

# Journal Highlights

## NEW FINDINGS FROM *OPHTHALMOLOGY*, *AJO* AND *ARCHIVES*

### **Ophthalmology**

#### **Graft Failure After Descemet's Stripping Automated Endothelial Keratoplasty**

April's *Ophthalmology*

Two studies focusing on failed grafts in Descemet's stripping automated endothelial keratoplasty (DSAEK) appears in this month's *Ophthalmology*.

Suh et al. conducted a histopathologic study of 19 failed DSAEK grafts and found 16 cases with attenuation of endothelial cells, 11 cases of fibrocellular tissue in the graft-host interface, five cases with retained Descemet's membrane and four cases with epithelial ingrowth. In addition, four DSAEK grafts had full thickness cornea at one edge.

In the second study, Oster et al. identified a strong relationship between donor tissue detachment and graft failure. They described the clinical and histological features of 16 graft failures from 15 patients and found that 75 percent of failed grafts had atrophic corneal endothelium. The authors also identified residual host Descemet's membrane in the graft and improper donor trephination.

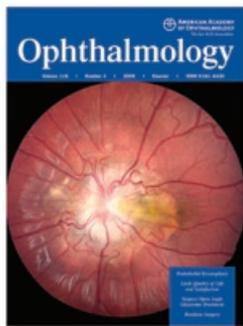
These studies show that potential causes of graft failure include the presence of interface material, retained

Descemet's membrane and epithelial ingrowth, and that a profound endothelial cell loss is also associated with graft failure.

#### **Intraocular Methotrexate for Uveitis and Uveitic Cystoid Macular Edema**

April's *Ophthalmology*

Taylor et al. evaluated the use of intravitreal methotrexate (MTX) to treat uveitis and uveitic cystoid macular edema (CME) and reported that this approach can effectively improve visual acuity and reduce CME.



The prospective case series involved 15 eyes of 15 patients with a unilateral exacerbation of uveitis and/or CME that reduced visual acuity to 20/40 or worse. Each patient received an intravitreal injection of MTX. Thirteen patients responded to

the injection with a rapid increase in visual acuity associated with decreased intraocular inflammation and/or macular thickness. Of these 13 individuals, four had a subsequent relapse about four months following the injection.

The authors note the side effects of systemic corticosteroid and immunosuppressive therapy are difficult to justify for unilateral ocular disease in these complex patients. However,

intravitreal MTX appears effective and allows for the reduction of immunosuppressive therapy in some patients.

#### **Combined Inhaled and Oral Corticosteroid Increases Cataract Risk**

April's *Ophthalmology*

Using 10-year follow-up data from the Blue Mountains Eye Study, Wang et al. confirmed that the use of both inhaled and oral corticosteroids can promote the development of nuclear, cortical and posterior subcapsular cataract (PSC) subtypes.

The study involved 3,654 Australians aged 49 and older. At baseline, 103 individuals were current users of inhaled corticosteroids and 120 were past users. In addition, there were 31 current and 147 past users of oral corticosteroids.

Current users of either type of corticosteroid had a greater risk than past users of developing nuclear cataract but not cortical cataract. In subgroup analyses, those patients who use a combination of both inhaled and oral corticosteroid, or who used the combination in the past, were at increased risk of PSC when compared to nonusers.

They conclude that high long-term risks of developing PSC and nuclear cataract are associated with combined inhaled and oral corticosteroids, and they stress the need for judicious use of these medications.

## Factors Associated With IFIS

April's *Ophthalmology*

**N**eff et al. identified factors associated with intraoperative floppy iris syndrome (IFIS).

Findings from an analysis of 899 eyes of 660 patients undergoing routine cataract surgery indicated that a significant percentage of IFIS occurred with no clearly identifiable risk factors. While IFIS was associated with use of tamsulosin and previous use of other alpha<sub>2</sub> antagonists, their use did not necessarily predict IFIS—several patients were identified to have IFIS with no history of alpha<sub>2</sub> antagonist use. In addition, the researchers found that IFIS was not necessarily bilateral and does not correspond to an increased complication rate during phacoemulsification.

They suggest that physicians take a detailed history of past and present medication use to help identify patients potentially at risk for developing IFIS.

## Significant Refractive Errors Uncommon in Preschool Children

April's *Ophthalmology*

**I**n a study of ocular disease among children aged 6 months to 71 months, **Giordano et al.** have found that significant refractive errors are uncommon.

The researchers examined 2,546 Caucasian and African-American preschool children in the Baltimore Pediatric Eye Disease Study using cycloplegic autorefraction. Hyperopia was the most common refractive error among both African-American and Caucasian children, but African-Americans were on average about 0.75 D less hyperopic than Caucasians. In addition, the researchers found no evidence for a myopic shift over this age range. Finally, spectacle use was rare in these children, even among those with clinically important refractive errors. Based on published prescribing guidelines, 5.1 percent of the children would have benefited from spectacle correction, yet only 1.3 percent had been prescribed correction.

## American Journal of Ophthalmology

### Reversal of Glaucomatous Disc Cupping

April's *AJO*

**T**he Collaborative Initial Glaucoma Treatment Study reports its findings about the effect of IOP lowering on the optic disc.

The authors randomized 348 eyes to medical or surgical treatment of open-angle glaucoma (OAG). Baseline and five-year stereoscopic optic disc photographs were assessed by two independent readers for change and confirmed by an independent committee.

Three hundred and three eyes (87 percent) of both treatment cohorts showed no change, 22 (6 percent) showed enlargement of the cup along any meridian and 23 (7 percent) showed a reduction in the cup along any meridian. Incidence of optic disc progression was higher in the medicine group (10 percent) than in the surgical group (3 percent). The incidence of reversal of cupping was higher in the surgical group (13 percent) than the medicine group (1 percent). Visual-field worsening was significantly associated with progression of optic disc cupping. Reversal of cupping was associated with lower postoperative IOP but was not associated with improvement of either visual acuity or central visual fields.

### Rate of Endophthalmitis in Open Globe Injuries

April's *AJO*

**A**ndreoli et al. report a case series evaluating the percentage of patients in whom endophthalmitis developed after open globe injury.

The authors reviewed the charts of 675 patients treated surgically for open globe injury between January 2000 and July 2007. Cases with at least 30 days of follow-up were included in statistical analyses (558 in total). A standardized treatment protocol was used in all cases. Intravenous vancomycin and ceftazidime were started on admission and were stopped after

48 hours. Patients were discharged on topical antibiotics, corticosteroids and cycloplegics. Surgical repairs were performed by the chief of trauma, who was on call for all open globe injuries. Data collection variables included timing of injury and repair, mechanism of injury, details of surgical repair and details of follow-up (including duration, presence of complications and vision). A primary outcome measure of endophthalmitis and secondary outcome measure of risk factors for endophthalmitis were then studied.

The overall percentage of endophthalmitis was 0.9 percent (three culture-positive cases and two culture-negative cases). Four of the five cases achieved final acuity of 20/80 or better. Risk factors for endophthalmitis included intraocular foreign body and primary IOL placement.

The authors conclude that a standardized protocol including surgical repair by a dedicated eye trauma service and 48 hours of intravenous antibiotics was associated with very low rates of posttraumatic endophthalmitis.

### Pars Plana Vitrectomy for Retained Lens Material After Cataract Extraction

April's *AJO*

**H**o et al. reviewed a case series to determine current clinical predictors and visual outcomes of patients who undergo pars plana vitrectomy (PPV) for retained lens material. The medical records of 166 patients who underwent PPV for retained lens material between January 2001 and January 2007 were reviewed. Main outcome measures included final visual acuity, development of glaucoma, retinal detachments and cystoid macular edema.

At the final examination, 120 patients (72 percent) had a visual outcome of 20/40 or better and 18 patients (11 percent) had a visual outcome of 20/200 or worse. In patients without any preoperative eye conditions, 83 percent achieved a final vision of 20/40 or better. Multivariate analysis showed that predictors for visual outcomes of

20/40 or better were presenting vision, insertion of a posterior chamber lens and absence of preoperative eye disease. Predictors for visual outcomes of 20/200 or worse were the absence of an anterior vitrectomy at cataract surgery, absence of a sulcus lens, presence of preexisting eye disease and development of glaucoma. Performing a PPV within seven days of cataract surgery was associated with a lower risk of developing glaucoma.

The authors recommend that the cataract surgeon perform an anterior vitrectomy, place a posterior chamber lens if possible and consult a retina specialist for a PPV within seven days to decrease the risk of developing secondary glaucoma.

### Lower Posterior Capsular Opacification With Silicone IOLs

April's *AJO*

**V**ock et al. compared posterior capsular opacification between two IOLs six months after surgery. Both lenses featured sharp-optic edges and open-loop haptics. One IOL was made of silicone and the other was made of hydrophobic acrylate.

One hundred and six eyes in 53 patients were included initially in this randomized, controlled, masked trial. Forty-four eyes of 22 patients with age-related bilateral cataract were available for the six-year follow-up. Each patient had standard cataract surgery and randomly received a silicone or hydrophobic acrylate IOL in the first eye, and the other type of IOL in the fellow eye. Follow-up examinations were at one, three and six years after surgery. The intensity of PCO was assessed using digital retroilluminated photos and the automated quantification of after-cataract (AQUA) software.

Six years after surgery, the AQUA scores were 2.3 for the silicone and 3.8 for the acrylic IOLs. The acrylic IOL eyes also had a significant increase in AQUA score from the three-year to the six-year follow-up. Nd:YAG laser capsulotomies were performed in two silicone and six acrylic IOLs.

The authors conclude that an angu-

lated three-piece hydrophobic acrylic IOL had more PCO six years after surgery than a silicone IOL of otherwise similar design. Apart from an optic material effect, differences in haptic design and the degree of optic edge sharpness may play a role.

### Chronic Anterior Uveitis in Children

April's *AJO*

**H**olland et al. described the clinical features of chronic anterior uveitis in children presenting to a referral center. They identified relationships between demographic, medical and ophthalmic factors at baseline and determined which factors predict new complications and vision loss during follow-up.

All children under the age of 16 at onset of chronic anterior uveitis were examined by one clinician from 1993 through 2006. Cross-sectional analyses compared baseline findings. Relationships between potential risk factors and incident adverse events were studied by Kaplan-Meier and Cox proportional hazards regression models. There were 115 patients (200 eyes) who met inclusion criteria, and follow-up ranged from 0.4 to 157.5 months. There were numerous strong relationships between eight defined complications at baseline in pairwise comparisons. Flare was the inflammatory sign most consistently associated with complications at baseline. Baseline factors that predicted new complications during follow-up included an age of less than three years, elevated cells, elevated flare, keratic precipitates, signs of intermediate uveitis and papillitis. Factors that predicted vision loss included male gender, increased flare, signs of intermediate uveitis, papillitis and baseline complications. Juvenile idiopathic uveitis and immunomodulatory therapy were not related to new complications.

The authors conclude that chronic anterior uveitis in children is associated with various vision-threatening complications that occur in combinations. Complications develop early in the disease course and patients with

more severe disease at presentation are at an increased risk of additional adverse events.

### Archives of Ophthalmology

#### Serum Cystatin C Level, Kidney Disease and AMD Incidence

February's *Archives*

**K**lein et al. examined the associations of serum cystatin C and chronic kidney disease (CKD) with the incidence of age-related macular degeneration.

The study consisted of 4,926 patients aged 43 to 86 at baseline, of whom 3,779 participated in one or more follow-up examinations over a 15-year period. AMD was determined by grading photographs of the macula. Persons were defined as having mild CKD based on a serum cystatin C value of between 45 and 60 ml/min/1.73 m<sup>2</sup> using the Modification of Diet in Renal Disease Study equation. Moderate/severe CKD was defined as a serum cystatin C value of less than or equal to 45 ml/min/1.73 m<sup>2</sup>.

The investigators reported that, while controlling for age and other risk factors, higher levels of serum cystatin C at baseline was associated with the incidence of early AMD and exudative AMD but not geographic atrophy or progression of AMD. Mild CKD was associated with the 15-year cumulative incidence of early AMD but not the incidence of other AMD endpoints.

They conclude that these findings show a relationship of serum cystatin C and CKD with the incidence of AMD. The underlying biological processes remain to be determined.

#### Characteristics of Glaucoma in Japanese-Americans

February's *Archives*

**P**ekmezci et al. reviewed the medical records of patients of Japanese descent who visited two private ophthalmology clinics in San Francisco within the last 10 years.

Glaucoma diagnoses were based on optic nerve head appearance and

glaucomatous visual field defects. Glaucoma was classified as primary or secondary and further subclassified as open-angle or angle-closure glaucoma. Primary open-angle glaucoma patients who never had a recorded IOP of greater than or equal to 21 mmHg were defined as having normal-tension glaucoma and those with a recorded IOP of less than 21 mmHg were defined as having high-tension glaucoma.

Among 1,732 patients, 112 had glaucoma (6.4 percent). Among 97 primary open-angle glaucoma patients, 19.6 percent had high-tension glaucoma and 80.4 percent had normal-tension glaucoma. Although normal IOPs were four times more common than high IOPs in the Japanese-American clinic population with glaucoma, the proportion of normal-tension glaucoma (80.4 percent) was still not as high as was described in a previous population-based study in mainland Japan (92.3 percent).

Presence of glaucoma was positively correlated with age, refractive error and IOP, while it was negatively correlated with central corneal thickness and BCVA. Controlling for age, correlations with IOP and visual acuity remained significant.

The authors conclude that glaucoma among Japanese in the United States may be different from other American ethnicities and possibly mainland Japanese. Ophthalmic practices should be aware of the differences, and diagnostic protocols should be patient- and ethnicity-based.

### Reduction of IOP With Anecortave Acetate

February's *Archives*

**R**obin et al. examined the IOP-lowering effect of anecortave acetate (delivered by anterior juxtasceral depot) in eyes with steroid-induced ocular hypertension following sub-Tenon's or intravitreal injections of triamcinolone acetonide.

Eight eyes of seven subjects with steroid-induced ocular hypertension with uncontrolled IOP on maximal tolerated medical therapy received 24 mg of anecortave acetate. IOP was then monitored for 12 months.

From a baseline IOP of  $31.3 \pm 11.3$  mmHg, eyes treated with anecortave acetate experienced a mean IOP reduction of 12 mmHg within one week and 14 mmHg by one month. Three of eight eyes remained controlled without

further IOP-lowering interventions, although two of these three eyes required one or more additional anecortave acetate treatments during follow-up. Five eyes failed to achieve adequate IOP levels, four of which ultimately underwent trabeculectomy within eight weeks of anecortave acetate therapy. There were no serious adverse events associated with either the medication or the injection procedure.

The authors conclude that anecortave acetate delivered by anterior juxtasceral depot may be a promising treatment modality for IOP reduction in eyes with steroid-induced ocular hypertension, noting that four of eight eyes were able to avoid trabeculectomy. They recommend that future studies be conducted to clarify the mechanism of action, to establish the safety and efficacy in a larger cohort, to identify the optimal dose and frequency of dosing and to explore the potential additivity to other IOP-lowering therapies.

*Ophthalmology summaries are written by Lori Baker Schena and edited by John Kerison, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. Archives of Ophthalmology summaries are written by the lead authors.*

## ROUNDUP OF OTHER JOURNALS

### Management of Flat Anterior Chamber After Trabeculectomy

*The Journal of Glaucoma*  
2009;18:13–20

**A** flat anterior chamber (FAC), which involves contact between the posterior surface of the cornea and either the iris, lens or vitreous, is a possible complication resulting from overfiltration in the early post-operative period after trabeculectomy. Monteiro de Barros et al. conducted a prospective evaluation of three different approaches to this condition. They focused on early grade 2 FAC, in which contact occurs between the entire iris and the corneal endothelium.

Thirty-six eyes with a FAC were randomized to three treatment groups: group one, anterior chamber reformation with viscoelastic substance; group two, anterior chamber reformation with balanced salt solution and concurrent drainage of choroidal effusion; and group three, pharmacologic therapy with atropine, phenylephrine and, in select patients, oral acetazolamide.

Treatment group two had a greater number of eyes with acuity decline of two or more lines than group three. Group one had more eyes with acuity decline of two or more lines than group three—but this was not significant. The decline in visual acuity was mainly from cataract or coexistent

macular changes.

The authors conclude that when visual acuity preservation is a primary concern, medicinal treatment alone may be the preferred treatment option. However, when control of IOP is a high priority, reformation of the anterior chamber with a viscoelastic substance may be a preferred option.

### Correlations Between Corneal and Scleral Thickness in Glaucoma

*The Journal of Glaucoma*  
2009;18:32–36

**M**ohamed-Noor et al. assessed 124 patients with and without glaucoma to determine the correla-

tion between central corneal thickness and anterior scleral thickness (ST) in the disease.

The study enrolled 31 consecutive patients with ocular hypertension, 31 patients with primary open-angle glaucoma, 31 patients with normal-tension glaucoma and 31 normal patients.

The investigators measured CCT with ultrasonic pachymetry and measured ST with ultrasonic biomicroscopy at the temporal quadrant. While results showed a correlation between CCT and ST among the normal-tension glaucoma group, no correlation was found among other patients.

The authors speculate that CCT and ST could potentially be associated with other characteristics of the sclera and choroid, therefore serving as a potential marker for a possible susceptibility of the optic nerve to glaucomatous damage. However, answering this type of hypothesis will require additional research.

### Cone Death Linked to Starvation in Mouse Model of Retinitis Pigmentosa

*Nature Neuroscience*  
2009;12:44–52

**P**unzo et al. have found evidence that starvation may be the cause of the slow demise of cones in retinitis pigmentosa, the most common type of retinal degeneration caused by a single disease allele. The researchers observed that while most mutations that cause retinitis pigmentosa involve the rod photoreceptor-specific genes, the cone photoreceptors also die as a result of such mutations.

To better understand this nonautonomous cone death, they analyzed four mouse models with mutations in rod-specific genes. The researchers noticed that the changes in many of the genes involved in cellular metabolism coincided with cell death onset. These changes reflected cones with a shortage of nutrients.

In addition, these cones demon-

strated signs of autophagy—a cellular self-digestion process—which is consistent with prolonged starvation. They also found that several aspects of the insulin/mammalian target of the rapamycin pathway regulating cellular metabolism were affected during the period of cone degeneration. This finding led the researchers to increase and decrease the insulin level and measure the survival of cones in one of the models. Mice treated with insulin had prolonged cone survival, while depletion of endogenous insulin produced the opposite effect.

The authors conclude that the nonautonomous cone death in retinitis pigmentosa in humans may, in part, be attributed to the starvation of cones. Thus, a potential therapeutic approach could involve treatments that improve cone nutrition.

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Roundup of Other Journals is written by  
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## 1/2H AD