

OSI

Ocular Surface Insight

Issue 15



**Ocular
Neuropathic Pain**

**Sjogren's –
A Dental Perspective**

**Are all preservatives contraindicated in
the management of dry eye disease?**

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“Innovation distinguishes between a leader and a follower.”

Steve Jobs

Welcome to the latest issue of **OSI**.

Just over a month now until OSI is running our first 2-day conference on the 24-25 June in London.

We have the Dry Eye Masterclass on Friday the 24th of June, it will be a great interactive day with both theory and practice. The day is supported by Scope our Platinum sponsors who have been working in partnership with us, to raise the awareness of this great opportunity to learn more about dry eye management and treatments. We also have additional industry support running the workshop from our gold sponsors: Lumenis, Daybreak, Rayner and Positive Impact.

Saturday the 26th of June is our symposium day, the programme offers world expert opinions and plenty of panel discussions to make it an interactive forum of innovation and updates of the very latest ideas and approaches in ocular surface treatment. Keep checking our website for the final programme.

In this issue of the OSI Magazine we have a very compelling article by Lyndon Jones and Wylie Tan preservatives and dry eye disease. We also have a great Q & A session with Connan Tam about the day to day running of a dry eye clinic.

Also make sure you read ‘Ophthalmology going greener’ by Yee Ling Wong, Maha Noor, Katherine L. James and Tariq M. Aslam.

The OSI team and I are really looking forward to seeing many OSI readers face to face, at our conference in June.

Samer Hamada

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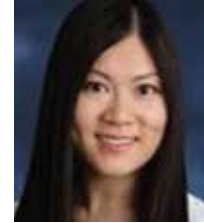
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Contents

- 6. What's in the news?
- 11. Beware of the Beast in Beauty
- 13. Are all preservatives contraindicated in the management of dry eye disease?
- 18. Sjogren's – A Dental Perspective
- 20. Ocular Neuropathic Pain
- 24. Q & A's with Connan Tam
- 26. Ophthalmology Going Greener: A Narrative Review
- 34. OSI Symposium & Dry Eye Masterclass (DRAFT PROGRAMME)



What's in the news?

Exploring contact lens opportunities for patients above the age of 40 years

Contact lenses offer a good option for patients with presbyopia, especially with improved optical designs available in modern multifocal contact lenses. Due to the ageing population, there is good opportunity to increase contact lens penetration by managing these patients better. However, multifocal contact lenses achieve low penetration in the market.

A questionnaire was administered to people aged above 40 years, to investigate their perceptions of contact lenses for presbyopia. Only people, with presbyopia, who were existing contact lens wearers or willing to try contact lenses were included. Participants were recruited from United Kingdom (UK), United States of America (USA), Netherlands, Germany, France, Spain, and Italy.

Data from 1540 participants above the age of 40 years was collected, 57.9% were females and 42.1% males. Overall, 50.8% of the participants wore contact lenses, but contact lens wear was less common amongst older participants. Some data supported earlier studies, such as 6.1% wore gas permeable lenses. However, only 25% of the contact lens wearers used multifocal contact lenses. The reasons the participants wanted to wear contact lenses were similar to younger patient such as sports or cosmesis reasons. Reasons why participants had dropped out of contact lenses included discomfort and dry eye related issues. Poor visual performance with contact lenses was a reason to dropout of contact lenses for the older participants.



The study highlights some failings by eye care practitioners in the management of patients with presbyopia. It seems that patients of this age group are seeking suggestions and recommendations from their eye care practitioner including upgrading contact lenses and dual wear options. The day-to-day problems encountered by the contact lens wearers in this study seem to be, in the main, things that could be easily tackled by additional counselling and instruction from the eye care practitioners.

Authors: Shehzad A Naroo, Manbir Nagra, Neil Retallic

Publication: Cont Lens Anterior Eye. 2022 Apr 16;101599.doi: 10.1016/j.clae.2022.101599.

Eye diseases during pregnancy: a study with the medical data warehouse in the eye clinic of the Ludwig-Maximilians-Universität München in Germany

The objective of this study was to analyse the most common ophthalmologic disorders in pregnant women seen in a hospital in Munich in Germany using a big data analysis system, as well as to compare the results obtained with those from other epidemiological studies that used different data acquisition methods.

The authors retrospectively analysed electronic health records of pregnant women who were seen at the ophthalmology department from 2003 to 2019 at the Ludwig-Maximilians-Universität München hospital. The main complaints that led to ophthalmic consultations during this period were evaluated, and the variation

in intraocular pressure of patients throughout gestational trimesters by analysing data from the data warehouse system.

A total of 27,326 electronic health records were analysed. Of participants, 149 (0.54%) required eye care during pregnancy. Their mean intraocular pressure was 17mmHg in the first trimester, 12mmHg in the second trimester, and 14mmHg in the third trimester. The most prevalent findings were dry eye (29.3%) and conjunctivitis (16%), and ametropia (16%). The most common posterior segment problem was diabetic retinopathy (4.6%). The lower mean intraocular pressure in the second and third trimester



found in our study is in accordance with other studies that used other method for data acquisition.

The results concluded that the most common ophthalmic conditions found in this study population were dry eye, conjunctivitis, and ametropia. The use of data warehouse proved to be useful for acquiring and analysing data from many patients. This study results are comparable with other studies in published literature that adopted different methodology.

Authors: Thiago Gonçalves Dos Santos Martins, Paulo Schor, Luis Guilherme Arneiro Mendes , Andreas Anschütz , Rufino Silva

Publication: Einstein (Sao Paulo). 2022 May 6;20:eAO6613. doi:10.31744/einstein_journal/2022AO6613.eCollection 2022.



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What's in the news?

Management Strategies for Evaporative Dry Eye Disease and Future Perspective

Dry eye disease (DED) is a common disorder that remains challenging from a clinical perspective. Unstable or deficient tear film is a major factor contributing to DED and the inability to resolve the loss of tear film homeostasis that accompanies DED can result in a vicious circle of inflammation and treatment-refractory disease.

Recently recognized as a multifactorial disease, the main etiological subtypes of DED are aqueous-deficient and evaporative which exist on a continuum, although evaporative dry eye (EDE) is the more frequent classification. Although attaining greater recognition in recent years, there is currently no consensus and no clear recommendation on how to manage EDE.

Clarity on the early diagnosis and treatment of EDE may facilitate the avoidance of progression to chronic inflammation, permanent damage to the ocular surface, and treatment-refractory disease. The purpose of this review was to

identify current best practice for management of EDE to help clinicians in providing accurate diagnosis and optimized treatment.

The authors summarized recent literature considering the role of the lipid layer on tear film stability, the importance of its composition and of its dynamic behaviour, and the link between its malfunction and the insurgence and maintenance of tear film-related diseases. They have provided an assessment of the best management of lipid-deficient EDE based upon an understanding of disease pathophysiology, while indicating the flow of current treatments and possible future evolution of treatment approaches. Lipid containing eye drops may be considered as a step closer to natural tears from artificial aqueous tears because they more closely mimic the aqueous and lipid layers and may be used in combination with other management approaches. As a next

step, they recommend working with a wider expert group to develop full guidelines to enable patient-centred management of EDE.

Dry eye is a multifactorial disease of variable presentation with the tendency to become a chronic disease for which it is essential to identify and treat the main pathogenic mechanisms involved and tailor the treatment to the individual patient. Early intervention is needed to prevent the vicious cycle of DED and may require a multi-faceted management approach. EDE is not just a problem of MGD but can be the result of anything affecting blinking, mucin spreading, aqueous layer volume and content. Lipid-containing eye drops may provide significant relief of symptoms by improving the lipid layer and its spreading ability and, as such, are an appropriate component of the overall management of lipid-deficient EDE; natural lipid-containing eye drops should be the preferred treatment.

Authors: Maurizio Rolando, Jesús Merayo-Llodes

Publication: *Curr Eye Res.* 2022 May 6;1-11. doi: 10.1080/02713683.2022.2039205.

What's in the news?

Autologous platelet-rich plasma eye drops versus artificial tear eye drops for symptomatic dry eye disease: A prospective comparative interventional study

The authors of this study set out to evaluate and compare the efficacy of autologous platelet-rich plasma (aPRP) eye drops and artificial tear (AT) eye drops in moderate to severe symptomatic dry eye disease (DED).

This prospective interventional study included 121 eyes of 61 patients of moderate to severe DED. Patients were divided into aPRP (31 patients) and AT (30 patients) group. Ocular Surface Disease Index (OSDI) score, tear film breakup time (TBUT) (s), corneal fluorescein staining (CFS) score, and Schirmer test score (mm) of both the groups were evaluated and compared

pre-treatment and post-treatment at the end of 3 months.

The mean age of the aPRP group and AT group was 52.8 ± 12.8 years and 55.5 ± 13.4 years, respectively. At the end of 3 months, OSDI score reduced more in the aPRP group as compared to AT group, and the mean difference (-22.7) was statistically significant ($P < 0.001$). There was no significant difference in post-treatment Schirmer test score between the two groups ($P = 0.44$). Post-treatment improvement in TBUT and CFS score in the aPRP group was significantly higher in the aPRP group as compared to that in the



AT group ($P < 0.05$). Bruising at the site of blood withdrawal was noted in two patients in the aPRP group.

The authors concluded that aPRP is safe and more effective than AT in treating patients with moderate to severe symptomatic DED.

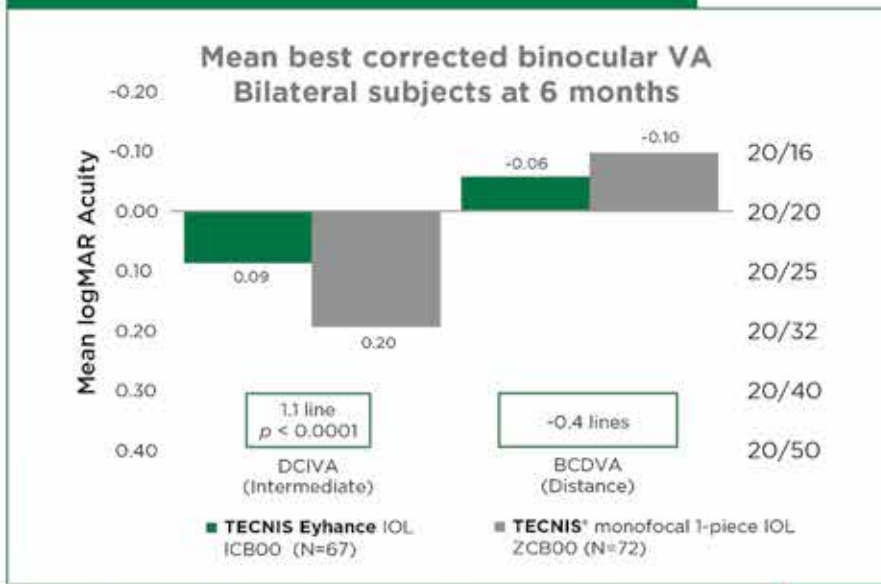
Authors: Preeti Rawat, Ritika Agrawal, Vijay Bhaisare, Shweta Wallia, Neetu Kori, Rishi Gupta

Publication: *Indian J Ophthalmol.* 2022 May;70(5):1549-1553. doi: 10.4103/ijo.IJO_2595_21.

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1. Data on File, Johnson & Johnson Surgical Vision, Inc., Sep 2018, DCF2018CT4015.
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1. VisuEVO® Instructions for Use (IFU). 2. VisuXL® Gel Instructions for Use (IFU). 3. Brancato R, Fiore T, Papucci L, et al. Concomitant Effect of Topical biguanine Q10 and Vitamin E to Prevent Keratocyte Apoptosis After Excimer Laser Photoablation in Rabbits. J Refract Surg 2002; 18:135-9. 4. VisuXL® Instruction for Use (IFU). 5. Postorino EJ et al. Efficacy of eye drops containing cross-linked hyaluronic acid and coenzyme Q10 in treating patients with mild to moderate dry eye. Eur J Ophthalmol 2010; 26: 25-31. 6. Muzzi M, Mancucci R. Poster presented at the Association for Ocular Pharmacology and Therapeutics (AOPT) 13th Scientific Meeting, Feb 16-19, 2017, Florence, Italy. 7. Fogagnolo P, et al. The Effects of Topical Coenzyme Q10 and Vitamin E D-α-Tocopheryl Polyethylene Glycol 1000 Succinate after Cataract Surgery: A Clinical and in vivo Confocal Study. Ophthalmologica 2012; 229: 26-31. † In an animal model.

Beware of the Beast in Beauty



Insights from the Cosmetic Surgery Panel, MCLOSA/OSI Joint Symposium 2021

By **Elsa Lee** MSc Ophth MBBS

Open a social media page and you are bound to be bombarded with beauty trends and cosmetic surgery. As mainstream aesthetic standards shift, cosmetic products and procedures have arguably consumed consumers. The result is a rise in ocular surface diseases (OSDs). At the MCLOSA/OSI Joint Symposium 2021, Ms Sabrina Shah-Desai and Ms Amy Gallant-Sullivan unmasked cosmetics-associated OSDs and shed light on their management.

As Ms Shah-Desai highlighted, an important cause accounting for the rise of OSDs related to make-up use is patient consumers' lack of awareness of the risks involved. To illustrate, concentrations of preservatives approved for consumer use are toxic to ocular surface and adnexal cells. Yet, the author has frequently been subjected to TikTok videos of beauty gurus' hack of applying liquid eyeliner in the conjunctival cul-de-sac. Instantiating this is a rise in periorbital dermatitis, a type 4 hypersensitivity often triggered by nickel in mascara, Thimerosal in contact lens solution, Kajal pencil, fragrances, and nail varnish, to name a few.

Worse clinical phenotypes include chronic blepharitis secondary to micropigmentation or permanent tattoos of eyebrows and eye liners, and topical anaesthetics induced dry eye disease (DED). Noteworthy culprits of dermatitis, tear film instability, and keratitis are glitter eye shadow and

makeup removal wipes. Fake lashes are similarly to blame. Longer lashes channel airflow directly onto the eye surface which accelerate drying and cause particle accumulation. Furthermore, cyanoacrylate-based lash extensions, lash glues contain latex, ammonia, and formaldehyde join forces in their offence. Avoiding fake lashes will not eliminate the harm if patients also opt for eyelash growth serums; FDA-approved Latisse contains prostaglandin analogues which may further irritation.

Invasive aesthetic procedures carry just as much risk. Periorbital Botox may precipitate hypometric blinks, OSD, and blepharitis, alongside the well-recognised entity of botox induced ptosis. More feared complications have been reported including blindness and ophthalmoplegia secondary to dermal filler injection. Cicatricial ectropion has occurred post laser and skin tightening treatments, as well as horizontal lid phimosis and recurrent congenital ptosis.

Emphasis of the myriad cosmetics related OSDs and sentiments on raising their awareness, are by no means solitary. In 'Eyes are the story – beauty and pharma', Ms Amy Gallant-Sullivan uncovered the surge in 'above-the-mask' makeup use in the context of a pandemic, yet cosmetic-related health awareness had failed to rise to the occasion. Poor application and misuse of

mainstream products often result in ocular irritation, allergy, contact dermatitis, meibomian gland and corneal epithelial cell toxicity, and contact lens dropout.

Ms Gallant-Sullivan notes that patients' make-up application processes impact diagnosis. For the secret biochemists, Ms Gallant-Sullivan's handy list of the top 10 ocular-surface-offending ingredients include argireline (acetyl hexapeptide-3 / acetyl hexapeptide-8), benzalkonium chloride (BAK), carbon black, formaldehyde, isopropyl cloprostenate, parabens, phenoxyethanol, retinols, chlorphenesin, and tea tree oil. Simple steps such as checking product ingredient lists could improve patients' symptoms caused by cosmetic use.

The top 10 blunders in aesthetics encompass Botox for Crow's feet, Botox-in-a-jar, eyelid tattooing, eyelash extensions, eyelash tinting, eyeshadow powder/glitter, OTC eyelash growth serums, retin-A, sharing makeup, and water-proof makeup.

Taming the beast of cosmetics-related OSD may become the bread and butter of ocular surface specialists with ever-evolving beauty crazes. As Ms Gallant-Sullivan and Shah-Desai reiterate, the first step tackling the beast in beauty lies in the foundation of eliciting a detailed history of product use and application patterns, as well as patient education.



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Are all preservatives contraindicated in the management of dry eye disease?

By **Wylie Tan**, MSc, OD, FAAO and **Lyndon Jones**, PhD, DSc, FCOptom, FAAO

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Introduction

Our understanding of dry eye disease (DED) with respect to its epidemiology, classification and treatment options has evolved a significant amount over the past 10 years. The TFOS DEWS II Management and Therapy report recommends a staged approach in the management of DED,¹ with ocular lubricants being a mainstay treatment option of many dry eye treatment regimens. There are a wide range of topical ocular lubricants available to treat dry eyes, some of which include preservatives, and some of which are preservative-free (PF).²⁻¹⁷

The preservative is the main component in topical preparations with the greatest potential to adversely affect the ocular surface. Hence, there is a general sense among eye care practitioners (ECPs) that PF drops are preferable and that preserved drops should be avoided where possible. However, is this necessarily accurate?

The purpose of this paper is to determine whether non-BAK preserved drops are safe to use and should be considered when choosing treatment options for the

management of mild to moderate forms of DED.

Dry Eye Disease

DED affects a large number of patients, and its definition recognizes that the disease process involves a loss of tear film homeostasis and subsequent ocular surface inflammation.¹⁸

The classification of DED includes two subtypes: Aqueous Deficient Dry Eye (ADDE) and Evaporative Dry Eye (EDE).¹⁸ It is acknowledged that both subtypes can co-exist and present as a mixed disease, with EDE or mixed disease being found in the majority of patients.^{18, 19}

Management of DED

The diagnosis of DED as ADDE, EDE or mixed disease has a significant bearing on the management and treatment of the condition. The TFOS DEWS II Management and Therapy Report recommended a staged management and treatment approach, and topical application of tear substitutes or specific medications is recommended for every stage of DED severity.¹ It is important to note that the recommendations provided in Step 1 are carefully considered, as this step includes a variety of management options that may be combined with treatment options typically considered for later stage disease. These included education of the patient in terms of the need for ongoing treatment over an extended period of time, modification of the local environment such as the use of locally placed humidifiers, lid hygiene measures and the use of all forms of ocular lubricants, including those that may be available in a preserved format.

¹ Skipping this important step and jumping straight to more complex, lengthy and frequently more expensive treatment options may not be in the best interests of the patient.

When choosing which drops to use to treat DED, it is important to consider the various components incorporated and the specific layers of the tear film it addresses. For example, lipid-containing drops (LCD) or lipid-stabilizing drops,

are particularly important for restoring the lipid layer of the tear film to prevent tear evaporation and are a valuable option in the management of patients with EDE.²⁰⁻²² Another important component to consider when choosing drops is whether the drops contain a preservative or not, as PF formulations have been shown to be beneficial in patients with a severely compromised ocular surface.²³ However, it is important to note that the majority of DED patients do not have severe disease, but rather, mild to moderate disease. While drops containing lipids are becoming increasingly available, they are not as commonly available as non-lipid containing formulations. If a patient with EDE or mixed DED would benefit from a lipid-based formulation but the product was not available in a PF product, would it be more appropriate to prescribe a lipid-based preserved drop or use a (potentially) inferior drop to manage the DED in a PF format?

Is it a problem to use a drop containing a preservative?

Considering that most dry eye patients are of the evaporative or mixed disease subtypes, LCDs are arguably the most appropriate formulation; however, there are very few PF LCDs on the market. If practitioners were to only offer PF options, this eliminates many choices for patients. In the staged approach for the management and treatment of DED recommended by the TFOS DEWS II Management and Therapy Report, PF formulations are recommended for more severe forms of disease, when preserved ocular lubricants and other initial management therapies are considered inadequate.¹ When using preserved ocular lubricants, it is imperative to have a deeper understanding of preservatives and their impact to the ocular surface to be able to provide optimal care for DED patients.

Preservatives in Ocular Lubricants

Benzalkonium Chloride

Preservatives are added to topical preparations to maintain the sterility of the drops in a multidose bottle.

The most commonly used preservative in topical drops, benzalkonium chloride (BAK) is an effective antimicrobial agent, but it has also been shown to be toxic to the ocular surface in laboratory, experimental and clinical studies.^{16, 24-29} Human ocular cells can absorb and accumulate BAK and higher concentrations and repeated use of topical drops containing BAK have been linked with worsening ocular signs and symptoms.³⁰ These dose-dependent and time-dependent effects of BAK are particularly relevant considering the long-term and cumulative use required to treat DED. Many studies on the effects of BAK on the eye have been related to the management of glaucoma, since glaucoma patients are required to use topical agents long-term, often requiring multiple doses throughout the day. Clinical studies with glaucoma patients using BAK-preserved drops long-term have shown an increase in prevalence and frequency of adverse ocular signs and symptoms in these patients.^{31, 32} "Switch" studies have consistently shown improvement in signs and symptoms when these glaucoma patients were switched from BAK-preserved to PF drops.³³ Given the abundance of evidence supporting the detrimental effects of BAK on the ocular surface, ECPs are correct in assuming that BAK is not recommended for DED patients of any type or severity and should avoid topical ocular lubricants containing BAK.

Alternative Preservatives

For mild to moderate DED, ocular lubricants that contain alternative preservatives other than BAK are available. These preservatives include polyquaternium-I (Polyquad® or PQ-1) and oxidizing preservatives, such as sodium perborate (GenAqua®; Dequest®), stabilized oxychloro complex (Purite®; OcuPure®), and Sofzia®.^{15, 34} Of these preservatives,

to-date PQ-1 has the largest body of evidence with respect to its performance in patients with DED.¹¹

PQ-1 and BAK are both quaternary ammonium compounds, but they differ markedly in their molecular size, modes of action, and molecular properties (Table 1). PQ-1 is a polymeric compound, which is about 27x larger than the molecular size of BAK.³⁵ Both compounds are effective preservatives through different modes of action. BAK causes cell death by using its smaller size to interact with and destabilize cell membranes and cause the release of cellular contents.³⁶ Its actions, however, are not specific to bacterial cells, so it is also toxic to mammalian ocular cells. In contrast, PQ-1 has a molecular size too large to enter mammalian cells, which makes PQ-1 less toxic to the eye than BAK.³⁷ PQ-1's mechanism of action as an anti-microbial agent involves damaging bacterial cytoplasmic membranes, causing cell leakage.³⁸ PQ-1's anti-microbial properties have been used in multipurpose (MPS) contact lens solutions for over thirty years with little to no reports of ocular toxicity or allergic responses in vivo. The concentration of PQ-1 in MPS solutions range from 0.0001% to 0.001%, which is similar to the 0.001% of PQ-1 that is typically used in preserving dry eye lubricants.¹⁵

Table 1. Differences between BAK and PQ-1

Studies analyzing the use of PQ-1

The in-vitro effects of PQ-1 and BAK on human epithelial cells has been previously studied.^{39, 40} When comparing the usage of PQ-1 preserved travoprost to BAK-preserved travoprost and BAK-preserved latanoprost, the cells exposed to PQ-1 travoprost showed significantly better cell viability, less

apoptosis, and less oxidative stress; PQ-1's toxicity level was comparable to that of buffer solution.³⁹

Other experimental studies have found PQ-1 0.001% to be less cytotoxic than BAK 0.02%, but comparable in toxicity to BAK 0.01% after 15mins.⁴⁰

Choy and co-workers examined the toxicity of three contact lens multi-purpose solutions (MPS); they found that all three solutions caused human epithelial cells to have reduced metabolic rates and damaged cell integrity, with the greatest effects seen in the PQ-1 containing MPS.⁴¹

These results seem contradictory to the well-known long history of safe use of PQ-1 in contact lens care solutions; MPS solutions are complex in nature, and since it is impossible to isolate the preservative, it is hard to say that the preservative was the causative agent of cytotoxicity in these studies.¹⁵

The effects of PQ-1 and BAK preserved drops have also been explored in various animal studies. Rat models exposed to 11-days of twice daily application of high dose PQ-1 (0.1% and 0.5%) versus BAK (0.1% and 0.5%) preserved drops showed that PQ-1 was much less toxic than BAK with respect to fluorescein staining, impression cytology, in vivo confocal microscopy, and histology.⁴² Rabbit eyes showed similar findings, with PQ-1 being less toxic to the ocular surface compared to BAK when rabbit eyes were exposed to one-day multi-dose use of PQ-1 vs BAK preserved drops.⁴³ A rabbit model using exposure to four weeks of prostaglandin analogs showed that BAK-preserved drops resulted in significantly increased inflammatory cytokine interleukin IL-6 markers and significantly decreased goblet cells density, whereas findings for PQ-1 preserved drop were similar to the control sample.⁴⁴ A study by Ubels and colleagues found that PQ-1 preserved artificial tears showed greater protection against corneal desiccation and better

Properties	BAK	PQ-1
Molecular size	Quaternary ammonium (smaller than PQ-1) - Contains both hydrophilic and hydrophobic elements	Polymeric quaternary ammonium (27x larger than BAK) - Contains hydrophilic element and no/very small hydrophobic element
Mode of action	Bactericidal - Enters cells, causing cell lysis	Cytotoxic - Disrupts cell membranes, causing cell leakage
Typical concentration in eye drops	0.004% to 0.02%	0.001%
Cellular uptake	Absorbed by mammalian cells	Not absorbed by mammalian cells

cell viability compared to drops preserved by BAK and Purite®.⁴⁵ Human clinical studies have shown similar results in support of PQ-1 use. Confocal microscopy studies showed BAK-preserved drops significantly reduced tear break up time and epithelial cell density compared to controls, whereas PQ-1 preserved drops had limited reactions to the ocular surface and was considered more suitable for maintaining corneal homeostasis than BAK.⁴⁶ A separate study that explored OSDI scores after 6 months of starting glaucoma medications preserved with BAK, PQ-1 and no preservative showed that PQ-1 preserved drops had statistically significantly lower OSDI scores than the other tested drops.⁴⁷ A study comparing the tolerability of PF versus PQ-1 preserved artificial tears in post-LASIK patients showed no significant differences between these drops.⁴⁸

PQ-1 has been used as a biocide in MPS contact lens care solutions for more than thirty years and has an excellent record of being well-tolerated.⁴⁹ The concentration of PQ-1 in dry eye drops is comparable to that found in a number of MPS solutions, at 0.001%¹⁵ and the few MPS studies that showed concern for efficacy and resultant

keratitis did not involve PQ-1 preserved solutions.¹⁵ Studies have documented solution-induced corneal staining (SICS) from MPS interactions with silicone hydrogel contact lens materials.^{50,51} However, given the complex formulation of MPS products⁴⁹ and an undefined mechanism for SICS, there is no conclusive evidence to suggest whether preservatives or other MPS components, such as surfactants, are the causative agent of SICS.⁵² An in vitro study found that the uptake of PQ-1 from MPS in silicone hydrogel materials is minimal, which suggests the amount of PQ-1 transferred to the ocular surface would be almost negligible.⁵³ A large, multi-site study examined physiological and subjective responses after the use of different combinations of care solution and lens materials, and the findings showed no significant difference between a PQ-1 preserved MPS versus a PF hydrogen peroxide control.⁵⁴

The use of PQ-1 preserved MPS care solutions is very common and these products have an excellent safety profile. Residence time, the duration that a drop remains on the ocular surface, is extremely short for artificial tears.⁵⁵ The uptake and subsequent release of PQ-1 from contact lenses onto the ocular surface between the back surface of the lens and the cornea

suggests that contact lens wearers may be exposed to PQ-1 for a longer period than users of artificial tears. Considering the long history of safety of MPS use among contact lens users, this further suggests that PQ-1 preserved lubricants would have limited potential for adverse effects on the ocular surface in patient with mild to moderate DED.¹⁵

Summary

While PF formulations are an important option, they are not the only option and not all patients require a PF approach. When ECPs limit their recommendations to only PF formulations, DED patients are not necessarily provided with the best tailored care that they can be offered. It is crucial to diagnose and treat the subtype of DED that the patient has. Mild to moderate cases of DED can still benefit from using lubricants that contain non-BAK-based preservatives. PQ-1 has a long history of use in both topical ocular lubricants and contact lens care, has an excellent safety profile and is distinctly different from BAK. PQ-1 is used to preserve a number of artificial tears that are designed to help with specific elements of DED.¹¹ This knowledge will increase the choices that ECPs have available to help them better manage their dry eye patients with mild to moderate disease.

References:

- Jones L, Downie LE, et al.: TFOS DEWS II Management and Therapy Report. *Ocul Surf* 2017; 15;3: 575-628.
- Gao M, Wu G: Chemicals in Preservative-Free Tears, Branded and Generic. *Eye Contact Lens* 2018; 44;3: 203-204.
- Tong L, Petznick A, et al.: Choice of artificial tear formulation for patients with dry eye: where do we start? *Cornea* 2012; 31 Suppl 1 S32-6.
- Moshirfar M, Pierson K, et al.: Artificial tears potpourri: a literature review. *Clin Ophthalmol* 2014; 8 1419-33.
- Pucker AD, Ng SM, et al.: Over the counter (OTC) artificial tear drops for dry eye syndrome. *Cochrane Database Syst Rev* 2016; 2 CD009729.
- Garrigue JS, Amrane M, et al.: Relevance of Lipid-Based Products in the Management of Dry Eye Disease. *J Ocul Pharmacol Ther* 2017; 33;9: 647-661.
- Ribeiro M, Barbosa FT, et al.: Effectiveness of using preservative-free artificial tears versus preserved lubricants for the treatment of dry eyes: a systematic review. *Arq Bras Oftalmol* 2019; 82;5: 436-445.
- Dauill P, Amrane M, et al.: Cationic Emulsion-Based Artificial Tears as a Mimic of Functional Healthy Tear Film for Restoration of Ocular Surface Homeostasis in Dry Eye Disease. *J Ocul Pharmacol Ther* 2020; 36;6: 355-365.
- Barabino S, Benitez-Del-Castillo JM, et al.: Dry eye disease treatment: the role of tear substitutes, their future, and an updated classification. *Eur Rev Med Pharmacol Sci* 2020; 24;17: 8642-8652.
- Yang YJ, Lee WY, et al.: A Meta-Analysis of the Efficacy of Hyaluronic Acid Eye Drops for the Treatment of Dry Eye Syndrome. *Int J Environ Res Public Health* 2021; 18;5.
- Srinivasan S, Manoj V: A Decade of Effective Dry Eye Disease Management with Systane Ultra (Polyethylene Glycol/Propylene Glycol with Hydroxypropyl Guar) Lubricant Eye Drops. *Clin Ophthalmol* 2021; 15 2421-2435.
- Garofalo R, Kunnen C, et al.: Relieving the symptoms of dry eye disease: update on lubricating eye drops containing hydroxypropyl-guar. *Clin Exp Optom* 2021; 104;8: 826-834.
- Aragona P, Simmons PA, et al.: Physicochemical Properties of Hyaluronic Acid-Based Lubricant Eye Drops. *Transl Vis Sci Technol* 2019; 8;6: 2.
- Bitton E, Perugino C, et al.: Comparison of Ocular Lubricant Osmolalities. *Optom Vis Sci* 2017; 94;6: 694-699.
- Walsh K, Jones L: The use of preservatives in dry eye drops. *Clin Ophthalmol* 2019; 13 1409- 1425.
- Warcoin E, Clouzeau C, et al.: Hyperosmolarity and Benzalkonium Chloride Differently Stimulate Inflammatory Markers in Conjunctiva-Derived Epithelial Cells in vitro. *Ophthalmic Res* 2017; 58;1: 40-48.
- Kathuria A, Shamloo K, et al.: Categorization of Marketed Artificial Tear Formulations Based on Their Ingredients: A Rational Approach for Their Use. *J Clin Med* 2021; 10;6.
- Craig JP, Nichols KK, et al.: TFOS DEWS II Definition and Classification Report. *Ocul Surf* 2017; 15;3: 276-283.
- Lemp MA, Crews LA, et al.: Distribution of aqueous-deficient and evaporative dry eye in a clinic- based patient cohort: a retrospective study. *Cornea* 2012; 31;5: 472-8.
- Craig JP, Tomlinson A: Importance of the lipid layer in human tear film stability and evaporation. *Optom Vis Sci* 1997; 74;1: 8-13.
- Lee SY, Tong L: Lipid-containing lubricants for dry eye: a systematic review. *Optom Vis Sci* 2012; 89;11: 1654-61.
- Baudouin C, Galarreta DJ, et al.: Clinical evaluation of an oil-based lubricant eyedrop in dry eye patients with lipid deficiency. *Eur J Ophthalmol* 2017; 27;2: 122-128.
- Nasser L, Rozycka M, et al.: Real-life results of switching from preserved to preservative-free artificial tears containing hyaluronate in patients with dry eye disease. *Clin Ophthalmol* 2018; 12 1519-1525.
- Baudouin C, Labbe A, et al.: Preservatives in eyedrops: the good, the bad and the ugly. *Prog Retin Eye Res* 2010; 29;4: 312-34.
- Liang H, Brignole-Baudouin F, et al.: Reduced in vivo ocular surface toxicity with polyquad- preserved travoprost versus benzalkonium-preserved travoprost or latanoprost ophthalmic solutions. *Ophthalmic Res* 2012; 48;2: 89-101.
- Datta S, Baudouin C, et al.: The Eye Drop Preservative Benzalkonium Chloride Potently Induces Mitochondrial Dysfunction and Preferentially Affects LHON Mutant Cells. *Invest Ophthalmol Vis Sci* 2017; 58;4: 2406-2412.
- Stalmans I, Lemij H, et al.: Signs and Symptoms of Ocular Surface Disease: The Reasons for Patient Dissatisfaction with Glaucoma Treatments. *Clin Ophthalmol* 2020; 14 3675-3680.
- Harasymowycz P, Hutnik C, et al.: Preserved Versus Preservative-Free Latanoprost for the Treatment of Glaucoma and Ocular Hypertension: A Post Hoc Pooled Analysis. *Adv Ther* 2021; 38;6: 3019-3031.
- Zhang R, Park M, et al.: Dose-dependent benzalkonium chloride toxicity imparts ocular surface epithelial changes with features of dry eye disease. *Ocul Surf* 2020; 18;1: 158-169.

30. De Saint Jean M, Brignole F, et al.: Effects of benzalkonium chloride on growth and survival of Chang conjunctival cells. *Invest Ophthalmol Vis Sci* 1999; 40;3: 619-30.
31. Jaenen N, Baudouin C, et al.: Ocular symptoms and signs with preserved and preservative-free glaucoma medications. *Eur J Ophthalmol* 2007; 17;3: 341-9.
32. Konstas AG, Labbe A, et al.: The treatment of glaucoma using topical preservative-free agents: an evaluation of safety and tolerability. *Expert Opin Drug Saf* 2021; 20;4: 453-466.
33. Uusitalo H, Chen E, et al.: Switching from a preserved to a preservative-free prostaglandin preparation in topical glaucoma medication. *Acta Ophthalmol* 2010; 88;3: 329-36.
34. Kaur IP, Lal S, et al.: Ocular preservatives: associated risks and newer options. *Cutan Ocul Toxicol* 2009; 28;3: 93-103.
35. Rolando M, Crider JY, et al.: Ophthalmic preservatives: focus on polyquaternium-1. *Expert Opin Drug Deliv* 2011; 8;11: 1425-38.
36. Freeman PD, Kahook MY: Preservatives in topical ophthalmic medications: historical and clinical perspectives. *Expert Review of Ophthalmology* 2014; 4;1: 59-64.
37. Tripathi BJ, Tripathi RC, et al.: Cytotoxicity of ophthalmic preservatives on human corneal epithelium. *Lens Eye Toxic Res* 1992; 9;3-4: 361-75.
38. Codling CE, Hann AC, et al.: An investigation into the antimicrobial mechanisms of action of two contact lens biocides using electron microscopy. *Cont Lens Anterior Eye* 2005; 28;4: 163-8.
39. Brignole-Baudouin F, Riancho L, et al.: Comparative in vitro toxicology study of travoprost polyquad-preserved, travoprost BAK-preserved, and latanoprost BAK-preserved ophthalmic solutions on human conjunctival epithelial cells. *Curr Eye Res* 2011; 36;11: 979-88.
40. Paimela T, Ryhanen T, et al.: The preservative polyquaternium-1 increases cytotoxicity and NF- kappaB linked inflammation in human corneal epithelial cells. *Mol Vis* 2012; 18 1189-96.
41. Choy CK, Cho P, et al.: Cytotoxicity and effects on metabolism of contact lens care solutions on human corneal epithelium cells. *Clin Exp Optom* 2012; 95;2: 196-206.
42. Labbe A, Pauly A, et al.: Comparison of toxicological profiles of benzalkonium chloride and polyquaternium-1: an experimental study. *J Ocul Pharmacol Ther* 2006; 22;4: 267-78.
43. Liang H, Brignole-Baudouin F, et al.: Polyquad-preserved travoprost/timolol, benzalkonium chloride (BAK)-preserved travoprost/timolol, and latanoprost/timolol in fixed combinations: a rabbit ocular surface study. *Adv Ther* 2011; 28;4: 311-25.
44. Lee HJ, Jun RM, et al.: Comparison of the ocular surface changes following the use of two different prostaglandin F2alpha analogues containing benzalkonium chloride or polyquad in rabbit eyes. *Cutan Ocul Toxicol* 2015; 34;3: 195-202.
45. Ubels JL, Clousing DP, et al.: Pre-clinical investigation of the efficacy of an artificial tear solution containing hydroxypropyl-guar as a gelling agent. *Curr Eye Res* 2004; 28;6: 437-44.
46. Marsovszky L, Resch MD, et al.: Confocal microscopy of epithelial and langerhans cells of the cornea in patients using travoprost drops containing two different preservatives. *Pathol Oncol Res* 2014; 20;3: 741-6.
47. El Hajj Moussa WG, Farhat RG, et al.: Comparison of Efficacy and Ocular Surface Disease Index Score between Bimatoprost, Latanoprost, Travoprost, and Tafluprost in Glaucoma Patients. *J Ophthalmol* 2018; 2018 1319628.
48. Astakhov YS, Astakhov SY, et al.: Assessment of dry eye signs and symptoms and ocular tolerance of a preservative-free lacrimal substitute (Hylabak(R)) versus a preserved lacrimal substitute (Systane(R)) used for 3 months in patients after LASIK. *Clin Ophthalmol* 2013; 7 2289- 97.
49. Kuc CJ, Lebow KA: Contact Lens Solutions and Contact Lens Discomfort: Examining the Correlations Between Solution Components, Keratitis, and Contact Lens Discomfort. *Eye Contact Lens* 2018; 44;6: 355-366.
50. Andraso G, Ryen K: Corneal staining and comfort observed with traditional and silicone hydrogel lenses and multipurpose solution combinations. *Optometry* 2008; 79;8: 444-54.
51. Jones L, MacDougall N, et al.: Asymptomatic corneal staining associated with the use of balafilcon silicone-hydrogel contact lenses disinfected with a polyaminopropyl biguanide- preserved care regimen. *Optom Vis Sci* 2002; 79;12: 753-61.
52. Khan TF, Price BL, et al.: Cellular fluorescein hyperfluorescence is dynamin-dependent and increased by Tetricon 1107 treatment. *Int J Biochem Cell Biol* 2018; 101 54-63.
53. Morris CA, Maltseva IA, et al.: Consequences of Preservative Uptake and Release by Contact Lenses. *Eye Contact Lens* 2018; 44 Suppl 2 S247-S255.
54. Berntsen DA, Hickson-Curran SB, et al.: Subjective Comfort and Physiology with Modern Contact Lens Care Products. *Optom Vis Sci* 2016; 93;8: 809-19.
55. Napoli PE, Satta GM, et al.: Spectral-domain optical coherence tomography study on dynamic changes of human tears after instillation of artificial tears. *Invest Ophthalmol Vis Sci* 2014; 55;7: 4533-40.

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Small Drops, Big Benefits

Sjogren's – A Dental Perspective

By Jack Livesey, BDS

Sjögren's Syndrome (SS) is an autoimmune exocrinopathy characterised by lymphocytic infiltration of exocrine glands in multiple sites, with dry mouth and dry eyes as a primary presenting symptoms (1). With an ever increasing proportion of the population attending the Dentist regularly, the profession plays active role in diagnosing disorders and diseases to allow early management and treatment (2).

Recent research indicates that over half of patients with primary SS experienced oral symptom as their first manifestation of the disease (6).

Undergraduate dental programmes include teaching on systemic disorders, their relevant symptoms and appropriate treatments. This article will focus on SS which has both ocular and oral symptoms. There are many disorders such as diabetes and Bechet's syndrome that are linked to both the eyes and mouth which may initially be identified by the patient's general dental practitioner.

SS can present as primary or secondary, when associated with another autoimmune disease (3). The criteria most widely accepted for the diagnosis of the syndrome are:

1. Ocular symptoms – persistent dry eyes > 3 months
2. Oral symptoms – Persistent dry mouth > 3 months
3. Ocular signs – Schirmer's Test, Rose Bengal Dye test
4. Positive histopathology
5. Oral signs – 1.5ml > unstimulated salivary flow/15 mins
6. Autoantibodies (3)

Dry mouth is a common complaint in dental care and this can mainly be attributed to medications used to treat the ageing population. Antimuscarinic medications which may cause dry mouth includes mydriatic and cycloplegic eye drops (4).

It is important for a practitioner to identify patients who are more at risk of developing SS. The disorder affects around 0.5% of the adult population, with prevalence increasing with age and a female to male ratio of 9:1 (5).

SS must be recognised as a systemic disease and patients can also suffer from fatigue, skin lesions, haematological problems, vulval dryness and gastrointestinal complaints (5).

The decreased saliva (hyposalivation) can result in difficulty eating, chewing, speaking swallowing and denture retention (7). The oral mucosa may appear erythematous and fissured and patients can develop fungal infections and may complain of halitosis.

The loss of the salivary buffering capacity leads to atypical patterns of tooth decay and a higher frequency of toothwear (8).

Dental professionals must also be aware ocular manifestations including itchiness, dryness, blurring of vision and discomfort. Systemic drugs, such as antihistamines can aggravate these symptoms (5).

An important factor to consider with SS is that those who suffer from the primary syndrome are 44 times more likely to develop malignant lymphoma.



This means special care is needed when a SS patient presents salivary gland swelling or lymphadenopathy. Regular dental check-ups are necessary as lymphomas may present initially in the oral cavity (9).

When SS is suspected, the professional, either a doctor, dentist or optometrist should ask relevant questions to highlight any other symptoms and allow appropriate referral. Diagnosis requires a labial gland biopsy to test for the presence of autoantibodies. Management of oral symptoms include chewing sugar free gum and saliva replacement therapies such as BioXtra

products. Advising the patient to sip water regularly throughout the day often provides substantial relief. Pilocarpine can be used to stimulate salivary and lacrimal glands but may not have an effect due to irreversible damage to the exocrine glands in the latter stages of SS (10).

Treatments of the ocular symptoms are palliative. Tear substitutes, if used persistently, can have a marked improvement on the patient's quality of life. A procedure to block the tear ducts preventing them from draining away is sometimes implemented. Unfortunately, there are still no

therapeutic treatments available.

More complex immune-modulatory treatments are used in severe cases. Immunosuppressive drugs and biological agents have been studied for the management of the disease but firm evidence is yet to be presented in relation to these (11).

Dental practitioners are essential in the early diagnosis and management of SS. Due to routine recalls of dental patient's Dental professionals are correctly placed to refer patients via the appropriate specialist pathway (5).

References:

1. Ngo DY, Thomson WM, Nolan A, Ferguson S. The lived experience of Sjögren's Syndrome. *BMC Oral Health* 2016; 16:7.
2. Oral Health Foundation. National Smile Month. [Internet]. 2017 [cited 2017 July 27]. Available from: <http://www.nationalsmilemonth.org/facts-figures/>
3. Jadhav S, Jadhav A, Thopte S, Marathe S, Vhathakar P, ChivteP, Jamkhande A. Sjögren's Syndrome: A Case Study. *J Int Oral Health* 2015; 7: 72-74.
4. Taubert M, Davies E, Back I. Dry Mouth. *British Medical Journal* 2007; 334: 534.
5. Carr A, Ng W, Figueiredo F, Macleod R, Greenwood M, Staines K. Sjögren's Syndrome – an update for dental practitioners. *British Dental Journal* 2012; 212: 353 – 357.
6. Fox P, Bowman S, Segal B. Oral involvement in primary Sjögren syndrome. *J Am Dent Assoc* 2008; 139: 1592-1601.
7. Turner M, Jahangiri L, Ship J. Hyposalivation, xerostomia and the complete denture: a systematic review. *J Am Dent Assoc* 2008; 139: 146-150.
8. Wan Nik W, Banerjee A, Moazzez R. Gastro-oesophageal reflux disease symptoms and tooth wear in patients with Sjögren's syndrome. *Caries Res* 2011; 45: 323-326.
9. Ellis G. Lymphoid lesions of salivary glands: malignant and benign. *Med Oral Patol Oral Cir Bucal* 2007; 12: E479-E485
10. Fox P. Salivary enhancement therapies. *Caries Res* 2004; 38: 241-246.
11. Pederson A M, Bardow A, Nauntofte B. Salivary changes and dental caries as potential oral markers of autoimmune salivary gland dysfunction in primary Sjögren's Syndrome. *BMC Clin Pathol* 2005; 5: 4

What's in the news?

Microbiologic Analysis of Removed Silicone Punctal Plugs in Dry Eye Patients

This study analyzed the microbiologic results of removing silicone punctal plugs due to uncomfortable symptoms in dry-eye patients. Patients who were diagnosed with dry eye and received silicone punctal plugs-SuperEagle Punctum Plug™ (EagleVision, Denville, NJ, USA) or Parasol Punctum Plug™ (Beaver-Visitec international, Inc., Waltham, MA, USA)-into upper or lower puncta that were removed due to discomfort from January 2018 to June 2020 were enrolled and reviewed retrospectively.

Out of the total 58 patients (64 eyes), 19 patients were male, and 39 patients were female. Protrusion without granulation (21 patients, 32.8%) was the most common reason for plug removal, followed by protrusion with granuloma

(19 patients, 29.7%). The positive rate of bacterial culture was 42.2% and *Klebsiella aerogenes* was the most common organism identified (18.5%).

Vancomycin showed the highest susceptibility of 100% among all the antibiotics, third generation cephalosporins were the most susceptible (88.5%) among cephalosporines, and levofloxacin was the most susceptible (81.0%) among quinolones. Among the patients who complained of discomfort after insertion of silicone punctal plugs, approximately 42% had a



positive result in bacterial culture. Therefore, when removing punctal plugs in such patients, a microbiological examination may be needed for the appropriate selection of antibiotics.

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Ocular Neuropathic Pain

By **Majid Moshirfar**; Erin E. Benstead; **Paige M. Sorrentino**; Koushik Tripathy

Continuing Education Activity

Ocular neuropathic pain is a diagnosis of exclusion which refers to the heightened perception of pain in response to normally non-painful stimuli. It usually presents without any visible objective exam findings, making it extremely difficult to identify. For this reason, it is often misdiagnosed as dry eye disease. This activity describes the etiology, epidemiology, evaluation, treatment, and management of ocular neuropathic pain. This activity also highlights the role of the interprofessional team in the recognition and management of this condition.



Objectives

Explain the etiology of ocular neuropathic pain.
Review the presentation of a patient with ocular neuropathic pain.
Describe the current treatment options available for ocular neuropathic pain.
Summarize interprofessional team strategies for improving the outcomes of patients suffering from ocular neuropathic pain.

Introduction

Ocular neuropathic pain is a diagnosis of exclusion which refers to the heightened perception of pain in response to normally non-painful stimuli. It usually presents without any visible objective exam findings, making it extremely difficult to identify.[1] For this reason, it often gets misdiagnosed as dry eye disease.

Ocular neuropathic pain may present with accompanying visible damage to tissue; however, it can also occur as a result of a physiological dysfunction of the nervous system.[1] With other corneal pathologies, the intensity of corneal pain often correlates with vital dye staining. However, in patients with ocular neuropathic pain, symptoms are severe and unaccompanied by equivalent signs, which is why ocular neuropathic pain is sometimes referred to as “corneal pain without stain” or “phantom cornea.”[2] This is the ocular analog of complex regional pain syndrome, systemic neuropathic pain, or reflex sympathetic dystrophy.

Other names for this condition include, but are not limited to corneal neuropathic pain, corneal neuralgia, ocular pain syndrome, keratoneuralgia, corneal neuropathic disease, and corneal allodynia.

Ocular neuropathic pain is an important differential to consider because many patients get misdiagnosed due to its significant overlap with dry eye disease. The disparity between signs and symptoms often results in patients being dismissed or considered malingering, hysterical, or psychosomatic.[3] As demonstrated by case reports, patients with extreme cases of this condition have even committed to suicide due to the severity of chronic pain.[4] An important first step in treating ocular neuropathic pain is to communicate the belief that the condition and the symptoms are real.[2]

The objective of this article is to provide a summary of the condition and review approaches for its treatment and management, as well as increase awareness of this underrecognized disease.

Etiology

Ocular neuropathic pain can result from injury to or disease of peripheral corneal nerves.[1] The healing process results in aberrant regeneration and upregulation of nociceptors in the corneal nerves, which leads to hyper-responsivity and an increased perception of pain to ordinarily non-painful stimuli. [5] Ocular neuropathic pain may also result from a variety of systemic conditions which alter the somatosensory pathway.[1]

A comprehensive list of potential underlying causes that can lead to or have been associated with ocular neuropathic pain and trigger the heightened pain response to non-noxious stimuli are listed below in Table 1 (adapted from Dieckmann et al.).[1][2][6]

Epidemiology

As stated in the above table, ocular neuropathic pain has many systemic associations. The four most common are depression, anxiety, fibromyalgia, and headache.[1] Following these are diabetes, celiac disease, HIV, and idiopathic small fiber neuropathies.[1]

The proportion of females with ocular neuropathic pain is higher than men.[7] Females also tend to have a higher incidence of associated conditions such as fibromyalgia and autoimmune diseases. While autoimmune diseases affect between 5 to 8% of the population, 78% of the affected are women.[7] This association may be contributory to the higher incidence of ocular neuropathic pain in women.

Pathophysiology

The human cornea is often referred to as one of the most potent pain generators in the human body.[6] Unsurprisingly, it is also among the most densely innervated tissues with approximately 7000 nerve terminals per square millimeter, making the cornea about 300 to 600 times more sensitive than skin.[6] Corneal nerves carry the sensation of touch,

pain, and temperature.[8] Most of the nerves of corneal subbasal plexus are unmyelinated (C fibers) and some are myelinated (Ad fibers).

Corneal nerves detect mechanical, thermal, and chemical stimuli. Input is perceivable as pain or a range of dysesthesias (unpleasant abnormal sensations)[6]:

Photoallodynia (pain sensation in response to a non-painful stimulus, light)

Burning

Irritation

Dryness

Grittiness

Pain protects tissue from injury. Detection of painful stimuli by nociceptors transmits via action potentials to higher order centers where the pain is perceived.[1] Iatrogenic damage, trauma, and inflammation of the ocular surface can result in damage to this system, which may increase the sensitivity of peripheral nerves.[1][3] This increased sensitivity, or peripheral sensitization, intensifies pain signaling. Chronic stimulation can cause sensitization of the central nervous system and thus increased awareness of pain and photoallodynia.[1]

History and Physical

Due to the complexity of mechanisms involved in ocular neuropathic pain, the subjective symptoms of corneal dysesthesia can vary significantly. Patients may describe feelings of burning, aching, boring, hot poker-like fire, foreign body, and photophobia. The symptoms may substantially affect the quality of life of the patients and may cause impaired functioning relative to activities of daily living.

The Ocular Pain Assessment Survey (OPAS) may help evaluate corneal and ocular surface pain as well as its impact on the quality of life.[6] Surveys are useful not only in diagnosing but also in monitoring the efficacy of therapeutic approaches.[3]

Patients may also present with blepharospasm that developed due to chronic corneal nociceptor hyperactivity.[2][9]

Evaluation

To verify a diagnosis of ocular neuropathic pain, viewing the cornea in vivo using a confocal microscope allows for detection of abnormalities of the corneal nerves.[6] Specific characteristics of the instrument also enable it to be a tool to differentiate among various causes of perceived ocular pain, gauge the relative contributions of central versus peripheral mechanisms, and monitor the success or failure of treatment.[10]

The use of esthesiometers can be used for the detection of mechanical nociceptor responses and allow quantification of nerve fiber functionality.[6] Findings of morphological changes and hypersensitivity of corneal nerves in patients with chronic symptoms suggest the presence of ocular neuropathic pain.[5]

Since the above diagnostic methods are not readily available to a majority of practitioners, ocular neuropathic pain is often considered a diagnosis of exclusion.

Patients may demonstrate an exaggerated pain response to touch, air, and drops. A thorough case history is paramount

to revealing the causation—whether that be the history of refractive or cataract surgery, ocular surface disease, infection, systemic disorders, systemic pain syndromes, etc. Clinicians often dismiss these patients due to the lack of clinical findings.[2]

Initial examination of an ocular neuropathic pain patient resembles a dry eye workup. The ocular surface should be assessed with vital stains, tear production measured via Schirmer test, and tear quality evaluated with tear break up time, tear osmolarity, and/or tear proteomics.[6]

The ocular surface will appear healthy, unlike cases of dry eye which may present with surface staining, abnormal tear osmolarity, etc.[1] When the patient has subjective complaints of corneal pain without objective findings, it should raise suspicion of ocular neuropathic pain. Examiners must keep in mind that it is also possible for dry eye to be comorbid with ocular neuropathic pain and it can be difficult to differentiate these two diagnoses when they present together.

Distinguishing between central or peripheral pain origins for ocular neuropathic pain can be helpful when determining treatments. A proparacaine challenge test can be used to make this determination.[1][6] If patients experience either complete or partial relief with topical 0.5% proparacaine hydrochloride they likely have peripheral or mixed combined forms, respectively. If no relief or there is a worsening of symptoms, then the patient has central sensitization of pain, which can be very challenging to treat.[1][6]

Treatment / Management

Severe pain sensation and light sensitivity prevent those afflicted with ocular neuropathic pain from performing activities of daily living and is associated with symptoms of anxiety and depression—even suicidal thoughts in extreme cases.[6]

Treatment strategies encompass several approaches[1][6][3]:

Ocular surface treatment

- Copious lubrication with artificial tears decreases the hyperosmolarity of tears and halts over-stimulation of corneal nociceptors. Preservative-free tear supplements are preferred if frequent instillation is needed.
- Topical and/or systemic antibiotics along with dietary supplements (omega3 fatty acids) to treat evaporative dry eye and blepharitis
- Bandage contact lenses
- Scleral lenses provide a cushion of fluid over the entire cornea, while some patients experience immediate relief, for some patients, the lenses can trigger pain due to severe hyperalgesia[1] PROSE contact lens (prosthetic replacement of the ocular surface ecosystem) is custom made rigid gas permeable lens with liquid reservoir and may be helpful in post-LASIK neuralgia.
- Compounded lacosamide 0.1% may combine with preservative-free saline inside the bowl of a scleral lens

Anti-inflammatory[6][1][1]

- Soft steroids such as fluorometholone or loteprednol to dampen surface inflammation
- Topical or oral NSAID agents

- Topical immunomodulators such as cyclosporine 0.5% or lifitegrast 5% is also an option, but their therapeutic effects are not immediate
- Tacrolimus 0.03% eye drops have been shown to improve tear stability and have an anti-inflammatory effect
- Topical or oral antibiotics such as doxycycline or azithromycin are useful adjunct therapy when meibomian gland dysfunction is present
- Amniotic membranes provide anti-inflammatory, anti-fibrotic, and neurotrophic effects; since not all patients can tolerate the polycarbonate ring of self-retained tissues such as PROKERA, the corneal amniotic membranes can be placed underneath a bandage contact lens

Neuro-regeneration:

- Autologous serum tears (20%)- Serum contains various growth factors which play a crucial role in neuro-regeneration and healing - these factors include nerve growth factor, transforming growth factor beta, insulin-like growth factor 1, epidermal growth factor, fibronectin, and substance P

Others [12][13][14]:

- Systemic analgesics, tricyclic antidepressants (10 to 15 mg at bedtime), and antipsychotics to treat associated non-ocular pain
- Anticonvulsants such as carbamazepine (200 mg/day), gabapentin (300 to 900 mg/day) or pregabalin (150 mg/day), which are also used to treat trigeminal neuralgia
- Low dose naltrexone (1.5 mg at bedtime), an opioid antagonist used off-label
- Opioid agonists such as tramadol (50 mg/day) may provide acute relief but require caution due to the potential for dependence
- Vitamin B has proven effective in herpes, diabetic neuropathy, and neuropathic pain
- Also assists with re-innervation and re-epithelization of the corneal surface - specifically, B12 increases serotonin levels and inhibits nociceptive neuronal activity

Alternative therapies [1][6][1]:

- Acupuncture treatment semi-weekly
- Electrical neurostimulation to treat chronic intractable pain with central sensitization
- Invasive neuromodulation therapies such as deep brain stimulation and Intrathecal analgesic infusions may provide relief for severe, intractable cases of neuropathic pain

Differential Diagnosis

As previously noted, ocular neuropathic pain is a diagnosis of exclusion. The following are essential to rule out[1]:

- Trigeminal neuralgia
- Oculofacial pain
- Referred pain
- Ocular surface disease
- Sinus dysfunction
- Ocular medication toxicity
- Contact lens-related problems
- Corneal disorder (abrasion, erosion, infiltrate, ulcer, etc.)

- Chemical injury
- Trauma
- Uveitis
- Post-herpetic neuralgia

Take, for example, ocular surface disease. The mechanism is as follows: reduced tear secretion leads to inflammation. Inflammation causes sensitization of nociceptive nerve endings, which leads to feelings of dryness and pain. In the long term, inflammation and nerve injury alter gene expression within the trigeminal ganglion, propagating ocular dysesthesias and neuropathic pain.[10] It is easy to see how this particular differential diagnosis is often a misdiagnosis of ocular neuropathic pain.



Prognosis

The prognosis of patients with ocular neuropathic pain dramatically varies. Patients often have chronic symptoms requiring a multimodal treatment approach.[2][6] Early interventions yield better outcomes.

Complications

For reasons other than the obvious, treatment and management of chronic pain is an arduous task. Patients with chronic pain become increasingly anxious about it, and anxiety correlates with increased susceptibility to pain – a vicious cycle.[3] Chronic pain is not only psychologically taxing but physically as well. Studies have found comorbidity with many other conditions such as chronic fatigue, joint pain, and depression.[15]

Deterrence and Patient Education

Preventative screenings for certain risk factors, including autoimmune diseases and systemic pain conditions, should be considered before planning refractive surgeries such as LASIK. This approach may reduce the risk of subsequent development of ocular neuropathic pain.[3] Additionally, since patients suffering from more severe cases of ocular neuropathic pain also more frequently report overlapping psychiatric disease, screening for pre-existing personality disorders which could predispose a patient to depression and suicidal thoughts are equally important.[16] Healthy-minded individuals are more equipped to cope with chronic pain for longer while they seek treatment and are less likely to resort to self-harm.

Patients with ocular surface disease indicated higher pain responses at non-ocular sites such as the forearm compared to those without the condition, which would indicate that patients with the ocular surface disease have a lower systemic pain threshold, as is consistent with central sensitization in dry eye patients.[5]

To reiterate, an important first step in treating ocular neuropathic pain is to communicate the belief that the condition is real.[2] The second is to actively screen for it.

Pearls and Other Issues

- Dry eye patients who fail to respond to dry eye treatments and have persistent symptoms without objective findings warrant further investigation

- An important first step in treating ocular neuropathic pain is to communicate the belief that the disease is real, as there is often a psychological component associated with this chronic pain
- Ocular neuropathic pain is a diagnosis of exclusion; a thorough case history is important along with an examination of ocular health

Enhancing Healthcare Team Outcomes

Given the challenges in both diagnosis and treatment of ocular neuropathic pain, the best approach to this condition is with an interprofessional team consisting of physicians, specialists (including neurology, psychiatry, rheumatology, ophthalmology and optometry), specialty-trained nursing, and when appropriate, pharmacists and psychological personnel, all communicating across disciplines to direct the case towards optimal clinical results. [Level V]

References:

1. Dieckmann G, Goyal S, Hamrah P. Neuropathic Corneal Pain: Approaches for Management. *Ophthalmology*. 2017 Nov;124(11S):S34-S47. [PMC free article] [PubMed]
2. Rosenthal P, Baran I, Jacobs DS. Corneal pain without stain: is it real? *Ocul Surf*. 2009 Jan;7(1):28-40. [PubMed]
3. Jacobs DS. Diagnosis and Treatment of Ocular Pain: the Ophthalmologist's Perspective. *Curr Ophthalmol Rep*. 2017;5(4):271-275. [PMC free article] [PubMed]
4. Theophanous C, Jacobs DS, Hamrah P. Corneal Neuralgia after LASIK. *Optom Vis Sci*. 2015 Sep;92(9):e233-40. [PubMed]
5. Galor A, Levitt RC, Felix ER, Martin ER, Sarantopoulos CD. Neuropathic ocular pain: an important yet undervalued feature of dry eye. *Eye (Lond)*. 2015 Mar;29(3):301-12. [PMC free article] [PubMed]
6. Goyal S, Hamrah P. Understanding Neuropathic Corneal Pain--Gaps and Current Therapeutic Approaches. *Semin Ophthalmol*. 2016;31(1-2):59-70. [PMC free article] [PubMed]
7. Fairweather D, Frisancho-Kiss S, Rose NR. Sex differences in autoimmune disease from a pathological perspective. *Am J Pathol*. 2008 Sep;173(3):600-9. [PMC free article] [PubMed]
8. Shaheen BS, Bakir M, Jain S. Corneal nerves in health and disease. *Surv Ophthalmol*. 2014 May-Jun;59(3):263-85. [PMC free article] [PubMed]
9. Belmonte C, Acosta MC, Merayo-Llona J, Gallar J. What Causes Eye Pain? *Curr Ophthalmol Rep*. 2015;3(2):111-121. [PMC free article] [PubMed]
10. Belmonte C, Nichols JJ, Cox SM, Brock JA, Begley CG, Bereiter DA, Dartt DA, Galor A, Hamrah P, Ivanusic JJ, Jacobs DS, McNamara NA, Rosenblatt MI, Stapleton F, Wolffsohn JS. TFOS DEWS II pain and sensation report. *Ocul Surf*. 2017 Jul;15(3):404-437. [PMC free article] [PubMed]
11. Moscovici BK, Holzchuh R, Chiacchio BB, Santo RM, Shimazaki J, Hida RY. Clinical treatment of dry eye using 0.03% tacrolimus eye drops. *Cornea*. 2012 Aug;31(8):945-9. [PubMed]
12. Moore RA, Derry S, Aldington D, Cole P, Wiffen PJ. Amitriptyline for neuropathic pain in adults. *Cochrane Database Syst Rev*. 2015 Jul 06;(7):CD008242. [PMC free article] [PubMed]
13. Derry S, Wiffen PJ, Aldington D, Moore RA. Nortriptyline for neuropathic pain in adults. *Cochrane Database Syst Rev*. 2015 Jan 08;1:CD011209. [PMC free article] [PubMed]
14. Pakravan M, Roshani M, Yazdani S, Faramazi A, Yaseri M. Pregabalin and gabapentin for post-photorefractive keratectomy pain: a randomized controlled trial. *Eur J Ophthalmol*. 2012;22 Suppl 7:S106-13. [PubMed]
15. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. *Pain*. 2011 Mar;152(3 Suppl):S2-S15. [PMC free article] [PubMed]
16. Crane AM, Levitt RC, Felix ER, Sarantopoulos KD, McClellan AL, Galor A. Patients with more severe symptoms of neuropathic ocular pain report more frequent and severe chronic overlapping pain conditions and psychiatric disease. *Br J Ophthalmol*. 2017 Feb;101(2):227-231. [PMC free article] [PubMed]



Q & A's with Connan Tam

Connan Tam



Edited by Åsa Baudin

1 What prompted you to begin a dry eye clinic?

During the routine Optometric eye examination, Optometrists have to cover many tests. What I found was that we generally try to tag on some dry eye treatment advice in the last 5 minutes of an appointment. When we researched more into dry eye investigations and treatment we realised that more time needed to be dedicated to this group of patients.

2 How did you gauge interest/ motivate pts to attend and be referred?

Being one of first dedicated dry eye clinics, we have been fortunate to have gained notoriety and have a good word of mouth.

3 Do you host any educational events on Dry eye for both pts and colleagues?

I have personally been involved with a few dry eye webinars that were provided for Optometrists. I am one of the Key opinion leaders for Lumenis and provide IPL training. The plan to host patient-oriented Q&A sessions are in the pipeline.

4 What % of pts complain of dry eye?

In our general Optometric clinic I would say up to 25% will mention some form of dry eye symptom. The number does seem to have increased due to people working from home and generally more screen time.

5 What % have clinical dry eye?

As a dedicated dry eye clinic the majority attending the Dry Eye Centre are confirmed to have clinical dry eye. In our general Optometric clinic, around half of the patients, if not more, will have dry eye signs. Whether they have clinical dry eye is difficult to determine without conducting the full diagnostic work up.

6 Do you have pts with concomitant dry eye due to other drops - ie: Glaucoma drops?

Not so much, these days most patients are offered non-preserved formulations so I see less dry eye that is related to glaucoma drops specifically.

7 Do pts complain of low mood/depression due to Dry eye?

I find that dry eye does affect mental health in a large number of patients. Being a chronic condition, certain patients find it really difficult to deal with their symptoms that are experienced during much of their daily lives. Personally, I feel that much of dry eye care involves managing the psychological aspects too.

8 What % have already tried drops before coming to you?

The majority of patients attending our clinic would have tried various drops and other remedies. Some may have also attended other clinics before coming to us.



9 Are you familiar/aware of other new treatments such as IPL?

I believe that we were the first to adopt IPL in UK. In 2013, we imported the first available IPL device shortly after we started the Dry Eye Centre. We are also the first in the country to have the new Lumenis Optilight IPL device. We are always on the look out for new treatments and welcome the fact that we are often asked to trial new devices.

10 Is this treatment option of use/interest for you?

For us, we feel that IPL is a great conservative treatment option to treat eyelid telangiectasia and meibomian gland dysfunction.

11 What's the referral process – Gp/other opticians?

We are a private clinic and so any referral is accepted. A GP referral is not necessary. Many of our patients are self referred but we do also have referrals from Optometrists, Ophthalmologists and GPs.

12 Do you use DEWS as a reference?

Absolutely! I think it wonderful that there is so much research is going into dry eye.

13 Do you use preservative free drops for all pts?

When possible yes we only prescribe preservative free drops and medications.

14 If not, what influences your decision to offer preserved drops?

If a patient responded well previously to a preserved drop or drug. Sometimes I will have patients who failed to respond to all the non -preserved versions of a medication, I will then try a preserved option.

15 What is your “go to” dry eye treatment?

I do not have a go to treatment. With the condition being so multifactorial it is important to tailor a treatment plan according to the findings.

16 When do you refer to an Ophthalmologist, what is the tipping point to refer on?

I would refer on if the dry eye is advanced where the patient may need more complex medication or surgical intervention. When there is a suspected systemic link to the dry eye it is important that they undergo further investigation and treatment.

17 What is your measure of success?

Apart from the regular objective markers of dry eye treatment, improvement of a patients symptoms has got to be the ultimate measure!

Ophthalmology Going Greener: A Narrative Review

By Yee Ling Wong, Maha Noor, Katherine L. James & Tariq M. Aslam

Abstract:

The combined effects of fossil fuel combustion, mass agricultural production and deforestation, industrialisation and the evolution of modern transport systems have resulted in high levels of carbon emissions and accumulation of greenhouse gases, causing profound climate change and ozone layer depletion. The consequential depletion of Earth's natural ecosystems and biodiversity is not only a devastating loss but a threat to human health. Sustainability—the ability to continue activities indefinitely—underpins the principal solutions to these problems. Globally, the healthcare sector is a major contributor to carbon emissions, with waste production and transport systems being amongst the highest contributing factors. The aim of this review is to explore modalities by which the healthcare sector, particularly ophthalmology, can reduce carbon emissions, related costs and overall environmental impact, whilst maintaining a high standard of patient care.

Key Summary Points:

The adverse health effects of climate change include spread of infectious diseases, cardiovascular and respiratory diseases secondary to wildfires, malnourishment due to droughts and flooding, and obesity, diabetes and heart disease owing to increasing motorisation and progressive agricultural activities.

The healthcare sector is a significant contributor to carbon emissions globally.

This review aims to explore methods by which the healthcare sector, particularly ophthalmology, can positively reduce waste production and carbon emissions.

Refinement of referral pathways, upskilling community optometrists, establishment of peripheral imaging and treatment 'hubs', utilisation of home devices alongside AI algorithms, and risk stratification of patients in ophthalmology outpatient settings can reduce unnecessary cost, waste production, and travel-associated carbon emissions.

Promoting sustainability in healthcare through acknowledgement, education (undergraduate and postgraduate medical, nursing, and optical bodies), policy development, and setting targets for carbon emissions are the next steps in the movement towards sustainable healthcare.

Introduction

"The life of every child born today will be profoundly affected by climate change. Without accelerated intervention, this new era will come to define the health of people at every stage of their lives."—The 2019 report of the Lancet Countdown [1].

Combustion of fossil fuels and biomass, world food production (via animal cultivation, irrigated agriculture) and mass deforestation have resulted in rapid increases in world energy production and the accumulation of heat-trapping "greenhouse gases" in the troposphere. Man-made gases from the use of halocarbons for refrigeration and insulated packaging accumulate in the stratosphere and destroy ozone, reducing shielding against harmful ultraviolet radiation. Industrialisation and the emergence of a world economy, with modern transport systems and electronic communication network, vast expansion of energy-intensive agriculture and livestock production, urban migration and increase in consumerism are all contributing to the global

environmental changes. Climatologists believe that the unusual weather patterns are signalling the beginning of a long-term change in the average temperature, precipitation and patterns of weather extremities. According to the Intergovernmental Panel on Climate Change (IPCC) report, global warming is predicted to reach 1.5 °C above pre-industrial levels between the years 2030 and 2052 if it continues at the current rate [2]. Such climate change and ozone depletion impact the Earth's natural ecosystem and biodiversity, depleting freshwater supply and the marine ecosystem that are essential to human health [3, 4].

Climate change and ozone depletion can lead to adverse health consequences. In the past 20 years, heat-related mortality in those above 65 years old has increased significantly (53.7%), reaching a total of 296,000 deaths in 2018. The negative consequences of climate change can be observed in every continent—from the ongoing spread of dengue virus across South America, the wildfires in Australia compromising cardiovascular and respiratory health, and the floods or droughts in China, Bangladesh, Ethiopia and South

Africa leading to the undersupply of food and malnourishment [5]. Modern lifestyle choices, with increasing motorisation replacing active transport modalities like walking and cycling, and the increase of red meat and dairy consumption (progressive agricultural activities) have led to an increased prevalence of diabetes and obesity and their subsequent chronic health issues. This has resulted in an increased reliance on healthcare and associated costs [6]. Yu and colleagues also elaborated the potential impact on eye health including increasing incidence of trachoma infections, vitamin A deficiency eye conditions, cataracts, allergic eye diseases, glaucoma and age-related macular degeneration (AMD) as direct or indirect consequences from extreme weather conditions [7]. Poor air quality has been shown to put additional pressure on emergency services; a study by Kings College London using data from nine English cities demonstrated that on high pollution days there is an increase in ambulance calls with 673 extra out-of-hospital cardiac arrests and admissions for stroke and asthma [8].



The Lancet Commission on Health and Climate sets forth the requirement of the health sector to tackle climate change, by identifying and mitigating the risks it poses to bring about a paradigm shift in the future delivery of healthcare [9]. Climate change not only poses the biggest health ‘threat’ but also creates an ‘opportunity’ for positive change in global health [10,11,12].

This review aims to explore ways in which the healthcare sector, in particular ophthalmology, can reduce carbon emissions along with related costs, environmental impacts and associated mortality and morbidity, whilst maintaining the best standard of care. We will explore ‘sustainability’ in ophthalmology, the ability to meet the needs of the current generation without compromising the needs of future generations [13, 14].

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Carbon Emission in Healthcare

In 2017, the healthcare sector was responsible for 4–6% of carbon emission globally [8]. The USA spends by far the

most on its healthcare system (with nearly one-fifth of GDP in 2013). After food service facilities, hospitals are the second most energy intensive commercial buildings in the USA [15]. The NHS (England’s National Health Service) employs over 1.5 million people to provide high-quality healthcare to a population of approximately 56 million people. This delivery of care contributes to 4–5% of the country’s total greenhouse gas and this value may well increase further if unchecked, with an ageing population and increasing healthcare expenditure [16]. Whilst emitting carbon, the NHS is also treating acute presentations and conditions attributed to such emissions [6]. Hence, in 2008, the Sustainable Development Unit (SDU) was created following the publication of the Climate Change Act (2008) to gain a better understanding of the association between climate change, health and healthcare. The NHS has since achieved a significant reduction in greenhouse gas emission and their associated costs whilst delivering and maintaining high standards of care.

In January 2020, the NHS England Chief Executive launched the Greener NHS campaign, aiming to make the NHS the world’s first net zero health service by 2040, with an 80% reduction by the years 2028–2032. It was noted that the NHS is “part of the problem as well as the solution.” In addition, The NHS Net Zero Expert Panel has been established to look at changes the NHS can make across the organisation both in its supply chain and wider partnerships. NHS emissions come from a number of sources, but transport contributes significantly. It is estimated that 6.7 billion road miles each year are from patients and their visitors travelling to access the healthcare sites [17, 18].

The Ophthalmology Carbon Footprint

Cataract Surgery

Ophthalmology has the highest surgical volumes and rapid turnover rates in the NHS with approximately 414,000 cataract procedures in England and 20,000 in Wales between the years 2017 and 2018 [19]. This makes cataract procedures an obvious target for reduction of carbon emissions. Morris and colleagues estimated the carbon burden accounting for 343,782 cataract procedures



in England in 2011 to be at least 63,000 tonnes of CO₂equivalent (CO₂eq) taking into consideration building and energy use, travel and procurement [20]. Somner et al. compared different techniques of cataract explantation [phacoemulsification vs. modified small incision cataract surgery (MSCIS)] and the environmental impact. They concluded that phacoemulsification is not only much more costly but has a significantly greater environmental impact compared to MSCIS. This is the result of disposable waste (paper and plastic) and the energy used by the phacoemulsification machine [21, 22]. In terms of cost-effectiveness, various studies carried out in India and Nepal have shown that the technique of MSICS is 1.4–4.7 times less expensive than phacoemulsification with similar visual outcomes and complication rates. It is therefore the predominant technique in developing countries and areas with limited resource but high volume and backlog [22,23,24,25,26]. Of course, in many

their disposable supplies but generates twice as much waste compared to that of the next highest site, indicating that packaging and waste management could be an issue [27].

Figure 1a shows an example of non-clinical waste generated in a cataract centre in the UK in preparation for a cataract case and Fig. 1b shows an example of clinical waste generated upon completion of a cataract case. During a non-complex phacoemulsification case, a total of 2.10 kg of waste was generated. It is important to recognise the amount of waste produced from each case depends on various factors such as the complexity of case (meaning more or less surgical equipment), the use of disposable equipment and packaging, the number of saline bottles used and the remaining volume of balanced salt solution, the number of surgeons operating affecting disposable gowns and gloves used.



Fig. 1

a Non-clinical waste generated in preparation for a phacoemulsification case. b Clinical waste generated following a phacoemulsification case

developed nations there are different socioeconomic conditions and healthcare infrastructures and expectations, and larger ‘real-world’ prospective analyses would be required to assess the long-term visual outcomes of different cataract surgery techniques, their carbon footprints and cost-benefit analyses.

In developed countries, single-use disposable instruments and equipment have contributed to a mass production of clinical and non-clinical waste, and significantly to carbon emissions. Morris et al. estimated that 53.8% of these emissions were from procurement, the majority due to disposable medical equipment [19]. Goel and colleagues published data on productivity, costs, carbon emissions and waste generation for every cataract surgery performed across nine participating sites internationally, using the “Eyefficiency” cataract surgery auditing tool. Service costs range from £31.55 to £399.34, solid waste weighs between 0.19 and 4.27 kg and carbon emissions range from 41 kg CO₂eq to 130 kg CO₂eq for each cataract case performed. Comparing the expenditure of medical supply and waste generation between two developed countries exposes an interesting difference. New Zealand has the highest expenditure on consumables with low waste generation indicating that the supply spending could be disproportionately high. The UK spends moderately on

By comparing UK cataract services with the Aravind Eye Care System (AECS) in India, notable differences in carbon generated are observed. At the AECS approximately 6 kg CO₂eq is generated per phacoemulsification procedure compared to approximately 130 kg CO₂eq in the UK, for every case performed [20]. This significant difference is due to the Aravind’s high volume approach providing up to 1500 cataract surgeries per day, thereby minimising the environmental footprint associated with electricity and energy use. They also reuse surgical gowns, blankets and certain surgical and pharmaceutical supplies (including multiuse solutions during cataract surgery and preoperative eyedrops). Contaminated instruments (instrument trays and phacoemulsification tip) would be sterilised in between each case, whereas non-contaminated instruments (fluid collection bags, plastic protectors on phacoemulsification machines and tables, intraoperative pharmaceuticals) would be sterilised at the end of the operating day to reduce environmental impact associated with repeated sterilisation. Despite reusing surgical supplies, cleaning gloves with alcohol and chlorhexidine, and simultaneously operating on multiple patients within a single operating theatre, the rate of postoperative endophthalmitis is no higher than European norms [28, 29]. However, because of stricter infection control guidelines, implementation of the Aravind model of practice is not currently feasible in countries such as the UK.

Reduce, Reuse, Recycle, Rethink and Research

The 5 R's of sustainability (Reduce, Reuse, Recycle, Rethink and Research) can be applied to reducing the environmental impact of ophthalmic surgery in a cumulative manner, whilst maintaining patient safety.

We can reduce energy consumption by simply turning off lights in operating theatres and switching off equipment when not in use. The use of light emitting diode (LED) lights, timer and motion detectors will also result in significant reduction in energy expenditure [30,31,32]. According to Kagoma and colleagues, operating theatres are almost always unoccupied up to 40% of the time over a 24-h period [33]. The Providence St. Peter Hospital, Washington reduced energy consumption by reducing its ventilation system output by 60% during unoccupied times [34].

Sensible ways to reduce the amount of waste generated should also be considered. Referring again to Fig. 1a and b, a major contributor to waste is plastic packaging, with the majority of the equipment being placed in plastic containers and double wrapped. The use of polypropylene plastic blue sterile wrap is not only damaging to the environment but will also incur a substantial disposal cost. There is an opportunity to work with industries to reduce the amount of waste derived from a single operation [33]. Understandably, ophthalmic surgeons have specific equipment they prefer for a certain surgical procedure, hence the existence of single packaging disposable surgical equipment, individually packed gloves and gowns according to size. Perhaps the creation of a surgeon-tailored pack with preferred equipment, gloves of their size and disposable gowns could reduce the amount of double packaging of each product.

Bartl [35] suggested that the reuse of materials is equally as effective at reducing waste as it avoids the side streaming of waste generated through recycling and occurs before the end-stage of material is reached. Kwakye and colleagues reported that switching from disposable to reusable surgical gowns in a single hospital led to a waste reduction of 23,000 kg of carbon, saving the hospital 60,000 USD over a 12-month period [36]. In a review article published by Guetter in 2018, decisions whether to use disposable or reusable materials such as drapes and surgical gowns are based on available scientific data and cost based on region, country, culture and customs. Data relating to infection rates is still controversial and more comparative studies are needed to look at savings and expenditures relating to reusable items [30]. Indeed, one can argue that the environmental impact of laundering of reusable textiles could potentially be more significant, especially when paired with harmful laundry chemicals and inefficient ageing hospital infrastructure (water and energy). The benefits of reuse of surgical equipment are also disputable because of the hidden costs associated with storage, damage of equipment in the process of sterilisation and instrument handling, and the risk of cross-contamination e.g. Creutzfeldt–Jakob disease (CJD), especially in vitreoretinal surgery when neural tissues are involved [37].

According to Southorn et al. [38] each operating room has the potential to produce up to 2300 kg waste every year, with almost 80% of the total waste generated preoperatively. This is variable depending on the surgical specialty, type of procedure, duration of surgery and surgeon preference of instruments and equipment. The amount of waste generated also differs from one country to another, more so in higher income countries [32]. Waste segregation is important

especially in healthcare not only from an ecological standpoint but also economical one as clinical waste is the most expensive to treat [30].

As of 2013, a meaningful recycling programme has taken place in about 80% of Australian hospitals, about 50% in the USA but less than 10% in the UK [32]. This difference may be due to varying abilities to segregate waste because of strict infection control rules and fear of contamination, leading to incineration of potentially recyclable items [38]. In a survey published in 2012, only 11% (n=780) of participating anaesthetists from Australia, New Zealand and England agreed that adequate recycling occurred in their theatre [39]. Of course, recycling also comes with its cost; the impact of carbon emissions from collection, sorting and re-processing needs to be considered. Furthermore, a significant proportion of recycled paper, scrap metal, with approximately 70% exported to China and Hong Kong in 2016, led China to impose a ban on waste imports. This raises questions about sustainability of recycling [32, 35]. In 2015, McGain and colleagues published a cohort study reporting that recycling did not lead to additional costs and that the overall impact of recycling (although savings may be small) may be magnified if adapted by the national healthcare system [40].

'Green initiatives, incentives or awards' may encourage surgeons and administrators to rethink the global and financial impact of the unnecessary waste produced [31]. Perhaps ophthalmologists can be invited to participate in an innovative competition to design a surgeon-tailored instrument pack based on each subspecialty in ophthalmology to best cut down unnecessary waste and cost, whilst maintaining patient safety.



As pre-existing literature on environmental impact on current ophthalmic practices is scarce, more research and publications are needed to help map out the carbon footprint of various eye care services especially relating to cataract surgery and glaucoma care in the community [7]. More data is needed on environmental impacts of healthcare activities, life cycle analysis of materials, and cost analysis. Innovative design of devices that minimise environmental impact whilst maintaining standard of care would also be useful [33].

Restructuring Ophthalmic Delivery of Care

Ophthalmology is one of the busiest specialties in the NHS with a predicted increase in demand by 30–40% over the next 20 years [41, 42]. As of 2019, primary care referrals have increased by 12% from 2013 to 2014. In England and Wales, approximately 2.5 million people 65 years and above have visual impairment related to cataracts leading to an increasing need for outpatient services. The demand for cataract surgery is predicted to rise by 50% in the next 20 years from year 2017. Glaucoma is the most common cause of visual impairment in people over 70 years old and is predicted to rise by 44% over the next 15 years [43]. Up to 20% of new referrals are for 'suspected glaucoma' and the number of 'false positive' referrals has increased following the introduction of the first National Institute for Clinical Excellence (NICE) glaucoma guideline [44, 45]. Inappropriate referrals to the outpatient ophthalmology service are estimated to be between 20% and 65% [46,47,48]. This leads to unnecessary costs, capacity issues, travel-associated carbon emission, and unnecessary (clinical and non-clinical) waste production. Filtering schemes like the Manchester Glaucoma Enhanced Referral Scheme (GERS) have resulted in a 53% reduction in false positive referrals between April 2013 and November 2016, whilst maintaining clinical efficacy with no cases of missed glaucoma or non-glaucomatous pathology [49, 50].

More Local Delivery of Care

As large quantities of greenhouse gases are generated by patients travelling to access hospital-based healthcare, smaller treatment centres or screening hubs for patients with chronic eye conditions like AMD could be established peripherally in a number of locations, reducing transport-associated carbon emission. The challenge associated with delivering care in this way is the initial investment required, especially when such schemes may not offer a financial saving [51]. As the NHS moves to a population-focused planning and delivery of healthcare through the Integrated Care Systems there is an opportunity for such services at a regional level. Furthermore, an upskilled optometry workforce provides the opportunity for care to be delivered from optometry practices already located across towns, cities, and suburban areas offering convenient and closer-to-home locations. This approach again aligns with the NHS England care closer to home strategy, providing a number of benefits not least the reduction in patient miles. Many community optometrists have taken up training to provide extended care services to patients, allowing continuing professional development for particular clinical interests, whilst offering additional income generation under their NHS contracts. Nationally, optometrists who specialise in certain areas of ophthalmology and ophthalmic specialist nurses are already undertaking outpatient appointments and intravitreal injections respectively. These new models of care would provide care closer to where patients live and often located by public transport routes with opportunities to walk or cycle, thereby significantly reducing patient miles.

Teleophthalmology/Health Information Technology

The use of teleophthalmology and health information technology can help save time, energy and raw materials like paper and plastic and their subsequent impact on the environment and our planet [52]. The collaborative effort of the Teleophthalmology Network in Scotland is one example of this approach. By supporting optometric practices to utilise smartphones attached to slit lamps, enabling ocular biomicroscopic videography, ophthalmologists are able to view a patient's examination features in real time without the patient attending, thereby streamlining the ophthalmic triaging system [53]. Purohit and colleagues published a systematic review targeting transport-associated emissions and found that the carbon footprint saved using telemedicine ranges between 0.7 and 372 kg CO₂eq per consultation [54]. Sharafeldin and colleagues undertook a review on economic evaluation that supports evidence of cost-effectiveness of teleophthalmology on chronic conditions like diabetic retinopathy and glaucoma [55]. An audit carried out in Western Australia consisting of 709 patients found that they were able to correctly diagnose 95% of patients via remote consultations and saved over 10 days of outreach clinics for 287 patients with cataract seen and managed [56]. The use of teleophthalmology or virtual consultations have exponentially increased during the COVID-19 pandemic, to provide outpatient appointments in a way that usual change management cycles would have taken significantly longer to achieve. Although this was not suitable for all patients and types of appointment, it helped keep in-person hospital attendances to a minimum, whilst reducing patient miles travelled. Older patients may struggle with the not-so-traditional way of healthcare provision and the initial learning curve of telemedicine. Obtaining accurate visual acuity and clinical examination for future comparison may be difficult and is no substitute for face-to-face clinical examination. Nonetheless, with the advancement of technology, teleophthalmology offers an opportunity to deliver some suitable services remotely and provides a way to reduce the carbon footprint of services whilst allowing access to care in geographically isolated areas [57, 58].

Home Tele-screening

The emergence of a variety of home devices for the monitoring of visual acuity, visual fields, and intraocular pressure for conditions such as diabetic retinopathy, AMD, and glaucoma also present as a movement away from traditional clinic visits and towards sustainability [59,60,61,62,63]. In particular, ForeseeHome™ (conducts preferential hyperacuity perimetry for monitoring AMD) [64], myVisiontrack™ (uses shape discrimination hyperacuity testing in AMD and diabetic retinopathy) [65], and Alleye™ (detects neovascular AMD and distinguishes between dry and wet AMD) [66] are US Food and Drug Administration (FDA) approved platforms for monitoring patients. Integration of these applications within existing monitoring programmes could help in substantially reducing carbon footprints.

Artificial Intelligence

The application of artificial intelligence (AI) approaches such as deep learning (DL) to ophthalmic imaging, including digital fundus photographs and visual fields, has been reported to achieve high accuracy in automating the screening and diagnosis of common vision-threatening diseases including diabetic retinopathy [67,68,69], glaucoma [70,71,72], AMD [73, 74], and retinopathy of prematurity (ROP) [75]. A DL algorithm system developed by Abramoff et al., IDx-DR,

has received FDA approval since 2018 for the detection of more-than-mild diabetic retinopathy in adults without physician-assisted interpretation [76]. Combining the use of 'imaging hubs' and AI technology would therefore be as a valuable adjunct in the mission towards improving sustainability in ophthalmology.

Promoting Environmental Sustainability

The International Agency for the Prevention of Blindness (IAPB) declared a climate emergency on the 22 April 2021 and released key resources that feature how the 'Eye Health Sector' can contribute to environmental sustainability. The key areas for actions which organisations can focus on to promote sustainability include acknowledging the climate emergency, the development of local and international frameworks, setting targets for carbon emission reduction, raising awareness, development of sustainable procurement policies whilst working with suppliers, reducing use of energy and water, minimising travel, reducing waste generated and finally implementing environmental sustainability in education [8, 77,78,79].

Both the General Medical Council (GMC) and Nursing and Midwifery Council (NMC) in the UK now require newly qualified doctors and nurses to be informed about sustainable healthcare and apply its principles and methods to their clinical practice [80, 81]. To promote this, medical

schools in the UK have already begun to incorporate lectures and student-selected modules on sustainable healthcare into their curriculum [82]. Optical governing bodies including Association of Optometrists (AOP), Association of British Dispensing Opticians (ABDO), and General Optical Council (GOC) are also prioritising sustainability, evident by the organisation of the forthcoming 'SEE Summit' [83].

The Centre for Sustainable Healthcare has described five principles for practising sustainable healthcare. The principles comprise prevention, patient empowerment (health promotion and education), lean pathways (telecommunication), low-carbon alternatives (e.g. avoiding use of greenhouse gases such as nitrogen oxide), and operational resource use (e.g. reducing packaging and water consumption) [84]. These could be integrated into postgraduate training and education for doctors and allied health practitioners, in the form of online short courses and induction modules [85], further supporting the drive towards sustainable healthcare.

Conclusion

The use of disposable equipment and instrumentation has been increasing proportional to the increase in demand on ophthalmic services and the increase in emphasis on safety, especially in developed countries. There is action we could take to reduce the environmental impact generated from our services whilst maintaining the highest standards of safety and care to our patients. It is vital for clinicians, healthcare professionals and their managerial teams, manufacturers and pharmaceutical companies to realise the cumulative waste generated and the harmful impact they cause the environment, public health, long-term morbidity and the life of our future generations.

References:

1. Watts N, Amann M, Arnell N, et al. The 2019 report of The Lancet Countdown on health and climate change: ensuring that the health of a child born today is not defined by a changing climate. *Lancet*. 2019;394(10211):1836–78.
2. IPCC. Global warming of 1.5 °C. An IPCC Special Report on the impacts of global warming of 1.5 °C above pre-industrial levels and related global greenhouse gas emission pathways, in the context of strengthening the global response to the threat of climate change, sustainable development, and efforts to eradicate poverty. Geneva: World Meteorological Organization; 2019.
3. McMichael AJ, Haines JA, Slooff R, et al. Climate change and human health: an assessment/prepared by a Task Group on behalf of the World Health Organization, the World Meteorological Association and the United Nations Environment Programme. Geneva: World Health Organisation; 1996.
4. McMichael T. Public health in Australia: a personal reflection. *Aust J Public Health*. 2010;17(4):295–6.
5. Watts N, Amann M, Arnell N, et al. The 2020 report of The Lancet Countdown on health and climate change: responding to converging crises. *Lancet*. 2021;397(10269):129–70.
6. The Royal College of Ophthalmologists. Sustainability in ophthalmology. https://www.rcophth.ac.uk/wp-content/uploads/2014/11/2013_PROF_222_Sustainability-in-Ophthalmology-May-2013.pdf. Accessed Jul 4, 2021.
7. Yu M, Khan I. Climate action in eyecare. www.eyenews.uk.com. Accessed Jul 21, 2021.
8. King's College London. Higher air pollution days trigger cardiac arrests and hospitalisations. <https://www.kcl.ac.uk/news/higher-air-pollution-days-trigger-cardiac-arrests-and-hospitalisations>. Accessed Aug 5, 2021.
9. Landrigan PJ, Fuller R, Acosta NJR, et al. The Lancet Commission on pollution and health. *Lancet*. 2018;391(10119):462–512.
10. Costello A, Abbas M, Allen A, et al. Managing the health effects of climate change. *Lancet*. 2009;373(9676):1693–733.
11. Pradyumna A, Guinto R. Climate change and health. *Lancet*. 2016;387(10017):430–1.
12. Lenzen M, Malik A, Li M, et al. The environmental footprint of health care: a global assessment. *Lancet Planetary Health*. 2020;4(7):e271–9.
13. Holden E, Linnerud K, Banister D. Sustainable development: our common future revisited. *Glob Environ Chang*. 2014;26:130–9.
14. WCED. Our common future. World commission on environment and development. Oxford: Oxford University Press; 1987.
15. Eckelman MJ, Sherman J. Environmental impacts of the U.S. health care system and effects on public health. *PLoS ONE*. 2016;11(6): e0157014.
16. Total healthcare expenditure in the United Kingdom from 1997 to 2019. 2021. <https://www.statista.com/statistics/317669/healthcare-expenditure-in-the-united-kingdom/>. Accessed Sep 26, 2021.
17. National Health Service England, Public Health England. Reducing the use of natural resources in health and social care. London: National Health Service England; 2018.
18. National Health Service England. Greener NHS campaign to tackle climate 'health emergency'. <https://www.england.nhs.uk/2020/01/greener-nhs-campaign-to-tackle-climate-healthemergency/>. Accessed Jul 4, 2021.
19. The Royal College of Ophthalmologists. National Ophthalmology Database Audit. <https://www.nodaudit.org.uk/u/docs/20/urxqilwxmw/NOD%20Audit%20Annual%20Report%202019.pdf>. Accessed Jul 7, 2021.
20. Morris DS, Wright T, Somner JEA, Connor A. The carbon footprint of cataract surgery. *Eye*. 2013;27(4):495–501.
21. Somner J, Scott K, Morris D, Gaskell A, Shepherd I. Ophthalmology carbon footprint: something to be considered? *J Cataract Refract Surg*. 2009;35(1):202–3.
22. Venkatesh R, van Landingham SW, Khodifad AM, et al. Carbon footprint and cost-effectiveness of cataract surgery. *Curr Opin Ophthalmol*. 2016;27(1):82–8.
23. Muralikrishnan R, Venkatesh R, Prajna NV, Frick KD. Economic cost of cataract surgery procedures in an established eye care centre in Southern India. *Ophthalmic Epidemiol*. 2004;11(5):369–80.

24. Gogate P, Deshpande M, Nirmalan PK. Why do phacoemulsification? Manual small-incision cataract surgery is almost as effective, but less expensive. *Ophthalmology*. 2007;114(5):965–8.
25. Ruit S, Tabin G, Chang D, et al. A prospective randomized clinical trial of phacoemulsification vs manual sutureless small-incision extracapsular cataract surgery in Nepal. *Am J Ophthalmol*. 2007;143(1):32–38.e2.
26. Amitava A, Khan A, Rizvi SA, Siddiqui Z, Kumari N, Grover S. Cost-effectiveness analysis should continually assess competing health care options especially in high volume environments like cataract surgery. *Indian J Ophthalmol*. 2015;63(6):496.
27. Goel H, Wemyss TA, Harris T, et al. Improving productivity, costs and environmental impact in International Eye Health Services: using the 'Eyeefficiency' cataract surgical services auditing tool to assess the value of cataract surgical services. *BMJ Open Ophthalmol*. 2021;6(1): e000642.
28. Thiel CL, Schehlein E, Ravilla T, et al. Cataract surgery and environmental sustainability: waste and lifecycle assessment of phacoemulsification at a private healthcare facility. *J Cataract Refract Surg*. 2017;43(11):1391–8.
29. Chang DF. Needless waste and the sustainability of cataract surgery. *Ophthalmology*. 2020;127(12):1600–2.
30. Guetter CR, Williams BJ, Slama E, et al. Greening the operating room. *Am J Surg*. 2018;216(4):683–8.
31. Brown C, Meals C. Four ways plastic surgeons can fight climate change. *Plast Reconstr Surg*. 2020;8(7): e2961.
32. Wyssusek KH, Keys MT, van Zundert AAJ. Operating room greening initiatives—the old, the new, and the way forward: a narrative review. *Waste Manag Res*. 2019;37(1):3–19.
33. Kagoma Y, Stall N, Rubinstein E, Naudie D. People, planet and profits: the case for greening operating rooms. *CMAJ*. 2012;184(17):1905–11.
34. Practice Greenhealth. The business case for greening the OR. https://www.c4sphg.org/HCW1_Presentations/GOR_FullSet_Guidance%20Docs_Web_042711.pdf. Accessed Jul 8, 2021.
35. Bartl A. Moving from recycling to waste prevention: a review of barriers and enablers. *Waste Manag Res*. 2014;32(9_suppl):3–18.
36. Kwakye G. Green surgical practices for health care. *Arch Surg*. 2011;146(2):131.
37. Armitage WJ, Tullo AB, Ironside JW. Risk of Creutzfeldt-Jakob disease transmission by ocular surgery and tissue transplantation. *Eye*. 2009;23(10): 1926–30.
38. Southorn T, Norrish A, Gardner K, Baxandall R. Reducing the carbon footprint of the operating theatre: a multicentre quality improvement report. *J Perioper Pract*. 2013;23(6):144–6.
39. McGain F, White S, Mossenson S, Kayak E, Story D. A survey of anesthesiologists' views of operating room recycling. *Anesth Analg*. 2012;114(5): 1049–54.
40. McGain F, Jarosz KM, Nguyen MNHH, Bates S, O'Shea CJ. Auditing operating room recycling: a management case report. *A A Case Rep*. 2015;5(3):47–50.
41. The Royal College of Ophthalmologists. New RCOphth Workforce Census illustrates the severe shortage of eye doctors in the UK. <https://www.rcophth.ac.uk/2019/01/new-rcophth-workforce-census-illustrates-the-severe-shortage-of-eye-doctors-in-the-uk/>. Accessed Jul 14, 2021.
42. NHS Digital. Hospital Outpatient Activity, 2017–18. <https://digital.nhs.uk/data-and-information/publications/statistical/hospital-outpatient-activity/2017-18>. Accessed Jul 14, 2021.
43. MacEwen C, Davis A, Chang L. Ophthalmology GIRFT Programme National Specialty Report. <https://gettingitrightfirsttime.co.uk/wp-content/uploads/2019/12/OphthalmologyReportGIRFT19P-FINAL.pdf>. Accessed Jul 14, 2021.
44. Ratnarajan G, Newsom W, Vernon SA, et al. The effectiveness of schemes that refine referrals between primary and secondary care—the UK experience with glaucoma referrals: the Health Innovation and Education Cluster (HIEC) Glaucoma Pathways Project. *BMJ Open*. 2013;3(7): e002715.
45. Shah S, Murdoch IE. NICE—impact on glaucoma case detection. *Ophthalmic Physiol Opt*. 2011;31(4):339–42.
46. Burr JM, Mowatt G, Hernández R, et al. The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and economic evaluation. *Health Technol Assess*. 2007. <https://doi.org/10.3310/hta11410>.
47. Bowling B, Chen SDM, Salmon JF. Outcomes of referrals by community optometrists to a hospital glaucoma service. *Br J Ophthalmol*. 2005;89:1102–4.
48. Vincent SJ, Vincent RA, Shields D, Lee GA. Comparison of intraocular pressure measurement between rebound, non-contact and Goldmann applanation tonometry in treated glaucoma patients. *Clin Exp Ophthalmol*. 2012;40(4):e163–70.
49. Forbes H, Sutton M, Edgar DF, et al. Impact of the Manchester Glaucoma Enhanced Referral Scheme on NHS costs. *BMJ Open Ophthalmol*. 2019;4(1):e000278.
50. Gunn PJG, Marks JR, Konstantakopoulou E, et al. Clinical effectiveness of the Manchester Glaucoma Enhanced Referral Scheme. *Br J Ophthalmol*. 2019;103(8):1066–71.
51. Tomson C. Reducing the carbon footprint of hospital-based care. *Future Hosp J*. 2015;2(1):57–62.
52. Yellowlees PM, Chorba K, Burke Parish M, Wynn-Jones H, Nafiz N. Telemedicine can make healthcare greener. *Telemed e-Health*. 2010;16(2):229–32.
53. NHS Scotland. 'Teleophthalmology Activation Guide'. 2020. <http://communityeyecare.scot.nhs.uk/telemedicine>. Accessed Aug 10, 2021.
54. Purohit A, Smith J, Hibble A. Does telemedicine reduce the carbon footprint of healthcare? A systematic review. *Future Healthc J*. 2021;8(1):e85–91.
55. Sharafeldin N, Kawaguchi A, Sundaram A, et al. Review of economic evaluations of teleophthalmology as a screening strategy for chronic eye disease in adults. *Br J Ophthalmol*. 2018;102(11):1485–91.
56. Bartnik SE, Copeland SP, Aicken AJ, Turner AW. Optometry-facilitated teleophthalmology: an audit of the first year in Western Australia. *Clin Exp Optom*. 2018;101(5):700–3.
57. Liu Y, Torres Diaz A, Benkert R. Scaling up teleophthalmology for diabetic eye screening: opportunities for widespread implementation in the USA. *Curr Diab Rep*. 2019;19(9):74.
58. Patel S, Hamdan S, Donahue S. Optimising telemedicine in ophthalmology during the COVID-19 pandemic. *J Telemed Telecare*. 2020. <https://doi.org/10.1177/1357633X20949796>.
59. Ittoop SM, SooHoo JR, Seibold LK, Mansouri K, Kahook MY. Systematic review of current devices for 24-h intraocular pressure monitoring. *Adv Ther*. 2016;33(10):1679–90.
60. Anderson AJ, Bedgood PA, George Kong YX, Martin KR, Vingrys AJ. Can home monitoring allow earlier detection of rapid visual field progression in glaucoma? *Ophthalmology*. 2017;124(12):1735–42.
61. Amirsolaimani B, Peyman G, Schwiegerling J, Bablumyan A, Peyghambarian N. A new low-cost, compact, auto-phoropter for refractive assessment in developing countries. *Sci Rep*. 2017. <https://doi.org/10.1038/s41598-017-14507-5>.
62. Ciuffreda KJ, Rosenfield M. Evaluation of the SVOne: a handheld, smartphone-based autorefractor. *Optom Vis Sci*. 2015;92(12):1133–9.
63. Wisse RPL, Muijzer MB, Cassano F, Godefrooij DA, Prevoo YFDM, Soeters N. Validation of an independent web-based tool for measuring visual acuity and refractive error (the manifest versus online refractive evaluation trial): prospective Open-Label Noninferiority Clinical Trial. *J Med Internet Res*. 2019;21(11): e14808.
64. Chew EY, Clemons TE, Harrington M, et al. AREDS2-Home Study Research Group. Effectiveness of different monitoring modalities in the detection of neovascular age-related macular degeneration: the Home Study, Report Number 3. *Retina*. 2016;36(8):1542–7.
65. Micheletti JM, Hendrick AM, Khan FN, Ziemer DC, Pasquel FJ. Current and next generation portable screening devices for diabetic retinopathy. *J Diabetes Sci Technol*. 2016;10:295–300.
66. Schmid MK, Thiel MA, Lienhard K, Schlingemann RO, Faes L, Bachmann LM. Reliability and diagnostic performance of a novel mobile app for hyperacuity self-monitoring in patients with age-related macular degeneration. *Eye*. 2019;33:1584–9.
67. Abramoff MD, Lou YY, Erginay A, et al. Improved automated detection of diabetic retinopathy on a publicly available dataset through integration of deep learning. *Investig Ophthalmol Vis Sci*. 2016;57:5200–6.
68. Gulshan V, Peng L, Coram M, et al. Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. *JAMA*. 2016;316:2402–10.
69. Raumviboonsuk P, Krause J, Chotcomwongse P, et al. Deep learning versus human graders for classifying diabetic retinopathy severity in a nationwide screening program. *NPJ Digit Med*. 2019;2:25.
70. Liu H, Li L, Wormstone IM, et al. Development and validation of a deep learning system to detect glaucomatous optic neuropathy using fundus photographs. *JAMA Ophthalmol*. 2019;137(12):1353–60.
71. Li F, Wang Z, Qu GX, et al. Automatic differentiation of glaucoma visual field from non-glaucoma visual field using deep convolutional neural network. *BMC Med Imag*. 2018;18:35.

72. Masumoto H, Tabuchi H, Nakakura S, Ishitobi N, Miki M, Enno H. Deep-learning classifier with an ultrawide-field scanning laser ophthalmoscope detects glaucoma visual field severity. *J Glaucoma*. 2018;27:647–52.
73. Grassmann F, Mengelkamp J, Brandl C, et al. A deep learning algorithm for prediction of age-related eye disease study severity scale for age-related macular degeneration from color fundus photography. *Ophthalmology*. 2018;125:1410–20.
74. Burlina PM, Joshi N, Pekala M, Pacheco KD, Freund DE, Bressler NM. Automated grading of age-related macular degeneration from color fundus images using deep convolutional neural networks. *JAMA Ophthalmol*. 2017;135:1170–6.
75. Brown JM, Campbell JP, Beers A, et al. Imaging and informatics in retinopathy of prematurity (i-ROP) research consortium. Automated diagnosis of plus disease in retinopathy of prematurity using deep Convolutional Neural Networks. *JAMA Ophthalmol*. 2018;136(7):803–10.
76. Abramoff MD, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. *NPJ Digit Med*. 2018;1:39.
77. Global Sight Alliance declares Climate Emergency and Calls for Urgent Action. IAPB, 2021. <https://www.iapb.org/news/global-sight-alliance-declares-climate-emergencyand-calls-for-urgent-action/>. Accessed Aug 10, 2021.
78. Call to Action for Environmentally Sustainable Practices in the Eye Health Sector. IAPB, 2021. https://www.iapb.org/wp-content/uploads/2021/04/IAPB_CAWG_CTAdocument.pdf. Accessed Aug 10, 2021.
79. Guide for Environmentally Sustainable Practices in the Eye Health Sector. IAPB, 2021. https://www.iapb.org/wp-content/uploads/2021/04/IAPB_CAWG_GUIDE-document.pdf. Accessed Aug 10, 2021.
80. General Medical Council. Outcomes for graduates. 2018. www.gmc-uk.org/education/standards-guidance-and-curricula/standards-and-outcomes/outcomes-for-graduates. Accessed Aug 10, 2021.
81. Nursing and Midwifery Council. Standards of Proficiency for Midwives. 2021. <https://www.nmc.org.uk/globalassets/sitedocuments/standards/standards-of-proficiency-for-midwives.pdf>. Accessed Aug 10, 2021.
82. Tun MS. Fulfilling a new obligation: teaching and learning of sustainable healthcare in the medical education curriculum. *Med Teach*. 2019;41:1168–77.
83. Association of British Dispensing Opticians. SEE Summit. 2021. <https://www.abdo.org.uk/dashboard/see-hub/see-hub-2/>. Accessed Aug 10, 2021.
84. Mortimer F. The sustainable physician. *Clin Med (Lond)*. 2010;10(2):110–1.
85. Gandhi V, Al-Hadithy N, Göpfert A, Knight K, van Hove M, Hockey P. Integrating sustainability into postgraduate medical education. *Future Healthcare J*. 2020;7(2):102–4.

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What's in the news?

High-Intensity Use of Smartphone Can Significantly Increase the Diagnostic Rate and Severity of Dry Eye



The purpose of this study was to investigate the effects of high-intensity use of smartphones on ocular surface homeostasis and to explore whether high-intensity use of handheld digital devices can cause false increase of dry eye diagnostic rate.

In this prospective self-control study, 60 subjects (120 eyes) were recruited and asked to read on smartphones provided by the same manufacturer for two consecutive hours. This study was conducted during 8:00 - 10:00 AM to eliminate the influence of digital equipment used the previous day. Ophthalmological examinations [non-invasive tear breakup time (NIBUT), fluorescein breakup time (FBUT), Schirmer I test, corneal fluorescein staining (CFS), bulbar conjunctival redness and meibomian gland (MG) assessment] and a questionnaire survey were conducted

before and after the reading test. Based on the collected data, the changes in ocular surface damage and subjective symptoms of the subjects were evaluated, and the differences in the diagnostic rate of dry eye before and after high-intensity use of smartphones were compared.

The diagnostic rate of dry eye was sharply increased (61.7% vs. 74.2%). The severity of dry eye also changed significantly, and the moderate and severe degree increased after reading (10% vs. 15%; 5% vs. 10.8%). The aggravated severity subjects had lower MG expressibility and more evident bulbar conjunctival redness compared to the non-aggravated severity subjects. After 2 h of continuous reading, NIBUT-First, NIBUT-Average and FBUT-Average were significantly decreased, while the proportion of BUT ≤ 5 s increased significantly.

Non-invasive keratograph tear meniscus height (NIKTMH) decreased significantly compared to the baseline level, while the proportion of NIKTMH < 0.20 mm increased significantly. No significant difference was observed in the Schirmer I test and CFS score between the two groups. Compared to the baseline, evident aggravation was observed in bulbar conjunctival redness. The Ocular Surface Disease Index (OSDI) was significantly higher than the baseline after the reading test.

The authors of this study concluded that diagnostic indicators related to dry eye are rapidly deteriorating after high-intensity smartphone use, especially those with lower MG expressibility and ocular redness. High-intensity smartphone use can increase the false positive rate of dry eye diagnosis by disturbing ocular surface homeostasis.

Authors: Chunyang Wang, Kelan Yuan, Yujie Mou, Yaying Wu, Xin Wang, Renjian Hu, Jinjin Min, Xiaodan Huang, Xiuming Jin

Publication: *Front Med (Lausanne)*. 2022 Apr 26;9:829271. doi: 10.3389/fmed.2022.829271.eCollection 2022.



Topics to Include:

TFOS Symposia: The Best in Dry Eye Disease!

Round Table 1: My approach to dry eye patients?

Innovation Part 1

Ocular motility, psychological impact in dry eye: new nexus?
 Vivior – Analyse our patient’s screen time
 Tear film optics
 Corneal nerves and Artificial Intelligence

Innovation Part 2

Biologics: “Corneal innervation”
 Biologics: Beyond Homeostasis
 Biologics: Tear film regeneration
 Biologics: Inlays (KeraNatural and Allotex)
 Biologics: Insulin eye drops
 Round Table 2: Artificial intelligence in dry eye disease

Ocular Surface Reconstruction:

Biological Tissues and components, and synthetic substrates for conjunctival cell transplantation.
 Conjunctival extracellular matrix, related disorders and development of substrates for conjunctival restoration

Keynote Lecture:

Molecules and hormones in Ocular Surface Disease

Ocular Surface Updates 1

ABCs of Conjunctivitis: Revisited!
 Diagnostic armamentarium of infectious keratitis
 “Urgent unmet needs in the care of bacterial keratitis: An evidence-based synthesis”
 “Fungal keratitis: A review of clinical presentations, treatment strategies and outcomes - The UK Outcomes “
 Tackling CLAK using a population health approach
 Contact lenses for drug delivery
 Round Table 3: Trends in managing infectious keratitis

Ocular Surface Updates 2

Can we stop permanent corneal deformation?
 Ocular Surface Disease in children: Early Intervention
 Cosmetics and DED/OSD
 Ocular rosacea

MCLOSA Seminar

Speakers to include:

Mr. Arthur Cummings
 Prof. Rohit Shetty
 Mr. Samer Hamada
 Dr. Damien Gatinel
 Prof. Christopher Liu
 Prof. Jennifer Craig
 Mr. Mohamed Elalfy
 Miss. Artemis Matsou
 Dr. Keyur Patel

Prof. James Wolffsohn
 Mr. Sheraz Daya
 Mr. David Lockington
 Prof. Giulio Ferrari
 Dr. Yan Ning Neo
 Mr. Damian Lake
 Mr. Sajjad Ahmad
 Dr. Pooja Khamar
 Miss. Andrena McElvanney

Prof. Michael Mrochen
 Prof. Darlene Dartt
 Dr. Catherine Jackson
 Mr. Ankur Barua
 Dr. Marguerite McDonald
 Miss. Rachna Murthy
 Prof. Jonathan Roos
 Mr. Nick Dash
 Miss. Nikolina Budimlija

Dry eye Masterclass 24 June 2022

Course Directors: Mr. Arthur Cummings, Prof. Rohit Shetty,

Mr Samer Hamada

Sample of Content:

DED – The basics

- What is new in DEWS II?
- Understanding the DED pathogenesis
- Classification of DED
- Perfecting patient history and role of questionnaire based assessment in your DED clinic
- Importance of external and systemic examination
- Optimising slit-lamp examination
- MGD grading and anterior blepharitis diagnosis
- Setting up a dry eye clinic
- Public Awareness (TFOS Current Project)

Clinical & Diagnostics

- Dry eye diagnostics at your fingertips- from basic to advanced and current diagnostics
- When should I plan a systemic investigation and connective disorder work-up?
- Refractive surgery and DED
- Cataract surgery and DED

- Cosmetics (surgical and non-surgical) and DED
- Masquerades including Demodex
- Pain without stain

Advanced Management of DED

- Stepwise management of DED- from conventional to advanced therapeutics.
- Dry eye in KC
- DED impact on the optical quality
- Management of severe aqueous deficient dry eye- punctal plugs, autologous serum
- Newer procedural therapies for DED

Workshops

- Diagnostics including invasive and non-invasive like NITBUT, TMH,
- Tear Osmolarity, and others
- MGD Assessment, Meibography, LLT
- MGD Management including eyelashes and lid margin, devices like Intense Pulsed Light, Miboflo, Punctal plugs
- Case-based customisation of DED management- One fit doesn’t suit all!

The 105th Oxford Ophthalmological Congress

Returns to an in-person meeting in 2022



Monday 4th July to Wednesday 6th July 2022

The Doyne Lecturer

Mr. Demis Hassabis
CBE FRS FREng FRSA

The Master's symposium

Chaired by Sir Professor Peng T. Khaw
Discovery and Delivery Glaucoma

The OOC programme also includes:

- Uveitis: there is more to life than steroids
- "Once upon a time..." Tales from the land of Paediatric Ophthalmology
- Genetics changing ophthalmology
- Cataract & Refractive Surgery
- Where do we go from here?
- The Cases

The social programme will be held at St. Annes & Worcester College.

The industry exhibition will be held at the Randolph Hotel.

We look forward to seeing you there.
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TREAT

DRY EYE



THEALOZ DUO

3% Trehalose,
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Effective prevention for moderate-severe Dry Eye patients³

Unique combination delivering significant OSDI improvements in moderate-severe Dry Eye patients³

PREVENT

USED TOGETHER, SOFTACORT® AND THEALOZ® DUO IMPROVE OUTCOMES IN DRY EYE DISEASE^{2,3}

Softacort® 3.35mg/ml eye drops, solution in single-dose container. **Abbreviated Prescribing.** Contains: Hydrocortisone sodium phosphate. **Information:** Please refer to Summary of Product Characteristics before prescribing. **Presentation:** 3 sachets each containing 10 single-dose units of 0.1ml. A single-dose container contains enough to treat both eyes. **Indications(s):** Treatment of mild non-infectious allergic or inflammatory conjunctival disease. **Posology and method of administration:** Adults & the Elderly: 2 drops 2-4 times per day in the affected eye. Treatment will generally vary from a few days up to a maximum of 14 days. Consider gradual tapering off down to one drop every other day to avoid relapse. Children: safety and efficacy is not established. **Contraindications:** Hypersensitivity to active substance or excipients. Ocular hypertension including that caused by known glucocorticosteroids. Herpes simplex and other corneal viral infections at acute stage of ulceration, unless combined with specific therapeutic agents. Conjunctivitis with ulcerative keratitis even at the initial stage. Ocular tuberculosis, ocular mycosis, acute ocular purulent infection, purulent conjunctivitis, and purulent blepharitis, stye and herpes infection that may be masked or aggravated by anti-inflammatory drugs. **Warnings and precautions:** Red eye: Do not prescribe for undiagnosed red eye. Ocular hypertension & cataracts: Monitor patients at regular intervals during treatment - prolonged use of corticosteroids has been shown to cause ocular hypertension especially for patients with previous IOP increase induced by steroids, and also cataract formation especially in children and the elderly. In children the ocular hypertensive response can happen more often, frequently and severely than in adults. Immunosuppression: Use of corticosteroids can result in opportunistic ocular infections due to delay or suppression or healing delay, and to the masking of symptoms. Viral keratitis: Not recommended but may be used if required only with a combined antiviral treatment and under close supervision. Perforations and thinning of cornea/sclera: Thinning of cornea and sclera (caused by diseases) may increase risk of perforations with use of topical steroids. Suspect a fungal infection with corneal ulcerations where a steroid has been used for a long time. Remove contact lenses when using Softacort. With blurred vision or other visual disturbances, consider referring patients for evaluating possible causes which may include cataract, glaucoma or rare diseases like central serous chorioretinopathy (CSR). Softacort contains phosphates. Children: Long-term continuous corticosteroid therapy may produce adrenal suppression. **Pregnancy:** Not recommended unless clearly necessary. **Lactation:** Risk to newborns/infants cannot be excluded. It is unknown if Softacort is excreted in human milk. **Driving & using machines:** Temporary blurred vision or other visual disturbances may affect ability to drive or use machines. Wait until vision clears before driving or operating machinery. **Undesirable effects:** Mild and transient burning and stinging immediately after instillation. Unseen with hydrocortisone, but have been observed with other topical corticosteroids: allergic and hypersensitivity reactions, delayed wound healing, posterior capsular cataract, opportunistic infections, herpes simplex infection, fungal infection, glaucoma, mydriasis, ptosis, corticosteroid induced uveitis, changes in corneal thickness, crystalline keratopathy, blurred vision. Very rarely, corneal calcification in patients with significantly damaged corneas. Prolonged use of corticosteroids has shown to cause ocular hypertension, especially with pre-existing or family history of increased IOP, and cataract formation. Children / elderly are more susceptible to IOP rise. Diabetics are more prone to sub capsular cataracts following topical steroids. In diseases causing thinning of the cornea, topical steroids could lead to perforation. **Overdose:** Rinse with sterile water. Discontinue treatment where prolonged overdose causes ocular hypertension. Symptoms from accidental ingestion are unknown, however, consider gastric lavage or emesis. **Storage:** Do not store above 25°C. Keep the single-dose containers in the sachet, in order to protect from light. Discard any unused contents immediately after administration. **Legal category:** Prescription Only Medicine (POM). **Basic NHS Price:** £10.99 for a pack of 30 single-dose containers. **PL No:** 20162/0024. **Sale and Supply:** Théa Pharmaceuticals Ltd, ICS Innovation Way, Keele University Science & Innovation Park, Keele, Newcastle Under Lyme, ST5 5NT **Date of preparation:** 05/10/2018.

REPORT ADVERSE EVENTS TO THÉA PHARMACEUTICALS LIMITED AND WWW.MHRA.GOV.UK/YELLOWCARD OR SEARCH FOR MHRA YELLOW CARD IN THE GOOGLE PLAY OR APPLE APP STORE.

References: 1. Softacort Summary of Product Characteristics. 2. Kallab M et al, Adv Ther. 2020;37:329-341. 3. Chiambaretta F et al. Eur J Ophthalmol 2017; 27(1):1-9.

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Théa
let's open our eyes