

# Journal Highlights

## NEW FINDINGS FROM *OPHTHALMOLOGY*, *AJO*, AND *JAMA OPTHALMOLOGY*

### ***Ophthalmology***

#### **Fungal Endophthalmitis From Contaminated Triamcinolone**

*Ophthalmology*

Published online Feb. 6, 2014

**S**mall et al. reported on an outbreak of fungal endophthalmitis linked to intravitreal injections of contaminated triamcinolone. For this retrospective observational case series, the researchers evaluated 17 eyes of 15 patients who were treated at a single retina practice. All had received injections of triamcinolone over a three-month period for macular edema or branch retinal vein occlusion; the triamcinolone had been obtained from a single lot that was prepared by a compounding pharmacy and subsequently found to be contaminated with *Bipolaris hawaiiensis*.

Fungal endophthalmitis developed in 14 eyes (82 percent). The median time to onset was 83 days (range, six to 322 days). While the patients' median preinjection visual acuity (VA) was 20/50 (range, 20/20 to counting fingers), their median VA at last follow-up was 20/400 (range, 20/30 to no light perception). With regard to presentation, patients typically sought treatment for painless loss of vision in

an eye that was white and quiet.

Cytologic or culture-positive confirmation of fungal infection was obtained in eight of 14 eyes (57 percent) after a number of vitreous taps and biopsies. All of the culture-positive specimens that were obtained by pars plana vitrectomy (n = 5) were identified as *B. hawaiiensis*. An investigation by the U.S. Centers for Disease Control and Prevention established that this outbreak was the result of contamination by the compounding pharmacy.

The researchers cautioned that the wide range in time to disease onset underscores the need to remain vigilant for the development of fungal endophthalmitis many months after injection. Further, they noted that in-office vitreous tap may be inadequate as a diagnostic tool.

#### **Ranibizumab for Diabetic Macular Edema: Three-Year Results**

*Ophthalmology*

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**S**chmidt-Erfurth et al. reported the three-year results of individualized ranibizumab treatment in patients with visual impairment due to diabetic macular edema (DME). They found that ranibizumab treatment was effective in improving and

maintaining best-corrected visual acuity (BCVA) and central retinal subfield thickness (CRST) outcomes with a progressively declining number of injections over the three-year period.

These results come from the core RESTORE study and a 24-month open-label extension of the core study. During the initial study, patients with DME were randomized to receive ranibizumab, ranibizumab plus laser, or laser alone. This phase 3 study demonstrated that ranibizumab alone or ranibizumab plus laser provided greater VA gains than did laser monotherapy.

Of the 303 patients who completed the core study, 208 completed the extension study. During this study phase, patients were eligible to receive individualized ranibizumab on the basis of prespecified retreatment criteria, and monthly visits were mandatory.

Results were as follows: 1) Patients originally treated with ranibizumab monotherapy or ranibizumab plus laser experienced an overall maintenance of their earlier BCVA and CRST outcomes. 2) Patients initially treated with laser monotherapy experienced a progressive improvement in BCVA and reduction in CRST. 3) Patients in all three treatment groups received a mean of fewer than three injections in the final year, and 19 to 25 percent of patients did not require any ranibizumab injections during the extension study. 4) The most frequently reported ocular adverse effects were cataract



and eye pain, and the most frequently reported systemic effects were nasopharyngitis and hypertension.

### Disc Torsion in Young Myopic Eyes

*Ophthalmology*

Published online Feb. 6, 2014

**L**ee et al. investigated the possibility of a link between optic disc torsion and visual field (VF) defects in young myopic Korean patients. They found evidence of a correlation, as the optic disc torsion in the eyes with VF defects was greater both in prevalence and degree than that observed in the patients' normal fellow eyes.

For this retrospective cross-sectional study, the investigators evaluated 39 Korean patients who had unilateral glaucomatous-appearing VF defects and myopia. The patients ranged in age from 20 to 50 years.

The researchers measured optic disc torsion and tilt ratio from disc photographs and performed logistic and linear regression analyses to investigate a number of parameters, including 24-hour peak, trough, and mean intraocular pressure (IOP) and retinal nerve fiber layer (RNFL) thickness. Overall, optic disc torsion was more prevalent in VF-affected eyes. In the multivariate analysis, the degree of optic disc torsion was associated with the presence of a VF defect, and the torsion degree and RNFL thickness were associated with the severity of the VF effect.

The researchers noted that a longitudinal study is needed to confirm whether VF-affected eyes with optic disc torsion are at increased risk of future optic nerve or VF progression.

### American Journal of Ophthalmology

#### Hoffer Q and Haigis Formulas for IOL Calculation in Short Eyes

April *AJO*

**I**n the first study to do so, Eom et al. performed a head-to-head comparison of the accuracy of the Hoffer Q and Haigis formulas according to the anterior chamber depth (ACD) in eyes with a short axial length (AL). They

found that the difference between the predicted refractive errors of the two formulas increased as ACD decreased in short eyes.

For this retrospective cross-sectional study, the researchers enrolled 75 eyes from 75 patients with an AL of less than 22 mm. All eyes had undergone uneventful cataract surgery and had been implanted with an AcrySof IQ intraocular lens (IOL). The median absolute errors (MedAEs) predicted by the Hoffer Q and Haigis formulas were compared, and the correlations between ACD and the predicted refractive error calculated using the two formulas were analyzed.

In a subgroup analysis, there were no significant differences between the MedAEs predicted by the two formulas when the ACD was deeper than 2.40 mm. However, in patients with an ACD of less than 2.40 mm, the Haigis formula proved more accurate. Thus, for these patients, surgeons should use either the Haigis formula or the Hoffer Q formula with more hyperopic correction, the researchers recommended.

#### Office Use of Anti-VEGF Agents for AMD Lagging Behind Studies

April *AJO*

**H**olekamp et al. used retrospective medical claims analysis to examine bevacizumab and ranibizumab utilization and disease monitoring patterns in patients with neovascular age-related macular degeneration (AMD) in clinical practice. The results indicate that patients in clinical practice receive fewer injections of ranibizumab or bevacizumab and are monitored less frequently than those enrolled in clinical trials.

Patients who received one or more injections of ranibizumab or bevacizumab during the 12 months after initial neovascular AMD diagnosis were included. Annual bevacizumab and/or ranibizumab injection utilization was assessed by year-of-first-injection cohorts: 2006 and 2007 (received either agent because of billing code overlap); and 2008, 2009, and Jan.-June 2010 (re-

ceived each agent). Outcome measures were time to first injection relative to neovascular AMD diagnosis and mean numbers of intravitreal injections, ophthalmologist visits, and optical coherence tomography (OCT) and fluorescein angiography (FA) examinations in 12 months.

In the 2006 and 2007 cohorts (n = 8,767), mean annual numbers of bevacizumab or ranibizumab injections were 4.7 and 5.0, respectively. Over 92 percent of patients in all cohorts received first treatment within three months of being diagnosed with neovascular AMD. In the 2008-2010 cohorts (n = 10,259), mean annual number of injections remained low, as did mean numbers of ophthalmologist visits (bevacizumab only) and OCT examinations (both agents); but there was no such trend in FA examinations.

Compared with treatment protocols validated by clinical trials published at the time, in clinical practice, patients with neovascular AMD received fewer bevacizumab or ranibizumab injections and less frequent monitoring from 2006 to mid-2011. The authors encouraged further research to evaluate this issue and visual outcomes that may be associated with reduced utilization.

#### TMP-SMX Reduces Recurrences of *Toxoplasma Gondii* Retinochoroiditis

April *AJO*

**F**elix et al. compared the effects of trimethoprim-sulfamethoxazole (TMP-SMX) versus placebo in reducing the risk of recurrences of *Toxoplasma gondii* retinochoroiditis. They found that TMP-SMX treatment resulted in a 100 percent reduction of recurrence over a one-year period, with no significant side effects noted.

This single-center, prospective randomized double-masked clinical trial was conducted in São Paulo, Brazil. A total of 100 patients with active recurrent *T. gondii* retinochoroiditis were included. In all cases, the initially active toxoplasmosis lesions were successfully treated with twice-daily TMP-SMX for 45 days. Subsequently,

five patients dropped out of the study.

The remaining patients were randomized to two groups; two patients were later lost to follow-up. The 46 patients in group 1 were treated with a single tablet of TMP-SMX every two days, while the 47 patients in group 2 were given a placebo tablet every two days. The primary outcome measure was the incidence of recurrent toxoplasmosis retinochoroiditis within one year, and the secondary outcome measure was a one-year change in best-corrected visual acuity.

No patients in group 1 experienced a recurrence of toxoplasmosis retinochoroiditis within 12 months; in contrast, six of those in the placebo group (12.8 percent) experienced a recurrence. Visual acuity improvements in the two groups were similar, and no treatment-limiting toxicity was observed.

### Staphylococcus Ubiquitous on Ophthalmology Clinic Surfaces

April *AJO*

**R**eem et al. screened environmental surfaces of an outpatient ophthalmic clinic for methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* (MSSA and MRSA) in order to identify the most commonly contaminated surfaces and to phenotype and genotype all collected isolates. In this single-institution, one-year prospective environmental study, the MSSA and MRSA bacteria that were isolated were highly diverse, indicating a constant introduction of clones over time. Doorknobs, slit-lamp headrests and chinrests, and computer keyboards were hot spots of contamination. Multidrug resistance was characteristic of MRSA strains.

Commonly touched surfaces in examination rooms and common areas were targeted and sampled on a quarterly basis for one year. Samples were collected using electrostatic cloths and swabs. Of 112 total samples, 27 (24 percent) and five (4 percent) were positive for MSSA and MRSA, respectively. Both community-associated and hospital-associated MRSA isolates were found. No single surface remained

consistently positive with the same isolate over time, and molecular analysis demonstrated high levels of diversity among isolates.

The authors proposed a surveillance protocol for important high-touch surfaces in ophthalmology clinics. They suggested that frequently contaminated surfaces must be targeted for routine cleaning and disinfection and offered an effective sampling protocol that could help to guide clinics' disinfection policies.

### JAMA Ophthalmology

#### Ten-Year Follow-up of AMD in AREDS

March *JAMA Ophthalmology*

**C**hew et al. described 10-year progression rates to the intermediate or advanced stages of AMD as part of Age-Related Eye Disease Study (AREDS) Report No. 36.

Participants in the original AREDS trial were followed for a median of 6.5 years. Once the trial was completed, the investigators observed 3,549 of the 4,203 surviving participants for an additional five years. The rates of progression to large drusen and advanced AMD (neovascular AMD or central geographic atrophy) were evaluated by means of annual fundus photographs assessed at a reading center. Best-corrected visual acuity was measured at annual study visits.

The researchers found that the risk of progression to advanced AMD increased with increasing age and severity of drusen. Women and current smokers were at higher risk of neovascular AMD. In the oldest participants with the most severe AMD status at baseline, the point estimate risks of developing neovascular AMD and central geographic atrophy by 10 years were 48.1 and 26 percent, respectively. Similarly, rates of progression to large drusen increased with increasing severity of drusen at baseline, with 70.9 percent of participants who had bilateral medium drusen progressing to large drusen, and 13.8 percent to advanced AMD in 10 years. Median visual acuity at 10 years in eyes that

had large drusen at baseline but never developed advanced AMD was 20/25; eyes that developed advanced AMD had a median visual acuity of 20/200.

The natural history of AMD (prior to anti-vascular endothelial growth factor therapy for many cases of neovascular AMD) demonstrates a relentless loss of vision, on average, in persons who developed advanced AMD. These progression data and the risk factor analyses may be helpful to investigators conducting research in clinic populations.

#### Heritabilities of Intraocular Pressure in the Korean Population

March *JAMA Ophthalmology*

**K**im et al. compared intraocular pressures (IOPs) in parents and their offspring in Korea.

Participants were from a family-based cohort study that examined data from the Korean National Health and Nutrition Examination Survey conducted in 2008 and 2009. Data were obtained from 9,700 participants.

The individuals were stratified into two groups (those with or without an IOP of 19 mmHg or more) based on the mean plus two standard deviations IOP value of the entire study population. The authors evaluated the impact of parents' high IOP on offspring's high IOP and the relationship between parental systemic disease and high IOP in their offspring.

IOP showed a heritable tendency from parents to their offspring in this Asian population, with the prevalence of high IOP in offspring increasing according to whether one or both parents had a high IOP. However, no association was identified between the offspring's IOP and parental diabetes mellitus, hypertension, obesity, or metabolic syndrome.

Ophthalmology summaries are written by Jean Shaw and edited by Susan M. MacDonald, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. JAMA Ophthalmology summaries are based on authors' abstracts as edited by senior editor(s).

## ROUNDUP OF OTHER JOURNALS

### Drug Choice for Treating Severe Anterior Uveitis in Children

*British Journal of Ophthalmology*

Published online Jan. 23, 2014

**D**oycheva et al. evaluated the long-term efficacy and tolerability of adalimumab and other tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) inhibitors when used to treat children with refractory, chronic antinuclear antibody (ANA)-associated anterior uveitis. They found that adalimumab and infliximab are effective and generally well tolerated, and they concluded that adalimumab is their preferred choice.

For this retrospective analysis, the researchers evaluated the records of 31 children with ANA-associated uveitis who had been treated with adalimumab, etanercept, or infliximab and followed for at least two years.

Of the 31 children, 23 were treated with adalimumab, five were treated with infliximab, and three received etanercept. Control of uveitis was observed in 78 percent (18/23) of those who received adalimumab and in 40 percent (2/5) of those who received infliximab. Etanercept proved ineffective, and those children were switched to one of the other drugs.

The researchers noted that their preferred TNF- $\alpha$  inhibitor is adalimumab, as it does not require hospitalization for administration, is easy to manage, and has fewer side effects than and superior efficacy to the other drugs in its class.

### Diffraction Trifocal IOL Outcomes

*Journal of Cataract & Refractive Surgery*

2014;40(1):60-69

**I**n one of the few studies of trifocal intraocular lens (IOL) technology, Mojzis et al. evaluated near, intermediate, and distance vision in presbyopic patients who had received a new diffractive trifocal IOL, the AT Lisa tri 839MP. They found that vision improved at all distances.

For this case series, European researchers evaluated 60 eyes of 30 patients (age range, 42 to 76 years) who underwent bilateral refractive lens exchange with implantation of the AT Lisa IOL. Outcome measures were uncorrected and corrected distance visual acuities (VAs) and intermediate and near VAs; keratometry; manifest refraction; and aberrations.

At the six-month follow-up examination, the researchers found improvements for all VA measurements. The postoperative refractive status was within the range of +1 to -1 D, and total internal aberrations decreased. No serious complications were noted.

### Global Burden of AMD Through 2040

*The Lancet Global Health*

2014;2(2):e106-e116

**F**or a meta-analysis, Wong et al. reviewed published reports of the prevalence of age-related macular degeneration (AMD) and provided projections of the worldwide number of patients in 2020 and 2040, taking into account information on ethnicity, region, and gender. Overall, they found that 8.7 percent of the worldwide population has AMD, and they projected that 196 million people will have AMD in 2020, with that number rising to 288 million in 2040.

The researchers found substantial evidence that early AMD is more prevalent in Europe than in Asia, although the rates of late onset are similar. In addition, the analysis confirmed that AMD, in all stages, is more prevalent in people of European ancestry than in those of African ancestry. Late prevalence was found to increase rapidly after age 75, especially in people of European ethnicity and in Europe and Oceania regions.

The largest projected number of cases is expected to emerge in Asia, in keeping with the area's growth in population. Approximately one-third of the world's cases of AMD will occur in

Asia, even though this region currently has the lowest prevalence.

### Severe Diabetic Retinopathy in Patients With Glucokinase Mutations

*JAMA*

2014;311(3):279-286

**I**n the first systematic assessment of the issue, Steele et al. evaluated the link between chronic mild hyperglycemia and the prevalence and severity of complications in patients with glucokinase (GCK) mutations. They found that these patients—who have had mild hyperglycemia from birth—had a low prevalence of micro- and macrovascular complications. Moreover, the GCK patients were less likely to experience diabetes-related complications than individuals who had lived with more severe hyperglycemia for a shorter period of time.

For this cross-sectional study, the researchers evaluated 99 patients who carried a GCK mutation (median age, 48.6 years), 91 unaffected family members who served as controls (median age, 52.2 years), and 83 unrelated patients who had been diagnosed with young-onset type 2 diabetes at age 45 or younger (median age, 54.7 years).

Overall, the prevalence of clinically significant microvascular complications was low in GCK patients and controls (1 and 2 percent, respectively). However, 36 percent of those with young-onset type 2 diabetes had evidence of clinically significant microvascular disease. This pattern held true for macrovascular disease, with such complications affecting 4 percent of the GCK patients, 11 percent of the control group, and 30 percent of the young-onset diabetics.

Retinopathy was present in 30 percent of GCK patients, 14 percent of controls, and 63 percent of those with young-onset diabetes.

Roundup of Other Journals is written by Jean Shaw and edited by Deepak P. Edward, MD.