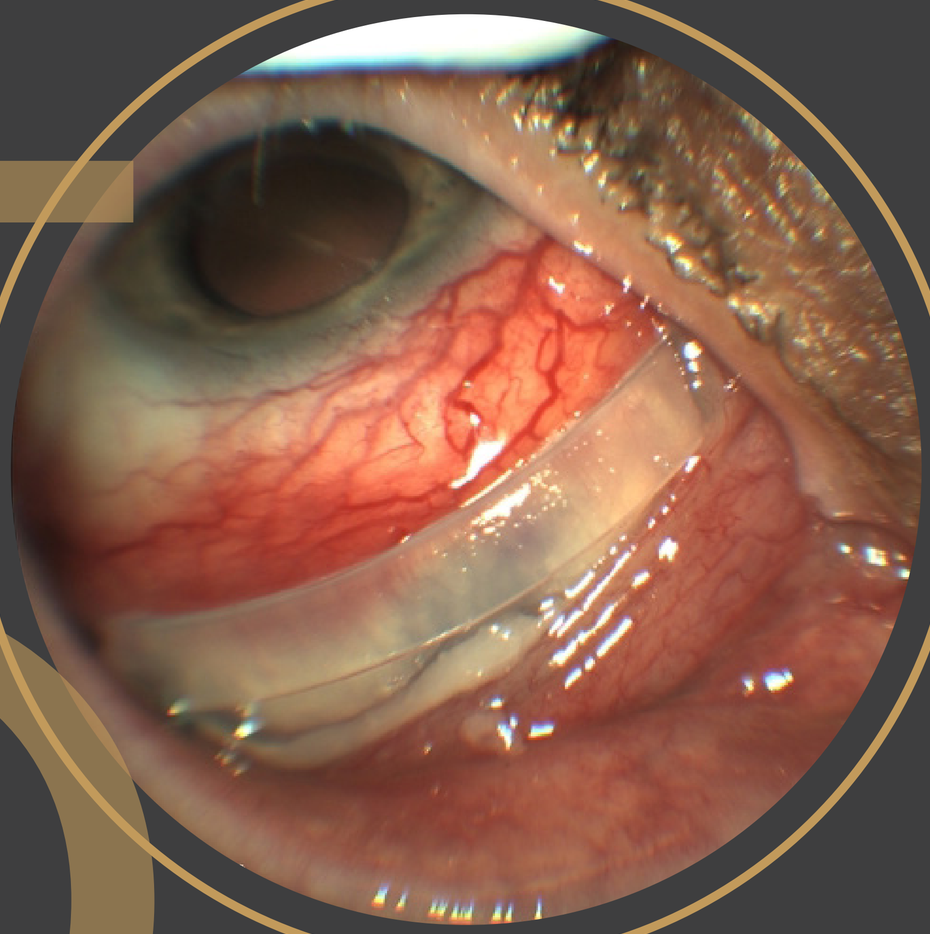

50 years of...

# VITREORETINAL SURGERY

Undoubtedly the development of pars plana vitrectomy in the 1970s transformed retinal reattachment surgery. It also opened the way to the development of macular surgery and surgery for the complications of diabetic retinopathy.

Robert Machemer and Jean-Marie Parel, recruited from Melbourne where he worked with Prof Gerard Crock, developed the prototype device with Storz Instrument Company. They conducted surgical training courses at Bascom Palmer Eye Institute in Miami to introduce retinal surgeons to the new instrumentation and techniques.

In 1975, Conor O'Malley and Ralph Heintz introduced the concept of three port pars plana vitrectomy with a 20-gauge Ocutome. All the ports were of the same gauge and hence interchangeable. This advantage with the smaller instrumentation meant that this system rapidly became adopted worldwide.

During the 1980s, Stanley Chang described the use of perfluropropane gas C3F8 for longer acting internal tamponade and then in 1988 he described the use of "heavy liquids" perflurocarbon liquids for intraoperative management of retinal detachment.

The development of smaller gauge instrumentation progressed through the late 1990s and in 2002, Gildo Fujui, Eugene De Juan and Mark Humayun published regarding a 25-gauge vitrectomy system. The flexibility of these instruments initially limited their adoption and Claus Eckhardt in 2005 published an account of a 23-gauge system which combined the positive feature of being transconjunctival but with increased rigidity and safety compared to the 25 system. Subsequent to this, the 25-gauge instruments have been strengthened and now are very widely used.

Macular surgery has now become routine practice. The results from full thickness macular hole repair and epiretinal membrane peel have improved significantly with smaller gauge surgery and the development of dyes to stain the epiretinal and internal limiting membrane to facilitate peeling. The primary success rate of full thickness macular hole repair is now routinely 85-90%. With transconjunctival sclerostomies, patients are more comfortable and day surgery predominates.

Machemer and the early adopters of vitrectomy would be astounded to learn that now the vitrectomy approach is being used to deliver gene therapy to patients with retinal dystrophies. Luxterna® (voretigene neparvovec-rzyl) developed by Spark Therapeutics Inc. has been given FDA approval for the treatment of biallelic RPE65-mediated inherited retinal dystrophy. This is just the first approved retinal gene therapy, with many more on the way.

In addition, the recent development of both epiretinal and subretinal retinal prostheses for patients with severe visual loss due to retinal dystrophic disease utilises the vitrectomy approach. These devices, which aim to provide visual information to patients who are non-navigational, have proven successful in aiding these patients with navigation and identification of objects. More recently, a subretinal device has been developed aiming to aid patients with severe geographic atrophy due to age related macular degeneration.

Interestingly within the last decade, a previously avoided space has become a surgical target. The suprachoroidal space is now being investigated for a number of interventions including our own suprachoroidal retinal prosthesis, developed in Melbourne.

We can only look forward to the next 50 years and what that brings in advancing technology, leading to improved outcomes for our patients.

***A/Prof Penny Allen***

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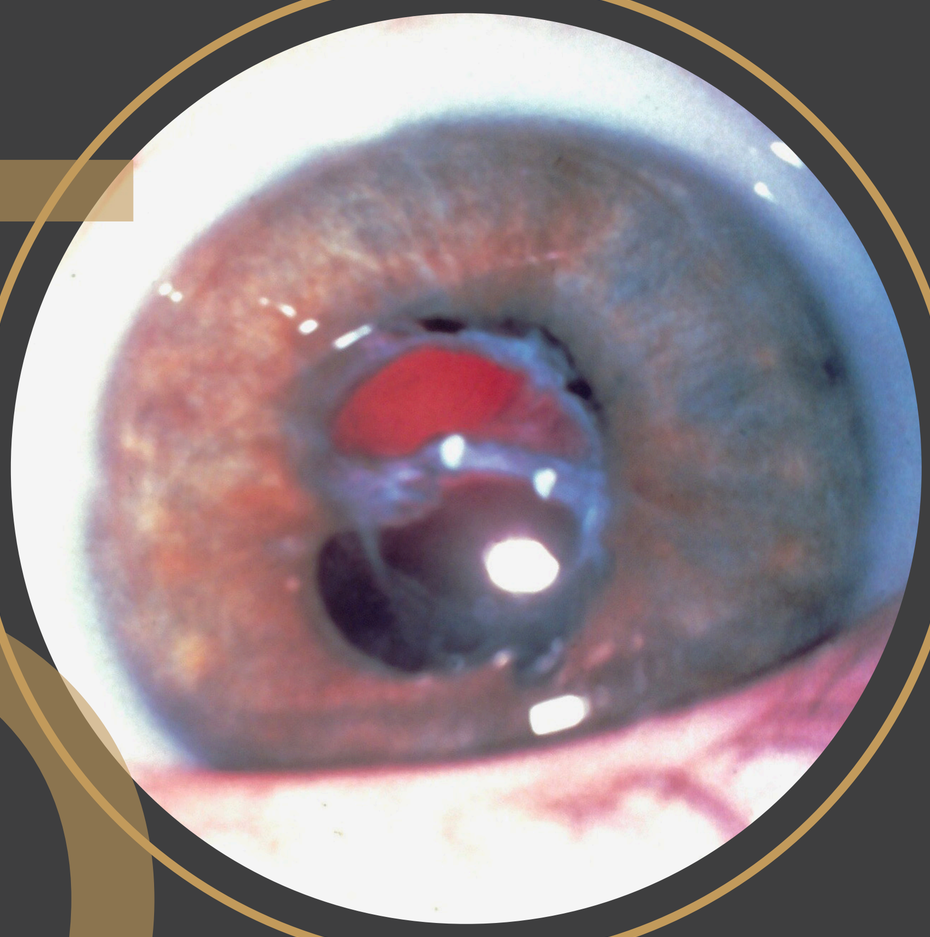

50 years of...

# PAEDIATRIC CATARACT SURGERY

Changes in cataract surgery in children over the last 50 years have produced significantly better visual outcomes.

Prior to the invention of YAG-laser for posterior capsular opacity and after cataract remnants due to extracapsular cataract surgery, needling discission was the usual approach.

The use of discission to remove cataracts in children was first described around 1960. This was an alternative to the standard intracapsular procedures being performed in adults, which required large incisions and significant postoperative care to allow for wound healing in an age without microsurgical techniques and the operating microscope.

A paper by Ira S Jones in 1960, the *Transactions of the American Ophthalmic Society*, discussed whether different surgical procedures for cataract removal were applicable to congenital cataracts of different aetiologies. His final analysis confirmed that needling could be used for all aetiologies. This technique has its advantages as it was through a small incision which did not require suturing. However, it often needed to be repeated to "clear" the visual axis.

Fast forward to 2019 and paediatric cataracts are performed using adult phaocoemulsification techniques. This is done with some technical modifications to allow for the decreased scleral rigidity and increased capsular elasticity found in children.

Now the biggest dilemma in paediatric cataract surgery is the choice of IOL power and the theoretically desired refractive error to allow for future eye growth, and likely myopic shift, versus the risk of induced hypermetropia and resultant amblyopia.

***Dr Wendy Marshman***

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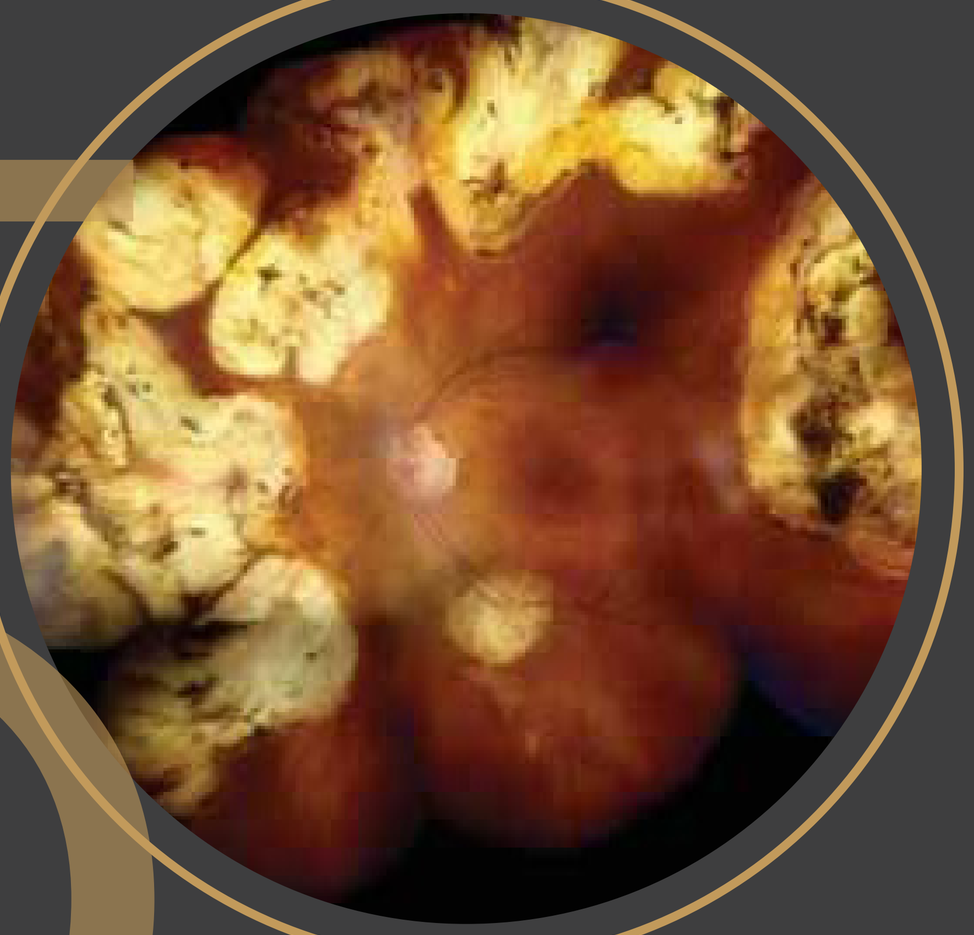

# 50 years of...

## THE RETINA

The 1971 Diabetic Retinopathy Study (DRS) showed that argon laser photocoagulation of the retina was a successful treatment for proliferative diabetic retinopathy. This was followed shortly after by the ETDRS which demonstrated efficacy of macular laser for oedema. Prior to this, a variety of treatments were used including pituitary ablation which carried a significant mortality rate. Despite being decades old, laser still has a role to play in the management of diabetic retinopathy as evidenced by the recent DRCRNet data from Protocol S in its five-year results in 2018.

Retinal imaging evolved from the development of fluorescein angiography, which initially allowed retinal specialists to view posteriorsegmentfunctionalityaswellasthestructuralinformation provided by colour photography. From this information, gifted clinicians such as J. Donald Gass and Alan Bird were able to describe a range of diseases and characterise their features.

More recently we have seen the rise of the digital age. Since 1991, OCT has revolutionised the viewing of the macula and eliminated any controversy about the presence of oedema. It has also allowed us to view in-vivo tissue to an almost cellular level. Further developments have followed, including scanning laser ophthalmoscopes, fundus autofluorescence, oct-angiography, adaptive optics and widefield imaging. It is now possible to take dozens of images of the retina in both en-face and cross-sectional views. If anything, we have gone from too little information to perhaps an excess. Diseases that were thought to be distinct entities have been shown to have overlapping features and likewise previously linked diseases have been shown to be separate conditions. The challenge now is to choose the correct imaging to display the pathological features and target treatment. Artificial intelligence systems are already being developed that use these digital images to help screen vast numbers of patients.

Recognition of the role played by VEGF in subretinal choroidal neovascularization in ARMD initiated the use of anti VEGF agents delivered by intravitreal injection. The efficacy of the treatment was confirmed in the MARINA and ANCHOR trials in 2006. The vitreous cavity was once considered a space to be violated at one's peril. Intravitreal injections are now the most commonly performed procedure by ophthalmologists and provide treatment for a range of ever increasing pathologies. These include macular degeneration, retinal infections, retinal vascular disease and, more recently, genetic therapies. In hindsight, the vitreous is almost the perfect location for local treatment. It is easily accessed with a small gauge needle, provides a reservoir for treatment, can be easily visualised and minimally traumatic to the eye. With increasing knowledge of the procedure and causes of post injection infection, guidelines have been developed to make the risk of infection minimal. The scale of the anti-VEGF revolution is hard to over-state. It has provided treatment for blinding conditions and revolution of anti-VEGF agents. It is likely more treatments will be trialled and released for use as intravitreal agents.

***Dr Xavier Fagan***

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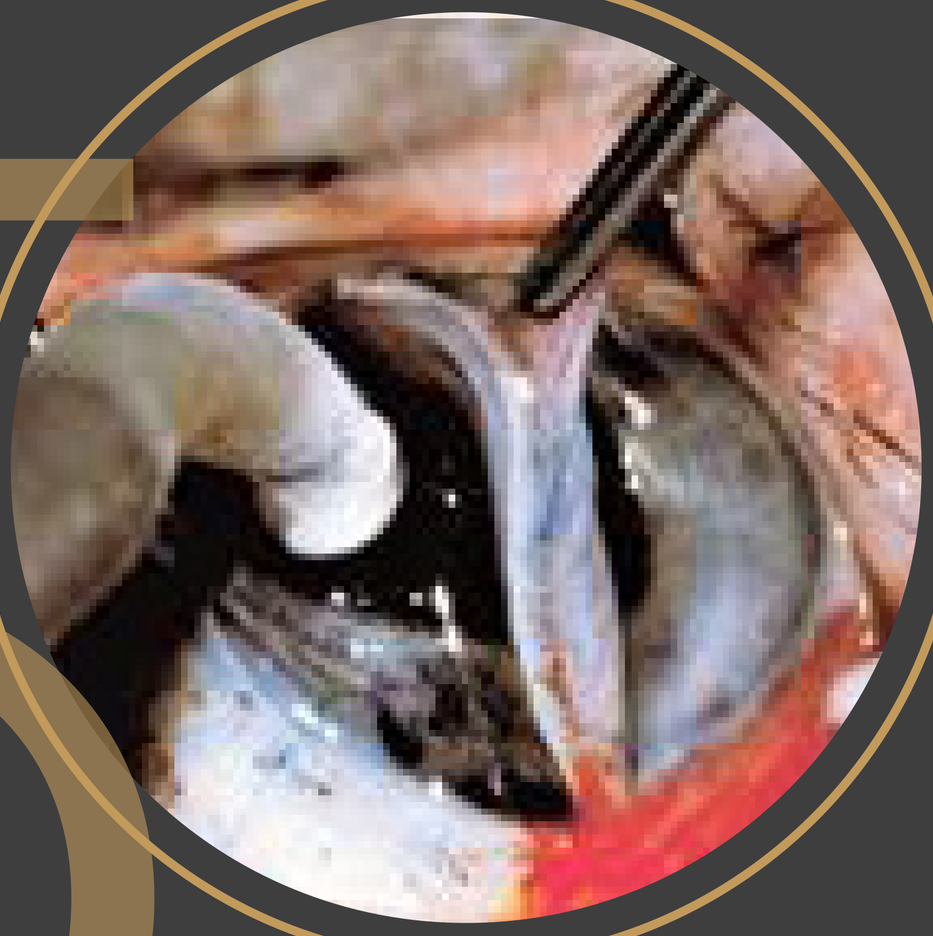

# 50 years of...

## CATARACT SURGERY

The last five decades have seen what must be one of surgery's most astonishing transformations. Cataract surgery was a high risk operation performed under a general anaesthetic, requiring several days in the hospital and leaving the patient with an oedematous cornea for several days to weeks, high astigmatism and thick aphakic glasses. It is now a low risk operation often performed with only sedation and topical anaesthetic as a day procedure with rapid recovery where the patient's new refractive situation is often spectacle independence for near and distance.

It is not just ophthalmic hubris to say that modern cataract surgery is now the most successful of all surgeries, one of the few where the patient frequently is left better functioning than they were prior to the development of the disease. What other common surgery can claim this, especially on a matter of such importance as sight?

This progress from intra-capsular, through extra-capsular to modern small incision phacoemulsification cataract surgery, has been built on hundreds of small, incremental advances and several large jumps forward. It is fair to say that it is also one of the great success stories of a partnership between surgeons and medical companies.

The number of advances are way too numerous to list here but extend across several fields; operative techniques and equipment (especially the introduction of phacoemulsification, improved fluidics and torsional phaco power), improved wound profiles and reduced size (and with this the elimination of the need for sutures), anaesthesia (with the introduction of sedation plus topical anaesthesia) and medication (with intracameral antibiotics). Then there is the jewel in the crown, the introduction of IOLs and decades of improvements not only in IOL technology (with foldable, aspheric, toric, multifocal and EDOF IOLs to name but a few) but also in IOL formulae and biometry.

In conjunction with the developments in cataract surgery, there has been a commensurate improvement in vitreoretinal and corneal grafting surgery. This often allows full rehabilitation of patients that have either pre-existing concurrent ophthalmic disease or experience an operative complication.

Other changes have been introduced to safeguard patients with specific risk factors, such as intracameral phenylephrine and dilation devices for small pupils and intraoperative floppy iris syndrome. This is an excellent example of the profession meeting the challenges of new risks to maintain patient safety.

The result has been surgery where the trauma to the eye has been reduced so dramatically that immediately the day following surgery, the vision has already greatly improved and the eye, to the casual observer, is normal with no external signs of inflammation.

As always, one change is built on the back of another and then allows for the next development, such as the replacement of the capsulotomy with a capsulorhexis allowing for the introduction of safe phacoemulsification surgery and foldable IOLs driving more astigmatically neutral small incision wounds.

I feel privileged to have had a career that has spanned most of these improvements. Change does not stop and I am sure in 20 years we will look back on present day surgery and feel it somewhat primitive. But, at almost 60 years of age and with my own cataract surgery not seemingly distant, I am incredibly grateful that I will be having modern, small-incision surgery with topical anaesthesia and a near vision IOL strategy. Now if only we have fully accommodative IOLs before my surgery is due!

***Dr Michael Loughnan***

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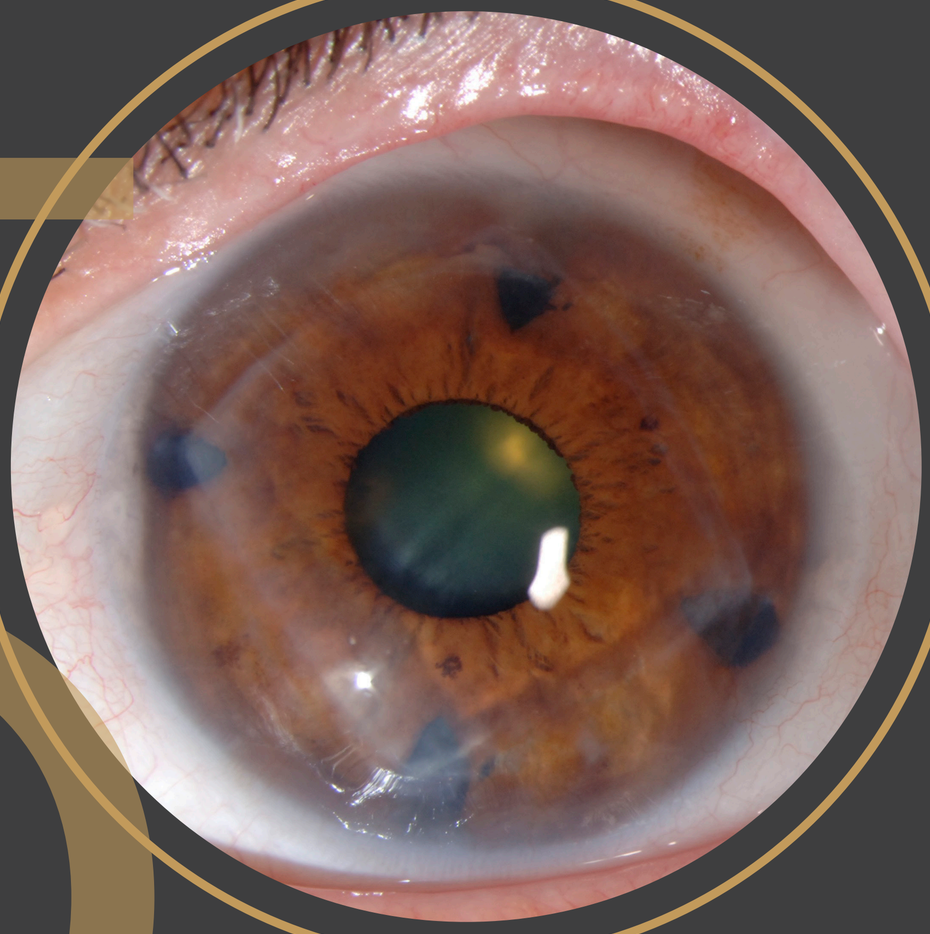

50 years of...

# CORNEAL SURGERY

In the seventies, corneal diseases were all treated with one operation: the penetrating keratoplasty. Whether the indication was the tectonic repair of a leaking cornea, removal of a worsening infection or attempting to regularise an ectatic cornea to improve vision, the abnormal cornea was removed and the donor tissue carefully sown into position. Arguments raged mainly over suture techniques and other tricks to improve outcomes.

Real patient data on outcomes, via Coster and Williams' work on the ACGR, highlighted high risk patients that might not do well with surgery. This applied some rigor to our decision to resist offering unlimited repeat grafts after failure. Despite this, suture related complications, rejection and prolonged recovery times after surgery limited the effectiveness of transplant surgery.

The revolution in lamellar surgery has transformed our outlook.

Endothelial keratoplasty techniques, developed by Terry and Melles and standardised by Price, Kruse and others, arose from the unanticipated ability of the graft to attach to the posterior stroma without the need for sutures or glue but with just the steady pressure of an intraocular air bubble.

The realisation that the transplanted donor stroma led to interface irregularities and haze, which then reduced the vision as well as increased the risk of rejection, led to a minimalist operation: transplants of just the endothelial layer with its supporting basement membrane (DMEK).

The ability to expand endothelial cells in the laboratory has opened the way for the possibility of cell therapy or a truly tissue engineered cornea.

Keratoconus remains a mysterious condition, affecting young people with poorly defined diagnosis, unclear aetiology and highly variable severity. Therapy 50 years ago was restricted to glasses. The newly developed rigid gas permeable contact lenses and graft surgery if best corrected vision remained poor.

Progression was carefully observed and eye rubbing was discouraged, but no real effective intervention was offered.

A group in Dresden explored the engineering principle of cross linking a polymer to reduce elasticity, stiffen the material to set the long term shape of the cornea. They took up the challenge of developing an effective but safe cross linking protocol that minimised scar formation, maintained vision and was safe to the endothelial cells but still halted progression. The initial recommendation was epithelial removal followed by 30 minutes' soaking with riboflavin and then a 30 minute session of irradiation with UV light at 3mW. This protocol stressed safety at the cost of both surgeon efficiency and the patient. A successful randomised control trial and widespread adoption has made a dramatic difference to sufferers, keeping most of those with good vision in glasses or contact lenses dramatically reducing the need for corneal graft surgery.

The discussion has now moved on to optimising the treatment regimen. Transepithelial treatment reduces pain and the risk of complications but at the cost of lower efficacy. Shorter soak times and higher intensity but reduced treatment times may have an equivalent effect as the Dresden protocol. Evaluation of definite signs of progression, earlier diagnosis and access to care are the current challenges. Deeper understanding of the fundamental basis of the condition will provide the next breakthrough.

***A/Prof Mark Daniell***

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# 50 years of...

# REFRACTIVE & CORNEAL SURGERY

Over the past half century, ophthalmology has seen the establishment and continued refinement of the refractive surgery subspecialty. Prior incisional refractive corneal surgical techniques lacked accuracy and predictability but planted the seeds for the development of a more refined method for modifying corneal curvature. This came in the form of the Excimer laser, which was developed as a result of trans-Atlantic collaborations between London and New York. Phototherapeutic keratectomy (PTK) emerged as a safe and precise method of correcting refractive error, which continues to be used until this day. A twenty year follow up data confirms the safety and efficacy of PTK, which remains an excellent procedure for laser vision correction in many patients.

Parallel to the improvements in corneal refractive surgery, we have benefited from advances in anterior segment imaging. A key development has been an appreciation of the importance of imaging the posterior cornea. This has resulted in a shift from classic Placido based corneal topography to a more three dimensional Scheimpflug corneal tomography. No refractive surgeon would consider laser vision correction without the reassurance of a normal tomographic map of the cornea, which is essential to exclude keratoconus and confirm that a safe residual stromal bed will remain after surgery.

The transition to lamellar corneal surgery has been a theme over recent decades. For laser refractive surgery, this meant the evolution from surface treatment with PTK to LASIK, characterised by creation of a corneal flap followed by Excimer laser ablation of the exposed stroma. Flap creation by a mechanical microkeratome has largely been superseded by the introduction of the femtosecond laser, reducing serious intraoperative flap related complications and affording precise control over flap dimensions. More recently, SMILE is an exciting addition to the refractive armamentarium. Using a femtosecond laser, a small lenticule of corneal stroma is cut and then manually excised from the cornea. This method avoids potential flap related complications and is growing in use.

Lamellar corneal transplant techniques have also evolved considerably. Fifty years ago, full thickness penetrating keratoplasty (PK) was used for most corneal transplants. While tried and tested, PK is far from a perfect procedure and transplants have become targeted to replace only the layer of the cornea which is diseased. Thus endothelial disease is now treated with endothelial keratoplasty (EK), with the implanted lamella of tissue becoming ever thinner as the years pass. We have moved on from Descemet's stripping (automated) EK (DS(A)EK), which includes a layer of corneal stroma to Descemet's membrane EK (DMEK). Anterior lamellar keratoplasty is preferred over PK in eyes with normal corneal endothelium, for example keratoconus.

A truly pivotal event for corneal surgery has been the development of corneal cross linking (CXL) for the treatment of progressive keratoconus. Early evidence for its efficacy comes from a landmark randomised controlled trial performed in Melbourne. Corneal transplant surgery for keratoconus will perhaps become a thing of the past as we move into the next 50 years as a College. It is with great interest that we corneal surgeons see what the future brings for our patients.

***Dr Georgia Cleary***

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# 50 years of...

## RETINAL DYSTROPHY DETECTION

The incidence of retinal dystrophies is estimated at 1 in 4000 per head of population. Inheritance can be autosomal dominant, autosomal recessive or X linked recessive with also sporadic cases.

Retinal dystrophies have marked clinical and genetic heterogeneity and currently mutations in more than 200 genes and an additional number of chromosomal locations that are known, but yet to be cloned, have been identified. Complicating the clinical picture is the fact that different mutations in the same gene can occur, causing different phenotypes within the same family.

It is not feasible to test all genes in all patients, but newer techniques including chromosome microarrays ( since 2000) and next generation sequencing ( since 2005) allow whole genome scanning which has the potential to find the "needle in the haystack" and with commercial companies investing in this technology, we should see a lowered cost and improved return on gene diagnoses.

The identification of these genes and being able to decode the proteins they produce, has allowed the beginnings of a new age of gene therapy for inherited blindness. The RPE 65 gene (discovered in 1997) encodes retinal specific protein 65 kd and is responsible for the conversion of all trans retinyl ester 11 to cis retinol in the retinal pigment epithelium. Mutations in this gene are responsible for Leber's Congenital Amaurosis, a severe and early onset form of retinal dystrophy affecting both rods and cones and usually leading to poor to no vision in infancy. Another 20 plus gene mutations have been identified in LCA but the RPE65 gene is of interest as there is now a gene therapy possible for this mutation which has been approved in the USA since 2017 and Europe from 2018.

Luxturna has been approved for treatment in children over the age of 1 and functional cDNA of the RPE65 gene is delivered to the retina on an adenoviral associated vector. The treatment is injected into the subretinal space between the RPE and photoreceptors after a pars plana vitrectomy. This treatment showed an improvement in the multiluminance mobility test ie increased light sensitivity but not always best corrected visual acuity, in the majority of patients. With clinical trials now having occurred for over 10 years, these results appear to be sustained. The cost of this novel gene therapy to affected individuals is reported to be very high but is the start of producing more light at the end of a very dark tunnel.

***Dr Wendy Marshman***

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