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December 2018

ADVANCING THERAPEUTIC OPTOMETRY

Dry eye
Diagnosis, management and therapy

Blepharitis
Dedicated eyelid cleanser vs baby shampoo

Beneath the surface
Systemic conditions related to DED

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NOVATEARS®

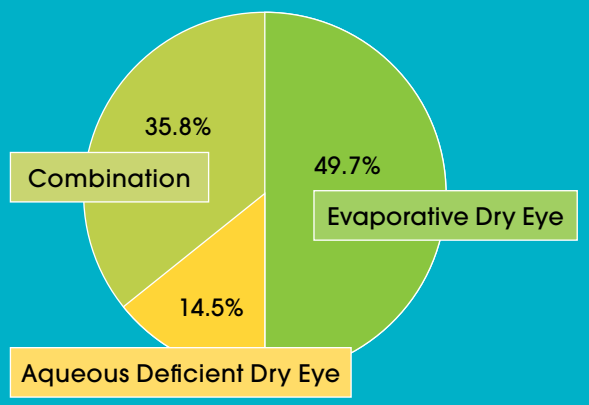
for Evaporative Dry Eye & Meibomian Gland Dysfunction

Evaporative Dry Eye is more common than previously thought

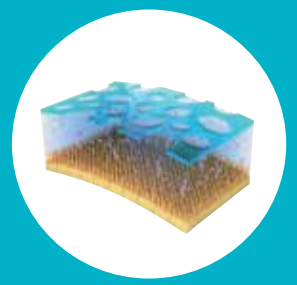
Aqueous Deficient Dry Eye Disease is caused by a lack of aqueous tear secretion which results in a concentrated and unstable tear film.

Evaporative Dry Eye Disease is caused by an increase in tear evaporation due to an abnormal tear film lipid layer or Meibomian Gland Dysfunction (MGD).

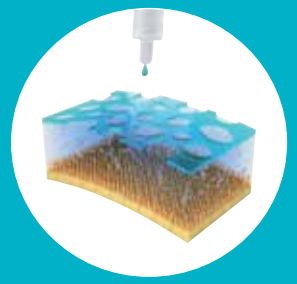
More than 85% of patients suffer from some form of Evaporative Dry Eye.[3]



Utilises patented EyeSol® technology to provide an innovative water-free mode of action



Lipid layer deficiency



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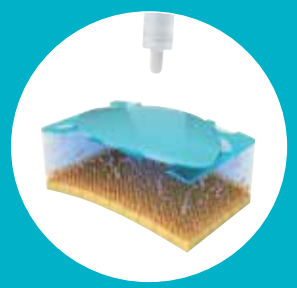
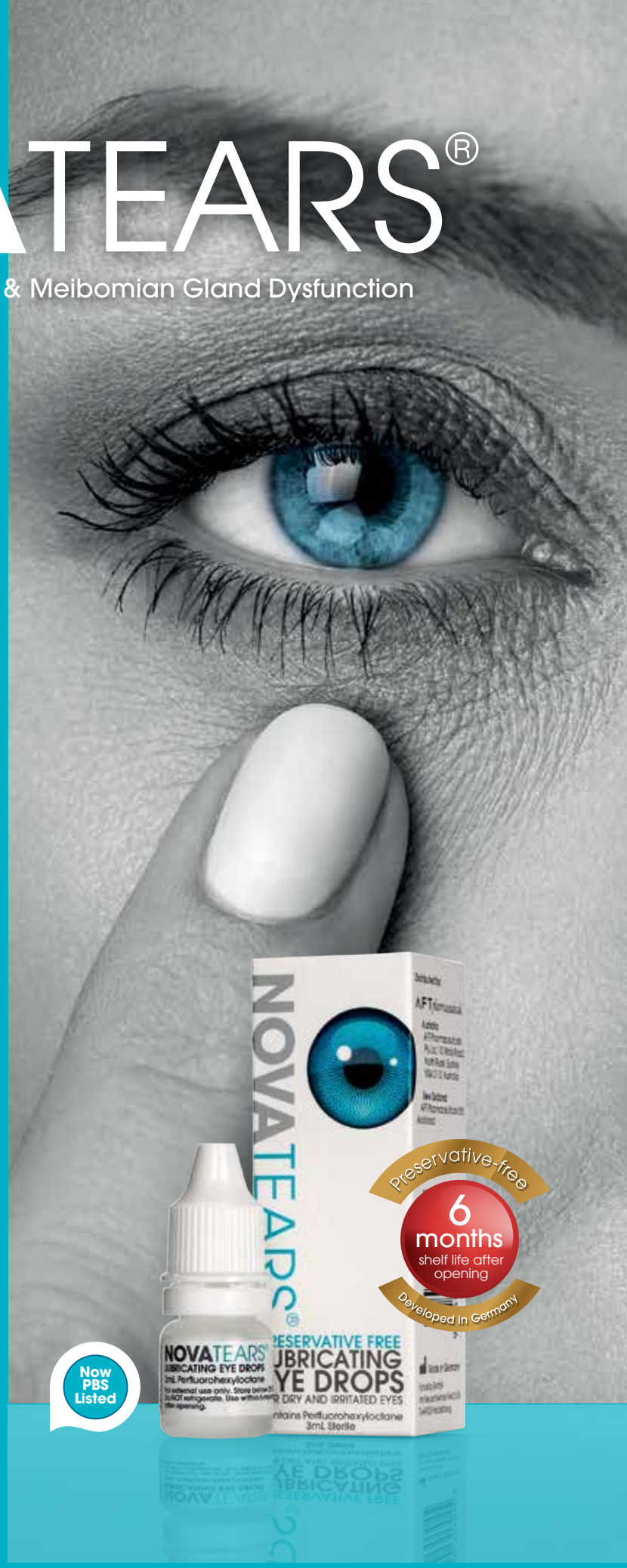


Spreads quickly and easily on the lipid layer

NovaTears® helps address a significant need by providing a specific therapeutic option for patients with Evaporative Dry Eye Disease.



STREAMLINED AUTHORITY CODE 6172

PBS Information: Authority Required (STREAMLINED): Severe dry eye syndrome in patients who are sensitive to preservatives in multi-dose eye drops.

References: 1. Steven, Philipp, et al. "Semifluorinated Alkane Eye Drops for Treatment of Dry Eye Disease – A Prospective, Multicenter Noninterventional Study." Journal of Ocular Pharmacology and Therapeutics 31 (8), 498-503 (2015). 2. Steven, Philipp, et al. "Semifluorinated Alkane Eye Drops for Treatment of Dry Eye Disease Due to Meibomian Gland Disease." Journal of Ocular Pharmacology and Therapeutics. 33(9), 678-685 (2017). Sponsored by Novaliq GmbH. 3. Lemp, M.A., Crews, L.A., Bron, A.J., Foulks, G.N. and Sullivan, B.D., 2012. Distribution of aqueous-deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study. Cornea, 31(5), pp.472-478. NovaTears® Eye Drops (Perfluorohexyloctane 100%, 3mL) are for the lubrication and relief of dry and irritated eyes. Do not use NovaTears® with contact lenses. If using any other eye medication, allow at least 15 minutes between using the other product and applying NovaTears®. NovaTears® should not be used in children under 18 years. NovaTears® should not be used while pregnant or breastfeeding. AFT Pharmaceuticals Pty Ltd, Sydney. ABN 29105636413.

AFT pharmaceuticals

Working to improve your health

December 2018 Anterior eye

In the 10 years since its founding, *Pharma* has been optometry's steadfast advocate for the use of ocular therapeutics.

In recent years, the growing number of patients with complaints about dry eye has encouraged optometric professionals to rapidly expand their knowledge of the condition. This, in turn, has yielded a better understanding of the myriad causes of dry eye disease as well as new tools for detection and therapies for treatment.

Still, we are at the beginning of a long trek. In an attempt to identify opportunities for improvement, in this issue, we discuss the complex topic of dry eye diagnosis and treatment, offering insight and practical recommendations on how to detect and manage the dry eye patients in your practice.

We also take this opportunity to advise of changes to the Editorial team.

Associate Professor Mark Roth BSc (Pharm) BAppSc (Optom) PGCertOcTher NEWENCO FAAO OAM has resigned as Clinical Editor. In the 10 years he held the position, Mark made an outstanding contribution to *Pharma*. Former Optometry Australia CEO Joe Chakman came up with the concept and approached Mark to take the helm of *Pharma*, and the publication's enduring success is thanks in no small part to his commitment to ocular therapeutics and his dedication to the profession of optometry. Optometry Australia takes this opportunity to warmly thank him for his contribution to *Pharma*.

We would like to introduce our new Clinical Editor, Kerryn Hart. Kerryn is Optometry Australia's Policy and Standards Advisor and is a Teaching Scholar at Deakin University's School of Medicine (Optometry). She holds a Master's Degree in Public Health, a Graduate Certificate in Ocular Therapeutics, a Postgraduate Diploma in Advanced Clinical Optometry and a Bachelor of Optometry.

This issue of Pharma offers 6 (4T) CPD points.

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Contact lens prescribing trends 2018

The 19th annual survey by Efron, Morgan and Woods

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The 19th annual survey of Australian contact lens prescribing was conducted between January and April, 2018. The same format as in previous years was employed. An email was sent to all members of Optometry Australia with a link to a questionnaire, and a request that this be downloaded, printed and completed to provide details of the first ten patients fitted with contact lenses after receipt of the questionnaire. The survey was specifically designed to be straightforward for optometrists to complete while capturing key information about their patients.

Practitioners were asked general questions about themselves. For each contact lens fitting, they were requested to complete the following details: date of fitting, new fitting or refitting, age and sex of patient, lens material, lens design, frequency of replacement, times per week of wear, modality (daily or extended wear) and care system. Practitioners were asked to return the photographed or scanned copies of the questionnaire by email.

Completed questionnaires relating to 381 contact lens fits were returned, which provides a sound basis for a meaningful analysis. Each fitting was given an annualised weighting based on the number of lenses fitted during the survey period and the time taken to complete the fits. This means that data generated by practitioners with a higher frequency of fitting contact lenses were afforded a higher weighting than those with a lower frequency of fits.

The discussion below will concentrate primarily on data relating to new lens fits, as opposed to refits. We believe that new fits are a more sensitive barometer of current patterns and future trends, whereas refits are more indicative of previous fitting behaviours.

In keeping with other markets around the world,[1] a majority of lenses (69 per cent) were fitted to females. The average age of contact lens wearers at the time of fitting was 40.2 ± 16.9 years. The age at fitting ranged from eight to 79 years. This is the first time that the average age at fitting in Australia has exceeded 40 years, and reflects a continual year-on-year increase. In 2000, the average age was 32 years.

Soft lens materials and designs

Soft lenses are still the main type of contact lens fitted, accounting for 87 per cent of new fits, representing a slight decrease from the last few years.[2]

Figure 1 is a composite of pie charts detailing the key findings of the 2018 survey in relation to soft lenses. Silicone hydrogels are still the

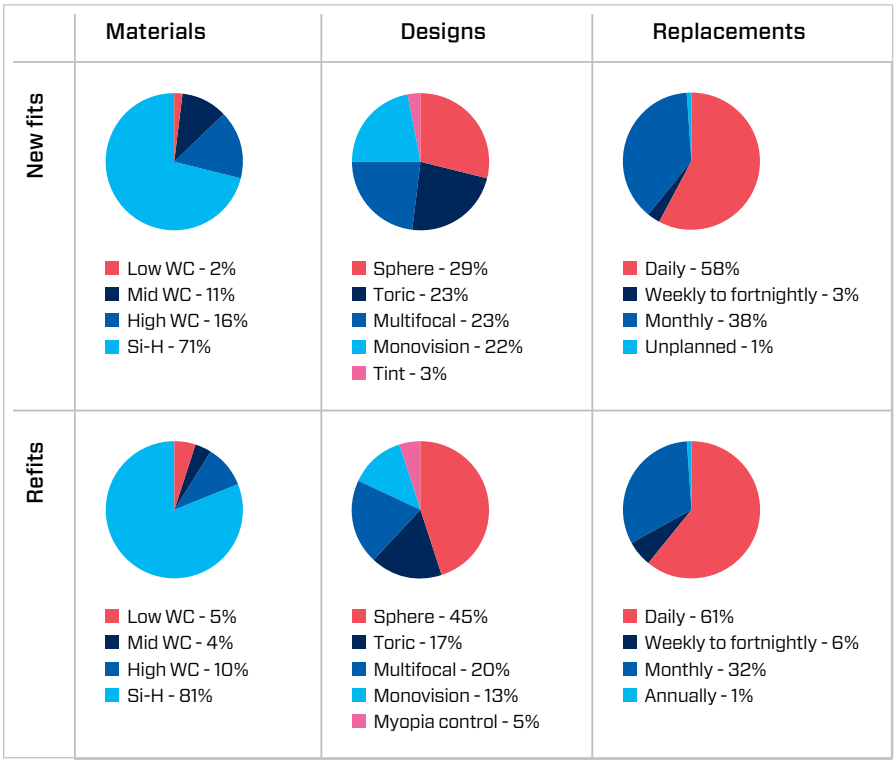

Figure 1. Detailed results for soft contact lens prescribing in the 2018 Australian survey (Si-H, silicone hydrogel; WC, water content)

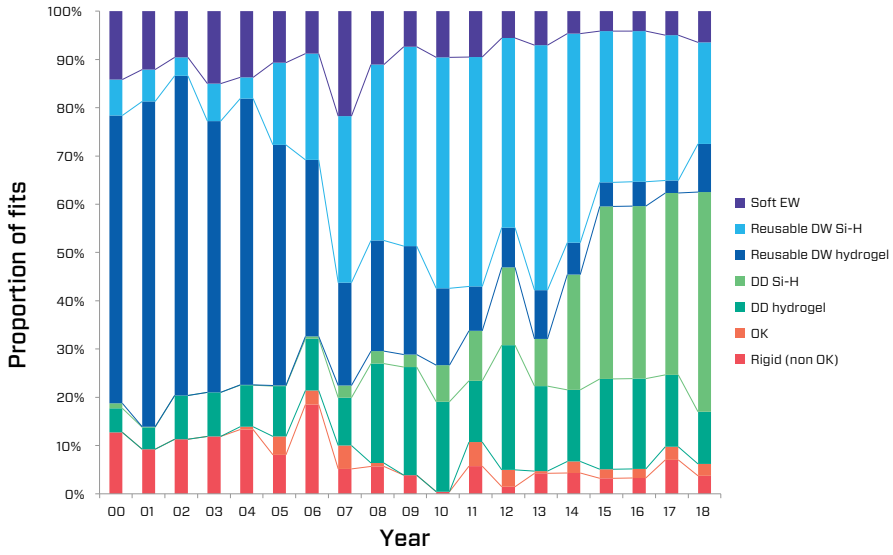

Figure 2. Proportion of all fits of various lens categories in Australia between 2000 and 2018 (EW, extended wear; DW, daily wear; Si-H, silicone hydrogel; DD, daily disposable; OK, orthokeratology)

dominant material, representing 71 and 81 per cent of materials prescribed as new fits and refits, respectively, with the balance comprising a mixture of low-, mid- and high-water content hydrogel materials. The remarkable penetration of silicone hydrogel materials since their introduction into the market at the turn of the century is illustrated in Figure 2. The reason for the popularity of this highly-oxygen-permeable material type is that it essentially eliminates hypoxic complications such as limbal and conjunctival redness, stromal oedema, corneal neovascularisation and epithelial microcysts.[3]

The key categories of lens designs are spherical, toric, multifocal, monovision, coloured (tinted) and myopia control. Spherical designs represented 29 per cent of new fits. Almost a quarter of soft lenses prescribed are in toric form (Figure 1).

Figure 3 shows trends in the proportion of toric lens fits as a proportion of all spherical and toric lens fits, since 2000. The gradual increase in toric lens fitting can be attributed to a combination of better toric lens designs being introduced—making such lenses easier to prescribe and fit—and a growing range of available toric parameters. The level of toric lens prescribing in Australia has consistently fallen short of that which would be expected if all lens wearers with ≥ 0.75 D of astigmatism were fitted with toric lenses (shown by the dotted line in Figure 3).[4,5]

The slight decline in toric lens prescribing between 2013–2016, as can be seen in Figure 3, was possibly due to accelerated prescribing of silicone hydrogel daily disposable lenses during this period, with the availability of toric designs lagging behind spherical designs for this lens type. As the data for 2017 and 2018 shows, this situation has now been rectified, with a wide range of parameters now available in toric silicone hydrogel daily disposable lenses and a commensurate increase in toric lens fitting.

Multifocal designs continue to be preferred to monovision for the correction of presbyopia. This trend, which has been evident since the turn of the century, can be attributed to improved multifocal lens designs. The fact that almost a quarter of soft lens fits are for the correction of presbyopia highlights the importance of this demographic in modern day contact lens practice. No doubt this will be a growing proportion of the market as pre-presbyopes fitted during the big growth period for contact lenses in the 1990s and 2000s advance towards manifest presbyopia. Indeed, this trend is consistent with the overall increase in the average age of lens wearers, as discussed above. Also, the possible future introduction of multifocal designs in toric form will likely boost the fitting of multifocal lenses.

As was the case in 2017, coloured (tinted) lenses only represented one per cent of new fits this year. Myopia control lenses incorporate special designs for arresting the rate of progression of myopia.[6] Although these lenses represented one per cent of new fits and two per cent of refits in 2017,[2] very few (0.2 per cent) new fits were recorded this year, although the proportion was greater for refits (five per cent). The small number of new fits might reflect the current paucity of specific lens designs for myopia control available in Australia and/or an overly cautious approach of contact lens practitioners who desire more evidence of the efficacy of such lenses.

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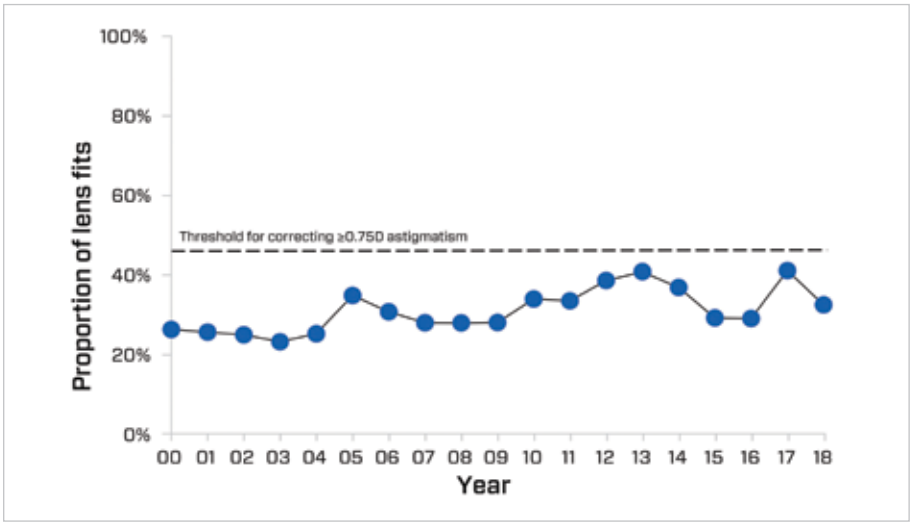

Figure 3. Percentage of all soft lenses prescribed as toric lenses in Australia between 2000 and 2018

Trends 2018

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Soft lens replacement and wearing modality

Virtually all soft lenses are replaced daily (62 per cent) or monthly (34 per cent). Trends since 2000 in daily disposable versus reusable soft lens fitting, in both hydrogel and silicone hydrogel materials, are shown in Figure 2. Daily disposable lenses, especially those made from silicone hydrogel materials, now dominate the market. As noted in our report last year, if this rate of prescribing daily disposable lenses continues at the same rate as has been apparent so far this century, virtually all soft lenses prescribed in Australia may be this lens type in the very near future.

Extended wear lens fitting, almost exclusively with silicone hydrogel materials, has remained constant at around eight per cent of all lens fits over the past decade (Figure 2).

Multi-purpose solutions remain the lens care option of choice for those wearing reusable lenses, representing 87 per cent of prescribed care regimens. The balance is made up almost exclusively of peroxide systems.

Rigid lenses

Of all rigid lenses prescribed, 39 per cent were orthokeratology fits. The slight increase in rigid lens prescribing in 2018 compared with recent years[2] perhaps reflects a renewed interest in large diameter rigid lenses and orthokeratology for temporary myopia relief and/or myopia control.

Australia versus the UK

We have conducted annual contact lens fitting in about 40 countries over the past few years.[1] This provides an opportunity to benchmark against international colleagues, and this year we compare contact lens prescribing in Australia against the UK (Figure 4). Seven key categories of lens type are represented. The outer and inner rings display the Australian and UK fitting data,[1] respectively.

Similar prescribing trends might be expected in Australia and the UK, in that both countries: (a) are island nations that are often used as 'test beds' by industry for trialling new products, (b) are dominated by large practice chains (with one major chain operating in both countries); (c) have a sophisticated base of registered practitioners with advanced university-based training; (d) have active contact lens organisations (the Cornea and Contact Lens Society of Australia and the British Contact Lens Association); and (e) have strong sales and marketing representation from the four major international contact lens corporations.

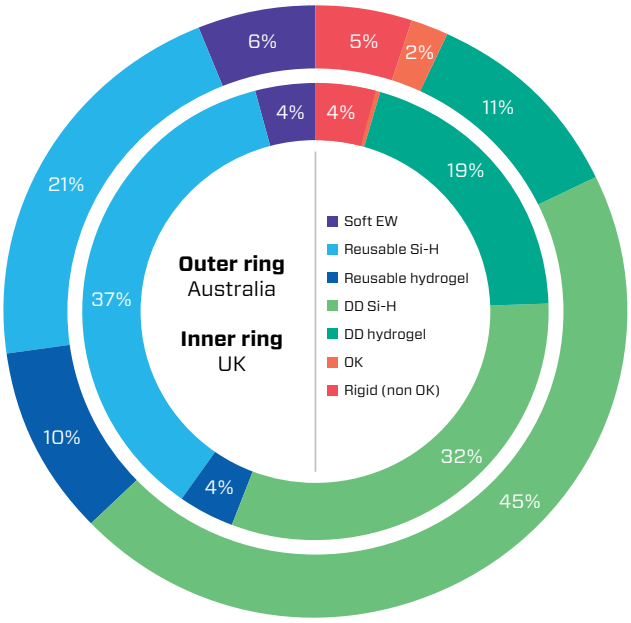

Figure 4. Percentage of all contact lenses prescribed in Australia (outer ring) compared with the UK (inner ring) (EW, extended wear; DW, daily wear; Si-H, silicone hydrogel; DD, daily disposable; OK, orthokeratology)

Indeed, inspection of Figure 4 confirms broad similarities between contact lens fitting in Australia and the UK. Although the overall extent of silicone hydrogel lens fitting is similar, Australian practitioners prefer to fit a higher proportion of daily disposable lenses made from this material. Whereas virtually all soft lenses were reusable hydrogel lenses towards the end of the 20th century, this modality now represents only 10 and four per cent, respectively, of all lens fits in Australia and the UK, although the reason for this difference between nations is not clear. More orthokeratology lenses are fitted in Australia, but the rate of fitting of other rigid lens types is similar.

Conclusions

The results of our 2018 survey indicate an increase in the average age of lens wearers and a high rate of prescribing daily disposable lenses in Australia. Silicone hydrogels are very firmly entrenched as the material of choice, representing around 78 per cent of all soft lens fits. High levels of contact lens fitting for presbyopia (especially multifocals), and astigmatism, continue at similarly high levels as have been observed since the turn of the century. ▲

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Can NovaTears solubolise meibum?

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A case report shows a surprising patient outcome

CASE REPORT

Obstructed, poor functioning or atrophied meibomian glands can lead to lipid layer disruption of the tear film and subsequent evaporation—and 86 per cent of dry eye sufferers demonstrate meibomian gland dysfunction.[1] Prevalence rates of dry eye can range from seven to 33 per cent.[2] Risk factors for dry eye include use of computers and devices, low relative humidity, medications, contact lens wear[2] auto-immune disease and rosacea.[3]

The 'new kid on the block' in the management of evaporative dry eye disease is NovaTears (AFT Pharmaceuticals). NovaTears is perfluorohexyloctane (EyeSol), a clear semifluorinated alkane (SFA), which has physically and chemically inert properties and excellent spreadability across the ocular surface, providing a more stable film against tear evaporation.

Patient A, a 60-year-old gentleman presented to our clinic complaining of a gritty and stinging sensation in his eyes over a few years, particularly under his left upper eyelid. His symptoms were increasing in severity and frequency and limiting his ability to use the computer for prolonged periods of time. He also experienced intermittent and unexplained watery eyes. His occupation involved significantly long hours of computer use (up to 10 hours a day) and he noted that while his symptoms were not as severe on the weekends, they were still present.

His oral medications included an angiotensin II receptor antagonist for hypertension, vitamin B and C supplements, and he reported having 'borderline' diabetes. His only past ocular history was a mild corneal abrasion from an injury to the superior aspect of his left eye about two-to-three years prior. He had severe osteoarthritis resulting in bilateral knee reconstructions, but no other health issues.

On examination, he was found to have an impaired fluorescein tear break-up time of about three seconds in each eye. His lashes and lid margins were clear and there was no conjunctival or corneal staining.

There was a persistent patch of evaporation noted on his left superior cornea which was attributed to his previous corneal abrasion (Figure 1). It was difficult to express any oil from his meibomian glands.

Meibography using infrared imaging on the Oculus Keratograph 5M showed healthy and functional meibomian glands in all lids (Figures 2A–D). The patient had done a lot of computer work the previous day and his eyes were quite gritty and watery. With a significantly high tear meniscus height (Figure 3), his non-invasive break-up time was around 12 seconds for each eye, which fell within an expected

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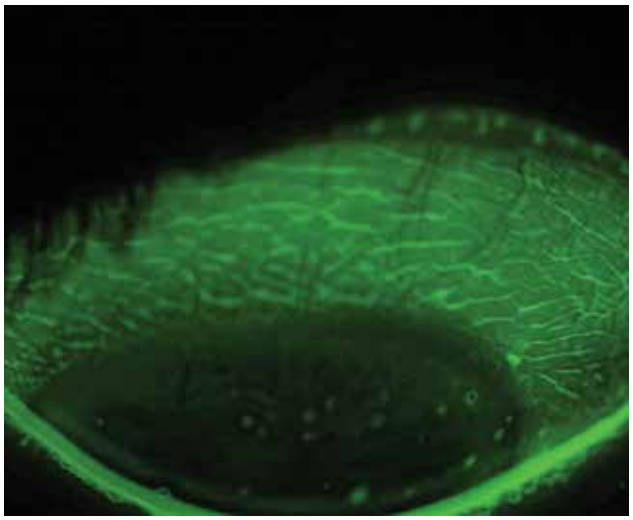

Figure 1. Examination reveals persistent patch of evaporation on the left superior cornea

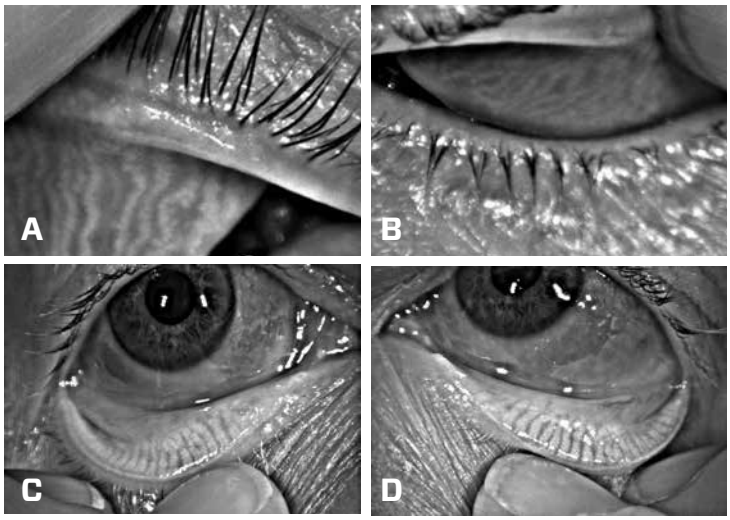

Figure 2A–D. Infrared meibography shows healthy and functional meibomian glands on all lids

NovaTears

From page 5

range and indicated a healthy tear film. However, videography using sodium fluorescein staining highlighted the underlying tear film instability causing the reflex tearing (Figure 4).

Treatment

The patient's first treatment included an in-room Blephasteam lid heating session and meibum expression. The melting point of meibum increases with inflammatory dry eye.[4] The Blephasteam device is designed to heat the eyelids for 10 minutes at a temperature higher than the ocular surface and lids; the heat assisting the meibum to soften prior to expression.[5] Despite this, it was still difficult to express meibum from any glands at the time of consultation. This is not unusual, so I asked him to start daily warm lid compresses using a heat bag for 10 minutes at home. I also recommended he use NovaTears to help his tear film stability while on the computer until we could improve his meibum consistency.

On reviewing the patient three weeks later, I learned that he had been away on holidays for a fortnight and had only commenced the lid compresses four days before seeing me again. He had, however, been using NovaTears daily and reported that he had significantly less tearing and no symptoms of grittiness, even after his return to work, which he attributed to the use of the artificial tear.

His only notable symptom now was a foreign body sensation in the area of his left upper globe, that had reduced in intensity and frequency. But most surprisingly, his meibum had softened significantly—light yellow oil was easily expressed from all lids without requiring heating prior.

That was certainly an unexpected result. Typically, I find two or three Blephasteam sessions are required before a result like this is achieved and, more commonly, only with an ideal management scenario of patients performing regular eyelid heating at home.

Discussion

Moderate-to-severe dry eye disease is associated with significant pain, limitations in performing daily activities, reduced vitality, poor general health, and often depression.[6] Patient A's productivity was most certainly affected by his dry eye symptoms and he was relieved to have found an effective management so quickly.

Typically, patients may require topical steroids, oral antibiotics or intense pulsed light (IPL) therapy to achieve healthier meibum, and often over a period of several weeks or months before achieving good meibum consistency.[7]

Kroesser et al.[8] found that high levels of topically-applied perfluorohexyloctane were maintained in the tears of rabbits for a minimum of four hours and significant levels were seen in meibomian glands up to eight hours after single and multiple doses. The highest exposure and longest presence of topically-applied perfluorohexyloctane were found in the anterior ocular tissues with only minor distribution into the posterior tissues observed. The researchers concluded that SFAs (including EyeSol), due to their lipophilic properties, are known to solubilise a number of lipophilic compounds. Further research has confirmed that topical application of perfluorohexyloctane significantly improves clinical signs of meibomian gland disease, including an improvement in the number of expressible meibomian glands.[9]

As meibum is a mixture of many different lipophilic compounds, it is likely that the SFAs might solubilise at least a number of them. While there may be other explanations for Patient A's decreased symptoms, I attributed the significantly-improved meibum quality (in essentially the absence of any other treatment) to his use of NovaTears.

Conclusion

Dry eye disease remains a challenging and complex condition to manage. Patients' signs and symptoms often are incongruous with each other, requiring treatment plans to take a very tailored

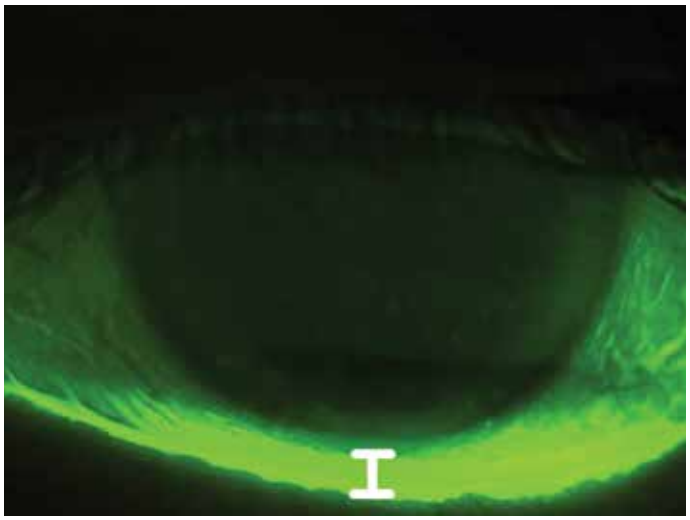

Figure 3. Significantly high tear meniscus height highlights the reflex tearing from the underlying impaired tear break-up time.

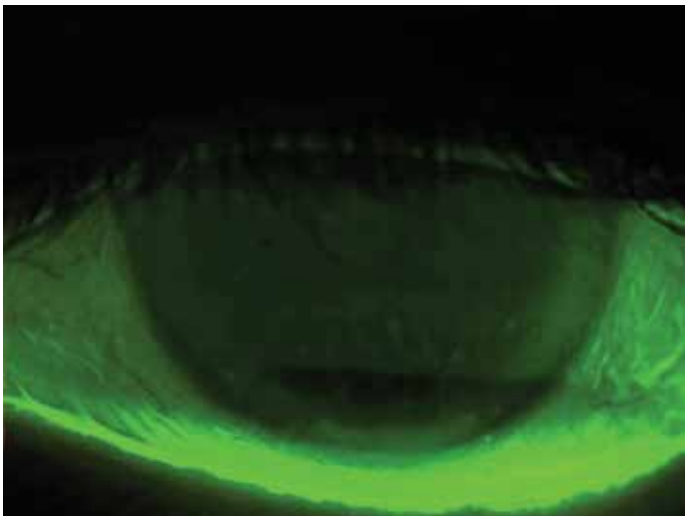

Figure 4. Videography using sodium fluorescein staining reveals the underlying tear film instability causing the reflex tearing

and individual approach. NovaTears may assist in the maintenance of a stable tear film in evaporative dry eye, and possibly even facilitate the melting of the inspissated meibum. It may be another powerful tool in our dry eye tool box.

Since September 1, 2018 NovaTears has been available on the PBS with Streamlined Authority Code (6172 x 5 repeats). Eligible patients with severe dry eye must be sensitive to preservative in multidose eye drops. NovaTears is available in a 3 ml bottle with a 4–5 times smaller droplet size than traditional water-based drops to minimise spill over, and can be used six months after opening. ▲

Jennifer Rayner is principal consulting optometrist and co-owner of Alleve Dry Eye Clinic in St Peters, South Australia. The clinic is dedicated solely to the diagnosis, treatment and management of dry eye.

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Topical immunomodulators

Clinical use for dry eye disease

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Whether it be a driving force or a response to the altered ocular surface, the inflammatory cascade in dry eye contributes to both the signs and symptoms of the disease, including the sensations of dryness, burning and visual fluctuations.[1] Both the initial and follow-up Dry Eye Workshops (DEWS) consensus definitions of dry eye disease included inflammation as part of its description, highlighting the contemporary understanding of this process in the pathogenesis of the disease.[2,3]

Anti-inflammatory therapy is therefore a viable route in managing the signs and symptoms of dry eye.[4] In ophthalmic therapy, corticosteroids are well known as potent treatments of inflammation, and short-term, high-frequency doses are effective in managing exacerbations of dry eye disease, improving patient signs and particularly symptoms. While effective in the short-term, corticosteroids have limited utility in chronic management due to associated risks of serious complications, including secondary infection, intraocular pressure rise and cataract formation.[5]

Chronic, pharmacological management of dry eye disease therefore requires alternative anti-inflammatory agents with more acceptable side-effect profiles. There are currently two commercialised molecules used to specifically target inflammation associated with dry eye disease without the side-effects associated with corticosteroids: cyclosporine and lifitegrast.

Both agents aim to decrease activity of T-cells, which become activated in dry eye and amplify inflammatory signals on the cornea and conjunctiva and recruit further immune cells to the diseased ocular surface.[6,7]

Cyclosporine

Cyclosporine is a large, hydrophobic, calcineurin inhibitor produced by the fungi Tolypocladium inflatum and Beauveria nevus.[8] Cyclosporine is used for chronic immunosuppression after organ transplantation, where its lack of bone marrow suppression is advantageous compared to other treatments.[8] However, the agent can still cause significant systemic effects, with more than 50 per cent of patients treated systemically experiencing complications such as nephrotoxicity, hepatotoxicity or hypertension. These complications are not seen with topical ophthalmic use, as cyclosporine does not appear to appreciably concentrate or is even detectable in the systemic circulation after use of upwards of three years.[8]

Ophthalmically, cyclosporine is prepared as 0.05% emulsions in single-use, unpreserved vials.[8] At this concentration, cyclosporine has been demonstrated in clinical trials to improve unanaesthetised Schirmer tear scores in moderate-to-severe dry eye patients, leading to the current label indication to increase tear production 'in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca.'[6]

The clinical trials for cyclosporine were unable to demonstrate improvement in patient symptoms compared to the control vehicle. Clinically, the drug is administered twice a day, with stinging on installation the most

Continued page 8

Lifitegrast and cyclosporine

From page 7

commonly reported adverse reaction.[9] The drug has also been observed to take upwards of three months to exert appreciable effects.[10] Thus in practice, it is common for patients to be initially prescribed a course of corticosteroids to manage the dry eye inflammation before cyclosporine is added. A relatively potent corticosteroid with low propensity to penetrate past the cornea and increase IOP such as fluorometholone alcohol is typically selected. The steroid is prescribed four times a day for approximately two weeks before adding cyclosporine twice a day while the steroid is tapered over a two-to-four-week period. The aim is to transition to using only cyclosporine indefinitely, with short-term corticosteroid use deployed in periods of disease exacerbation.

Lifitegrast

Lifitegrast is the latest molecule to reach commercialisation with an indication to manage dry eye. In contrast to cyclosporine formulations, the improvement of both a sign (inferior fluorescein staining score) and a symptom (dryness symptoms on a visual analogue scale, where patients indicated on a line their perception of dryness symptoms) were demonstrated in clinical trials, leading to a 5% lifitegrast ophthalmic solution used two times a day gaining FDA indication 'for the treatment of the signs and symptoms of dry eye disease (DED).'[7,11] Lifitegrast is the first entry in a new class of drugs known as 'LFA-1 antagonists,' specifically developed in the laboratory to target T-cell mediated inflammation on the ocular surface in dry eye.[12] By competitively binding with LFA-1 (lymphocyte functional associated antigen-1) expressed on activated T-cells, lifitegrast prevents interaction of LFA-1 with the overexpressed ICAM-1 (intracellular adhesion molecule-1) receptors on the surface of the epithelial cells of the conjunctiva and cornea in inflammation, decreasing further T-cell mediated inflammatory activation.[11-12]

Improvement in signs and/or symptoms were achieved within an 84-day study period across four clinical trials, with some suggestion that improvements may have occurred as early as 14 days.[13-16] One-year safety studies have also been conducted, with the majority of reported adverse reactions being mild-to-moderate in nature (irritation of instillation site) and no detection of the molecule within the plasma.[17] With the formulation only reaching market in 2016 in the United States, lifitegrast is early in its post-market surveillance period and hence it is too early to gauge its overall impact in dry eye management.

The promise of commercialised pharmacological formulations for dry eye is that they will aim to improve the signs and/or symptoms of the disease with simple, twice-a-day dosing from unpreserved solutions without the associated risks seen with corticosteroids.

In Australia, neither ophthalmic cyclosporine or lifitegrast have been approved by the Therapeutic Goods Administration (TGA). The application for ophthalmic cyclosporine was withdrawn by the sponsor after the TGA indicated that it was unlikely to be approved due to the inadequacy of the follow-up subgrouping statistical analysis used to allow the drug to reach the market in the USA and Canada.[18] Despite this, the drug can be accessed by patients in Australia through the Special Access Scheme, and resources are available for practitioners seeking to prescribe the formulation.

Lifitegrast has begun the process of approval with the TGA and it has already been recommended to be added to the Poisons Schedule under Schedule 4. For endorsed optometrists, it should also be noted that while cyclosporine does appear on the Optometry Board of Australia's Guideline for Use of Scheduled Medicines and so can potentially be prescribed, lifitegrast currently does not.[19] The drug would need to be added by the board and to relevant state or territory legislation before it could be potentially prescribed on optometrists' prescriptions. ▲

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Recurrent disciform keratitis

An optometrist's role (in NZ)

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The herpes simplex virus-1 (HSV) is a major cause of vision loss, affecting approximately 1.5 million globally and it is estimated that 90 per cent of adults are seropositive for the HSV antigen.[1-3] It has been reported that HSV keratitis can significantly affect quality of life in patients even when an active infection is not present due to an inflammatory response.[4] Ocular involvement of HSV can include both the anterior and posterior segments of the eye. HSV can affect all layers of the cornea from superficial epithelial disease to stromal keratitis and endotheliitis.[1]

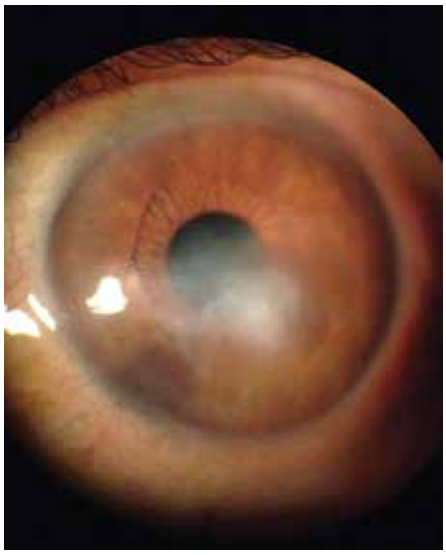

Figure 1. Post treatment for herpetic disciform keratitis (after second episode)

Stromal and endothelial keratitis has the greatest morbidity for the patient due to both corneal scarring and neovascularisation. It has been reported that herpetic disciform keratitis accounts for an estimated two per cent of initial HSV presentations but can be responsible for up to 20–48 per cent of recurrences.[1] For almost 20 years, the Herpetic Eye Disease Study (HEDS) has set the protocol for the management of herpetic eye disease, including the use of oral aciclovir as a prophylactic to reduce recurrences.[1,5,6]

Disciform keratitis is the most common type of endotheliitis and presents with a disc-shape of stromal oedema.[1,7] Associated ophthalmic signs include keratic precipitates and increased corneal thickness.[1,8] The HSV enters the host cell leading to host cell death. The virus is regarded as a 'broad cell tropic' as it can infect a variety of host cells including: epithelial cells, fibroblasts, neurons and lymphocytes.[1] The mechanism through which the virus enters the host cell varies depending on the cell type but generally occurs in two stages: 1) the viral glycoproteins bind to the receptors of the host cell and 2) the viral envelope fuses with the plasma membrane or undergoes endocytosis. Following fusion, viral nucleocapsid and proteins are released into the host cytoplasm where the proteins are transported into the nucleus.[1]

This case study illustrates the use of oral aciclovir for the management of recurrent disciform keratitis by an optometrist.

CASE REPORT

A 46-year-old male with a previous history of disciform keratitis presented with a sore left eye, photophobia and decreased vision.

On examination his unaided vision was R 6/18 (PH 6/6) L 6/12 (PH 6/12). The ocular health examination was unremarkable in the right eye. The left eye demonstrated moderate conjunctival hyperaemia; the cornea was oedematous with a central circular infiltrate with surrounding microcysts. Keratic precipitates were visible on the corneal endothelium.

Intra-ocular pressures were R 15 mmHg and L 15 mmHg with Perkins tonometry.

A differential diagnosis of recurrent herpetic disciform keratitis (second episode) was given and the patient was referred to a tertiary hospital for assessment and management by ophthalmology who confirmed the diagnosis. See Figure 1 (post treatment).

A year later, the patient presented again with recurrent disciform keratitis (third episode) with vision of hand movements only in the left eye. Ocular examination showed severe conjunctival hyperaemia, corneal oedema, microbullae, a central disciform infiltrate (3mm x 4mm) and grade two anterior chamber reaction. The patient was once again referred to a tertiary ophthalmology clinic for appropriate management.

A differential diagnosis of microbial keratitis was made (most likely herpes simplex but with a possible bacterial superinfection). The patient was admitted, and a corneal scrape was performed followed by topical and fortified cefuroxime and tobramycin, topical 3% aciclovir, topical cyclopentolate 1% three times a day and oral doxycycline 100mg daily. The polymerase chain reaction (PCR) was positive for viral HSV1. The patient was discharged four days after admission and presented to the optometrist on the same day with complaints of blurry vision. The ocular examination showed moderate conjunctival hyperaemia, central corneal staining and neovascularisation and large central corneal scar (2.8 mm x 2.5 mm) (Figure 2).

As this was the patient's third episode of herpetic disciform keratitis, prophylactic oral aciclovir 400 mg

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Keratitis

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was prescribed by the optometrist to use twice a day. Additionally, topical prednisolone acetate 1% was prescribed four times a day to reduce the corneal scarring. The patient was reviewed two weeks later.

On review, the conjunctival hyperaemia had reduced and the eye was white with a smaller central scar. The patient was advised to continue with the oral aciclovir indefinitely and to start tapering the prednisolone acetate 1% by one drop each week and was reviewed three weeks later.

During the final follow-up visit, the patient had a VA of 6/24 in the left eye and the ocular health examination showed the corneal scar had reduced in size and density but was located centrally and within the pupil (Figure 3).

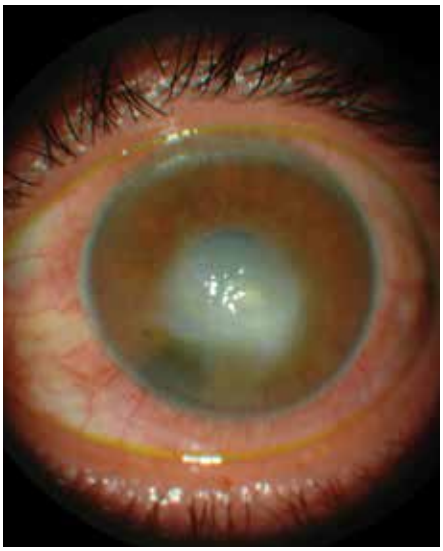

Figure 2. Examination reveals moderate conjunctival hyperaemia, central corneal staining and neovascularisation and large central corneal scar (after third episode following discharge from ophthalmology department)

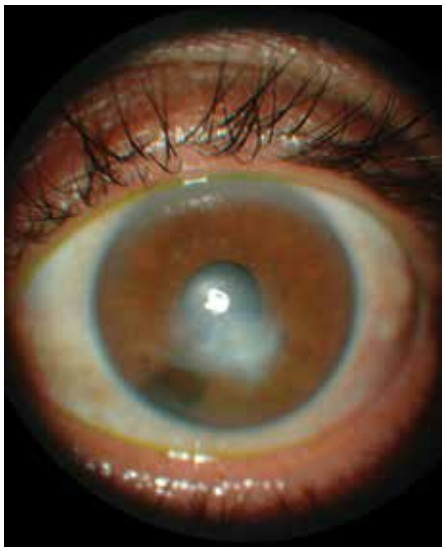

Figure 3. Final follow-up examination shows the corneal scar had reduced in size and density but was located centrally and within the pupil

Discussion

For the last two decades, the Herpetic Eye Disease Study (HEDS) I and II has provided protocols for herpetic eye disease. HEDS investigated the use of topical corticosteroids as well as oral aciclovir as adjunctive therapy for the treatment of herpetic stromal keratitis.[1]

The results of HEDS I showed the use of topical corticosteroids significantly reduced the time to resolution of 68 per cent of persistent or progressive stromal keratouveitis and is regularly used in the treatment of herpetic stromal keratitis.[1]

The results of HEDS II showed that prophylactic oral aciclovir (used at 400 mg twice a day) reduced the recurrence rate of HSV compared to the placebo group. This result was particularly important in those with a history of HSV stromal keratitis.[5,9,10]

Both HEDS I and II examined the role of aciclovir in herpetic eye disease, however newer generations of antivirals (such as valaciclovir) could also be used, although the literature on its role is limited.[11] Valaciclovir (a prodrug of aciclovir) is converted to aciclovir during first pass metabolism.[12] The conversion of valaciclovir to aciclovir also leads to an increased bioavailability of aciclovir by threefold to fivefold, compared to oral aciclovir. Given the increased bioavailability, 500mg of valaciclovir used once a day is as effective as 400 mg of aciclovir used twice daily in preventing recurrent herpetic eye disease.[11]

Both oral aciclovir and valaciclovir have good safety profiles. Commonly reported side effects include: nausea, headaches, vomiting and gastrointestinal upset.[1] Those with renal impairment will require adjustment to the dosage due to a risk of nephrotoxicity.

Conclusion

Oral aciclovir 400 mg can be used twice a day to reduce the recurrence of herpetic disciform keratitis. If available, valaciclovir 500 mg can be used once daily, as an alternative to aciclovir, to provide ongoing prophylactic cover. ▲

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CLINICAL AND EXPERIMENTAL OPTOMETRY

Pharma and Optometry Australia's official journal *Clinical and Experimental Optometry (CXO)* are collaborating to bring our readers up to date with some of the most interesting articles, reviews and original research available in the latest issues of *CXO*.

Does the temperature of an artificial tear affect its comfort?

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As part of our ongoing collaboration, Pharma and Optometry Australia's official journal Clinical and Experimental Optometry *bring our readers up to date with some of the most interesting articles, reviews and original research available in the pages of* Clinical and Experimental Optometry.

In this issue, Clinical and Experimental Optometry *Deputy Editor Maria Markoulli offers a brief look at a study published in September's issue of* Clinical and Experimental Optometry *that confronts one of the untested assumptions of optometry: refrigerated artificial tears offer a soothing effect to patients with dry eye.*

Bitton E, Crncich V, Brunet N. Does the temperature of an artificial tear affect its comfort? *Clinical and Experimental Optometry* issue 101, volume 5.

Dry eye disease has received a lot of attention of late, largely due to the publication of the 2017 consensus report of the Tear Film and Ocular Surface Dry Eye Workshop. One of the aspects highlighted in the report was that, despite the multitude of treatments available, there is a dearth in publications on their efficacy.[1]

The first port of call in dry eye management is most often the use of artificial tears, used for their palliative effect.

One recommendation often made clinically to patients with dry eye disease, without substantial evidence to back up the reasoning, is that patients should refrigerate their artificial tears prior to instillation. The hypothesis here is that chilled drops soothe dry eye disease.

Most artificial tears are marketed with recommended storage at room temperature, so in order to test the hypothesis that a lower temperature will be soothing, Dr Etty Bitton and colleagues from the Université de Montréal set out to determine if refrigerating artificial tears does indeed improve reported comfort.[2]

To do this, they recruited 18 people with mild or moderate dry eye disease

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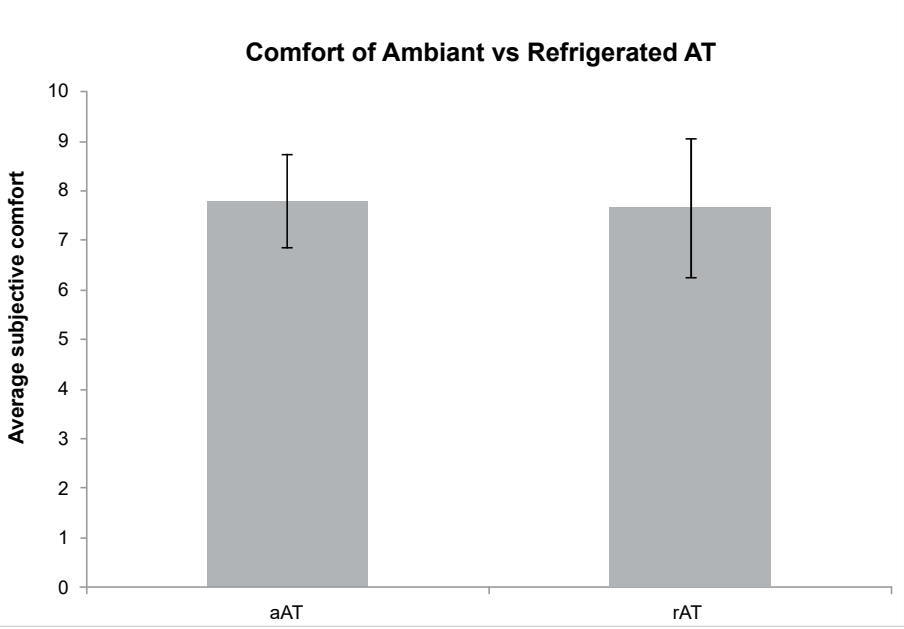

Figure 1. Comfort of ambient vs refrigerated artificial tears

CXO review

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based on their score on the Ocular Surface Disease Index questionnaire, a commonly-used tool to assess dry eye disease symptoms. Participants were also required to have normal corneal sensitivity at baseline.

They were instructed to instil Systane Ultra eye drops (Alcon Laboratories), once in the morning and once in the evening. Following a prompt by text or email, each time one eye received the drop at room temperature the other eye received the refrigerated drop. Participants were then asked to report their comfort on a 1-10 scale, 10 being excellent.

In order to confirm the effect of refrigeration on these drops, the team first compared the Systane Ultra drops at room temperature and after refrigeration by comparing their pH and osmolality. The laboratory testing showed that neither drop pH nor osmolality changed with refrigeration.

When the clinical measurements of comfort were evaluated, they found that there was no significant difference in comfort scores between the two temperatures at any time of day.

The recommendation to apply cold artificial tears is often made to patients with allergic eye disease. These findings suggest that while temperature may affect comfort in ocular allergy, this does not seem to be the case in dry eye disease.

The reason for the lack of efficacy found here with cold drops may in part be due to the differing pathophysiology between dry eye disease and allergic disease, where the latter is more affected by hyperaemia and hence symptoms are more likely to be alleviated by modulating ocular surface temperature. Another factor may be that the participants recruited in this study only had mild to moderate dry eye disease and therefore little ocular surface inflammation which may have changed the result. Nevertheless, the evidence at hand indicates that when managing dry eye disease, whether artificial tears are stored in the fridge or at room temperature, the end result for the patient will be the same. ▲

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GUIDE

TFOS DEWS II CHAIR-SIDE REFERENCE PAGES 14-16

Dry eye disease and management

Building up your practice via TFOS DEWS II

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Centre for Eye Health

Over the last 12 months, the University of New South Wales (UNSW) School of Optometry and Vision Science team has been applying the lessons from the 2017 TFOS DEWS II workshop to our own dedicated Dry Eye Clinic. This article summarises our approach to diagnosis and management of dry eye disease, and aims to give every clinician a 'how-to guide' to expand their dry eye skill set.

In diagnosing and managing dry eye disease, it is helpful to keep in mind the underlying pathophysiology of the disease and its definition. Dry eye is defined as 'a multifactorial disease of the ocular surface, characterised by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.'[1]

At its core, dry eye disease is thought to involve hyperosmolarity of the tear film.[2] This hyperosmolarity promotes an inflammatory cascade within the ocular surface which causes downstream ocular surface damage to the corneal epithelial cells and glycocalyx, the conjunctival epithelial and goblet cells and the lid wiper region of the eyelids.[2] The resulting tear film instability leads to further hyperosmolarity, perpetuating what has been aptly named the 'vicious circle' of dry eye disease.[3] Each one of these components can be assessed clinically with tools available to the clinician. To appropriately diagnose dry eye, one needs to look for each of these signs and provide intervention to break the vicious circle.

DIAGNOSIS

The TFOS DEWS II workshop recommendation for accurate diagnosis of dry eye is as simple as 1-2-3.[4]

Step 1: History and symptom-taking

When a patient presents with any symptoms, the first thing we do is put on our 'detective hat' to determine the cause of these symptoms. This is true for dry eye disease. Clinicians work through questions about the severity of symptoms, any association with mouth-dryness or enlarged glands (possible Sjögren's syndrome), the chronicity of the symptoms and any triggering events (such as recent ocular surgery or a change to medications), whether it is bilateral or unilateral (dry eye is usually symmetrical) and whether there are associated symptoms such as itchiness (possible allergy), swelling or crustiness (possible conjunctivitis) or discharge (possible infective keratitis or conjunctivitis). Clinicians also identify any risk factors and classify them as either 'modifiable' (contact lens wear, current preserved topical medication, androgen deficiency, systemic medication such as antihistamines) or 'non-modifiable' (older age, female sex, Asian ethnicity).

Step 2: Diagnostic testing

As per the definition of dry eye, the diagnostic process involves the assessment of symptoms and markers of homeostasis. With regards to symptoms, the use of validated questionnaires such as the Ocular Surface Disease Index (OSDI) or the Dry Eye Questionnaire-5 (DEQ-5) is highly recommended.[5,6] These can be printed and used in a paper format or downloaded as an app and they help stratify the severity of the symptoms and, more importantly, help monitor the impact of treatment.

The second part of diagnostic testing is to look for signs indicative of a loss of homeostasis. This involves measurement of tear osmolarity, tear break-up time (ideally the non-invasive form) and looking for the presence of ocular surface damage in the form of corneal, conjunctival or lid wiper staining. If any one of these is positive, it is important to move to the next step. If not, look to differentially diagnosing for other causes of these symptoms.

Step 3: Classifying the dry eye disease

Establishing whether the patient has evaporative dry eye disease, aqueous

Continued page 17

Dry Eye Definition: Tear Film & Ocular Surface Society (TFOS) Dry Eye Workshop II (DEWS II)

Examination and differential diagnosis workflow

Routine initial clinical exam

Signs consistent with dry eye

Symptoms consistent with dry eye

Diagnostic tests

Signs: one of the following

- Non-invasive tear break-up time (TBUT) < 10 seconds
- Osmolarity ≥ 308 mOsm/L OR a difference > 8 mOsm/L between eyes
- Staining
  > 5 corneal spots
  > 9 conjunctival spots

Symptoms

- Dry Eye Questionnaire (DEQ-5) ≥ 6

or

- Ocular Surface Disease Index (OSDI) ≥ 13

Result

Signs, no symptoms

Signs and symptoms: DRY EYE

Symptoms, no signs

Triaging questions

- How **severe** is the eye discomfort?
- Do you have any mouth dryness or swollen glands?
- How **long** have your symptoms lasted and was there any triggering event?
- Is your **vision** affected and does it clear on blinking?
- Are the symptoms or any redness much worse in **one eye** than the other?
- Do the eyes **itch**, appear swollen or crusty, or give off any **discharge**?
- Do you wear **contact lenses**?
- Have you been diagnosed with any **general health conditions** (including recent respiratory infections) or are you taking any **medications**?

+ Detailed anterior eye examination differential diagnosis where indicated by answers

Risk factors: Modifiable

Consistently shown

- Androgen deficiency
- Computer use
- CL wear
- Hormone replacement therapy
- Haematopoietic stem cell transplantation
- Environment (pollution, low humidity)

Medications

- Antihistamines
- Antidepressants
- Anxiolytics
- Isotretinoin

Dry Eye - TFOS DEWS II

Optometry
NEW SOUTH WALES
AUSTRALIAN CAPITAL TERRITORY

Dry eye is a multifactorial disease of the ocular surface characterised by a loss of homeostasis of the tear film and accompanied by ocular symptoms in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play aetiological roles.

Adapted from Craig et al. and Wolffsohn et al. [1,2]

Diagnoses

Neurotrophic condition (dysfunctional sensation)
Manage dry eye signs

Pre-disposition to dry eye
Preventative management

Preclinical state
Observe, educate/treat

Neuropathic pain
Refer for pain management

Sub-type classification
- Diagnostic tests

Aqueous deficient
(low volume)
- Tear meniscus height < 0.25mm

Can occur separately or together

Evaporative
(abnormal lipid or meibomian gland dysfunction [MGD])
- Meibomian gland expression
- Meibography
- Interferometry
- Blink and lid closure

Causes

Sjögren's

Non-Sjögren's
- Congenital
- Age-related
- Lacrimal gland obstruction
- Systemic medications
- Anterior eye surgery
- Contact lens wear

Ocular surface
- Vitamin A deficiency
- Mucin deficiency
- Iatrogenic
- Contact lens wear
- Age-related

Lid-related
- Obstructive
- Incomplete blinking
- Age-related

Probable	Inconclusive
Low intake of FFA	Smoking
Refractive surgery	Alcohol
Allergic conjunctivitis	Pregnancy
	Demodex
	Botox injection
Anticholinergics	Multivitamins
Diuretics	Oral contraceptives
Beta-blockers	

Risk Factors: Non-Modifiable

Consistently shown	Probable	Inconclusive
Age	Diabetes	Hispanic
Female	Rosacea	Menopause
Asian	Viral infection	Acne
MGD	Thyroid disease	Sarcoidosis
Connective tissue disorder	Psychiatric conditions	
Sjögren's syndrome	Pterygium	

TFOS DEWS II staged management and treatment recommendations

Adapted from L Jones et al. [3]

Step 1

- Education
- Modification of local environment
- Dietary modifications including oral essential fatty acid supplementation
- Identify and potentially modify offending systemic and topical medications
- Ocular lubricants of various types: if MGD is present, then consider lipid-containing supplements
- Lid hygiene and warm compresses of various types

Step 2

- Non-preserved ocular lubricants
- Tea tree oil treatment for Demodex (if present)
- Tear conservation (punctal occlusion / moisture chamber goggles)
- Overnight treatments (ointment or moisture chamber devices)
- In-office physical heating and expression of the meibomian glands (including device-assisted therapies)
- In-office intense pulsed light therapy for MGD
- Prescription drugs to manage dry eye disease
- Topical antibiotic or antibiotic/steroid combination applied to the lid margins for anterior blepharitis (if present)
- Topical corticosteroid (limited-duration)
- Topical secretagogues
- Topical non-glucocorticoid drugs (such as cyclosporine)
- Topical LFA-1 antagonist drugs (such as Lifitegrast)
- Oral macrolide or tetracycline antibiotics

Step 3

- Oral secretagogues
- Autologous/allogeneic serum eye drops
- Therapeutic contact lens options
- Soft bandage lenses
- Rigid scleral lenses

Step 4

- Topical corticosteroid for longer duration
- Amniotic membrane grafts
- Surgical punctal occlusion
- Other surgical approaches: tarsorrhaphy, salivary gland transplantation

Notes:

i. These steps are not designed to be used as a rigid, fixed process, but more an organisational tool

ii. Options within a step are not ranked by importance

iii. It is possible and likely that one or more options within each step will be needed/utilised

iv. Earlier steps should be continued if moving to later steps

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How-to guide

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deficient dry eye disease, or a mixture of both is critical to guide subsequent management of the patient.

Evaporative dry eye disease occurs when the structure and function of the meibomian glands is impaired. Clinicians should observe the meibomian gland orifices—looking for any signs of obstruction, keratinisation or telangiectasia. Pressure should also be applied to the eyelids in order to examine the quality of the gland expression. In observing the lid margins, signs of associated lid margin disease are observed, such as anterior blepharitis associated with colonisation of the lid margin with Staphylococcus species or cylindrical crusts on the lashes associated with Demodex infestation. This can be treated with various commercial lid hygiene products. If available, the meibomian gland structure can be examined with infrared photography or meibography and the thickness of the lipid layer measured with interferometry.

In aqueous deficient dry eye disease, the tear film volume can be estimated by measuring tear meniscus height or by using unanaesthetised Schirmer strips for five minutes or phenol red threads for 15 seconds.

MANAGEMENT AND THERAPY

Patient education

Once the diagnosis of dry eye is established as being either aqueous deficient, evaporative dry eye disease, or (more commonly) a combination of the two, the treatment goal will be to restore homeostasis of the tear film. It is important to educate the patient about several factors.

The chronicity of their condition and the need for ongoing management

Any environmental modifications they might be able to make, locally or externally. For example, contact lens users may need to be refitted and managed according to the TFOS Contact Lens Discomfort workshop.[7] If the patient is using preserved eye drops on a regular basis, there may be a benefit from changing to a non-preserved form. Externally, patients may need to adjust their seating arrangements at work to avoid air conditioning vents being directed at them.

Diet modifications such as general hydration and a healthy intake of essential fatty acids such as omega-3. The literature is equivocal about the latter, so keeping abreast with the latest research findings is important.

Management of dry eye is a stepped process. It should start at the simple end of the spectrum and becomes more complex as required with appropriate communication to patients at each step.

Management of evaporative dry eye disease and meibomian gland dysfunction

This involves treating any blepharitis, blinking abnormalities and meibomian gland dysfunction (MGD). The biggest factor contributing to dry eye disease is MGD. MGD is caused by obstruction of the orifices and/or qualitative or quantitative changes to the meibomian gland secretions. A patient with dry eye disease that has MGD as an aetiological factor therefore needs management that will involve clearing of the gland orifices, followed by gland expression. This can be done in-office with readily accessible tools.

To debride the lid margin, it is recommended that both eyes be anaesthetised topically.

It is then recommended to soak a sterile cotton bud in the same anaesthetic solution and run this along the lower eyelid margin in order to soften any keratinised material by breaking down tight junctions.

A drop of lissamine green is then instilled to help to define Marx's line, the mucocutaneous junction (Figure 1). Debridement should occur anterior to Marx's line, specifically, over the meibomian gland orifices as this will avoid damaging the posterior eyelid, specifically the fragile lid wiper region. The lid wiper region is in contact with the ocular surface and is prone to frictional damage, and it is best to avoid interference with this area.

Lid margin debridement involves use of a sterilised golf spud (or a sterile cotton bud) gently rubbed along the stained lower eyelid margin. The goal is to remove any obvious meibomian gland orifice obstructions or any superficial keratinisation. Lid margin debridement has been shown to be effective in improving both patient symptoms and meibomian gland function.[8,9]

The next steps involve clearing out any deeper obstructions of the meibomian glands by gently expressing the glands.

First, the meibomian glands are heated to facilitate their expression.

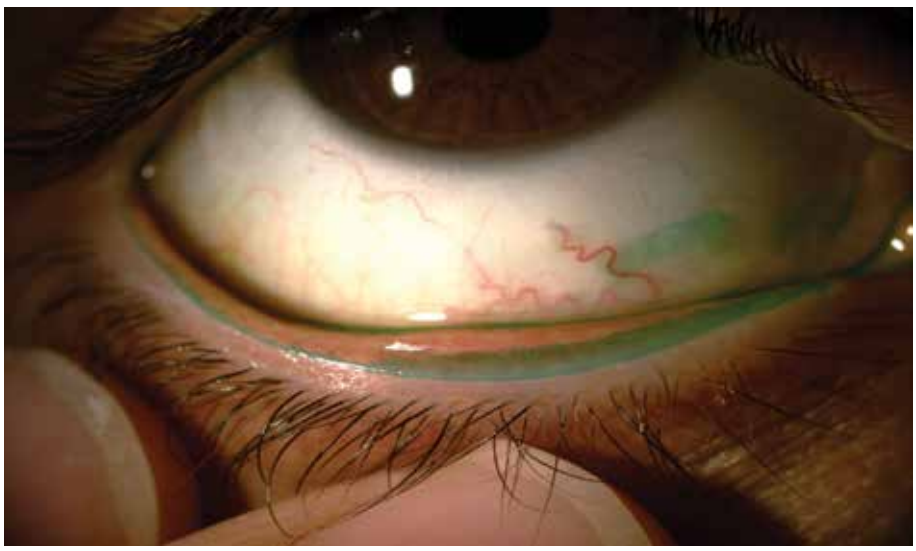

Figure 1. Lissamine green staining can be used to delineate Marx's Line and to identify any lid wiper epitheliopathy

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This should be preferably done using commercially-available warm compresses or with steam goggles. The glands are warmed for 10 minutes.

Both eyelids and lid margins are anaesthetised as described above and using one of the available instruments the glands are expressed.

A mastrota paddle or a sterile, moistened cotton bud is used to pull the eyelid away from the globe. Because this process involves applying a significant amount of pressure to the eyelids, we want to protect the globe itself.

Then use a finger or another cotton bud to apply pressure to the lower eyelid and encourage the glands to express their contents. Move along from the nasal to the central and then to the temporal regions of the eyelid and repeat two to three times per lower eyelid, depending on the patient's tolerance. At the UNSW Dry Eye Clinic, flat forceps, sterilised in the same manner as a tonometer probe, are used. This frees up one hand to allow eyelid manipulation. Patients need to guide the clinician with regards to the amount of pressure applied to the glands. It is important to warn patients that the procedure will leave their eyes looking somewhat red and feeling uncomfortable for the rest of the day. Typically, only the lower lid is easily manipulated with this procedure and so the upper lids are rarely expressed in this manner.

At the end of the procedure, the patient's eyes are checked for corneal staining again and then rinsed with unit dose sterile saline.

Patients can be reviewed within the month to determine efficacy of the procedure. If effective, gland expression can be repeated every three months. If gland expression has not improved signs or symptoms, use of specialised equipment such as the Lipiflow or Intense Pulsed Light is indicated.

Management of aqueous deficiency

Management of aqueous deficiency is approached in three ways:

The first and most accessible option is to recommend artificial tear supplements that target either the aqueous or lipid layer or both, allowing alignment of this selection to the diagnosis. When more frequent drop instillation is required, such as in excess of four times a day, non-preserved artificial tear supplements are indicated in order to minimise the risk of a toxic response to the preservative.

The second approach aims to conserve the existing tears using punctal plugs. This is somewhat controversial given that dry eye disease is often associated with inflammation. By blocking the puncta, inflammatory mediators could be trapped and hence perpetuating the vicious circle. Therefore, the advice is to bring the ocular surface inflammation under control before blocking the puncta.

The third aspect of managing aqueous deficiency involves promoting tear secretion. This can be done topically using drugs such as Rebamipide and Diquafosol which promote the secretion of aqueous and mucin, respectively. Unfortunately, neither are available in Australia. However, optometrists can refer to the patient's general practitioner for prescribing of oral secretagogues—such as oral pilocarpine—if desired.

Management of inflammation

Inflammation can be brought under control using relevant pharmacological intervention. The most obvious choice is the use of corticosteroids. Depending on the severity of the dry eye disease, the patient could be prescribed a milder steroid such as fluorometholone alcohol four times a day for a short period, tapering down and monitoring mid-way and at the end of the course of treatment. Of course, a stronger steroid could be used if the patient has more severe inflammation and if their profile allows for this.

The disadvantage of steroids are their IOP-raising effects and their association with cataractogenesis and the propagation of pre-existing infection. To that end, immunomodulators such as cyclosporine A or lifitegrast (if available) which target a specific part of the inflammatory pathway and do not elevate IOP can also be used. Topical antibiotics such as azithromycin are also used for their anti-inflammatory effects, as is systemic doxycycline and manuka honey in the topical eye drop form.

Conclusion

Dry eye disease is a multifactorial disease that requires a clinical approach that is multi-faceted in order to break the vicious circle and restore ocular surface homeostasis. To guide our management, we first need to determine whether the presenting patient has evaporative dry eye disease or aqueous deficiency, or a combination of the two.

The treatment process begins with simple therapies first and progresses to more complex therapies as required. One or more options within each category can be considered concurrently depending on the presentation. Importantly, dry eye disease, particularly in the early stages, is a condition that can be easily diagnosed and managed within the realm of optometric practice. ▲

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Beneath the surface: dry eye disease and systemic conditions

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Dry eye disease (DED) affects approximately 20 per cent of the Australian population, and is more prevalent in females and the elderly.[1,2] Obvious clinical signs such as ocular surface staining and reduced tear break-up time are often sufficient to diagnose the condition. As the understanding of DED grows, coupled with advances in ocular imaging, our ability to assess and diagnose dry eye has become far easier. For all concerned – the clinician, the patient, etc., it is vital to bear in mind that DED is a complex multifactorial disease.[3] Many dry eye signs and symptoms may not correlate. As optometrists, we must remain vigilant, always considering the relationship between DED and systemic conditions, especially autoimmune disease. Conditions such as diabetes mellitus, Sjögren's syndrome (SS) and rheumatoid arthritis are often associated systemic causes of DED.[2]

CASE REPORT

A 58-year-old Caucasian female presented with common dry eye symptoms of ocular redness, grittiness, foreign body sensation and watery eyes. After questioning, she also reported a persistent dry cough and dry mouth, long-standing, with an onset of over 20 years ago. At that time, she had seen numerous health care practitioners. Her management involved only using artificial tears multiple times a day offering minimal benefit. She denied any previous ocular surgeries, allergies, systemic conditions and impactful medications.

Completion of the Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire returned a positive symptom score of 20. Tear osmolarity using the I-PEN Osmolarity System was 312 mOsm/L in the right eye and 324 mOsm/L in the left eye. Assessment with the OCULUS Keratograph 5M showed low tear meniscus height of 0.10 mm (Figure 1), non-invasive keratograph tear break-up time (NIKTBUT) of five seconds and low lipid layer thickness on tear film interferometry in each eye. There was also moderate anterior blepharitis with signs of Demodex infestation. Sodium fluorescein showed patchy corneal staining centrally and inferiorly. Lissamine green staining was observed on the nasal and temporal bulbar conjunctiva in both eyes. Meibography revealed grade 2 meibomian gland dysfunction (MGD) (Figure 2). Gland expression using the Korb Meibomian Gland Evaluator found cloudy toothpaste secretions.

From the observable clinical signs, the patient was found to have a combination of aqueous-deficient and evaporative DED, along with anterior blepharitis and demodex.

Treatment

The patient was treated with in-office BlephEx and Intense Pulsed Light (IPL) therapies. For home maintenance, she used Optimel Manuka+ Dry Eye drops, OUST Demodex cleanser and the EyeGiene Insta-Warmth System.

After four months of treatment, the patient reported marked improvement in her symptoms, with her SPEED questionnaire score reducing down to nine.

Beneath the surface

With numerous obvious clinical signs indicating DED contributing factors, it is easy to focus solely on those areas. Although the patient's symptoms improved, the low tear meniscus height and her comment on dry mouth warranted further investigation. A report was sent to the patient's general practitioner for a blood workup to assess for systemic conditions, especially autoimmune diseases such as SS, rheumatoid arthritis, systemic lupus erythematosus and thyroid disease.

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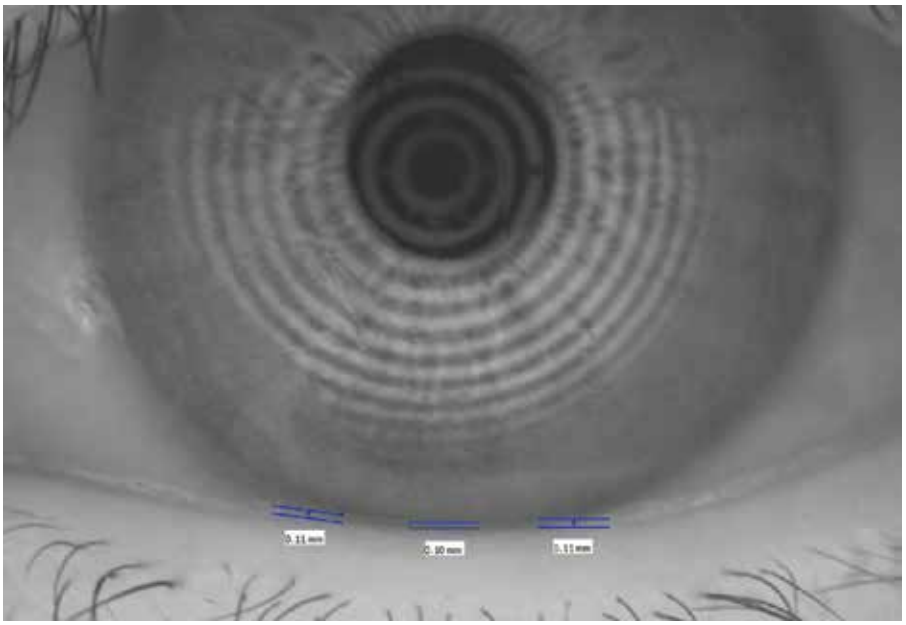

Figure 1. OCULUS Keratograph 5M measurement of the tear meniscus height

Systemic conditions

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The blood test results were inconclusive: auto-antibodies appeared to be negative however she had a weakly positive rheumatoid factor. The patient continued with further workup involving a salivary gland biopsy which confirmed the diagnosis of SS, likely secondary SS, due to her elevated risk of also having rheumatoid arthritis. The patient was referred to and is now under the care of a rheumatologist.

Sjögren's syndrome

SS is a chronic autoimmune disorder involving lymphocytic infiltration of the salivary and lacrimal glands, resulting in the hallmark symptoms of dry eye and dry mouth (xerostomia).[4] Dry eye is often one of the earliest symptoms of SS, and found to precede systemic complications by around 10 years.[5]

Depending on the degree of systemic involvement, compromised function of the exocrine glands can also lead to symptoms of muscle pain, joint pain, fatigue, dental issues, gastrointestinal problems and increased risk of lymphoma.[4]

SS occurs in two basic forms, classified as primary or secondary. With primary SS, the disease occurs in isolation, independent of other rheumatic conditions. With secondary SS, the disease occurs in association with other autoimmune conditions, most commonly rheumatoid arthritis or systemic lupus erythematosus.[6]

According to the Australian Sjögren's Association, SS is one of the most prevalent autoimmune disorders, affecting up to 0.5 per cent of all Australians.[7] Women account for more than 90 per cent of patients with SS, where females are nine times more likely to be affected than males. While it can occur at any age, it is most commonly diagnosed in women between 40 and 60 years of age.[6]

Workup of SS

There is no single test that can definitively diagnose SS. Symptoms are often non-specific and can mimic other systemic conditions, making diagnosis difficult and often delayed. A report to the patient's general practitioner or rheumatologist can start the process.

In 2016, an updated classification criteria for primary SS was approved by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR). The classification criteria include oral and ocular signs and symptoms, serological tests for auto-antibody biomarkers and histology of the salivary glands (Table 1). Each criteria or item is weighted, and a diagnosis of primary SS is established if an individual obtains a score greater than four. This criterion has a sensitivity of 96 per cent and specificity of 95 per cent.[8]

The inclusion criteria questions require any individual to answer affirmatively to at least one of the following questions:

1. Have you had daily, persistent, troublesome dry eyes for more than three months?
2. Do you have a recurrent sensation of sand or gravel in the eyes?
3. Do you use tear substitutes more than three times a day?
4. Have you had a daily feeling of dry mouth for more than three months?
5. Do you frequently drink liquids to aid in swallowing dry food?

Exclusion criteria include prior diagnosis of hepatitis C infection, acquired immunodeficiency disease, sarcoidosis, amyloidosis, graft-vs-host disease, previous head and neck radiation treatment and use of anti-cholinergic drugs.

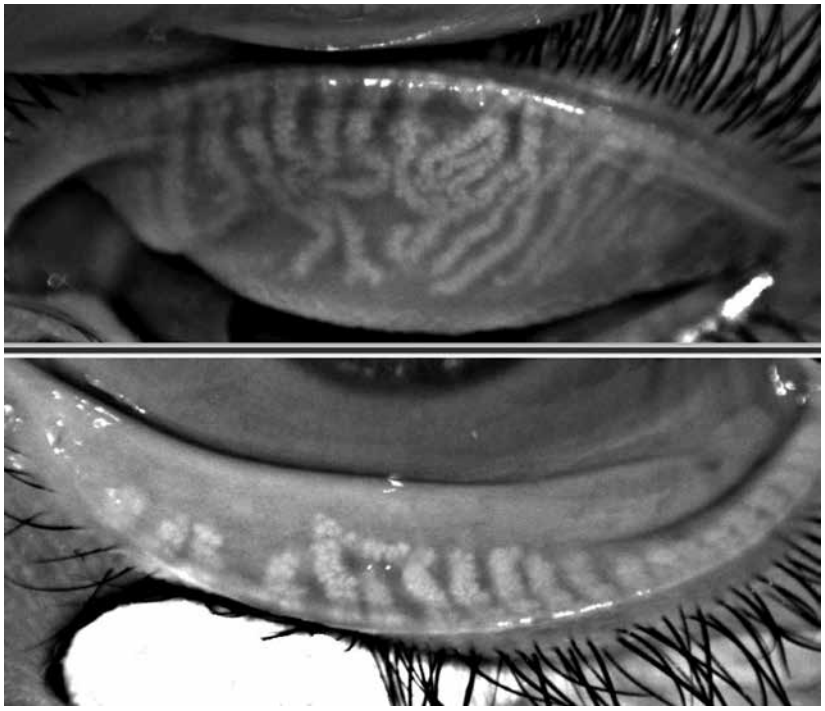

Figure 2. Meibography showing meibomian gland dysfunction using the OCULUS Keratograph 5M

IN-OFFICE TESTS

In practice, optometrists have access to a wide range of clinical tools and technology to assist in the diagnosis of DED. Some of the key tests in working up a dry eye patient, particularly a patient you suspect may have SS, can include:

Dry eye questionnaires

Surveys such as The Ocular Surface Disease Index (OSDI) and SPEED can provide valuable information relating to the patient's symptoms and the impact on their quality of life. The scores can also act as a baseline to monitor for disease progression or improvement after treatment.

Tear meniscus height and Schirmer's test

Both of these tests aid in the diagnosis

of aqueous-deficient DED. A tear meniscus height of less than 0.25 mm represents low tear volume. According to the ACR/EULAR classification criteria, a Schirmer's test result of less than 5 mm in at least one eye, unanaesthetised, is a risk factor for SS.[8]

Tear break-up time

In SS patients, TBUT ranged from 1 second to 15 seconds, compared to 4 seconds to 32 seconds in the non-SS control group.[9] A TBUT of less than 10 seconds indicates tear film stability and is indicative of DED.[10]

Ocular surface staining

Sodium fluorescein allows for evaluation of ocular surface integrity, whereas lissamine green and rose bengal stain dead and degenerated cells. The presence of rose bengal or lissamine green staining on the temporal conjunctiva was found to be higher in SS patients.[11]

Meibography and meibomian gland expression

Ocular surface inflammation can impair the function and structure of meibomian glands. SS patients were found to have higher levels of meibomian gland dropout, poorer meibomian gland expressibility and meibum quality compared to non-SS control groups. It is important to remember that SS patients can have a combination of aqueous-deficient and evaporative DED.[12]

Tear osmolarity

This has been recognised as a key mechanism of DED, and one that can be objectively and reliably measured. Tear hyperosmolarity damages the corneal and conjunctival epithelial cells, causing tear film instability and triggering inflammatory cascades, including the release of inflammatory mediators.

Normal tear osmolarity range can vary between instruments but is generally defined as less than 308 mOsm/L in both eyes and an inter-eye difference of less than 8 mOsm/L. In non-medicated SS patients, a mean tear osmolarity of 314.5 mOsm/L was found, whereas normal tear osmolarity was measured in SS patients on systemic treatment.[13]

Other clinical tests which are used more frequently overseas, mainly in the US, include the InflammaDry test which can detect the inflammatory biomarker MMP-9, and the Sjö test, an in-office blood test which tests for traditional SS biomarkers.

2016 ACR and EULAR classification criteria	
ITEM	WEIGHT
Labial salivary gland with focal lymphocytic sialadenitis and focus score > 1 foci/4mm^2	3
Anti-Ro positive	3
Ocular staining score > 5 in a least one eye	1
Schirmer's test < 5 mm / 5 min in at least one eye (unanaesthetised)	1
Unstimulated whole saliva flow rate < 0.1 mL/min	1

Table 1. The 2016 American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) classification criteria. An individual with a score of > 4 is classified as having primary Sjögren's syndrome (SS).

BE ALERT TO OTHER SYSTEMIC MASQUERADES

Diabetes

Many factors increase the risk of diabetes associated DED, including chronic hyperglycaemia, systemic hyperosmotic stress and diabetic neuropathy, which can compromise lacrimal gland function and tear film stability. The reported prevalence of DED in patients with diabetes ranges from approximately 20 per cent to 54 per cent, and is 50 per cent more common in women than in men. The risk of DED also increases with higher levels of glycated haemoglobin and with longer disease duration.[14]

Rheumatoid arthritis (RA)

An estimated two per cent of the Australian population have RA. The disease is three times more common among the female population, and women are more likely to develop the condition at an earlier age than men, with peak prevalence between 35 and 64 years of age. DED is the most common ocular complication, affecting between 44 per cent to 75 per cent of patients with RA. The severity of DED appears to be associated with longer disease duration, but not severity of RA.[15,16]

Systemic lupus erythematosus (SLE)

The prevalence of DED among patients with SLE is reported between 25 per cent and 36 per cent. Similar to SS, approximately 90 per cent of SLE patients are women, however, it most commonly affects younger women between 15–44 years of age, with peak incidence between 20 and 30 years of age. Approximately 15 per cent of SLE patients report onset of symptoms including DED before 18 years of age.[17, 18]

Grave's disease

DED affects approximately 15 per cent of patients with Grave's disease, with more common ocular complications such as exophthalmos and lagophthalmos, affecting more than 80 per cent of patients. It has been reported that signs and symptoms such as exophthalmos and lagophthalmos are more common in men, whereas ocular pain and DED are more common in women.[19]

Skin conditions such as Rosacea

Rosacea affects up to 10 per cent of the population with peak incidence between 40 and 60 years of age. It is 50 per cent more common in women than in men. Ocular side effects occur in approximately 65 per cent of patients with rosacea, with DED associated with higher levels of lid margin inflammation, anterior blepharitis, demodex and meibomian

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gland dysfunction.[20] It is important to be aware that, in some instances, skin conditions may not be immediately obvious due to the application of makeup.

Management

There is currently no cure for SS. Treatments aim to improve patient symptoms and quality of life. In SS patients, it is important to address and manage other co-existing ocular conditions such as anterior blepharitis, demodex, meibomian gland dysfunction and skin conditions.

Many dry eye and SS patients will respond well to conventional home therapies such as artificial tears, hot compresses, lid hygiene and topical anti-inflammatory eye drops. Advanced treatments such as Intense Pulsed Light and Lipiflow may also be useful in improving both the signs and symptoms of DED. SS patients may also benefit from treatments including punctal plugs, scleral lenses and topical cyclosporin. These treatments aim to boost tear volume, hydrate the cornea, and increase tear production respectively.

SS patients may also consider oral disease-modifying anti-rheumatic drugs such as Hydroxychloroquine (Plaquenil) to improve symptoms, especially in secondary SS. With these patients, co-management with the patient's general practitioner and rheumatologist is important due to potential for systemic and ocular toxicity.

Conclusion

Although clear clinical signs pointing to DED may be obvious, optometrists should remain vigilant and consider the association between DED and systemic conditions. In autoimmune conditions such as SS, symptoms including dry eye were found to precede systemic complications by approximately 10 years and predominantly affected women. Timely diagnosis can allow for more effective management of the condition and reduce the subsequent risk of more serious complications. ▲

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Blepharitis management

Study authors report that dedicated eyelid cleanser outperforms baby shampoo

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Blepharitis is one of the most frequently encountered ocular conditions in clinical practice (Figure 1) and is estimated to affect up to 47 per cent of patients presenting to eye-care practitioners.[1,2] Characterised by chronic inflammation of the eyelids, the condition can affect both the anterior and posterior eyelid lamellae, with involvement of the eyelashes, periocular skin, lid margins and meibomian glands.[1-3] Blepharitis can have a significant impact on the ocular comfort, vision quality and productivity of sufferers, and is associated with a myriad of signs and symptoms, including ocular surface irritation, conjunctival hyperaemia, palpebral erythema, eyelid crusting, dry eye syndrome and intermittent visual disturbance.[1,2] In the most severe cases, chronic inflammation of the ocular surface may also lead to the development of irreversible sight-threatening corneal damage.[2]

The complex multifactorial pathophysiological mechanisms underlying the development of chronic inflammation in blepharitis are not fully understood,[1-3] however, the over-colonisation of bacteria in eyelid tissue observed in blepharitis patients is thought to induce hypersensitivity reactions leading to ocular surface inflammation.[1] Moreover, the lipolytic exoenzymes released by colonising bacterial species, might also trigger further inflammatory cascades and contribute towards tear film destabilisation through the degradation of constituents of the surface lipid layer.[4] In addition, ocular infestation with Demodex mites is considered to be another important cause of blepharitis, through triggering an overactivation of host immune and inflammatory responses.[5]

The natural history of blepharitis is characterised by intermittent episodes of inflammatory exacerbations, which are often associated with higher levels of bacterial load.[1,2] In addition to the treatment of the acute inflammatory flares with antibiotics and anti-inflammatory medications, routine use of eyelid hygiene techniques and warm compress therapy are also commonly recommended for long term symptomatic control and the preventative management of inflammatory exacerbations.[1-3] Diluted baby shampoo has traditionally been recommended for this purpose and remains widely used today, although an increasing range of dedicated eyelid cleansing formulations continues to become commercially available.[3,6]

Study methodology

The clinical efficacy of a dedicated eyelid cleansing formulation (TheraTears SteriLid) was compared against a 1:10 diluted baby shampoo solution (Johnson's No More Tears) prepared in sterile conditions in a recent double-masked, randomised paired-eye trial conducted by the University of Auckland's Ocular Surface Laboratory.[7]

A total of 43 participants exhibiting clinical signs of blepharitis on slitlamp examination at baseline were recruited. Participants were randomised to apply the dedicated eyelid cleanser to one eye, and the diluted baby shampoo to the fellow eye, and then rinse, two times a day, for a period of four weeks. Investigator and participant masking were achieved through the supply of

Continued page 24

Parameter	Measurement	Dedicated eyelid cleanser treatment	Baby shampoo treatment
Blepharitis symptoms	SANDE score	Improved	Improved
	SPEED score	Improved	Improved
Anterior blepharitis signs	Seborrhoeic eyelash crusting	Improved	Improved
	Trichiasis	Improved	Improved
Ocular Demodex infestation	Eyelash cylindrical collarettes	Improved	No change
Meibomian gland health	Tear film lipid layer thickness	Improved	No change
	Meibomian gland capping	No change	Worsened
Ocular surface inflammation	MMP-9 expression levels	Improved	No change
Ocular surface desiccation	Superior lid margin staining	Improved	Improved
	Inferior lid margin staining	Improved	No change
Ocular surface epithelium goblet cell health	MUC5AC expression levels	No change	Worsened

Table 1. Summary of significant study results

Blepharitis management

From page 23

the two formulations in identical foam pump bottles labelled with the eye randomised to application.

A predetermined computer-generated randomisation schedule dictated treatment allocation to consecutively presenting participants thereby eliminating risk of bias in treatment allocation. Ocular surface characteristics, tear film quality, validated symptomology questionnaires, and conjunctival impression cytology markers were evaluated at baseline, and at the end of the four-week treatment period.

Clinical blepharitis signs and symptoms

A summary of the significant study results is provided in Table 1. Overall, the findings showed that four-week treatment with both the dedicated eyelid cleanser and diluted baby shampoo formulations was associated with improvements in clinical signs and symptoms of blepharitis.

Significant reductions in the SANDE and SPEED symptomology scores, as well as in superior lid margin staining, seborrhoeic eyelash crusting, and trichiasis grades were observed in both treatment groups. These findings would support current recommendations for the routine use of eyelid hygiene regimens in blepharitis patients for providing ongoing symptomatic relief.[1-3]

However, the dedicated eyelid cleanser also demonstrated superior clinical efficacy relative to diluted baby shampoo treatment in this cohort of blepharitis patients. A greater reduction in SANDE symptomology scores was detected, while improvements in inferior lid margin staining and cylindrical eyelash collarette grades were limited only to the dedicated eyelid cleanser treatment group. Cylindrical eyelash collarettes (Figure 2) are considered pathognomonic for ocular infestation with Demodex mites,[2] which is emerging as a significant cause for chronic blepharitis.[5] The clinical efficacy of the dedicated eyelid cleansing formulation in reducing cylindrical eyelash collarettes in the study was consistent with the anti-demodectic activity observed in a separate *in vitro* study conducted by the University of Auckland's Ocular Surface Laboratory, thought to be attributed to its tea tree oil and linalool constituents.[8]

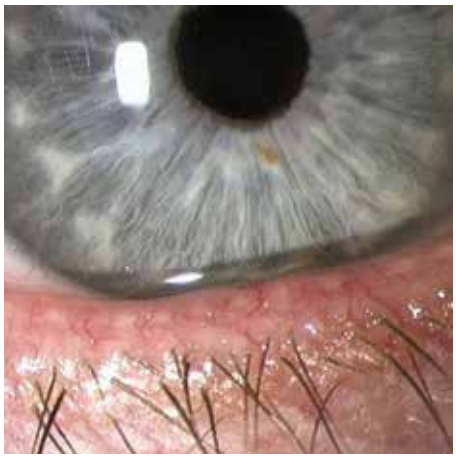

Figure 1. Slitlamp biomicroscopic signs characteristic of blepharitis

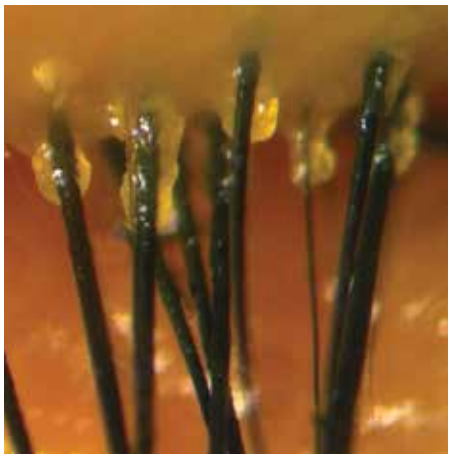

Figure 2. Cylindrical collarettes on slitlamp biomicroscopy

Biomarkers of ocular surface inflammation and goblet cell function

In agreement with the trends observed in clinical signs and symptoms, biomarker analysis of conjunctival impression cytology samples identified improvements in ocular surface inflammatory markers that were limited to the dedicated eyelid cleanser treatment. MMP-9 expression levels were observed to decrease significantly with the dedicated eyelid cleanser formulation, but no significant change was detected in the baby shampoo treatment group. MMP-9 is an important matrix-degrading enzyme,[9] which has been implicated in ocular surface inflammatory pathways.[10-12] The release of MMP-9 from corneal epithelial cells is thought to be triggered by signalling cascades related to tear film hyperosmolarity,[13] and elevated levels have been observed in patients with dry eye disease.[9,14] The reduction in MMP-9 expression levels would therefore further support the superior anti-inflammatory effects demonstrated by the dedicated eyelid cleanser treatment.

Interestingly, MUC5AC expression levels were observed to fall with baby shampoo treatment, but did not change with dedicated eyelid cleanser application. MUC5AC is a goblet cell-specific mucin, and a marker of goblet cell function and density within the ocular surface epithelium.[15-17] Goblet cell integrity can be compromised by ocular surface inflammation and tear film hyperosmolarity, resulting in a reduction in MUC5AC levels.[18] The decrease in MUC5AC levels observed with diluted baby shampoo treatment would suggest the possible presence of pro-inflammatory agents, which might potentially explain the smaller improvements in clinical signs and symptoms observed with baby shampoo than with the dedicated eyelid cleanser application.

It is conceivable that the pro-inflammatory agents within the baby shampoo formulation could partially offset its therapeutic benefits. In addition, meibomian gland capping was also observed to worsen with diluted baby shampoo treatment, but not dedicated eyelid cleanser application, and thought to be potentially associated with gland orifice keratinisation related to ocular surface inflammation.[19]

Subjective preference

Finally, a significantly greater proportion of participants expressed preference for the dedicated eyelid cleanser over the diluted baby shampoo formulation in this double-masked randomised study (Figure 3).

Given the chronic nature of blepharitis, routine long-term use of eyelid hygiene regimens are required to sustain symptomatic improvements.[1,2] The therapeutic potential of self-applied treatments can be limited by patient adherence to recommendations, which might be influenced by patient preference, adverse effects, perceived

efficacy and convenience.[20]

In addition to a higher level of patient preference and the larger reduction in SANDE symptomology scores observed in the dedicated eyelid cleanser group, it was noted that a greater proportion of participants reported ocular stinging with the baby shampoo treatment than with the dedicated eyelid cleanser.

Furthermore, although the dedicated eyelid cleanser is distributed commercially in foam pump bottles, this is not the case for undiluted baby shampoo. Patients with blepharitis who use baby shampoo solutions for eyelid hygiene regimens would therefore need to dilute and lather the formulation themselves prior to application, which might be perceived as a more inconvenient and time-consuming process, as well as risking dilution errors. The combination of the above factors would appear to favour longer term compliance with the use of the dedicated eyelid cleanser than with that of diluted baby shampoo solutions, despite the greater financial cost of the former.

Conclusion

In summary, the results of the double-masked, randomised paired-eye trial conducted by the University of Auckland's Ocular Surface Laboratory demonstrated that four-week treatment with both the dedicated eyelid cleanser and diluted baby shampoo formulation were associated with improvements in clinical signs and symptoms of blepharitis. However, the dedicated eyelid cleanser demonstrated superior clinical efficacy in blepharitis patients, and this was confirmed by conjunctival impression cytology biomarker analysis. The potential for diluted baby shampoo treatment associated with a decline in goblet cell health warrants further investigation in future research. ▲

Sang H Lee, Dr Isabella Cheung, Salim Ismail and Professor Trevor Sherwin, are acknowledged for their contributions as co-authors to the original manuscript as published in The Ocular Surface Journal in January 2018. (Sung J, Wang MTM, Lee SH, Cheung IMY, Ismail S, Sherwin T, Craig JP. Randomized double-masked trial of eyelid cleansing treatments for blepharitis. *Ocul Surf* 2018 Jan; 16 (1): 77-83. doi: 10.1016/j.jtos.2017.10.005)

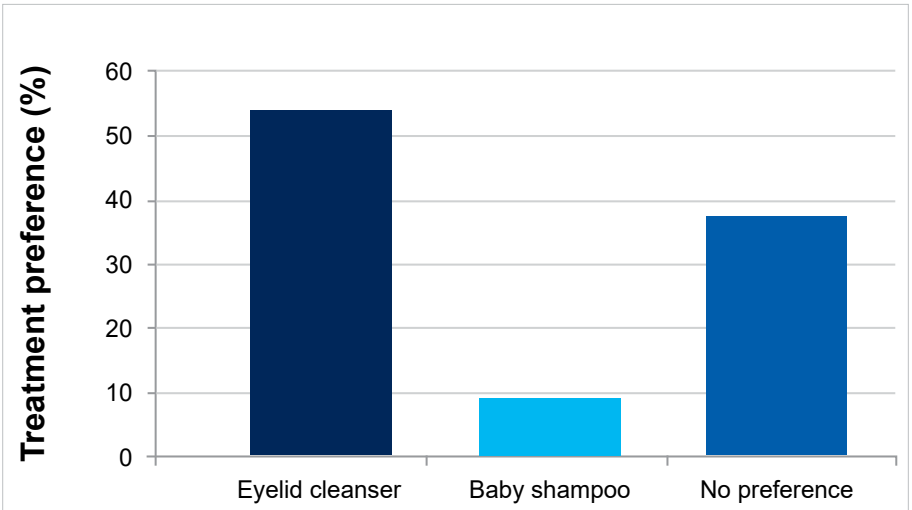

Figure 3. Subjective treatment preference of blepharitis patients in the double-masked randomised paired-eye trial. Each bar represents the percentage of participants that reported preference for the dedicated eyelid cleansing formulation, diluted baby shampoo solution, or expressed no preference.

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PBS list of medicines prescribed by optometrists

Revised November 2018

Note: To satisfy PBS criteria for combination antiglaucoma agent, patient must have been inadequately controlled with monotherapy

	Product	Max qty	Repeats
ANTI-GLAUCOMA PREPARATIONS			
Betaxolol eye-drops, solution, 5 mg (as hydrochloride)/mL, (0.5%), 5 mL	Betoptic, BetoQuin	1	5
Bimatoprost eye-drops 300 mcg/mL (0.03%), 3 mL	Lumigan, Bimatoprost Sandoz, Bimtop	1	5
Bimatoprost eye-drops 300 mcg/mL (0.03%) 30 x 0.4 mL unit doses	Lumigan PF*	1	5
Bimatoprost with timolol eye-drops containing bimatoprost 300 mcg/mL (0.03%) with timolol 5 mg (as maleate)/mL (0.5%), 3 mL	Ganfort 0.3/5	1	5
Bimatoprost with timolol eye-drops containing bimatoprost 300 mcg/mL (0.03%) with timolol 5 mg (as maleate)/mL (0.5%), 30 x 0.4 mL unit doses	Ganfort PF 0.3/5*	1	5
Brimonidine tartrate eye-drops 1.5 mg/mL (0.15%), 5 mL	Alphagan P 1.5	1	5
Brimonidine tartrate eye-drops 2.0 mg/mL (0.2%), 5 mL	Alphagan Enidin	1	5
Brimonidine with timolol eye-drops containing brimonidine tartrate 2 mg/mL (0.2%) with timolol 5 mg (as maleate)/mL (0.5%), 5 mL	Combigan	1	5
Brinzolamide eye-drops 10 mg/mL (1%), 5 mL	Azopt, BrinzoQuin	1	5
Brinzolamide 10 mg/mL (1%) eye-drops containing brimonidine tartrate 2 mg/mL (0.2%), 5 mL	Alphagan, Enidin	1	5
Brinzolamide with timolol eye-drops containing brinzolamide 10 mg/mL (1%) with timolol 5 mg (as maleate)/mL (0.5%) 5 mL	Azarga	1	5
Dorzolamide eye-drops 20 mg (as hydrochloride)/mL (2%), 5 mL	Trusopt, Trusamide, APO-Dorzalamide	1	5
Dorzolamide with timolol eye-drops containing dorzolamide 20 mg (as hydrochloride)/mL (2%) with timolol 5 mg (as maleate)/mL (0.5%), 5 mL	Cosopt, Cosdor, Dorzolamide/ Timolol 20/5 (AN, APO, Sandoz)	1	5
Latanoprost eye-drops 50 mcg/mL (0.005%), 2.5 mL	Lanpro, Latanoprost (APO, Actavis, GH, Sandoz), Xalaprost, Xalatan	1	5
Latanoprost with timolol eye-drops containing latanoprost 50 mcg/mL (0.005%) with timolol 5 mg (as maleate)/mL (0.5%), 2.5 mL	Xalacom, Xalamol 50/5, Lantim, Latanaprost/Timolol (AN, APO, Sandoz)	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 10 mg/mL (1%), 15 mL	Isopto Carpine	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 20 mg/mL (2%), 15 mL	Isopto Carpine	1	5
Pilocarpine eye-drops containing pilocarpine hydrochloride 40 mg/mL (4%), 15 mL	Isopto Carpine	1	5
Tafluprost eye-drops 15 mcg/ml (0.0015%) 30 x 0.3mL unit doses	Saflutan*	1	5
Timolol eye-drops 5 mg (as maleate)/mL (0.5%), 5 mL	Timoptol	1	5
Timolol eye-drops (gellan gum solution) 2.5 mg (as maleate)/mL (0.25%), 2.5 mL	Timoptol XE	1	5
Timolol eye-drops (gellan gum solution) 5 mg (as maleate)/mL (0.5%), 2.5 mL	Timoptol XE	1	5
Travoprost eye-drops 40 mcg/mL (0.004%), 2.5 mL	Travatan	1	5
Travoprost with timolol eye-drops containing travoprost 40 mcg/mL (0.004%) with timolol 5 mg (as maleate)/mL (0.5%), 2.5 mL	Duotrav	1	5

* Unit doses

	Product	Restriction	Max qty	Repeats
ANTI-VIRAL EYE PREPARATIONS				
Aciclovir eye ointment 30 mg/g (3%), 4.5 g	Zovirax	Restricted: Herpes simplex keratitis	1	0

NOTE: Zovirax (aciclovir 3% ointment) ceased production in 2018. At the time of printing (November 2018), replacement product AciVision (aciclovir 3% ointment) has TGA approval, but is not PBS listed.

PBS list of medicines prescribed by optometrists

Revised November 2018

	Product	Restriction	Max qty	Repeats
ANTIBIOTICS				
Chloramphenicol eye-drops 5 mg/mL (0.5%), 10 mL	Chlorsig	Restricted: For treatment of patients identifying as Aboriginal or Torres Strait Islander	1	2
Ciprofloxacin† eye-drops 3 mg /mL (0.3%), 5 mL	CiloQuin, Ciloxan	Authority required: bacterial keratitis	2	0
Framycetin sulfate eye-drops 5 mg/mL (0.5%), 8 mL	Soframycin		1	2
Gentamicin eye-drops 3 mg/mL (0.3%), 5 mL	Genoptic	Restricted: Suspected pseudomonal eye infection	1	2
Ofloxacin† eye-drops 3 mg/mL (0.3%), 5 mL	Ocuflox	Authority required: bacterial keratitis	2	0
Tobramycin eye-drops 3 mg/mL (0.3%), 5 mL	Tobrex	Restricted: Suspected pseudomonal eye infection	1	2
Tobramycin eye ointment 3 mg/g (0.3%), 3.5 g	Tobrex	Restricted: Suspected pseudomonal eye infection	1	0

†**NOTE:** must be in consultation with an ophthalmologist

ANTI-INFLAMMATORY AGENTS				
Dexamethasone eye-drops 1 mg /mL (0.1%), 5 mL	Maxidex		1	0
Fluorometholone eye-drops 1 mg/mL (0.1%), 5 mL	Flucon, FML Liquifilm		1	0
Fluorometholone acetate eye-drops 1 mg/mL (0.1%), 5 mL	Flarex		1	0
Hydrocortisone acetate eye ointment 10 mg/g (1%), 5 g	Hycor		1	0
Prednisolone acetate with phenylephrine hydrochloride eye-drops 10 mg-1.2 mg/mL (1%-0.12%), 10 mL	Prednefrin Forte	Restriction: Uveitis	1	0
TEAR SUPPLEMENTS		Restricted: Severe dry eye including Sjögren's syndrome		
Carbomer 980 eye gel 2 mg/g (0.2%), 10 g	Optifresh eye gel	As above	1	5
	PAA	As above	1	5
	Viscotears	As above	1	5
Carmellose sodium eye-drops 5mg/mL (0.5%) with glycerol 9 mg/mL (0.9%), 15ml	Optive	As above	1	3
Carmellose sodium eye-drops 10 mg/mL (1%), 15 mL	Refresh Liquigel	As above	1	5
Carmellose sodium eye-drops 5 mg/mL (0.5%), 15 ml	Refresh Tears plus	As above	1	5
Hypromellose eye-drops 3 mg/mL (0.3%), 15 mL (contains sodium perborate)	In a Wink Genteal	As above	1	5
Hypromellose eye-drops 5 mg/mL (0.5%), 15 mL	Methopt	As above	1	5
Hypromellose 3 mg/mL (0.3%) with carbomer 980 2 mg/g (0.2%) ocular lubricating gel, 10 g	HPMC PAA Genteal Gel	As above	1	5
Hypromellose 3 mg/mL (0.3%) with dextran eye-drops 1 mg/mL (0.1%), 15 mL	Poly-Tears, Tears Naturale	As above	1	5
Polyethylene glycol 400 mg/mL (0.4%) with propylene glycol 3 mg/mL (0.3%) eye-drops, 15 mL	Systane	As above	1	5

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PBS list of medicines prescribed by optometrists

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TEAR SUPPLEMENTS (cont.)		Restricted: Severe dry eye including Sjögren's syndrome		
Polyvinyl alcohol eye-drops 14 mg/mL (1.4%), 15 mL	PVA Tears, Liquifilm Tears	As above	1	5
Polyvinyl alcohol eye-drops 14 mg/mL (1.4%), 15 mL (contains sodium chorite/hydrogen peroxide as preservative)	Vistil	As above	1	5
Polyvinyl alcohol eye-drops 30 mg/mL (3%), 15 mL (contains sodium chorite/hydrogen peroxide as preservative)	Vistil Forte	As above	1	5
UNPRESERVED TEAR SUPPLEMENTS**		Authority required:		
Carbomer 974 ocular lubricating gel 3 mg/g (0.3%), single dose units 0.5 g x 30	Poly Gel	Severe dry eye syndrome in patients sensitive to preservatives in multi-dose eye-drops	3	5
Carbomer 980 eye gel 2 mg/g (0.2%), single dose units 0.6 mL x 30	Viscotears Gel PF	As above	3	5
Carmellose sodium eye-drops 5 mg/mL (0.5%), single dose units 0.4 mL x 30	Cellufresh Optifresh Tears	As above	3	5
Carmellose sodium eye-drops 10 mg/mL (1%) , single dose units 0.4 mL x 30	Celluvisc Optifresh Plus	As above	3	5
Hypromellose 3 mg/ mL (0.3%) with dextran eye-drops 1 mg/mL (0.1%), single dose units 0.4 mL x 28	Bion Tears	As above	3	5
Perfluorohexyloctane eye-drops (100%), 3mL	NovaTears	As above	1	5
Polyethylene glycol 400, 4 mg/mL (0.4%) with propylene glycol 3 mg/mL (0.3%) eye-drops, single dose units 0.8 mL x 28	Systane	As above	2	5
Sodium Hyaluronate sodium hyaluronate eye-drops 1 mg/mL (0.1%), 10 mL	Hylo-Fresh	As above	1	5
Sodium Hyaluronate sodium hyaluronate eye-drops 2 mg/mL (0.2%), 10 mL	Hylo-Forte	As above	1	5
Soy Lecithin 1% + tocopherol 0.002% + vitamin A palmitate 0.025% *eye spray*, 100 actuations	Tears again	As above	2	5
TOPICAL OCULAR LUBRICANT OINTMENTS				
Paraffin 1 g/g compound eye ointment 3.5 g	Polyvisc		2	5
Paraffin 1 g/g pack containing 2 tubes eye ointment 3.5 g	Polyvisc (2 pack), Ircal (2 pack), Refresh Night Time (2 pack)		1	5
Paraffin paraffin + retinol palmitate 138 mcg/g (0.0138%) (equivalent to 250 units/g vitamin A) eye ointment, 5 g	VitA-POS		2	5

****NOTE: UNPRESERVED TEAR SUPPLEMENTS**

Optometrists have two **Streamlined Authority Codes** for unpreserved tear supplements

- **4105** Hylo-Fresh and Hylo-Forte
- **6172** all other unit-dose ocular lubricants

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PBS Information: Authority Required (STREAMLINED): Severe dry eye syndrome in patients who are sensitive to preservatives in multi-dose eye drops.

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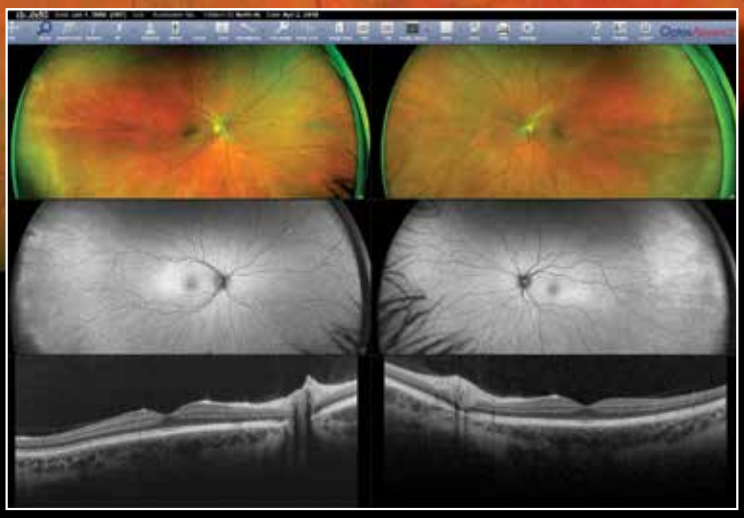

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