Welcome to Bausch and Lomb’s monthly research update.

With our background in clinical ophthalmic research, mainly of the anterior eye, Bausch and Lomb have asked us to produce an independent report of some of the interesting findings coming out of the research journals each month. As a busy practitioner, this should allow you to keep more up-to-date with cutting edge clinical research and allow you to locate the articles when you want to know more about a topic highlighted.

Welcome to latest issue of the Research Update in which the most recent issues of the ophthalmic journals listed below are reviewed. This month’s published research includes a range of really interesting papers relating to the anterior eye in particular. In the field of refractive surgery, permanent monovision in presbyopic myopes is explored, along with factors which may affect the incidence of post-LASIK dry eye. A diurnal pattern of tear osmolarity is described for the first time, and it has been observed that long-term dietary supplementation may be beneficial in patients with severe dry eye. Relating to cataract surgery, US data indicates that the incidence of cataract operations is continuing to increase, whilst further work suggests that cataract surgery to correct visual impairment may be linked to long-term survival in older persons. As usual, the update concludes with the most intriguing research paper title of the month and the most fascinating research finding.

<table>
<thead>
<tr>
<th>JOURNAL</th>
<th>VOLUME</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Journal of Ophthalmology</td>
<td>97(10)</td>
</tr>
<tr>
<td>Contact Lens and Anterior Eye</td>
<td>36(5)</td>
</tr>
<tr>
<td>Cornea</td>
<td>32(10)</td>
</tr>
<tr>
<td>Investigative Ophthalmology and Visual Science</td>
<td>54(9)</td>
</tr>
<tr>
<td>JAMA Ophthalmology</td>
<td>131(9)</td>
</tr>
<tr>
<td>Journal of Cataract and Refractive Surgery</td>
<td>39(9)</td>
</tr>
<tr>
<td>Journal of Optometry</td>
<td>6(3)</td>
</tr>
<tr>
<td>Journal of Refractive Surgery</td>
<td>29(9)</td>
</tr>
<tr>
<td>Optometry and Vision Science</td>
<td>90(10)</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>120(9)</td>
</tr>
</tbody>
</table>
Diurnal pattern of Tear Osmolarity

Tear osmolarity is a measure of the concentration of solutes in the tear film and can now be determined relatively easily in clinical settings using the TearLab Osmometer. This interesting study measured tear osmolarity and central corneal thickness (CCT) in 38 healthy subjects at bedtime (baseline), upon waking, and at regular intervals up to 8 hours after waking. Tear osmolarity was found to show diurnal variation, with the tear film being hypo-osmotic upon waking compared to bedtime, and tear osmolarity increasing after waking. CCT increased after sleep, but returned to baseline thickness within 4 hours. The association of tear osmolarity and corneal thickness/swelling indicates that tear film tonicity may be partly responsible for controlling corneal hydration.

Cornea 32: 1305-1310

Age-related thinning of Bowman’s Layer in the Human Cornea in vivo.

Bilateral laser scanning in vivo confocal microscopy was used by Germundsson and colleagues, based in Sweden, on 82 healthy subjects aged 15-88 years to examine changes in Bowman’s layer thickness with age. The results showed that between the ages of 20 and 80 years, Bowman’s layer loses one-third of its thickness, a decline of around 0.06 micrometres per year. The effect was observed in both eyes of participants, and the thickness of Bowman’s layer was not correlated with overall corneal thickness. The authors suggest these findings should be taken into account when planning surgical treatments involving the anterior cornea.

Investigative Ophthalmology and Visual Science 54: 6143-6149
Long-term supplementation in the treatment of keratoconjunctivitis sicca

Previous research has indicated that gamma-linolenic acid (GLA) and omega-3 (n3) polyunsaturated fatty acid (PUFA) supplementation may decrease the production of inflammatory mediators which are implicated in chronic dry eye. This double-masked placebo-controlled clinical trial examined the efficacy of 6 months of supplementation with GLA and n3 PUFAs in 38 postmenopausal patients with moderate/severe keratoconjunctivitis sicca (KCS). The Ocular Surface Disease Index score (based on patient symptoms) significantly improved with 24 weeks of supplementation, compared to placebo, whilst the topographic surface asymmetry index was also lower in those who received the supplement. Neither treatment had an effect on tear break up time, corneal/conjunctival staining or tear production, however the significant improvement in symptoms indicate promise for the treatment of moderate to severe KCS with supplementation.

Cornea 32: 1297-1304

Dry Eye After LASIK with a Femtosecond Laser or a Mechanical Microkeratome

Dry eye is the most common complication after LASIK, affecting up to 59% of patients. The LASIK flap may be created using a mechanical microkeratome or a femtosecond laser; this prospective study sought to determine whether the incidence of dry eye post-LASIK varied depending on how the flap was created. Eighty seven myopic patients underwent LASIK with femtosecond laser flap creation (n = 44) or microkeratome-assisted surgery (n = 43), and were followed up at regular intervals for 6 months post-operatively. Objective measures of tear break up time, Schirmer test and corneal staining were acquired, along with subjective reports of dry eye symptoms using the Ocular Surface Disease Index (OSDI). Both types of LASIK treatment were associated with significant increases in corneal staining and OSDI scores. Tear break up time reduced in both groups, but were significantly better (longer) in the femtosecond group. The authors suggest that further randomised studies are required to investigate whether femtosecond-assisted LASIK can reduce post-treatment dry eye.

Optometry and Vision Science 90: 1048-1056
A novel eyelid-warming device used for meibomian gland dysfunction

Heat therapy to melt meibum has previously been shown to be vital in successful management of meibomian gland dysfunction (MGD). The Blephasteam is a new commercially-available goggle-type device designed to deliver controlled, moist heat to the eyelids. This study examined the efficacy of the device in 25 normal subjects who received 10 minutes of treatment. Ocular thermography indicated a significant increase in temperature of both eyelids following use (approximately 2 deg C), with no change in corneal staining or IOP. Interestingly, even in these normal subjects, ocular surface redness was reduced following treatment. The data indicate that the device is safe and provides effective warming, suitable for MGD treatment.

*Contact Lens and Anterior Eye 36: 226-231*

Power profiles of daily disposable contact lenses

In this in vitro study, the authors used the Nimo TR1504 contact lens power mapper to evaluate the distribution of refractive power within the optic zone of daily disposable contact lenses, and assess the effect of lens decentration on power profile. Four brands of daily disposable lens were investigated; all lenses showed between 3 and 10 % increase in negative refractive power away from the lens centre. However, decentration of up to 1.0 mm had little effect, with the change in lens power compared to the well-centred position always measuring less than 0.25 D.

*Contact Lens and Anterior Eye 36: 247-252*

Cholesterol Deposition on Contact Lenses

Cholesterol is a common lipid deposited onto contact lenses. Walther and colleagues, based in Waterloo, Canada, sought to investigate the factors that influence cholesterol deposition on conventional hydrogel (CH) and silicone hydrogel (SiH) contact lenses in this laboratory-based study. The SiH lenses showed significantly higher levels of cholesterol deposition than CH materials and amongst the SiH materials, balafilcon A deposited the highest levels of cholesterol and lotrafilcon B the lowest. One limitation of the study is that it is not clear exactly how well these in vitro measures relate to the in vivo human eye.

*Optometry and Vision Science 90: 1057-1065*
Impact of soft contact lens edge design and mid-peripheral lens shape on the epithelium and its indentation with lens mobility

Wolffsohn and colleagues used simultaneous high-resolution optical coherence tomography and a high-speed camera to image soft contact lens movement and interaction with the ocular surface with each of various contact lens shape profiles and edge designs (chiselled or knife-edge). Data were obtained from 26 subjects on 4 visits immediately after insertion, and at 2 hours and 4 hours. Interestingly, vertical and horizontal contact lens movement did not change with time following insertion. Epithelial indentation (corrected for optical distortion) decreased post-insertion and changed following a blink. Vertical movement was affected by both mid-peripheral shape profile and edge design. The dual imaging system permits study of the effect of new contact lens designs on the ocular surface and movement.

*Investigative Ophthalmology and Visual Science* 54: 6190-6197

Monovision surgery in myopic presbyopes

Monovision surgery is associated with a number of potential disadvantages, so this study sought to investigate visual function and patient satisfaction in 40 myopic presbyopes undergoing a monovision excimer laser refractive procedure. Patients were followed up for 12 months post-operatively, providing useful information on the longer-term effects. All patients showed a reduction in distance and near stereopsis, which is a recognised effect of monovision. Glare symptoms decreased significantly during the 12 month follow up period. Notably, patient satisfaction significantly improved between 6 and 12 months, from around 40% at 6 months, up to approximately 85% at 12 months. The high levels of patient satisfaction suggest that monovision excimer laser treatment is a viable option for myopic presbyopes.

*Optometry and Vision Science* 90: 1092-1097
Increasing incidence of cataract surgery

A recent Swedish study indicated that the incidence of cataract surgery had levelled off after steadily increasing for around 30 years. This population-based study in Minnesota examined the incidence of first and second eye cataract surgeries between 1980 and 2011 to determine if a similar trend may be present in the United States. Incidence of cataract surgery peaked in 2011, with a rate of 1100 per 100,000. The 2005-2011 probability of second-eye surgery within 2 years of the first eye also showed a significant increase compared to 1998-2004 data. The results indicate a continuing steady increase in cataract surgeries, with 60 % of patients in the population examined having second eye surgery within 3 months of the first eye.

*Journal of Cataract and Refractive Surgery 39: 1383-1389*

Baseline Factors Predictive of Visual Prognosis in Acute Postoperative Bacterial Endophthalmitis

Post-operative bacterial endophthalmitis is a rare, but potentially devastating complication that may arise following cataract surgery. This French study included 99 patients with acute postoperative endophthalmitis and was undertaken to provide information on prognostic factors relating to this dreaded complication. The baseline (at presentation) characteristics associated with a good visual outcome included winter season, absence of intra-operative complications and initial VA. The key factor associated with a poor visual outcome was bacterial virulence, although infection of the right eye, corneal oedema and lack of fundus visibility were also relevant.

*JAMA Ophthalmology 131: 1159-1166*

Cataract Surgery and Improved Survival in Older Persons

The authors analysed data relating to cataract surgery and visual impairment amongst participants in the Australian Blue Mountains Eye Study, which is a large-scale population-based cohort study. Visual impairment was defined as a visual acuity poorer than 20/40; 354 participants aged 49 years and over had both cataract and visual impairment, or had undergone previous cataract surgery. Surgical correction of cataract was found to be associated with significantly better long-term survival in older adults, compared to participants with visual impairment who had not undergone cataract surgery. This interesting finding remained significant after adjustment for factors such as smoking status, body mass index, cancer and other comorbidities. The findings strongly support previous research which has linked visual impairment with poor survival.

*Ophthalmology 120: 1720-1727*
Capsular bag opacification with a new accommodating intraocular lens

Posterior capsular opacification is the most common long-term complication resulting from cataract surgery. Opacifying material may be fibrotic, which is particularly undesirable with new accommodating intraocular lenses (IOLs) which are designed to move or change shape to generate an increase in optical power. In this laboratory-based study, Floyd and colleagues describe use of a silicone oil-filled accommodating intraocular lens with large haptics to keep the anterior and posterior capsule separated. The accommodating IOLs were implanted into rabbit eyes, and examined after 6 weeks, compared to control IOLs. The implant appeared to be successful at preventing capsular opacification, by maintaining an extended capsular bag and may hold promise for future application in human eyes.

Journal of Cataract and Refractive Surgery 39: 1415-1420

Compliance with occlusion therapy for childhood amblyopia

Knowledge of the factors which limit compliance with occlusion therapy for amblyopia may allow these factors to be addressed, with the goal of improving the efficacy of treatment. This UK-based study explored compliance with occlusion therapy in 152 children participating in two smaller studies. Age, sex, amblyopia type and severity were not found to be associated with compliance. Compliance was found to be significantly reduced at weekends compared to weekdays, and was lower with both prolonged treatment duration and less-frequently scheduled follow-ups. Notably, the study identified that compliance with patching treatment averages less than 50 %, which is likely to limit the treatment effects significantly.

Investigative Ophthalmology and Visual Science 54: 6158-6166

Macular displacement following rhegmatogenous retinal detachment repair

This prospective study based in London investigated the incidence and magnitude of macular displacement following primary rhegmatogenous retinal detachment repair, along with associated symptoms. Post-operative assessment included fundus autofluorescence and optical coherence tomography. Macular displacement was found to be common, observed in around three-quarters of patients following repair of foveal-involving detachments, and also in 5 out of 17 cases where the fovea was spared. Most affected patients were symptomatic in the early post-operative period, describing bending of lines and/ or distortions of object size.

British Journal of Ophthalmology 97: 1297-1302
The association between residual astigmatism and refractive errors in a population-based study

This interesting paper included data from over 5,000 individuals aged 40-64 years participating in the Shahroud Eye Cohort Study in Iran. The purpose of the study was to explore the relationship between spherical and astigmatic components of refractive errors in a population-based study. Refractive error was determined by subjective techniques following autorefraction. As one might intuitively predict, increases in spherical refractive errors were typically associated with higher levels of astigmatism. Interestingly, cases of high hyperopia and high myopia mostly involved with-the-rule astigmatism, whereas most emmetropes generally showed against-the-rule refractive astigmatism. The data may be valuable in planning corneal refractive procedures.

*Journal of Refractive Surgery* 29: 624-629

Risk Factors and Genetics in Common Comitant Strabismus

The authors present a systematic review of previous literature to identify the key risk factors for the development of comitant strabismus. Identifying risk factors is important in enabling earlier diagnosis and management of associated amblyopia, and improving the likelihood of successful treatment. Forty-one relevant research papers were included in the review, which identified that the key risk factors for comitant strabismus are low birth weight; retinopathy of prematurity; prematurity; maternal smoking during pregnancy; anisometropia and hyperopia. A strong hereditary link was also identified, particularly in intermittent and accommodative strabismus.

*JAMA Ophthalmology* 131: 1179-1186
Most fascinating research finding this month...

Macular pigment, and its potential protective role in age-related macular degeneration, has received much interest in recent years. Stringham and Snodderly, based in Athens examined the effect of macular pigment on visual discomfort to short wavelength light, in normal pre-presbyopic individuals. Participants had a wide range of macular pigment densities (0.10- 0.71 at 30° eccentricity), as measured by subjective heterochromatic flicker photometry (as in the commercially available MPOD device). Higher density of macular pigment significantly reduced visual discomfort to short wavelength light. The authors suggest that macular pigment has a dual purpose of reducing visual discomfort and retinal protection from light damage, and that macular pigment interacts with non image-forming retinal input to achieve these effects.


Most intriguing research paper title this month...

*Human Corneal Anatomy Redefined. A novel pre-Descemet’s corneal layer: Dua’s Layer*

Dua and colleagues had previously hypothesised on the existence of a pre-Descemet’s posterior stromal layer based on surgical experiences performing deep anterior lamellar keratoplasty. In this study, they demonstrated the existence of this layer using 31 human donor sclerocorneal discs (median age 84 years). Using a big bubble technique and subsequent histology, the authors identified a well-defined, strong and acellular layer in the posterior cornea, which they termed “Dua’s layer.” The layer is approximately 10 micrometres thick, and consists mainly of type 1 collagen bundles. The recognition of this layer could have major implications on posterior corneal surgery and our understanding of corneal biomechanics and posterior corneal disorders such as acute hydrops.

*Ophthalmology* 120: 1778-1785