Australian College of Optometry's

– By Lewis Williams, PhD

Advances in anterior-segment treatments

Dr Sue Ormonde's second offering at the Australian College of Optometry's National Conference on 22-24 October in Melbourne related to the latest advances in anterior segment surgery. She opened with defects of the iris, natural, traumatic, and surgical (usually secondary to other, often more pressing issues necessitating surgical intervention with iris defects as collateral damage). Aniridia is probably the most common naturally occurring iris defect.

A key factor in any decision making is an assessment of the potential vision the affected eye might be able to provide. Once that assessment is available, a decision on whether a solution needs to be cosmetic-only, functional-only, or both has to be made.

The simplest form of treatment is a cosmetic contact lens, usually, but not always, with an opaque iris and a clear pupil. Hand-painted artwork that matches the appearance of the contralateral eye is a possibility although the number of suppliers of such a service is probably at an all time low as many custom laboratories fade from the manufacturing scene having been affected by the dominance of daily disposable, disposable, or frequent replacement stock contact lenses. Regardless, a suitable contact lens can provide a combined functional and cosmetic solution.

However, there are other solutions including surgical. One possibility is a so-called purse-string suture to close-up any gap in an iris but that has clinical ramifications for all clinicians involved with the patient subsequently because the treated pupil cannot be dilated thereafter. Unfortunately, leaving a pupil dilated also has sequelae as the iris tissue can become fibrosed and its dilated state can become permanent.

Whatever the cause may be, crystalline lens touch by the iris or parts thereof is a constant concern. An intraocular problem solver can be polymer (baked, black, PMMA) ring sector implant rings (e.g. the German Morcher Aniridia Implants) that are available in various patterns including one of numerous opaque sectors with an equal mark-space ratio.

Usually, the latter are applied as a complementary, overlapping pair with the sectors offset just one sector so that the artificial iris the devices form, is a complete circular artificial iris. Sector rings are only inserted at the time of cataract surgery and IOL implantation (curled into the capsular bag at the same time) and are known to be brittle meaning the less manipulation of the prosthetic before implantation and intraocularly the better. Because their appearance is not customizable they can still constitute something of a cosmetic problem once inserted but their functionality is high.

As an alternative, at least one manufacturer supplies a large hand-painted silicone elastomer-based artificial iris that is trephined to size and inserted in a similar manner to a rolled IOL via a small incision.

Moving from iris issues to anterior chamber IOLs, Dr Ormonde noted that it is often better to insert an ACIOL at a later date than at the actual time of cataract surgery. On the topic of penetrating keratoplasties in disastrous anterior segment events, e.g. corneal trauma, chemical burns, major infections, etc. the graft rejection rate can be as high as 25%.

The key to a better outcome is the presence/preservation of limbal stem cells because, without a set of healthy stem cells, the graft failure rate is high. The possibilities are a limbal autograft (tissue from the patient), a limbal allograft (tissue from another patient, preferably a close relative), or an epithelial transplant.

While an autograft is the logical answer, the transplantation of a significant amount (>6 o'clock hours of the limbal girdle) of the limbus from the fellow eye (assumed to be satisfactory unless the problem is bilateral in which case the choices are all difficult) runs the risk of creating a problem in that eye too so a

Sue Ormonde

conservative approach (<6 o'clock hours) is required.

The attendant need for systemic immunosuppression with allografts means the surgeon is committing the patient to immunosuppression for the rest of their life, a daunting prospect to most. Studies have shown that about 50% of allografts get an improvement in VA, but there is no substitute (other than the patient's own tissue) for having an unaffected identical twin.

Buccal mucosa from the patient has also been used in anterior segment repairs. However, while the rejection problem is avoided, the inescapable fact is that the cells are not limbal stem cells either. One possible solution now in use is the culturing of the patient's own limbal cells harvested from as little as 1 o'clock hour of the limbus and the cultured cells grafted on to the affected eye later.

Dr Ormonde described one case in which high-pressure concrete was sprayed into a workers eye destroying much of its anterior ocular surface. After the eye had settled, a penetrating keratoplasty was performed and a cultured amniotic membrane populated with limbal stem cells was applied. That resulted in re-epithelialization to such an extent that 6.5 years later a VA of 6/7.5 was achieved.

The Boston Keratoprosthesis that uses a donor cornea sandwiched between PMMA surfaces and grafted normally was also described. While some good results have been reported, fibrotic scarring and endophthalmitis are relatively common and the patient in committed to a rest-of-life need for steroids and antibiotics.

Other, last-resort possibilities include an osteo-odonto keratoprosthesis (OOKP – tooth-in-eye with PMMA cylindrical optic) which, despite a small visual field, has been known to provide approximately 6/6 vision. Glaucoma is a problem (disc can be examined, fields are very problematic, and IOP is immeasurable) and for treatment, only surgical solutions are possible. Furthermore, the bone component can start to absorb.

The history of medicine

The Sunday programme was introduced by Melbourne ophthalmologist, Dr Lewis Levitz who, over breakfast, presented an interesting, hour-long history of medicine including ophthalmology. The space available here does not allow justice to be done to his ambitious project – to use his words, 4,000 years of medical history in one hour. Historically, early humans noted the appearance of the tongue, they were aware of the heart's pulse and blood flow, but were averse to cutting the body meaning any 'discoveries' were dependent largely on observation of war wounds and trauma outcomes.

Fast forward a millennia or two to arrive at 129 AD when Galen, physician to the gladiators started to formalize primitive medicine using observation and reason to 'diagnose'. Galen noted arteries and veins, introduced couching for cataracts (in some remote, unserved parts of the earth, couching is still in use because it is better than the alternative – mature cataract blindness), had an understanding of motor nerves and the brain as the central nervous system 'co-ordinator', voice and the role the larynx played, and the liver's role in blood.

Fast forward another 1.5 millennia to arrive at 1628 and realize

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that William Harvey (physician, England) was discovering aspects of the heart, 72 beats per minute, the ventricle contained about 60 grams of blood, the heart was shifting 250 kg of blood per hour (about the weight of 3 men – it was 1628 after all), from which he deduced that the heart was a pump, a theory that was unacceptable at the time.

The stethoscope had to wait until 1816 when René Laennec (physician, France) used a roll of paper to form a crude stethoscope to hear the heart. That endeavour morphed into a hollow wooden cylinder for better results. Blood pressure was demonstrated in 1750, the mercury column as a means of measuring blood pressure (in a horse by direct arterial tapping) 1828, the inflatable cuff 1883, and Korotkoff sounds (physician, Russia) 1905.

Dr Levitz noted that by the auspicious year of 1950, we still had no idea of what blood pressures were 'normal' and it was 1960 before blood pressure became a treatable entity. It was until the CATIS randomized clinical trial published in 2013 in the *Journal of the American Medical Association* that established the real benefits of immediate blood pressure reduction in hypertensive and stroke patients.

Pseudoephedrine was known to the Chinese by 2,500 BC and atropine (from Atropa Belladonna or deadly nightshade a member of the tomato family) was used by society ladies to enhance their appearance (mydriasis) and was also used to kill emperors Augustus (14 AD) and Claudius (54 AD).

The analgesic effects of Meadowsweet were known for a long time (its salicylic acid content was the active ingredient) but is was not until 1897 that Bayer (Germany) chemist Felix Hoffmann (working under project leader Heinrich Dreser) discovered aspirin (acetylsalicylic acid) – the mechanism was not uncovered until 1971.

Later Dreser developed heroin, later still codeine so his projects' contribution to mankind are a mixed bag).

Lewis Levitz

Anaesthesia (ether initially although alcohol by mouth probably preceded that by 1,000 to 5,000 years) was first used by American dentist William Morton in 1846. Chloroform was used a year later. Topical ocular anaesthesia in the form of cocaine was first used by Austrian ophthalmologist Karl Koeller (on his own eye) in 1884.

In the same year William Halsted (surgeon, USA) injected cocaine into nerves and proceeded to performed a blood transfusion (on his sister) and a gall bladder operation (on his mother). His success was not met with universal approval at high levels of the medical establishment when the august journal *The Lancet* condemned anaesthesia on the basis that the patient must feel pain.

The concept of germs spreading disease was first proposed by Girolamo Fracastoro (physician, poet, mathematician, and geographer, Italy) in 1550 when he postulated that disease was spread by 'seeds', either chemical or living, and could be caught by, or communicated to, others.

The refinement of the microscope circa 1660s by Dutch tradesman and scientist Antonie van Leeuwenhoek allowed him to confirm the existence of blood cells. Cell multiplication was observed in 1840.

Rudolf Virchow (medical practitioner, scientist, and politician, from what was German Prussia, now Poland) discovered the connections between abnormal cells and tissues and disease. He also insisted on all medical advances being based on robust, well-researched science, a view that led him to fall foul of the medical publishing establishment of the time.

His problems proved to be so great that he and a like-minded colleague (Benno Reinhardt) started their own rigorous medical journal (*Archiv für pasthologische Anatomie und Physiologie, und für die klinische Medizin* [translation: Archive for Pathological Anatomy and Physiology and Clinical Medicine]), a publication that continues to this day (now known simply as *Virchows Archiv*).

Perhaps one of the greatest contributions to medical science that benefited the whole of the human race was the observations and developments surrounding vaccination by Edward Jenner (physician, England) in 1796. His work built on the risky but relatively common inoculation process in which a lesser disease was introduced deliberately with the intention of preventing the occurrence of a more serious and debilitating disease subsequently (e.g. cow pox to prevent smallpox [trialed in 1774 by Benjamin Jesty, farmer, England and others]). Initial work was the result of careful observation by several scientists but the basic technique was know in China and the Middle East well before any use in England or North America.

Louis Pasteur's work in France on fermentation and fermentation prevention by heat, added to scientific knowledge. However, Pasteur could never accept the concept of tiny organisms causing disease in such a large animal as the human.

The first antiseptic, carbolic acid (phenol in modern parlance), entered use circa 1869 following research by Joseph Lister (surgeon, England) that built on that of Pasteur. Lister's first antiseptic operation was performed in 1865. The alarmingly high hospital operation mortality rate of almost 65% was reduced to 15% by using Lister's methods. Lister went on to confirm the germ theory of disease and identify the causes of TB and cholera. Those were milestones in the history of medicine.

Other significant surgical advances are relatively recent, e.g. rubber gloves (1890), surgical masks (1897) but routine use of surgical gloves in the UK only entered the scene in 1960. While the details are now better understood, intuition still has a rôle in the practice of medicine regardless of the era of practice, e.g. in 3,000 BC people were advised to have clean hands, clean finger nails, and clean beards, Sushrata (India, era uncertain – range: 1,000 BC to 100 AD) wrote a medical text detailing treatment of 1,120 conditions including 51 eye conditions along with descriptions of surgical tools, herbal remedies, tissue grafting, plastic surgery, and wound care before, during, and after surgery.

The development of penicillin by Scot, Alexander Fleming in 1928 (with the involvement of Florey and Chain much of which is shrouded in claim and counterclaim) rounded out the general major developments in medicine.

An overview of cataract surgery rounded out the lecture. The name cataract can be traced to Greek or Arab words that translate to falling water (white water). Eye surgery is recorded in Egypt in 1,200 BC and cataract surgery some time later. Couching for cataract was described by Sushrata (see above).

Greek surgeon (but Rome citizen) Antyllus (2nd century AD) describes a small incision and sucking-out as the treatment for cataract, a method improved upon in the 10th century AD by Muhammad ibn Zakariya al-Razi (a Persian polymath).

Extracapsular cataract extraction (ECE) was first described by Jacques Daviel (ophthalmologist, France) in 1747.

The modern era owes much to Friedrich Von Gräfe (ophthalmologist, German Prussian) circa 1850 but perhaps the greatest advance is that of (Nicholas)