

Journal Highlights

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

Ophthalmology

Corneal Edema Ups Risk of Graft Failure

June's *Ophthalmology*

Findings from the Cornea Donor Study (CDS) indicate the risk of corneal graft failure following transplantation is significantly increased in eyes with pseudophakic/aphakic corneal edema or a history of glaucoma, compared with Fuchs' dystrophy. The CDS is a trial involving 1,090 patients undergoing corneal transplantation for a moderate risk condition.

Using data from the study, Sugar et al. found that five years following surgery, a preoperative diagnosis of pseudophakic/aphakic corneal edema increased graft failure risk approximately fourfold compared with Fuchs' dystrophy. In addition, patients who underwent prior glaucoma surgery and used preoperative glaucoma medication experienced a substantially increased graft failure rate. Data also showed that age, gender, diabetes, smoking and graft size were not strongly associated with graft failure.

The authors conclude that these findings confirm previous reports, mostly retrospective, concerning corneal transplants and graft failure. They

caution that the CDS procedures all involved full-thickness keratoplasty and did not take into account the newer endothelial keratoplasty techniques.

Comparison of Hybrid Thin-Flap LASIK Technique to PRK

June's *Ophthalmology*

Slade et al. created a hybrid approach to thin-flap LASIK. Thin-flap LASIK/Sub-Bowman keratomileusis (SBK) is a term that reflects the benefit of the type of flap used (planar and thin), the customization to the patient (myopic with a narrow refractive range) and the ablation of the excimer laser used.

In a contralateral eye pilot study involving 50 patients (100 eyes), the researchers compared this hybrid approach to photorefractive keratectomy to determine differences

in visual results, pain response, biomechanical effect, quality of vision and higher-order aberrations at one, three and six months following surgery. The authors found that at one month, the thin-flap LASIK/SBK group demonstrated significantly better visual acuity than the PRK group. By three months, vision in the groups had begun to equalize and at six months, there were no statistical differences.

They conclude that SBK may involve less pain, quicker visual recovery, fewer medications and an overall superior experience.

Electronically Monitored Glaucoma Drops Shed Light on Adherence

June's *Ophthalmology*

A study by Friedman et al. of glaucoma patients using eyedrops indicates that patients younger than 50, patients 80 or older, African-Americans and those in poor health have lower adherence to topical once-daily therapy. Those patients who admit to missing doses were also found to take less medication.

The study involved 196 patients with glaucoma being treated with a prostaglandin analog. Patients taking 75 percent or fewer doses during the eight-week period starting two weeks after the enrollment visit and ending two weeks prior to the three-month visit were compared with those patients taking more than 75 percent of doses. Less compliant patients were more likely to be younger than 50 or older than 79. They were also more likely to be African-American and to report less than excellent health, higher amounts of depression and lower income.

The authors suggest administering a survey of demographic factors and self-reported health to identify those who may be taking fewer than 75 percent of their drops.



Intravitreal Bevacizumab Superior to Macular Photocoagulation in DME

June's *Ophthalmology*

A three-arm trial of primary treatment alternatives for diabetic macular edema has shown the superiority of intravitreal injection of bevacizumab (IVB) either alone or in combination with intravitreal triamcinolone acetonide (IVT) over macular laser photocoagulation (MPC) in visual acuity improvement up to 24 weeks.

Soheilian et al. enrolled 129 patients (150 eyes) with clinically significant diabetic macular edema and no previous treatment. Three groups of 50 eyes were randomly assigned to the IVB group (1.25 mg of bevacizumab), the IVB/IVT group (1.25 mg of bevacizumab and 2 mg of triamcinolone acetonide) and the MPC group (focal or modified grid laser treatment). IVB injection yielded a better visual outcome at 24 weeks compared with macular photocoagulation. This effect persisted longer in the IVB group (up to 36 weeks) than the IVB/IVT group (up to 12 weeks). In the MPC group, no improvement in visual acuity was observed at any follow-up visit.

The authors are currently conducting a two-year follow-up study with these patients.

Gas Injection Alone Compared to Gas With Vitrectomy to Treat Retinal Detachment

June's *Ophthalmology*

Li et al. compared the efficacy of intravitreal gas injection against pars plana vitrectomy (PPV) with intraocular gas tamponade to determine the anatomic success rate and functional outcomes in patients with retinal detachment due to myopic macular hole.

The study involved 231 eyes of 231 patients who were randomly assigned to undergo intravitreal C3F8 gas injection (group A) or vitrectomy with intraocular C3F8 gas tamponade (group B). Twelve months following surgery, the retinal reattachment rate was 59.8

percent (52 eyes) in group A. This was significantly lower than group B at 74.5 percent (79 eyes). The researchers showed that PPV and low height of retinal detachment at baseline were associated with a higher retinal reattachment rate. The postoperative BCVA of the eyes with attached retinas was not significantly different between the two groups.

The investigators conclude that PPV results in a significantly higher anatomic success rate in patients with retinal detachment caused by macular hole.

American Journal of Ophthalmology

Aspherical vs. Spherical Silicone IOL

June's *AJO*

Ohtani et al. conducted a comparison of aspherical and spherical silicone IOLs of the same material and platform in patients undergoing bilateral cataract surgery.

Sixty-two eyes of 31 patients were randomized to receive a silicone aspherical IOL in one eye and a silicone spherical IOL in the other eye. Various parameters were measured at one, three, six and 12 months after surgery. There were no significant differences between IOLs with regard to BCVA, amount of IOL decentration and tilt, degree of posterior capsular opacification and all-distance visual acuity at any point after surgery.

Regarding corneal wavefront aberrations, there was no difference in third- and fourth-order root mean square (RMS). In ocular wavefront aberrations, aspherical IOLs showed significantly lower fourth-order RMS than spherical IOLs throughout the study, but not in third-order RMS. Contrast sensitivity under photopic and mesopic conditions was not different between IOLs, but contrast sensitivity under scotopic conditions was significantly better with aspherical IOLs than with spherical IOLs at all measurement points.

The authors conclude that the silicone aspherical IOL reduced ocular spherical aberration and improved

scotopic contrast sensitivity, and these results were consistent through the one-year follow-up.

Corneal Haze Formation After Thin-Flap Femtosecond LASIK

June's *AJO*

Rocha et al. evaluated the risk factors for interface haze formation after thin-flap femtosecond LASIK in a prospective study in patients with myopia.

The authors analyzed 199 consecutive eyes that underwent femtosecond laser LASIK with a Ladar 4000 excimer laser. Treated eyes were divided into two groups according to desired flap thickness: 90 μ m (106 eyes) and 100 to 110 μ m (93 eyes). The groups were also subdivided into low, moderate, high and severe myopia preoperatively, and according to depth of ablation intraoperatively.

Multiple parameters were measured and compared postoperatively. Corneal haze was observed in 32 eyes treated for moderate to high myopia at three months postoperatively. Thinner flaps and younger age were strongly associated with risk of postoperative haze. The degree of myopia, depth of ablation and self-reported history of dry eyes were not independently associated with an increased risk of corneal haze. Patients who developed any degree of haze had significantly higher logarithmic value of scatter values compared with those who did not develop haze. The mean postoperative BCVA was good in all eyes with haze.

Treatment of Stevens-Johnson Syndrome With Steroid Pulse Therapy

June's *AJO*

Araiki et al. performed a prospective study to evaluate the visual prognosis of patients with Stevens-Johnson syndrome (SJS) and its severe variant, toxic epidermal necrolysis (TEN), after institution of early high-dose systemic and topical corticosteroids.

Five patients with SJS or TEN and ocular complications at the acute stage

received intravenous pulse therapy with methylprednisolone within four days from disease onset. Topically, 0.1 percent betamethasone was applied more than five times daily for at least two weeks. Patients were evaluated over the next year.

At the initial examination, corneal or conjunctival epithelial defects and pseudomembranous conjunctivitis were present in all cases. Skin eruptions dramatically improved after steroid pulse therapy. Although ocular inflammation increased for several days, pseudomembranes disappeared and corneal and conjunctival epithelium regenerated within six weeks. At the chronic stage, all eyes had clear corneas with the palisades of Vogt, implying the presence of corneal epithelial stem cells. BCVA was 20/20 or better in all eyes. Five eyes showed superficial punctate keratopathy. No eye had cicatricial changes except for one with slight fornix shortening. No significant adverse effects of steroid occurred during all clinical courses.

The authors conclude that steroid pulse therapy at disease onset seems to have a demonstrable therapeutic effect in preventing ocular complications. Topical betamethasone also shows great promise for preventing cicatricial changes and corneal epithelial stem cell loss in the limbal region.

Relationship Between Diabetic Retinopathy and Sleep-Disordered Breathing

June's *AJO*

Shiba et al. tried to clarify the relationships of sleep-disordered breathing with nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) in a case-control study.

The study included 48 NPDR and 118 PDR patients who had undergone surgery. Pulse oximetry was conducted during the night, and the sleeping oxygen 4 percent desaturation index (number of oxygen desaturation events per hour exceeding 4 percent) and mean saturation of peripheral oxygen (SpO₂) percentage were calculated.

The authors diagnosed sleep-disordered breathing if the desaturation index was greater than five times per hour. The results were evaluated and compared between the two groups. These results and preoperative patient background factors were analyzed using multiple regression analysis to identify correlations with the diagnosis of PDR.

Twenty-nine percent of the NPDR and 48 percent of the PDR patients were diagnosed as having sleep-disordered breathing. The incidence of sleep-disordered breathing and the desaturation index were significantly higher in the PDR than in the NPDR group. Multiple regression analysis showed younger age and a higher desaturation index to be factors independently contributing to a diagnosis of PDR.

These results suggest that in diabetic retinopathy patients with nocturnal desaturation, reoxygenation caused by sleep-disordered breathing may relate to the development of PDR.

Archives of Ophthalmology

Topical Bevacizumab in the Treatment of Corneal Neovascularization

April's *Archives*

Dastjerdi et al. examined the safety and efficacy of topical bevacizumab (Avastin) in the treatment of corneal neovascularization.

Ten eyes from 10 patients with stable corneal neovascularization were treated with topical bevacizumab 1.0 percent for three weeks and were followed up to 24 weeks. Baseline and sequential follow-up corneal photos were compared to assess the size and extent of corneal neovascularization. For assessment of the condition, a novel quantitative method was used to measure three primary metrics: neovascular area, vessel caliber and neovessel invasion area. All local and systemic adverse events were monitored.

The patient population showed a significant reduction in two corneal neovascularization metrics: neovascular area and vessel caliber. From

baseline visit to the last follow-up visit, the mean reduction was 47.1 percent \pm 36.7 percent for neovascular area and 54.1 percent \pm 28.1 percent for vessel caliber. However, the decrease in neovessel invasion area (12.2 percent \pm 42 percent) did not achieve statistical significance. Visual acuity and central corneal thickness showed no significant changes. Topical bevacizumab was well-tolerated with no adverse events. No significant changes were found in mean arterial pressure at any follow-up visit.

The authors conclude that short-term topical bevacizumab therapy reduces the severity of corneal neovascularization without local or systemic adverse effects. Data from this study provide evidence that topical bevacizumab therapy could offer an alternative or adjunctive measure to conventional therapies in the treatment of this condition.

Forecasting Age-Related Macular Degeneration Through 2050

April's *Archives*

Rein et al. found that health care providers can expect a significant increase in age-related macular degeneration as the Baby Boom generation reaches retirement age. The study predicts that over the next 40 years, the aging of the U.S. population will lead to a large increase in early and advanced AMD. If used universally, existing medical treatments could reduce the expected number of cases of visual impairment and blindness attributable to AMD by as much as 35 percent.

The researchers estimated that by 2050 the number of people with AMD will double in the United States to more than 17.8 million. Without treatment, these patients would be expected to result in approximately 1.6 million cases of visual impairment and blindness in 2050—compared with between 400,000 and 600,000 cases today. In contrast, the projected number of cases would fall 35 percent to 1 million cases if all patients received perfect medical treatment by today's standards.

Treatment options include vitamin

prophylactic therapy for patients with early AMD and anti-VEGF injections for certain forms of advanced disease. The study found that the universal use of vitamin prophylactic therapy alone by all patients with early AMD could reduce visual impairment and blindness by 23 percent. In contrast, if used alone, anti-VEGF therapies would be expected to reduce visual impairment and blindness by only 17 percent. In their patented form, anti-VEGFs are far more costly than vitamins, but their use is targeted at the smaller group of patients who have developed advanced disease.

Retinal Effects of Tadalafil or Sildenafil Treatment

April's *Archives*

Cordell et al. examined the effects of two phosphodiesterase type 5 inhibitors (erectile dysfunction drugs) after six months of low-dose daily usage.

A total of 244 patients were randomized to either tadalafil (Cialis) 5 mg, sildenafil (Viagra) 50 mg or a placebo daily. Electroretinograms were recorded and other tests of ocular anatomy and visual function were

performed at baseline, three months and six months. There was no significant difference between either active treatment and placebo for the electroretinograms or other parameters measured. Retinal-function changes or visual symptoms that had been reported previously after single high-dose administrations of sildenafil were not observed. The only adverse event of an ophthalmologic nature was a retinal artery occlusion in a single patient in the placebo group.

The authors conclude that chronic low-dose use of these medications has no adverse effect on the retina under the conditions of this study.

Thrombospondin-1 and Pigment Epithelium-Derived Factor Levels in Patients With Diabetes

April's *Archives*

Wang et al. examined the levels of two major endogenous inhibitors of angiogenesis in vitreous samples prepared from normal and diabetic patients. The levels of thrombospondin-1 (TSP1) and pigment epithelium-derived factor (PEDF) were determined by Western blot analysis of vitreous samples.

All samples had very similar levels of PEDF. However, two forms of PEDF—high molecular weight and low molecular weight—presented in vitreous samples and migrated differently.

TSP1 was present at relatively high levels in control vitreous samples but its level varied widely among diabetic samples—from no change to almost no TSP1 present. The lower level of TSP1 was consistently observed in diabetic vitreous samples with a high molecular-weight isoform of PEDF.

The authors conclude that expression of a high molecular-weight isoform of PEDF in diabetic patients is associated with reduced levels of TSP1. Reduced levels of TSP1 favor a more proangiogenic state of endothelium and may promote the development and progression of more severe diabetic retinopathy. Therefore, the identity of the PEDF isoform present in the vitreous may be a predictor of the severity of diabetic retinopathy.

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

Retinal Electrical Stimulation Produces Predictable Visual Sensitivity

Investigative Ophthalmology & Visual Science

2009;50:1483–1491

In a step toward developing a working retinal prosthesis, Horsager et al. show that on the single-electrode level, retinal electrical stimulation can produce predictable visual qualia using a relatively simple linear-nonlinear model that predicts the relationship between electrical stimulation and sensitivity for a variety of temporally varying stimulation patterns.

The investigators studied two patients (ages 59 and 55) who underwent ocular implantation of 16-electrode

retinal prostheses. They used psychophysical techniques to measure the brightness of electrically generated percepts on single electrodes. Patients were asked yes-or-no questions to judge whether or not their retinal cells had been stimulated with the single electrodes. The authors found that the patients' perceptual responses to the retinal electrical stimulation was similar to models of ganglion cell-firing behavior during contrast adaption, human temporal integration of light stimuli and auditory processing found in cochlear implant wearers.

They note that for a retinal prosthesis to be successful, it must produce percepts consisting of areas of constant brightness across a range of brightness

levels—all while meeting complex engineering constraints. Models such as the one described in this study will help researchers select stimulation protocols that can meet these many constraints.

Confocal Scanning Laser Tomography vs. Optic Disc Photographs

Investigative Ophthalmology & Visual Science

2009;50:1682–1691

How does confocal scanning laser tomography (CSLT) compare to optic disc photography for detecting glaucomatous disc changes? According to a study by Chauhan et al., the technology compares well.

The investigators utilized topographic change analysis (TCA) software to detect topographic changes in the optic nerve head of the CSLT images. Comparisons were then made between TCA results and the findings from four expert observers who examined a series of conventional optic disc photographs. After a median follow-up of nine years with 18 CSLT images, comparisons were made for a range of liberal to conservative criteria and for individual and combined observer scores. For most criteria, the observers had either a high hit rate with low specificity or high specificity with a low hit rate when compared with the TCA.

The authors note that the agreement between the TCA and observer evaluation of disc photographs depended on criteria and observer. Ultimately, the TCA performed at least as well as either the individual or combined observer scores of disc photographs.

Preoperative Sub-Tenon's Levobupivacaine in Strabismus Surgery

British Journal of Ophthalmology
2009;93:329-332

Morris et al. have found that administering preoperative sub-Tenon's levobupivacaine to children undergoing squint surgery for strabismus does not result in lower pain scores compared with patients who did not receive this agent.

In this clinical trial, 27 patients (ages 1 to 16) undergoing strabismus surgery received sub-Tenon's levobupivacaine preoperatively and topical anesthetic eye drops at the end of the procedure. A control group consisting of 27 age- and sex-matched patients received only topical anesthetic eye drops at the end of surgery. The researchers took pain scores using the Wong-Baker Pain or FLACC (face, legs, arms, cry, consolability) assessments at 30 minutes, two hours, four hours, six hours and 24 hours postoperatively.

Roundup of Other Journals is written by Lori Baker Schena and edited by Deepak P. Edward, MD.

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