Comment on: A British Ophthalmic Surveillance Unit (BOSU) study into dysthyroid optic neuropathy in the United Kingdom

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In their British Ophthalmic Surveillance Unit (BOSU) study on dysthyroid optic neuropathy (DON), Wong and colleagues [1] report an annual incidence of 0.75 per million per annum, i.e. around 50 patients per year in the UK, which fits with previously published data [2]. Surprisingly however, almost half of their patients who were followed up for 9 months went on to have orbital decompression surgery (47%), despite initial medical therapy—and with a mean delay of only 2.5 months post presentation [1].

We should like to contrast this need for swift surgical intervention with evidence from our centre where we have for long used an alternative, ciclosporin-based medical regimen, unlike the BOSU study which reported predominantly i.v. methylprednisolone followed by oral steroid and occasional addition of radiotherapy (two patients), rituximab (1) or azathioprine (1). We retrospectively reviewed electronic case records spanning 23 years from our unit and identified 522 patients with thyroid eye disease (TED), of which 145 were considered sight-threatening as defined by EUGOGO [3], and 75 had DON. During the 12-month period of the BOSU study we saw one patient with DON at presentation. All 75 DON patients were followed up for between 2 and 10 years and had been treated with the Cambridge regimen: three pulses of i.v. methylprednisolone 10 mg/kg at 48-hour intervals, followed by low dose tapering oral prednisolone, starting at 30 mg, then 25, 20, 17.5, 15 mg (3 weeks at each dose) then subsequent reduction by 1 mg per month, and ciclosporin A (Neoral) starting at 2 mg/kg twice daily. As part of the regimen we

aim for a ciclosporin trough level of 150–200 micrograms/L during the first six months, then 100 to 150 mcg/L for the second six months and 50–100 mcg/L thereafter. Ciclosporin is then gradually withdrawn over six months after prednisolone has been stopped.

Seventy of the 75 DON patients (93%) recovered their pre-morbid visual acuities and 69 of 75 patients (92%) recovered pre-morbid visual fields. Interestingly, only five patients required surgical decompression of their orbits following our medical regime, with all five having presented with complicated or delayed presentations.

These data point to a potential role for ciclosporin in helping to reduce the need for orbital decompression surgery in DON. Previously, we have shown that ciclosporin therapy rapidly reduces the circulating anti-TSH receptor antibody, further evidence of its utility for TED [4]. Orbital wall decompression is associated with significant risks: the BOSU study reports one patient who developed perception of light vision following surgery and another developed intractable diplopia.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Eye and appearance characteristics of encephalocraniocutaneous lipomatosis

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Encephalocraniocutaneous lipomatosis (ECCL) is a rare neurocutaneous syndrome. The unique clinical manifestations of the disease include ocular edema or hamartoma, abnormal skin on the head and neck, and corresponding hair loss on the scalp. Historical literature on ECCL consists mainly of case reports and does not present the common features of the disease. We present the characteristic manifestations of the eye and skin to provide ophthalmologists with a fuller understanding of in ECCL.

Clinical information

Four patients, all male, aged 3–18 years, presented with ophthalmologic disorders caused by local or diffuse hyperplasia of the ocular surface and had irregular granule-like lesions on the head or neck and unilateral visible granular raised lesions on the tongue mucosal surface (Fig. 1). No brain abnormality was apparent on

skull computed tomography, and focal calcification was visible on the wall of the eye. All patients had normal intelligence and no history of seizures. ocular surface tumor was removed with conjunctival sac reconstruction or lamellar keratoplasty.

Pathological results: Two cases were corneal Sebaceous tumor (mature squamous tumor) and two cases were fibrous epithelial polyps.

Discussion

ECCL is a rare neurocutaneous syndrome with unknown etiology and multiple sporadic differences in ethnicity, gender, and family history. Since Haberland [1] described this syndrome in 1970, more than 60 instances of related disorders have been published worldwide, mainly reported via pediatrics, and neurosurgery cases [2, 3]. The main features of the syndrome include asymmetric skin damage to the head and neck, central nervous system abnormalities (CNS), ocular abnormalities, often bilaterally. hair loss in the local skin lesion area. The most common eye lesions in ECCL are ocular tumors around the eyeball and small skin nodules. Other rare eye abnormalities of the syndrome such as bilateral optic disk defects and lack of bilateral iris eyelid retraction have been reported [4].

The occurrence of ECCL may be related to genetic variation, and it is speculated that autosomal gene mutations lead to ectodermal dysplasia, while chimerism may be the cause of mesenchymal tumors and angiogenesis.

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Fig. 1 Appearance of ECCL.

A: Case 1. Left eye subconjunctival multifocal pink raised lesions. B: Case 2. Right corneal surface and left subconjunctival pink focal, smooth, bulging lesion. C: Case 3. Pink corneal smooth bulging lesion on the left cornea. D: Case 4. right eye conjunctiva, and substantial freshly appearing protrusion on the right side of the skin. E,F: case 1 and case 2. Side view: left scalp, face, and neck skin lesions and hairless area. G: case 4. Black lesions on the ipsilateral neck. H: Granular bulge of the left tongue mucosa

Syndromes that need to be differentiated from linear nevus sebaceous syndrome (LNS), and oculocerebrocutaneous syndrome (OCC). A diagnosis of OCC needs to include CNS cysts or hydrocephalus, small eyeballs with orbital cysts. Skin lesions of LNS are mainly located in the midline of the face forming a linear pattern. According to the revised ECCL diagnostic criteria (Table 1) by Moog [5] in 2009, The ECCL diagnosis of these four cases is clear.

This group of patients shared the following common clinical features of ECCL: (1) ocular lesions; (2) flaky

granular pigmentation of the area of skin loss; (3) granular mucosa visible on the surface of the tongue not observed in the previous literature. Ophthalmologists should consider the diagnosis of ECCL in their assessment if they encounter patients with these common characteristics.

There is no specific treatment for ECCL. The main ophthalmic approach is surgical removal of local bud tumors, with improvement of the cosmetic appearance as far as possible.

Table 1 Moog's revised diagnostic criteria for encephalocraniocutaneous lipomatosis (ECCL)

Eye	Skin	Central nervous system	Others systems
Major criteria	Major criteria	Major criteria	Major criteria
1. Choristoma, With or without associated anomalies	1. Proven nevus psiloliparus(NP)	1. Intracranial lipoma	1. Jaw tumor (osteoma, Odontoma or ossifying fibroma)
Minor criteria	2. Possible NP and ≥ 1 of minor criteria 3. ≥ 2 of minor criteria 2-5	2. Intraspinal lipoma 3. ≥ 2 of minor criteria	2. Multiple bone cysts 3. Aortic coarctation
1. Corneal and Other anterior chamber anomalies	Minor criteria 1. Possible NP	Minor criteria 1. Abnormal intracranial vessels,e.g. angioma,excessive vessels	
2. Ocular or eyelid coloboma	2. Patchy or streaky non-scarring alopecia (without fatty nevus)	2. Arachnoid cyst or other abnormality of meninges	
3. Calcification of globe	3. Subcutaneous lipoma(s) in Fronto-temporal region	3. Complete or partial atrophy of hemisphere	
	4. Focal skin aplasia/hypoplasia on scalp	4. Porencephalic cyst(s)	
	5. Small nodular skin tags on eyelids or between outer canthus and tragus	5. Asymmetrically dilated ventricles or hydrocephalus	
		6. Calcification(no basal ganglia	
Application of criteria for the diagnosis of ECCL			
Definite case			
1. Three systems involved,major criteria ≥ 2 ,or			
2. Three systems involved,proven NP or possible NP + ≥ 1 of minor skin criteria 2-5			
3. Two systems involved with major criteria,one of which proven NP or possible NP + ≥ 1 of minor skin criteria 2-5			
Probable case			
1. Two systems involved,major criteria in both			
2. Two systems involved,proven or possible NP			

Adopted and modified from ref. [5]

ECCL Encephalocraniocutaneous lipomatosis, NP nevus psiloliparus

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Comment on: Proposal for a new classification for ocular surface squamous neoplasia

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We read with interest Meel and Dhiman's recent proposal for a new classification for ocular surface squamous neoplasia (OSSN) [1]. The authors offer a modified criteria for conjunctival neoplasia that takes into account invasion (on ultrasound biomicroscopy (UBM)) and provides a rough guide for treatment. They suggest that OSSN of Grade III (with intraocular involvement present) should be managed with enucleation.

The potential of advanced ocular surface squamous lesions to invade through the sclera or cornea is well recognised with enucleation being the traditional management [2]. However, many studies over the past decade have shown success with globe-sparing therapy for these advanced lesions—and it is certainly our experience that invasive squamous lesions can be managed in this way [3]. Shields et al. showed that plaque brachytherapy is a safe and reliable alternative to globe removal for eyes with conjunctival squamous cell carcinoma (SCC) showing scleral invasion and/or intraocular involvement [2]. Further, Graue et al. demonstrated local tumour control in 75% of

recalcitrant conjunctival SCCs treated with electron beam radiotherapy [4].

The relevance of the American Joint Committee on Cancer (AJCC) staging of conjunctival SCC in guiding initial management was challenged in a recent work by Belleverie et al. [5]. They also suggest reclassification of the T3 category (diffuse vs deep invading) to better guide initial treatment. However, similar to previous reports, these authors also advocate the use of surface brachytherapy for scleral invasion of SCC [5].

The AJCC publications are recognised as authoritative guides for cancer staging and communicating information about cancer. Evidence-based staging is important to guide therapy and define prognosis, and the AJCC aims to help doctors design a treatment plan for individual patients. Meel and Dhiman's proposal include treatment in their modified staging system, and, although these management options are perhaps not available in their centre, we feel it would be useful to include staged options of therapy for advanced lesions as alternative to enucleation [1]. There appears to be an error in the classification table, listing Grade II lesions incorrectly as having no invasion into ocular coats on imaging, which contradicts the imaging findings and manuscript definitions of this grade.

We support the current classification system published by the AJCC, but agree with recent studies suggesting reclassification of the T3 category [5].

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Compliance with ethical standards

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Response to ‘Comment on: Proposal for a new classification for ocular surface squamous neoplasia’

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We thank McGrath and Salvi [1] for their valuable comments and suggestions.

There are no published guidelines for treatment of ocular surface squamous neoplasia (OSSN). Also, clinical spectrum of OSSN varies significantly between different continents like Africa and North America or Australia [2]. Clinical presentation is significantly delayed in resource-constrained countries, and hence use of conservative management options like plaque brachytherapy are not only limited by availability but also by feasibility.

The conventional method of treatment for OSSN is wide local surgical excision using a ‘no touch technique’ and cryotherapy of conjunctival edges. Topical treatment with chemotherapeutic agents and interferons has become popular in the past 1–2 decades due to the inherent benefits of topical treatment—treatment of a complete ocular surface, thus reducing the chances of microscopic residual disease, lesser side effects of treatment as compared to surgical excision, especially in giant or diffuse tumors and the relative ease of

administering treatment. Traditionally, enucleation is done for tumors with intraocular extension and exenteration for OSSN with orbital extension.

We agree with the authors that, technology-dependent treatment modalities, like plaque brachytherapy and proton beam therapy may not be available in resource-constrained countries. There are adequate reports in literature to show that brachytherapy effectively controls OSSN invading into the ocular coats and hence may be used as an adjuvant treatment in cases with incomplete tumor resection (Table 1) (the same has been added in the treatment options for grade II tumor in the revised table) [3]. However, its use in OSSN with overt (obvious on imaging (UBM) or clinically) intraocular extension is still being explored and needs to be evaluated in further studies [4]. We, at our center are now using adjuvant plaque brachytherapy in cases of invasive SCC, where there is microscopic residual disease in the ocular coats after surgery.

The proposed classification attempts to address the concerns with AJCC classification, as reported by previous studies and intends to give a rough guideline for treatment based on most commonly available treatment modalities [4]. While enucleation and exenteration remain the most common method of treatment for tumor with ocular and orbital extension, respectively, the treatment scenario for OSSN with

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Table 1 Proposal for the new classification (revised)

Group/grade	Limbal involvement (clock hours)	Maximal basal diameter (mm)	Imaging findings	Treatment recommended	Risk with upfront surgical excision
Grade I: OSSN with no invasion into ocular coats clinically ^a /on imaging (UBM)					
A (Small)	≤3	≤5	No invasion into ocular coats/globe on UBM	Surgical excision with edge control	Minimal risk of side effects
B (Large)	>3 to < 6	5–15	No invasion into ocular coats/globe on UBM	Immunotherapy/Immunoreduction f/b surgical excision	Moderate risk of side effects (Limbal stem cell deficiency, symblepharon formation)
C (Diffuse)	≥6	≥15	No invasion into ocular coats/globe on UBM	Immunoreduction with interferons f/b surgical excision	High risk of side effects, high risk of recurrence
Grade II: OSSN with invasion into ocular coats (sclera/corneal stroma) on imaging					
	Any	Any	Scleral or corneal stromal invasion on UBM	Excision with lamellar sclerectomy or keratectomy +cryotherapy of margins and base/adjuvant plaque brachytherapy for residual tumor at base	
Grade III: OSSN with intraocular invasion					
	Any	Any	Intraocular involvement present (clinically/UBM)	Enucleation	–
Grade IV: OSSN with intraorbital extension					
	Any	Any	Orbital extension on CT/MRI	Exenteration	–

UBM ultrasound biomicroscopy, *CT* computed tomography scan, *MRI* magnetic resonance imaging, *f/b* followed by

^aClinically as suggested by mobility of conjunctival lesions in non-limbal tumors

no or limited invasion has changed significantly. Surgery is mainly replaced with topical therapy or is used for residual disease after chemoreduction or immunoreduction. The proposed classification helps to decide treatment especially in this category. I thank the authors for picking up the printing error in Table 1 (grade II tumors are tumors with extension into ocular coats on UBM or clinically, the same has been corrected in the revised table).

Till the time, further studies evaluate and define the role of other possible treatment options for intraocular and orbital disease like external beam radiotherapy, brachytherapy, or intraorbital interferon injections for a possible staged management approach; this classification may help guide treatment with the more established treatment options [5, 6].

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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The positive impact of e-mail referrals on access to specialist macula services

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Patients suspected of having neovascular age-related macular degeneration (nAMD) requires rapid access to specialist clinics for confirmatory diagnosis and subsequent treatment. The Royal College of Ophthalmologists (RCOphth) guidelines [1] recommend <7 days delay between initial referral in primary care to assessment with a specialist in macular disease, and for those patients requiring treatment <7 days delay between specialist consultation and initial treatment. In order to achieve this the Oxford Eye Hospital utilises the ‘Wet AMD rapid access referral form’ developed by the Thames Valley Macular Group, adopted by the RCOphth and endorsed by the Macular Society and RNIB for all referrals to the dedicated rapid-access clinic for patients with suspected nAMD [2]. To address the concern that rapid-access referrals were being missed and booked into routine clinics, a streamlined e-mail referral system was created using a dedicated nhs.net email account from August 2014.

Despite this system being widely shared with primary care providers, many referrals to our service are via other routes. We have audited the delay in access to specialist clinic for each referral route for 98 new AMD referrals seen in clinic between January and March 2018. Only 33.7% of referrals were received thorough the dedicated e-mail address, with 19.4% via the walk-in eye casualty service or other sub-specialist clinics and the remaining 46.9% via the patients' general preactioners (GPs). Figure 1 shows

the delay between referral and first specialist review for patients in each of the three referral groups. No patients referred via their (GP) were seen within the 7 days target. The differences in the proportions of patients seen between the e-mail referral group and GP referral group within 2 weeks ($p = 0.0014$) and within 3 weeks ($p < 0.0001$) were statistically significant (chi-squared test).

Overall 28.6% of patients referred were found to have nAMD in at least one eye. Figure 2 shows the delay between referral and specialist review for those patients found to have nAMD and those with other diagnoses. It shows that many patients who are subsequently confirmed to have nAMD are facing delays in accessing specialist review.

This work shows that, while there are other challenges in seeing patients in a timely manner, the use of a dedicated e-mail referral system for nAMD can significantly reduce delays in patients being seen in specialist macular clinics compared to traditional GP-centred referral systems, and the importance of reinforcing the use of this system by optometrists and other providers of primary ophthalmic services in the community. It also highlights the need for more training of community optometrists to ensure that the rapid access pathway is used only for nAMD.

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Fig. 1 Delay between referral and specialist review by referral type

Fig. 2 Delay between referral and specialist review by diagnosis

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Compliance with ethical standards

Conflict of interest Susan Downes Disclosure: PI on relevant commercially sponsored trials in last 5 years: Novartis, Bayer, and

Alcon. Prof Susan Downes has received honoraria in the past 15 years from Novartis and Bayer for speaking at educational meetings, as well as travel expenses from Ely Lilly as chair for diabetic retinopathy screening meetings, and Novartis to attend educational meetings in Medical Retina pre 2010. She is a PI on a number of commercial trials (Novartis, Roche, Bayer, Allergan, among others), and has received a bursary for a research nurse practitioner, and equipment (visudyne pump for photodynamic therapy) and funding to carry out genetic testing for a research project from Novartis. She also has been a co-PI or PI on grants from Wellcome, UK Fighting Blindness RP, Fight for Sight and UK NIHR/CRN funding. The remaining authors declare that they have no conflict of interest.

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Accuracy of pinhole visual acuity at an urban Indian hospital

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The World Health Organization-endorsed rapid assessment of avoidable blindness (RAAB) survey employs pinhole acuity to distinguish between refractive error versus conditions not correctable with eyeglasses, but few studies have validated this approach [1].

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Methods

Ethical committees at the University of California, San Francisco and Narayana Nethralaya Eye Hospital approved this study. A consecutive series of patients aged ≥50 years visiting the refraction clinic at Narayana Nethralaya Eye Hospital (Bangalore, India) in September 2015 had presenting vision and pinhole vision assessed using an ETDRS chart in a fully illuminated room, and then had a manifest refraction by an experienced optometrist. Analyses are reported with bootstrapped 95% confidence intervals with resampling at the participant level to account for non-independence of eyes.

Results

We assessed 204 eyes from 104 individuals (mean age 63.4 ± 7.8 years, 51.9% female). Mean spherical equivalent after manifest refraction was -0.31 (95% confidence interval [CI]: -0.07 to -0.60). Mean uncorrected visual acuity was 0.43 logMAR units (95% CI: 0.38 – 0.49), mean best corrected visual acuity (BCVA) was 0.16 (95% CI: 0.13 – 0.19) and mean pinhole acuity was 0.15 (95% CI: 0.12 – 0.18). Pinhole acuity had high agreement with BCVA (intraclass correlation coefficient 0.97 , 95% CI: 0.96 – 0.98 ; Fig. 1). On average, pinhole acuity was less than a letter different from BCVA (mean 0.4 letters better, 95% limits of agreement by Bland–Altman method: four letters worse to five letters better). The magnitude of improvement on pinhole testing was correlated with the magnitude of spherical equivalent from refraction (Spearman's $\rho = 0.68$, $P < 0.001$; Fig. 2).

Of 204 eyes, 21 (10.3%) had visual impairment even after subjective refraction (BCVA worse than 20/60). When treated as a diagnostic test for visual impairment not correctable with eyeglasses, pinhole acuity provided high discriminative ability, with an area under the receiver operating characteristics (ROC) curve of 0.99 (95% CI: 0.97 – 1.0). Pinhole acuity worse than 20/60 was 85.7% sensitive (95% CI: 59.1–100%) and 100% specific (98.0–100%) for detecting visual impairment not correctable with glasses, and had a positive predictive value of 100% (95% CI: 81.4–100%).

Fig. 1 Correlation between measurements of best spectacle corrected visual acuity and pinhole acuity. Points are weighted; the area of the circles represents the number of observations at each coordinate

Fig. 2 Relationship between improvement with pinhole occlusion and refractive error. Eyes were stratified according to how many lines of improvement were achieved with pinhole occlusion. The distribution of spherical equivalent for each stratum is depicted as a box-and-whiskers plot

Conclusions

Previous studies of patients with diabetic retinopathy or low vision found that pinhole acuity was biased relative to BCVA, with pinhole acuity ~ 1 line worse than BCVA [2, 3]. In contrast, we found essentially no bias in this population from a refraction clinic in India. The reason for the discrepancy is unclear, but the pinhole occluder may cause more visual degradation in those with retinal pathology than in a general population like ours [2]. The estimates of sensitivity and specificity of pinhole acuity as a test for visual impairment are consistent with prior reports, and suggest that estimates of refractive error based on pinhole occlusion should not overestimate the prevalence of disease [4].

In summary, pinhole acuity agreed well with BCVA and was a specific test for visual impairment not correctable with eyeglasses. These results suggest that pinhole occlusion is a valid gauge of refractive error in the RAAB survey or other community-based surveys.

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Compliance with ethical standards

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Time to drop the phenylephrine from the paediatric cycloplegia protocol: informing practice through audit

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Cycloplegic retinoscopy is the gold standard refraction approach in children. Various protocols are in use to achieve cycloplegia during outpatient appointments. Many use not only the muscarinic antagonist, cyclopentolate (CP), which paralyses the ciliary muscle, but also the alpha-adrenergic agonist, phenylephrine (PE), which as a mydriatic paralyses the iris constrictor, but has no effect on the ciliary muscle. Whilst mydriasis facilitates visualisation of the retinoscopy reflex, there is a risk of underestimating hypermetropia. Published evidence suggests that repeated

instillation of CP only is effective even for brown and very dark irides [1–3].

To develop a Patient Group Directive (PGD) we carried out a two-cycle audit (CA18/PA/02). The first round evaluated our current protocol: blue iris, CP 1% once (0.5% if age < 3 months); brown iris, CP/PE 2.5% once; very dark iris, CP/PE twice, 10–15 min apart; repeated if pupils still constrict on pentorch illumination. As standard, we set full dilation in 90% within 30 min, i.e. the level expected for blue irides with a single CP drop [4].

In the second round, we only included children with brown or very dark iris, administering CP twice or three times, respectively, 10–15 min apart.

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Table 1 Ethnic background and iris colour of children assessed in this audit

	Round 1		Round 2	
	<i>n</i>	%	<i>n</i>	%
<i>Ethnicity</i>				
Afro-Caribbean	5	9	10	20
Asian	7	13	19	37
Caucasian	44	79	20	39
Chinese			1	2
Other			1	2
<i>Iris colour</i>				
Blue	32	57		
Brown	11	20	14	27
Very dark	13	23	37	73

Fig. 1 Proportion of well-dilated pupils in rounds 1 and 2 of the audit. Eyes with blue irides are well dilated after one application of cyclopentolate (CP). In brown irides, application of CP twice increases the proportion of well-dilated pupils, and in very dark irides, application of CP three times is effective. Phenylephrine does not appear to enhance this effect

We assessed pupil constriction to pentorch illumination, standard when deciding whether additional drops are required. We also noted time from instillation of the first drop to pentorch test.

We evaluated 107 consecutive children (Table 1). Round 1 found that pupils were dilated in 97% of children with blue, 73% with brown, and 23% with very dark iris (Fig. 1), at a mean 24 min (SD 18) after first drop. Repeat instillation increased success to 100%, 91%, and 85%, respectively. In

the second round, pupil dilation was achieved in all children with brown iris, and in 89% with very dark iris, at a mean 32 min (SD 13) after first instillation.

Our use of pupil constriction as outcome measure, which assesses mydriasis, not cycloplegia, is a limitation. However, as we found that better dilation is achieved without the use of PE, this audit has changed our practice and contributed positively to the development of the PGD.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Do corneas melt in the Scottish summer? A 10-year review of corneal perforations requiring cyanoacrylate gluing in theatre at a tertiary referral centre

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Previous studies have identified the potential role of temperature and barometric pressure in contributing to a flare of inflammatory symptoms in susceptible rheumatological patients, but this association is controversial and not definitive [1, 2]. Joint inflammation is due in part to the pro-inflammatory role of matrix metalloproteinases (MMPs); enzymes which also have a destructive role towards the corneal extracellular matrix [3]. We wanted to perform a 10-year review of corneal perforations requiring cyanoacrylate gluing in theatre at our university tertiary referral centre to assess for any seasonal association [4].

Patients who underwent emergency gluing procedures in theatre for corneal perforation at Gartnavel General Hospital, Glasgow between 2008 and 2017 were identified from theatre logbooks and their electronic records retrospectively analysed. Audit data included patient demographics, date of perforation, ocular co-morbidities and any associated systemic conditions.

There were 65 episodes in 43 patients of corneal perforation requiring gluing in this 10-year period. All identified cases were treated with application of cyanoacrylate glue. The majority of perforations (27/43; 63%) occurred in patients >60 years of age, and of female gender (25/43; 58%). Of the 43 patients, ten had an underlying systemic connective tissue disorder such as rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE), nine had infectious keratitis, six had an inflammatory ocular surface (rosacea, ocular cicatricial pemphigoid, blepharitis), five were graft failures, three had corneal ectasias, seven fell into the ‘other causes’ category (including trauma, exposure, post-LASIK), and no clear cause was documented in three patients. There

were five patients who had three or more episodes of perforation; underlying diagnoses in these patients included Logistic syndrome, SLE and rosacea keratitis.

There was a slightly higher incidence of corneal perforations in the spring and summer months (17 episodes in spring, 22 summer, 13 autumn, 13 winter). This association did not reach statistical significance (Chi-square $p = 0.485$). With respect to those patients with underlying systemic connective tissue disorders, eight episodes occurred in the spring/summer months and eight in autumn/winter (see Figs. 1 and 2).

Average temperatures in Scotland range from 3 to 15 degrees Celsius (°C), with mean and median temperatures of 9 °C. [See ‘Scotland’s Environment’ from the Scottish Government, accessible at <https://www.environment.gov.scot/media/1185/climate-climate.pdf>].

We did not identify an increase in corneal perforations according to traditionally colder seasons in Scotland; rather, there was a slightly higher incidence in the spring/summer. This was not statistically significant, possibly due to the small sample size and the lack of extreme temperatures between the Scottish seasons. We could not identify any reports linking weather conditions and corneal melting in the ophthalmic literature. Disease-modifying anti-rheumatic drugs have previously been shown to improve the visual outcome in rheumatological patients with corneal melting, but this only implicates the presence of cellular inflammation, not the contributing factors for a flare in the underlying inflammatory condition [5]. A larger prospective study analysing these factors would be required to explore any link between seasonal variation and corneal melting leading to perforation.

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Fig. 1 Graph illustrating number of corneal perforations requiring gluing by month of year from 2008–2017

Fig. 2 Clinical photographs illustrating use of cyanoacrylate glue in the management of corneal perforations, either as direct application or in association with a plastic disc (punched from the plastic drape by a skin biopsy trephine)

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

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Iatrogenic cannula-associated ocular injuries during anterior segment surgery: time to re-think luer-lock design?

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Cataract surgeons are aware of potential iatrogenic ocular injuries from accidental cannula release during injections of solutions or ophthalmic viscosurgical device (OVD) [1, 2]. Prevention advice is simple. Surgeons and theatre nurse practitioners should be aware of the complication, taught to check instrument security and comply with manufacturers user instructions. Surgeons should firmly hold the cannula base. Universal adoption of luer-lock syringes has been established. Despite these measures however, events still occur.

Although rare (with possible under reporting), incidence during cataract surgery is between 0.009 [1] and 0.07% [2]. Serious ocular injuries can occur with visual loss being reported particularly with retinal damage [2]. Despite efforts to increase awareness, events still occur. It appears the standard advice to check for tight adherence and hold the cannula hub during injection is not enough to adequately mitigate risk. Even apparently tight fitting cannulas have been reported to dislodge [3], with reports of both luer-lock adapter and cannula becoming detached from the syringe, acting as a projectile [4]. It is still possible that surgeon and theatre nurse both fail to screw and tighten the luer-lock connection or cross threading could occur.

The author (CW) has first-hand experience of being handed an OVD with the luer-lock being accidentally removed by the theatre nurse. Instead of the 'tip cap' of an Amvisc (Bausch and Lomb, Kingston Upon Thames, UK) being screwed off, the entire luer-lock system was removed (by a pulling motion) and cannula affixed, contrary to the

manufacturer's instructions (Fig. 1). A twisting/tightening motion can be performed by the surgeon, but unless direct visual inspection of the device is performed, it will not be immediately evident that the luer-lock has been removed. This poses a potential risk and cataract surgeons must be aware that inadvertent detachment of luer-locks is possible (depending on the individual product). It is the authors' opinion that device design should change making inadvertent removal of luer-locks impossible. If iatrogenic cannula injuries are to be completely eradicated from practice, closer liaison with instrument manufacturers is required. Development of integrated syringe-cannula systems to eliminate all possibilities of inadequately tightening or inappropriately removing luer-locks is needed. Simple statements that luer-locks never fail will not avoid future harm if human performance shortfalls cannot be eliminated from every possible step. The safest way to do this is at the manufacturing stage by moulding one-piece cannula-syringe devices, where syringe and cannula hub are moulded together eliminating the possibility of detachment by force or inadequate tightening.

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Fig. 1 Amvisc syringe assembly as provided out of packaging (**a**). The grey 'tip cap' (blue arrow) has to be screwed off the 'luer-lock' (red arrow) and then cannula (with luer) tightened within the luer-lock for correct assembly (**b**). It is possible to detach the luer-lock from the end of the Amvisc syringe, obviously going against the manufacturers instructions (**c**). However, this makes it possible for a surgeon to be handed an inappropriately assembled OVD that poses a danger of

forceful detachment (**d**). An Alcon Viscoat syringe assembly (**e**). The syringe tip has a non-detachable moulded luer-lock (red arrow) that cannot be removed. To act as a safeguard from failure to correctly tighten the luer-lock by rotating the cannula to the full length of the sleeve threads, the design is improved by the inclusion of a yellow cannula locking cap (**f**). By applying the locking cap against the cannula hub, the cannula cannot act as a projectile

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