Supplement to
AUSTRALIAN OPTOMETRY

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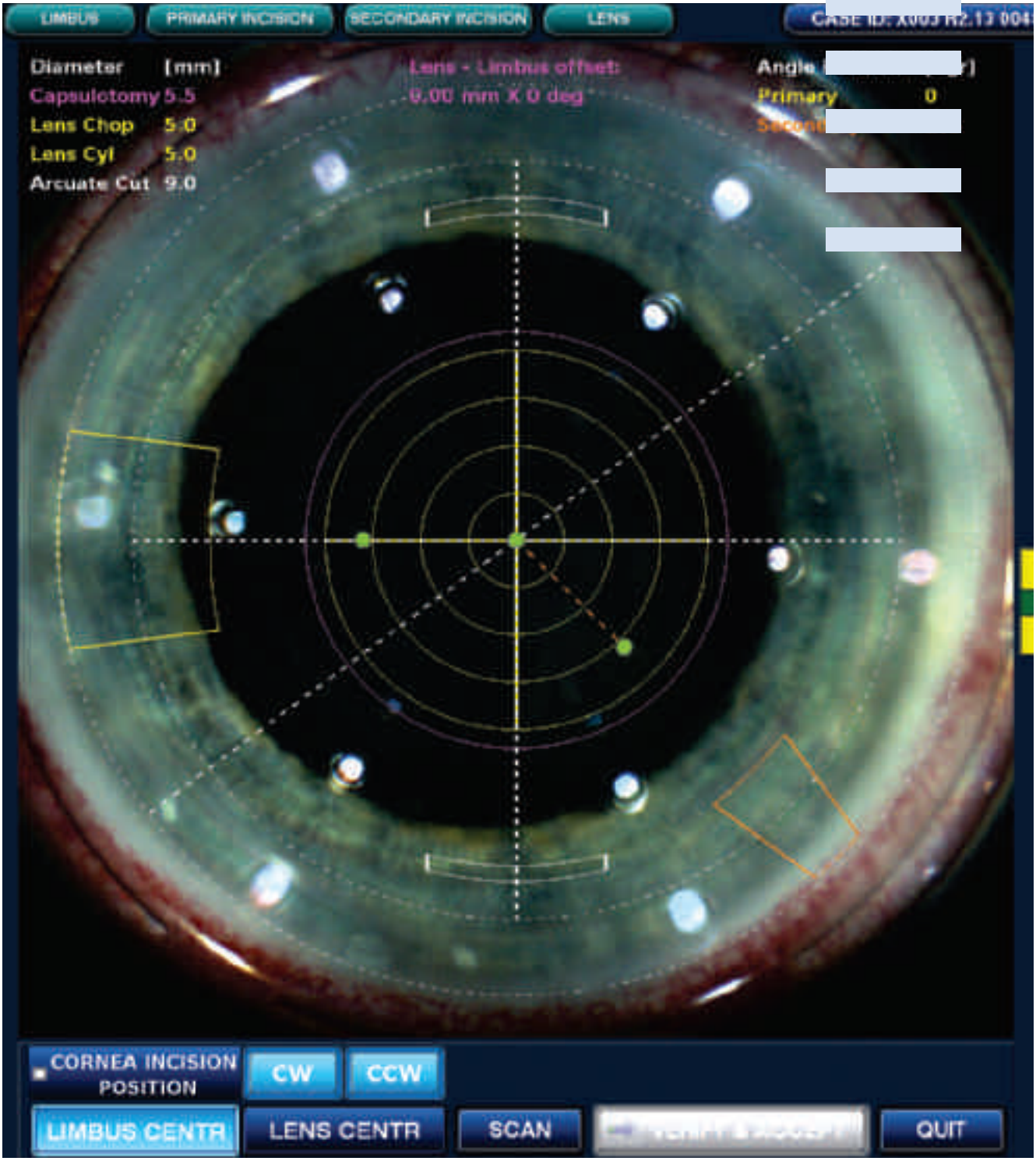
MARCH 2012



- **Femtosecond laser cataract surgery**
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1. Data on file. Alcon Laboratories, Inc. 2. Ketelson HA, Davis J, Meadows DL. Characterization of a novel polymeric artificial tear delivery system. Invest Ophthamol Vis Sci; 2008; 49: E-Abstract 112.

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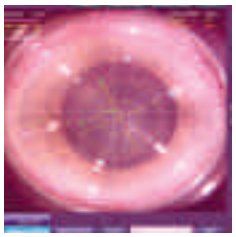
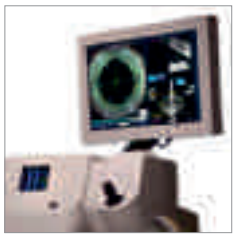

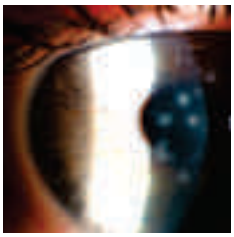
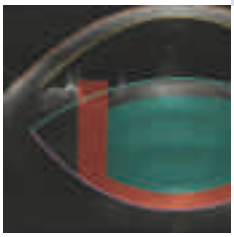

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COVER
Photo: Corneal and lenticular incision overlay viewed through video microscope of Alcon LenSx laser system

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How the technology

The recent introduction of femtosecond lasers to cataract surgery is a significant advance. This new and exciting technology has the potential to improve the safety and visual outcomes for thousands of Australians undergoing sight-restoring surgery each year.

Dr Tim Roberts
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Femtosecond lasers deliver ultra-short pulses of energy at near infrared wavelengths that disrupt tissue at a precise molecular level. They have been used in ophthalmology for many years, most commonly during LASIK, which has now become the standard procedure for performing refractive surgical procedures. The significant reduction in complications and improved safety and refractive outcomes have resulted in the wide acceptance of femtosecond lasers for LASIK procedures.

Cataract surgery is one of the safest and most successful major surgical procedures performed worldwide but the safety and refractive results still lag behind those of laser refractive surgery. The success of LASIK has stimulated interest in the use of femtosecond lasers for cataract surgery in an effort to improve outcomes and reduce complications.

Computer-guided laser cataract systems

This exciting new technology integrates high-resolution imaging systems with a femtosecond laser to perform key stages of the procedure with micron-level surgical precision. It advances an all-manual procedure to a more accurate laser procedure by creating precise and reproducible clear corneal incisions (with potentially less risk of wound leak and post-operative infection) and anterior capsulotomy (with greater accuracy and predictability compared to conventional manual capsulorrhexis), by fragmenting the lens nucleus (with reduced surgical time and energy levels compared to conventional phacoemulsification) and by correcting astigmatism with precise corneal relaxing incisions.

Several companies are developing laser systems for cataract surgery. The Alcon/LenSx system is currently the only one listed on the Australian Register of Therapeutic Goods for cataract surgery, with other systems expected to be registered for use in Australia in the near future. Each system incorporates different technology to image the anterior segment and dock the eye.

LensAR (Winter Park, FL) uses Scheimpflug imaging and a motorised servo-controlled head with a non-applanating suction fixation device that does not directly touch the cornea. OptiMedica (Santa Clara, CA) uses customised spectral-domain OCT imaging and a fluid-filled interface. Alcon/LenSx (Aliso Viejo, CA) uses pre-laser and real-time OCT images and a single-piece curved 13 mm diameter patient interface.

Potential benefits

- **Precise and reproducible corneal incisions**

Clear corneal incisions (CCI) remain the preferred method for surgeons accessing the anterior chamber during cataract surgery. The benefits of using CCIs are speed of recovery and improved visual outcomes;[1] however, an increase in the incidence of endophthalmitis, particularly since 2000, has been linked to the use of CCIs.[2] Manually created incisions make it difficult to control the length or architecture of the incision that may affect the stability of the wound under

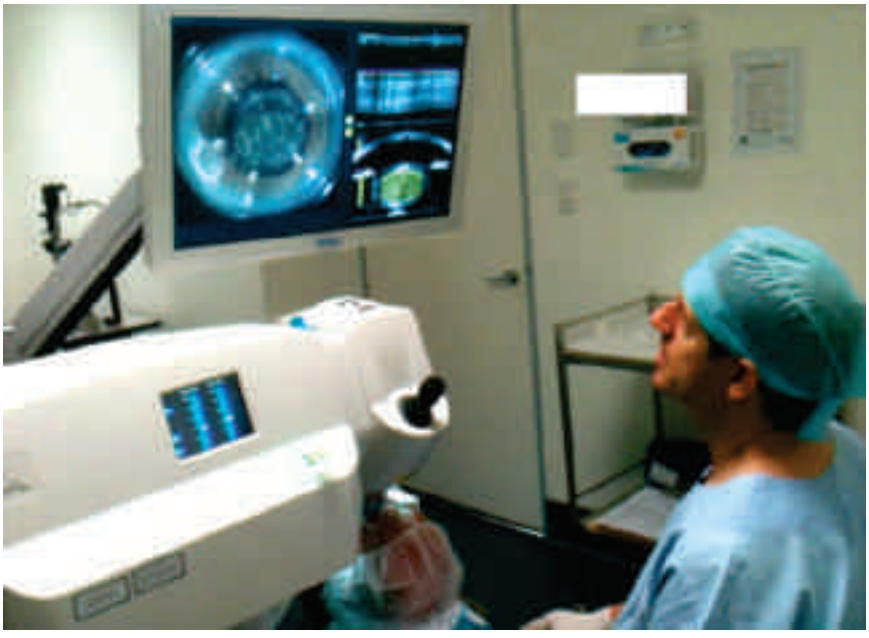

Figure 1. The procedure is performed under topical anaesthesia

works in a clinical setting

pressure following surgery and potentially allow leakage.

Laboratory studies on cadaver eyes show the femtosecond laser produces reproducible and stable incisions attributable to the controlled and more reproducible generation of squarer incisions and the multiplanar configuration of the corneal wound created.[3]

- **Accurate capsulotomy and refractive outcomes**

Precise capsulotomy size and contour is important in determining effective lens position and refractive outcomes.[4,5] A poorly-constructed capsulorrhexis can lead to an anterior capsule tear and subsequent complications.[6] A perfectly constructed, reproducible laser-cut capsulotomy should decrease complications and improve refractive outcomes. Laser-cut capsulotomies have greater accuracy and predictability compared to conventional manual capsulorrhexis with a 100 per cent accuracy of ± 0.25 mm[7] with a 12-fold improvement in precision.[8]

The anterior capsulotomy is the primary step in cataract surgery that can influence the position and centration of the IOLs (effective lens position) and consistent, well-centred capsulotomies are likely to reflect in more producible, better refractive outcomes.[9] We have found that with improved software and surgical experience, the incidence of anterior capsular tears is now extremely low.

- **Reduced phacoemulsification time**

Fragmenting the lens nucleus with the laser reduces the surgical time and energy levels compared to conventional phacoemulsification. Nagy's original paper with the LenSx laser showed that laser phacofragmentation resulted in a 43 per cent reduction in phacoemulsification power required and a subsequent 51 per cent decrease in phacoemulsification time. The laser units currently available employ varying treatment patterns and this may reflect the initial differences in results.

Further experience, in research and in clinical settings will help optimise these results across the board; however, it will remain to be seen whether this represents a clinically significant difference in safety to patients compared to current standard techniques. A review of the first 250 cases I performed, including the initial cases during the steep learning curve, found the average reduction in phaco time was 47 per cent. This suggests that the femtosecond laser may have further potential benefits in reducing corneal endothelium stress, although further short- and long-term studies on cell density are required.

Australian experience

We installed an Alcon LenSx system in Sydney in late March 2011 and the first laser cataract procedure was performed in April 2011. At the time of installation, this was the fourth such system installed worldwide (Budapest, Hungary; Texas and Utah, USA). Since then two units have been installed–one in Sydney and one in Melbourne–and one will be installed in Hobart early in 2012.

Our facility is a private multispeciality practice with an ambulatory day surgery centre and refractive laser facility located over two levels in suburban Sydney. The surrounding suburbs would be described as middle class. The eight surgeons operating at our practice have performed more than 1,000 laser cataract procedures. Worldwide, more than 170 ophthalmic surgeons have been trained using the LenSx laser and the total number of procedures performed is over 7,500.

Surgical procedure

We have located the laser in a purpose-built room adjacent to the entrance of the ambulatory day surgery centre. The patient walks in with assistance and is placed on the operative bed and the procedure is performed under topical anaesthesia (Figure 1). The eye is stabilised with a suction 'docking' system that allows imaging of the anterior segment and precise alignment of the laser delivery system (Figure 2).

Continued page 4

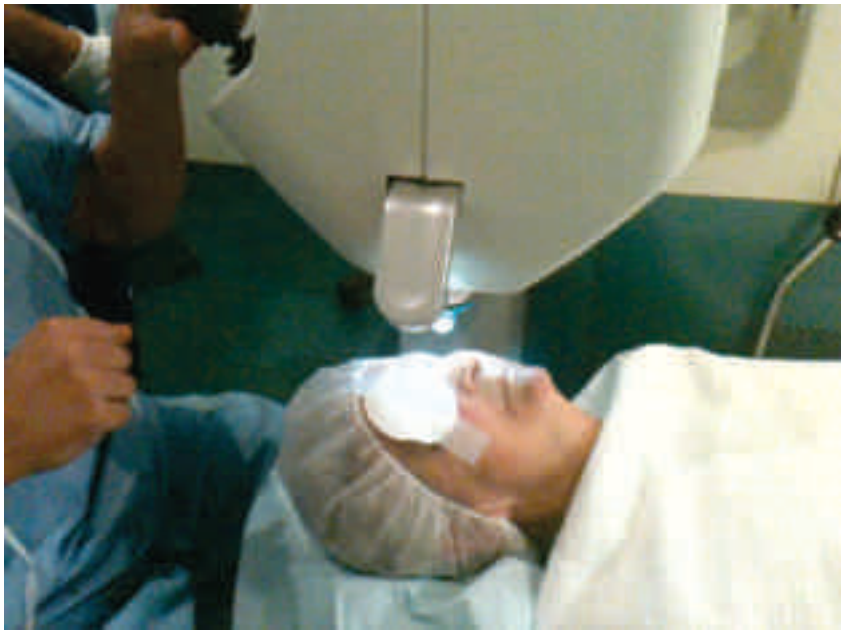

Figure 2. The eye is stabilised with a suction 'docking' system

Femtosecond: technology

From page 3

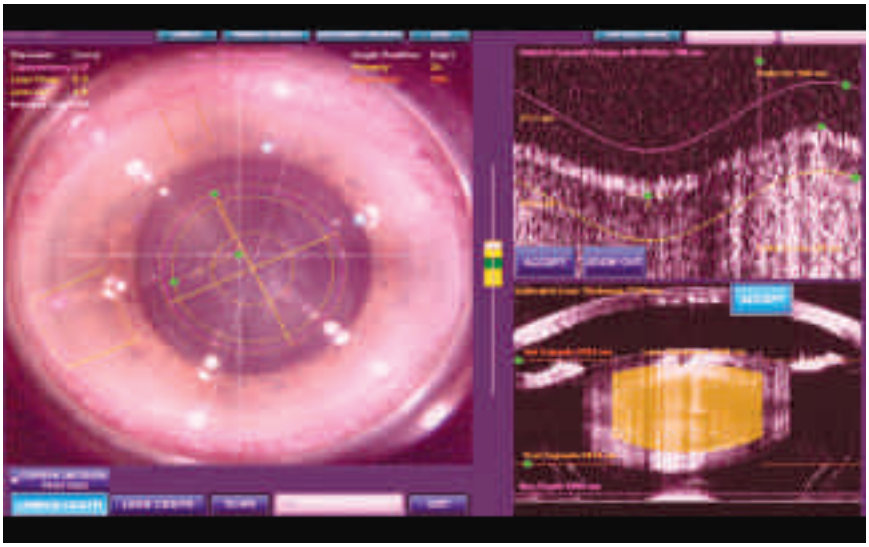

Figure 3. Live microscopic and OCT images in the surgical display

Application of the suction patient interface results in a rise in intraocular pressure, estimated to be approximately 50 mmHg.

The surgical display presents live microscopic and optical coherence tomography images of the anterior segment (Figure 3). During the capsulotomy, which takes 10-15 seconds, the femtosecond laser creates a circular incision in the anterior capsule at a preprogrammed diameter. The laser is then used to create incisions within the crystalline lens (nuclear fragmentation).

Finally, the laser creates corneal incisions to correct astigmatism (if required) and allow the surgeon to perform phacoemulsification. The patient is then escorted about three metres to the operating theatre where lens removal and IOL implantation is performed in a sterile environment (Figure 4).

All patients who are technically suitable, that is, those who have large enough pupils and palpebral fissure, now receive laser cataract and refractive surgery in our practice.

We analysed our early experience in a prospective trial and published the results of the first 200 cases.[10] There was a definite learning curve for all surgeons and previous experience with a femtosecond laser in the refractive setting helped flatten this learning curve. Since the initial installation, the unit has undergone several software upgrades. With greater surgical experience, femtosecond assisted cataract surgery now consistently results in a superior wound, more circular and more consistently sized capsulotomy, and a reduction in the average phacoemulsification energy and time than in routine manual surgery. The combination of these features should translate to a safer, more accurate outcome for patients.

The technology itself is continually evolving and improving and this will reduce the learning curve and the possibility of intraoperative complications. We await the results of ongoing prospective clinical trials and further research. The use of femtosecond lasers with cataract surgery is an exciting development for both patients and surgeons.

Dr Tim Roberts is a consultant ophthalmic surgeon, Royal North Shore Hospital, and clinical senior lecturer, Save Sight Institute, Sydney Medical School, University of Sydney.

References are available from j.megahan@optometrists.asn.au. Subject: Femtosecond surgery in a clinical setting, Roberts, 2012.

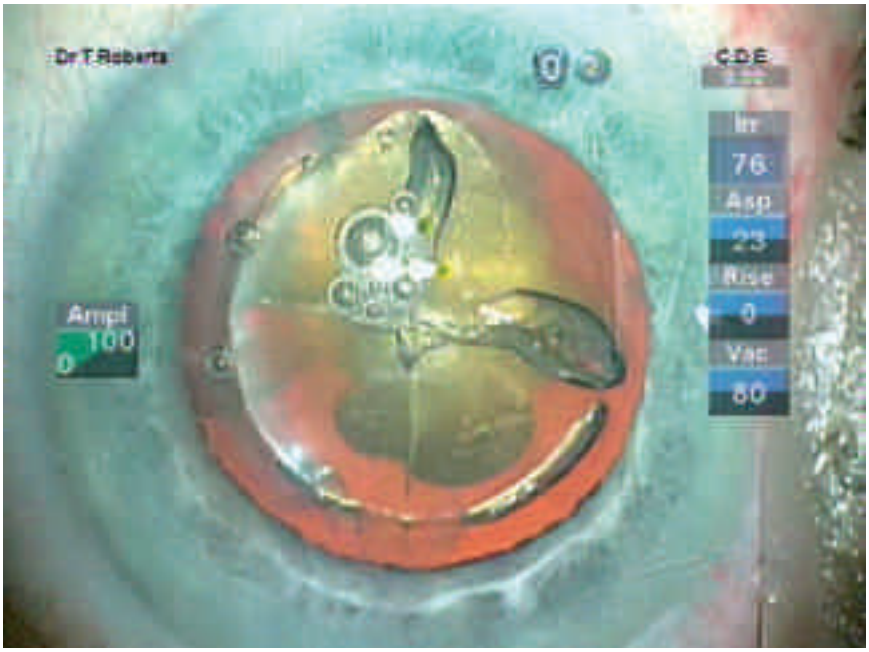

Figure 4. IOL implantation

Platform review

Globally, four companies offer competing systems, each with its own features and benefits.

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The emergence of femtosecond laser assisted cataract surgery as a major trend in developed countries including Australia challenges ophthalmologists and hospitals to analyse the technical and functional merits of competing platforms. Optometrists, too, will need to formulate opinions, as differing technologies will be presented to them as being optimal for their patients' care.

Currently there are four companies promoting femtosecond laser cataract surgery systems globally. As of February 2012, only one has TGA approval for use in Australia, the Alcon LenSx system. Three other companies will launch machines in Australia this year.

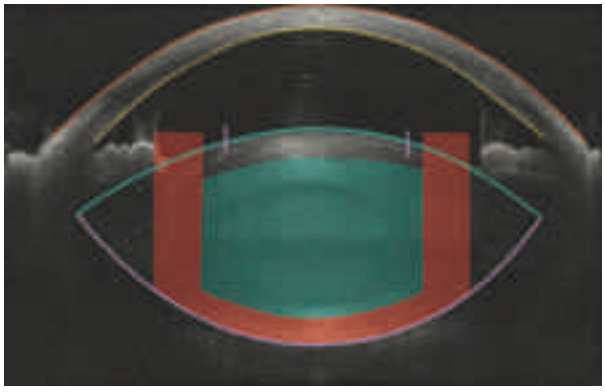
All systems share a basic model—there is a computerised user interface for the operator to control, a patient interface to contact and stabilise the eye, an imaging system to establish the position of the critical structures and target the laser, and the laser delivery module. Conceptual, biomechanical, software, hardware, optical and commercial modelling differences exist between the systems.

Alcon

The Alcon system uses OCT imaging and a curved solid patient interface, as does the Bausch + Lomb Technolas Victus system. Both systems applanate the cornea, which often causes folds on the endothelial surface. Optimedica initially researched solid curved patient interfaces, but concluded that the associated corneal ridges created a localised defocusing of both the diagnostic OCT beam as well as the therapeutic laser system. They observed that this accounted for localised skip areas (discontinuities) during the capsulotomy process. The skip areas can result in peripheral capsular tears and subsequent nuclear prolapse when the capsule is removed with forceps prior to commencing phacoemulsification. Optimedica concluded it should abandon the solid interface and designed a fluid bath interface.

Optimedica

Optimedica has called its interface 'Liquid Optics', as the fluid bath creates a plano concave lens that perfectly couples to and bathes the entire cornea after a secondary coupling of Optimedica's disposable contact lens interface to the fluid-filled cone creates the Liquid Optics. The patient interface is a truncated hollow cone with a gasket on its narrower end, which is applied to the globe and adheres to the limbus. Critically, the gasket's vacuum holds the eye firmly but the pressure on the cornea from the fluid bath is minimal, elevating the intraocular pressure by less than 20 mmHg in most cases. In contrast, applanation systems cause pressure elevations of 40-80 mmHg.



Sagittal view of the anterior segment with Optomedica's Catalys Precision Laser System

Lensar

Lensar also uses a fluid bath system, but uses a modified Scheimflug imaging system. Lensar uses a significantly longer laser pulse duration, up to 1,800 femtoseconds. Optimedica has a pulse duration of 600 femtoseconds.

Lensar has done extensive research into using its laser system to create peripheral cuts in presbyopic crystalline lenses, to re-establish bio-mechanical flexibility and accommodative function.

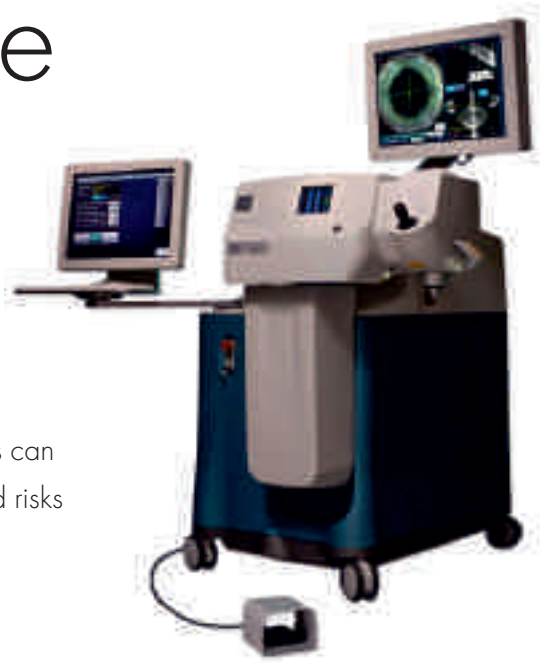
Bausch + Lomb

Bausch + Lomb (formerly Technolas Perfect Vision) has the Victus platform. It is trialling a modified solid curved interface with a built-in suction plate. Unlike other systems, its OCT system gives real-time imaging of the posterior capsule during the laser delivery, and can be configured to perform corneal surgical procedures including LASIK flap creation. Service and support is delivered for Alcon and Bausch + Lomb through their Australian divisions. Optimedica is represented by Designs For Vision, and Lensar through IQ Medical.

In my centre, I have chosen to implement the Optimedica system for a number of reasons. Its user interfaces are intuitive, and its imaging and treatment delivery are fast and highly automated, clearly identifying safety margin zones to protect the iris and posterior capsule. The Liquid Optics interface will produce excellent capsulotomies without skip areas and cause fewer sub-conjunctival haemorrhages, and the low intraocular pressure rise will reduce the risk of compromising vascular perfusion to the retina in the elderly cataract population. ■

Femtosecond laser cataract surgery

Better refractive outcomes



As awareness of this technology grows, optometrists can expect patients to ask for advice on the benefits and risks of the procedure.

Matt Oerding
Director Surgical Business
Alcon

The most common ophthalmic surgical procedure worldwide is cataract surgery with intraocular lens (IOL) implantation.

In developed countries such as Australia, manual phacoemulsification is predominant, consisting of a corneal incision, capsulorhexis, phaco-fragmentation and aspiration, which is followed by IOL implantation.

While refractive outcomes post-cataract are successful, they are not uniformly predictable in all patients, as each step is manually performed and dependent on the variability of the cataract and surgeon skill. Potential safety issues with standard cataract surgery include anterior and posterior capsular tears, corneal burns, endothalmitis and wound sealing corneal endothelial damage caused by the use of ultrasound energy.[1]

In 2011 more than 200,000 intraocular lenses were implanted in Australia using a manual phacoemulsification technique. Phacoemulsification was pioneered in 1967 by Charles Kelman who drew the idea from his dentist's ultrasonic probe. Cataract surgery and lens exchange using phacoemulsification is now over 40 years old and while significant improvements have occurred during that time, the basic principles have remained the same.

In early 2011, a significant change was made to cataract surgery with the introduction of the first femtosecond laser approved for commercial use in cataract surgery. Australia became the second country worldwide to have a commercial unit, which was installed in April 2011. Since then, additional units have been installed in Sydney and Melbourne, and the first unit in Tasmania was scheduled for installation in February 2012.

The promotion of these units by facilities to their patients and optometric referrers has started to raise awareness of laser cataract surgery as a privately-paid alternative to the conventional manual cataract surgery.

History

Use of femtosecond lasers in ophthalmic procedures is not new. Since 2001, over two million ocular procedures have been performed worldwide using femtosecond laser technology, principally for the creation of the corneal flaps in LASIK.[2] More recently, the use of femtosecond laser technology in cataract surgery has been demonstrated to enhance the safety and reproducibility of the three of most critical steps in the cataract procedure, which are corneal incisions, anterior capsulorhexis and lens fragmentation.[1,2] Performance of a precise anterior capsulorhexis is crucial in cataract surgery.

Mihaltz and colleagues[3] comment that '... a capsulorhexis with a 360 degree overlapping capsular edge prevents optic decentration, tilt, myopic shift, posterior and anterior chamber opacification due to symmetric contractile forces of the capsular bag and shrink wrap effect ... this technology also has the potential to reduce the risk of capsular tear and intraoperative complications during cataract surgery and reduced phacoemulsification power ...'

Worldwide there are four companies in various stages of commercialisation of femtosecond lasers optimised for cataract surgery. In Australia at the time of publication, the only laser approved for commercial use in cataract surgery was the Alcon LenSx laser system. The Alcon LenSx laser performs some of the most critical steps of cataract surgery that traditionally have been done manually: corneal incisions, anterior capsulorhexis and lens fragmentation.

A proprietary optical coherence tomography (OCT) system is used by the Alcon LenSx laser to provide real-time images of the anterior segment during cataract surgery. Prior to surgery, the surgeon customises the laser for the corneal incision, capsulotomy size and lens fragmentation.

Operation

Nagyl and colleagues[1] explain that '... the eye is docked to the laser and the integrated OCT captures three-dimensional images of all ocular structures within the anterior segment. These images are projected onto the video microscope screen along with overlays of the preprogrammed laser treatment. Prior to treatment the surgeon makes

any additional adjustments via a touch screen'.[2] During the treatment procedure a proprietary curved patient interface is applied to avoid eye movements. This causes a transient increase in intraocular pressure.[4,5]

The surgeon then chooses the order of the laser treatment. In a typical procedure, the cataract (lens) is fragmented, followed by the anterior capsulotomy and then the corneal incision; it takes about 40 seconds.

Laser cataract surgery does not completely replace the need for several steps in traditional cataract surgery. When the laser portion of the procedure is complete, the surgeon uses phacoemulsification equipment to remove the fragmented lens, performs cortical clean-up and then implants the IOL.[2]

The automated creation of the anterior capsulorhexis is precise and contributes to reduced IOL decentration, as well as an improved capsular edge/IOL overlap.[1] Better effective IOL lens position (ELP) can lead to better patient refractive outcomes.

Supporting studies

Development studies highlight the benefits of femtosecond laser technology. Results for anterior capsulotomy diameter showed that with an intended 5 mm capsulorhexis in porcine eyes, the average diameter was 5.88 ± 0.73 mm using a standard manual technique and 5.02 ± 0.04 mm using the Alcon LenSx laser.[1,2] Studies with lens fragmentation demonstrate a 43 per cent reduction in phacoemulsification power in the femtosecond eyes along with a 51 per cent decrease in phaco time.

Cunningham[2] comments that these findings have been translated to human eyes with the Alcon LenSx laser capsulotomies and phacofragmentation, demonstrating similar accuracy and effectiveness with minimal operative complications.[2]

At a breakfast symposium held prior to a Royal Australian and New Zealand College of Ophthalmologists meeting in November 2011, Dr Bob Cionni from Salt Lake City, USA, discussed several drivers to the introduction of femtosecond cataract surgery. He showed data from Dr Steve Slade of the USA that compared the refractive outcomes of LASIK and conventional cataract surgery with 85 per cent of patients able to see 6/6 post LASIK compared to only 35 per cent post conventional cataract surgery (Figure 1). One of the drivers was the need to improve refractive outcomes of cataract surgery.

The emerging popularity of advanced technology IOLs is also driving interest in laser cataract surgery. Due to its ability to produce a precise capsular bag and corneal incisions, laser cataract surgery should go hand in hand with advanced technology IOLs. Improving consistency in these manual steps of cataract surgery should lead to a more predictable effective lens position (ELP) for the IOL and more predictable refractive outcomes. The growing popularity of IOLs that also correct for astigmatism and presbyopia requires better refractive outcomes. Toric IOLs require minimal surgically-induced astigmatism and optimal IOL placement, and multifocal IOLs must have minimal residual refractive errors for optimal outcomes.

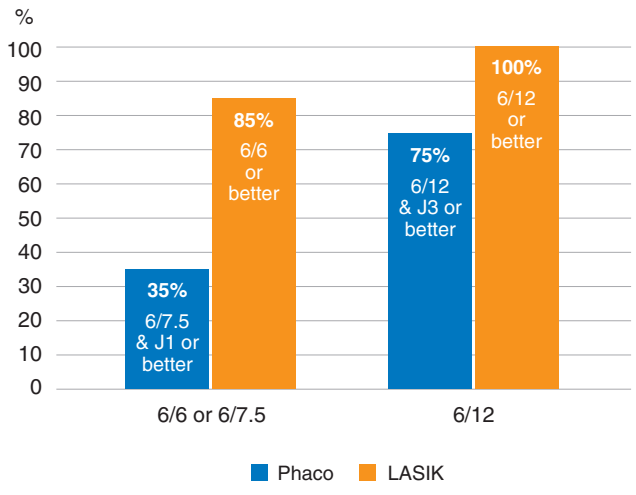
Future

The potential benefits of this new technology were largely theoretical until the recent Australasian Society of Cataract and Refractive Surgeons Congress in 2011 where laser cataract surgery was the hot topic that dominated most of the discussions at the meeting. Dr Cionni presented his early results comparing his manual cataract procedures to his LenSx cataract procedures. He found that there was a 42 per cent reduction of energy required during phaco for all grades of cataract with his LenSx cases.

He also found that 79 per cent of his LenSx patients were within 0.50 D of targeted refractive outcome, compared to 36 per cent with the patients who had undergone conventional cataract surgery. Although the cohort was small, the results were encouraging and have been consistent across other early studies and clinical experience from US and Australian surgeons.

Though early results for using femtosecond lasers to automate crucial steps in cataract surgery are encouraging, the cost of this new technology must also be considered. Facilities in Australia are charging patients an additional $800 to $1,000 per eye to have laser cataract surgery rather than conventional cataract surgery. Given that refractive results with conventional cataract surgery are generally good and complication rates are relatively low, patients must consider carefully the additional cost of this procedure.

As primary eye-care professionals, optometrists have a responsibility to educate patients and inform them of this new technology and the potential benefits of improved refractive outcomes, as well as the additional expense. In areas where lasers for cataract surgery have been installed, optometrists have already had patients asking them questions about this new technology and their suitability for it.



Source: Steve Slade MD

Figure 1. Refractive outcomes, LASIK vs conventional cataract surgery

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Novel ocular therapies from new cell sources

Stem cells and their derivatives are being used as a means of understanding ocular disease progression and as a source for transplantation.

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Melissa Mangala[*]
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Stem cells hold great promise for the treatment of eye disease and injury through the development of novel cell replacement strategies or new pharmaceuticals (Figure 1)**.**

A variety of stem cell types are currently under investigation. These include pluripotent embryonic stem (ES) cells derived from surplus pre-implantation embryos (donated from *in vitro* fertilisation programs);[1] induced pluripotent stem cells (produced by reprogramming somatic cells to an ES cell-like state);[2] and tissue-specific or 'adult' stem cells found in each ocular tissue.

These different stem cell types share a capacity for cell expansion while retaining the ability to produce specific ocular cell types. Notably, human ES and induced pluripotent stem cells possess a far greater proliferative capacity and differentiation ability than tissue-specific stem cells; that is, pluripotent stem cells can generate all cell types found in all ocular tissues, whereas tissue-specific ocular stem cells give rise only to cell types of a particular ocular tissue. Nevertheless, the combination of these two properties of cell expansion and differentiation potential is providing new ways to develop novel ocular therapies. This review aims to provide an overview of the different stem cell-based ocular therapies either in use or under development.

Stem cell therapies for corneal disease and injury

The human cornea is an innervated but avascular tissue composed of the corneal epithelium, Bowman's layer, corneal stroma, Descemet's membrane, and the corneal endothelium. Chemical or thermal burns, trauma or disease are common forms of vision loss and blindness associated with the cornea. In 2009, there were 1,679 corneal transplants in Australia and New Zealand.[3] Over the past 50 years, penetrating keratoplasty has become the dominant form of treatment for corneal damage; however, many corneal allografts are rejected over time. A recent study of the Australian Corneal Graft Registry has shown that while the short-term survival of full-thickness allografts is high (typically about 90 per cent at one year post-transplantation), long-term graft survival drops to about 46 per cent at 15 years post-transplantation.[4]

Similarly, international studies have shown that graft survival can be as low as 46 per cent at five years post-transplantation.[5] Poor graft survival is primarily due to the immune-mediated loss of donor endothelial cells. Large efforts have been made to find autologous modes of treatment to overcome allograft-related complications such as graft rejection and the requirement for immune-suppression.

When corneal damage is limited to the surface epithelium, an alternative to full-thickness allografts has been developed through the use of corneal epithelial stem cells located in the limbus, that is, limbal stem cells. These stem cells produce a population of transient amplifying cells that normally migrate to cover the central cornea, aiding in tissue homeostasis and repair.[6] These regenerative properties have enabled autologous limbal stem cells to be successfully used clinically in cases of unilateral, or partial bilateral, damage to the corneal surface.[7,8] For these treatments, cell culture following limbal biopsy produces a graft that is transplanted to the patient after removal of the conjunctival epithelium. Long-term clinical assessment of autologous limbal stem cell grafts is now possible and indicates a significant capacity for these grafts to repair corneal damage

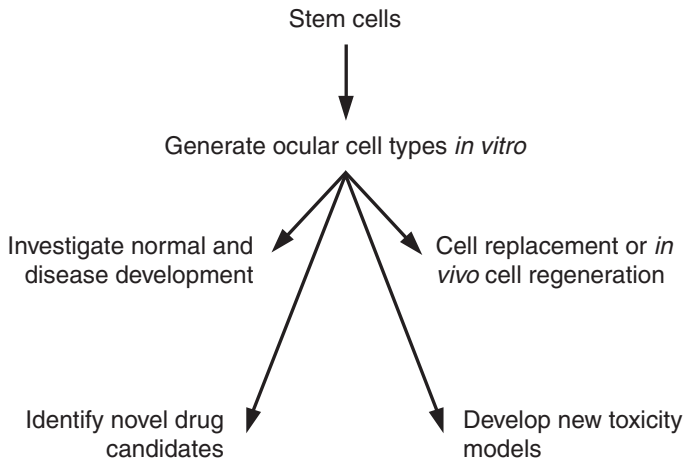

Figure 1. Potential applications of stem cell technology for the development of novel eye treatments

while increasing visual acuity and maintaining corneal transparency in the majority of treated patients.[9,10]

More recent research has, in part, focused on improving the cell culture substrates used in this procedure to improve graft integrity and thus aid both transplant manipulation and attachment. For example, an Australian proof-of-principle trial showed autologous limbal or conjunctival biopsies can be cultured on a commercially-available contact lens to provide a successful treatment method.[11] All three patients in this trial showed improvement in corneal transparency and visual acuity over the follow-up period of eight to 13 months, suggesting larger, long-term trials are worthwhile.

In cases of bilateral injury or disease, a patient's limbal stem cell population can be depleted to the point where clinical use of autologous limbal stem cells becomes unfeasible. To address this issue, alternative stem cell populations have been sourced with properties sufficiently similar to those of limbal stem cells. One such suitable alternative stem cell population is found within oral mucosa.

A small number of patients with clinically diagnosed bilateral limbal stem cell deficiency have been treated with autologous grafts derived from oral mucosa cultured on amniotic membrane or using cell sheet engineering.[12-14] Within the follow-up period of these studies (from three to 34 months) the visual acuity of many patients improved in the treated eye and the transplants remained transparent.[15] While these results hold promise for patients with limbal stem cell deficiency, larger patient cohorts need to be assessed to fully establish the long-term clinical benefits of this approach.

Stem cells for lens and cataract research

The ocular lens is a transparent, biconvex, avascular tissue that is encapsulated by a basement membrane, and its function is to focus light onto the retina. Within the lens, an anterior epithelial monolayer helps generate circulatory currents while also providing a pool of cells from which fibre cells are produced to both grow the lens and provide the necessary refractive index for lens function. Proper alignment of these differentiating fibre cells is critical for the maintenance of lens transparency.

Loss of lens function, predominantly through age-related nuclear cataract, is common and currently can be treated only surgically. As a result, cataract surgery is one of, if not the most commonly performed surgeries, placing a large burden on healthcare systems globally. In Australia, 180,000 cataract operations are performed annually, costing more than $320 million,[16] while in North America these figures are approximately 10 times higher.[17] In developing nations, inadequate access to surgery leaves many patients blind.

Due to population ageing, the incidence of cataract will almost double this decade, dramatically increasing the cost of cataract treatment.[18] Although effective at restoring vision, cataract surgery has a number of important complications. In particular, posterior sub-capsular cataract can arise in 20 per cent to 50 per cent of cases two to three years after primary cataract surgery.[19,20] While this can be treated in developed economies through laser-based posterior capsulotomy, this procedure adds to the financial and social burden of cataract and has its own complications.

Cataract surgery results in a loss of accommodative ability in patients, a situation that is yet to be resolved effectively by improved intraocular lenses. Therefore, there is significant scope to improve cataract treatment through the development of therapies that either avoid cataract surgery (for example, anti-cataract drugs) or enable lens accommodation after surgery (for example, full or partial lens regeneration).

Unlike the cornea, no regenerative medicine treatments have yet been devised that take advantage of the existing epithelial stem cell population within the lens. This is largely due to our incomplete understanding of the molecular mechanisms that control development of the exquisite cellular architecture required for lens transparency. Additionally, the position of the lens epithelial stem cells both within the eye and within the lens capsule makes it difficult to access these cells without inducing loss of lens transparency.

These difficulties have meant that until now, the majority of research into lens and cataract development has been restricted to imperfect animal-based models. However, the advent of pluripotent stem cell technology has provided a new source of lens epithelial cells that may overcome these technical barriers to improve cataract treatment. For instance, a variety of differentiation methods have been published that demonstrate the *in vitro* production of lens epithelial cells from non-human ES cells.[21,22] While the yield and purity of lens cells obtained via these methods is low, they nonetheless represent useful systems that may enable elucidation of the factors and mechanisms involved in lens and cataract development.

A more recent report describes a three-stage, defined growth factor treatment designed to mimic embryonic lens development from the blastocyst to neuroectoderm (via Noggin signalling), through the lens placode and lens vesicle stage (via BMP and FGF signalling), to lens epithelial and fibre cells (via FGF and Wnt signalling; Figure 2A).[23] This strategy represents a significant improvement in our ability to produce lens cells *in vitro*.

While the yield and purity of lens cells are increased by this approach, non-lens cells are still produced. The lens cells develop in an uncontrolled fashion into inappropriately organised and non-physiologically sized three-dimensional lens-like structures that do not accurately reflect the biology of the normal lens. Generating pure populations of lens epithelial cells and being able to control their differentiation into appropriately organised fibre cells and lens-like tissues are key steps that will aid investigation of novel cataract treatments.

Efforts to improve this three-stage lens differentiation method are underway in our laboratory and are aimed at eliminating the production of non-lens cells and ultimately, controlling the development of correctly-organised *in vitro* human lenses that focus light. Already this research is yielding promising results (Figure 2B) and can reasonably be expected to generate purified lens epithelial cells in the short-term.

Once large quantities of purified lens epithelial cells become available, a range of previously impractical research approaches will become accessible to investigate lens and cataract development. These include:

- **Anti-cataract drug identification**

The development of automated high-throughput screening equipment has enabled rapid and quantitative methods to study the interaction between cells and their microenvironment. Over the past 20 years, use of this screening equipment has transformed drug discovery in the pharmaceutical industry. Large quantities of human ES cell-derived lens epithelial cells will enable anti-secondary cataract drug screening to identify chemicals that inhibit lens cell survival, proliferation, migration and/or differentiation.

Continued page 10

Novel ocular therapies

From page 9

- **Improved ocular toxicity models**

Similar to the development of high-throughput drug screening assays, human ES cell-derived lens cells could be used to screen existing back-logs of candidate ocular pharmaceuticals to better assess their potential toxicity for accelerated drug discovery. In this way, use of imperfect whole animal or animal cell culture toxicity models could be avoided.

- **Lens regeneration to restore accommodation**

Biological restoration of accommodation after cataract surgery will require controlled growth of lens fibre cells around a malleable and/or biodegradable intraocular lens. While the full set of factors required for lens regeneration is not yet defined,[24,25] there is a significant body of evidence that demonstrates lens regeneration is possible both *in vivo* and *in vitro*. For example, lens regeneration has been studied in rabbits, dogs, cats, sheep and pigs. Importantly, human lens regeneration has been seen via the appearance of Soemmering's ring (an uncontrolled form of lens fibre cell regeneration following primary cataract surgery), suggesting that controlled lens fibre production may enable restoration of accommodation following cataract removal. Recently, O'Connor and McAvoy developed a culture system that generates functional *in vitro* lenses from explanted rat lens epithelial cells (Figure 2C).[24] By replacing the rat cells in this model with human lens epithelial cells derived from ES cells, it is anticipated that human lenses will be grown in the laboratory for use in defining the factors (and mechanisms) that underpin lens regeneration and primary cataract formation.

Stem cell research for retinal-induced blindness

In comparison to the lens, the larger number of cell types present within the retina make it a more complex tissue from a regenerative medicine perspective. These cell types include vascular, ganglion, amacrine, bipolar, horizontal and Müller cells, rod and cone photoreceptors, as well as the retinal pigment epithelium (RPE). Each of these cell types has its own specific function, tissue distribution and interconnectivity. Importantly, acute or chronic damage to any of these cell types can lead to blindness. In particular, age-related macular degeneration represents a major health burden, costing the Australian economy over $2.6 billion annually due to our inability to treat most macular degeneration patients.[26]

As with the lens, the ability to generate large numbers of normal retinal cell types through differentiation of human ES cells offers an opportunity to investigate normal and pathological retinal development, to undertake candidate retinal drug and/or toxicity screening, and to develop regenerative medicine strategies to restore or replace damaged tissue. Numerous methods have been reported to induce the differentiation of human pluripotent stem cells into retinal cells. This includes generation of ganglion and amacrine cells,[27] photoreceptors[28,29] and RPE.[30-32] However, similar to lens differentiation protocols, these methods generate the desired cell types in relatively low yield and purity, necessitating development of rigorous cell purification strategies. Fortuitously, the pigmentation that appears in mature RPE has enabled these cells to be manually excised from cultures of differentiating pluripotent cells.

Although laborious and inefficient, this method of purification is effective and studies using RPE purified in this way have shown it to be capable of restoring visual function in animal models of macular degeneration.[31,32] This therapeutic ability recently resulted in US Food and Drug Administration approval for phase 1 and 2 clinical trials using purified human ES cell-derived RPE to treat both age-related macular degeneration and Stargardt's macular dystrophy. These trials are being co-ordinated by Advanced Cell Technology (Inc) and as of July 2011, one

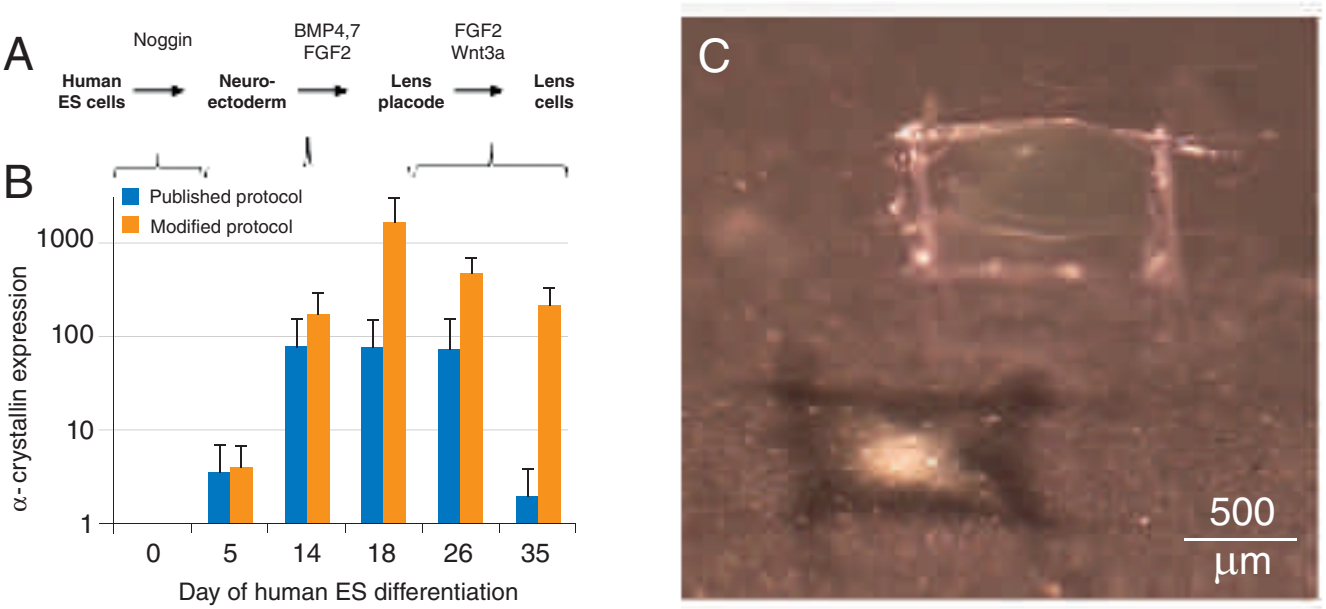

Figure 2. *In vitro* lens models. A. Three-stage protocol for differentiating human ES cells into lens cells. B. Investigations currently underway in our laboratory indicate this three-stage protocol can be further optimised (blue bars: published protocol; orange bars: increased Noggin in the first stage of differentiation). C. A functional *in vitro* lens generated from rat lens epithelial cells focusing light to a point.

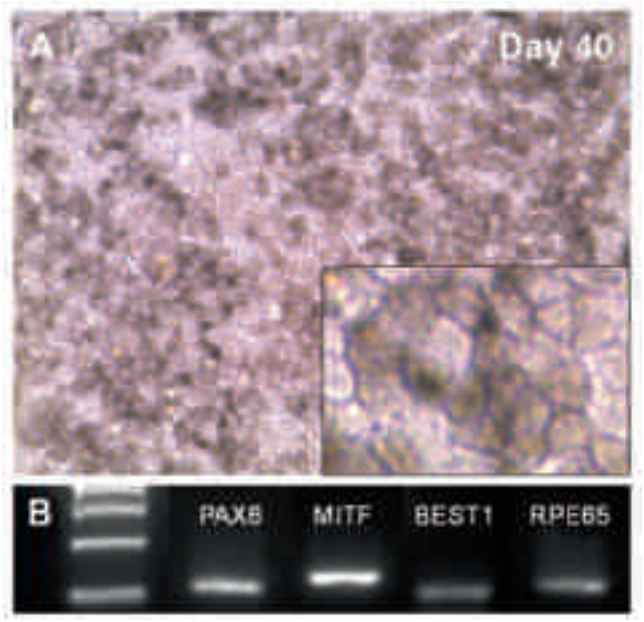

Figure 3. *In vitro* RPE. A. RPE generated from differentiating human ES cell cultures in our laboratory. B. PCR-based detection of gene expression in human ES cell-derived RPE: these cells express immature (PAX6, MITF) and then mature (BEST1, RPE65) RPE genes.

patient enrolled in each of these trials has undergone treatment at the Jules Stein Eye Institute (Los Angeles, US).

These pioneering clinical trials are a major advance in the development of novel therapies for currently costly and intractable blinding retinal disorders and their outcomes are eagerly awaited. In the meantime, to improve our understanding of how retinal diseases develop, further research is required to more accurately define the factors required during normal retinal development. Our laboratory is investigating the genes and growth factor signalling pathways involved in retinal development, particularly RPE (Figure 3).

Promising research from other human ES cell research groups indicate that one day it may be possible to generate full-thickness retina in the laboratory for transplantation. For instance, work from the Keirstead group (University of California, Irvine, US) has shown that rudimentary, immature retina can be produced *in vitro* from human ES cells,[33] and the Sasai group (RIKEN Centre for Developmental Biology, Japan) has shown that mouse ES cells can self-organise to produce an immature optic cup.[34]

In addition to RPE-based diseases, research is progressing into potential stem cell-based therapies for other retinal diseases. Proof-of-principle studies have shown that transplantation of photoreceptor precursors can provide retinal repair and improvement of visual function in mice.[35,36] However, before these studies can be translated into clinical trials, a range of fundamental issues need to be addressed including establishment of the most appropriate photoreceptor precursor to use, and the best photoreceptor source (for example, derived from human ES cells or retinal stem cells).

Progress is also being made investigating the potential for stem cell-based therapy for glaucoma. Globally, over 60 million people are affected by glaucoma with more than eight million progressing to bilateral blindness.[37] In Australia, approximately three per cent of people over 50 years are affected and about half of these are undiagnosed due to the asymptomatic nature of the early stages of open-angle glaucoma.[38] This costs the Australian economy over $1.9 billion annually, a figure that is expected to rise to $4.3 billion by 2025.[39]

The elevated intraocular pressure that occurs with glaucoma is thought to result in damage to retinal ganglion cells and the optic nerve, leading to a loss of visual fields.[40] Currently, there is no means of restoring visual field loss due to glaucoma. Instead, pharmacological or surgical intervention is aimed at lowering intraocular pressure to halt disease progression. While these approaches are often successful, the disease continues to progress in many patients. A range of cell-based approaches have therefore been investigated in an attempt to address visual field loss caused by glaucoma. This includes investigation of ES cell-derived retinal ganglion cells, neonatal rat oligodendrocyte precursors, bone marrow-derived mesenchymal stromal cells, and a human Müller cell line.[41,42]

Transplantation of some of these cell types into animal models of glaucoma have demonstrated an ability for neoroprotection,[43] suggesting that further development of these cell-based approaches might result in novel glaucoma therapies. However, key aspects for all of these approaches remain to be determined, including the optimal cell source and developmental stage of the transplanted cells, the most effective transplantation method and site, and how to stimulate effective integration of the transplanted cells.

Further developments

The above diverse studies demonstrate the promise of using stem cells and their differentiated derivatives as both tools for understanding ocular disease progression and as a source of cells for transplantation. With stem cell-based corneal treatments already in use and clinical trials of stem cell-derived RPE underway, it appears likely that stem cell-based ocular therapies will continue to be incorporated into clinical practice over the coming years. Of particular interest will be whether the development of patient-specific stem cells, created via cell reprogramming technologies, will lead to a new era of personalised regenerative medicine for the treatment of ocular disease and injury.

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References available on request from j.megahan@optometrists.asn.au. Subject: Ocular therapies from cell sources; O'Connor, Murphy, Mangala & Lim, 2012.

You see what you look for

Norman Smith
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OD DO MS FAAO FAOCO

Aggressive investigation reveals a lymphoid tumour of the conjunctiva in an 'itchy eye'.

Summer had finally arrived in Minnesota; we had gone from 18 degrees to a humid 35 degrees in just a couple of weeks. With allergy season suddenly on us, we had a good idea of what would be a popular problem in the coming weeks, and were mentally reviewing differentials and the latest in antihistamine eye-drops.

We greeted a frail-looking 90-year-old woman accompanied by her anxious daughter. The elderly woman told us how her eyes had begun itching a couple of weeks previously. She had used some of the eye-drops that had helped her the previous spring but she had used them all and wanted a new prescription.

On gross examination there was not much to see. No mucopurulent discharge, no diffuse pinkness; just deep-set eyes, a rather small palprebral aperture and the tissue-thin eyelids characteristic of advanced age. Even gently lifting the upper eyelid failed to disclose anything unusual.

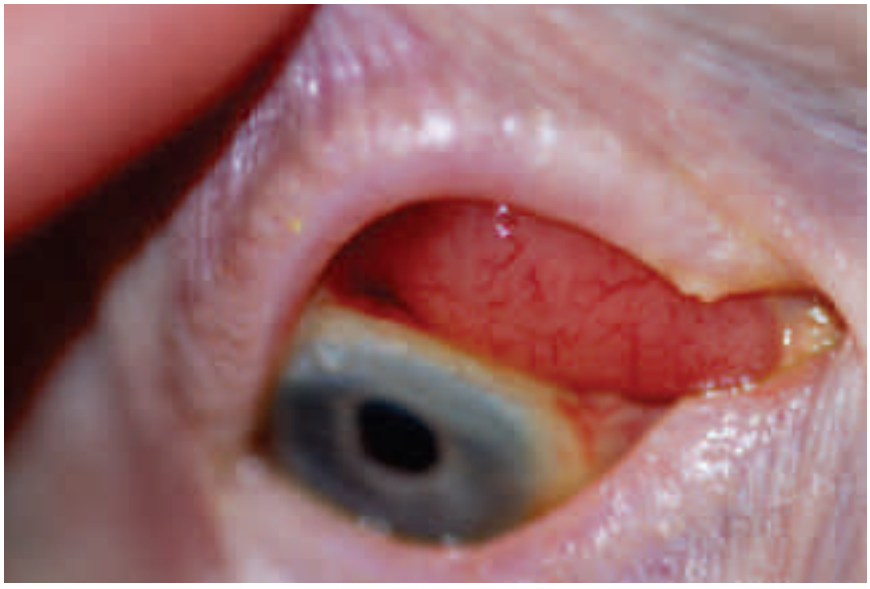
It is sometimes better to be a little mean in order to be kind. The fragile upper lid was moved more aggressively up and away from the globe and only then did an impressive salmon patch literally fall down into view.

Case study

The patient presented with a recent onset of itching eyes, particularly the right eye, with increasing blurriness and sensitivity to light. There was no discharge and only minimal irritation.

- On examination, her right eye visual acuity was 6/24+2 (20/80+2), which pin-holed to 6/7.5-2 (20/30-2) and left eye was 6/6-2 (20/20-2). Her ophthalmic history included bilateral cataract surgery and prior successful treatment for bilateral periocular lymphoma. There was no other relevant medical history.
- On slitlamp examination, she was found to have a trace of cells and pigmented keratic precipitates together with a fleshy salmon-pink swelling that occupied the entire superior forniceal conjunctiva.
- The remainder of the ocular examination revealed no other abnormalities.
- A conjunctival biopsy was performed. The histopathological evaluation report confirmed atypical lymphoid infiltrate consistent with the patient's previous diagnosis of low-grade B–cell lymphoma.
- The uveitis was treated with topical prednisolone 1%.

The patient was referred to oncology, which recommended radiation therapy. After consideration of her age and the possible side-effects, the patient chose to decline further treatment and is being monitored.



Discussion

This case is a good reminder that at any time, a combination of individual anatomy, circumstances and expectations can often result in surprising findings.

In this case, sufficient alarm bells went off that a more assertive investigation was warranted than might have been the case. Of note was the report of increased blurriness, photophobia and decreased vision. These symptoms suggest the need to exclude keratitis, glaucoma, uveitis, even perhaps meningitis or carotid-cavernous fistula.

Lymphoid tumours of the conjunctiva are commonly divided into three classifications:

- benign reactive lymphoid hyperplasia
- atypical lymphoid hyperplasia
- malignant lymphoma.

Malignant lymphomas may be further subdivided into:

- mucosa-associated lymphoid tissue lymphoma (MALT, sometimes also called a MALToma)
- non-MALT lymphoma.

The majority of conjunctival lymphomas are monoclonal proliferations of B

Continued page 13

Clinical QUIZ

TA, a 26-year-old teacher, presents with a seven-day history of red and watery eyes. Over the past four days she has developed progressive photophobia and mild blurring of her vision. She wears contact lenses intermittently but has not for the past three weeks. Her general health is good and she reports no allergies.

O/E her vision is 6/9 in each eye with correction (mild myopia). A bilateral follicular conjunctivitis and subepithelial infiltrates are noted. As seen in the Figure (right), some of the infiltrates are central and affecting her vision and ability to drive at night. The anterior chambers are deep and quiet and the remainder of the ocular examination is normal. No definite pre-auricular adenopathy is detected. She reports her fiancé had a similar conjunctivitis a week earlier, which had settled after 10 days. His vision is reportedly unaffected.

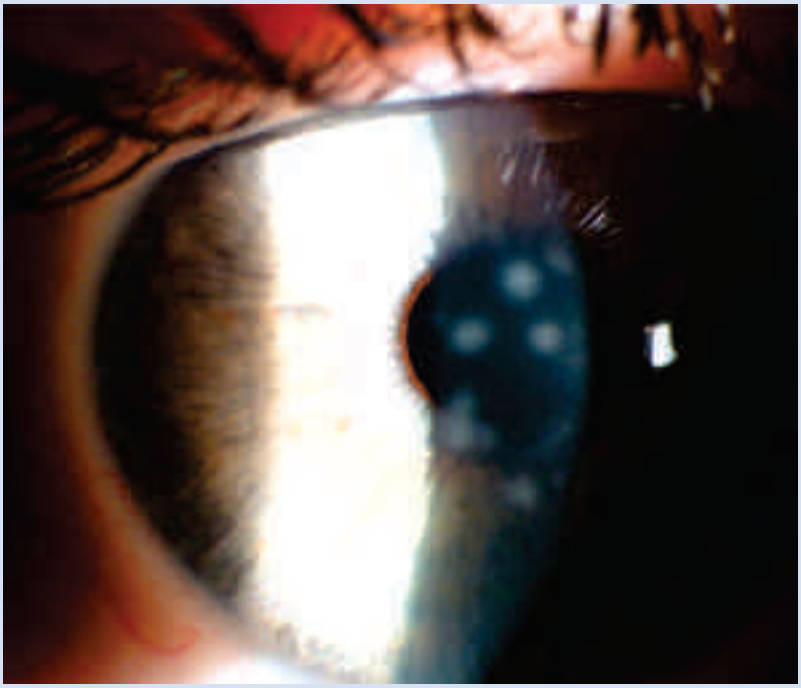


Photo: Gary Page

What are your diagnosis and management?

ANSWER PAGE 24

You see what you look for

From page 12

lymphocytes.[1,2] Lymphoid tumours of the conjunctiva are associated with systemic lymphoma in about 31 per cent of patients.[3]

MALT lymphomas are less aggressive, tend to remain localised to mucosal surfaces and have a better prognosis, while non-MALT lesions are considered highly malignant and invasive.[4] Biopsy is crucial in any case of suspicious conjunctival lesions. Once the presence of a conjunctival lymphoma is established, the most important element is differentiating between MALT and non-MALT varieties. In any case of biopsy-proven lymphoma, the patient should be given a complete medical evaluation to determine if systemic lymphoma is present.

Signs and symptoms

Periocular lymphomas typically arise in the conjunctiva, although rarely they may occur in the eyelid, lacrimal gland or orbit. These tumours occur most often in older individuals and in women. Lymphomas manifest under the conjunctiva as a mass that moulds around the eye with the characteristic 'salmon patch' appearance.

The most common presenting ocular symptoms are blurred vision, floaters and non-resolving uveitis. Pain and conjunctival hyperaemia (engorgement of blood vessels around the eye) are rare. Vision is often decreased. Biomicroscopic examination usually shows mild anterior segment inflammation with cells and flare, and keratic precipitates. Vitreous cells occurring in sheets are characteristic. Although the disease may begin with one eye, if untreated, bilateral involvement is common after several months.

Treatment

Chlamydia psittaci is most often considered responsible for conjunctival MALT lymphoma and recent studies show regression of ocular adnexal lymphoma after antibiotic therapy. The organism is found in about 80 per cent of cases by polymerase chain reaction (PCR).[5] Recent studies have shown that intralesional interferon may also be a viable form of therapy for MALT lymphomas of the conjunctiva.[6] Some success has been reported with chlorambucil. Regression may also occur with treatment using doxycycline 100 mg twice a day for three weeks. The most common form of treatment remains low-dose radiotherapy in multiple courses with proper shielding to prevent spread of radiation damage.

Prognosis

Although conjunctival lymphoma may be associated with systemic lymphoma, the ocular lesions have not shown a propensity to metastasise. The five-year survival rate for MALT lymphomas is reported to be 93 per cent;[7] however, many tumours recur, sometimes years after the initial occurrence and there can be transformation to a more malignant lymphoma. These patients should be monitored closely.

References available on request from j.megahan@optometrists.asn.au. Subject: MALT lymphoma, Smith & Skorin, 2012.

Can urine be used to monitor age-related

This is a summary of 'Identification of urinary biomarkers for age-related macular degeneration', undertaken by Guymer and Tao and colleagues and published in *Investigative Ophthalmology and Visual Science* in 2011.[1]

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Age-related macular degeneration (AMD) is a leading cause of vision loss in developed nations. Recent evidence suggests that the pathogenesis of this complex genetic disease may be traced to a defective regulation of the complement pathway, which results in chronic low grade inflammation.[2,3] Early AMD is characterised clinically by formation of sub-retinal deposits known as drusen, and pigmentary change of the retinal pigmented epithelium. It affects 15 per cent of those over 50 years of age. Only one to two per cent of this group will develop sight-threatening lesions of choroidal neovascularisation (CNV) or geographic atrophy (GA), also known as the late stages of AMD, which would lead to irreversible loss of central vision if left untreated.[4,5]

Rationale

Although the outcome of CNV has improved dramatically with recent advances in the treatment of this late form of the disease, there still remains no effective treatment for GA. Other than general lifestyle advice and antioxidant supplementation, there are no specific interventions to slow or reverse progression from early AMD to the late stages of the disease. Currently, there are trials of possible treatments for GA and intervention strategies developed for early AMD, but these advances are severely hampered by an inability to monitor the disease. What is needed is a tool that would measure progression of the early stages of the disease, predict risk of progression to the late and vision-threatening stages, and assess the efficacy of treatment.

Since AMD has been postulated to be a local manifestation of a systemic inflammatory process, several studies have investigated levels of inflammatory proteins in the serum as possible biomarkers of the disease, but with conflicting results.[6-8] Because using serum as a source of potential biomarkers has many challenges, other fluids such as urine have been tried. Urine offers relative abundance, ease of collection, stability and fewer proteins compared to serum.[9] Urine, unlike serum, is stable at room temperature for hours, making it ideal for repeated sampling for better disease monitoring.[10]

Interestingly, there are other findings that suggest that the kidney may also be affected in AMD. If this is the case, then there may be a particular pattern of proteins in the urine that would not necessarily be reflected systemically and therefore not picked up in the serum. The renal glomeruli and the choroidal vasculature complex are structurally similar, and there are several examples of kidney disease that are also associated with retinal changes.[11,12] In a rare form of kidney disease, membranoproliferative glomerulonephritis type 2 (MPGN type 2), there is deposition of material within the glomerular capillary walls and drusenoid deposits in the macula.[13,14] MPGN type 2 is associated with variants in the CFH gene—the same gene implicated in AMD.

The Blue Mountains Eye Study has also found evidence of kidney involvement in AMD—there is reduced renal function in AMD cases, with a decreased estimated glomerular filtration rate (eGFR) and creatinine clearance when compared with aged-matched controls. This raises the possibility that AMD may be a generalised systemic disease state with local organ manifestations as reflected by the mild abnormalities in renal function. The possibility of renal involvement in AMD made a strong case for considering urine as a source of pro-inflammatory biomarkers in AMD.

Our study investigated the level of urinary pro-inflammatory cytokines in subjects with AMD and control participants. Specifically, Transforming Growth Factor-β1 (TGF-β1) and Monocyte Chemoattractant Protein-1 (MCP-1), are both pro-inflammatory cytokines that are up-regulated in response to tissue injury and have been implicated in AMD. They are known to be involved in inflammatory responses in the kidney.[15,16] These cytokines, along with C3a-desArg, a break-down product of the complement cascade, are known to be involved in AMD, and reflecting the degree of inflammation,[17] were measured.

Results summary

Our cross-sectional study consisted of 103 AMD cases, comprising early AMD (51), geographic atrophy (GA, 19) or choroidal

macular degeneration?

If AMD is a local manifestation of a systemic inflammatory process that also affects other organ systems such as the kidneys, then urine could be a potential source of biomarkers for AMD.

neovascularisation (CNV, 33), and 54 unrelated controls, aged 73 ± 9 years, who attended the Royal Victorian Eye and Ear Hospital and private practice in Victoria, Australia.

AMD status was determined after grading retinal digital photographs, which were taken of both eyes of each participant. CNV status was confirmed through angiography and optical coherence tomography images. Urine cytokine levels were measured using immunoassay and the rs1061170 (Y402H) single nucleotide polymorphism of the complement factor H gene was determined.

Multivariate logistic regression analyses adjusting for age demonstrated significant associations of urinary TGF-β1 levels (Odds Ratio [OR] = 1.24 [1.02, 1.50], p < 0.031) and MCP-1 levels (OR = 1.07 [1.02, 1.12], p<0.008) with early AMD, and also MCP-1 levels with GA (OR = 1.10 [1.03, 1.17], p<0.003). There was no correlation between any of the three urinary protein levels and their corresponding serum levels (p = 0.057, p = 0.589 and p = 0.953 for TGF-β1, MCP-1 and C3a-desArg respectively). Urinary cytokine excretion results were further analysed according to allelic status of the Y402H variant of the CFH gene, available from 126 participants (82 per cent). Individuals with one or more copies of the C allele (Y402H) were 2.5 times more likely to have urinary MCP-1 above median levels (p < 0.040).

Study interpretation

Our results indicated that TGF-β1, which is known to have a pivotal role in the synthesis and deposition of extracellular matrix following renal tissue injury, was significantly elevated in the urine in early but not in late disease. Its elevation may reflect kidney changes early in the inflammatory disease process. Similarly, MCP-1 was also significantly elevated in early AMD but also in the late GA stage. MCP-1 has also been reported to be up-regulated in the retina of aged mice and in particular to have increased expression in the retinal pigment epithelium.[18]

We hypothesise that the increase in urinary MCP-1 level reflects local renal changes, perhaps as a result of local inflammation. Findings of significant associations of elevated urinary TGF-β1 and MCP-1 levels in early AMD make these markers potentially useful as biomarkers in monitoring early disease progression, and potential improvements with intervention.

Future direction

As with the development of any biomarker, the importance of longitudinal studies must be stressed. The selection of the cytokines targeted in this study was determined by existing knowledge in the area. Given this initial demonstration of the potential utility of urinary peptide analysis as marker for disease, broader proteomic analysis of urine of AMD may give rise to recognition of additional markers of this common and devastating disease.

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Drug delivery to the eye using contact lenses

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Contact lenses offer a reservoir for drugs to treat anterior and posterior eye conditions, in the open or closed eye, potentially reducing cost and risk.

The concept of using contact lenses as a delivery vehicle for drugs or biologics is not new. The idea dates back to at least the time when hydrogel lenses were first used for vision correction. Contact lenses used to deliver drugs have been tried with different degrees of success, depending on the indication, drug being delivered or polymer that is the delivery vehicle.

Most of the creative thought surrounding the concept dealt with delivery and treatment to the anterior segment of the eye. As has been shown more recently, if the correct drug is coupled with the right contact lens polymer and the drug is delivered in the correct manner, it is possible to deliver drugs to the retinal segment of the eye.[1]

Drugs

The types of compounds that have been delivered to the back of the eye include steroids and the more complex biological molecule ranibizumab (Lucentis). It has been shown using analytical chemistry techniques that these molecules may be taken into the matrix of the hydrogel material and then released.

The most important aspect of the release of a drug from the lens is that the molecule that one puts in must be the same as the molecule that comes out. If there is a variation, that may mean that the drug is altered in terms of clinical effectiveness or safety profile. For the regulators with whom I have spoken, this information is critical when designing potential clinical trials but also more specifically relative to the patient profile. Verification of molecular structure can be conformed using advanced analytical chemistry techniques such as HPLC and mass spectroscopy.

Polymers

There are as many types of polymers as there are drugs. This fact is often overlooked. The major difference is that most of these polymers, including the more common hydrogel contact lens polymers, are off-patent now. This is unlike the drug world, where many drugs are still on-patent. In some cases, this has been true for decades.

For the common hydrogel polymers such as etafilcon A (Acuvue) and polymacon (Sequence), it seems that the ability to take up a drug into the inside of the contact lens or cargo space is related to the amount of water associated with the lens. The more water that a material is composed of, the greater the amount of drug that can be incorporated into the polymer's cargo space. Data suggest that at least for hydrogel materials, higher water content lenses may be more useful.

There are three other points about drug release from polymers that are essential. First, the polymer must be comfortable to wear. If a lens polymer is uncomfortable, patients will not wear the product. Second, not all polymers can uptake drugs. Some polymers that form hydrogel materials will not take drugs into the cargo space. Third, the hydrogel can be used for vision correction.[2] There is no evidence that either base curve or power will affect the release of drug from the cargo space. This is critical for products that may be intended for use during waking hours.

Delivery

Most people who work or think in this field consider drug delivery in the awake or open-eye state but a key to success may lie in the closed-eye or sleep state. Experiments performed at the University of Calgary showed that delivery of steroids and biological molecules such as epidermal growth factor and ranibizumab is possible in the closed-eye state.[3]

From a patient standpoint, applying drugs in a closed-eye period may be more convenient and more efficient than attempting to insert contact lenses during an open-eye period. There is also the issue that an individual who uses the lenses as a delivery system during a closed-eye period does not require vision correction. This opens the possibility of using polymers that are not necessarily visually transparent, thus expanding the potential number of polymers from which manufacturers may choose.

One important issue with delivery that has plagued some studies is that not all polymers can be used for this purpose. This has been mentioned above in relation to the drugs themselves. Some polymers will not absorb a drug or biological molecules into the cargo space of the lens polymer and thus, no delivery of the drug is possible. Under these circumstances another polymer must be selected. Remember that this is an absolute requirement for individuals who are being treated for certain anterior segment conditions.

Continued page 17

Clinical QUIZ

A nursing home patient presents with a left red eye of two months duration, unresponsive to treatment by the nursing home medical staff with artificial tears and chloramphenicol eye-drops.

What are your diagnosis and management?

ANSWER PAGE 24

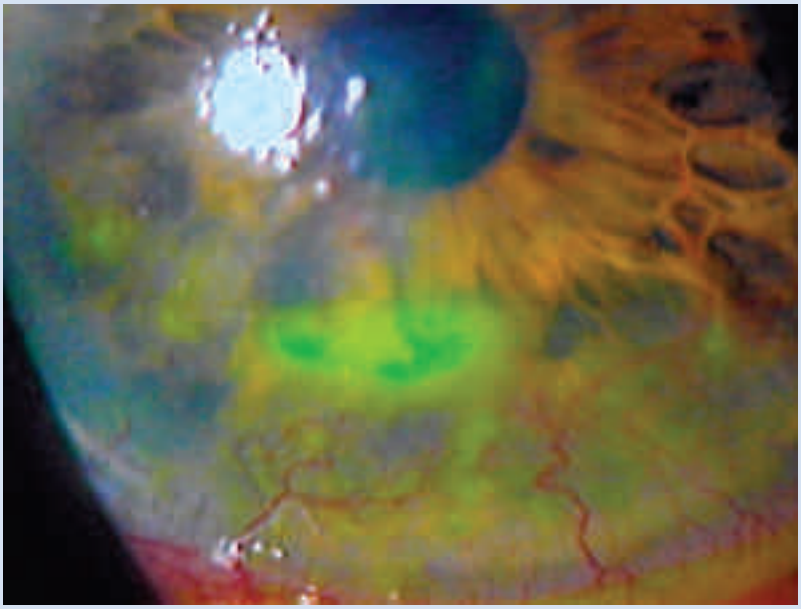

Photo: Graham Lakkis

Drug delivery to the eye using contact lenses

From page 16

As previously mentioned, it has been shown in animals that drugs may be effectively delivered to the posterior segment of the eye during a closed-eye period. Polymer compositions that are opaque open a new avenue that can be addressed in ophthalmology, namely, topical drug delivery by a medical device without any invasive surgery or vision correction.

One other issue that may be overlooked is the idea of using a topical drug delivery device in concert with other surgical techniques. This can be true for both anterior and posterior segment conditions. The release of epidermal growth factor from a contact lens to successfully treat non-healing epithelial defects in humans has been done in Canada (clinical paper in review). This was in combination with other topical medications that were being given or post-surgery. In a statistically insignificant number of cases, the release of epidermal growth factor from a contact lens provided accelerated growth at the wound site, compared to control or untreated eyes. There seems to be no difference with LASIK patients as the wounds heal so rapidly, assuming no other complication.

There is evidence that a contact lens used as a suitcase can deliver drugs and other biological molecules to both the anterior and posterior segments of the eye. This can be done in a less costly fashion and with less patient risk.

> **The most important aspect of the release of a drug from the lens is that the molecule that one puts in must be the same as the molecule that comes out.**

New products designed using the cargo space of a contact lens as a reservoir could provide efficient and much less costly treatment of anterior and posterior segment conditions than current treatments. In addition, these products could be used to correct vision. They may also be distributed by optometrists, under the supervision of physicians. This may make it easier to treat patients, especially in the developing world.

1. Schultz C, Poling T, Mint J. A medical device/drug delivery system for the treatment of glaucoma. *Clin Exp Optom* 2009; 92: 4: 343-348.
2. Schultz C, Morck D. Contact lenses as a drug delivery device for epidermal growth factor in the treatment of ocular wounds. *Clin Exp Optom* 2010; 93: 2: 61-65.
3. Schultz C, Breaux J, Schentag J, Morck D. Hydrogel contact lenses used to deliver drugs to the posterior segment of the eye. *Clin Exp Optom* 2011; 94: 2: 212-218.

Femtosecond laser capsulorrhexis improves outcomes in cataract surgery

The use of a femtosecond laser for anterior capsulotomy during cataract surgery has been found to produce more regularly-shaped and well-centred capsulotomies than manual techniques.

In a study, anterior capsulotomy was performed either with an intraocular femtosecond laser (n = 54) or using a manual continuous curvilinear capsulorrhexis (n = 57). Circularity and the area of capsulotomy, as well as intraocular lens (IOL) decentration were measured one week post-cataract surgery.

Circularity values were significantly better in the laser-treated group (p = 0.03); incomplete capsulotomies were observed in 28 per cent of eyes that underwent manual techniques compared with 11 per cent in the laser-treated group (p = 0.03). Laser-treated eyes also demonstrated a significantly better IOL/capsule overlap.

J Refract Surg 2011; 27: 8: 546-549.

Low degrees of astigmatism impair reading performance

The induction of low degrees of astigmatic refractive error has been shown to significantly reduce reading fluency in a population of university-aged students.

Thirty visually-normal adults (mean age: 21.7 ± 3.4 years) were assessed with optimal spectacle correction (baseline) and with two levels of astigmatism (1.00 D and 2.00 D) at both 90 degrees and 180 degrees, to induce both against-the-rule (ATR) and with-the-rule (WTR) astigmatism, respectively. Reading and eye movement fluency were measured using standardised tests, including the Discrete Reading Rate and Developmental Eye Movement test.

ATR astigmatism was shown to more significantly impair reading fluency than WTR astigmatism. Reading speed was reduced by 10 per cent for N16 print size for 2.00 D ATR astigmatism and by up to 24 per cent for smaller text sizes for 1.00 D ATR and 2.00 D WTR astigmatism.

The authors concluded that these findings have implications for the minimal prescribing criteria for astigmatic refractive errors.

Optom Vis Sci 2012; Jan 5 (Epub ahead of print).

Abstracts

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Vitamin D rejuvenates the ageing eye

Enrichment with Vitamin D(3) has been demonstrated to reduce retinal inflammation, decrease levels of amyloid beta and improve visual function in an experimental animal model of an aged eye.

Vitamin D(3) was administered by subcutaneous injection in aged mice (n = 14) for six weeks. Compared with an untreated group of age-matched controls, Vitamin D(3)-supplemented mice showed significant reductions in retinal inflammation and levels of amyloid beta accumulation. These changes were accompanied by a significant improvement in visual function as measured by the electroretinogram.

The authors proposed a potential role for Vitamin D(3) supplementation in reducing age-related visual decline.

Neurobiol Aging 2012; Jan 2 (Epub ahead of print).

Risk of retinal vein occlusion at high altitude

Three healthy young adults, with no known predisposing systemic factors, suffered retinal vein occlusion at high altitude.

Ascent at high altitude, defined typically as elevations above 2,700 metres, has been previously associated with thrombosis in lowlanders. In this case series, two males (31 and 37 years of age) and one female (40 years of age) were reported to develop a non-ischaemic central vein occlusion. In each case, vein occlusions were reported to occur at different durations of stay and at different altitudes. All three individuals showed complete recovery on descent to a lower altitude.

The aetiology of retinal vein occlusion at high altitude is not well understood; the authors postulated that hypobaric hypoxia at high altitude could be the unifying factor in the causation of retinal vein occlusion in these cases. They also proposed a potential role for anti-thrombotic prophylaxis in individuals embarking on extended sojourns at high altitudes.

High Alt Med Biol 2011; 12: 4: 393-397.

Ocular dangers of laser hair removal

Laser hair removal of the eyebrows can lead to permanent ocular damage and should be avoided. This case describes the induction of bilateral iritis and transillumination defects in a patient who underwent laser hair removal of the eyebrows.

A 41-year-old male presented to the Department of Ophthalmology (New York, NY) with bilateral eye pain and mild photophobia, two days post-treatment with a near-infrared (755 nm) alexandrite laser to epilate his eyebrows. No protective eyewear was worn during the procedure. At presentation, visual acuity was 6/6 in each eye. Ocular examination revealed Grade 2+ conjunctival injection and Grade 1+ anterior chamber cells in both eyes. Poor pupillary dilation and corectopia was evident in the right eye and the left eye showed no light response. Intraocular pressures and posterior fundus examination were unremarkable.

The patient was treated with topical steroids and cycloplegic drops for one month. Mild anisocoria and pupil irregularity persisted in both eyes at review.

Clin Ophthalmol 2011; 5: 1733-1735.

Cholesterol-lowering drugs reduce glaucoma risk

The long-term use of statins has been associated with a reduced risk of open angle glaucoma (OAG).

Participants in a prospective population-based cohort study underwent ophthalmic examinations, including intraocular pressure (IOP) and perimetry, at baseline and follow-up. The use of statins and non-statin cholesterol-lowering drugs was monitored. Associations between the use of cholesterol-lowering drugs and incident OAG were analysed.

Over a mean follow-up period of 9.8 years, 108 of 3,939 eligible participants (2.7 per cent) developed OAG. The hazard ratio for statin use was 0.54 (95% CI: 0.31-0.96, p < 0.05) and for non-statin cholesterol-lowering drugs 2.07 (0.81-5.33, p = 0.13). The positive effect of statins was

more pronounced with prolonged use. All analyses were adjusted for age, gender, baseline IOP, IOP-lowering treatment, family history of glaucoma and myopia. There was no effect of statins on IOP.

The authors concluded that these findings are consistent with the concept that statins have neuroprotective properties and may highlight a new OAG treatment modality.

PLoS One 2012; 7: 1: e29724. Epub 2012, Jan 4.

Descemet's membrane endothelial keratoplasty reduces graft rejection risk

The application of Descemet's membrane endothelial keratoplasty (DMEK) has been demonstrated to reduce the relative risk of an immunologic corneal rejection episode within two years post-surgery, compared with Descemet's stripping endothelial keratoplasty (DSEK) and penetrating keratoplasty (PK).

Patients treated with DMEK (n = 141) were retrospectively compared with cohorts of DSEK (n = 598) and PK (n = 30) patients treated at the Price Vision Group, Indianapolis, Indiana. Patient groups were matched for demographics, follow-up duration and indications for surgery. The post-operative steroid regimen and rejection criteria were identical in the three groups. The cumulative probability of a rejection episode both one and two years post-surgery was evaluated. Proportional hazards analysis was used to determine the relative risk of rejection episode.

DMEK eyes were reported to have a 15-fold lesser risk of experiencing a rejection episode than DSEK eyes (95% CI: 2.0-111, p = 0.008) and 20-fold lower risk than PK eyes (95% CI: 2.4-166; p = 0.006).

Ophthalmology 2012; Jan 2 (Epub ahead of print). ■

Baby boomers fail to see importance of nutrients for vision

Most baby boomers rank vision as the most important of their senses yet many do not attend regular eye examinations and are not aware that nutrients can help maintain good vision, according to a survey sponsored by Bausch + Lomb.

About 1,000 men and women aged between 45 and 66 years were questioned during the 'Eye on the Boomer' survey. The survey findings were released by the Ocular Nutrition Society at the American Academy of Optometry meeting in Orlando, Florida.

Although 78 per cent of participants declaring vision was their most important sense, and 55 per cent saying they worried about vision loss almost as much as heart disease and cancer, less than half had an annual eye examination.

Almost 60 per cent were not aware of the role of omega-3 fatty acids, 66 per cent were not aware of the role of lutein, and 89 per cent were unaware of the importance of zeanxanthin in their diet.

While more than half of respondents were taking vitamin and nutritional supplements to protect their joints, bones or heart health, just 18 per cent were taking supplements to support their eye health.

Twice a year testing of fields better than annual for detection

Researchers in the United States have found that biannual visual field testing for patients with glaucoma is more effective than annual testing at detecting disease progression.

The research, published in *Archives of Ophthalmology*, compared the visual field examinations of 381 patients included in the Advanced Glaucoma Intervention Study (AGIS) that had undergone at least 10 examinations and three or more years of follow-up.

The AGIS study included patients aged from 35 to 80 years with primary open-angle glaucoma; participants received biannual visual field examinations.

Two data sets, high frequency and low frequency visual field testing, were compared to determine whether more frequent testing led to earlier detection of glaucoma testing.

The low-frequency group—with a median of 12 field tests over three or more years—was created by removing every other test from the original high-frequency data set.

Results showed that progression was 69 per cent more likely to be detected in the high-frequency set.

Clever contact lens monitors blood glucose levels

A contact lens that monitors blood glucose levels in diabetic patients is being developed by researchers in the United States.

The research, a collaboration between the University of Washington and Microsoft Research Connections, aims to replace regular blood tests and provide real-time information to the wearer, allowing them to react quickly to fluctuations in insulin and glucose levels.

People with type 1 diabetes must check their blood glucose levels several times a day, which can be invasive and time-consuming. The contact lens, using natural user interface technology, will monitor glucose levels through tears rather than blood and is non-invasive.

Researcher Babak Parviz said that to some degree, what was in the blood also appeared on the surface of the eye. 'This contact lens, in principle, can give us information about what is happening inside the body without actually going into the body or collecting a blood sample,' he said.

Uveitis often misdiagnosed by non-ophthalmic practitioners

Ian Clemens
BScOptom GradCertOcTher

Uveitis is a disease characterised by inflammation. As its name suggests, it occurs in the uveal tissues of the eye: the iris, choroid and ciliary body. The aetiology is often unknown and treatment is non-specific, aiming to prevent complications by reducing the associated inflammation.

Uveitis can be acute or chronic and is generally classified according to the site of the inflammation: anterior (iritis or iridocyclitis), intermediate (pars planitis), posterior (choroiditis, retinitis and chorioretinitis) or panuveitis (usually in endophthalmitis).[1] Acute anterior uveitis (AAU) is the most common presentation of acute uveitis and is responsible for about 75 per cent of all cases of intraocular inflammation.

Often recurrent, uveitis has numerous causes and over 50 per cent of the people it affects are HLA-B27 positive. It most commonly affects people between the ages of 20 and 50 years. It is uncommon in patients younger than 10 years and older than 70 years. Attacks, by definition, resolve totally within three months and are not caused by any significant pathology or inflammation in other ocular tissues.[2]

Uveitis appears over several hours or days and characteristic symptoms are pain, redness and photophobia. It is primarily but not always unilateral. Common signs of uveitis are peri-limbal injection of the conjunctiva and the presence of anterior chamber cells and flare. The affected pupil may be sluggish and slightly miotic. Other findings may include hypopyon, iris anomalies such as posterior or anterior synechiae (PS or AS), iris atrophy, raised or lowered intraocular pressure (IOP) and hypopyon.

The corneal stroma or epithelium may be

Case report

A 62-year-old female (SF) holidaying from Tasmania presented to our central Victorian practice with a red, sore, watery right eye (RE). She explained that the eye had been troubling her for about a week.

She had initially presented to a GP in Mildura who diagnosed conjunctivitis and prescribed chloramphenicol eye-drops. She continued her travels while diligently using the drops but her symptoms did not improve. Three days later, she presented to the emergency department of the Albury Base hospital with the same complaint. The clinician diagnosed 'an allergy' and prescribed both Bleph-10 and Albalon-A eye-drops. In both cases, she was not given a thorough red eye work-up. Neither practitioner examined her with a slitlamp and both failed to measure her visual acuity.

Three more days had passed with no improvement and she found herself in Castlemaine. Within a few hours, she presented at our practice and my staff, following practice procedure for a patient with unilateral red-eye, interrupted me and asked if I would see her straight away. No matter how heavily booked I am, I never say 'no' to a red eye.

History revealed the convoluted journey to my chair as described above. She had a red, sore right eye. She was mildly photophobic. The eye had mild epiphora and felt worse in the evening. Her general health was good and she was not taking any medications. She wore spectacles only for near tasks. She felt her right eye vision was 'a bit blurry' and that her left eye was perfectly normal. The patient had no history of cold sores or other herpetic infections.

Her vision was measured at R = Count Fingers L = 6/6. The RE vision did not improve with a pinhole. She was surprised at the degree of visual degradation in the RE but noticed this only when the LE was occluded.

Slitlamp examination of the RE revealed significant corneal oedema, multiple 'mutton fat' keratic precipitates (KP) spread over the inferior endothelium, 3+ cells in the anterior chamber, peri-limbal conjunctival erythema and a hazy view of the iris (Figure 1).

The RE pupil was miotic and fixated. There did not appear to be any anterior synechiae. There was no fundus view due to the corneal oedema, AC cells and flare. The LE was normal. Intraocular pressures

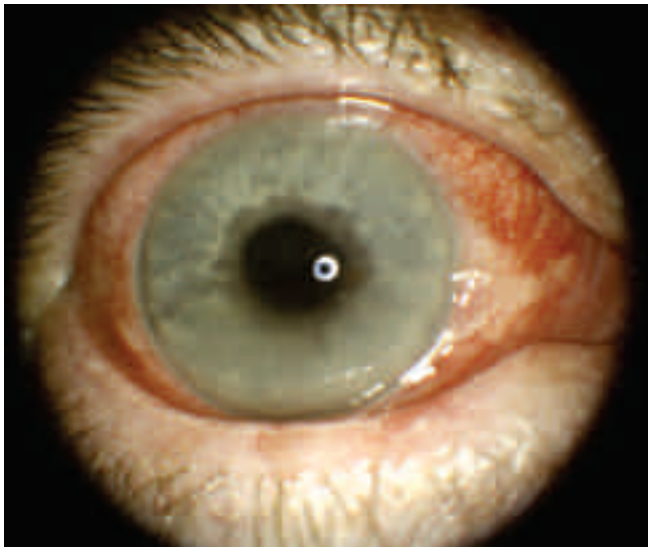


Figure 1. Initial presentation

Therapeutic management swings into action, bringing welcome relief to a patient suffering the pain of uveitis.

affected if either herpes zoster or herpes simplex virus is involved. The endothelium may have some keratic precipitates (KP) that are large and appear greasy ('mutton fat' KP) or can be fine and small, although the 'mutton fat' type is more common in chronic anterior uveitis. The affected lid will often spasm due to the commonly described deep, boring pain and can swell, leading to pseudoptosis. Topical anaesthesia does not provide relief from the pain of AAU.[3,4]

I find this case study (below) interesting because four years ago I would have had to refer SF to an ophthalmologist to treat her condition but now, after gaining my therapeutic endorsement in 2008, I can effectively and safely manage this type of patient myself.

This makes my practice both more interesting and professionally satisfying. Studying therapeutics also gave me a much better understanding of uveitis and it is amazing how much more knowledge you retain when you are expected to know how to treat something in the future.

The delay in an accurate diagnosis also highlights the need for optometrists to collaborate with GPs and other medical departments to assist with ocular diagnosis and treatment. The need for closer working relationships is important, as most emergency departments and GP clinics are disadvantaged by not having access to a slitlamp and tonometer. Expertise to perform such tests as gonioscopy and indirect ophthalmoscopy is clearly lacking in non-ophthalmic practitioners, leading to frequent misdiagnosis in primary care medical settings.[5]

This case shows that once a thorough history and work-up demonstrate a diagnosis of acute anterior uveitis, primary care optometrists can perform a vital role in the management and timely treatment of this condition.

1. Bartlett JD, Jaanus SD. Clinical Ocular Pharmacology, 3rd ed, 1995.
2. Gutteridge IF, Hall AJ. Acute anterior uveitis in primary care. *Clin Exp Optom* 2007; 90: 2 : 70-82.
3. Jackson TL, ed. Moorfield's Manual of Ophthalmology, 2008 edition.
4. Catania LJ. Primary care of the anterior segment, 2nd ed, 1995.
5. Statham MO, Sharma A, Pane AR. Misdiagnosis of acute eye diseases by primary health care providers: incidence and implications. *Med J Aust* 2008; 189: 7: 402- 404.

(IOPs) were RE 18 and LE 17 mmHg measured by non-contact tonometer. There was no significant staining of the corneal epithelium. Gonioscopy showed wide open anterior chamber angles, though the view was poor due to the oedematous cornea.

After the examination, I asked a few more questions and found that the patient had no arthritis or joint pain, no mouth ulcers, gastrointestinal disorders or lung conditions and no psoriasis. She felt confident that she had never experienced this type of complaint before.

A diagnosis of acute anterior uveitis (AAU) was made and she was prescribed g. prednisolone acetate one per cent (Pred Forte) to be used hourly (q1h) and g. homatropine two per cent bid. I asked her to instil six drops of Pred Forte into the RE in 'the hour before bed tonight'. I arranged to review her three days later, when her schedule allowed.

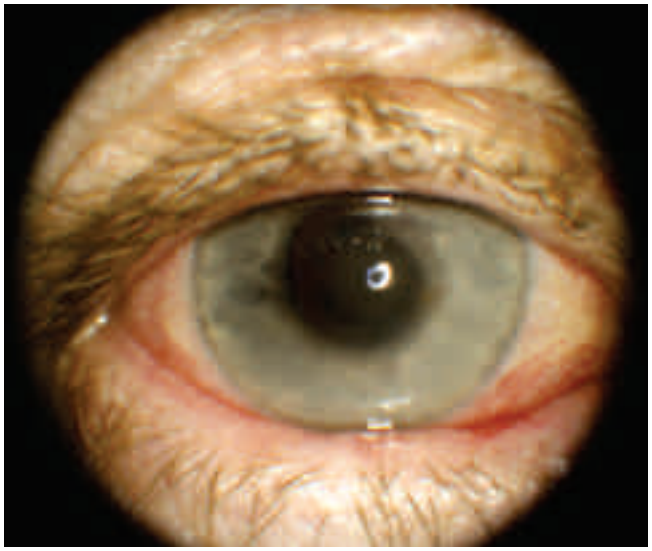


Figure 2. Three days after treatment

On review, she reported that her RE was much better and her vision had improved. She was no longer photophobic and the epiphora had ceased. Vision was R = 6/60 (pinhole 6/24) L = 6/6. IOPs were R = 16 and L = 13 mmHg. Her RE pupil was dilated. There were fewer KP and there were 2+ cells in the anterior chamber. The corneal oedema was still present. The fundus view was still poor (Figure 2).

The patient was happy that her signs and symptoms had improved but I counselled her that in a significant case of AAU, complete resolution would take some time. I asked her to cease the homatropine but continue with the Pred Forte q1h. A review was elusive. She told me she was leaving to return to Tasmania in three days. After consulting my trusty internet search engine, we agreed that she would attend the Launceston Eye Hospital within a few days of getting home with a letter I wrote documenting her recent history ... and could she possibly ask the attending physician to report their finding back to me?

I called SF at home a few days later and she told me her eye was 'getting better every day' and that she had an appointment at the eye hospital the following day.

About two weeks later, I received a letter from SF thanking me for the treatment she received at our practice. I find this sort of feedback extremely rewarding and I shared it with the staff member who had assisted the patient that day.

Another two weeks passed when a report regarding SF arrived on my desk from the eye hospital reporting that SF's vision had returned to R = 6/6- and that her AC was free of cells and that she was currently tapering the Pred Forte. ■

Environment takes its toll on the eye

Pollen, dust, pollution, computer use, air conditioning–some of the factors that cause people to be bothered by ocular symptoms and sensitivities.

Both outdoor and indoor environmental conditions influence eye health.

As an indication of the need to be cognisant of environmental conditions, the World Health Organization has defined 'Sick Building Syndrome' (SBS) to include symptoms related to indoor air conditions such as irritation of eyes, nose and throat, dry mucous membranes and skin.[1] Researchers have, in fact, linked poor indoor air quality with eye irritation.[1-8] Eye symptoms such as dryness, irritation and tiredness are observed when the precorneal tear film is unstable.[9] Destabilisation of the tear film can result from a decrease in lacrimal gland secretion and other gland dysfunctions brought about, in part, by the ambient environmental conditions and interactions with any pollutants present.[10] High room temperature and low relative humidity, for example, have been identified as risk factors leading to tear film instability.[5,11]

In addition to adverse environmental conditions found inside offices and enclosed places, external pollutants such as smog affect eye health.[12] Tear lysozyme, a critical component in ocular surface defence, has been shown to decrease in concentration with exposure to smog pollution,[12] potentially increasing the risk of developing irritative red eye problems and infections.[13]

To identify common ocular symptoms with respect to incidence, impact on quality of life, management strategy and overall satisfaction with available treatments, a global online survey, the NSIGHT Study, was conducted by Market Probe Europe.[14] Three thousand eight hundred participants in a 15- to 65-year-old vision corrected population, across seven countries, were enrolled in the study. Environment-related symptoms reported by patients included those associated with allergy/sensitivity (red eyes, sensitive eyes, itchy eyes), and workplace environment (dry eyes, watery eyes, tired eyes, eye strain).

Patients were also asked to report the frequency of these symptoms and how bothersome they found the symptoms (reported as 'not bothered', 'slightly bothered' or 'significantly bothered'). Questions regarding availability of a solution for the problem were also solicited. The survey additionally reported patients' sensitivities to pollution, air conditioning, computer use, long days, eye make-up, pollen/dust/hay fever, and contact lens wear.

Study results

A large number of patients reported experiencing symptoms associated with environmental conditions, the vast majority of whom reported these symptoms to be either slightly or significantly bothersome. Many of the symptomatic patients had no solution to their problems irrespective of the cause (Table 1).

Of those surveyed, 55 per cent reported either slight or significant sensitivities to environmental conditions of pollen, dust, hay fever and pollution, and to computer use. In addition, 47 per cent of the subjects described their eyes as being either slightly or significantly sensitive to air conditioning (Table 2).

Analysing the data for respondents reporting slight or significant sensitivity according to age (Figure 1) showed that peak sensitivity to pollution and allergens occurred within the 20-30 year age group.

	Experienced symptom	Bothered by symptom	No solution for symptom
Sensitive eyes	36	88	50
Watery eyes	27	74	66
Itchy eyes	40	84	44
Puffy/swollen eyes	22	79	57
Red eyes	33	57	60
Eye strain	58	85	53
Dry eyes	38	88	28
Tired eyes	69	87	43

Table 1. Percentage of patients who reported symptoms. Of those who experienced the symptoms, the percentage who reported the symptom to be either slightly or very bothersome and the percentage without a solution for the problem are included in the table.

	All patients	Contact lens wearers	Spectacle wearers
Pollution	55	58	55
Air conditioning	47	61	46
Computer use	72	74	72
Long days	72	79	72
Cosmetics & make-up	30	38	30
Pollen, dust, hay fever	55	56	55

Table 2. Percentage of patients who reported eye sensitivities to each condition overall, and differentiated into contact lens and spectacles wearers

Dr Jennifer P Craig
PhD MCOptom FAAO FBCLA
Dr Alexis KS Vogt
PhD

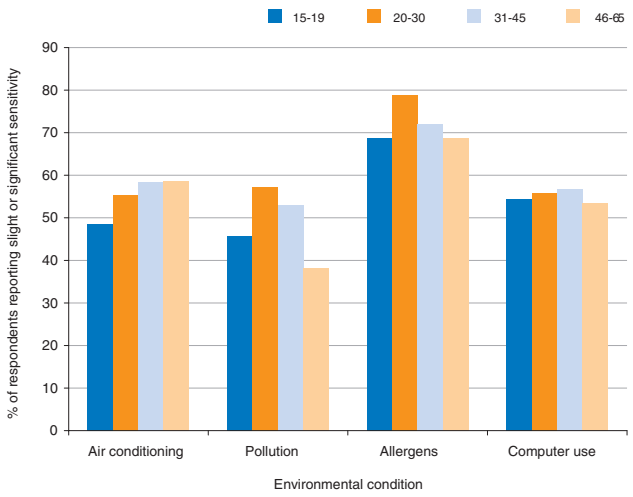


Figure 1. Percentage of respondents who reported slight or significant sensitivity to environmental conditions, according to age category

Sensitivity to air conditioning showed a trend of increasing with age. The variation of sensitivity to computer use was less age-dependent.

Geographic location was also found to have an impact on ocular symptoms. The largest percentage of patients who reported being significantly bothered by environmental factors live in Asia (Figure 2).

In addition to observing geographic trends, the data also highlighted gender trends. In categories of sensitivity to pollution, air conditioning, pollen, dust and hay fever, and computer use, more women than men reported slightly to significantly bothersome symptoms, particularly in relation to sensitivity to air conditioning where 56 per cent of women compared to 38 per cent of men reported sensitivity (Figure 3).

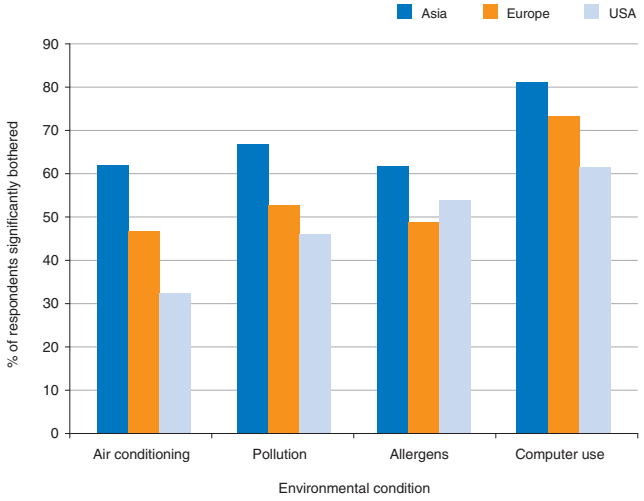


Figure 2. Percentage of respondents 'significantly bothered' by environmental conditions, according to geographic location

NSIGHT Study comparison to dry eye literature

The NSIGHT Study was not a study of dry eye disease but it is interesting to compare the results to those reported in the dry eye epidemiology literature as they are consistent in some instances. For example, the geographic differences in environmental symptoms noted in the NSIGHT Study are consistent with the regional differences in prevalence of dry eye disease, which ranges from seven per cent in the United States to 33 per cent in Taiwan and Japan.[15-20] The gender disparity noted in the NSIGHT Study is also consistent with the dry eye literature, which shows the most marked disparity post-menopausally.[21-23]

Continued page 24

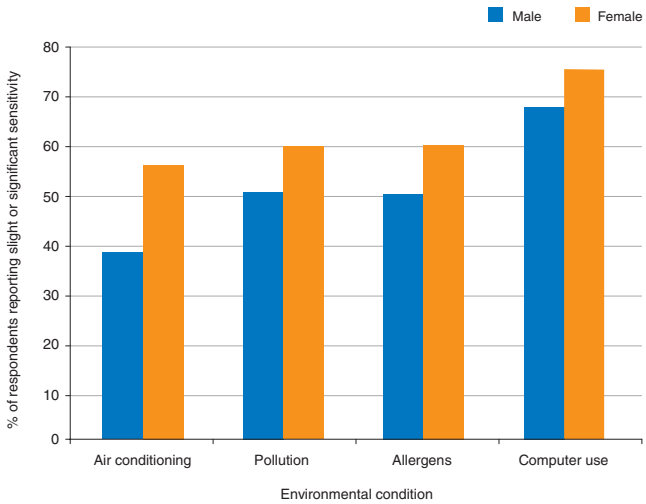
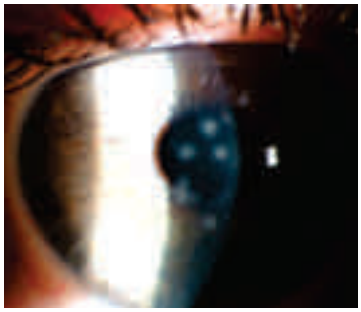


Figure 3. Percentage of respondents who reported slight or significant sensitivity to environmental conditions, according to gender

Clinical QUIZ ANSWERS

From page 13



Diagnosis

Post adenoviral keratoconjunctivitis subepithelial infiltrates

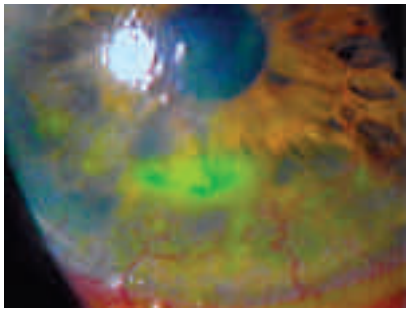
Due to the impact of the infiltrates on TA's vision and lifestyle, we elected to treat her with Flarex qid OU in addition to lubricants q2h OU.

There was a rapid improvement in vision over the next five days and following a slow taper of her steroids over four weeks she remained symptom free. At her last visit one month after starting treatment, she remained with some faint subepithelial infiltrates, which she was aware may take months to resolve. She was lost to follow-up after moving interstate at the end of the school year.

EKC is commonly encountered in optometric practice. Generally the disease is self-limiting and treatment consists of symptomatic relief with lubricants, and counselling regarding its contagious nature. Occasionally topical steroids are indicated in the presence of significant symptoms, membranous conjunctivitis, or post-viral corneal changes.

Gary Page

From page 17



Diagnosis

Herpes simplex epithelial and stromal keratitis

Slitlamp examination showed epithelial dendritic changes centrally over the pupil with inferior mid-peripheral stromal scarring and extensive superficial and deep corneal vascularisation. Possible aetiologies included exposure keratopathy, trauma and herpes simplex keratitis.

The appearance was consistent with that of advanced herpetic keratitis.

Treatment was commenced with topical acyclovir ointment q3h. At one week, the central dendrites had resolved down to a moderate superficial punctate keratopathy, but the inferior ulceration had not re-epithelised.

Topical steroid drops (prednisolone acetate 1.0%) were prescribed, which helped close the inferior defect. The vascularisation did not regress. Final visual acuity was count fingers at one metre due to pre-existing disciform macular scarring secondary to exudative AMD.

Graham Lakkis

Environment takes its toll on the eye

From page 23

Some dissimilarity is noted with regard to age. Although the prevalence of dry eye disease has generally been shown to increase with age,[19,21,22] the environmental symptoms reported in the NSIGHT Study showed varying trends with age, depending on the environmental condition. For example, the peak age group that reported sensitivities to pollution in the NSIGHT Study was aged between 20 and 30 years, whereas there was no obvious trend with age for patients reporting sensitivity to computer use. The reason for this difference is not clear from the data but is believed to perhaps reflect the adverse environmental conditions to which participants within this age group, predominantly, are exposed.

Conclusion

The NSIGHT Study highlighted the influence environmental factors have on ocular comfort. Outdoor as well as indoor environmental factors cause ocular symptoms that are both common and bothersome. With so many patients experiencing environmental symptoms but lacking a solution, this study's findings suggest that there is a need for eye-care professionals to be more active in addressing the symptoms caused by environmental factors.

References available on request from j.megahan@optometrists.asn.au. Subject: Environment takes its toll, Craig & Vogt, 2012.

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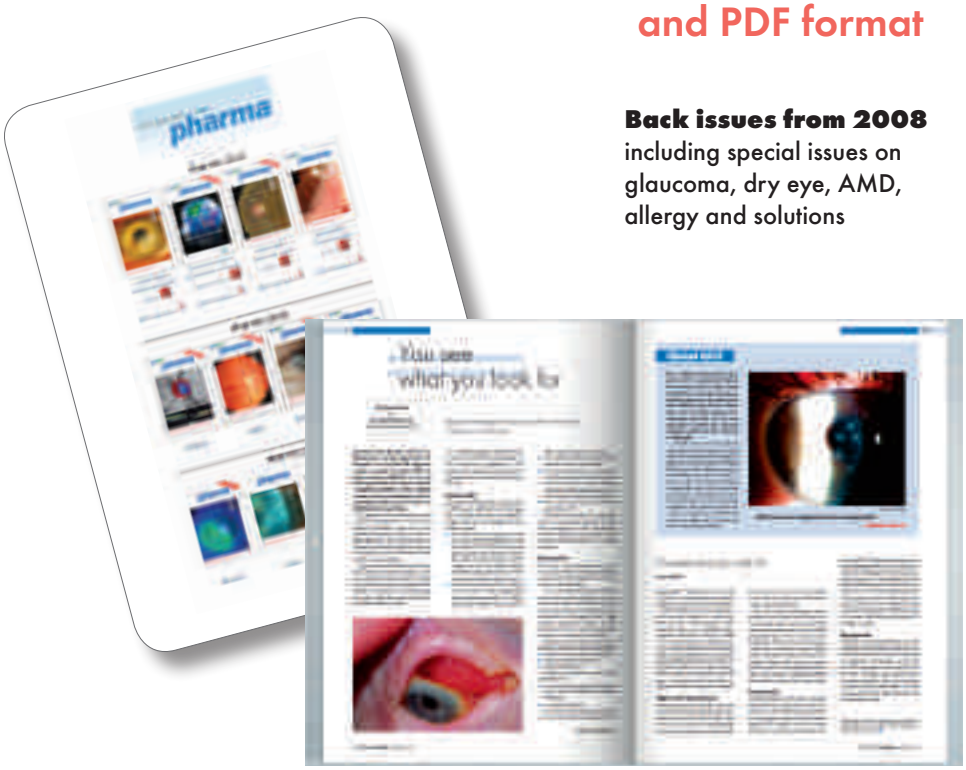

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