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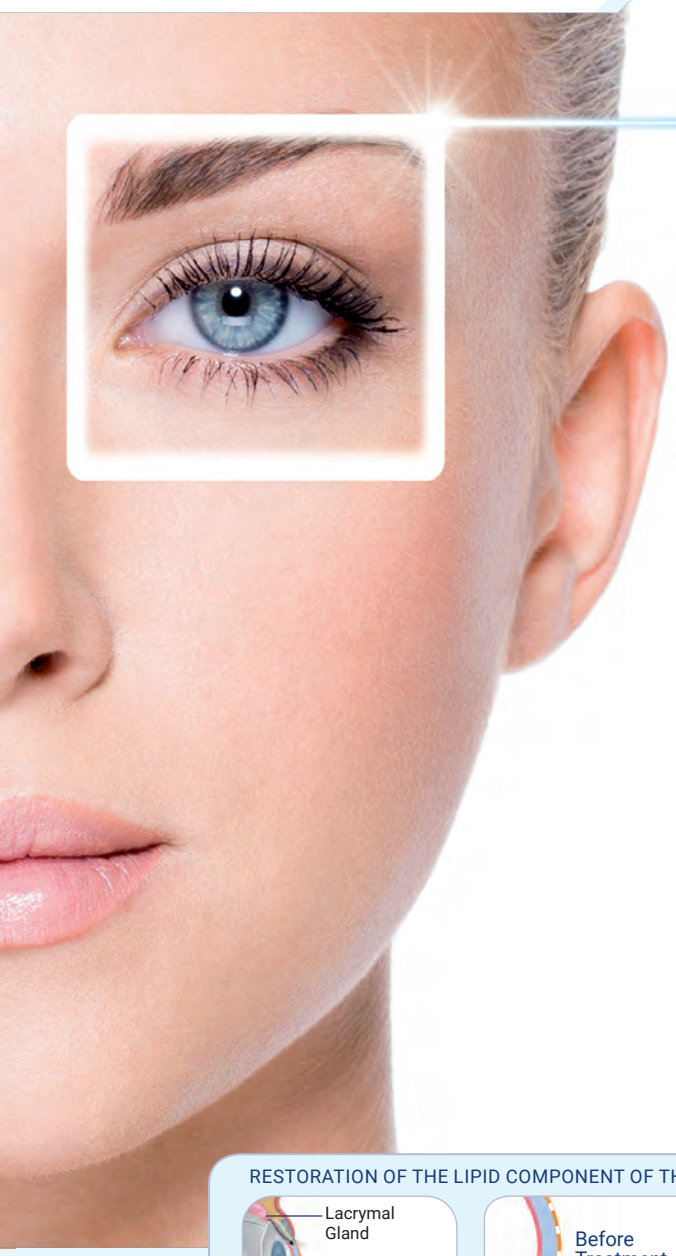

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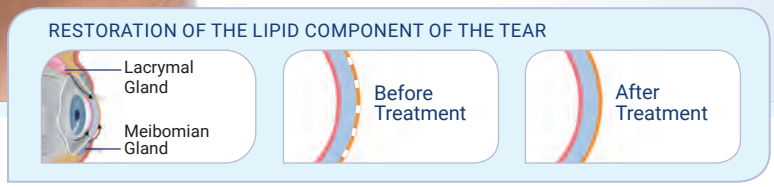

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March 2020
Collaborative care

A note from Angelica Ly, Guest Clinical Editor

As eye care professionals, we take pride in being part of a world-renowned health care system, but what can we do as individuals to shape it? The authors in this issue of *Pharma* teach us that we can practice in novel ways to truly embrace the ever-evolving scope of our profession.

The rising demand for eye care services associated with our ageing population is unprecedented, and patients are slipping through the cracks. Given that the average life expectancy exceeds 80 years, a single glaucoma patient diagnosed at 50 and reviewed every six months will need a minimum of 60 appointments over their lifetime. There are 201,062 patients with glaucoma in Australia, this amounts to over 12 million assessments for the management of just one disease. Each and every practicing optometrist has a potential role in easing this tidal wave of need for ongoing care.

We can also work more synergistically with general practitioners, our colleagues in primary care. As Dr Kalloniatis so aptly describes in her article, ongoing communication between clinicians is a genuine facilitator of better patient care.

Collaborative care is indeed all about ensuring that the patient sees the right professional for the right care at the right time. Delays, suboptimal treatment outcomes and vision loss should be minimised through early detection. As articles in this issue show, as practising optometrists, we can regularly shift roles from problem-solvers to diagnosticians to coordinators of care and back. We also play an invaluable role in screening for drug toxicity and during pregnancy.

I especially love Dr Lindsay McGrath's expression 'shared care networks.' Use of the word 'network' over 'models' imparts dynamism and interconnectedness. Let's interconnect, let's network and share in the expertise of one another and our professional colleagues in academia, pharmacy, general and specialty practice.

This issue was designed with a rich passion for collaborative care, and I enjoyed collaborating with the *Pharma* team in putting it together. Happy reading!

Cover: 'Collaboration' by Yvonne Lin
Selected for its clever symbolism on the theme of this issue, Yvonne Lin's image shows the hands of Kalasha girls from Northern Pakistan, united during an annual harvest festival. Yvonne is an avid photographer and a practicing member of Optometry Australia; more of her stunning images can be seen on Instagram @vonlin.

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To treat or not to treat:
the value of optometry-led collaborative care for glaucoma

Henrietta Wang
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Research Staff Optometrist
Centre for Eye Health

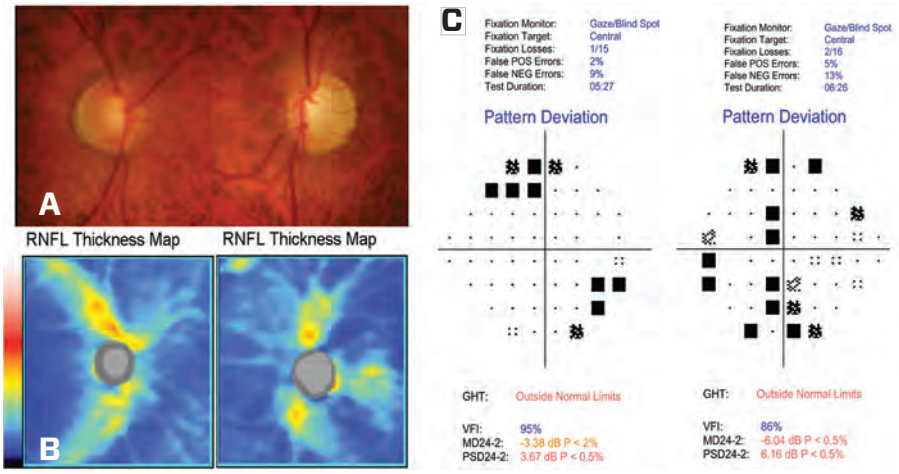

Figure 1. Clinical results from visit number 1. 1A: Fundus photography shows thinning of the neuroretinal rim inferiorly in the right eye, and both superiorly and inferiorly in the left eye. 1B: Cirrus OCT RNFL thickness map showing wedge-like defects inferotemporally in the right eye and both superotemporally and inferotemporally in the left eye. 1C: Humphrey Field Analyzer 24-2 visual field results which were not concordant with the structural findings.

As every practicing optometrist knows, although glaucoma can have severe, irreversable visual consequences,[1] access to the early detection and treatment through eye-care providers can significantly improve visual outcomes.[2]

Using prevalence data from the National Eye Health Survey conducted in 2016,[3] it is estimated that there are over 200,000 Australians currently living with glaucoma. With an increasing ageing population, this number is projected to continue to rise with a corresponding rise in the demand for eye-care services.

In the public sector, already scarce health care resources will be spread even more thinly across the growing population. Consequently, there is increasing demand for alternative pathways offering diagnostic services and ongoing care to patients identified as glaucoma suspects or those diagnosed with early or stable glaucoma.[4-6]

One such pathway is the Glaucoma Management Clinic at the Centre for Eye Health (CFEH) which is a shared-care model providing both optometric and ophthalmologic services specifically for glaucoma.[5] The goal of this pathway is to reduce the strain on public health care systems, thus freeing up resources for more complex patients requiring vital ophthalmological attention.

The following discusses a case of glaucoma seen at the CFEH in collaboration with an ophthalmologist from the local health district. The case study highlights the key advantages of the alternative pathway offered by CFEH, stepping through the clinical findings from initial diagnosis to ongoing management.

CASE REPORT

Visit number 1

A 57-year-old Caucasian male was referred to the CFEH for a glaucoma assessment. He denied any visual symptoms such as blurry vision, red and sore eyes, or haloes around lights. His personal ocular histories were unremarkable, although he did report that his mother has normal tension glaucoma. His medical history was routine and did not reveal any glaucoma-specific risk factors. His entrance test findings are summarised in Table 1.

Dilated fundus examination showed small obliquely inserted discs with deep cups. The neuroretinal rim appeared thin superiorly and inferiorly in the right eye, and inferiorly in the left with corresponding loss of retinal nerve fibre layer (RNFL) reflectivity (Figure 1A). There were no disc haemorrhages in either eye. Optical coherence tomography (OCT) was concordant with the funduscopic results (Figure 1B). Visual field results showed superior and inferotemporal regions of depression OD and a cloverleaf pattern defect OS however these results did correlate to the structural findings

	OD	OS
Refraction and visual acuity (VA)	-3.75/-0.75x75 (6/6-1)	-3.75/-1.00x111 (6/7.5-2)
Intraocular pressures (applanation)	15 mmHg	19 mmHg
Central corneal thicknesses	616 microns	604 microns
Slitlamp examination and gonioscopy findings	• CBB all quadrants with heavily pigmented trabecular meshworks and posterior iris bowing • Bilateral Krukenberg's spindles and subtle peripheral iris transillumination defects	

Table 1. Summary of entrance test findings at the initial visit

(Figure 1C).

Taken together, the results were suggestive of at least a structural pigmentary glaucoma, and referral to an ophthalmologist was recommended for consideration of treatment.

Visit number 2

Eight months later, the patient returned to the CFEH Glaucoma Management Clinic, his entrance tests findings are shown in Table 2.

	OD	OS
Visual acuity (VA)	6/6-2	6/7.5
Intraocular pressures (applanation)	18mmHg	19mmHg
Slitlamp examination and gonioscopy findings	• Bilateral Krukenberg's spindles with no visible iris transillumination defects • Open angles with heavy pigmentation of the trabecular meshwork • 'Pigment reversal' sign in both eyes (see Figure 3 for representative example)	

Table 2. Summary of entrance test findings at visit number 2

Stereoscopic fundus flicker comparison showed no change in the disc or peripapillary appearance in either eye. There was no evidence of structural change in either eye with OCT imaging (Figure 2A). Similar to the initial visit, his visual field results were unreliable and did not appear to match his structural findings (Figure 2B).

What is your management plan for this patient?

To develop a cohesive and evidence-based management plan, we must answer the two following questions: (1) what is the natural history of this presentation and (2) what additional clinical information is necessary?

The importance of natural history

The definition of glaucoma – much like the scope of optometry – has evolved significantly over the past few decades. Previously, a high intraocular pressure (IOP) was thought to be the defining characteristic of glaucoma, however this has since evolved to include a constellation of features with a shift in focus to characteristic structural changes at the optic nerve.

Notably, disease progression is no longer required to make the diagnosis with the newest definition of glaucoma by Casson et al,[7] who describe it as 'potentially progressive.'

This definition is consistent with the natural history of specific subtypes of glaucoma which may not progress and subsequently may not require interventions. It's vital for clinicians to understand the natural history of their patient's glaucoma because it can guide decision-making regarding the necessity of treatment.

PDS

Specific to our case, pigment dispersion syndrome (PDS) can be classified into two broad categories: active and inactive.[8]

In active PDS, there is liberation of pigment as a result of friction between the anterior zonule bundles and iris pigment epithelium. Liberated pigment can deposit along anterior segment landmarks such as the corneal endothelium, anterior and posterior lens capsules and the anterior chamber angle with subsequent implications for IOP.[9] Increases in IOP induced by the liberation pigment can result in glaucomatous changes to the optic nerve and visual field.

With age-related changes to lens thickness and pupil size, and erosion of the iris pigment epithelium in the areas of contact, PDS can reach the inactive stage known as the 'burnout phase' whereby IOP stabilises.[9,10]

While the stabilisation of IOP can help patients already on treatment reach target IOPs more easily, a subset of patients will continue to progress despite the IOP normalisation. This is thought to be due to an intrinsically programmed apoptotic process that continues independent of IOP.

In other PDS patients reaching the burnout phase, such as the case discussed in this article (without stimulus for progression such as increased IOPs) their glaucoma stabilises without intervention.[10] As such, longitudinal data from long-term monitoring is key in helping clinicians differentiate between these subgroups.

Ancillary testing and decision-making

In addition to the barrage of routine clinical tests, there are several ancillary tests that can be readily implemented by clinicians to ascertain the disease stage of their patients with PDS. These can include characterisation of the diurnal IOP profile, photo-documentation of

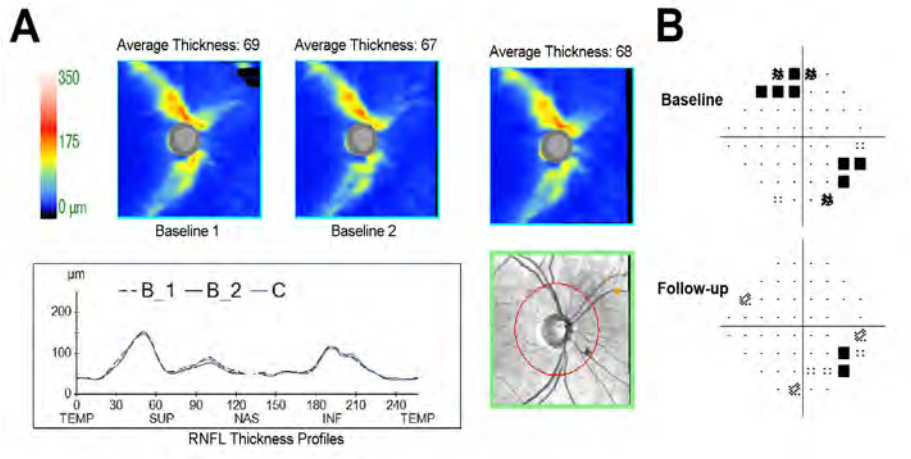

Figure 2. Clinical results from visit number 2. 2A: Cirrus OCT RNFL guided progression analysis showed no change in the RNFL profile of the right eye. 2B: Visual field results showed apparent improvement in the visual field, however, the results remain discordant with structural findings.

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Glaucoma care

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anterior segment structures such as iris transillumination defects and gonioscopy, and the use of provocative testing.

In brief, there are several options available for IOP phasing, ranging from 24-hour monitoring in a hospital setting to IOP self-monitoring devices such as the Icare HOME instrument. This test can not only help characterise a patient's diurnal IOP fluctuation profile but also has the potential to detect peaks occurring outside of typical office hours.

Understanding a patient's IOP fluctuation profile can assist with stratifying risk of conversion or progression and assessing whether IOP fluctuation is the underlying cause for progressive disease despite an adequate in-office IOP reduction.

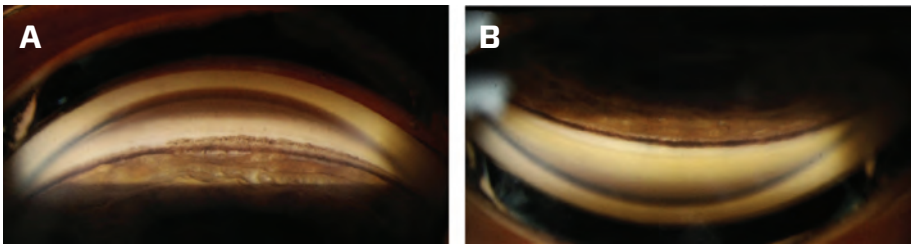

Figure 3. Representative gonioscopy photographs showing 'pigment reversal sign' whereby the inferior angle (3A) becomes less pigmented than the superior angle (3B) in a patient with pigment dispersion syndrome.

> The majority of ancillary tests can be performed in an optometry-led environment, hence our role as clinicians is pivotal in ascertaining the most correct diagnosis and management plan for these patients.

Additionally, careful photo-documentation of anterior segment findings can help clinicians determine the stage of PDS in their patients.

Features suggestive of burnout PDS include: the filling-in of iris transillumination defects through migration of adjacent iris pigment epithelial and 'pigment reversal sign' with gonioscopy (Figure 3), whereby the inferior angle appears less pigmented relative to the superior angle due to the directionality of aqueous convection currents.

Another ancillary test often used in the assessment of patients with PDS is provocative testing. One such example is exercise. Exercise-induced IOP elevations are thought to trigger pigment showers and subsequently has the potential to highlight IOP elevations, particularly in active patients. While there are no guidelines for the intensity or duration of provocative testing, this test can be useful to guide IOP-lowering treatments aimed at preventing exercise-induced IOP spikes.

Long-term management plan

As the clinical picture is suggestive of stable 'burnt out' pigmentary glaucoma, given the relatively short follow-up period, a six-month review period with IOP phasing in the interim was recommended for this patient in the CFEH Glaucoma Management Clinic with ophthalmology input.

The majority of ancillary tests can be performed in an optometry-led environment, hence our role as clinicians is pivotal in ascertaining the most correct diagnosis and management plan for these patients.

Conclusion

With the rate of increase in the ageing population exceeding the growth of the eye-care workforce in Australia, there is growing demand for alternative, collaborative pathways to accommodate patients identified as glaucoma suspects or those diagnosed with early or stable glaucoma.

As this case report shows, understanding the natural history of certain subtypes of glaucoma can assist clinicians in determining whether intervention is required; ancillary testing can provide additional information to help clinicians with stratifying risk of progression in patients with glaucoma; and finally, collaborative care pathways have the potential to provide timely care to glaucoma suspects and patients with early or stable glaucoma that are not prioritised in current public health care pathways. ▲

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A general practitioner's approach

Vascular work-up, papilloedema, hypertensive crisis and suspected thyroid eye disease

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Optometrists and general practitioners (GPs) play an important role in primary health care. This article aims to highlight a GP's approach to preventative health activities around cardiovascular disease (CVD) and give a GP's perspective on the management of hypertensive crisis, papilloedema and suspected thyroid eye disease (Graves' ophthalmopathy).

Primary prevention is about identifying patients at risk prior to the development of disease. Vigilance on behalf of all clinicians involved in patient care can improve outcomes. CVD occurs in 18 per cent of Australians and accounts for 36 per cent of all deaths and 6.9 per cent of all disabilities.[1]

Our patients' cardiovascular (CV) health can be determined by a number of modifiable and non-modifiable risk factors. Importantly, a number of modifiable risk factors associated with CVD also directly contributes to ocular complications like age-related macular degeneration (AMD), cataracts, inflammatory eye disease, thyroid eye disease, retinal ischemia, hypertensive retinopathy and diabetic eye disease.[2–4]

Which of your patients should be encouraged to see their GP?

A GP's approach to evidence-based preventative health activities is outlined in The Royal Australian College of General Practitioners *Guidelines for preventive activities in general practice 9th editio*n (Red Book).[5] One of the primary screening tools utilised is the 'assessment of absolute CVD risk' which combines risk factors to calculate the probability that an individual will develop a cardiovascular event (myocardial infarction, stroke) or other vascular disease within five years.[5]

It is considered reasonable that we complete this assessment at least every two years in all adults aged over 45, or 35 for Aboriginal and Torres Strait Islander (ATSI) patients. Information required to complete this assessment includes the patient's age, sex, smoking status, cholesterol (total and high-density lipoprotein-cholesterol), systolic blood pressure, diabetic status and the absence or presence of left ventricular hypertrophy (LVH). Using the Australian Cardiovascular disease charts (Figures 1 and 2) patients are stratified into Low (< 10 per cent), Moderate (10–15 per cent) and High Risk (> 15 per cent).

Evaluation of CVD risk generates discussion regarding modifiable risk factors and allows patients to focus on reducing these risk factors. This can be achieved through lifestyle changes, as well as appropriately prescribed pharmacotherapy like lipid-lowering agents, anti-hypertensives and medications directed towards smoking cessation.

In summary, all adults aged over 45—or 35 for ATSI patients—should be encouraged to see their GP for a CVD risk assessment and start the dialogue about how improving their modifiable risk factors can not only improve their ocular health but their general health as well.

Papilloedema

Papilloedema is defined as optic disc swelling that is due to raised intracranial pressure (ICP).[6] It is an important examination finding which requires urgent investigation to determine the underlying cause.[6] This sort of presentation requires careful evaluation by an appropriately-trained eye care professional to ensure that other causes of optic nerve swelling are excluded, and to differentiate true from pseudopapilloedema.[7]

The potential causes of raised ICP are varied and include intracranial mass lesions, cerebral oedema, increased cerebrospinal fluid (CSF) production, decreased CSF absorption, obstructive hydrocephalus, obstruction of venous outflow or idiopathic intracranial hypertension.[6]

To determine the cause of papilloedema the patient requires urgent neuroimaging and may also require a lumbar puncture, which is most efficiently arranged via the local Emergency Department. A GP could help facilitate this process, but given the urgency of the situation, they may not be immediately available. In some scenarios, it may be appropriate for the GP to arrange urgent outpatient imaging. Once the cause of the patient's papilloedema has been determined, a GP's strength is the co-ordination and oversight of appropriate longer-term follow-up.

Hypertensive crisis

From a preventative health point of view, a GP should aim to measure the blood pressure (BP) of any patient aged 18 years or older at least every two years. They interpret these BP measurements in the context of the patient's absolute CVD risk assessment.[5]

In general, a GP is happy with BPs of ≤ 140/90 mmHg for adults and BP ≤ 130/80 mmHg for adults with a chronic disease.[5] GPs generally act on high readings once a trend has been established: consistently high readings on two or more occasions.[5] The exception is a patient presenting with a hypertensive crisis, which is a very uncommon presentation to a GP, but one not to be missed.

Most patients with significantly elevated blood pressure (systolic pressure ≥ 180 and/or diastolic pressure ≥ 120 mmHg) are well. This means they have no acute, end-organ injury (severe asymptomatic hypertension).[8] Your clinical suspicion that a patient is in hypertensive crisis should be raised if you record a BP ≥

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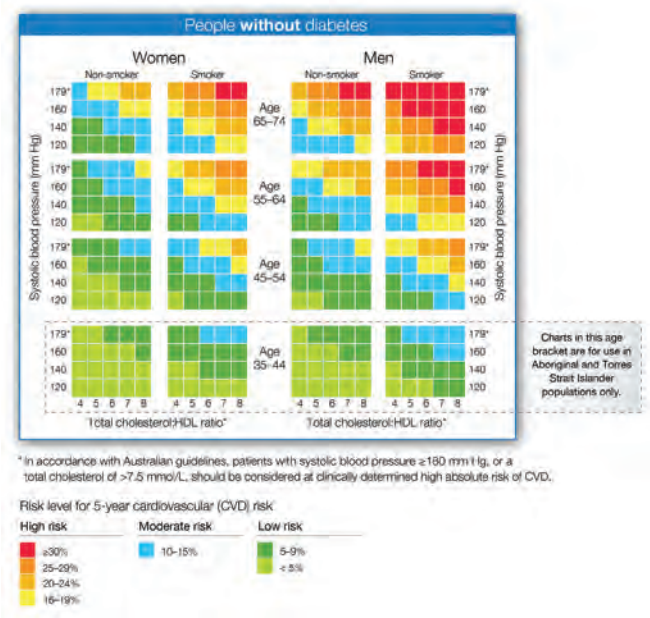

Figure 1. The Australian cardiovascular disease chart, risk without diabetes*

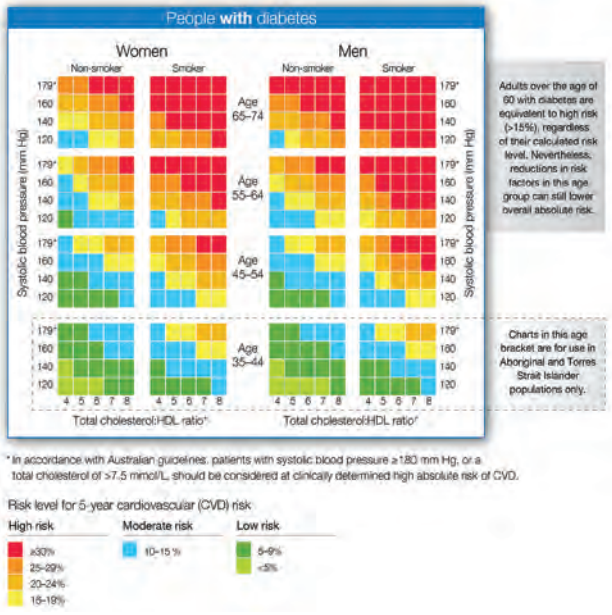

Figure 2. The Australian cardiovascular disease chart, risk with diabetes*

A GP's approach

From page 5

180/ ≥ 120 mmHg and they are unwell. In broad terms, an unwell patient would exhibit concerning symptoms such as focal neurological symptoms (think: stroke), nausea/vomiting, any pain (headache, chest pain, abdominal pain, severe back pain), difficulty breathing and/or pregnancy (pre-eclampsia).[8] Specific ocular examination findings would include evidence of moderate to severe hypertensive retinopathy (fresh flame haemorrhages, exudates [cotton-wool spots] or papilloedema).[8]

If the patient appears otherwise well with a high BP reading, it would be reasonable for them to review with their GP within 24-48 hours. If they are unwell, even if their BP is < 180/120 mmHg, it is likely they need urgent medical assessment. It is most appropriate to call an ambulance or ensure they can safely and quickly present to the local Emergency Department.

Suspected thyroid eye disease (Graves' ophthalmopathy)

Graves' disease is an autoimmune disorder involving the thyroid-stimulating hormone (TSH) receptor antibodies (TRAb). These antibodies essentially mimic the effects of TSH, thereby stimulating thyroid function, with the extrathyroidal TSH receptor expression linked with the pathogenesis of Graves' ophthalmopathy.[9,10]

Graves' ophthalmopathy is characterised by excessive tearing, periorbital oedema and proptosis. Extraocular muscle thickening and dysfunction can also lead to presentation of diplopia. Severe presentation can be sight-threatening related to optic nerve compression, elevated intra-ocular pressure due to elevated episcleral venous pressure or significant corneal ulceration primarily due to exposure. Graves' ophthalmopathy affects approximately 20 per cent of those with a diagnosis of Graves' disease. A patient's presentation of Graves' ophthalmopathy will often accompany clinical features of thyrotoxicosis.[10]

A GP would defer to an optometrist or an ophthalmologist to determine visual function, but management of vision-threatening Graves' ophthalmopathy would require ophthalmological intervention. GPs are familiar with managing the non-ocular complications of Graves' disease and assist in the diagnosis of Graves' disease through initial investigations which include thyroid function tests, thyroid antibodies and if appropriate, a radionuclide thyroid scan.

GPs would commonly assess for clinical signs/symptoms of thyrotoxicosis which include tachycardia, hypertension, weight loss, diarrhoea, tremor, hyperreflexia, heat intolerance, anxiety and pretibial myxoedema.[11] The symptom profile of a thyrotoxic patient can be quite broad with the severe end of the spectrum requiring urgent in-patient admission. For those patients who are amenable to outpatient treatment, GPs will often initiate treatment (carbimazole, beta blockers) and arrange outpatient specialist review to discuss definitive treatment such as radioactive iodine or surgery.[9] Smoking leads to worsening of Graves' ophthalmopathy[10] and therefore smoking cessation is essential.

Ultimately, a GP wears two hats, and while there is much to be gained in preventative health, they are often at the forefront of the identification of acute medical illnesses which require urgent medical intervention. As colleagues and members of a multi-disciplinary care team, optometrists can also have an impact in identifying suitable cases for referral. By presenting a GP's viewpoint, the hope is that a context for ongoing communication between clinicians will be provided and better patient care will be facilitated. ▲

*Diabetes charts reproduced with permission from the National Heart Foundation of Australia from National Vascular Disease Prevention Alliance. Absolute cardiovascular disease risk management.

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A GP's approach

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Visit the Australian absolute cardiovascular disease risk calculator (www.cvdcheck.org.au) for further education and information.

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Spotting the difference:

Collaborative care of low-risk pigmented choroidal lesions

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With the increasing number of retinal imaging devices in optometric practice, choroidal naevomelanocytic lesions are a frequent incidental finding among primary eye-care providers during routine examination.[1] Pigmented intraocular tumours can be defined as any melanocytic abnormality of the inner layers of the eye, and include intraocular tumours (benign, indeterminate or malignant lesion of the uvea, retina, retinal pigment epithelium or optic nerve) metastases, scarring or hyperplasia associated with degenerative, inflammatory or neovascular disease.[2]

Failure to distinguish between benign and malignant lesions can result in delays of care, suboptimal treatment outcomes and greater frequency of loss of vision or the eye. Suspicious or atypical lesions require long-term periodic surveillance, with intervals set depending on risk factors addressing the risk of malignant change. Early identification of change is imperative and may be improved with ocular imaging technology and specialist expertise.

The increasing detection and referral rate for pigmented choroidal lesions may burden specialist care by false positive referrals of benign lesions.[2] It is well documented that choroidal naevi are present in 5-10% of the population. Efficiency of referral and follow-up of low risk lesions could likely be improved by referral refinement schemes and shared-care networks integrating optometrists with a special interest and ophthalmologists trained in ocular oncology or retinal disease.

Suspicious pigmented choroidal lesion

A suspicious choroidal naevus can have overlapping clinical features of a small choroidal melanoma, including tumour size (>5mm), location, presence of subretinal fluid and orange pigment.[1] Differentiation between these two entities requires both funduscopic evaluation along with specialised ancillary imaging – including autofluorescence, ultrasonography and spectral domain optical coherence tomography (OCT).

Choroidal naevi can develop suspicious features which can predict transformation to a choroidal

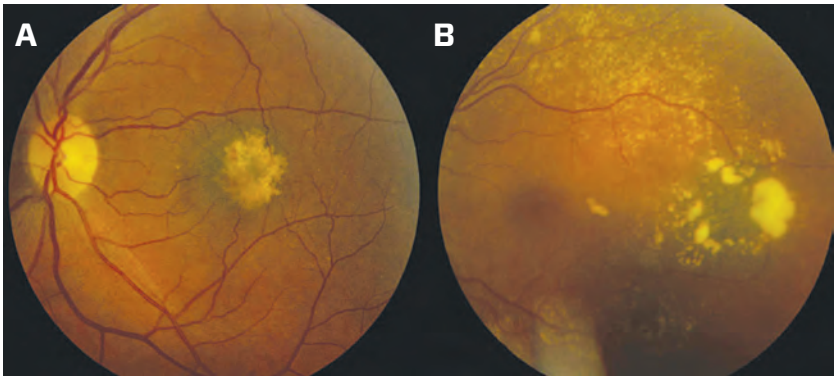

Figure 1. Choroidal naevi with drusen. A: At the macula and B: midperiphery

T	Thickness greater than 2 mm
F	Fluid, Subretinal
S	Symptoms (flashes/floaters/shimmers)
O	Orange pigment (lipofuscin)
M	Margin closer or equal 3 mm from optic disc
U	Ultrasonographic Hollowness
H	Halo absent
D	Drusen absent

Table 1. Characteristics of Choroidal Melanocytic Lesions Predictive of Neoplasm or Growth [TFSOM-UHHD] – 'To find small ocular melanomas use helpful hints daily'[3]

melanoma. Eight such characteristics have been defined by Shields et al. as detailed in Table 1.[3] Typically, a small melanoma displays two to three of these risk factors. Pigmented lesions with no risk factors carry a three per cent risk of growth over five years.[4] The presence of three or more risk factors is associated with a more than 50 per cent risk of tumour growth in five years.[4]

Approximately 98 per cent of naevi have overlying drusen – similar to those seen in macular degeneration, and indicate slow growth and chronicity (Figures 1A and 1B). Another factor to consider is the presence of a halo, which is seen in five per cent of choroidal naevi.[3] This refers to a pigmented naevus surrounded by a circular band of depigmentation (Figure 2), less commonly associated with melanoma. Presence of subretinal fluid is a strong risk factor for growth, however, subtle fluid can be difficult to assess clinically. Chronic fluid is usually associated with overlying retinal cysts, while active acute fluid leak from a malignant lesion may have localised serous detachments (Figure 3A and 3B).

Case 1: Lipofuscin never lies

A 30-year-old female was referred by her optometrist with a pigmented lesion at the left macula. She initially sought examination due to a one-week history of blurred vision in the left eye. She had no significant past ocular or medical history. On examination, her vision was R 6/6, L 6/6. Fundus examination of the left eye revealed a pigmented lesion of the choroid measuring 5 x 5 mm (Figure 4A and 4B). Although she had symptoms related to subretinal fluid, there was no lipofuscin and the lesion measured 1.5 mm in thickness (Figure 5A). The lesion had two risk factors (fluid and margins close to optic disc) at presentation, and was monitored closely.

At six weeks review, the lesion was unchanged in basal dimensions. Fundus examination and autoflourescence confirmed new lipofuscin and increasing subretinal fluid (Figure 4C and 4D and Figure 5B). With these risk factors, the lesion was diagnosed as a small choroidal melanoma and treatment was recommended with photodynamic therapy. Eighteen months post

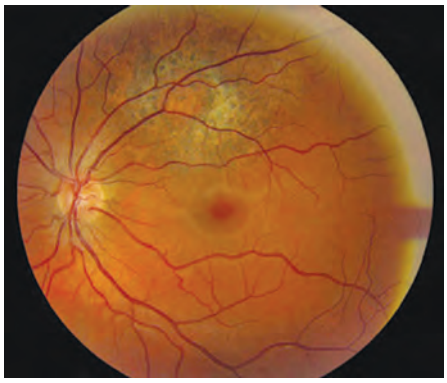

Figure 2. Halo naevus – central pigmented area with a surrounding yellow halo. These naevi represent 5 per cent of choroidal naevi, and are associated with reduced rate of transformation to choroidal melanoma.

treatment, the patient had a paracentral scotoma, but uncorrected central vision of 6/6 in both eyes. The patient was monitored longterm by her ophthalmologist and optometrist alternating six monthly.

Case 2: They grow up so quickly

A 65-year-old female was referred by her optometrist with a large suspicious choroidal lesion in the left eye. She was asymptomatic. Visual acuity was R 6/6 and L 6/6. Fundus examination revealed a peripheral pigmented lesion measuring 8 x 8 mm. There was drusen overlying the lesion and no subretinal fluid (Figure 6A). There were no risk factors for growth, therefore the

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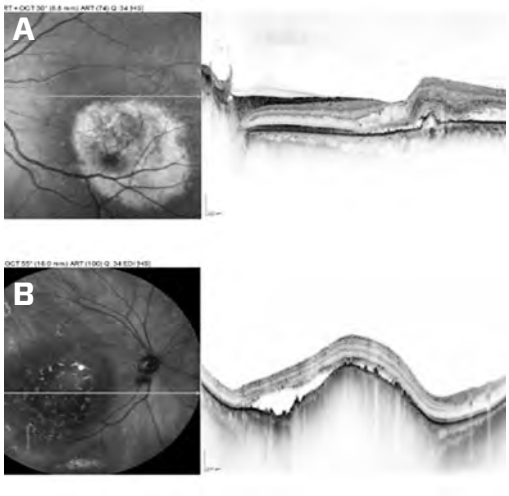

Figure 3. A: OCT through superior aspect of choroidal naevus showing intraretinal cystic oedema and drusenoid pigment epithelial detachment. B: OCT through a choroidal melanoma with subretinal fluid temporally.

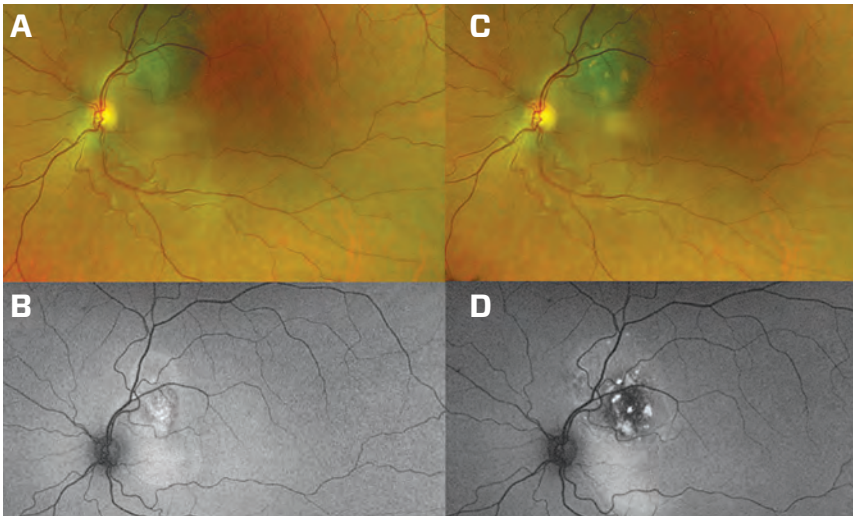

Figure 4. A: Optomap colour photograph of suspicious choroidal naevus. B: Autofluorescence at presentation shows mild hyperautofluorescence of the lesion itself and slight hyperautofluorescence at the macula in the area of subretinal fluid. C: Colour photograph at review highlighting slight increase in size and new lipofuscin. D: Autofluorescence confirms lipofuscin.

Choroidal lesions

From page 9

patient was returned to the care of her optometrist for annual screening. She was recommended to seek earlier review should she notice flashes, shimmers or blur in her vision.

Two years later, the patient presented for a spectacle prescription update, complaining of some peripheral flashes. Her optometrist noted a significant change in thickness of the choroidal lesion. The optometrist contacted the ocular oncology team urgently, and the patient was reviewed promptly.

Her choroidal naevus showed signs of transformation to melanoma – including increased thickness (to 4 mm), subretinal fluid and ultrasonographic hollowness (Figure 6B). She proceeded to plaque brachytherapy and was able to avoid enucleation, thanks to her astute optometrist and prompt referral. The patient was monitored for recurrence with her ophthalmologist for five years after treatment, then returned to shared care monitoring with her optometrist.

Shared care benefits for all

Although imaging is integral to better diagnosis and differentiation of pigmented choroidal lesions, additional contributing factors include clear communication between the referring and intermediate care party, judicious screening of incoming referrals, rapid access to ophthalmological opinion, evidence-based practice and optometric staff with specific training in the diagnosis of pigmented lesions – beyond the basic competencies of tertiary optometric training.

Though there is usually a high agreement between optometrists and ophthalmologists grading pigmented lesions using defined assessment strategies such as 'TFSOM-UHHD,' there must also be a note of caution.[5] In certain cases, there is a grey area between a suspicious naevus and small melanoma, and sometimes experienced ocular oncologists will classify a lesion as indeterminate (Figure 3A), to be followed closely for signs of increasing suspicion. In general, these cases should be referred appropriately and are kept under specialist care to be monitored closely.

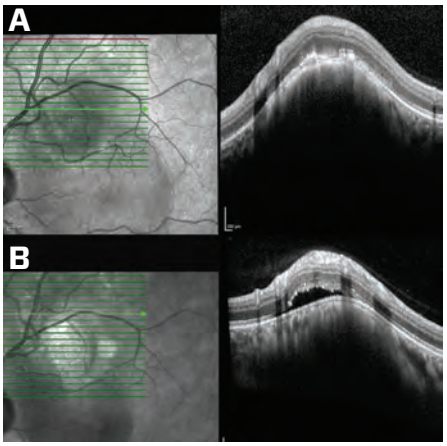

Figure 5. OCT of choroidal naevus at two visits. A: Confirming lipofuscin and B: with subretinal fluid overlying the lesion.

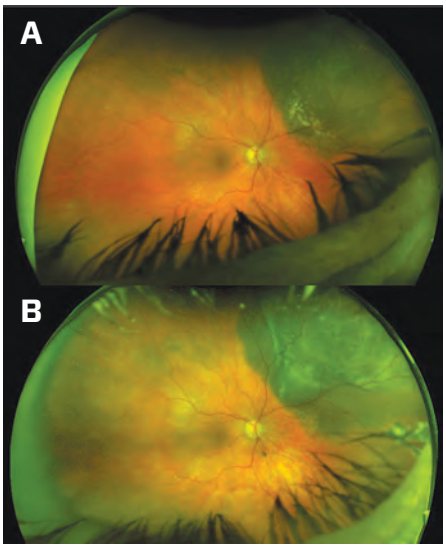

Figure 6. A: Choroidal naevus at presentation and B: at two-year review, note increasing thickness, basal dimensions and suspicious for subretinal fluid

Optometrists who provide the best collaborative care are those who are progressive, are involved in regular continuing education and who keep up to date with technology (including autofluorescence, ultrasonography and optical coherence tomography, as described above) and innovation for diagnosis and monitoring of eye disease. The most important part of co-management is the collaboration and open communication between both parties to ensure the best possible care is given to the patient.

For optometrists involved in co-management with an ophthalmologist already – or keen to become involved – it can be useful to spend a session in the ophthalmology practice. This gives a unique opportunity for education and assimilation, as well being able to provide invaluable feedback to both parties about the combined care being provided. It would be logical to commence a shared care relationship for a particular patient group (glaucoma, age related macular degeneration, tumours) rather than all patients initially – such that experience can be gained, and a relationship with the treating ophthalmologist formed.

From the optometrist's point of view, co-management can enhance the patient's perception of their care provider. They see that optometrists can handle primary care – from red eyes to retinal disease – and can act as support for cases that require a specialist.

From the ophthalmologist's perspective, shared care with optometrists allows focus on patients who require in-depth care and management, while optometrists can handle stable review patients. This is particularly true for rural and remote patients who find it financially or geographically challenging to attend specialist review appointments for checkups.

One thing we know for certain: workloads will continue to increase for both optometrists and ophthalmologists. The population is ageing, and we must make sure that our patients' ocular health and vision are optimised to support them into their ninth and tenth decades. Despite increasing demand for services, we now have a good balance, with short wait times for optometrists who can help regularly review stable patients and triage patients requiring specialist care. ▲

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Accessing advanced dry eye management options

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Navigating the Special Access Scheme (SAS) and producing autologous serum eye drops

When it was released in 2017, the second Tear Film & Ocular Surface Society Dry Eye Workshop (TFOS DEWS II) report detailed our current understanding regarding the diagnosis and management of dry eye.[1] The consensus regarding dry eye management suggested a stepwise approach, with lifestyle modifications and artificial lubricants recommended with milder presentations, and more aggressive therapies including pharmaceuticals or surgery with more severe cases where mild therapies prove inadequate.[2]

To access some of these more advanced forms of dry eye treatment, optometrists are required to co-manage and coordinate with numerous members of the patient's health care team including general practitioners and ophthalmologists, as well as other specialised organisations such as pharmacies or the Australian Red Cross Blood Service.

This article will discuss some of the processes involved with accessing two of the more specialised treatments for dry eye, cyclosporine and autologous serum eye drops, in Australia.

TREATMENT 1

Cyclosporine ophthalmic drops in Australia: The Special Access Scheme

One of the key concepts highlighted by the DEWS reports was the definition of dry eye and the recognition of the important role inflammation plays as part of the disease pathophysiology.[3] Anti-inflammatory therapy, such as the use of corticosteroids, thus has a role in managing the disease and significantly improve signs and symptoms.[2]

However, while corticosteroids are effective, they are not considered a long-term solution for chronic dry eye management due to the associated risks and adverse effects with their prolonged use. Cyclosporine A, an immunomodulator, has been specifically formulated as an ophthalmic emulsion and can be used safely long-term to manage dry eye associated inflammation pharmaceutically.

Cyclosporine, as an active ingredient, is currently listed as one of the drugs which can be prescribed, pending state or territory legislation, by endorsed optometrists by the Optometry Board of Australia for ophthalmic use.[4] However, at the time of this writing, the commercial formulation of this drug (0.05% cyclosporine ophthalmic emulsion) is available in the United States and Canada but has not been approved by the Therapeutic Goods Administration (TGA) in Australia and so is nominally not commercially available.

How to get it

The absence of a ready commercial supply in the Australian market does not immediately prevent the prescribing of cyclosporine ophthalmic drops to patients should they be indicated. One option is for the formulation to be ordered compounded, although this requires access to a compounding pharmacy with experience manufacturing ophthalmic emulsions which may not be readily accessible. [For more on this, see Alison Haywood's article 'Personalised medicines for eye care' in this issue of *Pharma*.]

Alternatively, the commercial formulation of these drops can potentially be acquired through the Special Access Scheme (SAS). The SAS allows for patients to be prescribed and dispensed therapeutic goods which are not currently on the Australian Register of Therapeutic Goods (ARTG) in exceptional circumstances. These 'unapproved' goods are stated to have not been evaluated by the TGA for safety or efficacy, putting the onus on the prescribing practitioner to justify their use clinically and ensuring that alternatives available on the ARTG have been considered before unapproved goods are attempted to be accessed through this pathway.[5]

The SAS is broken into three distinct categories: A, B and C, which reflect the anticipated use of the scheme. Category A is reserved for prescribing agents to patients who are seriously ill and is unlikely to be relevant to the therapeutic practice of optometry.

Category C: notification pathway

Category C is a notification pathway for drug formulations considered to have an established history of use, such as use in other jurisdictions or countries.

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Special Access Scheme

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Specific formulations and indications for their use accessible through Category C are listed within legislation and must be prescribed by a medical practitioner. 0.05% Cyclosporine ophthalmic eye drops are currently listed in the legislation with the indication to help tear production decreased due to dry eye, which is in line with the listed indication for the commercial formulation of this ophthalmic drop.[6]

Optometrists, whether endorsed or not, can thus gain access to the commercial formulation for their patients by co-ordinating with their general practitioner, with the medical practitioner notifying the TGA through the Category C forms.

Category B: application pathway

Alternatively, Category B, an application pathway, may be utilised by endorsed optometrists directly. In Category B, the patient's diagnosis, details of the drug being requested and the clinical justification for use of the product are submitted on forms to the TGA for consideration and approval, after which the prescription, application and approval letter may be brought to the pharmacy for the supply to be dispensed.

Category B applications may take some time—from several days for commonly applied products, to longer if the TGA has to assess and evaluate data—so if the drug is needed urgently, it may be preferable to work with the patient's general practitioner to access the drug via Category C.

Category C is a notification pathway, so no acknowledgement from the TGA after lodgement is required; Category B, on the other hand, requires approval before the drug can be dispensed.

The TGA has also moved to an online system for submission of applications or notifications (tga.gov.au), further streamlining the process and reducing some of the administrative burden for prescribing practitioners.[5]

Practitioners should be aware of their responsibilities to the TGA and their patients if using the SAS.

Patients should be informed that the substance being prescribed has not been evaluated by the TGA or listed on the ARTG and is thus unapproved. As such, providing and documenting informed consent for the use of the medicine is critical. Practitioners are also required to inform the TGA immediately if there are any adverse reactions when using unapproved products accessed through the scheme.

Finally, for this specific scenario, not all pharmacies may be able to source commercial cyclosporine ophthalmic drops, so it may also be helpful for practitioners to search for and liaise with potential pharmacies in the local area prior to prescribing the drops through the SAS to provide adequate guidance to patients.

TREATMENT 2

Autologous Serum: The Australian Red Cross

Serum is the component of blood after the removal of white and red blood cells, as well as the components involved with clotting (fibrinogens). The resulting fluid contains proteins, antibodies, growth factors and electrolytes and other substances, some of which are thought to be useful in lowering inflammation and promoting healing of eyes damaged in dry eye.

Autologous serum is formed from the patient's own blood and involves collection by the Australian Red Cross Blood Service in the eastern Australian states or other organisations such as Cell and Tissues Therapies WA elsewhere.[7]

How it's used

To prepare the serum into ophthalmic drops for dry eye, approximately 470 mL of blood is collected from patients to make their own drops. The blood is allowed to clot at room temperature before being centrifuged to isolate the serum. The serum is diluted with saline to form a 20 per cent serum solution which is placed within 20 metres of tubing.[8]

The tubing is heat-sealed at approximately 7 cm intervals to produce single-use segments which are then stored frozen for up to a year.[8] Approximately 1,200 segments are produced from a single blood-drawing session which, depending on the frequency of administration (between three and eight times a day) by the patient, may be sufficient for almost an entire year.[8]

Patients are required to cut out the number of segments for use the next day using alcohol swabbed scissors and allow them to defrost in the refrigerator. As there are no preservatives, open tubes are to be discarded after use and cannot be refrozen or otherwise reused.[8]

While effective in reducing signs and symptoms of dry eye, from a practical perspective, there have been reports that the tubes are difficult to use, particularly for those who have poor vision. The need for advance defrosting also requires a certain level of planning by patients, reducing their convenience.[8]

How to get it

Autologous serum drops are produced by the Australian Red Cross Blood Service on a compassionate basis only and require an order from an ophthalmologist due to the time, cost and labour involved in their preparation.

Optometrists seeking autologous serum for their severe dry eye patients are thus required to co-ordinate with the patient's ophthalmologist so that these drops can be successfully ordered, prepared and supplied. It should also be noted that patients are required to meet the requirements for blood donation to produce autologous serum eye drops, potentially preventing patients with severe

cardiovascular or respiratory co-morbidities having autologous drops made.

New Zealand

In New Zealand, the New Zealand Blood Service has experimented with allogenic rather than autologous eye drops from healthy donors to meet this gap since 2007, demonstrating them to be effective and more importantly, safe, considering the testing that the blood services do to detect infectious organisms. Serum eye drops from healthy donors may thus represent an avenue for increased serum eye drops being used therapeutically. [9]

Conclusion

As these two examples show, to effectively manage serious cases of dry eye disease with some of the more advanced treatment modalities, co-ordination with numerous members of the patient's health care team as well as outside organisations may become necessary.

Optometrists should be well prepared to serve the role of overall co-ordinators of patient's dry eye disease and stay informed of the pathways through which therapeutic options can be accessed. ▲

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How does NovaTears work?

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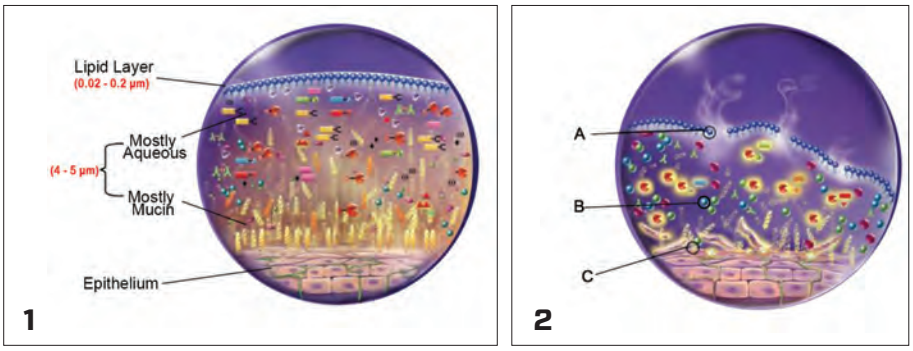

Figures 1 and 2. Healthy tear film (Figure 1) and unstable tear film (Figure 2) typically characterised by a (A) discontinuous lipid layer and (B) hyperosmolar aqueous layer with (C) reduced mucins and goblet cells.

Deficiency in quality and quantity of the tear film is often considered the primary defining characteristic of dry eye disease (DED). The tear film is a complex, dynamic multi-component structure composed of an underlying aqueous-mucous layer and a superficial lipid layer, which synergistically maintain homeostasis on the ocular surface. Functionally, the aqueous-mucus layer improves the wettability and corneal adhesion of the tear film, while the lipid layer tends to form a superficial protective 'blanket' having an occlusive effect.

When healthy tear film is compared to unhealthy tear film, as shown in Figures 1 and 2, 'holes' in the blanket of an unstable tear film (A), as typically observed in evaporative DED and meibomian gland dysfunction (MGD) due to altered lipid quality and/or quantity, can increase evaporation of the underlying aqueous layer of the tear fluid, thus increasing the tear film osmolarity (B) and causing epithelial cell apoptosis (C). As such, 'artificial tears' that replenish the aqueous component of the tear film are often used as first-line therapy in DED.

Artificial tears

Although most frequently used to manage tear film deficiencies, the term 'artificial tears' is a misnomer as most products do not mimic the complex composition of human tears and, contrary to their name, typically 'supplement' rather than 'replace' the tear fluid.

Most artificial tears are isotonic or hypotonic aqueous eye drops with added viscosity building agents such as carboxymethylcellulose, hydroxypropyl guar or sodium hyalorunate, which increase the ocular residence time. They typically function by augmenting the aqueous layer and transiently reducing tear fluid osmolarity; however, their effect is generally short-lived due to rapid drainage from the ocular surface.

Lipid-based eye drops, on the other hand, contain amphiphilic lipids and/or surfactants, which fortify the tear film lipid layer to minimise evaporation. Due to their more sustained effect, they are often superior to non-lipid eye drops in the management of evaporative DED, especially when it is associated with MGD. Moreover, in a recent study comparing non-lipid and lipid-based eye drops, the latter resulted in a significantly greater improvement in tear film lipid layer thickness and consequently a greater reduction in tear evaporation in DED patients exposed to desiccating environmental stress.[1]

This has encouraged the development of several lipid-based tear supplements, including oil-in-water microemulsions (Cationorm, Santen SAS) and ointments (for example VitA-POS, AFT Pharmaceuticals). Liposomal sprays such as ActiMist (Optrex Ltd.) and Tears Again (Optima Pharmazeutische GmbH), which replenish the phospholipid layer at the aqueous-lipid interface, have also shown significant improvement of tear film parameters.[2]

Problematic eye drop ingredients

A significant concern with long-term eye drop use is the presence of preservatives, which can further compromise the ocular surface and exacerbate ocular discomfort, especially in patients with DED who already have a deficient tear film.[3] Large amounts of surfactants typically used in most lipid-containing eye drops may also exacerbate DED symptoms by transiently destabilising the tear film.[4] Consequently, several

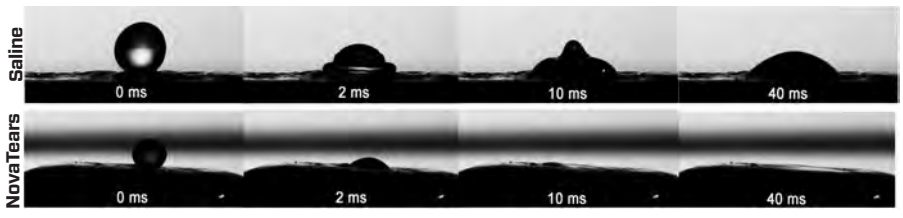

Figure 3. Representative images showing the spreading dynamics of saline (top) and NovaTears (bottom) on the corneal surface under typical conditions for dispensing eye drops.

preservatives and surfactants have been listed in the TFOS DEWS II Iatrogenic Report as potential dry-eye -causing agents.[5]

To reduce preservative exposure, novel multi-dose bottles such as the COMOD system used in the Hylo eye-care range, or single-use eye drops in sterile packaging, are preferred but have proven to be a more expensive and less sustainable alternative for regular use. As such, non-aqueous lubricating vehicles that are safe for ocular use and do not require any preservative may be a solution to this dilemma. This principle has been explored by Novaliq GmbH, with their patented technology using a novel optically transparent, non-aqueous semifluorinated alkane that is pharmaceutically inert and well tolerated on the ocular surface.[6] This preservative-free, lipid-layer stabilising product is currently marketed as EvoTears (URSAPHARM) in Europe and NovaTears (AFT Pharmaceuticals) in Australia and New Zealand.

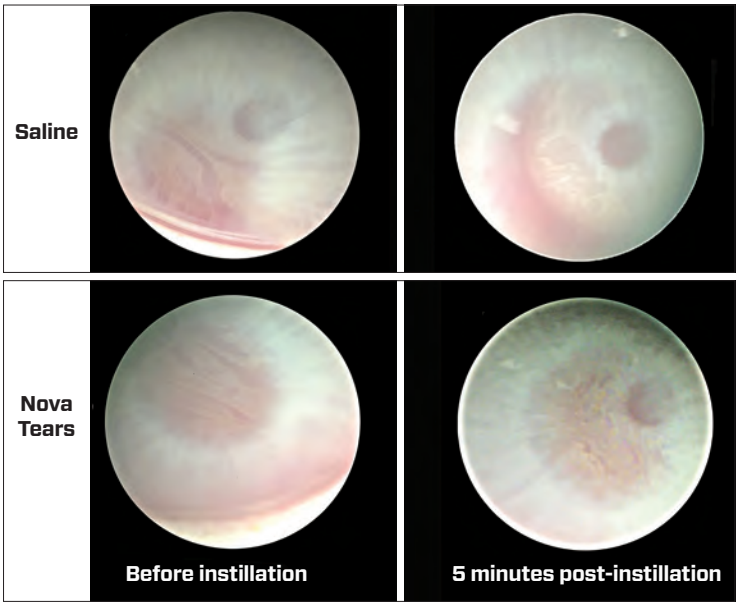

Figure 4. Representative images showing the lipid layer patterns before (left) and after (right) instillation of saline (top) and NovaTears (bottom) into healthy rabbit eyes. Typically, a Grade 3 wavy lipid layer pattern was observed at baseline, which did not improve after instillation of saline. However, instillation of NovaTears resulted in a significant improvement of the lipid layer pattern (coloured fringes, Grade 5) at 5 minutes.

NovaTears and tear fluid dynamics

Multicentre clinical trials have demonstrated improved therapeutic outcomes after instillation of NovaTears four times a day for six to eight weeks in patients with mild-to-moderate hyperevaporative DED[7] and MGD.[8] The mechanism by which NovaTears exhibit these beneficial effects was further elucidated at the University of Auckland, New Zealand.

Using high speed photography, it was observed that due to its ultralow interfacial tension, the contact angle of NovaTears on the ocular surface was practically zero resulting in enhanced spreadability in comparison to saline (Figure 3).[9] Moreover, due to the lower surface tension, smaller droplets of NovaTears could be dispensed, overall leading to less wastage of the dose.

NovaTears also resulted in a significant improvement of the lipid layer grade immediately after administration of a single dose in pre-clinical studies performed in healthy rabbit eyes (Figure 4). Moreover, the lipid layer grade, which correlates with the quality and thickness of the tear film lipid layer, consistently improved on repeated dosing, with the improvement being statistically significant after twice-daily instillation for at least five days.

Similarly, a transient improvement in tear fluid thickness was also reported in a recent study performed in 48 patients with mild-to-moderate DED using ultrahigh-resolution optical coherence tomography. On repeated administration, tear fluid thickness gradually increased over time with a simultaneous improvement in other DED signs and symptoms.[10] These observations may once again be attributed to the unique spreading dynamics of NovaTears on the ocular surface with its amphiphilic nature enabling stabilisation of the superficial lipid layer to strengthen the tear film barrier.

Conclusion

NovaTears can provide a safe, surfactant- and preservative-free alternative for the management of evaporative DED and associated MGD. Multiple pre-clinical and clinical studies have demonstrated the lipid layer stabilising properties of NovaTears, which can be attributed to its unique spreading dynamics. These enable NovaTears to fill the 'holes' in the lipid layer of a compromised tear film, resulting in fortification of the superficial protective 'blanket' and minimisation of tear evaporation. ▲

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Glaucoma community collaborative care program

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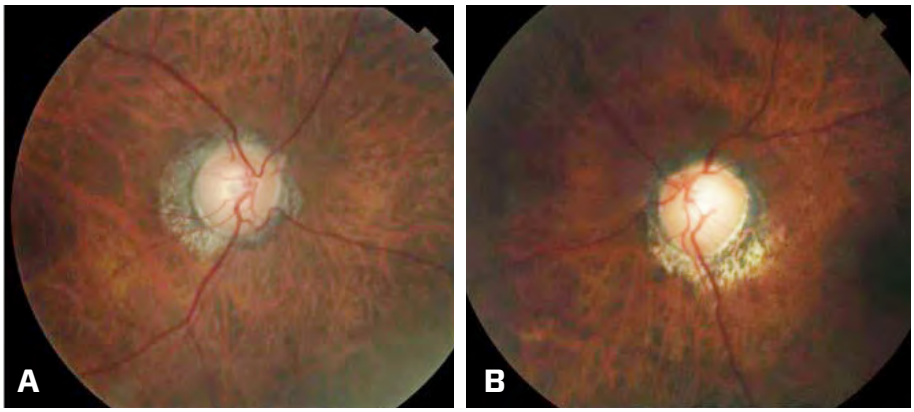


Figures 1A and 1B. Right and left optic nerve head photos, respectively

Glaucoma is a progressive optic neuropathy that places an increasing burden on Australia's health system as our population ages. Despite advancing research and technology, it continues to be the most common cause of irreversible blindness worldwide.[1] The absence of a cure for glaucoma and the progressive nature of the disease means patients require lifelong monitoring and treatment from the time of diagnosis. The goal of glaucoma management is to minimise disease progression and preserve sight for the duration of the patient's lifetime. For some patients this can be achieved with topical agents, laser or surgery. For others, these treatment options will still result in disease progression and they may require intensive specialist input and multiple operations.

In this article, we lay out the background and rationale for a new community-optometry-based collaborative care model for glaucoma patients launched by the Royal Victorian Eye and Ear Hospital in March 2019. This plan will potentially ease the travel and waiting time demands for hundreds of patients and allow more timely care for high-risk patients.

The growing demands of glaucoma

By 2040 it is predicted that 111.8 million of the world's population will have glaucoma.[2] About one in 200 Australians will develop glaucoma by the age of 40.[3] With our current life expectancy at 81 years (male) and 85 years (female),[4] a growing cohort of patients will require up to 40 years of regular eye appointments to manage the condition. This amounts to years of travelling to appointments, taking leave from work, out-of-pocket consultation fees and medication expenses. The cumulative cost of private health care is also unaffordable for many Australians with glaucoma. This increases demand on the public health system. The limited capacity of the public system means lengthy waiting times to access care, which in turn can lead to suboptimal outcomes for patients.

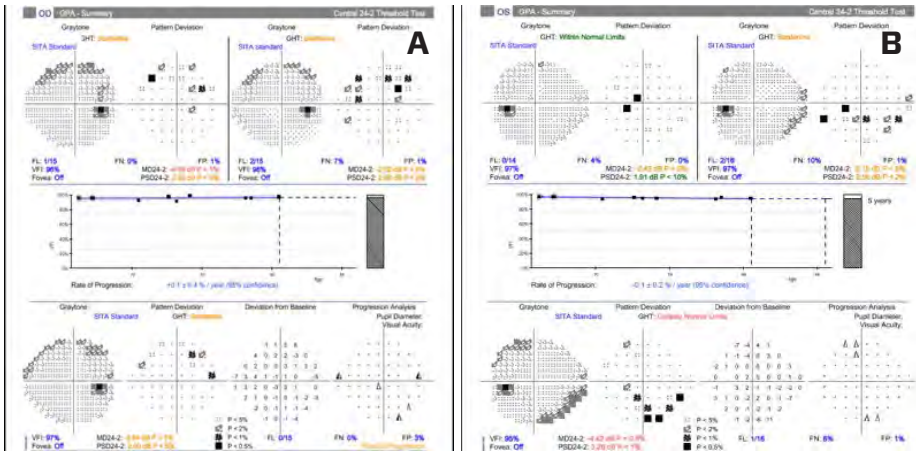
What is collaborative care?

Collaborative eye-care models combine regular monitoring of stable patients in a community optometry practice with ophthalmological review at prescribed intervals, or sooner if required. To be effective, such models require excellent collaboration and regular communication between optometrists and ophthalmologists.

Since the unmet demand for public hospital ophthalmology appointments is not isolated within Australia alone, other countries have faced this ongoing challenge with the development of inter-disciplinary collaborative eye-care models.[5,6] Effective collaborative practice is beneficial to patients, health systems and the economy. However, multi-site collaboration has many facets, which can make it challenging to develop and implement. It is logistically complex, requires a secure and reliable mode of information transfer, and clearly defined roles and guidelines for the disciplines involved. Other centres in Australia have also trialled various models of ophthalmology-optometry collaborations for glaucoma;[7-13] however, as successful implementation of new collaborative care schemes is highly dependent on contextual factors,[14] it is important to develop models and guidelines specific to the location.

The largest ophthalmology service in Victoria, The Royal Victorian Eye and Ear Hospital delivers more than 120,000 ophthalmology appointments annually. Since 2014, the Eye and Ear began adapting to meet the growing demands of glaucoma care via three key avenues.

To minimise potentially unnecessary appointments for false-positive referrals, the referral and triaging guidelines were reviewed by senior members of the Glaucoma Unit. Secondly, in 2016 a collaborative off-site clinic was established at the Australian College of Optometry to manage non-specific or low-risk referrals. Both of these approaches are now embedded within the hospital's model of care.



Figures 2A and 2B. Humphrey Visual Field Guided Progression Analysis Summary right and left, respectively

The glaucoma community collaborative care program

The third strategic change within the Glaucoma Unit at the Eye and Ear is expanding its collaborative care program and improving access for glaucoma patients. This involves recruiting a network of optometrists across the state to participate in a pilot program where eligible patients with glaucoma will be monitored in a shared-care arrangement between the Glaucoma Unit and a participating community optometrist. This concept is not novel to the Eye and Ear, as a pilot program called the National Eye Health Demonstration Project had previously been conducted that included the shared management with community optometrists of not only glaucoma, but also age-related macular degeneration and diabetic retinopathy.[15] However, the new program is aimed solely at addressing the needs of glaucoma patients and is proposed as an ongoing service at the Eye and Ear.

Expressions of interest were sought from registered optometrists across metropolitan and rural Victoria for an initial two-year participation of up to 30 community optometrists. Articles calling for participants were featured in trade publications including *Insight*, Optometry Australia's news blog and *MiVision*. Key regional areas with the highest concentration of glaucoma patients were identified, and recruitment of participating optometrists was targeted at these locations. The selection of participating optometrists was based on practice location, specific equipment availability in the individual practices, optometrist availability, and previous experience in collaborative care.

As part of the program, the Glaucoma Unit has developed an ongoing education series to support the participating optometrists commencing in early 2019. These sessions provide opportunities to enhance glaucoma management strategies, as well as strengthen the collaborative relationship between the glaucoma medical team and optometrists in its small group interactive teaching style and open discussions.

CASE REPORT

As one of the first patients included in the program, Mr OW described being able to be followed up closer to home as a major advantage. The 80-year-old male was initially referred to the Glaucoma Clinic in 2005. Originally from Ghana and with a previous diagnosis of primary open angle glaucoma, he also had a history of left ocular trauma in 1978 and had been left aphakic after primary repair in the United Kingdom. Subsequently he underwent a secondary implant of an anterior chamber intra-ocular lens in 1993 after moving to Australia. He went on to have standard phacoemulsification surgery on his left eye in 2004. His highest IOPs registered while under care at the Eye and Ear were 28 mmHg in the right eye and 26 mmHg in the left eye. He has a family history of glaucoma (brother).

He is currently pseudophakic in both eyes and was enrolled in the program with controlled intraocular pressures of 14 and 15 mmHg in the right and left eye respectively. His corneal pachymetry is 549 and 542 µm. He uses Xalacom NOCTE in both eyes and Azopt BD in the left.

Mr OW had his first visit at the designated optometrist in the Glaucoma Community Collaborative Care Program (G3CP), six months after his Eye and Ear Hospital appointment. The local optometrist identified a left optic disc haemorrhage in his left eye and referred him back sooner for review.

Disc haemorrhages are characteristic linear haemorrhages perpendicular to the optic disc and occur on the superotemporal or inferotemporal disc margin most commonly. They are normally located in the prelaminar optic disc, cross the peripapillary zone, and extend into the adjacent superficial retinal nerve fibre layer.[16-18]

The aetiology of optic disc haemorrhages remains an area of active research and has not yet been characterised. A mechanical theory hypothesises that disc haemorrhages result from mechanical shearing at the lamina cribrosa[19] or because of damage to the capillary network at the border of retinal nerve fibre layer defect enlargement.[20] Essentially, this theory suggests that the primary insult is neurodegenerative, and the haemorrhage is a secondary event resulting from tissue damage. Other authors suggest various vascular aetiologies, for example, ischaemic microinfarction in the optic nerve head[21] or perturbation of the blood-retinal barrier.[22,23] In this theory, a yet unknown primary vascular problem increases tissue susceptibility to damage.

Description of prevalence of disc haemorrhages is quite varied and its reported prevalence in different types of glaucoma also varies. Using the Blue Mountain Eye Study as an example, disc haemorrhages were present in 13.8 per cent of participants with open-angle glaucoma (OAG; eight per cent of patients with high-pressure glaucoma and 25 per cent of patients with low-pressure glaucoma), 1.5 per cent of patients with ocular hypertension, and one per cent of normal subjects.[24]

Although disc haemorrhages are strongly associated with glaucoma, there are other causes. Diabetes mellitus, optic disc drusen, ischaemic optic neuropathies, vascular diseases of the retina, systemic hypertension, leukaemia and systemic lupus erythematosus

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Glaucoma

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are among a few. Posterior vitreous detachment can also cause optic disc haemorrhage.[25,26] A thorough history and close evaluation for evidence of non-glaucomatous optic neuropathies, disc oedema, retinal abnormalities or retinal vasculature changes may help to distinguish these entities as a potential cause of disc haemorrhage.

When associated with glaucoma, disc haemorrhage was a risk factor for perimetric progression in the Collaborative Normal Tension Glaucoma Study (CNTGS).[27] A large review investigating prognostic factors for visual field progression in patients with OAG found a clear association between visual field progression and disc haemorrhage in patients with NTG.[28] In the Early Manifest Glaucoma Trial the number of patient visits with disc haemorrhages increased the risk of perimetric and photographic optic disc criteria for progression.[29]

Mr OW's original appointment with the hospital was planned for six months after his visit to the optometrist. However due to the noted left disc haemorrhage, he was reviewed in six weeks at the Glaucoma Service after his visit to the optometrist and there was no progression in the visual field or disc appearance following clinical assessment. In fact, Mr OW's visual fields have been stable in both eyes for 15 years. His myopic changes in his fundi make the optical coherence tomography retinal nerve fibre layer analysis less reliable. The disc haemorrhage was no longer present, which was expected. No change in management was necessary and Mr OW continues to be a part of the G3CP with frequent follow-up visits shared between the optometrist and the Eye and Ear to closely monitor for progression.

Conclusion

The aim of the program is to provide greater access through regular community-based eye care, with patients being reviewed closer to home, reducing travel time and costs, as well as facilitating better access to Eye and Ear appointments. There will be ongoing communication between optometrists and the Eye and Ear Glaucoma Unit about the patients' progress to reduce the risk of adverse outcomes. With lower risk patients having regular reviews in the community, this will increase capacity for patients with more severe or unstable glaucoma to be seen at the Eye and Ear.

Specifically, patients with stable mild glaucoma (glaucomatous disc changes, visual field MD index < 6 dB, field loss not within central 10°) will be suitable for community monitoring, as will patients with moderate disease (glaucoma disc changes, visual field MD index 6-12 dB, field loss not within central 10°).

We hope this initiative will help to build robust, mutually-beneficial and lasting relationships with participating optometrists and ophthalmologists, promote continuing professional education and most importantly, benefit both low-risk glaucoma patients and those requiring more advanced care. ▲

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Demystifying Bull's Eye Maculopathy

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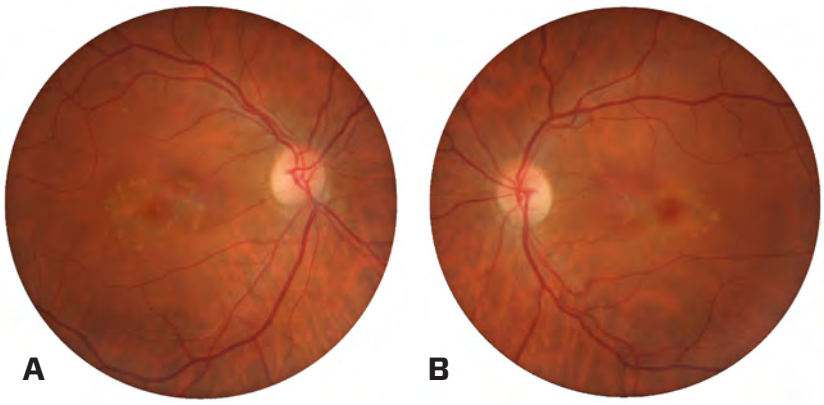

Figures 1A and 1B. Posterior pole photography shows bilateral hypopigmented oval rings centred at the fovea (OD > OS).

Drug-induced retinal toxicity can occur from the use of a number of systemic medications. Plaquenil (hydroxychloroquine) is an established drug for treating autoimmune and dermatological conditions such as systemic lupus erythematosus, rheumatoid arthritis, and discoid lupus with an emerging role in oncology including non-small cell lung cancer, chronic lymphocytic leukaemia.

Plaquenil can cause irreversible toxic retinopathy, a condition that can potentially produce vision loss and for which there is no treatment other than discontinuing the drug. Screening of patients taking Plaquenil aims at detecting any signs of retinopathy as early as possible—and before vision loss occurs. Equipped with modern imaging techniques and a sound understanding of the results, optometrists are in an ideal position to undertake this screening role. But first, we need to be familiar with the presentation of Plaquenil retinal toxicity and debunk a few common myths surrounding this condition.

CASE REPORT

A 48-year-old Caucasian female was referred to the Centre for Eye Health (CFEH) for a macular assessment. She felt her vision—particularly in the right eye—had deteriorated over the last 12 months. There was no family history of macular disease or blindness. Her entrance tests (Table 1) showed normal visual acuity and colour vision, but reduced contrast sensitivity and abnormal Amsler findings.

Fundoscopy and posterior pole photography (Figures 1A and 1B) showed bilateral hypopigmented oval rings centred at the fovea (OD > OS).

Spectral domain-optical coherence tomography (SD-OCT) (Figure 2A) revealed marked loss of parafoveal outer retina and retinal pigment epithelium (RPE) with associated homogenous signal hyper-transmission into the underlying choroid in the right macula. In the left macula (Figure 2B), parafoveal outer retinal loss was also evident, including attenuation of the outer nuclear layer (ONL), thinning and disruption of the external limiting membrane (ELM) and ellipsoid zone (EZ), although the RPE involvement was less pronounced.

Correspondingly, fundus autofluorescence (FAF) exhibited a ring of hypo-autofluorescence. (Figures 3A and 3B).

Humphrey Field Analyzer central 10-2 threshold perimetry (Figures 4A and 4B) showed a dense ring scotoma extending approximately 6-8 degrees from fixation, concordant with the structural findings. Inspection of the raw data also revealed the depression in the central points, more so in the right eye than the left.

To make the diagnosis, the missing piece of the puzzle lies in the medication history. This patient took Plaquenil for three years prior to 2010 and the indication for use was not disclosed. She also could not recall the drug dose and appeared within a healthy weight range. She was diagnosed with Plaquenil retinopathy in 2010 by her ophthalmologist and subsequently stopped taking the drug.

Her last ophthalmological review was in 2015. In 2018, when she presented at

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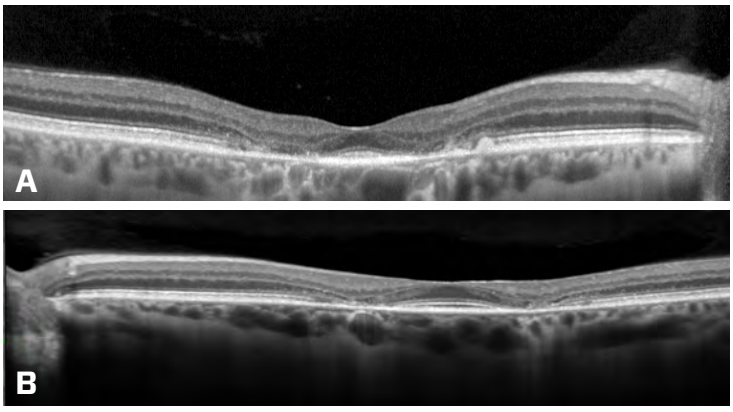

Figures 2A and 2B. SD OCT retinal nerve fibre layer imaging

	OD	OS
Best-corrected visual acuity	6/6	6/6
Contrast sensitivity (Mars)†	1.32	1.44
Amsler grid	Positive ring scotoma	Positive ring scotoma
Standard D15 colour vision	Pass	Pass

Table 1. Entrance test results
†Normal range is 1.72 to 1.92 log units for patients under 60 years old.

Bull's Eye Maculopathy

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the CFEH, there was evident parafoveal photoreceptor and RPE damage in a Bull's eye pattern, presumably caused by the Plaquenil, and unfortunately, there is no treatment to reverse the damage. To establish the rate of progression, this patient was referred back to her ophthalmologist who first diagnosed the retinopathy.

This case serves as a reminder of the importance of routine screening and early detection and segues into a discussion on myths surrounding Plaquenil retinopathy.

Myth number 1: Bull's eye maculopathy is pathognomonic for Plaquenil retinopathy

Bull's eye maculopathy is a general term used to describe maculopathy with the characteristic appearance of a dark central area at the fovea with a parafoveal zone of depigmentation.[1] Other than drug toxicity, it can occur in inherited macular disorders including cone dystrophy/degeneration, benign concentric annular macular dystrophy, and fundus flavimaculatus.[2] Broadly, the earlier age of onset, diminished visual acuity, impaired colour vision, and absence of concurrent medication history aids in differentiating inherited disease from acquired toxicity.

Plaquenil retinopathy does not always develop in a parafoveal (bull's eye) pattern, which is defined as a ring pattern two to six degrees from the centre of the fovea. In a study involving 201 patients with Plaquenil retinopathy, 12 per cent developed a pericentral pattern (retinal changes eight degrees from the fovea) near the vascular arcade.[3]

Although this pattern can be seen in all races, it is much more prevalent among patients of Asian ethnicity.[3] Consequently, the methods of screening should be adapted based on race.

Firstly, while central 10-2 visual field is the mainstay screening protocol for non-Asian patients, 24-2 or 30-2 visual field tests should be conducted on patients with Asian heritage, as reflected in the screening guideline by the American Academy of Ophthalmology (2016).[4]

A suspicious defect found in any of the central four test points in the 24-2 or 30-2 field should be taken seriously and subsequently confirmed with 10-2.4 Secondly, a singular OCT foveal line scan or radial scans are insufficient due to the lack of coverage of the pericentral zone. Clinicians should perform posterior pole volume scans and scrutinise each B-scan carefully for focal thinning or loss of the photoreceptor layers, including the ONL and/or EZ, and RPE, particularly if there are areas of reduced sensitivity in the visual field.

Myth number 2: If the VA is 6/6, the retinopathy must be mild

Due to the preservation of the photoreceptors and RPE in the foveal zone, such as in our case, patients with Plaquenil retinopathy can retain excellent visual acuity despite significant field loss. Visual acuity is neither a sensitive nor a reliable metric to describe the severity of toxicity. (Melles et al).[5] classified the toxicity stage based on SD-OCT and visual field (Table 2) with progressive outer retinal thinning and corresponding field loss in the mild-to-moderate stages, and eventual RPE involvement in the severe stage. RPE damage is visible on SD-OCT and can be confirmed by hypo-autofluorescence on FAF imaging. Fundus changes can be none-to-minimal in a mild and moderate stage of toxicity. A bull's eye fundus appearance, in our case, implies RPE loss and severe toxicity.

Myth number 3: Retinopathy will not deteriorate if the patient ceases the drug

Progression of Plaquenil retinopathy can occur even after the drug is discontinued and is dependent on the severity of toxicity. Marmor et al monitored 11 patients with established retinopathy for 13 to 40 months after the drug was stopped, and found that while visual field changes were inconsistent, OCT showed little visible change in early and moderate cases, but progressive thinning and loss of ellipsoid zone in severe cases.[6] Similarly, Kellner et al[7] found no progression in retinopathy without RPE damage, and progression in those with RPE damage. The authors also found that progression may be complicated by cystoid macular oedema and epiretinal membrane formation.[7]

In another study involving 15 patients with a mean follow-up of 26 months, OCT showed that progression occurred in 75 per cent of early toxicity and 100 per cent of severe eyes.[8] The most frequent anatomical changes were ONL thinning at fovea, EZ and RPE disruption at the parafoveal region.[8] The mechanism of progressive Plaquenil retinopathy after drug cessation is unclear. The binding and accumulation of the drug by melanin in the RPE cells

Stage of plaquenil retinopathy	SD-OCT	Visual field	Funduscopy
Mild	Isolated parafoveal thinning of the outer retina	Corresponding isolated field defects (contiguous scotoma points)	None
Moderate	Parafoveal outer retina thinning on both side of the fovea	Partial or full ring scotoma	Minimal to none
Severe	Outer retina thinning and RPE disruption	Severe field loss	Bull's eye maculopathy

Table 2. Staging of Plaquenil Retinopathy (adapted from Melles et al[5])

and the slow clearance of the drug from the body (months) may explain progression for some patients, but the question of why the progressive retinopathy extends for many years remains unanswered.[9]

Myth number 4: Annual screening applies to everyone

The American Academy of Ophthalmology (AAO) 2016 Hydroxychloroquine and Chloroquine retinopathy screening guideline recommends baseline screening before or within the first year of drug use and commencement of annual screening after five years for patients without major risk factors.[4] Major risk factors are high dose (> 5.0 mg/kg real weight for Plaquenil), duration of use (> 5 years), renal disease (defined as reduced glomerular filtration rate), tamoxifen use and presence of macular disease.[4]

If a number of risk factors are present, screening may be indicated before five years or more frequent than the yearly schedule. The duration of screening is not specified by the AAO guideline or the manufacturer, although it is likely to be required indefinitely.[9]

Myth number 5: Patients should be advised to discontinue the drug as soon as retinopathy is evident

The benefits of drug cessation should be carefully weighed against the medical risks that are managed. Early retinopathy carries minimal risk of vision loss and the consequence of stopping Plaquenil can be life-threatening for some patients. Therefore, while we can advise the patient and the treating practitioner about the risk of vision loss, we should refrain from recommending treatment alteration to the patient directly. Instead, the decision should be made in conjunction with the ophthalmologist, the prescribing medical practitioner and the patient.

Key messages

Plaquenil is a widely used drug in autoimmune conditions. Screening for Plaquenil retinal toxicity is critical as the damage is irreversible. The goal of screening is to recognise the signs at an early stage and to prevent central vision loss.

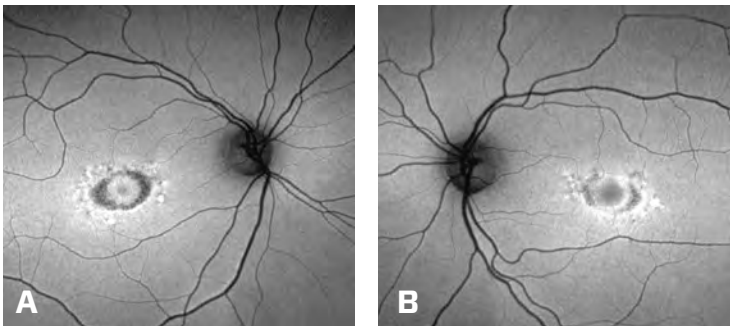
Modern screening supports the use of SD-OCT, and visual field as primary tests, as well as FAF as a useful adjunctive test. Optometrists without access to these techniques should refer to fellow colleagues or ophthalmologists.

Not all patients with Plaquenil retinopathy present with the classic parafoveal pattern, those with Asian ancestry typically display early damage in a pericentral pattern, thus require wider field structural and functional investigation.

Optometrists should be acquainted with the latest screening guideline and inform the ophthalmologist and the prescribing medical practitioner promptly once definitive signs of retinopathy are recognised.

The decision of drug cessation should be made in conjunction with the ophthalmologist, the prescribing medical practitioner and the patient. ▲

The author would like to thank Dr Angelia Ly for reviewing and input into this article.



Figures 3A and 3B. Fundus autofluorescence (FAF) exhibits a ring of hypo-autofluorescence.

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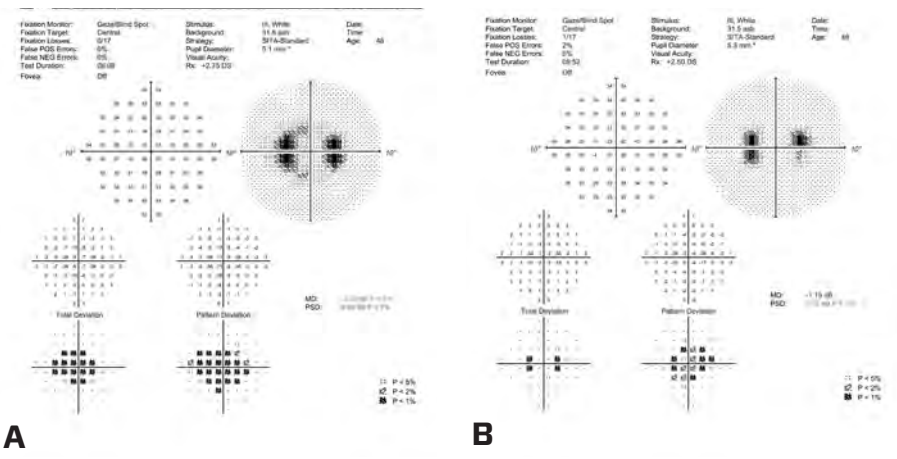

Figures 4A and 4B. Humphrey Field Analyzer shows dens ring scotoma extending approximately 6-8 degrees from fixation

Personalised medicines for eye care

Working with compounding pharmacists

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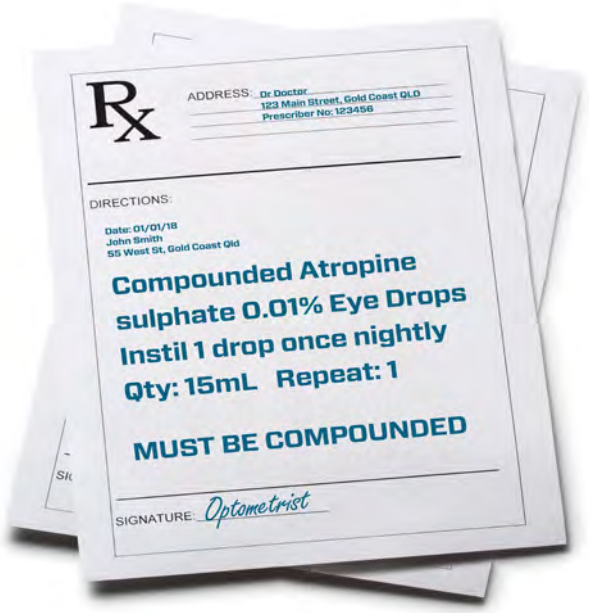

Figure 2. Example of a script for atropine eye drops

Compounding, also referred to as 'extemporaneous dispensing' is the supply of a single 'unit of issue' of a therapeutic product intended for a specific person in response to an identified need.[1,2]

These compounded products are prepared in a community or hospital pharmacy and must be safe, efficacious and of a consistently high quality.[1] The preparation of these compounded products is governed by a number of professional standards and guidelines[1-4] and pharmacists are required to meet the Pharmacy Board of Australia and relevant state guidelines. No additional training or formal certification is required for a pharmacist to prepare compounded products.

Compounding pharmacists can work with optometrists and ophthalmologists to meet patient needs, when commercial products are not available or those commercially-available are not suitable for patients.[2] Examples of requests for compounded preparations for eye care include antibiotics (gentamicin, tobramycin), antifungals (clotrimazole), antivirals (acyclovir) and N-acetylcysteine for cataracts.

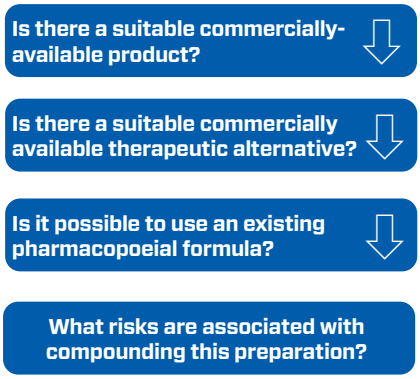

Figure 1. Compounding decision support and risk assessment tool (adapted from the Professional Practice Standards[2])

How are eye drops compounded?

Ophthalmic products are sterile preparations that if prepared extemporaneously are governed by additional guidelines for 'complex compounding' since they involve special competencies, equipment, processes and facilities for their preparation.[1,2,4] Criteria to provide quality, patient-centred compounding services are detailed in the Professional Practice Standards.[2]

The standard includes a compounding decision support and risk assessment tool (Figure 1) to assign a risk-rating related to the product, personnel and patient.[2]

Ingredients and formula

Ophthalmic products are sterile, liquid, semi-solid or solid preparations that may contain one or more active pharmaceutical ingredients (APIs) intended for application to the conjunctiva, the conjunctival sac or eyelids. A number of monographs for ophthalmic products exist in professional formularies such as the British Pharmacopoeia (BP), United States Pharmacopoeia (USP) and the Australian Pharmaceutical Formulary (APF).[1] When a non-pharmacopoeial formula is used, the pharmacist is required to cite references relating to the stability, safety, and efficacy of the product.[2] Since ophthalmic preparations are required to be sterile, an aseptic manufacturing process is usually employed, when the nature of the dosage form (for example: too viscous to filter) precludes the use of routine sterilisation methods.[5]

Sterilisation

Sterilisation is achieved by filtration (most applicable to use in a community pharmacy) or by heating in an autoclave, according to specifications detailed in the BP.[1] Sterile compounding is required to be undertaken within cleanrooms and ancillary areas, using isolators,

laminar flow cabinets, and laminar flow workbenches that meet Australian Standards, using protective clothing and equipment specifically designed for, and dedicated to, the preparation of these sterile products.[4] Dedicated ingredients are required from approved sources (such as TGA-registered sources) and measuring equipment must be appropriately sterilised.[2]

Water for injections (sterile water used to dilute or dissolve drugs) is usually used as a vehicle for eye drops, and sodium chloride is added to ensure the drops are approximately isotonic with lachrymal secretion.[1] Some formulas may require buffers, which need to be carefully selected, since they can reduce the stability of certain medicines if heat sterilisation is used.[1] If a thickening agent is required, ingredients such as hypromellose 4500 may be added.[1] Thickening agents moisten, soothe and lubricate the surface of eye and retain the drop on the eye for longer, however at high concentration their viscosity might make it difficult to sterilise the final product by filtration.[6] Since patients can develop sensitivity to preservatives over time with repeated application of a product, alternative preservatives can be substituted or preservative-free single-use units may be used.[1]

Packaging

Compounders have access to a wide variety of packaging options that can be discussed with the prescriber to ensure stability of the product and to accommodate any patient preference. The volume of product in each container is generally limited to discourage prolonged storage.[7]

Tips for patients

The APF provides instructions for pharmacists on counselling patients on the appropriate administration of eye drops, ointments and gels; relevant cautionary advisory labels that are to be attached to the primary container.[1] Flyers are also available online from Safe Medication.[7] Pharmacists will also advise patients to store products away from children and pets. Ophthalmic products are generally required to be stored below 25°C, unless otherwise specified, for example where the API or other excipients in the product may be sensitive to elevated temperatures. The compounding pharmacist will also provide the patient with product information in the form of a Consumer Medicines Information (CMI) leaflet, which outlines safe use, storage and expiry.

Compounding atropine 0.01% eye drops

Control of myopia progression, particularly in children, has become an important goal, due to the increased global prevalence of myopia and the increased risk for ocular pathology associated with high myopia.[8,9] A recent review of the epidemiology and pathophysiology in myopia by Wu et al[8] highlights clinical trials using atropine in school-aged children. Recent clinical trials have demonstrated that low-dose atropine (0.01%) slows myopia progression, with significantly less side-effects compared to higher concentration preparations.[8,10]

Note: Low-dose atropine (0.01%) eye drops are not commercially available, and may be prepared by a compounding pharmacist in appropriate sterile facilities.

When a prescriber requests atropine 0.01% eye drops

The following case outlines the process that a compounding pharmacist would take when presented with a request from the prescriber. (Figure 2 provides an example prescription). It is important that the prescriber clearly states on the prescription that the product is to be compounded, to prevent the accidental dispensing of the commercial 1% product. The existing commercial product (Atropt Eye Drops) cannot be used since it contains 100 times the concentration of atropine (Table 1).

Can the commercial product be diluted?

While the commercial product could be diluted to contain the correct amount of atropine, and sterility can be maintained via filtration, dilution will have altered the concentration of excipients present with potential to affect both the stability and solubility of the atropine and the preservative efficacy as well as the consistency (thickness).

Step 1. Design of an appropriate formula

A drug (salt) is chosen based on its solubility and stability: Atropine sulfate a weakly basic drug, which has the following solubilities in 100 mL (water 0.22g; ethanol 50g; glycerol 3.70g).[11] Degradation of atropine sulfate is primarily due to hydrolysis, with the rate of hydrolysis increasing at temperatures above that of room temperature. Stability and solubility is thus optimum for aqueous atropine in an acid solution (pH 3-4).[12] Atropine sulfate is also susceptible to light degradation and this should be reflected on in the choice of the immediate container and/or advice to protect the product from light during preparation and during use by the patient.[6]

Step 2. The form of the drug that will be used to compound the product is chosen

Pure raw material may be used, but this is limited by the amount that can be weighed accurately (due to capacity of the balance). A commercial product for example, a 0.6 mg/ml and 1.2 mg/ml injection, which may also be used as a source of atropine, has the added advantage that it is sterile.

Step 3. The excipients to deliver and optimise the stability of the drug are chosen.

These are included to preserve the solution (benzalkonium chloride, disodium edetate, benzyl alcohol) maintain pH at about 4.5 (boric acid,

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Atropt Eye Drops® 1%	Compounded low strength eye drops (0.01% strength)
Atropt Eye Drops® 1% contains 1g of atropine sulfate per 100mL. 1g = 1000mg, therefore, Atropt Eye Drops® 1% contain 1000mg of atropine sulfate per 100mL.	Compounded low strength eye drops (0.01% strength) needs to contain 10 mg (0.01g) per 100mL.
10mg is 100 times less than 1000mg.	

Table 1. Calculation showing that the compounded product will need to contain *100 times less* the atropine concentration of the original product.

AUDIT	involves pharmacists complying with legislation and checking their own practice against standards.
QUALITY ASSURANCE	ensures the quality of compounded products and must include training, SOPs, documentation, verification, testing, cleaning, disinfecting and safety, containers, repackaging, labelling and storage and responsible personnel.
QUALITY CONTROL	documenting policies and procedures ensures quality control, which verifies that the quality assurance processes are in place to achieve the desired result.
RISK ASSESSMENT	risk identified to avoid adverse events should be followed by a plan to either eliminate or mitigate the risk. KEY AREAS – pharmacy premises, product, personnel, patient.

Figure 3. Checklist for complex compounding

Compounding

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sulphuric acid, hydrochloric acid) and maintain isotonicity (sodium chloride).

Best practice standards are applicable to all pharmacists, no matter the level of complexity of the compounding undertaken. Figure 3 details processes that pharmacists undertake for complex compounding from an internal or external audit for assessing risk in terms the pharmacy, product, staff and patients.

Optometrists interested in prescribing compounded products should identify a pharmacy equipped to compound sterile preparations, since these products require specialised equipment and facilities. (The current PBS List on the Optometry Australia website, provides a brief state-by-state directory of ophthalmic compounding pharmacists). A visit to the compounding pharmacy will provide the prescriber with further confidence that the pharmacy will be able to provide a service to meet the eye care needs of their patients. ▲

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CLINICAL AND EXPERIMENTAL

OPTOMETRY

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One of the most commonly-encountered ocular surface conditions in Australia, thanks to our ultra-violet exposure, is pterygium, with a prevalence of approximately seven per cent in patients aged 49 years or older.[1] This tends to occur on the nasal interpalpebral zone and encroaches onto the cornea (Figure 1), although it can also infrequently occur in the temporal region. The sentinel finding is the growth of a fibrovascular membrane across the limbus, usually arrowhead in morphology.[2]

Progression of a pterygium further onto the cornea can impact vision by virtue of inducing astigmatism and, in later stages, by encroaching directly onto the visual axis. The only way to deal with this condition definitively is by surgical removal.

The most likely differential diagnosis is a pinguecula, a well-defined lesion, also in the interpalpebral zone that does not encroach onto the cornea, and so does not impact vision. Pingueculae occur in up to 70 per cent of the Australian population and tend to be stationary and occasionally inflamed with congested vessels. Unlike pterygia, pingueculae do not impact vision or cross the limbus, and rarely need surgery. Both, however, can cause some degree of discomfort due to the disturbance to the tear film.[3] Both these conditions need to be further differentiated from conjunctival

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*.

Accuracy of diagnosis of pterygium by optometrists and general practitioners in Australia

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neoplastic conditions which will be more vascular in appearance and irregular in consistency and shape.

Primary care clinicians such as optometrists and general practitioners play a role in the management of pterygia and will refer to an ophthalmologist for surgery when pterygia start to impact on either the vision or the cosmesis of the patient. Accurate differential diagnosis is therefore important.

Dr Lawrence Hirst, a Queensland-based ophthalmologist, made the observation that pingueculae were frequently misdiagnosed by general practitioners as pterygia, and so decided to compare the accuracy of general practitioner diagnosis to that of optometrists, using his own diagnosis as the benchmark.

To that end, Drs Hirst and Jane Smith examined 1,511 patients who had been referred to Dr Hirst over a nine-month period based on the diagnosis of a pterygium by either their general practitioner (549 cases) or their optometrist (962 cases).

General practitioners were 13.28 times more likely to incorrectly diagnose a pterygium than optometrists. When pterygia were misdiagnosed, they were incorrectly named as pingueculae by both clinician groups. General practitioners were more likely to only refer one patient during the nine-month observation period, while optometrists tended to refer more often.

The authors conclude that general practitioners misdiagnose pterygium more often than optometrists, most likely reflecting the available equipment, the in-depth ocular training and experience of optometrists versus the multi-disciplinary nature of general practitioners' practice.

These findings also support the concept that the optometrist is the central primary eye health care provider and that active collaboration needs to be encouraged between optometrists and general practitioners to ensure appropriate management of conditions such as pterygia. ▲

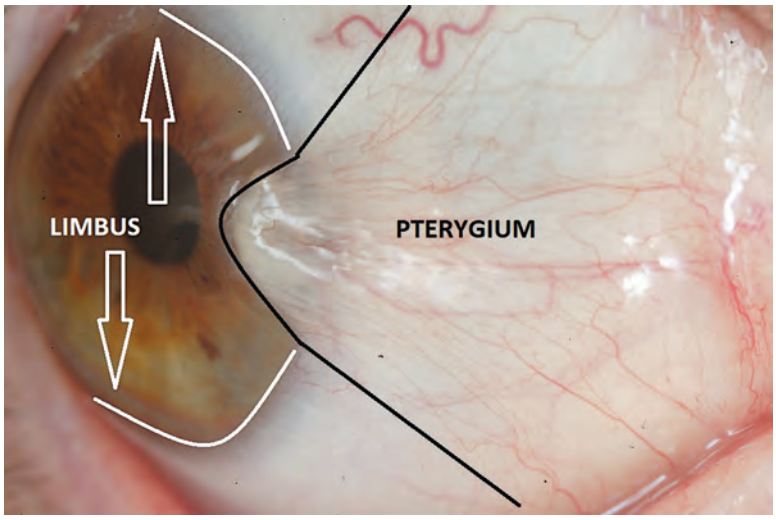

Figure 1. External photograph of a nasal pterygium which is crossing the limbus (arrows)

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Pregnancy and the eye

Ocular changes and pregnancy

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It's vital that optometrists are aware of the ocular changes associated with pregnancy, as well as the risks involved in the use of ophthalmic medications during pregnancy. The hormonal effects of pregnancy cause changes in many organ systems, including the eye. The ocular changes during pregnancy are typically transient, and may be classified as physiologic, pathologic, or modifications of pre-existing conditions.

The optometrist's role may differ depending on the condition encountered. For benign or minor conditions, the responsibility may be to counsel and reassure or to manage the minor condition independently through complete resolution. However, some conditions may need referral to ophthalmology for further evaluation or management.

Rarely, the investigation of an ophthalmic complaint may reveal a serious life-threatening condition. In this situation, the optometrist must make the appropriate referral to the obstetrician or to the emergency department for urgent care.

Physiologic changes

Typically, physiologic changes associated with pregnancy are transient and seldom pose a significant risk to long-term vision. Physiologic changes during pregnancy most commonly affect eyelids, cornea and intraocular pressure (IOP). Hyperpigmentation of sun-exposed skin (known as 'chloasma' or 'melasma') may affect the eyelids or periorbital skin. The condition is self-limited, and often resolves post-partum.[1] Because the skin change is benign, no treatment or referral is necessary.

Corneal changes during pregnancy have been well-documented and include an increase in thickness and curvature, which may result in changes in refractive error. Historically, it has been advised to wait several weeks post-partum to prescribe spectacle or contact lenses.[2] However, there are few studies that systematically examine refractive changes in pregnancy. Pizzarello found that pregnant women who complained of vision changes had myopic shifts of nearly one dioptre, all of which returned to near pre-pregnancy levels.[3] Similar findings were observed in a study of pregnant Nigerian women, which found the shifts occur most frequently during the third trimester.[4]

Pregnancy has also been identified as a potential risk factor for post-LASIK corneal ectasia.[5] For this reason, it is recommended to postpone pregnancy for one year following laser refractive surgery and to postpone refractive surgery for three to six months following pregnancy and lactation, and only once the refraction has stabilised.

Contact lens intolerance has been reported in 25–30 per cent of pregnant women. Corneal sensitivity is reported to decrease during pregnancy, so contact lens intolerance may be related to a decrease in tear production, or other pregnancy-related changes in the cornea, conjunctiva or lids.[6] The appearance of transient Krukenberg spindles without other signs of pigment dispersion syndrome have been reported.[1]

Intraocular pressure decreases by approximately 10–15 per cent during the pregnancy, most notably during the second half of pregnancy, and there is a decrease in diurnal fluctuation of IOP. No decrease in aqueous production has been demonstrated, so the decrease in IOP is likely due to increased trabecular outflow and/or reduced episcleral venous pressure. IOP returns to pre-pregnancy levels approximately two months post-partum.[7] The effect of pregnancy on pre-existing glaucoma has not been well studied, nor have the risks of glaucoma management been fully established.

Pathologic changes

Two key pathologic changes associated with pregnancy of which primary eye care professionals should be aware include: central serous chorioretinopathy and pregnancy-induced hypertension.

CSC

Central serous chorioretinopathy (CSC) is a spontaneous, localised serous detachment of the neurosensory retina from the underlying retinal pigment epithelium. It is typically self-limited, but may be recurrent or chronic. It is much more common in men than women, and pregnancy is a well-documented risk factor for the development of CSC. It is thought that increased levels of endogenous corticosteroids during pregnancy may be the reason for the increased incidence during pregnancy. Other risk factors include smoking, Helicobacter pylori infection and obstructive sleep apnoea. Patients with a history of CSC prior to pregnancy should be advised that it may recur during pregnancy; however, there are no recommendations for additional examinations during pregnancy.

CSC in pregnancy is most common in the third trimester, and is more likely to have yellow subretinal fibrin deposits compared to CSC in men and non-pregnant women.[8] It typically resolves by one to two months post-partum, but has been reported to recur in subsequent pregnancies.[1,9]

Optical coherence tomography (OCT) is a non-invasive diagnostic tool that allows for diagnosis of CSC without the need for invasive intravenous fluorescein angiography. CSC during pregnancy is not associated with fetal risks.

PIH

Pregnancy-induced hypertension (PIH) includes pre-eclampsia and eclampsia. Pre-eclampsia includes hypertension and proteinuria. Eclampsia is diagnosed when a pre-eclampsia patient develops seizures. Eclampsia is a life-threatening

emergency, and immediate attention must be given. Both pre-eclampsia and eclampsia have been reported to cause vision disturbances including blur, photopsia and visual field defects.

Clinically, the most common ocular finding of PIH is localised or generalised constriction of the retinal arterioles. Other findings of hypertensive retinopathy (intraretinal haemorrhages, cotton wool spots) may also be seen.

All vision changes associated with PIH should be taken very seriously, as they may indicate an impending seizure and require immediate care. The appropriate referral of such a patient is an immediate referral to the obstetrician rather than to a retinal specialist.[10] Severe vision loss is rare but possible in PIH. Serous exudative retinal detachments as well as cortical blindness have been reported. Fortunately, both conditions tend to resolve days to weeks following delivery.

Pre-existing conditions

Pregnancy is an independent risk factor for worsening of diabetic retinopathy. Pre-existing diabetes is present in 1 in 167 pregnancies in Australia.[11] The more severe the level of retinopathy at conception, the more likely there will be progression during pregnancy.

Other risk factors for progression of retinopathy include duration of diabetes and poor pre-pregnancy glucose control. Gestational diabetes is not associated with diabetic retinopathy. While regression of retinopathy is common in the post-partum period, some women will continue to experience worsening for up to one year following delivery. Therefore, careful monitoring of diabetic patients during the first year post-partum is important.[10,11] Examination recommendations vary depending on the organisation, but there are some common guidelines.

A comprehensive eye examination is recommended in the first trimester for all pregnant women with pre-existing diabetes. Depending on the level of retinopathy found during the first trimester, additional examinations are recommended later in the pregnancy. For example, the American Academy of Ophthalmology recommends an eye exam for pregnant patients with diabetes every three to 12 months if no retinopathy or mild nonproliferative retinopathy (NPDR) is present, and an exam every one to three months if the retinopathy is severe NPDR or worse.[12]

Pan-retinal photocoagulation (PRP) is safe during pregnancy. Typically reserved for patients with proliferative disease, several guidelines recommend PRP earlier in pregnant patients (at the level of severe non-proliferative retinopathy).[10]

Treatment of diabetic macular oedema (DME) in pregnant women is more controversial. Data is lacking as to the natural history of DME during pregnancy, and the American Academy of Ophthlamology guidelines recommend delaying focal laser treatment in pregnant patients.

Anti-VEGF injections have emerged as a more recent treatment option for DME. Their use during pregnancy is controversial, however, as they may cause systemic side effects to the mother and foetus, including loss of pregnancy.[12] Several case reports have been published in which spontaneous miscarriage occurred shortly after intravitreal anti-VEGF injections. While causation cannot be determined, Polizzi and Mahajan recommend that anti-VEGF be utilised only when the benefit to the woman justifies the risk to the foetus.[13]

The optometrist plays an important role in the care of the diabetic patient. Unless the patient presents with retinopathy requiring treatment, the optometrist can provide the examination and testing such as fundus photography and optical coherence tomography (OCT), and can make the appropriate recommendations regarding follow-up care. If the retinopathy requires treatment, a referral to an ophthalmologist or retinal specialist is appropriate. In all cases, whether or not treatment is needed, the optometrist has an obligation to communicate the examination findings and recommendations with the patient's general practitioner and obstetrician.

Use of ophthalmic medications during pregnancy and lactation

Caution should be used when administering or prescribing medication to a pregnant woman. Topical medications may be absorbed through the nasolacrimal mucosa and may pass through the placenta or be excreted in breast milk, creating a potential risk to the foetus or neonate. Limited data is available on the safety of medication use in pregnancy, particularly the use of topical medications. A review by Chung suggested that the topical ophthalmic use of medications during pregnancy presents very low risk of harm due to the small amounts of medication absorbed.[14] However, general guidelines for use of ophthalmic medications during pregnancy and lactation include: avoid medications if possible during the first trimester; avoid unnecessary drugs throughout pregnancy; use the smallest dose and shortest duration necessary to achieve the desired therapeutic effect; and use digital nasolacrimal occlusion or gentle eyelid closure for several minutes following instillation to reduce systemic absorption. Consulting with the patient's obstetrician or pharmacist about the utilisation of pharmaceutical agents is appropriate in some situations. Finally, the patient should be informed about the medication choices and the information (or lack thereof) related to the safety of the proposed treatment. Information is available from a variety of sources. The drug package insert may contain information related to pregnancy and lactation, although many drugs have not been well studied. Texts such as *Drugs in Pregnancy and Lactation* (Brigg, et al) provide information on many medications. Websites such as mothertobaby.org also provide referenced, scientific evidence on a variety of medications. However, ophthalmic (topical) medications are often overlooked in such references.

Diagnostic agents

Topical anesthetics and sodium fluorescein dye used in a routine ophthalmic examination are considered safe during pregnancy. Mydriatic and cycloplegic agents are all assigned Category C (animal reproductive studies have shown an adverse effect on the foetus, but there are no adequate human studies), but their topical ophthalmic use has not been studied extensively. Generally, dilated eye exams are deferred until post-partum. While non-mydriatic wide-field photography does not replace pupillary dilation, it may be appropriate in lieu of dilation in routine cases. However, in situations in which dilation is important for diagnosis, such as a patient with a complaint of photopsia or a patient with pre-existing diabetes, the benefit of the dilation outweighs the risks, and dilation should

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be performed. Chawla et al reported that the use of dilating drops during pregnancy is safe.[15]

Anti-infective agents

Consideration must be given to the risk and benefit of treating an ocular infection during pregnancy. While unnecessary medications should be avoided, a pregnant patient should not be required to suffer needlessly.

Non-pharmacologic measures such as warm compresses and lid scrubs for blepharitis, or saline rinses for mild bacterial conjunctivitis, may be considered in lieu of drug therapy. However, a bacterial keratitis presents significant risk of permanent vision loss if not treated promptly. The optometrist should not hesitate to treat painful and/or sight-threatening infections with medication.

Topical anti-bacterial agents in Category B (presumed safe) include azithromycin, erythromycin and tobramycin. Topical fluoroquinolones are all labeled Category C (unknown safety) except for besifloxacin, which reports no available human data. Given a variety of available Category B topical medications, it would be prudent to avoid the fluoroquinolones in the treatment of conjunctivitis. However, given their efficacy in treating bacterial keratitis, the benefit of their use in a corneal ulcer likely outweighs any small risk involved.

Systemic antibiotics may be needed in the case of a soft tissue (lid) infection. Penicillins and cephalosporins, commonly utilised in the management of internal hordeolum or preseptal cellulitis, are considered safe during pregnancy. Likewise, erythromycin and azithromycin are considered safe to use. Tetracycline and its derivatives should be avoided in both pregnant and lactating women due to the possibility of bone and teeth abnormalities in the foetus/infant.

Oral antivirals acyclovir, valacyclovir, and famciclovir are Category B medications and are generally considered safe during pregnancy. Given the potential complications of untreated herpetic infections, the benefit outweighs the risks of antiviral therapy.

Anti-inflammatory and allergy agents

Most topical antihistamine agents are designated Cateory C. Despite this designation, there are no reported adverse effects from topical antihistamine agents. Limited use for symptomatic patients when non-pharmacologic intervention is insufficient in relieving symptoms, is probably safe during acute episodes of significant ocular allergy. While systemic corticosteroids are a relative contraindication during pregnancy, there are no known teratogenic effects of topical steroids.[14,15] When considering the potential risks of untreated anterior uveitis, the benefits of topical steroid therapy likely outweigh the risks.

Anti-glaucoma agents

Brimonidine is the only Category B glaucoma medication. However, since brimonidine can cause severe central nervous system depression in neonates and infants, it should be discontinued prior to delivery and avoided during lactation.[16] Topical beta-blockers have been associated with foetal bradycardia. However, systemic beta blockers are often used by obstetricians to treat systemic hypertension in pregnant women; as such, topical timolol, particularly in the lowest concentration used once daily, is probably safe during pregnancy. Some experts recommend discontinuing several days prior to delivery to avoid foetal bradycardia.[14-15] Prostaglandin analogs are associated with premature labour or miscarriage in animal studies. Although there are case series in the literature in which pregnant women were exposed to latanoprost with no adverse pregnancy outcome, this class of medication should be avoided during pregnancy. Oral acetazolamide has been associated with teratogenic effects on the foetus. No reports of adverse effects have been reported from topical carbonic anhydrase inhibitor use.[17]

Because intraocular pressure is often reduced during pregnancy, it may be possible to manage glaucoma without medication or with limited medication to reduce the risk of harm to the foetus. Laser trabeculoplasty may also be an appropriate option for pregnant patients who need additional IOP lowering.

Summary

Pregnancy is responsible for many changes in the eye. Physiologic changes, while benign, may result in the pregnant patient presenting to the optometrist for care. Pathologic changes may also bring the pregnant patient in for evaluation. It is important for the optometrist to be familiar with the benign and more serious complications associated with pregnancy. In the event that medical therapy is indicated, a cautious approach is indicated to minimise potential harm to both the mother and the developing foetus. ▲

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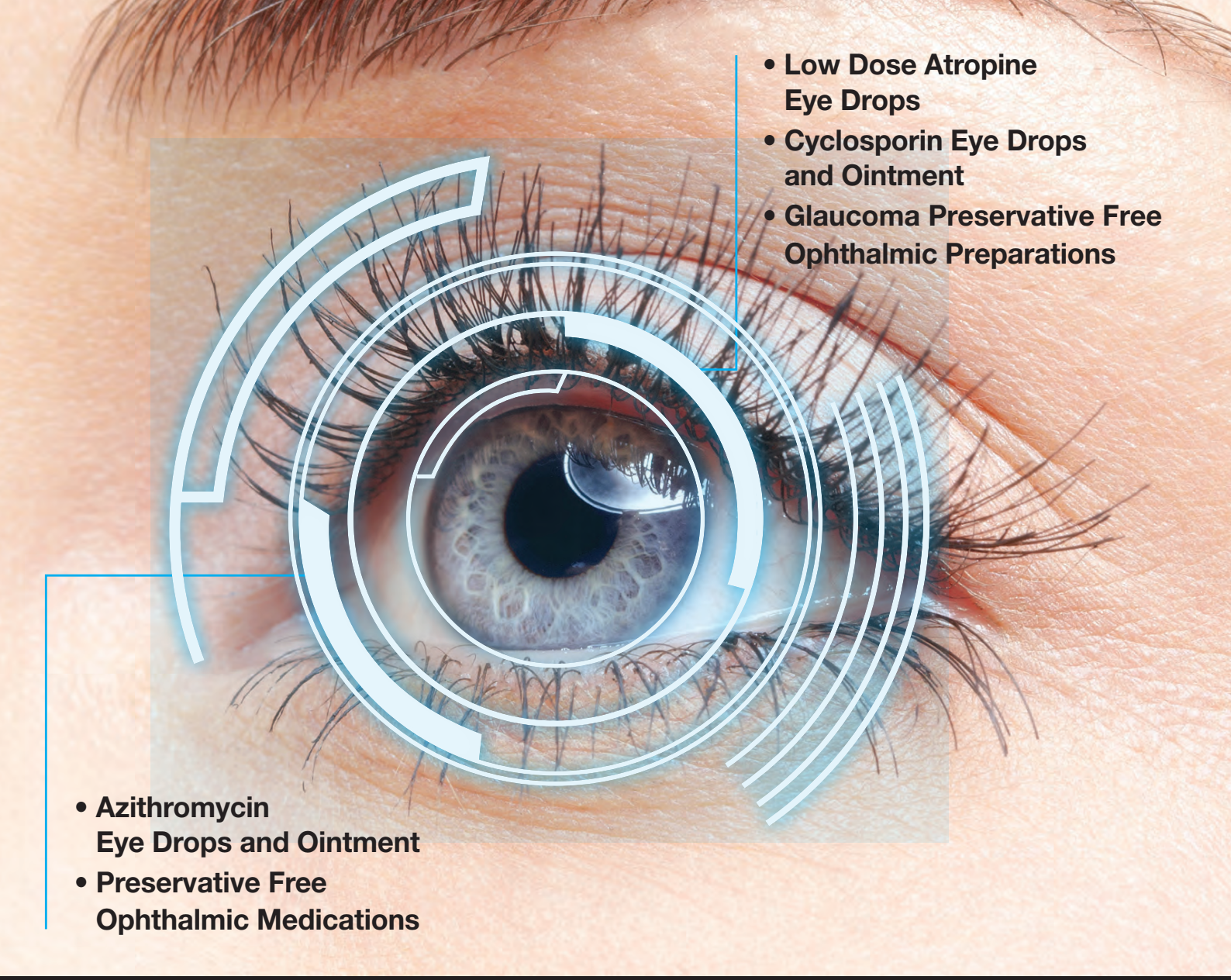

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