additional tools, patient reporting capabilities and a telemed platform that are explained in more detail below.

BULBAR REDNESS - Accurate measurement and tracking of bulbar redness is a vital part of any anterior surface diagnosis. The bulbar redness mode provides instant grading from 0-4 of a selected area along with a measurement of the percentage of vascularity. The comparison mode can



be used to compare bulbar injection of two areas of interest on the same patient and generate a heat map for further improved patient education.

LID REDNESS - For objective measurement of inverted upper and lower lids, the lid redness tool detects palpebral conjunctival redness and uses the same zero to four scale seen in bulbar mode. Results are presented instantly in the industry standard five-sector grid.

CORNEAL STAINING - Accurate evaluation of fluorescein staining is a key component of any anterior eye assessment and something that is vulnerable to a significant level of subjective variation. When an area of interest has been highlighted, using the standardised corneal grid if preferred, the points of stain or fluorescence are displayed clearly in red and an accurate count of the punctuates in each section is recorded.

OTHER TOOLS – There are a host of additions to the main functions that allow for exact measurements, direct annotations and powerful enhancements of every image. And for every session a report is generated and saved to the patient file; this can be easily exported to a PMS/ EMR and mailed directly to the patient.

TELEMED/TELEHEALTH - The latest version of the AOS software comes complete with a telemed platform which enables secure, easy-to-use remote communications with patients. The live video calling feature is activated with one click and can be accessed by patients on any smart device or pc. The patient facing mobile app is a tool that captures images easily and transfers them directly into the patient record in the AOS software. From here, analysis of the image takes place and reports can be generated without having to see the patient in practice, all the while conforming to GDPR and HIPAA compliance.

Patient education is the key challenge that AOS helps overcome, the introduction of enhanced imaging and grading improving compliance with treatment. Explaining why the treatment options have been recommended, visually and objectively, and giving a score which, the patient can easily relate to is something that occurs in other medical fields and is an experience they expect when they see an ECP.

repeatable system has obvious benefits.

the practice.

The AOS grading has been shown to be between 98.2% -

99.8% accurate and repeatable and significantly reduces inter clinician variability - subjective and often inaccurate

Tracking and monitoring a pathology with a consistent,

Being able to offer safe, secure and easy to use remote

maximised chair time value and increased revenues for

services has become a business requirement over the past

year and the benefits of this flexible way of treating patients are clear - safer, less time-consuming care for the patient,

grading is replaced with consistency, accuracy and objectivity.



AOS is HIPAA and GDPR compliant, is registered as a Class 1 medical device and has been subject to several validation studies including 'Evaluating a new objective grading software for conjunctival hyperaemia' by Byki Huntjens at City University of London.

AOS is intuitively designed to fit within the workflow of an every-day practice and its core features improve patient evaluations, covering any condition/pathology which affects the ocular surface.

The addition of a telehealth platform into the latest version enables ECPs to deliver the type of flexible service that has over the last year, become vital.

For anyone who is interested in digital imaging and grading of the anterior eye, for those that want to deliver the type of flexible, educational experience patients want and deserve, for those that want better patient outcomes and want to maximise in-practice chair time AOS is a must-have piece of software.

For more information on how AOS can become a tool for success for your business go to **aos-hub.com** 

\*source: http://openaccess.city.ac.uk/16492/1/Anterior\_eye\_health\_recording.pdf www.aos-hub.com

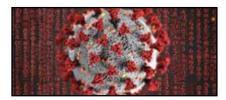
## What's in the news? Ocular MRI Findings in Patients with Severe COVID-19: A Retrospective Multicenter Observational Study

COVID-19 is a pandemic infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), negatively affecting various organs such as the central nervous system. COVID-19 has been reported to be associated with ophthalmological abnormalities, such as conjunctivitis, chemosis, retinopathy or optic neuritis. MRI orbital abnormalities have been reported but no MRI studies have been published about globe abnormalities to the best of our knowledge.

This paper reports a series of patients with severe COVID-19 presenting with abnormal MRI findings of the globe.

#### **Study Population**

A total of 129 patients (43/129 [33%] women and 86/129 [67%] men, mean age  $63 \pm 14$  years) was included for analysis from March 4th to May 1st 2020 (Figure 1). Among them, 9/129(7%) patients (1/9 [11%] woman and 8/9[89%] men, mean age  $56 \pm 13$  years) had abnormal MRI findings of the globe consisting in the presence of one or several nodules of the posterior pole of the globe. 2/9 (22%) patients had diabetes, 6/9 (67%) were obese, 2/9(22%) had hypertension and none of them had asthma.



This study showed that 7% of patients with severe COVID-19 presented with one or several nodules of the posterior pole of the globe. This rate is in line with the prevalence of 5.5% of ocular manifestations among COVID-19 patients. Patients affected by severe COVID-19 were reported to be more at-risk to develop ocular manifestations. Screening of these patients is recommended to provide appropriate treatment and improve the management of potentially severe ophthalmological manifestations.

https://doi.org/10.1148/radiol.2021204394

Authors: Augustin Lecler, MD, PhD, François Cotton, MD, PhD, François Lersy, MD, Stéphane Kremer, MD, PhD, Françoise Héran, MD on behalf of the SFNR's COVID Study Group.



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# A woman surgeon in the time of COVID

J. J.



By Nancy Al Raqqad FRCSGlasg

It has become clear without doubt that the COVID 19 pandemic has changed the face of humanity all over the world. Not only it has affected our daily practice and the way we took our lives for granted. It has also helped sculpt our perspectives and diversify our practice.

In this regard this unprecedented time has given me some space to look around more often, embrace our fast life track with more ease and reflect on myself, my family and my career in a different way.

We can never deny that we were all hit by a wave of denial at first. The first few weeks of the pandemic with the escalating news put us in a state of gear up waiting for the next step and as people of science, evidence plays a major role in our digestion of any news or change of track. Thus after denial came a state of suspense of questioning our next step and prioritizing our goals in life... and when lockdowns started to shatter the world and death toll to rise we sundered to its sentence... and despair started to take over.

I always try to handle life in a positive way. Believing that if life gives sour lemon turn it into a sweet lemonade... looking for an escape of the burden of responsibility, the fear of getting sick and catching the CoVID curse or spreading it through my contact with patients to loved ones or sterilizing all what my hand gets hold of or fighting to stay healthy physically and mentally... as a dynamic person and I have always believed that static means death and dynamic means life.. so came out with moving on a different plane to stay alive and keep our minds busy with reviewing our practice and learning more about our selves meanwhile waiting for the clouds to disappear. Like my fellow colleagues I became more absorbed in the philosophical view of life... going back to the basics of survival, of mingling more with our family members and trying to distract our under-used hands with something as near as possible to our practice. We came up with continued education through virtual meetings and discussions. We adopted new hobbies and learnt new skills. Women reverted to in home dining and refining cooking skills while men practiced gardening reading and instrumental music training. We embraced the sun more often... the value of exercise and healthy eating habits and the value of family and support.

My practice as an ophthalmologist and cornea and refractive surgeon was affected on a large scale too. In early 2020 hospitals were reserved for the seriously ill or emergency eye cases and thus selective cataract and refractive procedures were delayed giving way to Covid patients care.

Corneal donation was also affected as we used to rely on half of our transplants on local sources while importing the rest from corneal banks in the USA. This too had been put on a halt. Delay of grafting for those on the waiting list put more pressure on our service and our patients. Psychological and medical pressure escalated and it was our duty to spread reassurance in a time we the surgeons had no definite answer to where the world was going. As the year started to unfold and more understanding of the virus we were fighting waived in our horizon glimpse of hope and accommodation of our practice pattern evolved. After all, we cannot stay locked down with fear watching our skills loosing stamina as days passed by. My team and I started to streamline the patients offering optimum protection for both sides, avoiding those of old age, lowered immunity and the ones with good vision who can be postponed. We started to PCR test our patients before any surgical procedure to protect the staff and other patients and limited the number of cases in theater per day.



This way we accommodated our practice, our sense of achievement, and our patients safety in one setting.

The need for travel and move around also embarked heavily on us and we tried to bridge the pattern of our conferences by staying in contact with our fellow colleagues and friends through social media and virtual meetings. In fact, we strengthened our acquaintances and increased our knowledge that was reserved to those who could afford attending international meetings, something we wouldn't have done in the old days.

As a Mum of four and head of cornea team in a tertiary referral hospital, a wife and an officer, I tried to minimize the burden of responsibility and focus on what I can do rather what I couldn't. That spirit helped me navigate through times of supreme stress when I needed to keep my immunity and sanity at full!

Vaccines against Covid 19 are being rolled-out the world is split into two groups, those who believe is the savior and those who don't. Being a surgeon and a science believer, and now that I have taken my second dose of the vaccine I can only pray for freedom of fear, possible reverse to our norms while taking all the lessons learned through this global test towards appreciation and gratitude.



Nancy Al Raqqad FRCSGlasg Consultant Cornea, Cataract and refractive surgeon Amman-Jordan Nrakkad@yahoo.com

## What's in the news?

# Patient-reported burden of dry eye disease in the UK: a cross-sectional web-based survey

The objective of this study was to compare socio demographics and vision-related quality of life (QoL) of individuals with or without dry eye disease (DED); and to explore the impact of DED symptom severity on visual function, activity limitations and work productivity.

The design of the study was a Cross-sectional web-based survey and the setting UK general population. The participants were all adults  $\geq 18$  years with (N=1002) or without (N=1003) self-reported DED recruited through email and screened.

All participants completed the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25), with six additional questions (items A3-A8), and the EuroQol 5 dimensions 5 levels. DED participants also completed Impact of Dry Eye on Everyday Life questionnaire, 5-item Dry Eye Questionnaire and the Standardised Patient Evaluation of Eye Dryness questionnaire along with the Ocular Comfort Index, Work Productivity and Activity Impairment and the Eye Dryness Score (EDS), a Visual Analogue Scale.

The results showed that baseline demographic and clinical characteristics were similar in participants with versus without DED (mean age, 55.2 vs 55.0 years; 61.8% vs 61.0% women, respectively) based on recruitment targets. Scores were derived from NEI VFQ-25 using the new 28-item revised VFQ (VFQ-28R) scoring. Mean (SD) VFQ-28R scores were lower in participants with versus without DED, indicating worse functioning (activity limitations, 73.3 (12.3) vs 84.4 (12.3); socioemotional functioning, 75.3 (21.5) vs 90.3 (16.2); total score. 71.6 (12.8) vs 83.6 (12.6)). Higher percentages of problems/inability to do activities were observed among those with versus without DED. The impact of DED on visual function was worse for participants with more severe DED symptoms, as assessed by EDS. In addition, a higher EDS was associated with worse symptoms on common DED scales and a worse impact on work productivity.

In conclusion DED symptoms were associated with negative effects on visual function, activities and work productivity, whereas worse DED symptoms had a greater impact on vision related QoL and work productivity.

Authors:

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# Ocular Surface Insights from Across the Pond: Neurotrophic Keratitis

By Seema Nanda OD

★ If the Wi-Fi symbol on a mobile phone shows no bar (indicating a poor signal) the connection is lost and a call cannot be completed.

★ Similarly, if the corneal nerves degenerate, the impaired innervation or poor signal, cannot be sent to the trigeminal nerve, the connection is lost so the ocular surface cannot heal adequately.

★ This illustration of faulty communication depicts the rare condition known as Neurotrophic Keratitis (NK).

Neurotrophic keratitis, or neurotrophic keratopathy, is a disease caused by damage to the corneal nerves that affects less than 65,000 people in the USA.1 In a healthy cornea, there are about 7,000 nerve endings per square mm.2,3 These nerves are essential to the health of one's eyes as they help with reflexes of blinking and tearing to maintain a healthy ocular surface.1 The nerves provide protection and nourishment to the ocular surface due to the avascular nature of the cornea. Akin to an entire electric grid shutting down, when this neural network is injured, moderate neurotrophic keratitis can ensue and become more severe. Consequently, an increased risk of ulcer formation, corneal melt, and subsequent scarring can occur, which contributes to a patient's permanent loss of vision.<sup>1</sup>

Symptoms of neurotrophic keratitis may include: changes in tear viscosity, redness in the eyes, and blurred vision.5,7 Some individuals with neurotrophic keratitis may not have any symptoms at all, since their damaged corneal nerves no longer sense feeling.<sup>1,5</sup> The hallmark in diagnosing a neurotrophic cornea is the reduction in corneal sensitivity or complete anesthesia of the ocular surface.<sup>4</sup> The clinical diagnosis can be deduced with the patient's complete medical history and an ocular examination; however, the treatment can be elusive and reasonably challenging until now.

Several clinical causes of NK result from (1) common diseases in the herpes family – simplex or zoster, (2) recurrent epithelial erosions from trauma or surgery, or (3) toxicity from prolonged use of topical ocular medications. Hypoesthesia can occur, thus resulting in the neurotrophic condition when the trigeminal ganglion - including the ophthalmic branch - becomes damaged.<sup>3</sup> Another cause involves individuals who are known to be poor wound healers who may also suffer from this keratopathy due to sensory loss. Characteristically, inadequately controlled diabetics may develop neuropathies of their extremities in their hands and feet. Comparably, these patients may also develop denervation of nerves in their corneas leading to a neurotrophic keratopathy.

NK can be divided into three stages based on severity, according to the Mackie Classification system. Stage I is characterized by alterations of the corneal epithelium, which are dry and opaque, with superficial punctate keratopathy and mild corneal edema. Stage II is depicted by development of epithelial defects, often near the center of the cornea. Stage III is categorized by ulcers of the cornea, accompanied by stromal edema and/or melting that may result in corneal perforation.3 The key in differentiation from other corneal maladies requires checking a decrease in corneal sensitivity.

The simplest way to perform the test for corneal sensitivity is to lightly brush the affected cornea with a cotton-wisp or frayed dental floss to initiate the blink response. A more quantitative approach to measure corneal sensation is the use of the Cochet-Bonnet aesthesiometer. A nylon filament protrudes from the device to a maximum length of 6 cm. Initially, 1-2 cm of the filament extended out and touches the injured cornea. If a tear or blink response cannot be elicited, then the nylon thread is extended out further until a response is attained. Notably however, sectoral hypoesthesia may be observed in patients with herpetic disease; therefore, all quadrants should be checked and documented accordingly.<sup>4</sup>

Until recently, treatment options in mild conditions have been limited to bandage contact lenses along with prophylactic antibiotics. Moderate cases have involved the use of autologous serum eyedrops and amniotic membranes. However, in more severe and recalcitrant situations, a tarsorrhaphy has been warranted to avert further deterioration and sloughing of corneal tissue.8 Today, with the advent of an ophthalmic solution produced from recombinant human Nerve Growth Factor (rhNGF), an eyedrop that aids in the closure of persistent corneal epithelial defects is finally available. The drop, known as cenergimin-bkbj 0.002%, is administered every two hours, six times per day for eight weeks in the affected eye and can be given to patients as young as two years of age.

To understand the significance of this novel therapy, one needs to study how endogenous NGF is essential in corneal homeostasis. NGF acts through receptors to support corneal innervation and integrity. They are maintained by three pathways as an integral part to the development, survival, growth and delineation of corneal cells.<sup>10</sup> Initially,



NGF plays a role in nerve function and stimulates the regeneration and survival of the sensory nerves.<sup>2,5</sup> Afterward, it binds receptors on lacrimal glands and promotes sensory-mediated reflex tearing secretion.<sup>1,10</sup> Finally, it stimulates proliferation, differentiation, and survival of corneal epithelial cells.10 The mechanism of action is believed to be through the action of the specific high-affinity (TrkA) and low-affinity (p75NTR) receptors in corneal epithelial cells to support corneal healing. The concept of endogenous NGF is not new, as it was discovered in the 1950s. Yet the ability to create a structurally identical molecule that is ten times more potent than in vitro NGF and preservative- free, is clearly an accomplishment.

Pivotal studies in both the Europe Union (EU) and United States (US) have demonstrated the effectiveness of cenergimin-bkbj 0.002% over the eight-week treatment course monitored by 48 weeks of follow-up. The EU arm, also known as the REPARO study, determined the dosage (10 vs. 20 mcg/ ml) and its effectiveness compared to placebo. Upon completion of the EU protocol, the US trials duplicated the model using the now-defined REPARO dosage of 20mcg/ml for an eight-week therapeutic regimen; and later tracked by 24-weeks of follow-ups.12 In the EU report, 72% of the moderate or severe cases of NK completely healed: they

also remained stable for one year in 80% of the cases, as was with the US model showing similar outcomes of 65.2% completely recovered. <sup>9,12</sup> Adverse reactions to the solution may cause mild to moderate eye discomfort, such as eye pain during treatment. Instillation site pain was noted in 16% of participants and 1 to 10% exhibited corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing.<sup>9,12</sup>

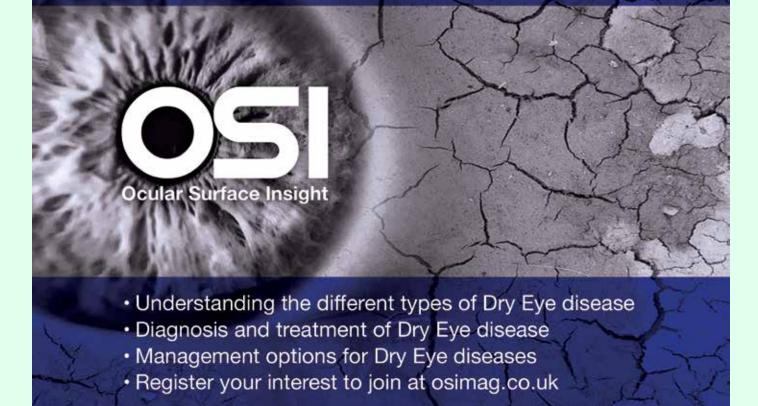
In summary, several conditions can lead to neurotrophic keratitis, including: herpes viruses, ocular surgery or trauma, diabetes, and even dry eye disease. Therapeutic options have been minimally palliative and relatively unsatisfactory to date. However, with the introduction of the recombinant human Nerve Growth Factor in cenergimin-bkbj 0.002%, the medication can mirror the body's own NGF, thereby inducing corneal innervation, tear secretion, with subsequent cell propagation and division. Clinical studies in both the EU and US confirm greater rates of corneal healing due to this innovative eyedrop formulation. Ultimately, treatments such as cenergimin-bkbj 0.002%, will provide the eyecare practitioners with another means to help those patients with poor corneal innervation so they can finally get the signal they need to make a connection.

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# Dry Eye Masterclasses 202

Developed by Mr. Samer Hamada, Prof. Arthur Cummings and Prof. Rohit Shetty



# Cataract surgery in ocular surface disorders

By Francesco Aiello MD, PhD, FEBO, FEBOS-CR

Cataract surgery is the most commonly performed surgical procedure worldwide. It guarantees appreciable visual outcomes in uncomplicated cases. However, when cataract is associated with ocular surface comorbidities, its surgical management and post-operative visual prognosis may not be comparable with the one of the uncomplicated cases. Among these conditions, chronic cicatrizing conjunctivitis (i.e., Stevens-Johnson syndrome, ocular cicatricial pemphigoid, allergic keratoconjunctivis), Mooren's ulcer, peripheral ulcerative keratitis (PUK) and limbal stem cell deficiency must be considered.

It must be noted that in this context, the formation of cataract occurs at an early age, due to the ongoing local inflammatory state and/or as the result of prolonged topical steroids use. Additionally, surgical-induced trauma to ocular tissues may represent the trigger for the reactivation of the local inflammatory response. Hence, a careful preoperative, intraoperative and postoperative planning is crucial in the surgical management of such unusual cases.

Specifically, whenever one of these conditions is identified in a patient requiring cataract surgery, it is highly recommended to await until the local inflammation is fully controlled and the disease is in the quiescent phase. Notably, it has been proposed to wait for at least 3 to 6 months after the resolution of the last inflammatory flair before performing the surgical procedure.

The eventual presence of metaplastic corneal epithelium/corneal pannus, scarred and shortened conjunctival fornices, mispositioned eyelids with deranged lashes must be preoperatively investigated, to guarantee a proper intraoperative management. Consequently, peribulbar or retrobulbar anesthesia, rather than subtenon block, is generally advocated in such cases to avoid conjunctival inflammation and further scarring. Also, topical anesthesia should be avoided since the duration of the surgical procedure may be longer than the one of uncomplicated surgeries. Also, general anesthesia may be considered in the presence of short fornices, or when lid sutures, canthotomies or fornix reconstruction are additionally needed.

The use of lid speculum should be judicious. In fact, not only may the mechanical stress induce the reactivation of the local inflammatory state, but also lid speculums may not be suitable in the presence of very short fornices. The evidence of an uneven corneal epithelium or the presence of stromal opacity are other issues to be addressed before the surgery. In fact, an inadequate intra-procedural visualization might derive and furtherly complicates an already challenging operation. At the pre-operative encounter, the use of diffuse light at the slit-lamp may simulate the intraoperative visualization with the surgical microscope. In the presence of difficult view during the surgery, the use of non-axial light as a light pipe or a chandelier (to be held into the anterior chamber or inserted through the pars plana) might help. Besides, the use of hydroxypropyl methylcellulose (HPMC) 2% onto the ocular surface might enable visualization through irregular corneas.

The selection of the incision-site location is crucial to ensure a safe and sound cataract surgery, especially in the presence of concomitant disorders of the ocular surface. The site of incision largely depends on the location of corneal scar or thinning and on the presence and location of an eventual symblepharon. In the presence of peripheral corneal opacity, it is strongly suggested to choose the incision-site location to continuously and properly visualize the tip of the instruments during each of the

surgical steps. In other words, try to avoid the incision site to be located opposite to the corneal lesion. In the case of peripheral corneal thinning, scleral incisions are preferable after conjunctival dissection. In such cases, it has been suggested not to suture the conjunctiva back after the surgery. In fact, limiting the local vascular supply might damper the inflammatory reaction, furtherly preventing corneal thinning.

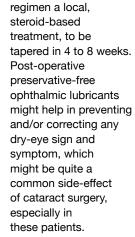
Contrariwise, patients suffering from chronic cicatrizing conjunctivitis may benefit from corneal incisions. In fact, trauma-induced dispersion of conjunctival antigens may propell the inflammatory reaction.

The choice of the type of surgery largely depends on the concomitant corneal, scleral and conjunctival state. Both phacoemulsification and extracapsular cataract extraction (ECCE) have



acceptable visual outcomes. However, when corneal scarring impedes proper visualization or in the presence of a very dense cataract, ECCE is advocated.

In all these cases, capsular dye is an indispensable tool to enhance visibility during surgery, especially while performing rhexis. Finally, a careful and strict follow-up is strongly advisable to promptly identify and manage any inflammatory flair. The continuation of any local (i.e., cyclosporine 0.02%) or systemic (i.e., methotrexate, cyclophosphamide) immunosuppressive treatment is therefore suggested during the peri-operative period. Furthermore, it may be helpful to add to the therapeutic



All of this suggestion may aid the surgeon to properly handle such unusual and complicated cases.

Acrylic intraocular lenses (IOL) with square edges are highly suggested in this context, as they have been described to reduce the incidence of posterior capsule opacification. In addition, large optic (6.5 mm) IOLs are recommended in order to avoid post-operative decentration. And in the sulcus allocation of the IOL is proposed whenever intraocular visualization is scarce, in order to avoid the "half in the bag" issue. Not all the difficulties will be eventually overcome, but these measures may aid to optimize cataract surgery management and short-term outcomes. However, long-term success will be only guaranteed by the effective control of both the local inflammatory state and of the associated ocular surface disorder.



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References: 1. Eykappo (chloramphenicol) Summary of Product Characteristics. 2. Novelia® PureFlow Technology. http://www.nemera.net/wp-content/uploads/2015/06/Flyer-NOVELIA\_April20151.pdf (Accessed February 2021). 3. Novelia@ PureFlow Technology, https://www.nemera.net/wp-content/uploads/2014/06/WP-Novelia-alternativetofi Iters-June 2015 (Accessed February 2021). 4. MIMS February 2021.

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eye drops solution chloramphenicol

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10ml



# Flap Thickness during LASIK Evolution

By Caitriona Kirwan FRCSI(ophth), Azher Eldouri FRCS, Michael O'Keeffe FRCS



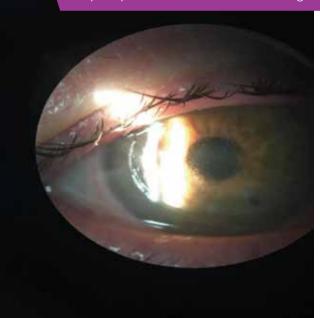
## Introduction

Since its inception in the 1990's, Laser in-situ keratomileusis (LASIK) has become the world's most popular form of refractive surgery. Monitoring developments over the years, gives insight into how a surgical procedure can evolve often through trial and error. In the early days of LASIK, corneal flaps were either free cut or hinged. The flaps were sutured at the completion of stromal ablation and the eyes were padded for 24 hours. Quite accidentally it was discovered that the flaps were adherent to the underlying stroma and sutures were not required. For many years LASIK flaps were created using a mechanical microkeratome. The introduction of femtosecond laser for flap creation marked a major milestone in the history of LASIK. Flap thickness has also seen major changes.

In the early 1990's, mechanical microkeratomes permitted creation of corneal flaps with diameters ranging from 7.5 to 8.5 mms. Flap creation commenced on the temporal side of the cornea with formation of a 1mm hinge in either the nasal or superior cornea. The superiorly located hinge was to become the most desirable location, as these flaps were better able to withstand the upward and downward motion of the eyelid, hence reducing the risk of flap dislocation. Flap thickness of between 130 and 180 µm's could be selected but the desired depth of cut was not always achieved. Unexpected thick flaps resulted in a thinner than desired residual stromal bed thickness, which was found to increase the risk of kerectasia. Sometimes very thin flaps were created. Button holes, whereby a flap was not cut but the blade skimmed the surface cutting only the central cornea was a dreaded complication often resulting in visual loss due to corneal distortion. On occasion a free flap

was created and these were sutured using 10/0 nylon. It subsequently emerged that repositioned flaps remained in-situ without sutures due to the suction effect created by the endothelial cell pump mechanism.

In the year 2000, a bladeless, femtosecond laser system emerged that could cut corneal flaps. The femtosecond laser is a solid-state laser that emits pulses of a wavelength close to the infrared spectrum of extremely short duration femtoseconds. This laser is based on principles of photodestruction. It has a similar action to the Nd: YAG laser system. This laser permits the creation of much thinner flaps of more predictable and uniform thickness than the traditional mechanical microkeratomes.



#### Flap displacement and folds following LASIK

Without doubt, the advent of femtosecond laser signified a huge forward leap from the microkeratome. It has made LASIK safer with fewer flap related complications. This technology allows greater flexibility and reproducibility in flap creation. As confidence in the technology grew and in an effort conserve stromal bed thickness and allow treatment of greater refractive errors, flap thickness reduced to as little as 80 microns. With a flap of 80 microns, the cut was made just deep to Bowman's layer. However, these ultra-thin flaps were beset with problems such as folds and dislocation and were subsequently abandoned in favour of slightly thicker flaps. We the authors cut flaps of 100 to 110 microns for some time. We recorded a 5% incidence of folds and dislocation within the first 24 hours. Placement of a bandage contact lens (BCL) in the eye at the completion of LASIK, intense lubrication including lubricant ointment overnight failed to meaningfully reduce the risk. More recently we cut 120micron flaps, which has eliminated these problems, and we no longer insert a BCL. We feel that this thickness strikes a good balance between tissue preservation and unwanted flap complications.

In conclusion, LASIK with femtosecond technology has been a game changer in refractive surgery. However, we believe that there is a lower limit to flap thickness.



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# The top five tools I cannot live without when diagnosing Ocular Surface Disease. Slit lamp.

By Brian Tompkins & Dr. Keyur Patel

Every writer has a pen, every chef has a knife and every optometrist has a slit lamp. It featured prominently, for good reason, in our previous list of 'The top five tools I cannot live without when diagnosing ocular surface disease' and can be used in 90 percent of dry eye investigation without having to invest in additional tools.

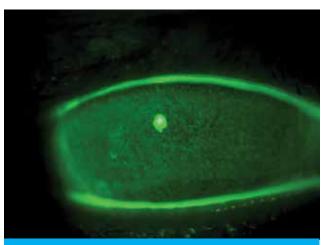
The bio-microscope is an essential weapon in our eye care armoury and it is something that we use day in, day out in every examination. It is essential in contact lens fitting and aftercare and, when used properly, allows us to do so much of our everyday work.

Combining an adjustable light source shone through a slit of variable width and/or height with a microscope, usually binocular, the slit lamp began life as an instrument more commonly used by ophthalmologists but has gone on to be a staple item of equipment for optometrists and contact lens opticians, with its development overseen by a number of optical physicists.

It allows for close surface examination of the anterior eye, from the tips of the eyelashes to the back of the crystalline lens. By adding auxiliary lenses such as Goldmann or Volk



Keyur's Topcon DC4 Digital Slit Lamp



Medica Mentosa secondary to buffered saline in a scleral lens – Topcon DC4

lenses it can also be used to inspect the posterior section, including the vitreous and the retina.

An early incarnation of the device was first demonstrated by Allvar Gullstrand at Heidelberg in 1911 by focusing the image of a red hot rod through the slit. A decade later, Ida Mann together with Harrison Butler introduced the use of the slit lamp to England.

Her enthusiasm for the slit lamp was clear and in her memoirs she wrote:

"This beautiful instrument utilised the principle of the fluorescence of living transparent tissues in a focused beam of light... it was like cutting a microscopic section through live tissue and many things undreamt of were revealed. These discoveries were of great importance, as they increased our powers of accurate diagnosis."

While the technology around slit lamps has evolved greatly since those early days, the basic principles remain the same. Digitisation has been a game-changer and a bio-microscope's efficacy can be enhanced further by attaching a camera to facilitate image capture and recording for referral capability, for comparison of treatment efficiency and, some would say, most importantly, for patient education.



Demodex Blepharitis – Topcon DC4

It has never been easier to take good quality pictures. All of us carry around in our pockets a device capable of taking incredible images. The smartphone is a wonder of modern-day technology, complete with cameras that are plenty good enough for the day-to-day needs of most eye care professionals. Clearly, you can go the extra mile and invest in more specialist equipment if you deem it necessary but simply harnessing the power of your phone can make a difference.

With it being so easy to capture high quality images and video there really is no excuse for not doing so. The technology is there, it's straightforward to use and it significantly enhances the patient experience – allowing them to clearly visualise their condition and better understand treatment pathways.

Good quality images should be part and parcel of our everyday record keeping. It is our duty, as outlined by professional bodies, to keep comprehensive patient records. As the College of Optometrists states;

#### "Full records are essential to facilitate the clinical management of the patient and continuity of care."

By breaking down the slit lamp into four main sections we get a clearer picture of both its purpose and its capabilities.

#### Light Source

The latest evolution of 21st century slit lamps come with a halogen or LED light source, that allows for an extremely bright light to be achieved. LED is widely regarded as the best option as it stays cooler, allowing for improved patient comfort.

When it comes to light, the techniques used dictate the need. It's important to have a clear and bright diffuse option and a precise slit beam that can be used to accurately analyse tissue and illuminate different structures.

It's worth noting that as the technology of light sources evolves over time, this can have an impact on patient records, as the light temperature on images taken on updated equipment can also appear different to those taken on older devices when you are comparing and contrasting.

#### Magnification

Magnification needs vary hugely according to the examination technique. Very low magnification allows an overview of the eye/lids and general adnexa. The eyepieces are generally fixed but many models can increase magnification by having changeable eyepieces. The optics then have additional magnification options. Some can change between 5x and 50x just at the turn of the wheel.

#### **Filters**

We typically use four different filters, depending on the individual needs of the patient.

White Light: More than 90 per cent of our time on the bio-microscope is spent using white light. This is the most flexible and covers the vast majority of ocular assessment.

**Cobalt Blue**: This built-in enhancement filter is used for sodium fluorescein evaluation and works best in conjunction with a Wratten filter.

**Red Free**: This green(ish) filter helps to enhance blood vessels, which can be useful when looking at neovascularization or telangiectastic vessels.

**Infra-Red**: The newest addition to the filter range, allowing IR assessment of the meibomian glands.



Brian's Zeiss Slit Lamp with Custom Digital Camera and custom-made LED Lamp

#### Digital add-ons

Imaging and video through a beam splitter attachment has been around for many years and the ability to take an image and attach it to a patient record was a huge step in record keeping and as an educational tool.

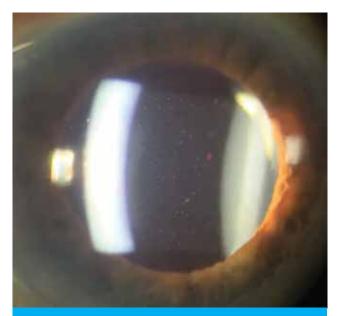
The ability to take a digital image, with instant review, has meant that multiple images can be taken over a short period, allowing the practitioner to not only take multiple images with different set ups, but to choose there and then which is the most clinically accurate and educate the patient sitting in their chair about what you have just seen, and the best way to manage the condition for optimal output.

It allows the patient to take part in the journey of their ocular condition as they can watch their progress and see for themselves the changes made through our interventions.

Slit lamp adaptors now allow us to take an image with a smart phone, meaning ECPs can take quickly and easily take images in the highest resolution possible to give in-depth clarity.

Here at TK&S we are passionate about the technology we have at our disposal. We are always looking to push boundaries and adopt new technology that can make a difference to our patients. Bio-microscopes form a key part of that but for us it is more about the add-ons creating a natural evolution of the device rather than reinventing the wheel itself.

For example, Brian's slit lamp which takes pride of place in his examining room is at least 50-years-old. It is a beautiful object and the crisp optics work perfectly, with 21st century lighting adaptations and recording equipment attaching to it to maximise its potential. Keyur, meanwhile, has the very latest Topcon machine, complete with LED illumination and in-built digital camera.



Anterior Chamber Cells – iPhone 12 with Slit Lamp Adaptor (4K), Courtesy of Hamza Mussa @thecrazyoptom

They are very different in style but ultimately similar when it comes to the end result for the patient.

Whichever end of the scale you opt for, the most important thing to consider is what is right for you. Try them, experiment with them, get comfortable with them. Your next slit lamp is going to be with you for a long time and you're going to work closely together every day. It's a decision that will have a profound effect on the way you work so take your time and get it right, both for you and your patients.



Greasy Tear Film – Topcon DC4

#### What does the future hold?

We always have one eye on the future and are keen to be aware of what lies in store around the corner. One area which is currently seeing exciting advances in technology is the 'drone slit lamp'. This allows ECPs to operate a machine remotely – whether that be from a separate room within the practice to keep a safe distance during the COVID-19 pandemic or event from an entirely different continent if the patient had a particularly rare condition that no local optometrist was able to examine.

The flexibility that drone slit lamps afford is potentially game-changing, allowing practitioners to work remotely and giving patients access to a worldwide network of specialist ECPs.

A study by the Canadian Ophthalmological Society compared the use of a mechanised remotely operated stereoscopic drone slit lamp compared with a conventional slit lamp in assessing anterior segment pathology in ophthalmology patients.

It found there was substantial agreement between the two when assessing AC depth, cell, and flare. Sensitivity and specificity for assessing these findings ranged from 88.2% to 100%. The study concluded that the drone slit lamp

"provides excellent capability for examination of anterior segment pathology in live patients, performing similarly to a conventional slit lamp". As part of our research for this article, we spoke to John Gelles, director of the Specialty Contact Lens Division at The Cornea and Laser Eye Institute & CLEI Center for Keratoconus in New Jersey.

John has been at the vanguard of drone slit lamps and said:

"Generally all drone slit lamps are simply digital slit lamps with remote controlled servo motors for movement. By using two cameras, stereoscopic views are possible, and this can all be viewed with the use of VR headsets or side-by-side images with prism eyewear, which gives an even higher image quality."

"Connectivity via modern broadband, or better still 5G, allows for low latency communication for real-time evaluation."

"Though high-quality examination is possible, limitations remain. There is currently no ability to perform a physical evaluation or procedure, for example you don't yet have the ability to flip a lid or remove a foreign body. But this will change with the ability to create remote-controlled attachments similar to the da Vinci Surgical System."



Fuchs Endothelial Corneal Dystrophy – Topcon DC4

In short, the future is here, now. Let's embrace it, use it and reap the benefits.

If anyone has any specific questions around anything in this article, from dry eye to drone slit lamps, please feel free to email us at dryeye@tkso.co.uk and we will respond.



## Q & A's with Dr E. Daniel

#### Edited by Vivian Ho

Association of meibomian gland morphology with symptoms and signs of dry eye disease in the Dry Eye Assessment and Management (DREAM) study". The Ocular Surface, Volume 18, Issue 4, 2020

Why was it important to study the association between symptoms and signs of dry eyes disease and MGD morphology<sup>1</sup>?

The inconsistency of associations between the ocular signs and symptoms of dry eye have thwarted scientists for several decades in finding the best therapies for the disease. Newer tear functions tests have also failed to establish concrete associations. Imaging of the meibomian glands by various modalities including infrared photography has shown us the rich diversity of the morphological structure of the meibomian glands observed in the normal population and in patients with dry eye. Many previous investigators have introduced and investigated some of the morphological features, but none have focused on all the morphological features described in our study. Our hope was to find a consistent association between some of these morphological features and the signs and symptoms of dry eye.



Are you surprised with the study results that most MG morphologic features did not correlate with the symptoms and signs of MGD in the DREAM study2 patients? And why do you think that's the case?

Going by the undeniable failure to find consistent correlations in dry eye by experienced investigators it did not surprise us that most MG morphologic features did not correlate with the symptoms and signs of MGD. The DREAM study focus was to find out if omega-3 fatty acids offered a benefit over a placebo in dry eye subjects. Meibography was possible only in a few DREAM sites that had the oculus machine. The evaluation of the meibography images did not begin until much later when funding was procured for that purpose and this precluded adequate certification of the imagers. This resulted in many images being ungradable because of poor eversion of the lids and we had to decide to limit our analysis to the middle third of the lids. Our DREAM cohort was composed of dry eye subjects with moderate to severe dry eye and did not have a control of normal eyes.

#### Reference:

1) Association of meibomian gland morphology with symptoms and signs of dry eye disease in the Dry Eye Assessment and Management (DREAM) study". The Ocular Surface, Volume 18, Issue 4, 2020

2) Dry Eye Assessment and Management Study Research Group, Asbell PA, Maguire MG, et al. n-3 Fatty Acid Supplementation for the Treatment of Dry Eye Disease. N Engl J Med. 2018;378(18):1681-1690. How important do you think meibography imaging is to the diagnosis and management of MGD? Would you recommend the use of such imaging device based on your study results?

Meibography imaging has provided us with the opportunity to look at the meibomian glands in detail. Evaluation of the meibography images is still in its infancy and this modality of imaging has much to offer in the future and no dry eye examination would be complete without meibography.

What additional information has your research findings on MG morphology and dry eye disease added to the existing evidence? How may we address any of the remaining uncertainties in future studies?

Our research findings brought out certain surprising results. We had hypothesized that the morphological features of meibomian glands we looked at had degrees of severity and our external eye disease specialists derived a composite score by their perceived degrees of severity. To our surprise we found that the presence of tortuous meibomian glands were good for dry eyes as they correlated with longer tear break up time and longer Schirmer test lengths. We also found ghost glands to be less frequent in the eyes of subjects with Sjogren's syndrome. These types of glands that are present in almost all eyes that show meibomian gland atrophic changes in dry eye subjects have not received much attention but may be an important morphological feature to investigate in future studies. Histopathological studies on these glands would be extremely useful. Our finding needs to be validated in future larger studies. Going forward, I think that longitudinal studies with meibography images that have good lid eversion and focus, taken at regular intervals through several years, both in dry eye subjects as well as normal controls will give us a comprehensive insight into whether and how much these MG morphological features play a role in dry eyes.



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# Keratoconus: Can it be caused by atopy and contact lens wear?

By Samer Hamada

Keratoconus has been defined as a multifactorial disease, where there are genetic and environmental factors involved in the disease pathology. The role of mechanical stress on the cornea has been extensively studied over the last few years. It is believed that eye rubbing can trigger keratoconus to manifest in genetically predisposed individuals. Some studies also suggest that eye rubbing alone without the presence of keratoconus genes would still cause keratoconus to appear and progress. It has been shown that the mechanical stability of the cornea is weakened as a result of biochemical changes induced by eye rubbing. If we apply the same logic then one would assume that any source of ocular surface inflammation and instability could lead to destructive changes of the biomechanical stability of the cornea. It has been established that there is a positive association between keratoconus and various ocular surface inflammatory diseases, ranging from dry eye disease to atopic eye disease and other inflammatory and vascular disorders, to severe autoimmune-related eye diseases. If we observe a cohort of keratoconic patients we will find that dry eye disease is a prominent comorbidity. The real question is, could keratoconus develop as a result of inflammatory changes which affect the tear film? If that is correct then subsequently could we really manage a progressive keratoconus or stop keratoconus occurrence, by modifying ocular surface factors or optimising ocular surface? Ocular surface microenvironment optimisation has been key in treating dry eye disease, so would it be useful to treat keratoconus?

Allergic eye disease including vernal and atopic kerato-conjunctivitis is another cause of poor ocular surface stability. It is unclear whether atopy has a direct effect on keratoconus progression or if eye rubbing in patients with atopic disease is the direct cause of keratoconus. However inflammatory markers are present in keratoconus patients who were not known to have allergic eye disease or dry eye disease. One may think that eye rubbing is to blame, especially as there have been cases of unilateral keratoconus observed on the side of the dominant hand. The debate is whether eye rubbing related corneal trauma alone is responsible for keratoconus without the presence of triggering inflammatory biomarkers for example in the absence of known surface



inflammatory markers. One study estimated that one out of three keratoconus patients had atopy. There are obviously various confounding factors including defining those with atopic disorder. One of the largest meta-analysis by Hashemi et al (Cornea. 2020) could help in this controversy. The authors looked at various risk factors of keratoconus by reviewing 29 studies on subjects from 15 countries. What they found was interesting, the risk to develop keratoconus was three times higher in subjects who had abnormal eye rubbing on a daily basis, compared with those who did not have the habit of rubbing their eyes. Conditions such as asthma, allergy, and eczema were all identified as risk factors in the subject group, however atopy did not increase the risk of keratoconus. The authors concluded that the atopy is a causal pathway to keratoconus and can be considered as an indirect cause.

The second point I want to discuss here is whether contact lenses wear would contribute or be considered as a risk factor for keratoconus. The role of chronic inflammatory changes associated with contact lenses in causing keratoconus, remain controversial. We know that most keratoconic patients will need contact lenses to improve their vision, but the question is if contact lenses wear through exertion of external pressures would trigger the progression of keratoconus? So why could contact lenses have this destructive effect on the cornea? There are many reports discussing how contact lenses interfere with normal corneal physiology and affect the ocular surface, corneal and conjunctival epithelium, stream, and even endothelial cells of the cornea. One common example of how contact lenses could affect the corneal curvature is a corneal warpage, which is not unusual to see in patients with chronic contact lens wear. The effect of contact lenses goes further, affecting keratocytes apoptosis and even the cornea endothelial cells shape and sizing (increased cells polymegathism and pleomorphism). Is this chronic irritation from daily contact lens wear or is it the trauma to the ocular surface and cornea from inserting and removing contact lenses on a daily basis? We should not forget that contact lens wearers are more likely to rub their eves due to ocular surface irritation. Some believe that the traumatic effect from the contact lenses manipulation, insertion and removal is

insult to the corneal epithelium and stroma by the chronic use of contact lenses. It has been established that prolonged contact lens wear can induce mechanical micro-trauma of the corneal epithelium, stimulating the release of various types of cytokines such as interleukin-1 and the effect on reduction of keratocytes cell density. There has also been evidence of up-regulation of various degrading enzymes that are directly linked to the oxidative stress and degradation of corneal collagen layers, such as MMPs mainly MMP-9 and MMP-13 in patients with keratoconus who wear rigid contact lenses. Confocal microscopy of those patients found depletion of keratocytes from the anterior corneal stroma. Furthermore, it is known that tear film of contact lenses wearers is of high osmolarity and is rich with pro-inflammatory mediators. There is then no doubt that contact lens wear can contribute to dry eye syndrome. The release of inflammatory mediators and feeding into the vicious circle of dry eve disease, which will allow for worsening of ocular surface inflammation, leading to destructive changes on the corneal collagen layers. The contact lenses effect can be summarised by the following:

Micro-trauma to corneal Epithelium Imbalanced surface microenvironment Pro inflammatory status Keratocytes apoptosis Collagen destruction However, we know that there are many patients who stop wearing contact lenses after 10 or 15 years of use and the keratoconus continued to progress. The argument here is whether the destruction has started already, and cessation of contact lens wear would not influence that process. The decision of what to advise patients regarding stopping or reducing contact lenses wear remains a clinical decision by the treating eye specialist. However, there is no question that optimising the ocular surface and minimising the micro-trauma from contact lenses use must be considered when allowing the patient to continue their contact lens use. Moreover, educating patients on risks associated with contact lenses and specific techniques to minimize eye trauma when inserting or removing contact lenses must be considered. More importantly, ensuring that any dry eye disease (which is commonly present among contact lenses wearers) is proactively managed.



The association between keratoconus and dry eye disease, atopic diseases, and contact lenses use, remains a controversy with no clear evidence to suggest whether there is a direct cause and effect relationship. In the light of limited evidence to suggest one way or the other it is important that patients at risk are treated carefully and appropriately to minimise the chance of keratoconus progression.



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Monday 12th July 9.00am - 5.00pm

Cornea & Cataract Day Birmingham Park Regis Hotel

UKISCRS are moving the planned 24th May meeting to, what we hope will be, an in-person\* meeting on Monday 12th July.

- Programme features: -
- A Corneal morning of Cases & Videos
- Chaired by: Prof. Srinivasan
- Topical debates

- Room 101

- Decision making for the Ocular Surface
- An afternoon of Cornea with Bita Manzouri & her all female Panel

It is our intention that the faculty, council and industry will be on-site.

We are so looking forward to seeing you! Register on the website (limited numbers).

\*The meeting will run as a 'Safer Accredited Event' with the 'All Secure Standards' in place

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