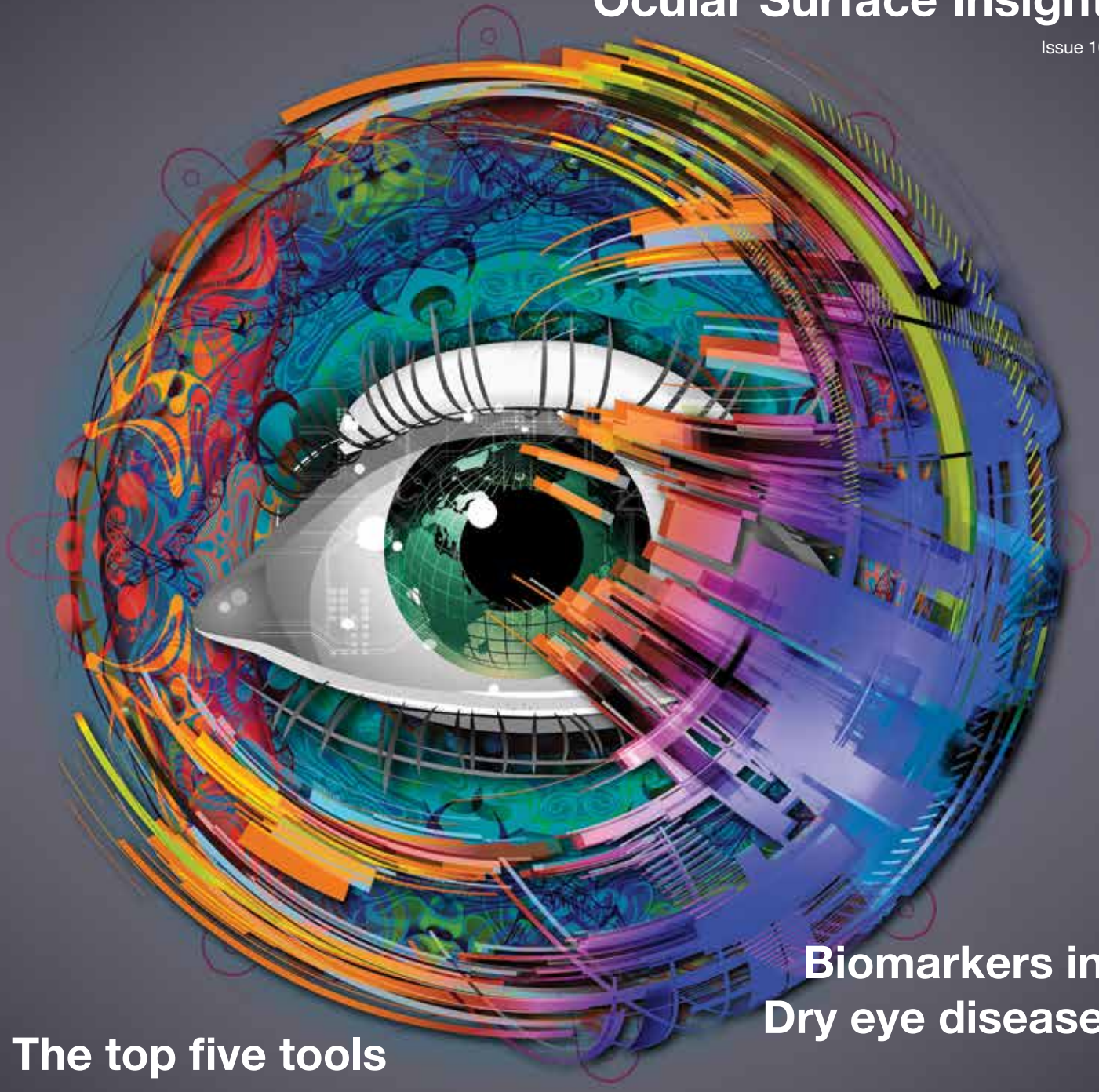
OSI

Ocular Surface Insight

Issue 10



Biomarkers in Dry eye disease

The top five tools I cannot live without when diagnosing Ocular Surface Disease

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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

"Details matter. They create depth, and depth creates authenticity."

Neil Blumenthal

Welcome to the Winter issue of OSI.

Welcome to the OSI Magazine!

On the day I am writing this the UK is in another lock down. This is due to the recent surge of new Covid -19 cases, in order to protect the NHS from being overwhelmed. Here at OSI, we promise to offer you a range of interesting stories during these difficult times.

Behind the scenes, the editorial team are working on the modules to deliver Dry Eye Masterclasses in the new year. This intensive course will cover the very latest approaches and best practice, when diagnosing and treating dry eye from the most innovative clinicians in our field. We aspire to question and inspire, never to bore or lecture.

Details will be available on our website: www.osimag.co.uk to register.

We live in a world of information overload, but there is always a risk that something essential is being lost or overlooked. On that note, if you are looking for the best diagnostic tools to assist you with ocular surface disease, Brian Tompkins and Keyur Patel have rounded up the tools they cannot live without! Another article from Artemis Matsou is great at demonstrating the fact that diagnosing dry eye doesn't have to take up a lot of clinic time, with useful step by step tips.

Thanks for reading.

Samer Hamada

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Ocular Surface Insight

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Contents

What's in the news?

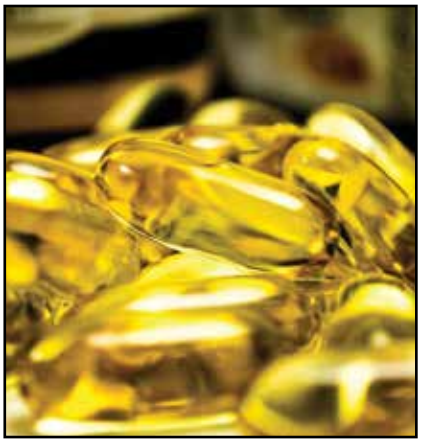
A systematic review of the effect of omega-3 supplements on meibomian gland dysfunction

Meibomian gland dysfunction (MGD) is the leading cause of dry eye syndrome (DES). Many ocular disorders including DES and blepharitis can be linked to MGD. If we treat MGD, we can treat related diseases easily.

The purpose of this systematic review is intended to determine the efficacy of omega-3 supplementation in MGD patients.

This systematic review method included an electronic search on PubMed and Clinicaltrials.gov to include all randomized clinical trials (RCTs) using omega-3 as a treatment for MGD.

The result from the database search yielded to one RCT and six clinical trials through the MEDLINE of a total of 350 participants for the systematic review and meta-analysis study.
The investigated treatment group (omega-3 group) had a positive effect on MGD protection in the invasive sodium fluorescein-tear break up time (NaFl-TBUT) score compared with the placebo group (odd ratio = 8.72, 95% confidence interval: 4.73, 16.09; $p < 0.001$). These data suggest that the odd ratios of the omega-3 group to control group increased the likelihood of the improved stated outcome tear break up time (TBUT) being achieved in the treatment group. No evidence of publication bias was detected in the funnel plot inspection or the Egger's statistical test ($p = 0.2944$).



Conclusions:
A moderate daily dose of omega-3 may be a beneficial therapeutic for MGD. Omega-3 has been beneficial in many diseases, such as heart attack prevention and age-related macular degeneration, and this systematic review emphasizes its protection against MGD. In addition, this review emphasizes the precision of non-invasive TBUT (NITBUT) compared with invasive NaFl-TBUT which may suggest the importance of NITBUT in the clinic.

Ther Adv Ophthalmol. 2020 Oct 16;12:2515841420952188.doi:10.1177/2515841420952188.

Author: Mashael Al-Namaeh.

Massive Demodicosis of the Eyes in a Patient with Sjögren Syndrome: A Case Report

Demodex mites infestation, typically asymptomatic, is a problem for patients with weakened immune systems because it often takes the form of symptomatic, massive infection. The Demodex mites play an important role in the occurrence of a range of eye surface diseases such as Demodex blepharitis, Meibomian gland dysfunctions, conjunctivitis and corneal changes. The ocular infection is closely related to the systemic invasion. Our goal was to minimize infestation and alleviate the symptoms of massive demodicosis so as to prevent further damage to the cornea.

The research case involves a 61-year old woman diagnosed with secondary Sjögren syndrome due to rheumatoid arthritis. On the background of the autoimmune disease, corneal perforation of the left eye occurred that was cured by surgery.
Then during the follow-up visit the patient was found (microscopically) massively infected with Demodex mites and the developed symptoms were particularly severe.

The patient was treated with adequate dry eye syndrome and demodicosis therapy which significantly reduced the number of Demodex mites and improved the patient's condition.

The authors concluded that they wish to draw the attention of the physicians of different specialties that special care should be taken with respect to the therapy of dry eye syndrome and ocular demodicosis in patients with immunological disorders to achieve therapeutic success and avoid particularly dangerous consequences of these diseases.

Acta Parasitol. 2020 Oct 31. doi: 10.1007/s11686-020-00297-w.

Authors: Marta Ziaja-Sołtys , Magdalena Kołodziejczyk , Beata Rymgayłło-Jankowska , Dominika Wróbel-Dudzińska , Ewa Suchodoła-Ratajewicz , Dominika Szlonzak , Tomasz Żarnowski , Anna Bogucka-Kocka.

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

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Santen UK Limited (Email medinfo@santen.co.uk or telephone: 0345 075 4863).

1. Baudouin C et al. Br J Ophthalmol 2014;98:1168 - 1176
2. Craig J et al. Ocul Surf 2017;15(4):802 - 812
3. Leonardi A et al. Eur J Ophthalmol 2016;26(4):287 - 296.

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

What's in the news?

The UK National Artificial Eye Questionnaire study: predictors of artificial eye wearers' experience part 1-comfort and satisfaction

The objective with this study was to report associations with comfort and with appearance satisfaction in artificial eye wearers.

The method for this was through Multicentre, observational, cross-sectional study, nationwide within the National Health Service England. The National Artificial Eye Questionnaire (NAEQ) was completed by 951 respondents. Multiple regressions assessed associations between the experiences of artificial eye wearers, routine management, changes over time, baseline and demographic parameters and their reported comfort, satisfaction with appearance and prosthesis motility.

The results showed that better comfort levels were associated with needing less lubrication ($\beta = 0.24$, $p < 0.001$), older age ($\beta = 0.17$, $p = 0.014$), less discharge ($\beta = 0.16$, $p < 0.001$), less frequent cleaning ($\beta = 0.16$, $p = 0.043$), and male gender ($\beta = 0.06$, $p = 0.047$). Greater satisfaction with the appearance of the artificial eye was associated with better perceived motility ($\beta = 0.57$, $p < 0.001$). Black ethnic origin predicted a lower satisfaction with the appearance ($\beta = -0.17$, $p = 0.001$). Greater satisfaction with the motility was associated with a better appearance rating ($\beta = 0.51$, $p < 0.001$), longer time of having an artificial eye ($\beta = 0.13$, $p < 0.001$), older age ($\beta = 0.11$, $p = 0.042$), and a shorter adjustment time

($\beta = -0.07$, $p = 0.016$). Of the testimonials concerning appearance aspects, the majority (21/45, 46.7%) were related to the effect on social interactions.

The results suggest that more attention should be given to the "dry anophthalmic socket syndrome" as a key cause of discomfort. Young patients are concerned particularly about the motility of the artificial eye. Over time satisfaction with the artificial eye movement is likely to improve.

Eye (Lond). 2020 Oct 26.doi: 10.1038/s41433-020-01236-9.

Authors: Yinon Shapira , Emma Worrell , Andre S Litwin , Raman Malhotra .

Mediterranean diet and risk of Sjögren's syndrome

Non-genetic risk factors for Sjögren's syndrome (SS) are poorly understood. Adherence to a Mediterranean diet has been associated with reduction in other autoimmune diseases. We examined the association of Mediterranean diet with SS.

New patients attending a single centre warranting investigation for primary SS (pSS) were recruited into the Optimising Assessment in Sjögren's Syndrome cohort established in Birmingham, UK (2014-2018). Participants were classified into pSS and non-SS sicca, considered as cases and non-cases, respectively, and asked to complete an optional food frequency questionnaire on their diet before onset of symptoms. A semi-quantitative Mediterranean diet score (MDS) was calculated (possible range=0 to 18). Using multivariate logistic regression, corrected for energy intake, body-mass index, sex, age, symptom duration, and smoking status, we examined the association of MDS with SS.

Dietary data were available for 133/243 (55%) eligible patients (n=82 pSS and n=51 sicca). In the adjusted model, a higher total MDS (mean ± SD, 9.41±2.31 points) was associated with lower odds of pSS (OR 0.81, 95% CI 0.66-0.99; p=0.038) per one unit of MDS. Among MDS

components, the strongest association was seen with fish with OR 0.44 (95% CI 0.24-0.83; p=0.01) in the comparison between <1 portion/week and 1 to 2.5 portions/week. Higher galactose, vitamin A-retinol-equivalents and vitamin C showed associations with lower odds of pSS in multivariate analysis, where the association of vitamin C was attenuated when adjusted for MDS.

The conclusion from this abstract was that when adjusted for potential confounders, adherence to the Mediterranean diet was associated with lower likelihood of having pSS.

Clin Exp Rheumatol. Jul-Aug 2020;38 Suppl 126(4):216-221.Epub 2020 Oct 23.

Authors: Aleksander Machowicz , Isaac Hall , Paola de Pablo , Saaeha Rauz , Andrea Richards , Jon Higham , Ana Poveda-Gallego , Fumiaki Imamura , Simon J Bowman , Francesca Barone , Benjamin A Fisher

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*The study results are related to the haptic design.

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1. DOF2019OTH4015 - Study NXGT-103-MER3 - Proof of Concept Study for Next-Generation IOL Models MER003 and MER004. Aug. 28, 2019. **2.** Tognetto D, et al. Quality of images with toric intraocular lenses. *J Cataract Refract Surg* 2018;44(3):376-381. REF2020CT4232. **3.** Read SA, et al. The visual and functional impacts of astigmatism and its clinical management. *Ophthalmic Physiol Opt* 2014;34:267-294. REF2019CT4417. **4.** DOF2019OTH4003 - **TECNIS Synergy**® IOL - 6-month POC data. 23 April 2019. **5.** DOF2019OTH4002 - Weeber H - MTF of the **TECNIS Synergy OptiBlue** IOL, and other models. 27 March 2019.

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The top five tools I cannot live without when diagnosing Ocular Surface Disease

By **Brian Tompkins** and **Dr Keyur Patel**, TK&S Optometrists
Edited by **Daniel Owens**

Even before the onset of COVID-19, Ocular Surface Disease was a known and growing problem. Since the pandemic took over our lives it has only increased, with a population stuck on screens all day and it has become something that we see plenty of here at Tompkins Knight & Son Optometrists.

As a practice we strive for contact lens excellence and Dry Eye has always been one of our areas of specialism to minimise the effects of contact lens discomfort and dropout. As such we attract patients from all over the UK with a range of issues, some mild, some severe, looking for specialist advice.

It is a condition we are learning about all the time, with new technologies and treatments coming online and changing the way we manage OSD. It is evolving, and we are having to evolve with it too. We enjoy that challenge and embrace the opportunities it gives us.

The publication of the TFOS DEWS II report presented us with a resource, which underpins every stage of our treatment strategy. This acts as a reference point for all our decisions, allowing us to pinpoint the right process, in the right way, at the right time.

With that in mind, TFOS DEWS II is arguably the single most important tool at an optometrist's disposal when diagnosing OSD but we wanted to share five other diagnostic tools we use day in, day out to treat our patients.

Technology plays a pivotal role in all we do, and it's something we have invested in to take our diagnostics to another level. Our patients know that when they come to see us no stone is left unturned in terms of analysing their condition. Our state-of-the-art diagnostics enables us to decide the best patient pathway to achieve the best possible vision and comfort.

These are the five 'diagnostic tools' we simply cannot live without.

1. Questionnaires

As a practice, we are huge advocates of technology but arguably the most important aspect of any diagnosis involves little more than a few simple questions and answers.

Patient questionnaires are vital. They provide a comprehensive overview of a person's medical history, their general health, their lifestyle needs and ocular demands. Questionnaires act as an efficient triage process - essential in COVID times - allowing us to have a clear picture of the patient's needs.

In the longer term we would expect the current paper trail to be replaced by video conferencing and telemedicine but, for now, questionnaires are an effective starting point for the investigative process.

We have been doing lifestyle questionnaires for all new patients for some time now. Previously, all contact lens and dry eye patients received an OSDI questionnaire to complete but this has now been extended to all new patients as many are unaware of ocular surface disease issues.

All patients now receive this as a digital questionnaire set to complete online before their appointment.

Their answers are frequently enlightening and drill down on the potential causes of the dry eye and a clearer understanding of the level and type of treatment required. A number of patients have subsequently been found to be struggling with near vision or binocular vision rather than purely dry eye problems. Without the OSDI process, this would not have been apparent.

Our insistence on a dry eye work-up prior to even applying a lens means we can identify challenging patients, and set-up management protocols to enable greater contact lens success and minimise drop-out.

Across the profession, contact lens drop-out is a cause for concern but with these protocols in place our drop-out rate is extremely low.

There are many questionnaires out there and each practitioner will find the one that works best for them. Our preference, after trialling many, has been the OSDI giving us the comprehensive analysis we demand.

2. Bio-microscope

The bio-microscope, complete with videography capability, is an essential weapon in our eye care armoury. Every optometrist in the land has a bio-microscope for every day use in every patient and their efficacy can be enhanced further by attaching a camera to facilitate image capture and recording for referral capability, for comparison of treatment efficiency and for patient education.

The slit lamp is as essential to an optometrist as a cooker is to a chef, we simply can't do the job without one. The addition of a camera however, elevates it to another level entirely. Recording capability is the natural next step in 21st century optometry. The technology is there, it's straightforward to use and it makes a significant difference to the patient experience – allowing them to clearly visualise their diagnosis and better understand treatment pathways.

Several brands and models are available and it's a case of finding the right one for you and your needs.

3. Oculus K5M

This Oculus keratograph is an exciting new addition to the consulting room. It is something we use for a multitude of tasks every single day.

It is an advanced corneal topographer and meibographer that includes a full dry eye suite.

This allows a comprehensive step-by-step investigative protocol for the eyelids, the conjunctiva, cornea, tear film, lipids, blink pattern, non-invasive break-up time and every aspect of the ocular surface with and without ocular staining.

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.

Never forget, the K5M is essentially a topographer giving us ocular surface maps to illustrate the inefficiencies of vision experienced by dry eye patients.

4. Tear analysis

Once the initial non-invasive examinations are complete, our clinical technician takes chemical tear samples.

Osmolarity is a key feature of the TFOS DEWS II report and a key indicator of ocular surface disease. The TearLab ™ is now an essential part of any dry eye investigation and we currently rely heavily on Inflammadry ™ to assess for MMP9 as many low-grade inflammatory conditions will affect ocular comfort and future contact lens comfort.

Again, this thorough approach to diagnosis puts us in a far better position for long-term results. It's all too common to hear tales of people 'blaming the lens' but if you have a proper analysis of what's going on at the early stages of diagnosis you have a far better chance of success.

5. Advanced Ophthalmic Systems (AOS) AI grading system

One of our philosophies as a business is to 'never stand still'. Soon after Eduardo Mangieri, Karl Hans Jeebaun and Gerard Kool created and launched AOS back in 2014 we became early adopters of their technology and we have never looked back since.

With four clinicians, two examination rooms and a multitude of imaging devices, the consistency this system provides us is absolutely vital.

As well as inter-clinician consistency, it allows for a greater level of patient education by being able to show them the effects of their treatment and management.

The AOS software independently grades bulbar redness, lid redness and fluorescein staining (in particular punctate stain count).

A digital ruler (area and linear), allows independent, repeatable measurements on separate devices to track corneal abnormalities (such as keratitis) and then demonstrates to our patients the benefits of continued treatment.

The digital Wratten filter has helped when we have not been able to get a patient to the slit lamp, and the recent addition of the companion app has meant that we have been able to ask patients to take their own images, knowing that they will be transmitted directly and securely for us to analyse.

The latest feature to be added is the ability to securely tele-consult with patients.

Often patients will experience flare-ups, when they are not in or near your chair and the ability to see and capture images of the signs at the time of symptoms is crucial for effective management.

AOS is propelling modern optometry into the future, with game-changing AI clinical grading. Advances in telemedicine are only going to continue and some form of pre-appointment web-based video interaction with patients could well become standard in years to come. The AOS is allowing us to get ahead of the curve.

These are the five tools we cannot live without. They allow us to do our job better than ever and ensure our patients receive the best possible care at all times.

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Eyzeetan (bimatoprost/timoloi) Eye Drops Prescribing Information (please refer to the full SmPC before prescribing) Indications: Reduction of intraocular pressure (IOP) in adult patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to topical beta-blockers or prostaglandin analogues. **Available strengths:** 0.3mg/ml bimatoprost + 5mg/ml timolol Eye Drops, in 3ml solution. Dosage and method of use: One drop in affected eye(s) once daily, administered either morning or evening, at the same time each day. If a dose is missed, treatment should continue with the next planned dose. If more than one topical ophthalmic drug is being used, administer drugs at least 5 minutes apart. Systemic absorption reduced by using nasolacrimal occlusion or closing eyelids for 2 minutes. Advise patients to wash hands before use, avoid allowing the container tip to touch the eye. If handled improperly, contamination of ocular solutions can cause ocular infections. Use with caution in patients with hepatic or renal impairment. Eyzeetan is a sterile solution that does not contain a preservative. Safety and efficacy in children under 18 not established. **Contraindications:** Hypersensitivity to active substances or excipients; reactive airway disease including bronchial asthma or a history of bronchial asthma, severe chronic obstructive pulmonary disease (COPD); sinus bradycardia, sick sinus syndrome, sino-atrial block, second or third degree atrioventricular block, not controlled with pace-maker. Overt cardiac failure, cardiogenic shock. **Special warnings and precautions for use:** Before initiating treatment, inform patients of possibility of eyelash growth, periorbital skin hyperpigmentation and increased iris pigmentation. Increased iris pigmentation likely to be permanent. Hair growth may occur in areas where Eyzeetan repeatedly in contact with skin surface – avoid drops running onto cheek or other skin area. Patients taking concomitant systemic beta-blocking agent should be closely observed – effect on intra-ocular pressure or known effects of systemic beta-blockade may be potentiated. Use of two topical beta-adrenergic blocking agents not recommended. Patients with cardiovascular diseases and receiving hypotension therapy with beta-blockers should be critically assessed and other active substances considered. Cardiovascular disease patients should be monitored for disease deterioration and adverse reactions. Use with caution in patients with first degree heart block, severe peripheral circulatory disorders, mild/moderate COPD, asthma (respiratory reactions including death due to bronchospasm in asthma patients has been reported), corneal diseases, labile diabetes or those with spontaneous hypoglycaemia, active intraocular inflammation, aphakic or pseudophakic patients with torn posterior lens capsule, or with known risk factors for macular oedema. Inform anaesthetist before surgery as Eyzeetan may block systemic beta-agonist effects of adrenaline. While on beta-blockers, patients with a history of atopy or severe anaphylactic reaction may be more reactive to repeated challenge with allergens and may be unresponsive to usual dose of adrenaline used to treat anaphylactic reactions. Choroidal detachment has been reported with use of aqueous suppressant therapy (e.g timolol) after filtration procedures. If using other prostaglandin analogs, monitor for changes to intraocular pressure. Do not use in patients with contact hypersensitivity to silver. Beta-blockers may mask signs of hyperthyroidism. **Effects on ability to drive and use machines:** If transient blurred vision at instillation, wait until vision clears. **Interactions:** If more than one topical ophthalmic drug is being used, administer drugs at least 5 minutes apart. Potential additive effects resulting in hypotension and/or marked bradycardia when administered concomitantly with oral calcium-channel blockers, beta-adrenergic blocking agents, anti-arrhythmics, digitalis glycosides, parasympathomimetics, guanethidine. Potentiated systemic beta-blockade reported during combined treatment with CYP2D6 inhibitors. Concomitant use of ophthalmic beta-blockers and adrenaline may result in mydriasis. **Pregnancy:** Should not be used in pregnancy or breast-feeding unless necessary. If administered until delivery, carefully monitor newborns. **Side effects:** For full list of side effects, consult SmPC. 'Very common', 'Common' and 'Serious' side effects are included in this prescribing information. Very common (≥1/10) side effects: conjunctival hyperaemia. Common (≥1/100 to <1/10) side effects: headache, dizziness, punctate keratitis, corneal erosion, burning sensation, conjunctival irritation, eye pruritus, stinging sensation in the eye, foreign body sensation, dry eye, erythema of eyelid, eye pain, photophobia, eye discharge, visual disturbance, eyelid pruritus, visual acuity worsened, blepharitis, eyelid oedema, eye irritation, lacrimation increased, growth of eyelashes, rhinitis, blepharal pigmentation, hirsutism, skin hyperpigmentation (periocular). Uncommon Serious (≥1/1000 to <1/100) side effects: conjunctival oedema, iris hyperpigmentation, iritis, deepening of eyelid sulcus, eyelid retraction, dyspnoea. Serious (frequency unknown) side effects: hypersensitivity reaction including eye allergy, angioedema, allergic dermatitis, cystoid macular oedema, eye swelling, vision blurred, bradycardia, bronchospasm, asthma. **MA number:** PL 35533/0103 **Cost:** £14.16 for 0.3mg/ml bimatoprost + 5mg/ml timolol x 3ml **MAH:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire, GU32 3QG. **Legal category:** POM. **Date reviewed:** May 2020. **Version number:** 1010421347 v 2.0

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† Based on EY bottles vs UDVs

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Ocular Surface Disease 101

By **Seema Nanda**, OD

The perplexing task of treating the ocular surface occurs when countless conditions attack the cornea concomitantly. Clinicians may diagnose Dry Eye Disease (DED) initially by observing superficial punctate staining via the slit lamp, then complications may follow with persistent epithelial defects or recurrent corneal erosions. These issues could lead to neurotrophic ulcers which can become even more difficult to handle. Accordingly, treating at the earliest onset of ocular surface inflammation can mitigate further destruction of the corneal surface.

Ocular surface disease can be divided into aqueous or lipid deficiencies. These classifications can be further separated into the component layers of the tear film: the lipid layer may be reduced due to poorly functioning meibomian glands, while, the aqueous layer may be impaired due to an inadequately performing lacrimal gland. If the doctor can recognize each of these elements, analyze each part, and accept that the problems can occur alone or together, then the practitioner will be able to manage the cornea in a more systematic way.

Diagnostic testing can help detect levels of dry eye disease. Surveys can be used to measure patient's baseline symptoms, such as the DEQ-5 (Dry Eye Questionnaire-5), a simple five question form used to determine if a patient suffers from aqueous and/or lipid deficiency. Objective tests that can also be implemented include: matrix metallopeptidases (MMPs), tear break up time (TBUT), Schirmer's, and slit lamp evaluation of tear meniscus. Dry eye specialists prefer the MMP-9 test for its specific targeting of the inflammatory component in dry eyes. To diagnose and follow inflammation accurately will allow the doctor to better tailor a management approach.

Dry eye symptoms can be simplified as mild, moderate, or severe conditions. For mild cases, preservative-free artificial tears are excellent options. They contains an inactive ingredient, such as sodium hyaluronate, which anecdotally soothes the corneal surface. For moderate conditions, twice-daily use of MGD drops combined with supplements can provide relief to the deficient lipid profile.
For severe symptoms, additional therapies should be implemented which includes the consumption of high-quality supplements that contain fatty acids, specifically gamma linoleic acid (GLA) and alpha linoleic acid (ALA), which help to prevent this deterioration of the tear film. The combination of GLA - from black currant seed oil - with eicosopentanoic acid (EPA) and docosahexanoic acid (DHA) - from ultrapure US Pharmacopeia verified fish oil - aids in blocking the formation of proinflammatory prostaglandins while simultaneously stimulating production of anti-inflammatory prostaglandins. GLA works through its metabolite, dihomo-gamma linoleic acid (DGLA) to stimulate the tear-specific prostaglandin E-1, which reduces inflammation and supports tear production.
Consequently, this adjunctive therapy can help reduce inflammation and maintain corneal smoothness while improving symptoms of DED.
The progression of corneal problems can be slowed when the introduction of suppliments is started early.
These individuals should be monitored after four to six weeks of therapy to observe improvement in their dry eye complaints.

Another way to reduce active surface inflammation, would be the use of topical steroids and nonsteroidal anti-inflammatory drugs (NSAIDs).

Short-term use and the need for tapering steroids may be reasonable to prevent a possible rebound effect or spike in intraocular pressure. NSAIDS such as, cyclosporine ophthalmic emulsion 0.05%, cyclosporine ophthalmic solution 0.09%, and lifitegrast ophthalmic solution 5%, can be paired with steroids to help reduce inflammation for long-term therapy.

Topical remedies may not be sufficient in dealing with corneal deterioration as ocular surface disease advances. Consequently, the use of cryo-preserved amniotic membrane (CAM), could aid in these situations. CAM can be utilized as a treatment option for many corneal disorders due to its regenerative healing properties. When used with GLA, it can prevent further deterioration of the ocular surface. The efficacy can be seen in patients with moderate diffuse corneal punctate coalescing fluorescein staining which correlates with symptoms of moderate to severe dry eyes.
The insertion of amniotic membrane can resolve punctate erosions within one week. Normally, healing time for these types of lesions may take three months or longer, depending on severity. The acceleration of corneal restoration transformed the impaired cornea from a period of several months to that of a few days with cryo-preserved amniotic membrane, which is typical even in unmanageable cases. Inserting CAM as an anti-inflammatory is recommended to be worn for 3-5 days while taking nutritional GLA supplements.

Patients should return to the clinic at close intervals until they are stable and then extend visits out as conditions improve. Those patients who do not get regular follow-up visits are at higher risk of relapse. Fortunately, multiple therapies are now available to treat challenging corneal cases. Once these innovative approaches are implemented, both the patients and practitioners will be happier with their outcomes.

Seema Nanda, OD

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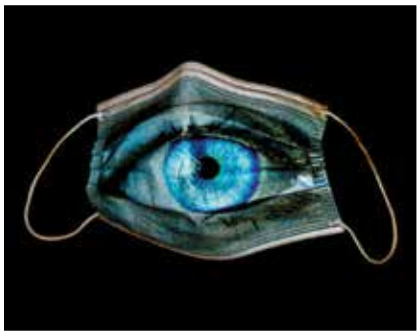
What's in the news?

Impact of the COVID-19 lockdown on digital device-related ocular health

Since the declaration of the lockdown due to COVID-19, the usage of digital devices has gone up across the globe, resulting in a challenge for the visual systems of all ages. The purpose of this study is to assess the impact of the lockdown on digital device usage, and consequently, the ocular surface health implications and circadian rhythm abnormalities related to digital eye strain.
An open online survey was sent through various social media platforms and was open for a period of 2 weeks.

For the results a total of 407 usable responses were obtained; the average age of respondents was 27.4 years. Typically, 93.6% of respondents



reported an increase in their screen time since the lockdown was declared.
The average increase in digital device usage was calculated at about 4.8 ± 2.8 h per day.The total usage per day was found to be 8.65 ± 3.74 hours. Sleep disturbances have been reported by 62.4% of people. Typically, 95.8% of respondents had experienced at least one symptom related to digital device usage, and 56.5% said that the frequency and intensity of these symptoms increased since the lockdown was declared.

The study highlighted the drastic increase in use of digital devices after the initiation of the COVID-19 lockdown, and along with it, the slow deterioration of ocular health across all age groups. Awareness about prevention of digital eye strain should be stressed, and going forward, measures to bring these adverse effects to a minimum should be explored.

Indian J Ophthalmol. 2020 Nov;68(11):2378-2383. doi: 10.4103/ijo.IJO_2306_20.

Authors: Aleksander Machowicz , Isaac Hall , Paola de Pablo , Saaeha Rauz , Andrea Richards , Jon Higham , Ana Poveda-Gallego , Fumiaki Imamura , Simon J Bowman , Francesca Barone , Benjamin A Fisher

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1. Selected polysaccharides at comparison for their mucoadhesiveness and effect on precorneal residence of different drugs in the rabbit model. Drug Dev. Ind. Pharm. 35, 941-949, 2009

2. Open-label randomized clinical trial on the efficacy and tolerability of Hydramed in the treatment of dry eye syndrome. Data on file.

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Assessing and managing dry eye, an Irish public healthcare system perspective

By **Brendan Cummings**

Dry eye of some degree is everywhere but where and when dry eye patients see an ophthalmologist varies hugely across healthcare settings. In refractive surgery settings, it's more often than not the case that the ophthalmologist is the one to bring up the subject at the pre-op assessment while the patient is often asymptomatic. Any amount of dry eye in this setting can lead to a patient's expectations not being met for a variety of dry-eye related reasons such as inconsistent pre-op refractions to post-op dry eye symptoms.

In the public system we often do not have the time to address issues our patients are not complaining about. The dry eyes we see are either in the Eye Emergency Department, in a non-dry-eye clinic, or extremely unwell patients intubated in the ICU.

For the patient attending a walk-in eye emergency department with dry-eye symptoms (as was often the case pre-COVID) we are sometimes quick to dismiss their complaints as trivial/ non-sight threatening and send them home with a prescription for lubricants and a leaflet on blepharitis. I have found this approach ineffective as these patients will often return with the same complaint a few weeks to months later claiming the problem is back. Patients can tell when an examination is rushed and are less likely to follow instructions from a doctor who hasn't given them the attention they feel their complaint deserves. As with almost every situation in medicine, a thorough and detailed history is the cornerstone of the consultation. For this reason, when assessing a patient in the ED whom I have a suspicion dry-eye is causing their symptoms I will have them give me as much of a symptom history as they feel they need to (within reason) and I will carefully and obviously examine the eyelid margins at the slit-lamp making sure to evert the lids and express meibum from the meibomian glands using a cotton-bud. I examine every patient with fluorescein and cobalt blue light and count out loud, under my breath but loud enough for the patient to hear, how long before I see tear film breaking up. I then examine the cornea for SPEEs or signs of exposure keratopathy. I am now equipped to give the patient a diagnosis, which is what

they have often waited hours to receive. "You have a condition called blepharitis/ meibomian gland dysfunction/rosacea/ etc, and it explains the majority of the symptoms you are complaining of," is usually my line. More often than not patients seem relieved that they have something 'wrong' with their eyes and haven't been 'wasting my time', as they often quietly fear. I then explain the cause of their dry eye symptoms to them referencing parts of my slit-lamp. "The oil produced by the glands in your eyelids is too thick and congested to protect the watery part of your tear efficiently", "the layer of tears on the front of your eye should stay stable for more than ten seconds but yours starts to break up and evaporate after only three seconds." "I can see some evidence of the dryness on your cornea and we need to start to reverse this process before it gets worse."
Now when I explain how and why to perform hot compresses, lid massage, lid hygiene, how often to use lubricants, the patient is invested in the process and much more likely to take ownership of the problem and follow instructions. These patients also tend to return to the ED much less often than the ones we throw lubricants at as they walk in the door.

Assessing dry eye outside of the 'emergency' setting where we are in a non-dry eye clinic often happens towards the end of the consultation after having assessed and dealt with the primary concerns such as explaining to the POAG patient that their pressures are a little higher than optimal and there is some evidence of visual field progression meaning we are going to have to escalate treatment for them. "OK thanks, doctor. Just one more thing, is the glaucoma making my eyes scratchy all the time?". It's these times when we realise just how annoying dry eyes can be for patients. Living life with uncomfortable eyes is often as much of a concern for patients as slowly losing vision. In these cases, assessment of the ocular surface is a routine part of my glaucoma examination. We try our best to use preservative free drops as much as possible with glaucoma patients as often dry-eye symptoms in this population are as a result of drop toxicity.

I have cancelled a handful of lower-lid lateral tarsal strip surgeries on the morning of surgery when, during the consent, the patient's description of their symptoms fits much better with epiphora secondary to blepharitis than entropion! Most of the time these patients have been put on the 'minor-ops' waiting list by a junior working in an oculoplastic clinic following a GP referral for watery eyes. Skimming over a dry eye assessment can potentially lead patients under a scalpel they have no business being under and having a procedure done that isn't addressing their symptoms, even if they do have a little lower lid laxity!

The easiest dry eye assessment used to be wondering up to ICU with a fluorescein drop and a hand held slit-lamp to see how dry an exposed cornea under high flow oxygen could get, then handing over a tube of ophthalmic ointment to the ICU nurse and asking for it to be applied every 2 hours before getting lost trying to find your way back to the ophthalmology clinic. These days getting up to an ICU involves so much PPE you can't see a red-reflex so now I just send the ophthalmic ointment with instructions.

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A lump on the cornea?
Clinical and immunohistochemical observations of corneal myofibroblastic proliferation with a differential diagnosis

Authors: Magdalena Edington, Fiona Roberts, David Lockington

Affiliation: Tennent Institute of Ophthalmology, Glasgow, UK

Introduction

We report a case of an enlarging corneal nodule, unresponsive to medical therapy, and the subsequent histological findings following surgical excision. We wish to remind the reader of the differential diagnosis of benign and malignant corneal nodules, and the need for histology when there is diagnostic uncertainty.

Case Report

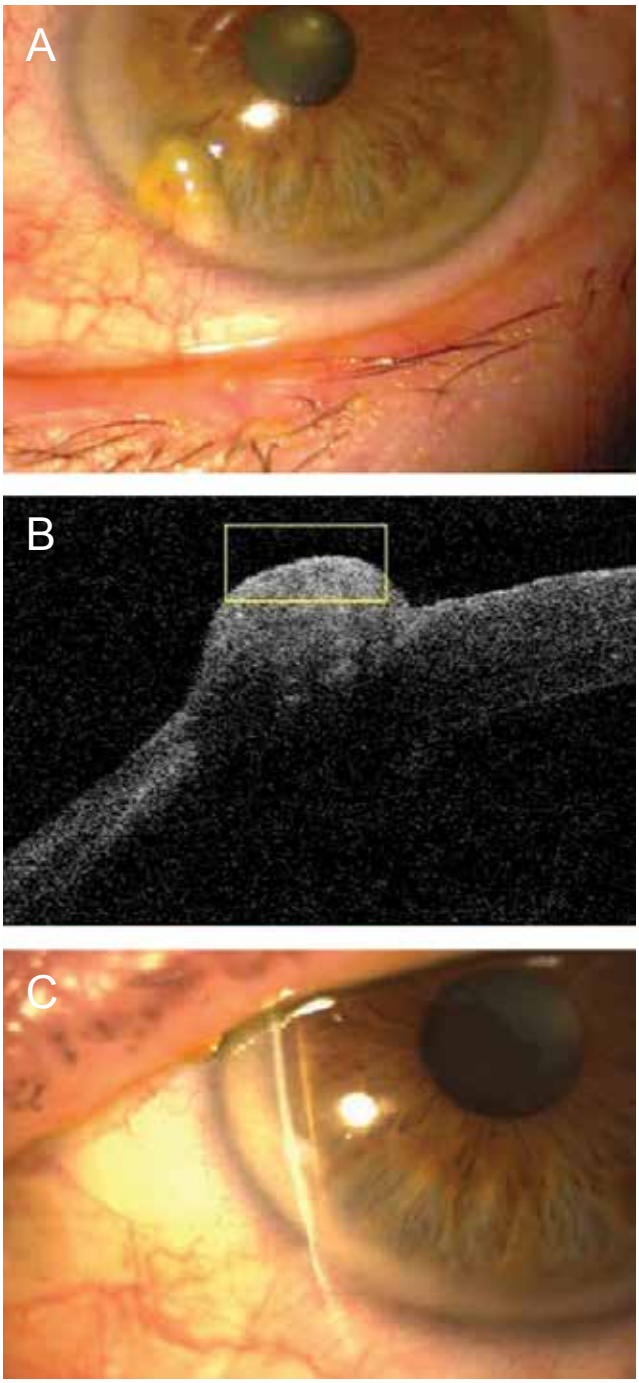
A 72-year-old female presented with a two-month history of intermittent foreign body sensation in her left eye. She had been initially treated in primary care with topical antibiotics for presumed conjunctivitis, but symptoms persisted and the patient noticed a 'white blister' on her cornea. She had no significant past ocular history, and no contact lens wear. Her medical history included hypertension and cardiac arrhythmia, for which she was receiving aspirin, bendroflumethiazide, atenolol, and warfarin.

On examination unaided distance visual acuity was 6/6 and 6/9 in her right and left eye respectively. She had mild blepharitis but the conjunctiva was not injected. The right cornea was clear; the left had an elevated gelatinous nodule measuring 1.5x2.7 mm with blood vessels from the limbus to the centre of the lesion [see Figure 1]. The remainder of the eye examination was unremarkable.

An inflammatory phlyctenule was suspected, and the patient was treated with oral Azithromycin 500mg once daily for three days, lubricants and topical steroids (Prednisolone) six times a day, tapered over a month. At review, she reported slight improvement in foreign body symptoms but felt the lesion was increasing in size. This was confirmed by photography and anterior segment OCT [see Figure 1]. Due to patient concern regarding the increasing growth, an excisional biopsy was performed. Intraoperatively, the lesion was easily dissected from a clean surgical plane above Bowman's membrane. Macroscopically, it was surprisingly dense and not compressible. Following excision, the patient was symptom free, with no recurrence of the lesion at 5-year follow up.

Histological examination showed the nodule to consist of a cellular spindle cell proliferation covered by a hyperplastic epithelium. By immunohistochemical staining the spindle cells were positive for smooth muscle actin, but negative for cytokeratins, S100, CD34, Desmin, CD117 and ALK [See Figure 2]. There were only occasional mitotic figures and the Ki67 proliferation index was very low. The sample lacked

Figure 1:



inflammatory cells typical in phlyctenules, and any hyaline or clumped collagen as would be expected in Salzmann nodules. The findings were consistent with a myofibroblastic proliferation. They were reminiscent of late stage mature nodular fasciitis.

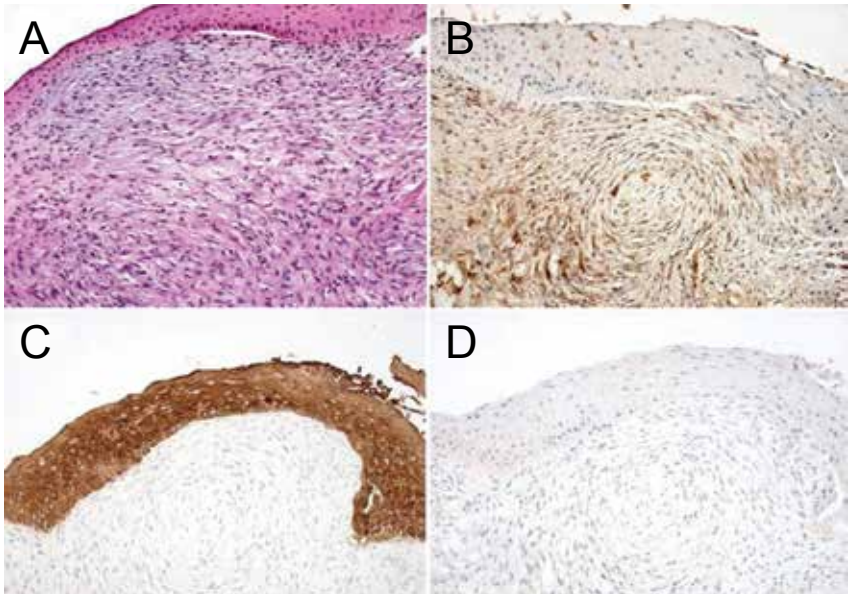
Discussion

Acquired corneal lesions are most commonly due to localised infection or inflammation, but if atypical, it is crucial to rule out ocular surface squamous neoplasia (OSSN). Over 95% of OSSN cases originate at the limbus, and lesions can have variable appearance, from pearly grey to reddish brown, with a papilliform or gelatinous surface. [1] The lesion can be vascularised, but this is not diagnostic. Clinically patients can be asymptomatic or complain of an irritated red eye.
The differential diagnosis of corneal lesions includes phlyctenules, Salzmann's nodular degeneration, and atypical corneal scarring such as keloid. Histopathology remains a useful and reliable diagnostic tool in the presence of worrying features or unresponsiveness to medical treatment.

Phlyctenulosis is a nodular inflammation of the peri-limbal tissues, which usually occurs secondary to an allergic hypersensitivity response of the cornea. Patients typically report ocular irritation and photophobia. Corneal phlyctenules usually appear as a white mound adjacent to the limbus, with a radial pattern of vascularized conjunctival vessels. Histologically, they are composed of lymphocytes, histocytes and plasma cells. [2] In contrast, in Salzmann nodular degeneration grayish, elevated nodules are often discovered in the upper and lower thirds on the cornea, relative to the position of the eyelids. Chronic exposure of an irregular corneal surface results in localized replacement of Bowman's layer by hyaline and clumped collagen fibrils, leading to superficial scarring. [3] There are also clinical cases of extreme keloid scarring of the cornea, reported even without preceding ocular trauma. [4]

In our patient, excisional biopsy was performed to rule out a malignant OSSN process as the lesion was enlarging despite medical therapy, was atypical, and had a blood supply. Histology showed a cellular spindle cell proliferation with a tissue culture type appearance in areas. This contrasts with the poorly cellular scarring seen in Salzmann nodular degeneration and the inflammation present in phlyctenules. Myofibroblastic proliferations occur in many sites either as reactive proliferations or as tumours (benign or malignant). Nodular fasciitis is a myofibroblastic proliferation that usually occurs in soft tissue. Frequently there are numerous mitoses but these diminish at a late stage, as does the proliferation index. In the ocular region it is best known in the orbit, although it has been described in an epibulbar location in association with floppy eyelids and in the sclera. [5, 6] Nodular fasciitis usually occurs in younger individuals although it has been described in all age groups. In our case the myofibroblastic proliferation was confined to the cornea but given the lack of recurrence following removal it is likely that the underlying reactive process is the same. A similar myofibroblastic proliferation forming a white nodule in the anterior corneal stroma has been previously described in children without a history of previous trauma or inflammatory disease. [7]

Figure 2:



This patient had a rapidly growing benign lesion on her cornea, which resolved with surgical excision. Histological examination was able to identify a rare diagnosis, but also reassure the patient. Excisional biopsy should be considered in any clinical situation where there is diagnostic uncertainty.

Acknowledgement

We thank the patient for granting her consent to share these images for publication.

Figure 1

Figure 1: Photograph at presentation (1a), and post-surgical excision (1c). 1b shows anterior segment OCT through nodule revealing that the growth is subepithelial and does not breach Bowman's membrane.

Figure 2

Histology slides revealed a 3mm nodule consisting of spindle cell proliferation covered by a hyperplastic epithelium; with no evidence of significant cellular atypia or mitotic activity (2a). Immunohistochemical staining revealed spindle cells positive for smooth muscle actin (2b) but negative for cytokeratin (2c), Desmin, S100, CD34, CD117 and ALK (2d). Ki67 proliferation index was very low.

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Q & A's with Prof. Craig

Randomized trial of topical periocular castor oil treatment for blepharitis. Ocul Surf 2020 May 15

Edited by **Vivian Ho**

Prof. Jennifer Craig

1

How did you come up with the amazing idea of studying Castor Oil in blepharitis patients?

I had the good fortune of meeting Dr. Emma Sandford in 2017. Emma's a natural health ophthalmologist in the Bay of Plenty, in the North Island of New Zealand and she excitedly shared with me her anecdotal success with topically applied 100% cold pressed castor oil in patients with anterior blepharitis. I was interested as this is a common, underdiagnosed condition that's relatively poorly managed in clinical practice. Emma's rationale for its use was the recognised anti-inflammatory and anti-microbial properties of castor oil. We discussed the need to back up her clinical findings with scientific evidence and from there we designed a randomised controlled trial, where both clinicians and participants would be masked, to allow us to demonstrate whether or not castor oil could truly make a difference.special infection control measures that were adopted by your department during the pandemic.

2

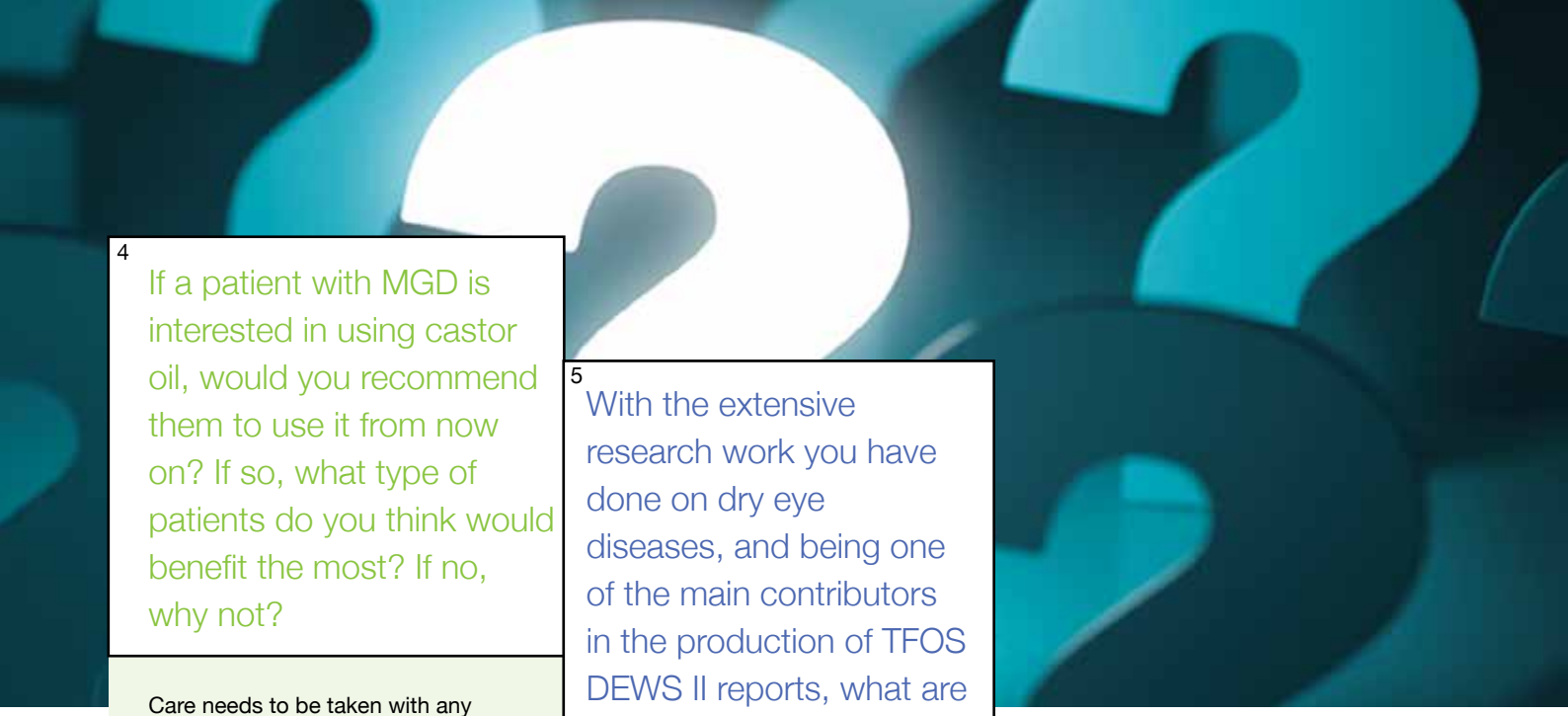
Your clinical result shows encouraging results with a significant reduction in OSDI and DEQ-5 symptom scores after the 4-weeks treatment, as well as improvement in eyelid margin thickening, telangiectasia, eyelash matting, madarosis, cylindrical dandruff and lid wiper epitheliopathy. How does Castor Oil contribute to such improvement?

The results are encouraging, but we need more studies to be able to prove this definitively. We suspect there's probably a combination of factors contributing to disrupting what has become known as 'the vicious circle of dry eye disease'. This vicious circle is a self-perpetuating cycle of tear film instability, hyperosmolarity, ocular surface inflammation and epithelial damage. Castor oil may be helping to break this cycle by helping to reduce the bacterial load on the eyelid margins, either from a direct effect on the bacteria and/or by helping to reduce debris on the lid margin. A reduced bacterial load limits the presence of bacterial exotoxins that destabilise the tears. There may also be some anti-inflammatory activity from the castor oil which might further contribute to reducing inflammatory mediators within the tears and supporting a more stable tear film. Finally, it's possible that the oil might contribute to the tear film lipid layer by migrating across the lid margin and supplementing the natural tear film oils.

3

The treatment did not show any changes to the tear film parameters, Demodex load or meibomian gland characteristics. What do you think the reasons are?

This study was only a 1-month trial and while we saw some of these parameters changing in a positive direction, I would expect we would need a longer trial, with more participants, to demonstrate some of these other effects. This is especially true in the case for indirect effects such as meibomian gland function improvement which is more likely to show up as a downstream benefit of interrupting the vicious circle of dry eye disease, in the longer term. We know *Demodex* are challenging to manage, and are treated most often with tea tree oil products. There's not currently evidence to show that castor oil is effective in treating *Demodex* but even if there's not a direct effect on the mites, removing its food source by cleaning up the lid margins, might be beneficial in the longer term.



4

If a patient with MGD is interested in using castor oil, would you recommend them to use it from now on? If so, what type of patients do you think would benefit the most? If no, why not?

Care needs to be taken with any products used on and around the eyes, therefore patients with MGD should seek advice from their eye care professional in the first instance. It seems from our research that periocular application of castor oil might be best suited for ameliorating the signs of anterior blepharitis rather than posterior blepharitis, at least in the shorter term, but more research is needed in this area and my recommendation would be to wait until a commercial product, that has undergone appropriate testing, becomes available.

5

With the extensive research work you have done on dry eye diseases, and being one of the main contributors in the production of TFOS DEWS II reports, what are your current management approaches in patients suffering with MGD?

After a thorough assessment to evaluate factors that might be contributing to the MGD, I take a logical and multifaceted approach to management. I start by optimising the lid margin, and this often includes managing bacterial and/or demodex load with dedicated lid cleansers, and in-office microblepharoexfoliation if necessary. I might also debride the lid margin to remove excess keratinisation where this is impeding flow of meibum from the gland orifices. The second stage involves encouraging meibum outflow from the glands by applying warm compresses (heated to at least 40°C for 10 minutes), using a latent heat device, or performing an in-office treatment such as thermal pulsation or IPL. Warming treatments will usually be accompanied by therapeutic gland expression. Finally, if the tear lipid layer remains suboptimal in quality, following these gland therapies, I may use systemic antibiotic treatments such as a low dose doxycycline, oral azithromycin, or omega 3 essential fatty acid supplementation. For patients whose natural oils remain deficient after treatment, artificial tear drops or sprays with lipid components, can help to supplement the natural oil layer, and improve its function.

6

With your extensive research on MGD management (1-4), e.g. eyelid massage device, intense pulsed light therapy, Manuka honey microemulsion and castor oil, which treatment modality works best for your MGD patients? And how do you decide which patients would benefit from a certain type of treatment?

I treat every patient I see as an individual, so I tailor my choice of treatment(s) to the patient based on diagnostic tests which let me know the dry eye subtype and severity. I also take into consideration the patient's medical and ocular history, including any modifiable and non-modifiable risk factors, and also their lifestyle, dexterity as well as likely treatment costs, as any of these factors can impact compliance. I'm pleased to see an increasing range of therapeutic strategies for our patients which gives us a greater number of options, although we need better evidence through carefully designed clinical trials to confirm treatment safety and efficacy, and to help identify the best products for specific dry eye subtypes and severities.

Reference:

i. Randomised trial of the clinical utility of an eyelid massage device for the management of meibomian gland dysfunction. Cont Lens Anterior Eye 2019 12 26;42(6):620-624.

ii. Randomised double-masked placebo-controlled trial of the cumulative treatment efficacy profile of intense pulsed light therapy for meibomian gland dysfunction. Ocul Surf 2020 Apr 30;18(2):286-297.

iii. Randomized masked trial of the clinical efficacy of MGO Manuka Honey microemulsion eye cream for the treatment of blepharitis. Ocul Surf 2020 Jan 20;18(1):170-177. Epub 2019 Nov 20.

iv. Randomized trial of topical periocular castor oil treatment for blepharitis. Ocul Surf 2020 May 15.

Dry Eye and Increased Face mask Wear – MADE (Mask Associated Dry Eye)

By **Nathan Little**

Mandated facial mask wear has been proven in reducing the spread of the novel SARS-CoV-2 virus which causes Covid-19, however mask wear, while beneficial in reducing the spread of the disease does have unintended outcomes for the ocular surface. Recent articles have referenced an increase in dry eye disease related to mask wear. This new phenomenon was designated as Mask Associated Dry Eye (MADE) and was first referenced by Darrell E. White MD in Ocular Surface Magazine in June, 2020.[1] Given the continued global impact of Covid-19 and the increase in face coverings a subsequent proliferation of mask related ocular surface disease and MADE could be on the horizon. The UK government issued the compulsory requirement for face coverings back in July, 2020 which included an extensive list of indoor and outdoor circumstances.[2] Due to government guidelines the UK saw an increase of mask wear in public places by 75% from March to September, figure 1 below.[3] A recent poll from YouGov also indicated interesting data pertaining to the frequency of travel outside the home and the type of face covering worn, Figure 2. An estimated 94% of the population left the domicile in the past week and 90% wearing a mask/face covering during that time. Notably, 69% of Britons wore washable and reusable masks as part of their travel routine. While the numbers of Britons wearing a face covering is promising (over 90%) this increase and the requirement for new behavioral habits does not come without faults and a proliferation in poor mask hygiene.[4] Figure 3 below shows that only 13% of all those wearing washable face coverings are cleaning them correctly, with 66% washing at a maximum every 2-3 wears (and 15% not cleaning the face mask at all). [4]

The apparent increase in mask time and the unsettling statistics on mask hygiene point to an upcoming increase in MADE and potentially other ocular surface diseases. Recent articles by Moshirfar et al. and Darrell E. White theorized that the increase in air flow from the dynamics of wearing the face covering may have an effect on the tear film stability. [1,5]

The increase in air flow to the ocular surface from the mask updraft may result in air convection to the ocular surface increasing tear film evaporation.[5] Feedback from different mask wearing cohorts described a distinct feeling of increased air flow upwards from the mask to the ocular region and the same patient cohort presented increased symptoms from the Ocular Surface Disease Index, including increased corneal staining and a reported increase in dry eye post cataract surgery.[5]

In addition to an increase in patient presentations for dry eye symptoms and increase in staff complaints of dry eye was also described.[5] It can be hypothesized that in addition to increased air flow from updraft that in these cases of eye care provider (ECP) staff the use of tape or other adherent materials used to hold a mask in place may have affected the normal biomechanics of the lid.[5]

The prolonged effects of the mask wear have not been quantified extensively in literature but ocular surface irritation and even exposure keratopathy have been reported as a result of mechanical ventilation and or lagophthalmos in some instances.[5]

Given the clear lack of documentation of ocular surface disease and the alike related to mask wear and MADE it is safe to say that eye care providers (ECPs) will need to consider MADE and other ocular surface diseases caused by mask were moving forward.

The prevalence of Covid-19 and mask wear will not diminish for the foreseeable future which may very well cause an increase in dry eye disease symptoms for patients, staff and even the ECP. In addition to dry eye symptoms, increased mask wear and the subsequent deterioration of the tear film may also pose a risk for increased transmission of Covid-19. This area of ocular surface disease is one to watch and may very well be a growing segment in the future.

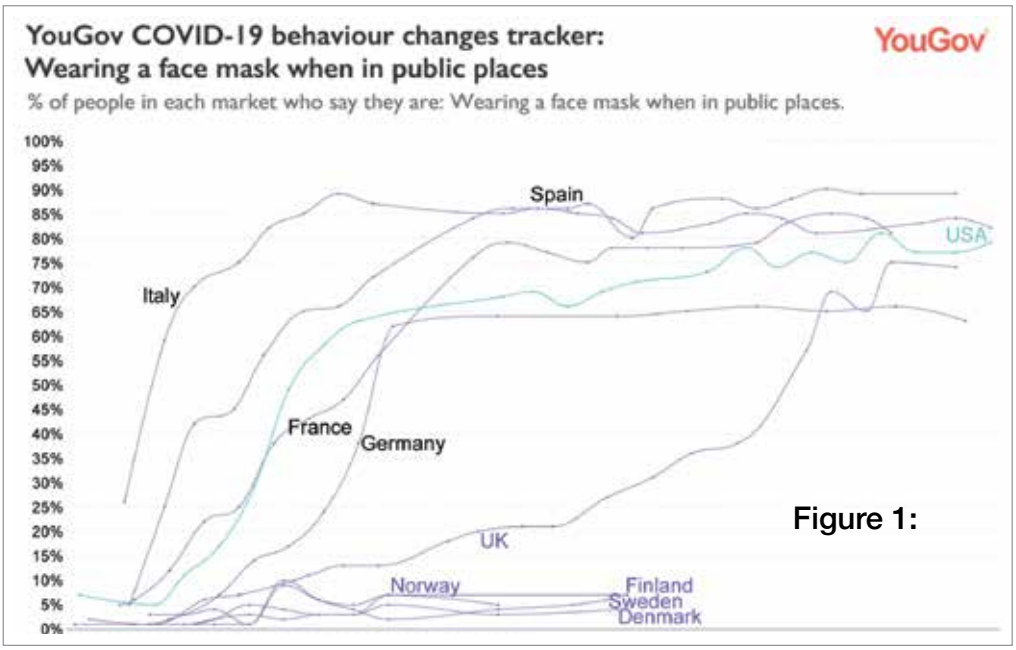


Figure 1:

1. https://www.healio.com/news/ophthalmology/20200622/blog-a-new-coronavirusassociated-eye-disease
2. https://www.gov.uk/government/publications/face-coverings-when-to-wear-one-and-how-to-make-your-own/face-coverings-when-to-wear-one-and-how-to-make-your-own
3. https://yougov.co.uk/topics/international/articles-reports/2020/03/17/personal-measures-taken-avoid-covid-19
4. https://yougov.co.uk/topics/health/articles-reports/2020/08/31/just-13-reusable-mask-wearers-are-washing-them-fre
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7362770/

Figure 2:

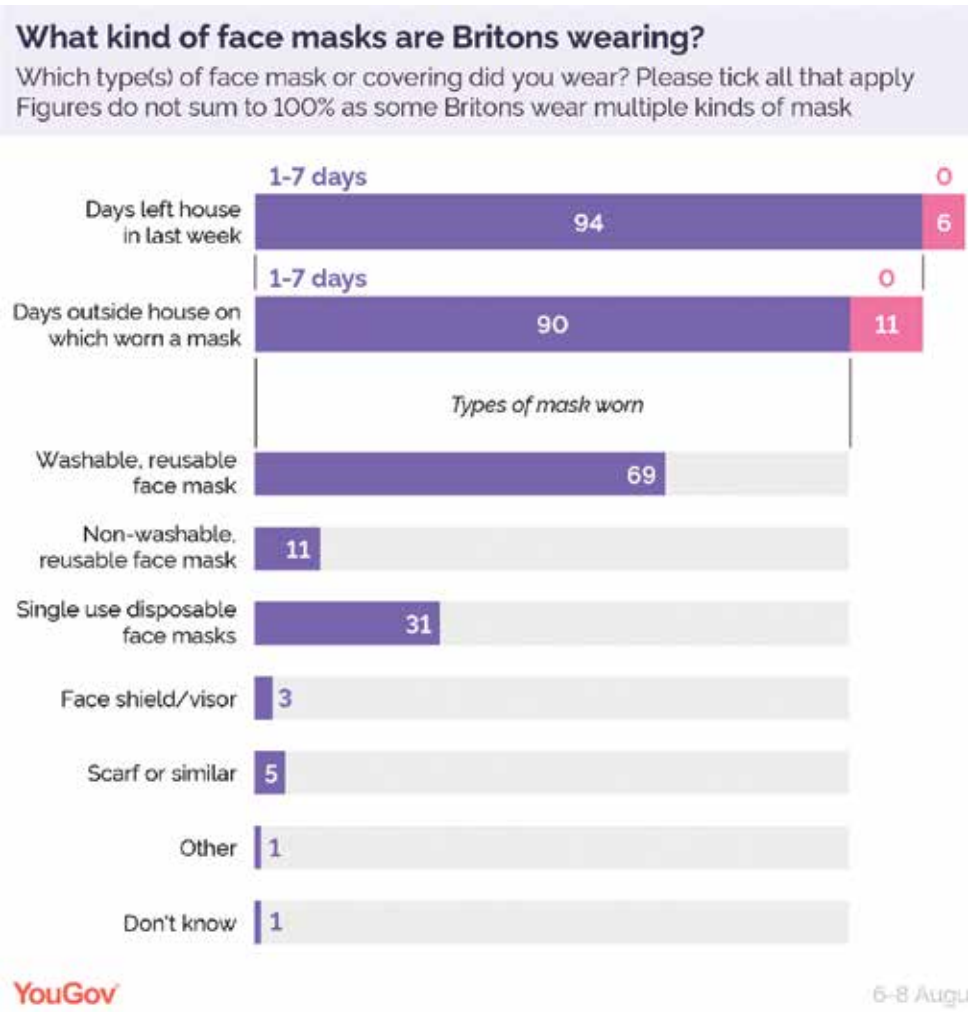


Figure 3:

Shotgun metagenomic sequencing to determine corneal infection

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Vito Romano – St. Paul's eye unit, Royal Liverpool University Hospital, Liverpool, UK

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Mohit Parekh – UCL Institute of Ophthalmology, London, UK

Corneal infections are the main cause of corneal scarring leading to reduction of vision or in the most serious cases, to blindness. Being an avascular tissue, cornea provides an immune privilege resulting in a slower recovery following an infection[1]. Often, an urgent treatment is required in cases of corneal infections to reduce any possible damage in the deeper layers of the tissue. Therefore, diagnosis of the primary causative agent becomes mandatory. Conventional diagnostic methods detect the presence and the class of an organism leading towards a broad spectrum antibiotic use, as the primary measure of treatment. Metagenomic shotgun sequencing-based technologies allow a hypothesis-free approach to identify full taxonomic and functional profile of an organism. Although conventional diagnostic methods can be used for quick identification of the causative agent, a detailed taxonomy and functional profile of an organism could be advantageous for target validation purposes and specific treatments.

The conventional shotgun approach was based on Sanger sequencing method. However, with the recent advances in the field, next-generation sequencing that produces millions of shorter reads (between 25-500 bp) in a short period of time result in high coverage compared to Sanger sequencing. Metagenomic shotgun sequencing allows to sufficiently determine the species/ strain using downstream bioinformatics platform. As it provides millions of reads, it is possible to obtain an overview of a complex microbiome with high sensitivity. Next-generation shotgun sequencing is also advantageous as it can detect the total microbiome from as little as 1ng volume of the sample. Many studies have shown the clinical potential of this technique which includes deep characterization of microbiome[2] for both, acute and chronic stages[3], human host response analyses and its applications in oncology.

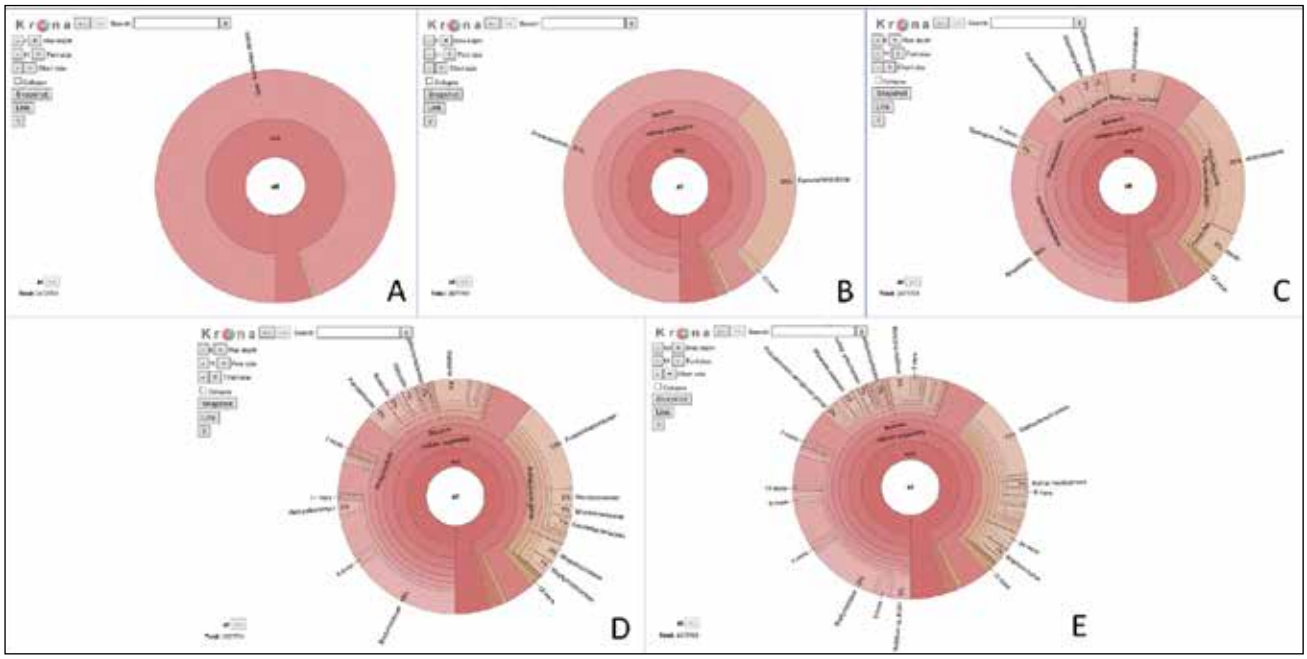
In a recent report, we showed that although conventional diagnostic approach reasonably suspected herpetic keratitis in a patient (92 bp positive HSV-DNA – type 1), shotgun sequencing confirmed the presence of HSV along with the last available taxonomical profiling of the virus i.e.

1. Simplexvirus – 124,439 reads
2. Human_alphaherpesvirus_1 – 124,091 reads
3. Human_alphaherpesvirus_2 – 36 reads

These results were achieved using 1.9 ng/µL of DNA concentration (114 ng in 60 µL) of the total sample volume[4]. Conventional diagnosis using PCR and histology requires a relatively higher amount of samples for analysis that are difficult to obtain in most of the clinical samples[5]. However, as the ocular surface microbiome hosts organisms from environment, not all the identified organisms are a cause of infection. In fact, as the microbiome of each individual is different, comparing to a standard control becomes fairly difficult unless a significant amount of samples are collected and analyzed.

Next generation sequencing technologies heavily rely on the analysis of the downstream bioinformatics data.

Figure 1:



It becomes difficult for a clinician to analyze huge datasets obtained for individual patients routinely therefore decoding the data is required. For example, the Krona chart (Figure 1) shows the taxonomical profile detected from the genetic material obtained from the ocular surface of a patient suffering from Acanthamoeba keratitis. These data require further downstream analysis to find the causative agent from the entire pool of the genetic material.

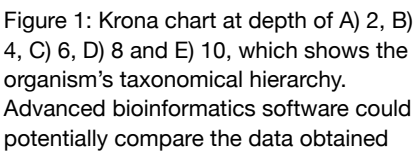


Figure 1: Krona chart at depth of A) 2, B) 4, C) 6, D) 8 and E) 10, which shows the organism's taxonomical hierarchy.

Advanced bioinformatics software could potentially compare the data obtained against resistance profiles, thus transforming next generation sequencing into a widespread practically and clinically feasible technique. The sensitivity and enrichment or depletion methods, laboratory workflow, reference standards for downstream analysis, bioinformatics challenges, regulatory issues, associated costs, determining the presence of actual live organisms and turnover time could be considered as current limitations when such techniques are deemed for routine clinical practice[6]. The turn-around time and costs are predicted to be significantly reduced with advances in this field. Conventional diagnostic method and metagenomics could hence be considered simultaneously to acquire data and create large databases and online platforms that could be used in the future as a reference to correlate and make this technique highly specific both in terms of diagnostics and treatments.

> "Next generation sequencing technologies heavily rely on the analysis of the downstream bioinformatics data."

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The QUICK Dry Eye Screening Test

By **Artemis Matsou**

Dry eye syndrome (DES) - also called dry eye disease- is a chronic, multifactorial disorder of the tears and ocular surface, characterized by a loss of homeostasis of the tear film, as defined by the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II[1]. Ocular symptoms typically include burning sensation, gritty feeling or foreign body sensation, redness, stinging, itching, photophobia, blurred vision or fluctuating visual disturbance, increased lacrimation, difficulty wearing contact lenses or driving at night. DES can have a substantial impact on visual function, ocular comfort, quality of life and work productivity[2]. It can also adversely affect the outcomes of cataract and refractive surgery.

Dry eye disease is frequently classified into two etiological sub-categories: aqueous tear deficient DES (reduced tear volume) and evaporative DES (deficient lipid layer)[3]. Regardless of the exact subtype, loss of tear film homeostasis results in a vicious circle of ocular surface inflammation, tear film hyperosmolarity and instability contributing to a self-perpetuating disease, with potential irreversible damage to the ocular surface[1,3]. The prevalence of DES ranges from 5% to 50%, but can be as high as 75% among certain populations, with the elderly and women more likely to be affected[4, 5]. A number of risk factors have been associated with dry eye syndrome (table 1), such as personal, environmental/ lifestyle factors, clinical and autoimmune conditions, drug induced and surgical/traumatic[6].

However, there is no single "gold standard" sign, symptom that correlates perfectly with dry eye[1], and more importantly, there is no single diagnostic tool. DES diagnosis is usually based on a combination of tests and patient-reported symptoms and continues to challenge ophthalmologists worldwide.

Currently, there is a number of diagnostic tools available: from traditional tests such as tear film break-up time (TFBUT) and ocular surface staining to testing for factors such as MMP-9 and osmolarity.

There are also instruments to image and quantify the tear film and the condition of the meibomian glands. But this leads to the question: are there too many tests available? How practical is to perform all of them? Which ones can offer a quick but accurate diagnosis? For a diagnostic test to be widely adopted as a key test, it will need to be quick, effective, inexpensive, easy to perform and available in clinical practice.

We hereby suggest **the QUICK Dry Eye Screening Test** (figure 1), which will allow the detection of dry eye disease in the majority of patients during a clinical consultation, using simple, readily available tools.

Equipment required:

- Fluorescein Sodium Sterile Ophthalmic Strips. Each strip is impregnated with 1.0mg of Fluorescein Sodium.
- Non-preserved sterile normal saline drops
- A slit lamp

eyelid manipulation and intraocular pressure check.

The QUICK Dry Eye Screening Test

1. (10 secs): Fluorescein instillation

The fluorescein strip is moistened with a small amount of normal saline drops (a single drop is sufficient), without touching the dye impregnated end of the strip. The fluorescein is then applied by gently touching the bulbar conjunctiva of the inferior cul-de-sac without touching the cornea.

2. (10 secs): Tear meniscus height

The tear meniscus height is assessed as an indicator of tear volume. The quantitative evaluation of the tear menisci is considered the most direct approach to study tear film volume. The meniscus is assessed in the centre of the lower eyelid without lid manipulation shortly after a blink. A tear meniscus height less than 0.25 mm is suggestive of dry eye.

3. (25 secs): Tear film break up time (TFBUT)

The patient is asked to blink naturally three times in order to distribute the dye across the ocular surface and then to cease blinking until instructed to blink again and to stare straight ahead.

The tear film is observed under the cobalt blue light of the slit lamp and diffuse illumination. The time (in seconds) between the last blink and the appearance of the first dry spot or hole in the tear film is measured and equal to the TFBUT (figure 2).

The reference value for DES diagnosis is a TFBUT of less than 10secs and it has been found to be relatively specific in screening patients for tear film instability[7]. Three TFBUT readings should ideally be obtained and averaged for each eye.

4. (15 secs): Ocular surface fluorescein staining.

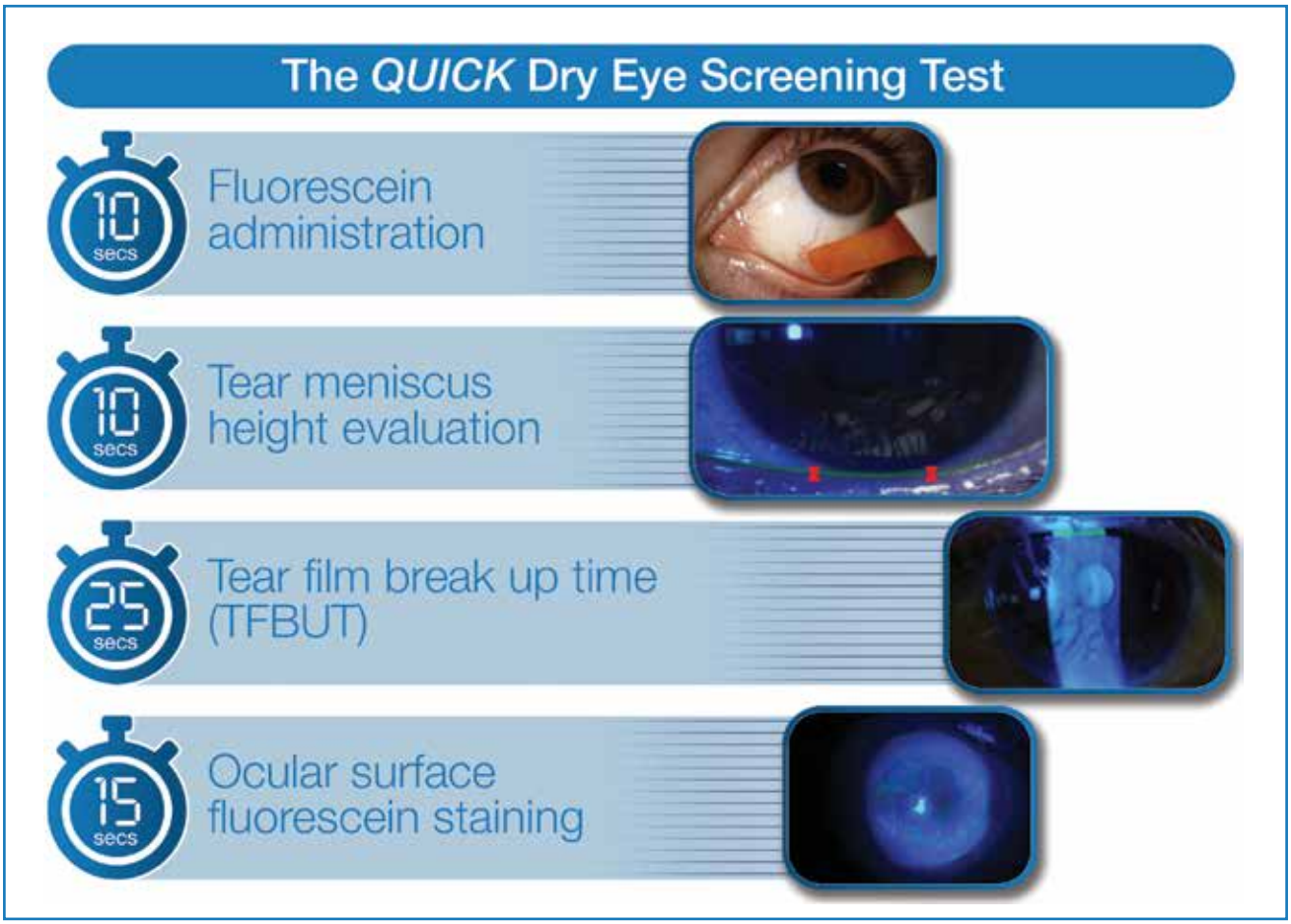
Table 1: Risk factors for dry eye syndrome:

Risk factors for dry eye syndrome					
Personal	Environment/ lifestyle	Medical conditions	Autoimmune diseases	Drug-induced	Surgical/traumatic
Female gender Older age Asian ethnicity Contact lens use Low dietary intake of omega-3 fatty acids Vitamin A deficiency	Low humidity or windy environments Air-conditioning Prolonged Reading for long periods Driving extended periods Cigarette smoking or smoke exposure Prolonged exposure to display monitors (computer, tablets, etc.)	Bell's palsy Parkinson disease Depression Perennial/seasonal allergies Diabetes mellitus Rosacea/ acne Glaucoma Thyroid disease Hepatitis C	Rheumatoid arthritis Sarcoidosis Sjögren syndrome Connective tissue disease	Anticholinergics Oestrogens Antipsychotics Glaucoma medications Antivirals Oral contraceptives Beta-blockers Opioids Diuretics Selective serotonin reuptake inhibitors Systemic chemotherapy	Refractive laser surgery Ocular injury

Given the high prevalence of DES and its potential for ocular surface damage and adverse effect on quality of life, one can appreciate the need for prompt and accurate diagnosis of the problem.

It is worth noting that the following measurements should be performed prior to instilling any other drops to the patient's eyes, and before any other invasive tests are conducted such as

Figure 1: The QUICK Dry Eye Screening Test:

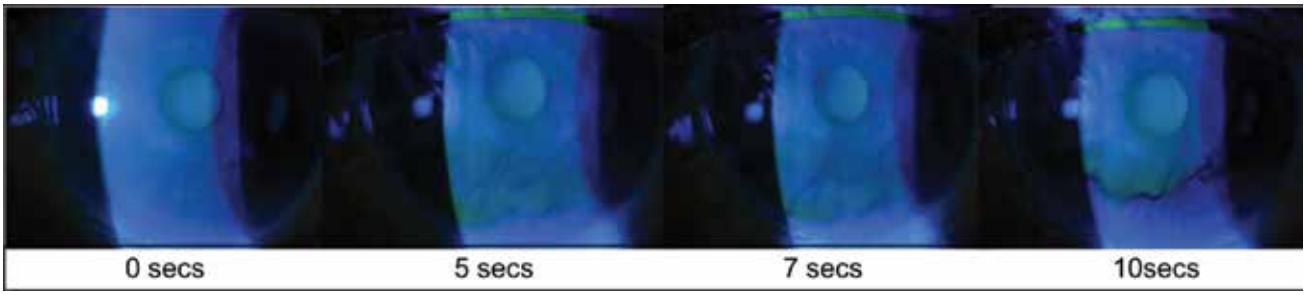


The fluorescein staining evaluation of the cornea and conjunctiva should be carried immediately after TFBUT. Fluorescein dye is taken up when corneal and conjunctival cells experience a compromise to their integrity, such as a disruption in superficial intercellular tight junctions[8]. Under the cobalt blue light these areas will appear bright green.
The typical staining pattern of the cornea and conjunctiva in dry eye syndrome includes epithelial punctate staining in the intrapalpebral region. The degree of staining of the ocular surface can be graded using various grading systems. Corneal and conjunctival staining have been shown to be informative markers of disease severity.

The suggested **QUICK Dry Eye Screening Test** should allow a rapid but reliable screening for dry eye syndrome in all settings and can be easily performed by all types of eye care professionals; opticians, optometrists, healthcare assistants specializing in eye care and ophthalmologists, and requires minimal training. The simplicity and tangibility of this test, along with its time and cost-effectiveness make it highly reproducible and attractive for wider adoption. It's easy to do, fits well into clinic flow, is inexpensive and offers reliable results; all the desirable qualities of a good screening tool.
Patients identified to have abnormal measurements and findings strongly suggestive of dry eye syndrome via this approach, can then be referred for further investigations, while patients with normal values and lack of concerning signs are spared from more elaborate testing as these steps can safely rule out dry eye syndrome in most cases.

Considering that dry eye syndrome is one of the most underdiagnosed conditions in eye care today, it is essential that all patients are screened for it. In fact, it is advisable to assume that all patients have dry eyes until proven otherwise, even for those without symptoms. This test should be performed to all patients due to undergo ocular surgery such as cataract surgery. The benefit in doing so is two-fold. Firstly, DES can induce errors in IOL power calculation, increasing the risk of a post-operative refractive surprise[9]. Secondly, DES can affect the post-operative healing process, triggering or exacerbating post-operative ocular surface

Figure 2: Tear Film Break-Up Time: the most frequently performed test of tear film stability in clinical practice. It is measured as the time that elapses between a complete blink and the appearance of the first break in the tear film:



inflammation due to elevated inflammatory cytokines in the tear film, leading to slower recovery and discomfort which can persist for many months after surgery, compromising quality of life[10-11].

As a consequence, untreated DES can jeopardize visual, refractive outcomes and patient satisfaction despite the absence of technical issues. It is therefore recommended that DES is proactively addressed in order to mitigate these risks, in all cataract candidates.

Integrating the QUICK Dry Eye Screening Test in routine practice can also prove priceless in refractive and premium IOL cataract surgery, as often patients with low grade or asymptomatic DES will undergo a costly procedure, only to end up dissatisfied with the outcome due to untreated dry eye disease. Diagnosing and managing DES in these circumstances not only prevents patients from blaming postop problems on the surgery, but also improves accuracy of measurements[12].

In summary, despite the army of available diagnostic tests for dry eye disease, ranging from the simpler, traditional and inexpensive to the newer, more sophisticated but costly high-tech devices, there is still no single test that can be universally diagnostic.

The evaluation of DES is often regarded quite cumbersome and therefore overlooked by many eye care professionals.

The QUICK Dry Eye Screening Test provides a simple, quick and reliable way to screen for dry eye syndrome in the general population, and identify those who would benefit from further investigations and treatment.

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Biomarkers in Dry Eye Disease

By **Samer Hamada**

Dry eye disease (DED) has so far been established as a chronic inflammatory condition, of the ocular surface. Despite our expanding knowledge and the growing number of diagnostics, there remains a challenge in the diagnosis and management of dry eye disease. This is particularly more challenging when there is a mismatch between signs and symptoms, which is the case in a large percentage of dry eye patients. In order to facilitate better diagnosis and management of DED, an increasing number of biomarkers have been investigated and utilised in clinical research as well as clinical practice settings.

What is a Biomarker?

A biomarker is an indicator of normal biological or pathological process, or the response to treatment. It should be objective, reproducible, and provide a value that is reliable, specific and sensitive to the process, micro-environment, and organ. In research and clinical trials, specific biomarkers would help patients selection and monitoring response to specific therapies.

Imaging Biomarkers

Imaging biomarkers were adopted quickly due to ease of use, non-invasive, and their high impact on disease diagnosis and management. Some of the examples of imaging biomarkers are:

- Noninvasive break-up time (NIBUT) to measure tear film stability
- Tear menisci height, area, radius, and depth to measure tear film volume
- Infrared meibography quantitative and morphologic parameters to assess meibomian glands
- Confocal assessment of corneal dendritic cells and other inflammatory cells to assess ocular surface inflammation
- Confocal assessment of subbasal corneal nerves (quantitative and morphologic parameters) to study corneal innervation

Tear film Biomarkers

Scientists have tested the possibility of using tear film biomarkers to help in the diagnosis, and treatment dry eye disease. The Pubmed search engine has hundreds of articles, related to the analysis of tear film cytokines, chemokines, and other proteins in relation to ocular surface inflammation including dry eye disease. Eye specialist are hoping that the use of biomarkers detection, will help to better understand more about the pathophysiology of DED. This will enable us to predict those at risk of dry eye disease, and potentially guide the treatment.

There have not been many advances on treatment level in dry eye disease and this is largely due to limitations of our in-depth understanding of the pathophysiology of DED. Many of the new therapies failed to get the regulatory approval due to the low success rate. With more information about biomarkers, we will be able to achieve better therapies, to develop and to monitor its efficacy.

In an ideal world it would be great, if we knew that dry disease is associated with specific parameters. This would help to detect those at high risk of dry disease, or even potentially a screening program, diagnostic program, or a criteria to identify disease severity and response to treatment. Furthermore it might answer frequently asked questions by patients, such as what is the long-term prognosis of the disease. It would be amazing to be able to tell contact lens wearers or those attending your practice seeking refractive laser surgery, or other refractive procedures what is the risk of them developing a dry eye disease immediately or in the long term after surgery, likewise on the long-term use of contact lenses.

There are hundreds of biomarkers which are used to as diagnostics, monitoring, or predicting biomarkers. It will be very underestimating to suggest that one or group of biomarkers would be enough to define DED when we know that it is, by definition, a multifactorial disease. The hope is that biomarkers would help to categorise DED and allow for more effective therapies, equally important if It would be used in the diagnosis of DED.

Bearing in mind that dry disease is essentially an immune-mediated inflammatory disease, the ocular surface biomarkers would be mostly those which gauge presence, and magnitude of inflammation. It will be a game changer if we were able to identify those markers, that correlate well with dry eye disease. All types of ocular surface inflammatory diseases might contribute to raised inflammatory biomarkers, and hence currently known biomarkers will not be able to differentiate dry eye disease from other inflammatory eye diseases. However, the levels of markers could help to know whether a dry eye treatment is working or not.

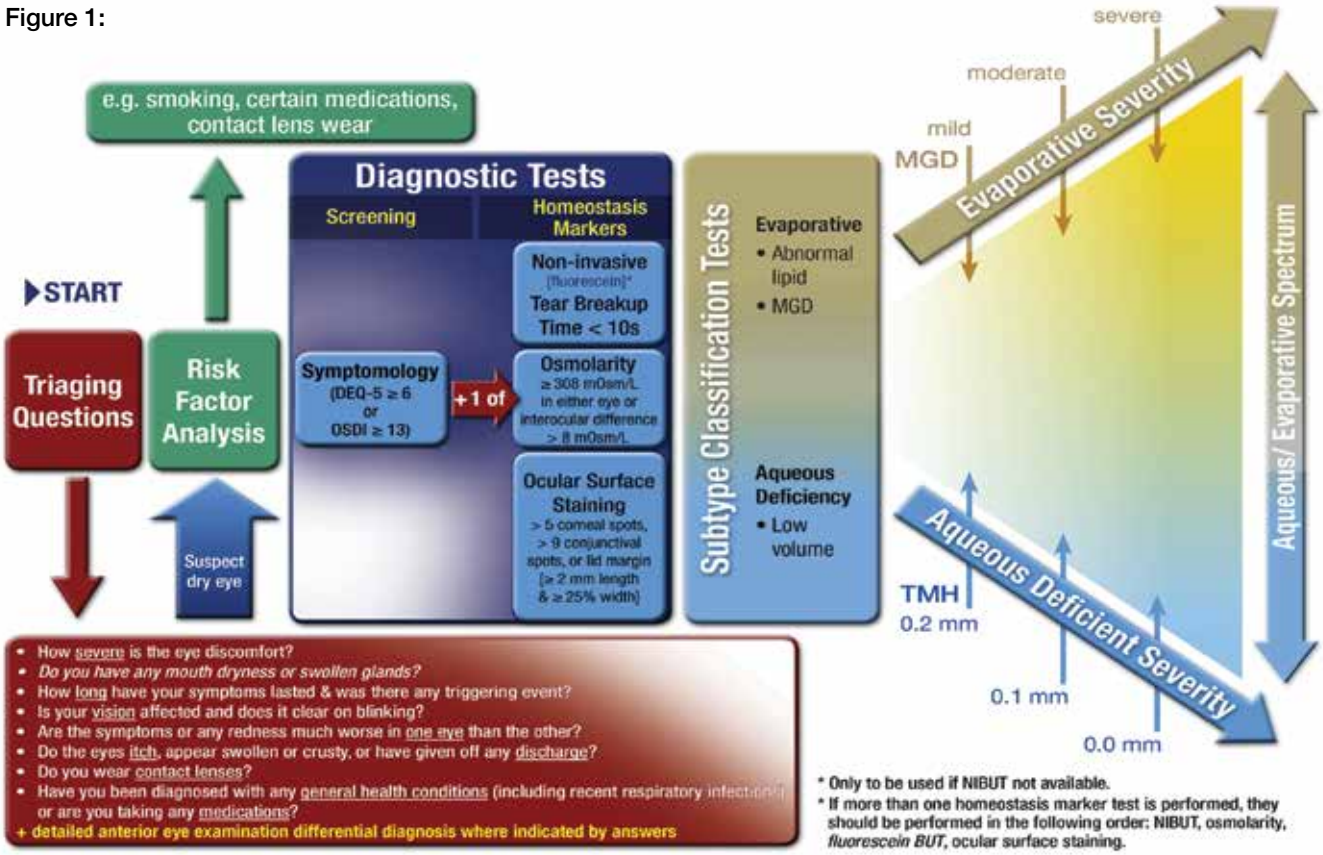
Types of Tear film Biomarkers

In measuring ocular surface biomarkers, there are two main approaches, that to take a tear sample or to perform impression cytology (IC).

Among tens of inflammatory markers that were mainly studied in clinical research, HLA-DR is the most common biomarkers of inflammation in dry eye disease which were studied through impression cytology. However there is a big variation among various studies of what is normal and what is more indicative of DED. The use of IC remains a research tool at the moment.

More easily to sample and measure are tears. Tear biomarkers originate from lacrimal gland, ocular surface, epithelial

Figure 1:



cells, stromal immune cells, and meibomian glands, and blood.
Tear biomarkers can be divided into:
1- Ocular surface inflammation: Inflammatory biomarkers are the most widely studied and investigated. I will discuss inflammatory markers in more detail, later in the article.
2- Lacrimal gland dysfunction: there is marked change in the level of lactoferrin, lysozyme, EGF, and aquaporin-5 (AQP5)
3- Oxidative stress (late lipid peroxidation products and antioxidant defence markers)
4- Contact lens intolerance (lactoferrin, lysozyme, lipocalin, phospholipase 2)

Inflammatory biomarkers

Many inflammatory mediators are released in the tear film and these include cytokines, chemokines and MMP-9. Additionally, products of lipid metabolism have been associated with DED such as prostaglandin E2 (PGE2), Arachidonic acid (AA), docosahexaenoic acid (DHA), eicosapantaenoic acid (EPA), secretory phospholipase A2 (sPLA2), and leukotriene B4 (LTB4).

Sampling of the tear film can be performed through many methods like microcapillary tubes, Schirmer strips, and minisponges. The main tear film markers that were constantly elevated in patients with DED compared to controls are: TNF-α, IL6, IL-17a, and IL8.

- TNF-α measures the overall level of ocular surface inflammation
- IL-6 is useful to inform on the status of ocular immunity and to measure if a treatment is effective
- IL-17a is secreted by specialised T helper 17 cells (Th17)
- IL-8 major chemotaxis that mediate macrophage and epithelial innate immunity

While the above biomarkers have been extensively studied in clinical research, in clinical practice there are only two main biomarkers what have been studied and had FDA approval: tear osmolarity and MMP-9. Both have been in clinical practice for many years and provide objective assessment of ocular surface inflammation.

Tear Osmolarity

The TFOS DEWS II report redefines dry eye as:
"a multifactorial disease of the ocular surface characterised by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."
High osmolarity is an objective biomarker to diagnose DED as well as to monitor repose to treatment. It is one of the diagnostic criteria as per TFOS DEWS II.

Figure 1: Dry Eye Disease diagnostic test battery, TFOS DEWS II Diagnostic Methodology report, Wolffsohn JS, Arita R, Chalmers R et al. TFOS DEWS II Diagnostic Methodology report. Ocul Surf. 2017 Jul;15(3):539-574. PMID: 28736342.

Matrix Metalloproteinases-9 (MMP-9)

It has been in clinical practice since the FDA approved InflammaDry. However, the MMP-9 might not differentiate DED from other ocular surface inflammatory diseases such as allergic eye disease. Additionally, there is poor correlation between MMP-9 positive levels and DED symptoms.

Electrophoresis of tear proteins

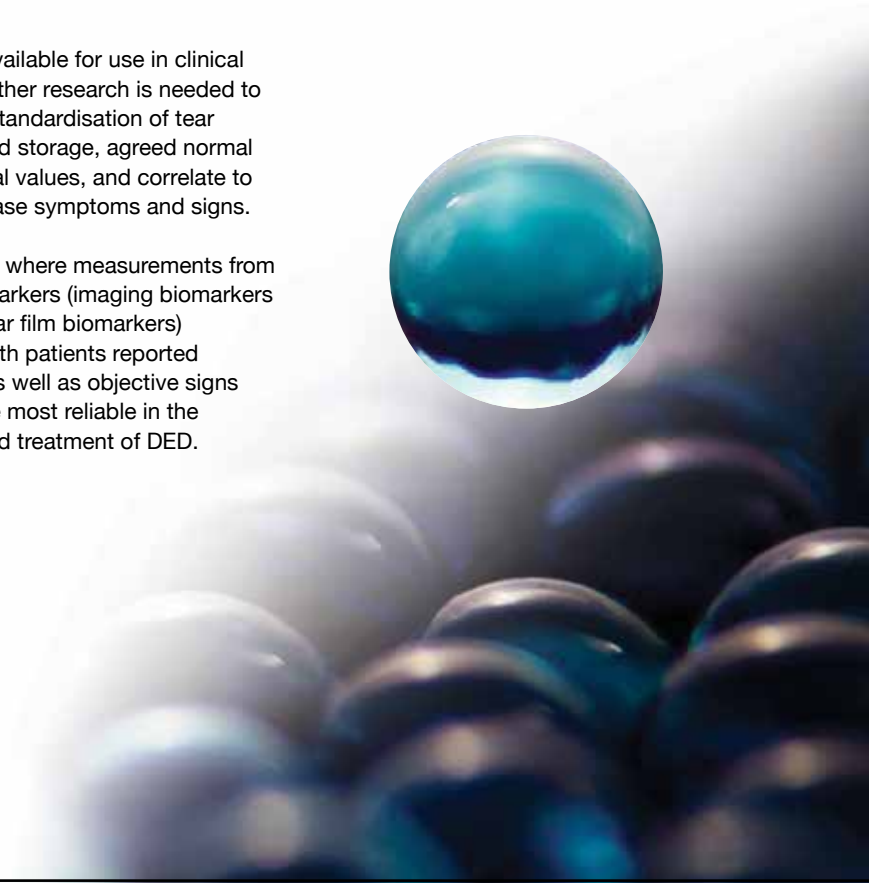
Electrophoresis of tear proteins using automated system (Hyrys–Hydrasys SEBIA, Evry, France). A four-tear protein panel consisting of lactoferrin, lysozyme, albumin and 20–60 kDa proteins, detected on Sebia electropherogramsis. It is useful tool for early diagnosis of tear film alterations, and monitoring of therapy. The quantification of many proteins in a single analysis using a small quantity of unconcentrated reflex tears, is the main advantage of this technique. It is suggested that it could be used as a routine test in diagnosis,

and management of dry eye disease and high-risk groups (computer users, contact lens wearers, cataract surgery, and glaucoma).

Decreased levels of lactoferrin, lysozyme, lipocalin, growth factors and mucins, as well as increased levels of albumin, tear albumin, cytokines/ chemokines and MMP activation are the main features for DED. The levels of these biomarkers may be used to distinguish between Sjögren's syndrome DED, and non-Sjögren's syndrome DED, aqueous deficiency dry eye (ADDE) from evaporative dry eye (EDE), or offer a measure of disease severity.

The lack of agreed value and standardisation, complexity of analysing tear products that require specialist labs, and difficulty collecting a very small sample of tears, limit the use of tear film biomarkers in clinical settings. The exception remains for the tear osmolarity and MMP-9 which are readily available for use in clinical practice. Further research is needed to include the standardisation of tear collection and storage, agreed normal and abnormal values, and correlate to dry eye disease symptoms and signs.

An approach where measurements from several biomarkers (imaging biomarkers as well as tear film biomarkers) combined with patients reported symptoms as well as objective signs would be the most reliable in the diagnosis and treatment of DED.



What's in the news?

Èyes Are The Story: The nexus between eye care and beauty

The quest to enhance human beauty with eye makeup began over six thousand years ago. Today it continues with an unrelenting passion.[1]

Many people apply several types of eye makeup multiple times a day, every day, in order to look younger and more attractive.[2] However, there is a sinister side to cosmetics. Many formulations contain chemicals that can act as carcinogens, neurotoxins, mutagens and endocrine disruptors, which in turn, may cause damage to the eye, including irritation, allergic reactions, contact dermatitis, blepharitis, meibomian gland and corneal toxicity, and dry eye disease.[1,3,4] Amazingly, few clinicians or patients are aware of these ocular hazards.[5]

Because of my work with the ophthalmic industry, I realized the unmet need for ocular-surface-friendly makeup. Eighteen year ago, I began researching the impact of cosmetics on eye health. Accordingly, I created a new line of optocosmetic and skincare products, Èyes Are The Story, in collaboration with laboratories in the USA, Canada, and Italy. I launched this brand through ÈSSIRI Labs, which I founded in 2016. These products are science-based, clinically tested, adherent to EU regulations, and uniquely formulated for sensitive eyes, contact lens users, and sufferers of dry eye disease and digital eye strain. Èyes Are The Story products avoid many of the ocular-surface-toxic ingredients found in mainstream cosmetics and skincare.

Embellishing the safe beauty movement, we are encouraging a new conversation about optimal eye protection and endocrine health. The nexus between eye care and beauty is a hot topic, so Èyes Are The Story prompts eye care practitioners to engage patients in discussions about their use of cosmetics and aesthetics treatments. According to a survey, 89% of women don't talk to their eye doctor about their beauty routines, and 70% of respondents don't consider ingredients when buying makeup.[5] Because so many chemicals in beauty products can harm our eyes, it's important that patients and doctors discuss these makeup routines.

It is important to pay close attention to what one uses on or around the eyes, as makeup can impact ocular health and vision, for both the short and long term. After all, Èyes Are The Story.

1. Wang J, Liu Y, Kam WR, Li Y, Sullivan DA. Toxicity of the cosmetic preservatives parabens, phenoxyethanol and chlorphenesin on human meibomian gland epithelial cells. Exp Eye Res 2020;196:108057.
2. https://www.scienceofpeople.com/makeup/ accessed 29.10.2020
3. Chen X, Liu Y, Kam WR, Sullivan AG, Sullivan DA. Toxicity of cosmetic preservatives on human ocular surface and adnexal cells. Exp Eye Res 2018;59:193-205.
4. Wang MT, Craig JP. Investigating the effect of eye cosmetics on the tear film: current insights. Clin Optom (Auckl) 2018;10:33-40.
5. Odell LE, Sullivan AG, Periman LM. Beauty does not have to hurt. Advanced Ocular Care. 2016;7(5):42-47.

Author: **Amy Gallant Sullivan**

Bandage contact lens and topical steroids are risk factors for the development of microbial keratitis after epithelium-off CXL

Tzamalis A, Romano V, Cheeseman R, Vinciguerra R, Batterbury M, Willoughby C, Neal T, Ahmad S, Kaye S.
BMJ Open Ophthalmol. 2019 Feb 16;4(1):e000231. doi: 10.1136/bmjophth-2018-000231. PMID: 30997402; PMCID: PMC6440609.

Although relatively rare, infectious keratitis has been reported to occur after CXL and many factors have been proposed to increase its incidence.
In a retrospective cohort study, we attempted to identify common risk factors for microbial keratitis after epithelium-off corneal cross-linking (CXL) for progressive corneal ectasia, mainly focusing in the role of bandage contact lens (BCL) and topical steroids applied after the procedure.

Therefore, all subjects undergoing epi-off CXL were divided into 2 groups regarding their postoperative management: those receiving a BCL, topical antimicrobial and steroids (Group1) and those managed only with a topical antimicrobial until complete epithelial defect healing (Group2).

1273 eyes of 964 patients were identified and enrolled in the analysis, 316 eyes in Group1 and 957 eyes in Group2.

9 eyes of 8 patients (0.71% of treated eyes) developed a microbial keratitis at a time-point 1 to 5 days after CXL. All cases of microbial keratitis were noted in Group1 (incidence=2.85%) and none in Group 2 ($p<0.0001$). Following treatment, there were no significant differences in the presence of persisting corneal haze or scarring between the two groups ($p=0.57$), when cases of microbial keratitis were excluded. Patients developing microbial keratitis were found to be atopic in a higher frequency (75%). Staphylococcus aureus was the only pathogen identified, being isolated from the cornea in 7 patients, from the conjunctiva in 2 patients and the nose in 3 patients. Further parameters such as age, gender, preoperative minimum corneal thickness, history of atopic disease, bilaterality of treatment and preoperative Kmax were evaluated but none of them was shown to increase significantly the risk of infection in contrast to the use of BCL and steroids in the early postoperative period ($p=0.005$).

In conclusion, our results would suggest that avoiding the use of BCL and delaying the introduction of topical steroids until epithelial healing, may significantly reduce the risk of developing microbial keratitis and does not seem to increase the risk of persistent corneal haze.

What's in the news?

The relevance of daylight for humans

Daylight is ubiquitous and is crucial for mammalian vision as well as for non-visual input to the brain via the intrinsically photosensitive retinal ganglion cells (ipRGCs) that express the photopigment melanopsin. The ipRGCs project to the circadian clock in the suprachiasmatic nuclei and thereby ensures entrainment to the 24-hour day-night cycle, and changes in daylength trigger the appropriate seasonal behaviours.
The ipRGCs also project to the perihabenular nucleus and surrounding brain regions that modulate mood, stress and learning in animals and humans. Given that light has strong direct effects on mood, cognition, alertness, performance, and sleep, light can be considered a "drug" to treat many clinical conditions. Light therapy is already well established for winter and other depressions and circadian sleep disorders. Beyond visual and non-visual effects via the retina, daylight contributes to prevent myopia in the young by its impact on eye development and is important for Vitamin D synthesis and bone health via the skin.
The sun is the most powerful light source and, dependent on dose, its ultraviolet radiance is toxic for living organisms and can be used as a disinfectant. Most research involves laboratory-based electric light, without the dynamic and spectral changes that daylight undergoes moment by moment. There is a gap between the importance of daylight for human beings and the amount of research being done on this subject. Daylight is taken for granted as an environmental factor, to be enjoyed or avoided, according to conditions.
More daylight awareness in architecture and urban design beyond aesthetic values and visual comfort may lead to higher quality work and living environments.
Although we do not yet have a factual basis for the assumption that natural daylight is overall "better" than electric light, the environmental debate mandates serious consideration of sunlight not just for solar power but also as biologically necessary for sustainable and healthy living.

Pharmacol. 2020 Oct 28;114304. doi: 10.1016/j.bcp.2020.114304.

Authors: **Anna Wirz-Justice, Debra J Skene, Mirjam Münch**

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Rizwana Khan

"BIG Data and Cataract Surgery":
Paul Ursell

Plenary president's lecture:
"My journey so far and our journey going forward"
Professor Sathish Srinivasan

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The Panel

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