OSI

Ocular Surface Insight

Issue 12

Ocular surface considerations in glaucoma care: more than meets the eye

Corneal topography: putting dry eye on the map

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1. Holden, BA, Fricke, TR, Wilson, DA et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology. 2016; 123:1036–42. Available from: doi: DOI: 10.1016/j.ophtha.2016.01.006

Ocular Surface Insight

"If the doors of perception were cleansed, everything would appear to man as it is - infinite."

William Blake

Welcome to the Summer 2021 issue of **OSI**.

Welcome to the OSI Magazine!

As COVID 19 restrictions are reduced and a return to normal is underway, activities in hospital and private eye clinics are getting very busy and waiting lists are growing. What steps can we incorporate into our practices which could save time or reduce the waiting lists.

We are dedicated to finding ways of keeping the ocular surface healthy, perhaps by taking dry eye disease and ocular surface irregularities more seriously in the first instance. By ensuring patients understand how to manage their symptoms with a clear treatment regime, prescribing preservative free medication to make sure the ocular surface is not compromised. If we follow these basic steps, we may be able to reduce referrals, and free up clinic waiting lists?

This issue of OSI has a lot of interesting articles that I am sure you will enjoy. Arthur Cummings and Dan Stack are covering the current topic of 'The ocular implications of working from home'. What can we learn from this new phenomenon and how can we improve the related conditions for patients. Brian Tompkins and Dr Keyur Patel are back with their 3rd instalment of "The top five tools I cannot live without when diagnosing 'Ocular Surface disease', this instalment is putting Topography on the map. Ejaz Ansari is sharing his highly successful framework for screening, diagnosing and treating ocular surface disease before surgery. Another highlight is a case study from Stylianos Georgoulas et al on how relatively small steps in glaucoma treatment regimens can make a huge impact on a patient's quality of life.

Finally, we are really thrilled to announce that OSI will have a joint one day symposium with The Medical Contact Lens & Ocular Surface Association (MCLOSA). This exciting collaboration will take place on the 26th of November in London. We really look forward to seeing everyone there in person after too many zoom calls!

Have a happy and healthy Summer!

Samer Hamada

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What's in the news?

The physical and mental burden of dry eye disease: A large population-based study investigating the relationship with health-related quality of life and its determinants

This large cross-sectional population-based study investigated the relationship between dry eye disease (DED) and health-related quality of life (HR-QoL).

Dry eye and HR-QoL were assessed in 78,165 participants (19-94 yrs, 59.2% female) from the Dutch population-based Lifelines cohort, using the WHS and the SF36 questionnaire, respectively. Logistic regression was used to assess the relationship between DED and below median Physical Component Summary (PCS) and Mental Component Summary (MCS) score, corrected for age, sex, education, BMI, and 52 comorbidities.

Overall, the results showed that, 8.9% of participants had DED. Participants with DED had an increased risk of low PCS (OR 1.54 (95% CI 1.46-1.62)) and MCS scores (OR 1.39 (95% CI 1.32-1.46), corrected for age and sex. This risk remained significant after correction for comorbidities ($P < 0.0005$). Increasing DED symptom frequency was associated with decreasing HR-QoL ($P < 0.0005$). Undiagnosed DED subjects had a significantly increased risk of low mental HR-QoL with increasing dry eye symptoms compared to diagnosed subjects ($P < 0.0005$). Compared to allergic conjunctivitis, glaucoma, macular degeneration and retinal detachment, DED showed the highest risk of low HR-QoL. Compared to other common systemic and chronic disorders, such as depression, rheumatoid arthritis, and COPD, DED was distinctive by having a substantial reduction in both PCS and MCS.

The conclusion of the study was that DED is associated with substantial reductions in both physical and mental HR-QoL, also after correction for associated comorbidities. Not having a diagnosis is associated with worse mental HR-QoL in subjects with severe DED. Our results underline the importance of recognizing dry eye as a serious disorder.

Ocul Surf. 2021 May 24;21:107-117.doi: 10.1016/j.jtos.2021.05.006.

Authors: Mathias Kaurstad Morthen , Morten Schjerven Magno, Tor Paaske Utheim, Harold Snieder, Christopher J Hammond, Jelle Vehof

The relationship between alcohol consumption and dry eye

The purpose of this study was to assess the association between dry eye disease (DED) and alcohol consumption using a large population-based cohort.

There were 77,145 participants (19-94 years, 59% female) from the Dutch Lifelines cohort were cross-sectionally assessed for DED using the Women's Health Study (WHS) dry eye questionnaire. Alcohol intake was assessed using self-reported food frequency questionnaires. The relationship between DED and alcohol use was analyzed using logistic regression, corrected for age, sex, BMI, smoking status, education, income, and 55 potentially confounding comorbidities.

Overall, 30.0% of participants had symptomatic dry eye. Alcohol use significantly increased the risk of symptomatic dry eye in females (odds ratio [OR] 1.095, 95%CI 1.045-1.148), but not in males (OR 0.988, 95%CI 0.900-1.084). Contrarily, in male drinkers, increasing alcohol intake (in 10 g/day) had a protective effect on symptomatic dry eye (OR 0.962, 95%CI 0.934-0.992), which was not seen in females (OR 0.986, 95%CI 0.950-1.023). Alcohol use and intake had a sex-specific effect on all outcomes of DED assessed: symptomatic dry eye, highly symptomatic dry eye, clinical diagnosis, and WHS definition dry eye.

This large population-based study found alcohol use to have a clear sex-specific effect on DED, presenting as a risk-factor only in females. This adds to the evidence of sex-specific pathophysiological mechanisms of dry eye and illustrates the importance of sex stratification in studies investigating DED. The mild protective effect of increased alcohol intake in male drinkers is advised to be interpreted with caution, as alcohol's other health effects might be of greater clinical significance.

Ocul Surf. 2021 May 21;21:87-95.doi: 10.1016/j.jtos.2021.05.005. Online ahead of print.

Authors: : Morten Schjerven Magno, Tishelle Daniel, Mathias Kaurstad Morthen, Harold Snieder, Nomdo Jansonius , Tor P Utheim , Christopher J Hammond , Jelle Vehof

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What's in the news?

Alternative therapies for dry eye disease

Dry eye disease (DED) is a multifactorial disease affecting approximately 5-50% of inividuals in various populations. Contributors to DED include, but are not limited to, lacrimal gland hypofunction, meibomian gland dysfunction (MGD), ocular surface inflammation, and corneal nerve dysfunction. Current DED treatments target some facets of the disease, such as ocular surface inflammation, but not all individuals experience adequate symptom relief. As such, this review focuses on alternative and adjunct approaches that are being explored to target underlying contributors to DED.

Recent findings in neuromodulation, stem cell treatments, and oral royal jelly have all been studied in individuals with DED and lacrimal gland hypofunction, with promising results. In individuals with MGD, devices that provide eyelid warming or intense pulsed light therapy may reduce DED symptoms and signs, as may topical Manuka honey.

For those with ocular surface inflammation, naturally derived anti-inflammatory agents may be helpful, with the compound trehalose being farthest along in the process of investigation. Nerve growth factor, blood-derived products, corneal neurotization, and to a lesser degree, fatty acids have been studied in individuals with DED and neurotrophic keratitis (i.e. corneal nerve hyposensitivity). Various adjuvant therapies have been investigated in individuals with

DED with neuropathic pain (i.e. corneal nerve hypersensitivity) including nerve

blocks, neurostimulation, botulinum toxin, and acupuncture, although study numbers and design are generally weaker than for the other DED sub-types.

Several alternatives and adjunct DED therapies are being investigated that target various aspects of disease. For many, more robust studies are required to assess their sustainability and applicability.

Curr Opin Ophthalmol. 2021 Jul 1;32(4):348-361.doi: 10.1097/ICU.0000000000000768.
Authors: Rhiya Mittal, Sneh Patel, Anat Galor

What's in the news?

Effectiveness of 0.66% Povidone-Iodine Eye Drops on Ocular Surface Flora before Cataract Surgery:

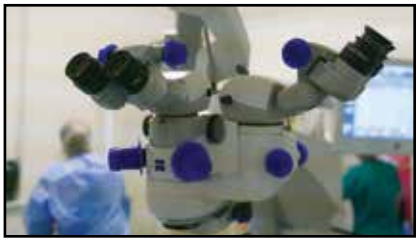
A Nationwide Microbiological Study

A multicenter, nonrandomized, prospective, controlled study was conducted to evaluate, as perioperative prophylactic treatment, the anti-infective effectiveness of 0.66% povidone-iodine eye drops (IODIM®) against the bacterial flora of the conjunctival surface of patients who undergo cataract surgery.

Eye drops containing 0.66% povidone-iodine were applied to the eye undergoing cataract surgery; the untreated contralateral eye was used as control. One hundred and twenty patients set to receive unilateral cataract surgery were enrolled in 5 Italian Ophthalmology Centers and pre-treated for three days with 0.66% povidone-iodine eye drops.

The contralateral eye, used as control, was left untreated. Conjunctival swabs of both eyes were collected at the baseline visit and after three days of treatment, just before the cataract surgery.

A qualitative and quantitative microbiological analysis of bacterial presence was evaluated by means of bacterial culture, followed by identification. Methicillin resistance determination was also performed on staphylococci isolates. Bacterial load before and after treatment of the eye candidate for cataract surgery was evaluated and compared to the untreated eye.



Reduction, or no regrowth on the culture media of the bacterial load was observed in 100% of the study subjects. A great heterogenicity of bacterial species was found. The 0.66% povidone-iodine eye drops, used for three days prior to cataract surgery, were effective in reducing the conjunctival bacterial load.

The 0.66% povidone-iodine eye drops (IODIM®) might represent a valid perioperative prophylactic antiseptic adjuvant treatment to protect the ocular surface from microbial contamination in preparation of the surgical procedure.

J Clin Med. 2021 May 19;10(10):2198.doi: 10.3390/jcm10102198

Authors: Rosario Musumeci, Pasquale Troiano, Marianna Martinelli, Matteo Piovella, Claudio Carbonara, Scipione Rossi, Giovanni Alessio, Luisa Molteni, Claudio Giuseppe Molteni, Laura Saderi, Giovanni Sotgiu, Clementina Elvezia Cocuzza

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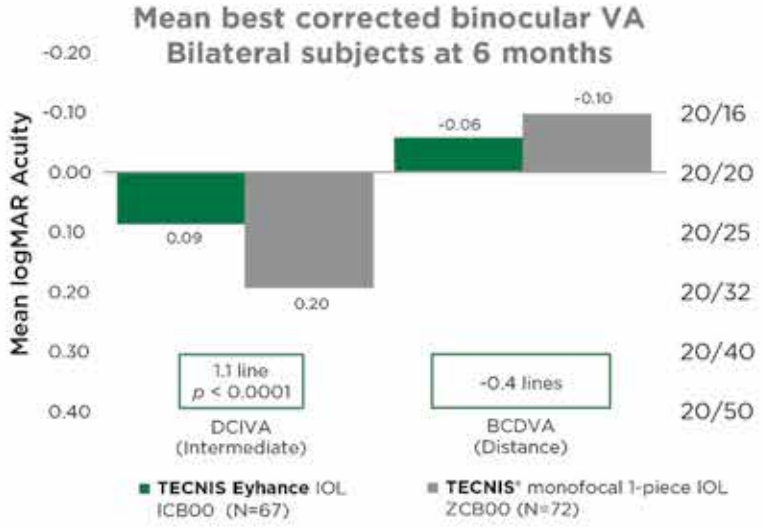

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Reference

1. Data 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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To reduce possible systemic absorption, perform punctal occlusion for one minute immediately after instilling each drop. If more than one topical ophthalmic medicinal product is being used, the medicinal products should be administered at least five minutes apart. **Paediatric population:** No data are available. **Contra-indications:** Known hypersensitivity to any ingredient. **Warnings and Precautions:** Latanoprost may gradually change eye colour by increasing the amount of brown pigment in the iris and this may be permanent. Unilateral treatment can result in permanent heterochromia. Change in eye colour has predominantly been seen in patients with mixed coloured irides, is usually within the first 8 months of treatment, rarely during the second or third year, and has not been seen after the fourth year of treatment. The rate of progression of iris pigmentation decreases with time and is stable for five years. The effect of increased pigmentation beyond five years has not been evaluated. No further increase in brown iris pigment has been observed after discontinuation of treatment. Iris pigmentation is not associated with any negative clinical sequelae. However, regular monitoring is advised and treatment discontinued if appropriate. Exercise caution in patients with asthma as some cases of exacerbation of asthma and/or dyspnoea have been reported. Use with caution in patients with a history of herpetic keratitis, and avoid in cases of active herpes simplex keratitis and in patients with history of recurrent herpetic keratitis specifically associated with prostaglandin analogues. Caution should also be used for chronic angle closure glaucoma, open angle glaucoma of pseudophakic patients, pigmentary glaucoma, inflammatory and neovascular glaucoma, inflammatory ocular conditions, congenital glaucoma, aphakic patients, pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, patients with known risk factors for cystoid macular oedema, or during the perioperative period of cataract surgery. In patients with known predisposing risk factors for iritis/uveitis, latanoprost can be used with caution. Periorbital skin discolouration has been observed mainly in Japanese patients. This is not permanent and may reverse while continuing treatment. Eyelashes and vellus hair in the treated eye and surrounding areas may change by increasing length, thickness, pigmentation, number of lashes or hairs and misdirected growth of eyelashes. Eyelash changes are reversible upon discontinuation of treatment. MONOPOST contains macrogolglycerol hydroxystearate (castor oil polyoxyl hydrogenated) which may cause skin reactions. No long-term safety data are currently available on this excipient. **Fertility:** No effect on fertility from latanoprost in animal studies. **Pregnancy:** Do not use MONOPOST during pregnancy. **Lactation:** Do not use or stop breast feeding. **Driving and Using Machines:** In common with other eye preparations, instillation of eye drops may cause transient blurring of vision. Until this has resolved, patients should not drive or use machines. **Interactions:** Paradoxical elevations in intraocular pressure have been reported following ophthalmic administration of two prostaglandin analogues. Therefore, the use of two or more prostaglandin, including analogues or derivatives, is not recommended. **Undesirable Effects:** The majority of adverse events relate to the ocular system. Most ocular adverse events are generally transient and occur on dose administration. **Infections and Infestations:** *Rare:* Herpetic keratitis. **Nervous System Disorders:** *Uncommon:* Headache; Dizziness. **Eye Disorders:** *Very common:* Iris hyperpigmentation; mild to moderate conjunctival hyperaemia; eye irritation (burning, grittiness, itching, stinging, foreign body sensation); eyelash and vellus hair changes of the eyelid (increased length, thickness, pigmentation and number of eyelashes). *Common:* Punctate keratitis, mostly without symptoms; blepharitic eye pain, photophobia, conjunctivitis. *Uncommon:* Eyelid oedema; dry eye; keratitis; vision blurred; macula oedema including cystoid macular oedema; uveitis. *Rare:* Iritis; corneal oedema; corneal erosion; periorbital oedema; trichiasis; distichiasis; iris cyst; localised skin reaction on the eyelids; darkening of the palpebral skin of the eyelids. *Very rare:* Periorbital and lid changes resulting in deepening of the eyelid sulcus. **Cardiac Disorders:** *Uncommon:* Angina; palpitations. *Very rare:* Unstable angina. **Respiratory, Thoracic and Mediastinal Disorders:** *Uncommon:* Asthma; dyspnoea. *Rare:* Asthma exacerbation. **Skin and Subcutaneous Tissue Disorders:** *Uncommon:* Rash; pruritis. **Musculoskeletal and Connective Tissue Disorders:** *Uncommon:* Myalgia; arthralgia. **General Disorders and Administration Site Conditions:** *Uncommon:* Chest pain. **Paediatric Population:** No data are available with Monopost. Report any suspected adverse reactions via www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. **Overdose:** Apart from ocular irritation and conjunctival hyperaemia, no other ocular side effects are known if MONOPOST is overdosed. Treatment should be symptomatic. **Storage:** Store below 25°C. After first opening of the sachet: use the single-dose containers within 10 days. After first opening of the single-dose container: use immediately. **Legal Category:** POM. **Basic NHS Price:** £8.49 for 30 pack, £25.47 for 90 pack. **PL Number:** PL 20162/0015. **PL Holder:** LABORATOIRES THEA, 12 RUE LOUIS BLERIOT, 63017 CLERMONT-FERRAND CEDEX 2, France. **Date of Preparation:** 27/02/2020

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References: 1. Rouland, J.F. et al. Br J Ophthalmol. 2013; 97(2):196-200 **2.** Miniuk-Hojlo, M. et al. Eur J Ophthalmol 2019; 29(2): 210– 215 **3.** Munoz-Negrete, F.J. et al. Clinical Ophthalmol 2016; 11: 551-5662 **4.** MIMS. Available at: http://www.mims.co.uk/Accessed 12/02/2020

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Théa let's open our eyes

MONO0002-FEB2020

Ocular surface considerations in glaucoma care: more than meets the eye

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Background

Ocular surface disease (OSD) is a visually significant ocular co-morbidity that is prevalent in 40-59% of all glaucoma patients (Jaenen et al., 2007). The majority of patients depend on topical therapy to reduce intraocular pressures and therefore prevent visual loss. These drops however contain several excipients, including preservatives, that are known to negatively affect the ocular surface and tear film, resulting in a reduced quality of life for patients (Badouin., 2008).

In cases of refractory glaucoma, despite the use of maximal tolerated medical therapy, trabeculectomy remains the surgical gold standard. First described in the 1960s by Kearns and Watson, trabeculectomy surgery involves the formation of an alternative transscleral route for aqueous towards the subconjunctival space by creation of a trans-scleral fistula, resulting in the formation of a filtering bleb. Unfortunately, ocular surface complications following trabeculectomy surgery are not rare and frequently remain under-recognised (Ono et al., 2013).

Case

A 74-year-old Caucasian female with a known history of bilateral primary open angle glaucoma (POAG) was reviewed at the Addenbrooke's Hospital glaucoma service, after being lost to follow up for more than a year.

Her past medical history included a left sided cerebellar abscess during childhood, resulting in cerebellar ataxia. At the age of 60, she suffered from a cerebrovascular stroke involving her cerebral hemispheres and left occipital lobe. This resulted in a bilateral facial palsy, neurotrophic cornea and a right sided homonymous hemianopia. To address her right 7th nerve palsy, she had a mid-facial lift and right lower eyelid lift through a plastics service. At the age of 72, a right 1.6g upper eyelid gold weight was performed by an oculoplastics team to address significant corneal exposure, with preoperative lagophthalmos measuring 8mm in her right eye and 1-2mm in her left eye (Figure 1). She had been prescribed ocular lubricants including Celluvisc hourly PRN with Lacri-lube ointment nocte to continue indefinitely.

Figure 1. External photographs. Right eyelid with 1.6g gold weight in-situ. Right lagophthalmos is minimal and functional eyelid closure is achieved. A 2 mm left eye lagophthalmos is present.

Historical records showed that this lady had moderate POAG and baseline intraocular pressure (IOP) in the 30s, with a cup to disc ratio of 0.6 in the right eye and 0.5 in the left eye. Humphrey visual fields (HVF) had previously detected moderate field losses in both eyes (Figure 2). She had been prescribed a fixed combination of Duotrav (travoprost and timolol) therapy nocte OU and Trusopt (dorzolamide) PF BD OU. Simbrinza (brimonidine and brinzolamide) had been trialled, although this was subsequently stopped due to development of a marked allergic reaction. She had not responded to selective laser trabeculoplasty.

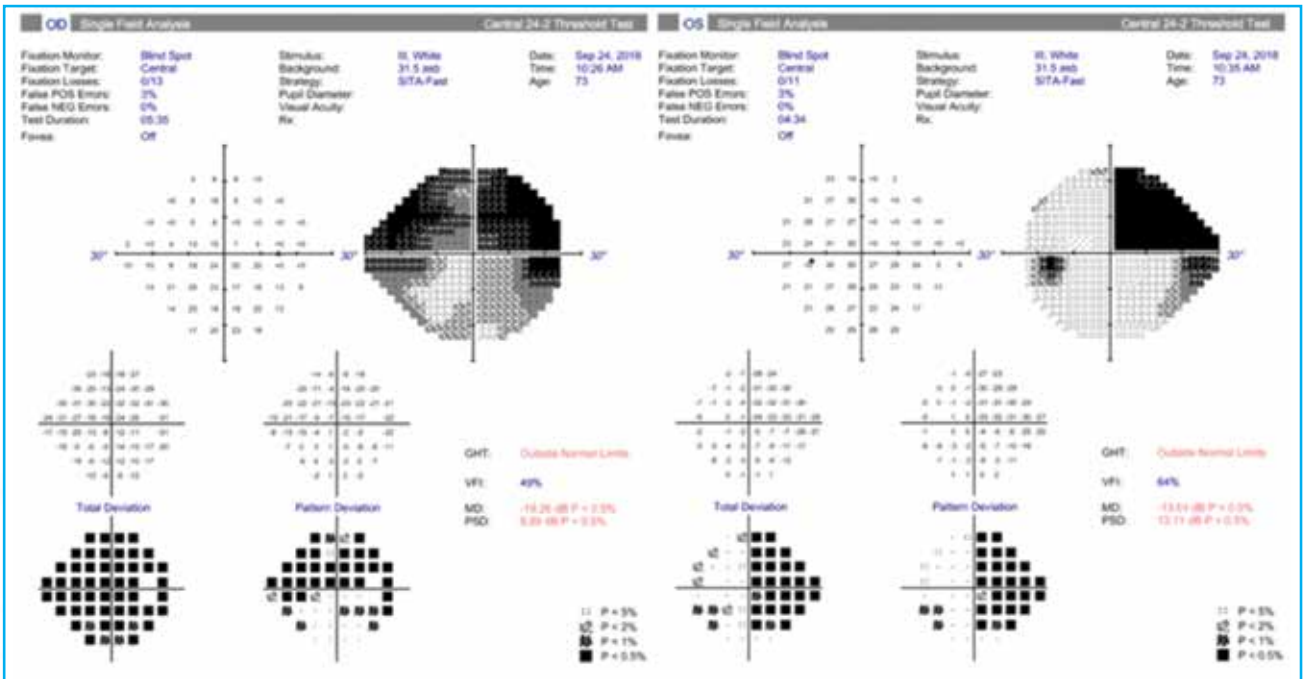

Figure 2. Humphrey visual field 24-2. Visual fields obtained from historical records confirm bilateral glaucomatous field losses in both eyes at baseline, worse right compared to left. A right upper homonymous quadrantanopic field defect is present, consistent with a previous left occipital stroke. These fields were performed 14 months prior to being lost to follow up with our service.

On the initial assessment after she was re-referred to our service, she had an IOP of 54mmHg right eye and 50mmHg in the left eye, with a best corrected visual acuity (BCVA) of 6/36 right and 6/9 left. She had reduced blink with poor Bell's phenomenon noted in both eyes. Confluent punctate epithelial erosions were noted bilaterally and nasal pterygiums OU. Bilateral nuclear sclerotic cataract was noted. Cup-to –disc ratio was 0.9 in both eyes, with bilateral advanced neuro-retinal rim thinning. Mean deviation on HVF measured -27.83dB right eye -23.12 dB in the left eye, confirming significant glaucomatous disease progression (Figure 3).

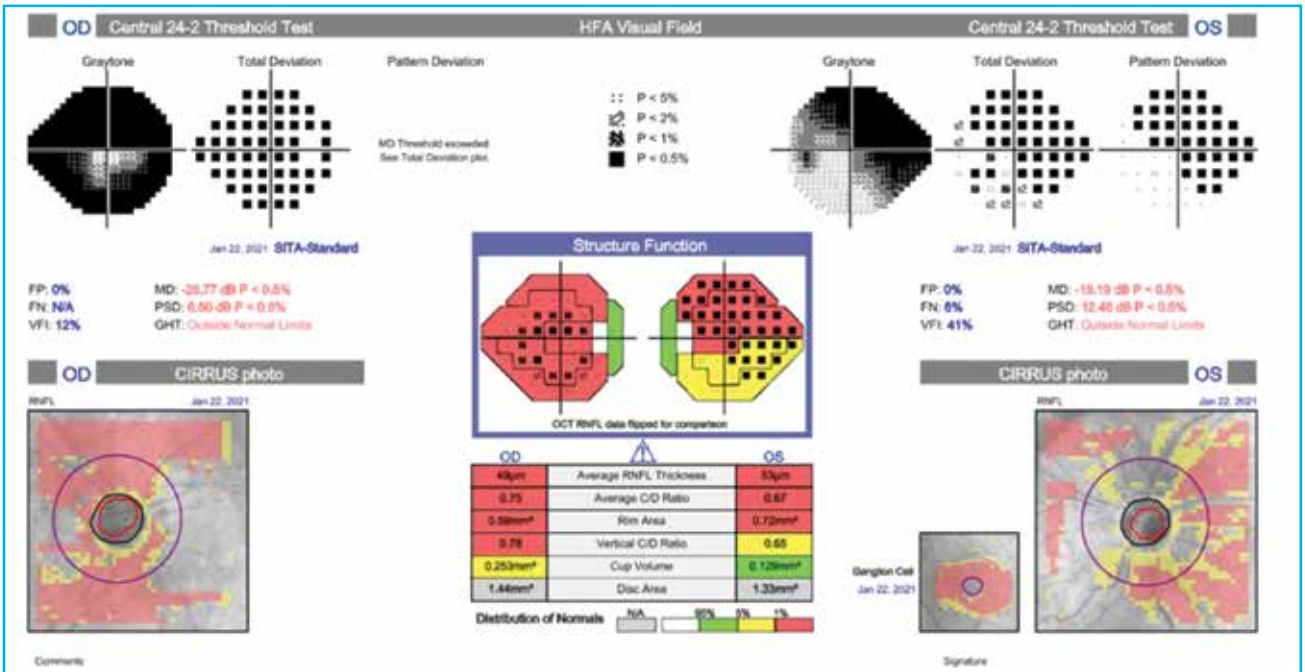

Figure 3. Combined report of the optical coherence tomography optic disc and 24-2 Humphrey field test, performed on follow up testing. Advanced retinal nerve fiber layer thinning is noted in both eyes. Visual field confirms significant progression of glaucoma, compared to baseline.

On further questioning, the patient admitted that she had self-ceased all her topical therapy, as she felt that these were making her eyes very uncomfortable, red and inflamed. The patient was educated regarding the importance of medication compliance. Her topical glaucoma was recommenced and an urgent right trabeculectomy was arranged. The patient was commenced on Diamox (acetazolamide) 250mg BD as bridging therapy. In addition, Hylo-Forte (sodium hyaluronate) eyedrops QDS and Xailin eye ointment were also added on to her regime, given that a poor ocular surface was likely contributing to her multiple eyedrop intolerances.

The patient underwent an uncomplicated right trabeculectomy with Mitomycin C (0.2mg/mL) applied to the sclera for 3 minutes. Post –operatively she was prescribed preservative free Dexamethasone 0.1% eyedrops 2-hourly, although her compliance with this regime was noted to be variable. Her right eye vision fluctuated in this postoperative period, with BCVA between 6/36 to counting fingers and relating to the variable state of a dry ocular surface. Given her poor vision, she was referred to the sensory team in social services and additional support in the home was organised for the patient, for food as well as help with instillation of eyedrops.

At weeks 3 to 6 after surgery, she developed significant postoperative scarring and vascularization around the bleb. Both releasable sutures associated with the trabeculectomy were removed within 4 weeks from the day of surgery, and she underwent 2 episodes of bleb needling with 5-fluorouracil (5mg in 0.2ml injection) in combination with subconjunctival dexamethasone (3.3mg in 0.1mL). Despite this intervention, it was deemed that her trabeculectomy remained only partially functional (Figure 4).

Figure 4. Trabeculectomy bleb of the right eye 15 months after surgery. Vascularization is present, with a significant degree of postoperative scarring. The bleb remains mildly flat and is partially functional. Intraocular pressure is under control with the use of a single combined drop of preservative free Fixapost.

A sequential trabeculectomy in the left eye was performed 6 weeks after her initial right eye surgery. The left eye had lagophthalmos fluctuating between 2-4 mm in her clinical visits. Priority was given to reducing her intraocular pressure through an expedited trabeculectomy. Given her tendency towards aggressive postoperative scarring, a higher concentration of mitomycin 0.4mg/ml was utilized.

Postoperatively, she developed significant left corneal epitheliopathy and dellen, in part related to mitomycin C used during her surgery, a pre-existing element of neurotrophic cornea as well as worsening of her facial nerve palsy. An oculoplastics referral was made, where insertion of a 1.2 g gold weight in the left upper lid was performed on the second month post trabeculectomy of her left eye. The patient was also switched to Thealoz Duo eye drops 2-hourly for her dry ocular surface. Similar postoperative scarring responses meant that although initial IOP was maintained at 8 mmHg, it rose to 16 mmHg, and by week 3 the releasable sutures were removed to increase flow through the filtering bleb (Figure 5).

Figure 5. Trabeculectomy bleb of the left eye 14 months after surgery– the bleb is elevated. It remains partially functional. Intraocular pressure is under control with the use of a single combined drop of preservative free Fixapost.

At present, this patient has maintained a BCVA of 6/12 in the right eye and 6/9 in the left eye. Fixapost preservative free eyedrops (Latanoprost and Timolol) were commenced in both eyes, to augment her partially functioning trabeculectomies. This has achieved an IOP of 12 mmHg to 15mmHg in the right and left eye and has halted the progression of glaucoma (Figure 6). Her ocular surface shows few punctate corneal erosions with the regular use of 2 hourly Thealoz duo and Viscotears gel nocte in both eyes, and the patient remains compliant and happy on her current topical eyedrop regime.

Figure 6. Glaucoma progression analysis Visual Field Index shows stabilization of glaucoma and improvement of visual function after trabeculectomy surgery (blue arrows) and optimization of the ocular surface with preservative free lubricants.

Discussion

This case demonstrates how a dry and inflamed ocular surface may have many causes, and that OSD can present an added degree of complexity in the successful management of a patient's glaucoma. Rationalization of eyedrops in order to optimize the patient's ocular surface and prompt surgical intervention to stabilize her glaucoma and eyelid pathology was required.

Preservation and maintenance of a healthy ocular surface is multifactorial, relying on adequate blinking of the eyelids for lubrication of the ocular surface (Aragona et al., 2021). A combination of bilateral neurotrophic cornea and worsening lagophthalmos in the context of facial nerve palsy, related to our patient's previous stroke resulted in significant OSD. In particular, our patient was not only prone to developing glaucoma-OSD from her topical IOP lowering medications, but predisposed by the status of her ocular adnexa (Kastelan et al., 2013). In cases of dysfunctional or incomplete blink response, the lack of ocular protection may potentially lead to corneal problems such as conjunctival infections, acute or chronic keratitis, corneal ulcerations, and reduction of visual acuity (Biglioli et al., 2020).

The relationship between the status of the ocular surface and the success rate of trabeculectomy is well established and has been the subject of many research studies (Baudouin et al., 2004), (De Groef et al., 2013). Factors such as dry eyes, eyelid position, eyebrow ptosis, prior strabismus surgery and poor Bell's phenomenon can ultimately affect the success of glaucoma surgery (Nijm et al., 2020). Dry eye disease and inflammatory signalling related to it can significantly contribute to conjunctival scarring (Lee et al., 2013), leading to failure of the surgery. In our patient, an inflamed ocular surface likely promoted aggressive postoperative scarring responses, resulting in partially functioning trabeculectomies. Conversely, dry eye disease may be exacerbated in patients with functional filtering blebs. Cytotoxics used to augment trabeculectomy surgery such as Mitomycin C and 5 -Fluorouracil can also affect ocular surface function, promoting the development of glaucoma-OSD (Ji et al., 2016).

The chronic use of topical medical treatment can be toxic to ocular epithelial cells (Ammar et al., 2010) and can lead to neurotrophic keratopathy (Lee et al., 2013). On a physiological basis, corneal nerves and epithelial cells work synergistically through the release of trophic factors essential in ocular haemostasis and wound healing (Müller et al., 2003). Thus, a reduction in corneal sensation can promote the development of corneal epithelial defects and ulcers (Semeraro et al., 2014). Ocular surface complications , such as dellen formation secondary to trabeculectomy is not uncommon, as elevation of the limbus is necessary for bleb formation (Jampel et al., 2005). Previously identified risk factors for dellen formation include a history of superficial punctate keratopathy and a history of diabetes mellitus (Ono et al., 2013). Our patient developed corneal dellen after left eye trabeculectomy, which resolved after prompt surgical intervention with a gold weight to address lagophthalmos, as well as the regular use of preservative free ocular lubricants.

The use of preservatives in topical treatment is well known to be associated with higher OSD occurrence and secondary poor quality of life (Kumar et al., 2020). Our patient was initially commenced on a combination of eyedrops including DuoTrav and Simbrinza, which contain preservatives such as polyquad and benzalkonium chloride (Steven et al., 2021). The burden of frequent instillations of these medications, and her persistently poor ocular surface had a significant impact on her quality of life. This was reflected by her discomfort with instillation of topical therapy and eventual noncompliance, amalgamating in suboptimal IOP control and significant glaucomatous progression. We found that converting her regime to preservative free Fixapost and Thealoz Duo eye drops drastically reduced her ocular surface issues and improved compliance. We recommend the routine use of preservative-free eyedrop regimes where possible, and find that patient education remains the key to maximize compliance with these regimes.

Our case demonstrates the intimate relationship between glaucoma treatment and the important effect that this therapy has on the ocular surface, as well as the reciprocal nature of this relationship. Through the use of surgery and preservative

free eyedrop regimes, we were able to maximize this patient's quality of life. Collectively, this case demonstrates the importance of a multidisciplinary team approach to such complex patients, where systematically addressing the significant ocular co-morbidities that may impact a patient ensures that best outcomes are achieved.

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What's in the news?

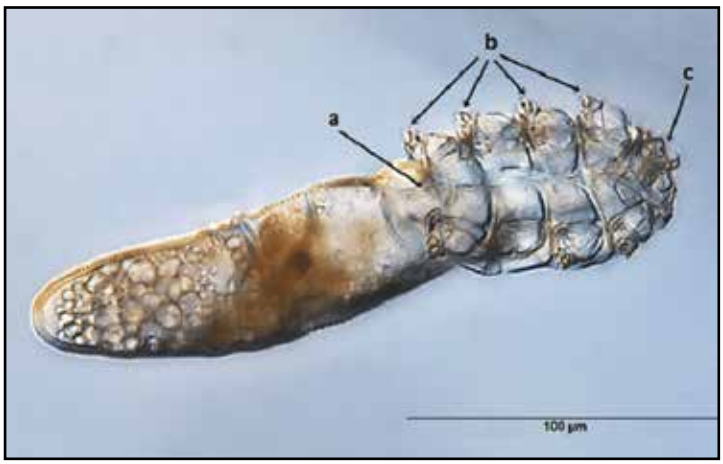
Corneal Effects of Tea Tree Oil

The purpose of this study is to report a case of corneal epithelial defects resulting from topical treatment of blepharitis with tea tree oil (TTO).

A 44-year-old man with a 1 year history of blepharitis non-responsive to eyelid hygiene was found to have signs of Demodex infestation. He was treated with a topical, off-label 50% TTO solution. Shortly afterward, the patient complained of bilateral ocular discomfort.

Slit-lamp examination revealed conjunctival injection and a corneal epithelial defect in both eyes. Treatment with lubricant, antibiotic, and steroid eye drops as well as bandage contact lenses was required to facilitate corneal healing.

Topical use of off-label, 50% concentration TTO can result in corneal epithelial defects. Eye care professionals should remain aware of this risk and only use approved, low-concentration TTO products when treating Demodex-related blepharitis.



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Authors: Brindhan Tharmarajah, Minas Theodore Coroneo

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New algorithm (ASCRS) establish the essential nature of point-of-care testing for ocular surface disease diagnosis and treatment

Regardless of visual goals, be it comfortable contact lens wear, successful refractive surgery or premium cataract surgery, achieving optimal outcomes requires a healthy, optimised ocular surface.

The tear film is the first refractive surface of the eye - 70% of the total refractive power occurs at the tear film[1]. As such, ocular surface health is crucial for obtaining reliable refractive measurements. The accuracy of these measurements supports the success of surgical outcomes, and ultimately patients' satisfaction with their vision[2].

The American Society of Cataract and Refractive Surgeons (ASCRS) now recommends a specific ocular surface disease (OSD) algorithm to evaluate the ocular surface prior to surgery[1].

The new algorithm considers osmolarity and MMP-9 essential tests for the identification of Visually Significant Ocular Surface Disease (VS-OSD). VS-OSD adversely impacts surgical outcomes and should be addressed prior to surgery.

A Structured Approach

The ASCRS recommends that symptoms are captured through a validated questionnaire. Eye care providers can capture subjective information about patients' ocular surface discomfort, visual symptoms, and the overall impact of these conditions on day-to-day activities.

However, not all patients with VS-OSD present with symptoms, and additional testing should also be performed to avoid mis-or under-diagnosis. Therefore, the ASCRS regards osmolarity and MMP-9 tests as essential, particularly in evaluation of asymptomatic patients.

Objective data drives decision making

Performing objective tear testing has multiple benefits. Tests can be performed before the patients sees the clinician, thereby reducing chair time. Osmolarity provides value to rule-in AND to rule-out OSD. In addition, osmolarity helps direct an appropriate treatment plan, expands patient education and improves therapy compliance.

Conclusion

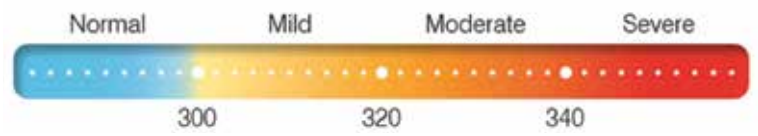
Use the ASCRS OSD algorithm to:

- incorporate a structure to identify VS-OSD
- improve diagnosis with essential point of care tests
- track therapy in weeks vs. months

... and thereby optimise surgical outcomes.

Osmolarity testing

Tear hyperosmolarity triggers a cascade of dry eye events that damage surface epithelial cells.[2] The TearLab Osmolarity System measures the osmolarity of tears with easy-to-interpret data, making the results informative whether normal or abnormal. An inter-eye difference of >8 mOsm/L or an elevated reading >300 mOsm/L is considered abnormal. Studies show that the toxicity of an abnormal tear osmolarity initiates cellular damage at levels >308 mOsm/L.[3] The TearLab Osmolarity Test provides a quick and simple method for



determining tear osmolarity using nanolitre volumes of tear fluid collected directly from the eyelid margin. This feature allows for tear collection in even the driest patients.

Benefits of Osmolarity testing

- ✓ Early, accurate DED detection
- ✓ Immediate, objective insight into ocular surface health
- ✓ Sets the stage for additional dry eye services
- ✓ Save chair time
- ✓ Efficient tracking of therapeutic response
- ✓ Enables you to have data-driven scientific conversations with your patients about their dry eye condition

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The keratoconus conundrum: the inflammatory - environmental interplay

By **Samer Hamada** & **Artemis Matsou**

Keratoconus (KC) is an ectatic corneal disorder, first described by Dr John Nottingham in 1854 in his treatise entitled 'Practical observations on the conical cornea and on the short sight and other defects of vision connected with it' [1]. His observations were further supported by other ophthalmologists conducting research in the field, such as Sir William Bowman.

Nevertheless, 167 years later and keratoconus pathophysiology and associations remain a mystery and a challenge for researchers. Extensive research conducted over the last 20 years has led to considerably better understanding of many aspects of keratoconus origin and the natural course of the disease, whilst inciting a new era in keratoconus management, which has particularly soared thanks to the enormous technological advances of the last few decades.

"Nevertheless, 167 years later and keratoconus pathophysiology and associations remain a mystery and a challenge for researchers."

This clinical entity is characterized by progressive corneal stromal thinning and structural weakening of the cornea with conical protrusion in the areas of greatest thinning [2]. It leads to progressive myopia, irregular astigmatism, scarring and visual compromise with blurry, distorted, reduced vision. It is a leading cause of corneal transplantation in the developed world affecting young individuals, most often seen in teenagers or young adults. Numerous hypotheses on its pathophysiology have been suggested, including genetic, environmental, inflammatory and even behavioural factors [3-6]. The classic dogma of KC being a degenerative, non-inflammatory disease has been challenged, with recent research indicating a crucial role of inflammation in the disease onset and progression [7, 8]. Certain environmental factors such as ocular surface disease, atopy and contact lens wear, and behaviours, such as excessive eye rubbing have also been strongly linked with KC development and progression.

The inflammatory hypothesis

The preocular tear film is a complex mixture of substances secreted from multiple sources. It has a dynamic nature, while any alterations in its composition have a direct effect on the structures it overlies; the cornea and the conjunctiva, collectively comprising the ocular surface. The tear film has been a powerful source of crucial information about the ocular surface microenvironment and has been utilized by a number of studies to investigate the biochemical changes in conditions such as keratoconus [7, 8].

"There is growing evidence of significant dysregulation of these immune pathways in keratoconic eyes"

Elevated levels of inflammatory mediators, such as proinflammatory cytokines, tumour necrosis factor, interleukins, cell adhesion molecules, and matrix metalloproteinases (MMPs) have been detected in keratoconic eyes compared to normal controls in a number of studies [9, 10].

Inflammatory cytokines such as Interleukin 1 (IL-1), IL-6, IL-17, TNF-α (tumour necrosis factor-alpha), transforming growth factor-β (TGFβ) and other growth factors, have all been detected at greater concentrations in keratoconic corneas. These proinflammatory molecules are implicated in corneal wound healing, activation of proteolytic enzymes that degrade corneal collagen and induction of keratocyte apoptosis. There is growing evidence of significant dysregulation of these immune pathways in keratoconic eyes.

And while the extent of the inflammatory contribution in keratoconus pathogenesis is uncertain, their involvement in the tissue degradation process seen in KC is becoming increasingly apparent.

- The Interleukin 1 (IL-1) cytokines (IL-1α, IL-1β) are released by injured corneal epithelial cells into the tear film and corneal stroma after tissue damage. They augment inflammation and abnormal wound healing in KC, induce keratocyte apoptosis and enhanced tissue damage by stimulating overexpression of MMPs that directly degrade corneal collagen [11, 12].
- IL-6 levels are increased in KC corneas compared to normal, while eye rubbing, contact lens wear, vernal and atopic keratoconjunctivitis seem to augment IL-6 production. A strong correlation between IL-6 and KC stage, keratometry, pachymetry and corneal hysteresis has also been reported [8, 11].
- IL-17 is implicated in the tissue degenerative processes observed in KC (stromal thinning- weakening) through activation of corneal fibroblasts and myofibroblasts and subsequent metalloproteinase production [12].
- TNF-alpha is considered one of the pathogenic protagonists and principal mediators of the inflammatory component of KC, as its upregulation has a detrimental effect on the cornea. The significantly higher concentrations of TNF-α found in KC tear film and corneal samples leads to over-activation of MMPs and abnormal degradation of stromal collagen [13].
- TGFβ is involved in the restoration of tissue after injury. In the human cornea, it regulates extracellular matrix (ECM) reorganization. A dysfunctional TGF-β axis has been implicated in the pathogenesis of keratoconus, through overexpression of inflammatory mediators, the protease cascade of MMPs, and promotion of corneal fibrosis in KC [2, 9].
- Other growth factors such as the nerve growth factor (NGF), the vascular endothelial growth factor (VEGF) and epidermal growth factor (EGF) have also been implicated in disrupted corneal homeostasis, on the account of causing damaged corneal epithelial cell proliferation and pathologic corneal wound healing response in KC eyes [11].
- Matrix metalloproteinases (MMPs) have been in the spotlight of the research on KC pathogenesis, with much speculation over their contribution to disease onset and

progression. An imbalance and dysregulation of the proteolytic activity of MMPs can lead to tissue remodeling and degradation of ECM components, which is the hallmark of corneal ectasia. The more widely studied MMPs are MMP-9, MMP-1 and MMP-2 [14, 15].
The association of MMP-9 (gelatinase B) with keratoconus seems to be the most comprehensively investigated so far, as it constitutes the primary matrix-degrading enzyme in the human cornea. Over-expression of MMP-9 in keratoconic corneas compared to controls has been reported across a number of different studies. A positive correlation between the severity of KC and MMP-9 levels and negative correlation between corneal pachymetry and MMP-9 levels has also been suggested.
Significantly higher expression of MMP-1 has been detected in the tear film of keratoconic eyes compared to controls, with a 1.9 times higher level of proteolytic activity in the tear film of KC subjects.
Significantly raised levels of MMP-3, -7, -13 were found in the tear film of keratoconic eyes compared to controls by Balasubramaniam et al [16], along with raised levels of MMP-13 (collagenase 3) in normal corneas after 60 seconds of eye rubbing.
Kolozsvari et al [11] showed increased tear expression of MMP-13 in KC eyes and a strong positive correlation of MMP- 13 with the severity of the disease.

It is therefore clear that various studies have independently reported an inflammatory microenvironment being present in eyes with keratoconus compared to normal controls, with higher expression of a number of inflammatory mediators and degrading enzymes, leading to oxidative stress, keratocyte apoptosis and extracellular matrix degradation- thinning-ectasia. This undeniable evidence of an inflammatory component in KC, generates further questions into the reasons why inflammation is present, and which factors - if any- can provoke this inflammatory state.

The environmental insults

In addition to the discovery of the inflammatory microenvironment of KC, what has also come to light over the years, is the association of keratoconus with several ocular surface disorders, or systemic diseases with ocular surface implications. Strong links between KC and various environmental factors which were previously considered a coincidental correlation have been suggested.

- Atopy and allergic diseases: The increased incidence of atopy in keratoconus patients has been well represented in the literature since the beginning of the 20thth century. However, the evidence has been conflicting as to whether the atopy itself or eye rubbing- the indirect consequence of atopy induced itch- is a causative factor of keratoconus.
In their multivariate case-control study, Bawazeer et al [17] showed that while a history of atopy was significant in the univariate analysis, eye rubbing was the only risk factor that was significant in both the univariate and multivariate level, invalidating a direct association between atopy and KC. It is estimated that approximately one out of three patients with KC has an underlying atopic disorder, although the prevalence of atopy varies widely in the literature (between 1.8% and 57%), due to different definitions of atopy/ allergy and lack of standardized classification [18]. In a large meta-analysis on the prevalence and risk factors of KC by Hashemi et al [19], although asthma, allergy, and eczema were all identified as effective risk factors for keratoconus, atopy per se did not increase the risk of the disease. As a result, atopy can be considered an essential component of the KC causal pathway, but only an indirect cause of keratoconus.
- Vernal keratoconjunctivitis (VKC)/ Atopic keratoconjunctivitis (AKC): The association between VKC/ AKC and KC is also well known, with a reported incidence of up to 26.8% of KC among VKC patients [20]. Kera toconus in association with VKC tends to begin at a much younger age, progress at a faster rate, escalate to a more advanced stage, while acute corneal hydrops is also more common in this group [21]. The association of AKC with KC has been reported less frequently in the literature, however a recent large matched cohort study concluded that the incidence rate of KC was 2.49 times higher in AKC than controls. Even after adjusting for potential confounders, AKC patients were 2.25 times more likely

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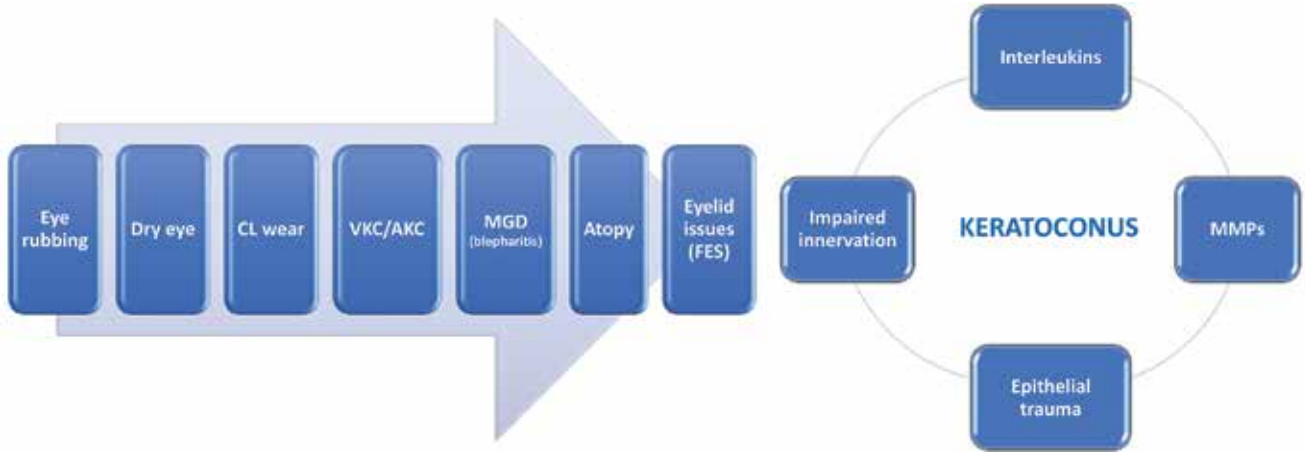

to develop KC [22]. Except for the mechanical stress caused by chronic eye-rubbing related cornea trauma in allergic states, a number of inflammatory cytokines, MMPs and lysosomal enzymes have been found elevated in the tear film of patients with AKC/VKC during active and quiescent phases of the disease. A vicious cycle starting with conjunctival inflammation, leading to frequent and intense eye rubbing and release of inflammatory cytokines and degrading enzymes has the potential to

either cause corneal deformation and ectasia or induce faster and more severe progression.

- Eye rubbing: Intense and prolonged eye rubbing is now a recognized independent risk factor for development/progression of KC, to the extent that de novo development of KC secondary to vigorous eye-rubbing has also been reported. The prevalence of eye rubbing in keratoconic patients ranges in the literature from 66% to 73% and can be the result of: ocular disease, dry eye syndrome, conjunctivitis, trichiasis, blepharitis, allergic eye disease, skin conditions (rosacea, periocular eczema), "removal relief" in contact lens wearers or behavioural [6, 23, 24]. Forces applied on the globe during eye rubbing can cause IOP elevations as high as 205-310mmHg. Distending IOP forces that are in excess of the corneal resistance to them is a known mechanism of permanent corneal deformation and keratectasia [25]. In addition, the epithelial trauma sustained from cyclic shear stress during eye rubbing and the corneal biomechanical fatigue, can lead to corneal thinning, loss of rigidity, tissue weakening and conical protrusion. Increased enzyme activity and enzyme denaturation is also a direct consequence of the increased corneal surface temperature during eye rubbing, with subsequent upregulation of collagenase activity. Finally, the levels of inflammatory and tissue degrading enzymes have been found significantly elevated after 60 seconds of eye rubbing in non keratoconic eyes, indicating the additional insult in the vulnerable KC prone corneas [26].

> "Evidently, keratoconic eyes present with dry ocular surface resulting from inadequate tear and mucin production, flawed corneal innervation, goblet cell loss and aberrant proteome alterations."

- Contact lens (CL) wear: CL wear and removal can be a trigger for eye rubbing ('removal-relief' rubbing), but also for mechanical micro-trauma on the corneal epithelium, thus stimulating the release of apoptotic cytokines and upregulation of degrading enzymes [24]. Contact lens wear induces an anoxic environment, mechanically stimulates the epithelial cells and favours a pro-inflammatory and matrix-degrading environment with keratocyte apoptosis and ECM remodeling. Ironically, the majority of KC patients rely on CL wear for visual correction. Currently, no strong evidence exists to suggest that contact lens wear should be avoided in KC patients.
- Dry eye: An increased prevalence and greater severity of signs and symptoms of dry eye has been reported in keratoconus patients when compared to non-KC control groups across several studies. It seems that KC subjects have greater tear film instability, with significantly lower tear film break-up time (TFBUT), higher fluorescein and Rose Bengal corneal and conjunctival staining scores, and they present predominantly decreased mucin production [27]. The drier state of the ocular surface in these individuals and its potential association with KC progression could be explained by: i) the corneal irregularity, as the conical elevation may disturb the tear film thickness and uniformity causing interrupted continuity- the most elevated areas such as the apex of the cone would be expected to be more affected, ii) reduced corneal sensitivity, since reduced density and abnormal morphology of the corneal sub-basal and stromal nerves has been reported in KC, iii) reduced goblet cell density, which has been detected in KC eyes on impression cytology and found related to KC severity, leading to reduced mucin production, iv) the subclinical ocular surface inflammation associated with dry eye can trigger the inflammatory cascade insinuated in KC [28]. Evidently, keratoconic eyes present with dry ocular surface resulting from inadequate tear and mucin production, flawed corneal innervation, goblet cell loss and aberrant proteome alterations.
- Meibomian gland dysfunction (MGD): Although the association of MGD with keratoconus has not been widely investigated, there is evidence that keratoconic eyes demonstrate a higher dropout in meibomian glands when compared to controls, even in the absence of clinical signs of blepharitis, while KC patients demonstrate an increased prevalence of signs and symptoms of MGD [29]. Possible mechanisms include repetitive micro-trauma from chronic mechanical rubbing (caused by the itching triggered from MGD), as well as release of inflammatory molecules such as MMP-9 which are found increased in MGD. Chronic exposure of the inferior cornea to an amplified pool of inflammatory mediators/matrix-degrading factors, aggregated in the inferior tear meniscus of MGD eyes, can have a significant impact on disease onset, progression and severity, while reversible keratoconus-like topography has been de\scribed in a rosacea-MGD case.

> "Prompt and adequate management of allergic eye disease, VKC and AKC, dry eye and MGD, and timely treatment escalation are imperative."

- Floppy eyelid syndrome (FES): A significantly higher level of FES in KC patients (up to 71%) has been reported [30]. Upregulation of MMP-9 has again been identified as a possible link between the two conditions, as have the ocular surface mechanical trauma sustained in FES due to abnormal eyelid and tarsal laxity and also the associated dry eye disease.

Can we call the shots in keratoconus onset and/or progression?

An ideal scenario for all corneal specialists and ophthalmologists dealing with keratoconus, is to be able to control and modify all possible factors that can trigger the onset or define the progression of keratoconus. Aside from the genetic predisposition, which consists a separate similarly complex issue, being in a position to manipulate epigenetic processes that can trigger KC or lead to progression is an alluring concept that could have a profound impact on the future approach in keratoconus management. Unfortunately, very few strategies exist currently in that direction. Amongst them, a crucial one has been identifying eye rubbers and counselling them thoroughly on the impact that this action has on their cornea. Prompt and adequate management of allergic eye disease, VKC and AKC, dry eye and MGD, and timely treatment escalation are imperative. The observed high frequency of raised MMP-9 levels in KC eyes, has led to the suggestion that point-of-care tear fluid MMP-9 testing would

be meaningful to be incorporated as part of the standard evaluation of KC patients along with keratometry and corneal tomography. Topical Cyclosporine A (CSA) has been suggested as an effective way of reducing MMP-9 levels, thus reducing the inflammatory stimulation in tears of KC eyes, while even a progression-arrest effect has been proposed, which however needs to be validated with further studies [31]. Future studies on targeted, specific anti-cytokine therapies such as TGFβ pathway blockage, or IL-1α and IL-1β inhibitors would also be appealing.

Beyond doubt, exploring non-invasive ways to manage keratoconus through manipulation of environmental factors or local ocular surface forces present an attractive alternative, which could materialize in the near future with the advent of molecular, biochemical and immunochemistry research strategies.

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What's in the news?

Smart Eye Camera:

A Validation Study for Evaluating the Tear Film Breakup Time in Human Subjects

This study aimed to demonstrate the efficacy of a "Smart Eye Camera (SEC)" in comparison with the efficacy of the conventional slit-lamp microscope by evaluating their diagnostic functionality for dry eye disease (DED) in clinical cases.

This retrospective study included 106 eyes from 53 adult Japanese patients who visited the Ophthalmology outpatient clinics in Keio University Hospital from June 2019 to March 2020. Tear film breakup time (TFBUT) and corneal fluorescence score (CFS) measurements for the diagnosis of DED were compared between the conventional slit-lamp microscope and SEC.

The objective findings of DED showed that there was a strong correlation between the conventional slit-lamp microscope and SEC with respect to TFBUT and CFS results (Spearman's r = 0.887, 95% confidence interval [CI] = 0.838-0.922, and r = 0.920, 95% CI = 0.884-0.945, respectively).

The interobserver reliability between the conventional slit-lamp microscope and SEC showed a moderate agreement (weighted Kappa κ = 0.527, 95% CI = 0.517-0.537 and κ = 0.550, 95% CI = 0.539-0.561 for TFBUT and CFS, respectively). The diagnostic performance of the SEC for Asia Dry Eye Society diagnostic criteria showed a sensitivity of 0.957 (95% CI = 0.841-0.992), specificity of 0.900 (95% CI = 0.811-0.927), positive predictive value of 0.880 (95% CI = 0.774-0.912), and negative predictive value of 0.964 (95% CI = 0.869-0.993). Moreover, the area under the receiver operating characteristic curve was 0.928 (95% CI = 0.849-1.000).

The conclusion reached was that Compared with the conventional slit-lamp microscope, SEC has sufficient validity and reliability for diagnosing DED in the clinical setting.

Translational relevance:
The SEC can portably evaluate TFBUT in both basic research and clinical care.

Authors: Eisuke Shimizu, Hiroyuki Yazu, Naohiko Aketa, Ryota Yokoiwa, Shinri Sato , Taiichiro Katayama , Akiko Hanyuda , Yasunori Sato, Yoko Ogawa , Kazuo Tsubota.

Transl Vis Sci Technol. 2021 Apr 1;10(4):28.doi: 10.1167/tvst.10.4.28.

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VISU/UK/VIEVO/0015 Date of Prep: January 2021

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the eye health company

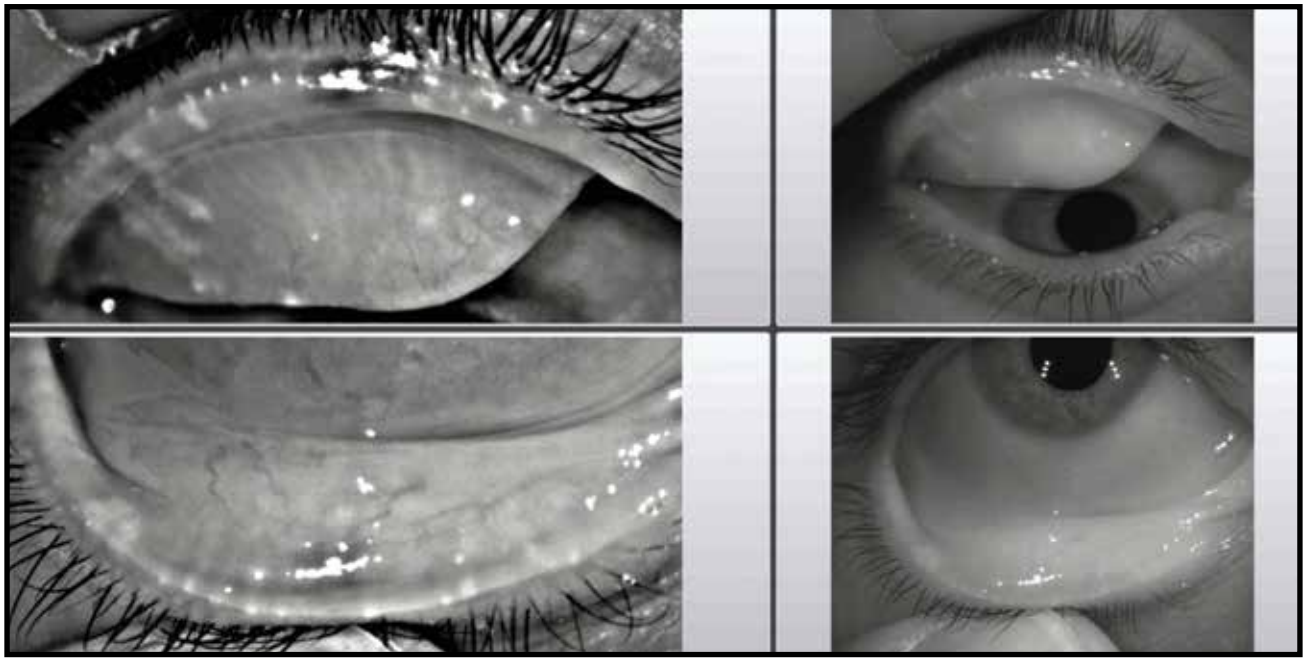
Establishing a healthy ocular surface enables premium post-operative outcomes.

Rely on a consistent framework for screening, diagnosing and treating ocular surface disease before surgery.

By **Ejaz Ansari**, FRCOphth, MD

With the latest advancements in intraocular lens (IOL) and refractive laser technology, e.g. LASIK, patients increasingly expect premium vision.

To them this means that, since they are making a significant out-of-pocket investment, they want to be spectacle free for virtually all situations and conditions. Fortunately, with a systematic approach, surgeons can be empowered to deliver on the promise of today's technology, providing new possibilities for patients' postoperative vision.



To have success with premium procedures, surgeons must have confidence in their surgical skills, clinical processes, and their staff. Consistently nailing the refractive target is imperative, and it requires the elimination of any preventable presurgical errors. The accuracy of important measurements such as biometry, and in turn IOL selection, depends on the health of the corneal surface. Un-controlled dry eye disease (DED) and other ocular surface disease (OSD) have been deemed by the American Academy of Ophthalmology (AAO) as a "contraindication" to keratorefractive surgery due to the fact that the accompanying irregularities in the tear film cause light scatter, higher order aberrations and image degradation. (1-4) Anterior blepharitis can increase the risk of endophthalmitis, and any eye surgery will worsen the symptoms of existing OSD.(5)

The Problem

OSD in patients presenting for cataract surgery is more prevalent than may be recognized. Trattler and colleagues looked at 136 patients (≥55 years of age) undergoing cataract surgery in their Prospective Health Assessment of Cataract Patients' Ocular Surface (PHACO) multicenter observational study.(6) They sought to determine the incidence and severity of DED in this group; the mean age was approximately 71 years, and almost 60% had never complained of foreign body sensation. A surprising finding in this study was that 80% of these patients in fact had signs of dry eye disease, with less than 25% having had a previous diagnosis. The study concluded that 15%-20% of patients would not have been identified with dry eye had they not been tested for dry eye in their pre-surgical consults.

Similar to the PHACO study, Gupta and colleagues reported the incidence of

OSD in patients presenting for cataract surgery to be more than 80%. Of significance, a large majority of patients who were asymptomatic and with no previous history of dry eye disease, 83%, had an abnormal tear osmolarity or matrix metalloproteinase-9 (MMP-9) level. (7)

As we know, dry eye is exceedingly common and highly prevalent in cataract-age patients. Many patients presenting for surgery have signs like abnormal osmolarity or MMP-9, each diagnostic markers of OSD, yet no symptoms and no previous OSD diagnosis. This makes it crucial that surgeons systematically screen, diagnose, and treat all patients prior to surgery.

The Disconnect

Each year, both the European Society of Cataract & Refractive Surgeons (ESCRS) and the American Society of Cataract and Refractive Surgery (ASCRS) conduct clinical practice surveys of their respective memberships. Sixty percent of respondents to the 2019 ESCRS Clinical Trends Survey said that they systematically check the ocular surface for all preoperative laser vision correction patients, 22% said they do for most cases, 12% only check the ocular surface when patients present with dry eye symptoms, and 6% said they rarely to never check. (8) For preoperative cataract surgery patients, less than half—47%—said they always assess the ocular surface, 27% said they do in most cases, 23% said they do only when patients present with dry eye symptoms, and 3% said they rarely to never check the ocular surface.

In the 2018 ASCRS clinical survey results, 90% of respondents agreed that mild to moderate dry eye significantly impacts keratometry and IOL power calculations, as well as patient satisfaction after cataract or refractive surgery. Nearly 90% say that inflammation and hyperosmolarity are involved in the pathogenesis of dry eye. (9) Beyond that, however, the survey reflected a lack of conformity, with many respondents unaware of current recommendations and most not using modern diagnostic tests. In fact, 45% percent said they do not incorporate a dry eye questionnaire; 63% perform Schirmer testing on a case-by-case basis; nearly 60% incorporate fluorescein staining at the initial point of care, while 58% incorporate rose bengal or lissamine green staining case by case.

The Solution

To address these educational gaps, members of the ASCRS Cornea Clinical Committee developed a consensus-based practical diagnostic OSD algorithm to aid surgeons in efficiently diagnosing and treating visually significant OSD (VS-OSD) before performing any type of refractive surgery.(5)

Scan for Ascrs Preoperative OSD Algorithm:

Although treating all OSD patients is important, the authors note that not every subtype requires delaying surgery, hence their choice to classify OSD as VS-OSD or non-visually significant (NVS-OSD).

In addition to being consensus and evidence-based, the group's stated goal for the algorithm were for it to be reliant on techniques and objective testing that take chair time into consideration. This dry eye guideline stands apart from other work as it is designed specifically for preoperative patients. Because signs and symptoms are poorly correlated—as well as being more pronounced in the cataract surgery population—the ASCRS algorithm is applicable even if patients do not complain of OSD symptoms.

Questionnaire

The group began by creating a new modified questionnaire specifically for pre-operative cataract and refractive surgery patients. They added extra questions to the SPEED tool to help screen for other subtypes of OSD that are relevant in the refractive setting and adapted items from Dr. Steven Dell's Cataract & Refractive Lens Exchange Questionnaire to address what the group called the "interplay between patients' expectations and the implications" of paying out of pocket for premium technology.

Non-invasive objective testing
Independent of the questionnaire's findings, a technician can proceed with the two noninvasive objective tests ASCRS determined to be "essential": tear osmolarity and inflammation (MMP-9). These two point-of-care tear tests are sensitive and specific for diagnosing DED even, as demonstrated in the Gupta study and recognized by the ASCRS Cornea Clinical Committee, in an asymptomatic population (5,7).

Osmolarity -
Tear hyperosmolarity is central to the definition of DED and the TearLab Osmolarity System (TearLab Corp.) and other osmometers are easy to integrate into clinic flow. (10,11) This test is validated, and with in-office quality control procedures to ensure accuracy, can reliably assesses tear osmolarity; >307 mOsm/L differentiates between normal and mild-to- moderate DED patients. An intereye difference > 7 mOsm/L is also considered abnormal, and variability, a hallmark of the disease, has been shown to correlate with increasing disease severity. (11)

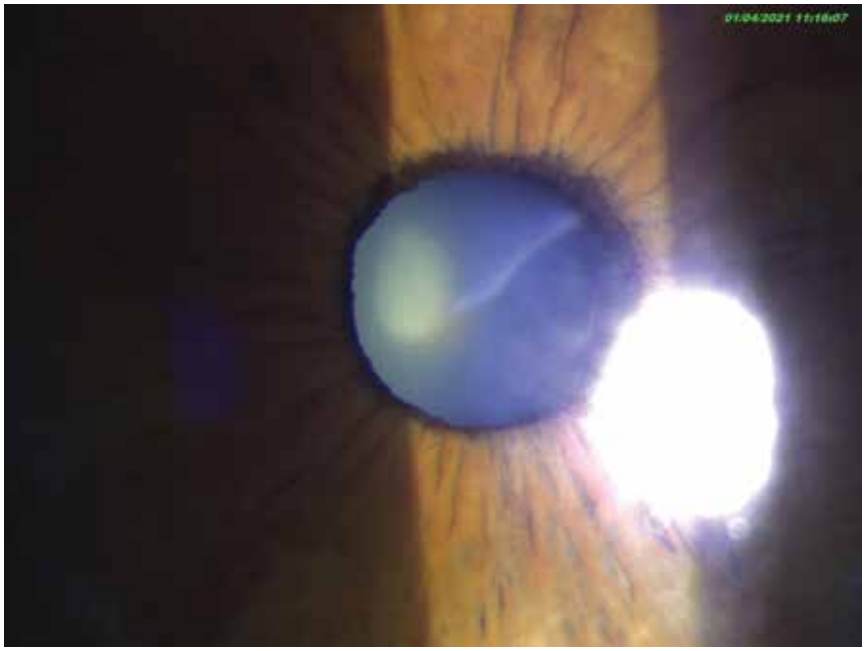
Inflammation - MMP-9 plays a key role in the breakdown of the ocular surface. (12) This marker can also be measured in tears using the sensitive and specific InflammaDry test (Quidel Corp).
A reading is considered positive if MMP is ≥40 ng/mL. (13) Patients with inflammation will likely benefit from anti-inflammatory therapy.

The ASCRS guidelines note that further diagnostic tests can be done to identify OSD subtypes, stating a preference for noninvasive options over invasive ones. Optional objective tests include lipid layer thickness, meibography, noninvasive tear breakup time, quantification of tear meniscus height, tear lactoferrin levels, topography/ tomography, aberrometry and ocular scatter index.

Exam

Of course, the clinical exam is paramount. The group advises a quick, focused ocular surface examination keeping in mind the phrase "Look, Lift, Pull, Push," to confirm the subtype, severity, and visual significance of OSD.

If, by following the ASCRS Algorithm, VS-OSD is found, preoperative refractive measurements and the surgery itself should be postponed until homeostasis is restored to the ocular surface. Treatment of VS-OSD in preoperative patients requires a more aggressive and multifaceted approach to speed the process and minimize surgical delays – estimated at 2-4 weeks. If patients have NVS-OSD, surgeons may proceed with surgery but the ASCRS guidelines emphasize the need for patient education and expectation management.



Treatment

To quickly achieve corneal health, the ASCRS guidelines recommend beginning at Step 2 or later of the TFOS DEWS II treatment guidelines. (14) They state that a combination of medical and procedural interventions based on disease subtype and severity will dictate the best approach in the preoperative patient. With DED being widely recognized as a multifactorial disease involving tear composition, ocular surface inflammation and lid margin disease, the available therapies continue to expand.

Conclusion

For a practice to achieve excellent, repeatable visual outcomes for all surgical patients, it must successfully identify and treat dry eye patients. This requires in-office procedures and clinical protocols that are developed and adhered to by the practice leaders. Once a system is in place for pre-surgical assessment of the ocular surface, its steps and importance must be thoroughly communicated to the entire practice, ensuring staff buy in and consistency of routines. Training and education should be ongoing, with the staff recognizing that they play an essential role in implementing the game plan that will ultimately improve visual outcomes for all surgical patients.

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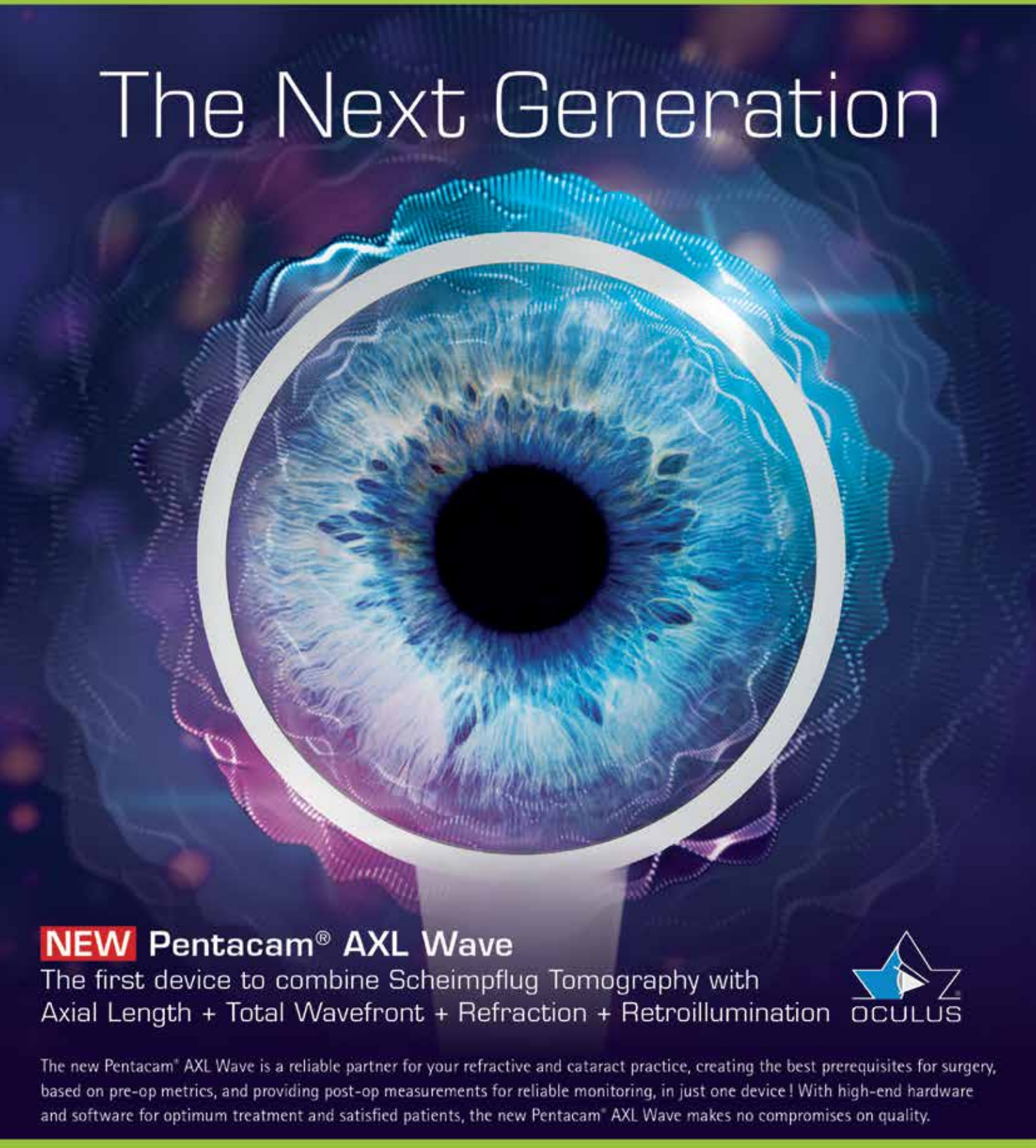
The Next Generation



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Corneal topography - putting dry eye on the map

By **Brian Tompkins & Keyur Patel**

The march of technology is allowing us as eye care professionals to access an ever-increasing range of patient data – equipping us with a deeper knowledge base from which we can develop multiple treatment pathways. Corneal topography can now create increasingly detailed 3D maps of the cornea's shape and curvature, enabling accurate detection of corneal diseases and irregular corneal conditions.

There are essentially three types of technology used in corneal topography.

Placido disc topography (eg Oculus K5M, Medmont, Topcon Myah)

Placido disc reflection systems measure the curvature, irregularities, tear film quality, foreign and other parts of the anterior cornea. The reflection is highly dependent on the tear film, which reflects the light.

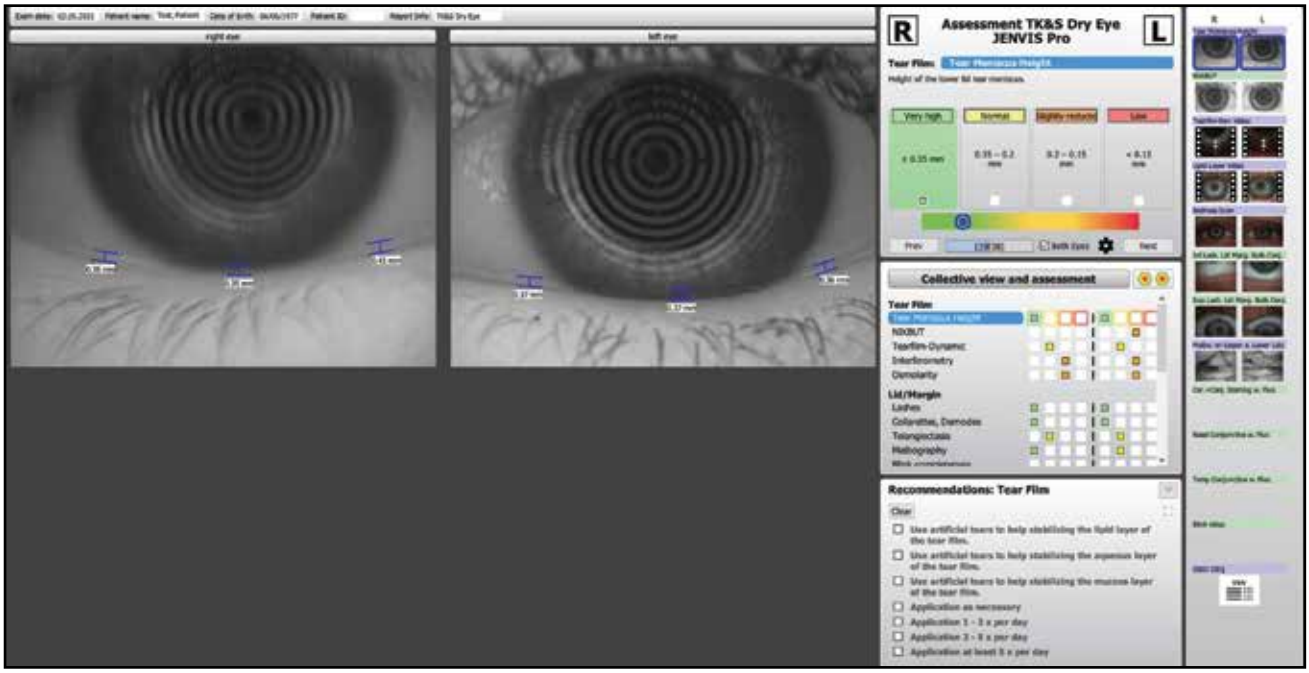
Scheimpflug (e.g Oculus Pentacam) and scanning-slit topography (e.g Bausch and Lomb Orbscan)

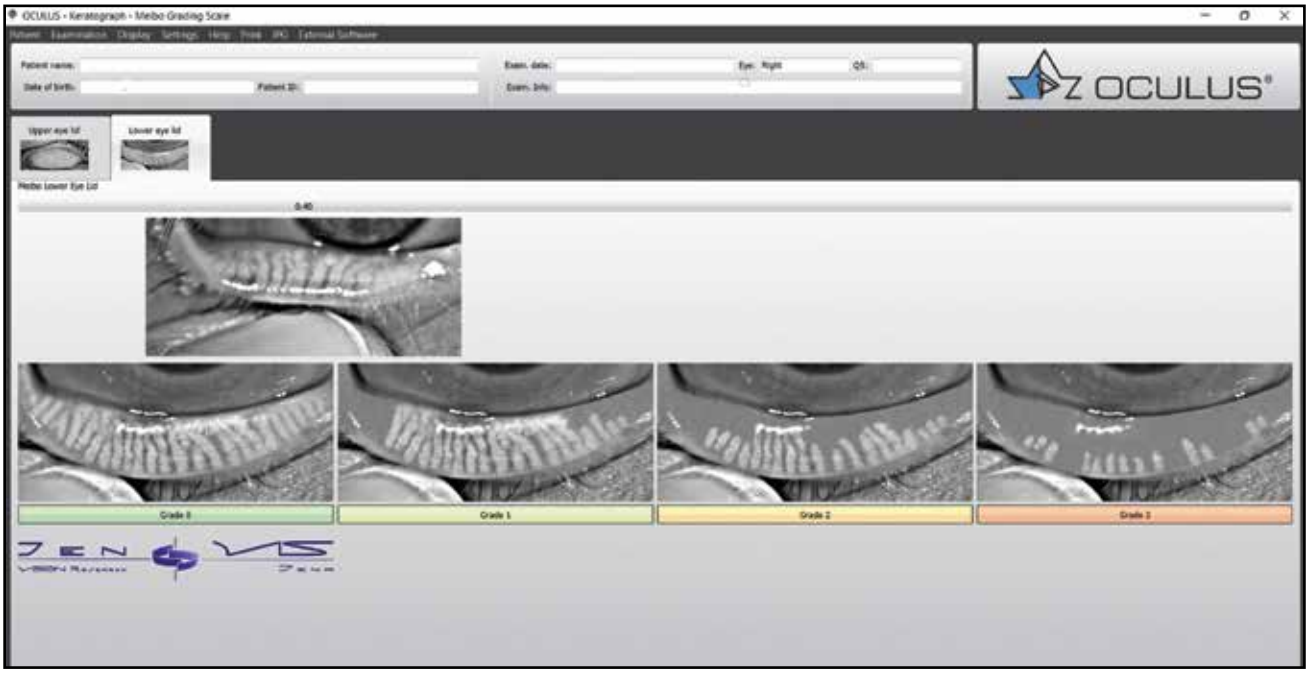
These two systems provide information about the anterior and posterior cornea using a slit beam, as opposed to measuring reflection as with placido disc systems.

As well as different types of corneal topographer, there are different types of topographic maps available as part of the non-invasive testing.

Axial display map

This is the most traditional way of viewing a topography image, as it is known for its overview of the corneal power.





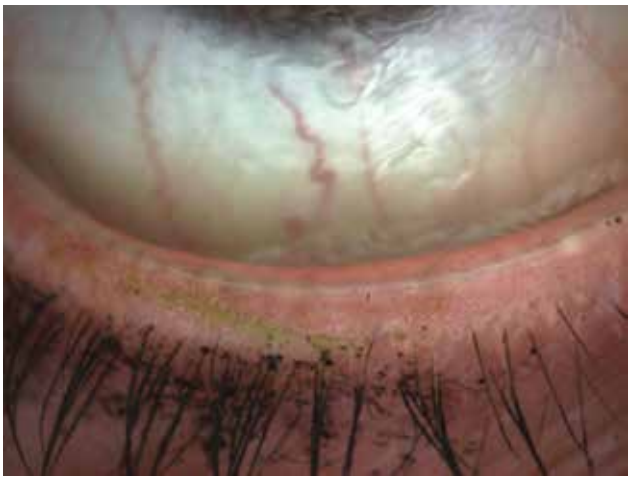
Tangential display map

This type of map provides an accurate measurement of the cornea's power and curvature, and is therefore helpful in fitting contact lenses, especially ortho-k lenses. This map can also be used to evaluate the power of a contact lens while the lens is on the eye.

Elevation display map

This map is used to determine the true shape of the cornea and is crucial for selecting the best contact lens design for an irregular cornea.
Most multimodal/combination devices use Placido disc systems to capture the data.

Here at TK&S we have an Oculus K5M. This placido-ring based corneal topographer also allows meibography and has a full dry eye suite of assessments, and it has proven an invaluable addition to our consulting room. It features a built-in real keratometer and a colour camera optimised for external imaging. It's something we use for a multitude of tasks every single day. It allows a comprehensive and guided step-by-step investigative protocol and reports for the eyelids, the conjunctiva, cornea, tear film, lipids, blink pattern, non-invasive tear break-up time and every aspect of the ocular surface with and without ocular staining.



It has become part and parcel of everyday practice and we now use our Oculus K5M for a wide variety of tasks in general practice. Any symptom in eye examination that indicates blur can be put down to fluctuating ocular surface quality. All contact lens-related vision issues can have an ocular surface element of problems, and it is crucial to examine ALL contact lens patients prior to fitting to determine the efficiency of tears etc to ensure success.

Our 'go to' measures to help analyse the tears in the best way are Non-Invasive Keratograph Break Up Time and Meibography. These allow a really quick assessment of possible immediate and future problems as well as illustrating blink patterns.

The COVID-19 pandemic appears to have triggered a rise in dry eye cases, most likely due to increased screen work with people working from home during the various lockdowns and spending more time on digital devices.

The JENVIS dry eye reports can be tailored and customised to the individual needs of the patient and the practice. This makes it brilliant for patient education, referral and management of the treatment protocols. It allows a quantitative and qualitative assessment of the intervention.

The ocular surface maps delivered by the K5M illustrate the inefficiencies of vision experienced by our dry eye patients and, when presented in a fully-personalised step-by-step guide with comprehensive data, provides the patient with a detailed snapshot of their condition and suggested treatment pathways which can also be used by other health care professionals.

The wealth of data we glean from dry eye assessments on the K5M helps form our suggested next steps, which typically include adopting the 30/30/30 rule, taking a break away from the screen every 30 minutes, resting or closing your eyes for 30 seconds and blinking 30 times.

With dry eye disease on the rise, high level assessment and appropriate treatment is essential if we are to make our patients as happy as possible and minimising their discomfort. A top-quality device enables us to do this quickly and easily, once again showing the power of technology and highlighting the importance of embracing the latest advances in optics.

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Presentation: 10ml bottle. **Main Ingredients:** Sodium hyaluronate, L-carnitine, Zinc chloride, Sodium Phosphate dibasic, Sodium phosphate monobasic, Sodium chloride, Virgin castor oil, Tween 80, Water. **Indications:** For the relief of medium to severe dry eye and to provide protection against the external environment. Also suitable for use overnight. **Dosage and method of use:** Instill 1 or 2 drops in the affected eye as required. **Warnings:** This product is not normally intended for continuous use for more than 30 days; if the symptoms persist consult your doctor. After administration, in rare cases, a slight temporary blurring of vision may occur due to the viscosity of the solution. If you wear soft contact lenses, remove them before applying product and do not replace the lenses for at least 15 minutes. After opening, use within 8 weeks. Consult doctor or pharmacist before using if pregnant or breast-feeding. **Contraindications:** Known hypersensitivity to ingredients. This product contains phosphates. It is not recommended for use in patients with significant damage to their corneal surface (such as pronounced erosion or corneal ulcer) as rare cases of calcification of the cornea during use of phosphate-containing eye drops have been reported in such patients. **Legal Category:** Class IIa Medical Device. **Cost:** £6.99 **Legal Manufacturer:** NTC S.r.l. Via Luigi Razza, 3-20124-Milan, Italy. **Distributer:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire, GU32 3QG, UK. **Date last reviewed:** September 2020. **Version number**: 1010448671 v 3.0

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10104331016 v 1.0 October 2020

The ocular implications of working from home

By **Don Stack** FAOI & **Arthur Cummings** FRCSEd

The COVID pandemic has forced unprecedented changes in all our lives. This dramatic upheaval in lifestyle has resulted in many outcomes, some positive, others more challenging.

The real consequences and paradigm shifts will take many years to be fully appreciated. Certainly, as eyecare professionals, we need to be cognitive of these developments and consider how the visual demands of our patients are evolving.

It is widely reported that home office workers typically work longer hours, take fewer breaks, and have a perception they need to be always available to answer emails and partake in video conferencing. The nuances around video conferencing are remarkably interesting and are only beginning to be understood. The most common complaints reported by remote workers are tiredness, dry eyes, postural difficulties, headaches, and eye strain (Computer Vision Syndrome). While the "Internet of Things" has and continues to enhance all our lives, we recognise that increased screen time affects all sectors of society, most notably the myopic shift in the younger age groups.

Opticalrooms have been delivering onsite corporate eyecare in Ireland since 2013 – both full time within employee Wellness Centres and, on-demand in the form of mobile pop-up clinics. With the ongoing current restrictions and employees currently based offsite we needed to pivot to find an alternative to our previous business model.
We were introduced to Vivior, a technology start-up company from Zürich, Switzerland, who have developed a glasses-mounted wearable that can assess the patient's visual demands remotely.

The Vivior Monitor can be easily attached to any spectacle frames and, because it weighs only 14 grams, the patient is not inconvenienced by the monitor while wearing it on their glasses. During the period that it is worn (at least four days/36 hours), the monitor measures the following data using various sensors:

- distances to objects in the visual field
- light conditions in the visual field
- ambient UV and blue light absorption
- head movement and position

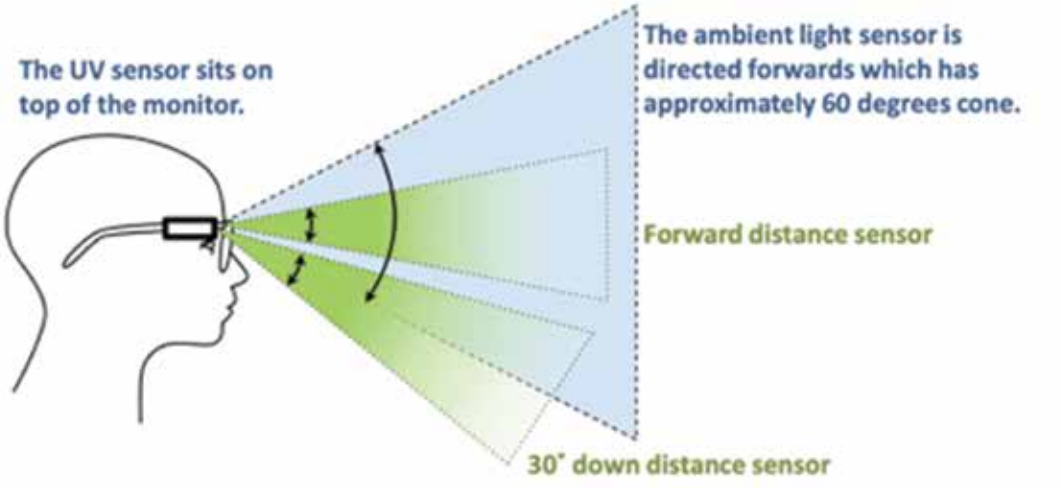
The data gathered from the monitor is stored anonymously in the cloud and processed using artificial intelligence to determine the type and duration of visual activities (such as reading, working on a computer, time outdoors, etc.).
We find the report generated to be a far more informative guide to lens selection than the typical questioning of the patient about their habits and daily routines.

Patients appreciate leveraging the latest technology to optimize their visual performance. On this basis, personalized solutions can be implemented to correct the patient's vision, particularly for progressive spectacle lens selection as well as IOL's.

In the corporate space, the monitor allows us to offer an alternative to the office ergonomic tests and use the findings to better understand the WFH (working from home) employee's workstation, e.g. their lighting, posture, distance from their monitor, range of devices used and, importantly for many, a measurement of the exposure to (HEV) blue light. HR departments within companies realise that eye strain associated with CVS is being reported by their employees and welcome a better understanding and any beneficial interventions possible. Vivior has developed an elaborate ergonomic report for our corporate clients that is more detailed and informative about the home office worker's working habits. This report allows us to advise the employee on VDU best practices and recommend a better home office set-up to enhance their comfort and performance.

The Vivior Sensors

The Accelerometer, gyroscope and magnetometer are in the monitor.



Two distance sensors, one straight and one tilted down 30 degrees. Each of those sensors has a detection cone of 25 degrees.

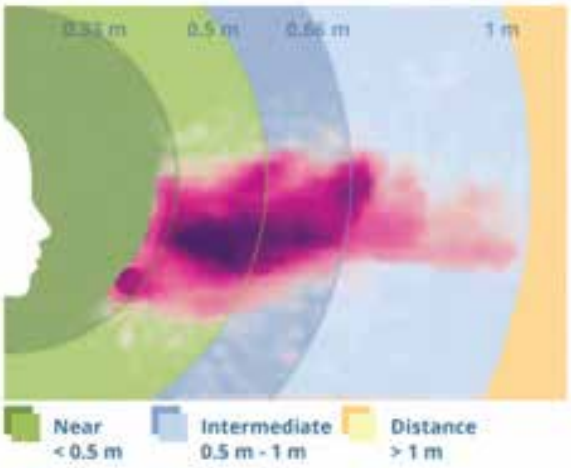
A marked escalation in employees complaining of dry, irritated eyes is also common, related to the frequency that the employee breaks visual fixation from their monitor. With the report details, we can combat this by offering solutions to help restore a more normal blink rate and offer relaxation in their accommodative effort. Helpful hydration tips, setting fixed times on tasks, regular breaks and perhaps keeping a preservative-free lubricant eye drop by their computer, are all potential suggestions in our final recommendations to the employee. The well known 20-20-20 rule helps if you can remember to do it: every 20 minutes, take a 20 second break by looking 20 feet away. If you cannot look 20 feet away due to restrictions in your workspace, simply close your eyes for 20 seconds. Another immensely helpful tool is to advise people that are on screens the whole day, to turn the situation around and allow their PC use to help, rather than exacerbate the dry eye situation. How does this work? Instruct them to squeeze the eyelids closely together every time that they press the "Enter" key. The squeeze needs to be so forceful that someone observing them would notice it. Do this for 4 to 6 weeks and then you can forget about it. Just like with Pavlov's bell and his salivating dogs, you would have conditioned your brain to blink properly (without any observer being able to notice it) every time that you press "Enter." This ensures a good flow of Meibum during the workday rather than the typical halt in production to poor blinking habits.

An important point to note is that the Vivior monitor does not have a camera or any sound recording capability, thus ensuring the patient can continue to work and go about their normal day with confidence and without feeling any intrusion in their lives.

Continues on page 32...

Report for workplace configuration "Laptop"

Your Vision Usage Profile



Introduction

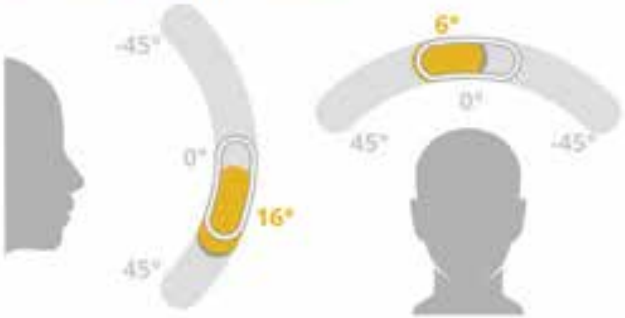
The workplace report aims to provide assessment of your current workplace configuration and behaviour based on objective data acquired with the Vivior monitor. It further provides recommendation to minimise the risk of such office syndrome symptoms as headache, eye strain and neck pain that are caused by inadequate workplace settings and work behaviour.

The statistics below is derived from a workplace configuration identified as Laptop: laptop screen is used as the main display.

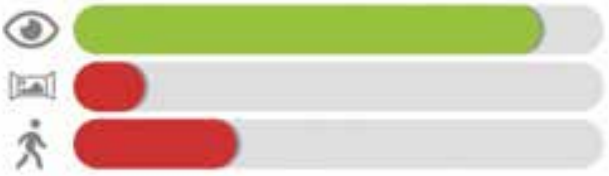
Distance Screen [cm]

Measurement time [hh:mm]

Head orientation



Break scores



Ambient illuminance [lux]

Head flexion activity

Colour Temperature [°K]

Head rotation activity

Light balance

Interestingly, the results from the monitor allow us to make recommendations above and beyond what we would have uncovered within our clinics. Armed with this comprehensive report, while discussing the patients' working style or visual demands, we can frequently make recommendations related to previously unavailable information e.g., improve the ambient lighting, adjust the monitor and/or chair to correct head tilt/flexion, time on tasks without breaks, and blue light filtering lenses to reduce HEV exposure etc.

Overall, the use of this innovative monitor sets us apart and is greatly appreciated by patients who expect/require optimal visual performance. The clinical report is easy to interpret and clearly guides us to the appropriate lens selection as well as any tints and/or coatings for a particular patient.

Both of us agree that using objective data leads to better diagnoses, better understanding of the patient's issues and hence, better therapies in the form of the best choice of progressive spectacle lens or the best IOL design for lens replacement surgery.

Working from home is vastly different to working in the office. We need to be aware of this and do our part in making patients more comfortable, both in terms of ergonomics and their ocular surface health.

Affiliations:

1. Don Stack: Optometrist/Director Opticalrooms Ltd., Ireland
2. Arthur Cummings: Ophthalmologist, Wellington Eye Clinic, Dublin, Ireland

Financial disclosures:

1. Don Stack: Vivior (Corporate Distributor Ireland)
2. Arthur Cummings: Vivior (Medical advisory board member)

Recurrent Corneal Erosion and use of the excimer laser

By **Ms. Caitriona Kirwan** & **Prof. Michael O'Keeffe**

Institute of Eye Surgery

Introduction

The corneal epithelium is squamous stratified 50µm thickness. It comprises 5 – 7 cell layers and rests on a basal membrane, Bowman's layer. The corneal epithelium is renewed every 15 days from the stem cells present at the limbus. The epithelium is supplied by sensory nerves which emerge vertically from the anterior stroma. The cornea is one of the most sensitive structures in the body. The healing of the corneal epithelium is extremely rapid. Epithelial cells migrate at a rate of at least 60µm per hour to cover an epithelial defect.

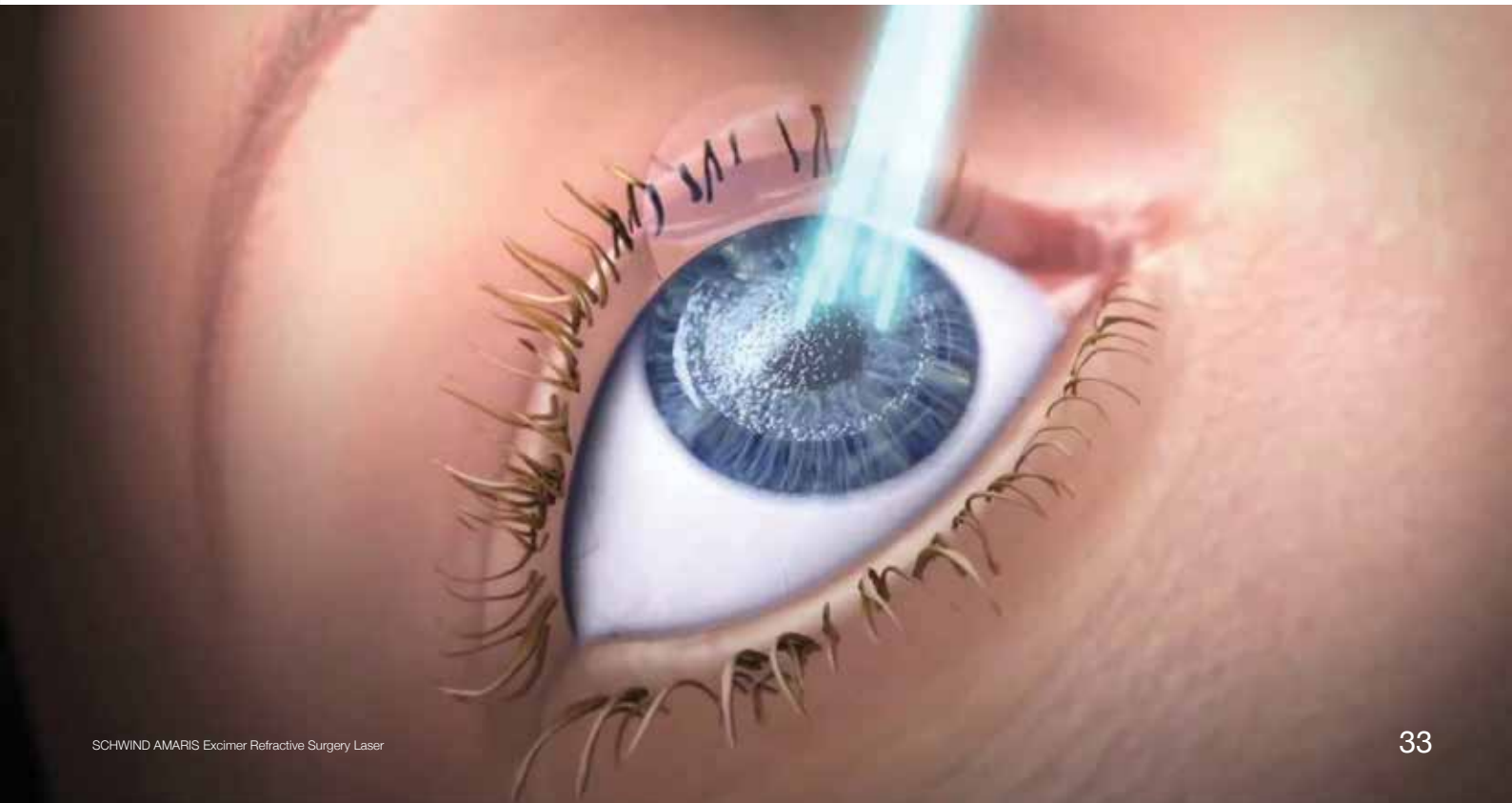
As the cornea is one of the most sensitive tissues of the body even minor trauma such as a finger nail, edge of a book page or any sharp object can result in a corneal epithelial defect. This causes sharp pain foreign body sensation, epiphora, photophobia and lid closure. Immediate treatment involves local anesthesia to examine the eye, pupil dilation to alleviate spasm, topical antibiotics, eye patching or bandage contact lenses. The majority heal within 72 hours. Most would add lubricants afterwards for a month. 90% resolve but about 10% result in recurrent corneal erosion.

Recurrent erosions are painful, frightening and incapacitating. They occur in early morning, are abrupt with sharp pain, foreign body sensation epiphora, and photophobia. They can recur weekly, monthly resulting in absence of employment. In such cases the patient continues with low grade symptoms of mild pain, foreign body sensation. They cannot work and develop anxiety and depression. In some patients there is no presenting trauma but persisting corneal disorders such as corneal dystrophy, lattice, Reis- Bucklers, macular and granular dystrophies, bullous keratopathy. Others have superficial basement membrane dystrophy such as finger print or map dot.

I have experienced some very interesting histories. A school teacher spent a week in bed, she had been treated medically and it was only after surgery that she got relief. Three other patients developed recurrent erosion following a trial of sunglasses in a store where the tag was attached to the inside arm instead of the bridge of the glasses. One such patient developed a severe psychological problem with significant medical legal implications. Such an insignificant eye injury can lead to a much larger problem.

Medical treatment is the first line or mainstay of treatment with hyperosmotic solution such as muro 128. Lubricants topical corticosteroids, bandage contact lenses and patching during the acute phase. Surgical treatments include debridement anterior stromal puncture and excimer laser using photo therapeutic keratectomy. The latter involves using the excimer laser to treat Bowman's layer so that by roughening this surface the corneal epithelium will permanently adhere to it. The early results of PTK were good but many of the erosions reoccurred. I changed my technique to photo refractive keratectomy (PRK). It resulted in far fewer recurrences. It eliminated any preexisting refractive error but in others it induced a refractive error. Patients were warned that this could occur but most felt that an induced refractive change and glasses was a small price for a pain free existence.

In Summary, PRK has been very successful, particularly in patients with recurrent erosions due to basement membrane dystrophies. It is also an excellent procedure in traumatic recurrent erosions.



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Q & A's with Prof. Tong

Meibomian gland dysfunction is the primary determinant of dry eye symptoms: Analysis of 2346 patients

(The Ocular Surface, Volume 18, Issue 4, October 2020, Pages 604-612)

Edited by **Vivian Ho**

Prof. Tong

1
Why did you conduct the study examining the contributions of clinical signs of dry eyes, and the predisposing factors to the magnitude of dry eye symptoms?

In busy clinics, there is limited time to assess patients. Ultimately, no one knows which signs are important enough that they have a direct bearing on human suffering, and should be the focus of our treatment.

2
What is your approach to the management of dry eye disease?

I seek to alleviate modifiable factors and treat with as few pharmacological and non-pharmacological modalities as possible, starting from lower cost options. The aim is to optimise quality of life, so treatment should be individualised. Most cases of dry eye should not need specialists, and there should be adequate resources such as optometrists in the community to manage them. Hospital physicians should only manage complex and severe cases, such as Sjogren's syndrome and ocular graft versus host disease.

3
Do you check for tear osmolarity or use any MGD imaging device such as the infrared meibography? If not, do you think these are useful to the assessment of DED?

We only use these tests in special circumstances or as part of research protocols. For example we perform meibography to evaluate long-term prognosis of the eyelids. In Singapore, most patients are unwilling to pay for additional DED tests if they don't directly change the treatment. One exception may be patients undergoing cataract surgery with toric or multifocal intraocular lenses.

4
In your study cohort, a reduced number of liquid meibum expressing glands (NLMEG, less than two per eyelid) on force expression and the presence of inferior fornix papillary reaction were found to be the most important factors that contributed to the magnitude of dry eye symptoms:

a)
Why did you include these two assessment parameters in additional to the standard dry eye tests (TBUT, Schimer's, cornea staining)?

These tests have been included because they are part of the external eye examination for ocular surface diseases which could cause tear dysfunction.

b)
Would you recommend anti-histamine as an additional treatment to dry eye patients with signs of inferior fornix papillary?

Yes, we recommend topical anti-histamine and mast cell stabilisers for such patients.

5
What are the key messages from your research findings? How may we address the remaining uncertainties in future studies?

Meibomian gland dysfunction tends to be more severe in patients with more severe dry eye symptoms. Treatment of the eyelids and objective monitoring of the eyelids is therefore recommended for all dry eye patients.
Concurrent allergies should be examined for and treated in dry eye patients. Experimental models can be used to understand ocular surface inflammation and tear dysfunction in meibomian gland dysfunction and in ocular allergies. Improvement in imaging techniques will help to document inferior fornix papillary reaction.

6
What type of patients present to your dry eye clinic? How do you perform dry eye assessment on them?

A broad range of patients with dry eye is referred to my clinic. We assess them based on a standard panel of clinical tests including slit lamp biomicroscopy, tests for tear stability and eyelid examination.

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Routine removal of all corneal graft sutures is not without risk

By **Nicholas Woo**, **Kanna Ramaesh** FRCOphth, **David Lockington** FRCOphth, PhD

In cases of high astigmatism following keratoplasty, selective removal of individual corneal sutures can reduce cylindrical magnitude and improve visual acuity (VA). Traditionally, removal of all residual sutures by 2 years has been encouraged to reduce the risk of inflammation, neovascularisation, microbial keratitis and ultimately graft rejection. [1-4] Heinzelmann's recent publication highlighted topical immunosuppression use following suture removal. [5] We recently reviewed a patient with 6/7.5 unaided VA following DALK who underwent removal of all residual graft sutures at 2 years, resulting in significant astigmatic increase and vision reduction (6/24 unaided).

In light of this, we retrospectively reviewed 25 consecutive cases of keratoplasty patients who underwent removal of all residual graft sutures (ROGS) in theatre in the subsequent period at the Tennent Institute of Ophthalmology, Glasgow.

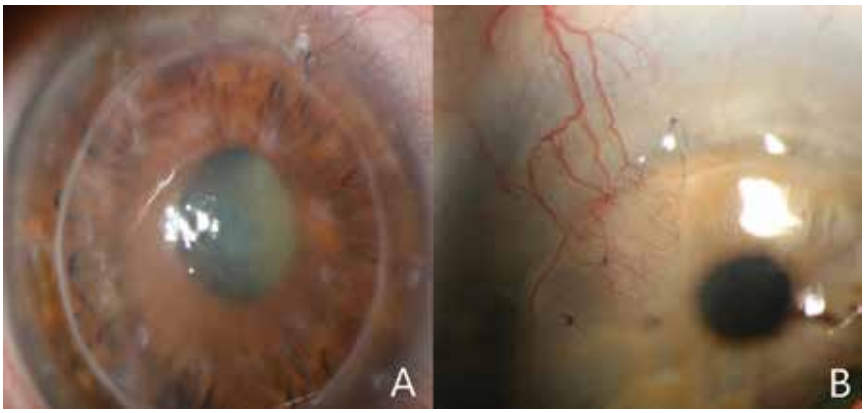
We identified 17 male and 8 female patients (mean age 36.5 years, range 19–81) in 30 months from April 2016. All sutures were interrupted, equating to removal of 313 residual individual sutures. Keratoplasty sutures were removed in 11 PKPs, 11 DALKs, and 3 tectonic corneal grafts. The mean time interval from keratoplasty to ROGS was 21 months (range 14-53). All suture material was completely removed in 12 cases. In 13 cases, fragments of suture material remained buried without protrusion (total of 25 retained suture remnants; median 2/case, range 1-4). [See Figure 1]

The cylinder magnitude assessed by corneal topography increased in 37.5% of eyes, but remained stable or decreased in 62.5% (total range -7.1 to +5.8 dioptres). Following ROGS, unaided VA decreased by 2 lines in 11 eyes (with reduced BCVA in 5). Complications included localised wound dehiscence, graft rejection, and corneal perforation in 3 separate cases.

We have demonstrated that unaided vision can deteriorate following non-selective total ROGS, with unpredictable astigmatic shifts. As graft clarity and wound integrity can be negatively affected following ROGS, we agree that suture removal is not without risk. [1-5] Our small study confirms that the traditional "complete suture removal by 2 years" strategy should be approached with caution. Due consideration should be given to the risk/benefits of keratoplasty suture removal on an individual patient basis.

Legend:

Figure 1: Clinical photo showing retained suture remnants [A] and associated neovascularisation [A+B] following removal of corneal graft sutures.



Acknowledgments: A version of this paper was a poster presentation at the Royal College of Ophthalmologists Annual Congress in Glasgow in May 2019.

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Ocular Surface Insights to Genetic Testing

By **Seema Nanda**, OD
Clinical Director: Nanda Dry Eye & Vision Institute, Houston TX USA

The Background

Patients come in for their annual eye exam with complaints of the usual blurred vision with excessive computer usage. They constantly rub their eyes and use copious amounts of artificial tears to lubricate their poorly wetting corneas. Refractions are performed and patients can barely discern the 20/20 line. Slit lamp findings reveal mild punctate keratopathy, so the doctor assumes the blur is due to their dry eyes. Accordingly, new contact lenses are dispensed and they leave.

The preceding typical scenario is performed in doctors' offices everyday around the globe. The patients' refractive error illustrated a mild increase in their astigmatism, which was not a cause of any significant concern. The topographical measurements also demonstrated unremarkable findings. Unfortunately, years can pass before a confirmation of keratoconus may become present. But, now with the advent of genetic testing, a more definitive way to predict the likelihood of developing corneal problems is finally available.

Before this breakthrough, four main procedures have been used to detect keratoconus conclusively. First, in-office protocols customarily entailed retinoscopy to detect the classic 'scissors-reflex' seen with keratoconus; however, many practitioners today use auto-refractors which bypasses this common finding.[1] Second, a marked increase in astigmatism at an oblique axis can be regarded as another red flag; still, if this rise is subtle from year-to-year, then this finding also may be overlooked. Third, keratometry readings are similarly good indicators of progression, especially if steeper corneal curvatures are noted. Nevertheless, if the cone is not central nor in one's visual axis, this finding too can be missed, which will lead to a delay in diagnosis. Fourth, the use of corneal tomography or topography can capture the early stage of form-fruste keratoconus, but can be cost-prohibitive in a clinical setting. Since all these methods have their limitations, the latest technique of genetic testing has come into the limelight. It can detect corneal anomalies from dystrophies to degenerations, especially in those individuals who have a family history of keratoconus, with a simple swab of one's cheek.

The Benefits

A major benefit of genetic testing is early detection, which can allow for better management of patients who may have keratoconus. For example, if a young adult wants to have LASIK surgery, and the clinician performs all the necessary tests to determine if patient would be a good candidate, the doctor could still miss early signs of the condition. With genetic testing, if that LASIK candidate is diagnosed with keratoconus, an alternative option with a Refractive Lens Exchange (RLE) or Implantable Collamer Lens (ICL) could be inserted to mitigate the condition. Another more advantageous use would be to detect the condition and then discuss preventative therapies with cross-linking in those patients with higher probability of development of the disease.

Risk assessment is another benefit of genetic testing and is one approach to gauge patient management of their potential disease progression. In those patients with low risk, that is, minimal clinical evidence of keratoconus, but with a family history of the condition and/or comorbidities, evaluation would be prudent every six to twelve months. On the other hand, patients with a greater likelihood for progression should be monitored more regularly at four to six-month intervals. For example, individuals who are younger, with symptoms of atopy and/or allergic conjunctivitis, are more prone to rubbing their eyes, which has shown an increased incidence of keratoconus. Also, people who have notably larger amounts of astigmatism, that is both asymmetrical and oblique, but with no significant corneal findings, are also at greater risk for developing keratoconus. Testing of immediate family members, especially younger siblings, should also be considered and preventive measures with cross-linking should be discussed.

A third benefit of genetic testing is the ability to test for other genetic markers. Although, the majority of patients encountered in clinics may have keratoconus, with a higher prevalence rate in men (60.6%) than women (39.4%), other corneal conditions can also be identified as well.[3,6] Approximately one in 1,100 people may have corneal dystrophies and present with symptoms of vision loss, eye pain, dry eye, and sensitivity to light or glare.[3,4,5]

These dystrophies are variable and may develop early in childhood or as later years, in their fifties or sixties.[3,8] Currently, there are 70 different genetic mutations (TGFBIs) that have been found to cause corneal dystrophy.[7] A custom panel is utilized that can examine more than 1,000 variants across 75 genes for keratoconus and more than 70 TGFBI mutations which include: Granular Type 1 and 2, Lattice Type 1, Reis-Bucklers and Theill-Behnke Corneal Dystrophy.

The Method

The doctor obtains a buccal, or cheek, swab from the patient and sends it to the Avellino lab for evaluation. For keratoconus, a detailed report, uploaded to a HIPPA-compliant portal, will show the Risk Score categorized as “LOW”, “MEDIUM”, or “HIGH.” The report will also include a variant analysis and interpretation. For the corneal dystrophy, “YES” or “NO” diagnoses with relevant additional variant analysis and interpretation will be included. Genetic counselors also would be available to provide support and answer questions for the eyecare


Clarissa Leahy/Getty Images

professionals and their patients. Incredibly, these genetic tests are already available in the US, Europe, Japan, Korea, and China.

Currently, with greater advances in technology, genetic testing can be offered in practices worldwide that will help clinicians potentially preserve vision with an early diagnosis. An innovative test for corneal disorders that uses DNA-sequencing to assess risk in developing keratoconus and definitively diagnosing five major corneal dystrophies, can be revealed quickly with a few strokes of a swab.

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What’s in the news?

The effect of daily life activities on intraocular pressure related variations in open-angle glaucoma

The recent advent of continuous intraocular pressure (IOP) telemetry has led to an increased awareness of the importance of IOP fluctuations, and theories have emerged that IOP variations could play as much a role in glaucoma progression as the mean level of IOP.

The aim of the present study was to evaluate the direct effect of common daily activities on IOP-related profiles. Primary open-angle glaucoma and glaucoma suspect patients were prospectively enrolled from specialist clinics at the University of California San Diego (UCSD), USA.

Patients were fitted with a SENSIMED Triggerfish (TF) contact lens sensor (CLS) and were instructed to return to their usual daily activities for 24 h. They were asked to record each specific activity or event in a diary.

The protocol was repeated twice. The following events were recorded: “walking/cycling”, “resistance training”, “yoga/meditation”, and “emotional stress”.

CLS measurements recorded 60-to-30 min prior to each event were used as a baseline reference, and all IOP-related fluctuations for 120 min after the start of each event were reported in relation to this reference. Forty relevant events from 22 CLS recordings in 14 patients were retrieved from the diaries.

- Walking/cycling (n = 10) caused a small but statistically significant elevation of the IOP-related profile during the activity ($p = 0.018$).
- Resistance training (n = 11) caused a persistent elevation of the IOP-related profile from the onset of the activity ($p = 0.005$) through 120 min after the activity was stopped ($p = 0.007$).
- Yoga/meditation (n = 4) caused a sustained drop in the IOP-related profiles through to 120 min, although this was not statistically significant ($p > 0.380$).
- Emotional stress (n = 13) was as sociated with a gradual elevation of the IOP-related profile from the start of the stressful stimulus. Both early and late variations were statistically significant ($p = 0.038$ and $p = 0.021$, respectively).

The present study suggests that emotional stress and resistance training may be associated with persistent IOP-related profile elevation.

Sci Rep. 2021 Mar 23;11(1):6598.doi: 10.1038/s41598-021-85980-2.

Authors: Kevin Gillmann , Robert N Weinreb, Kaweh Mansouri

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Upcoming Event:

Face to face meeting

Wed 10th – Fri 12th November

The UKISCRS Annual Congress 2021

Jury's Inn Hinckley Island Hotel

Programme:

Young Ophthalmologist Programme:
- Dry lab education
- How training has been affected by COVID
- Rapid Fire Papers, Video & Posters

Plenary Symposium:
Service Delivery – Post COVID

Sessions:
- Refractive Cataract Surgery
- Corneal
- Expert Video Cases

Medal Lectures:
- Lifetime Achievement Award
  Prof Michael O'Keefe
- The Pearce Medal Lecture
  Prof Tara Moore
- The Choyce Medal Lecture
  Mr Richard Packard

A not to be missed Congress with a Celebratory Awards Dinner!

Please visit our website for up to date information on all of our events and how to become a member:

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DR. PIETER GOUWS, UK

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