

# Journal Highlights

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

### *Ophthalmology*

#### Periocular Corticosteroid Injections in Uveitis

November *Ophthalmology*

In a retrospective analysis, Sen et al. evaluated the risks and benefits of periocular depot corticosteroid injections in patients with uveitis. They found that the injections were effective in treating active intraocular inflammation, with visual acuity improving in 50 percent of patients within six months. However, cataract and ocular hypertension were significant concerns, affecting a substantial minority.

For this multicenter study, the researchers evaluated 914 patients (1,192 eyes) who had received one or more periocular corticosteroid injections. Bilateral uveitis was present in 80 percent of the patients, and 11.1 percent were on systemic corticosteroids or immunosuppressive drugs at the time of the initial injection. Main outcome measures were control of inflammation; improvement of visual acuity (VA) to 20/40 or better; improvement of VA loss attributed to macular edema (ME); and the incidence of cataract, cataract surgery, ocular hypertension, and glaucoma surgery.

Six months after injection, 72.7 percent of eyes had achieved complete control of inflammation, and 49.7 percent showed an improvement in best-corrected VA to 20/40 or better.

Among a subset of patients with VA less than 20/40 attributed to ME, 33.1 percent of eyes improved to 20/40 or better.

With regard to complications, at the 12-month follow-up mark, the incidence of cataract in initially phakic eyes was 20.2 percent, and 13.8 percent of these eyes underwent cataract surgery. The incidence of ocular hypertension was 34 percent for an IOP of 24 mmHg or greater and 15 percent for an IOP of 30 mmHg or greater. Glaucoma surgery was performed in 2.4 percent of all eyes.



#### Long-Term Outcomes With Boston Type 1 Keratoprosthesis

November *Ophthalmology*

Srikumaran et al. evaluated the long-term outcomes of surgery with the Boston type 1 keratoprosthesis. They found that a large number of patients achieved and retained useful vision over a seven-year period, although the risk of complications rose with time.

For this retrospective case series, the researchers evaluated 133 patients (139 eyes) who underwent prosthesis implantation. Eyes were followed up for a mean of  $46.7 \pm 26$  months, with all but four eyes having at least six months of follow-up. Main outcome measures included visual acuity (VA),

postoperative complications, and device retention.

Preoperatively, only 10.8 percent of eyes had VA of 20/200 or better; this rose to 70 percent after implantation. Overall, the probability of maintaining VA of 20/200 or better at the seven-year mark was 50 percent, and

the researchers estimated the seven-year retention rate to be 67 percent.

With regard to complications, the seven-year cumulative incidence was 49.7 percent for retroprosthetic membrane formation, 21.6 percent for glaucoma surgery, 18.6 percent for retinal detachment, and 15.5 percent for endophthalmitis. Therefore, the researchers called for close follow-up of eyes undergoing this implantation.

#### Preventing Depression in AMD Patients

November *Ophthalmology*

Rovner et al. investigated whether an integrated model of mental health and low vision treatment could have an impact on depressive disorders in patients with age-related macular degeneration (AMD). The researchers found that the combined intervention program cut the incidence of depression in half when compared with standard outpatient low vision therapy.

For this study, 188 patients were randomized to receive low vision therapy plus either behavior activation or supportive therapy. Behavior activation was defined as structured behavioral therapy that aims to increase adaptive behaviors and achieve valued goals, while supportive therapy was defined as nondirective psychological treatment that provides emotional support and is similar to standard low vision treatment.

At the end of the four-month study period, 87 patients had completed the behavior activation/low vision rehabilitation (BA+LVR) treatment, and 76 had completed the supportive therapy/low vision (ST+LVR) treatment. Of those in the BA+LVR group, 11 (12.6 percent) developed a depressive disorder. By contrast, 18 in the ST+LVR group (23.4 percent) developed a depressive disorder.

A mediational analysis suggested that the integrated treatment approach (BA+LVR) prevented depression to the extent that it enabled AMD patients to remain socially engaged. The authors thus concluded that promoting interactions between ophthalmology, optometry, rehabilitation, psychiatry, and behavioral psychology might prove important as the population ages.

### Intravitreal Aflibercept vs. Laser for DME

November *Ophthalmology*

**K**orobelnik et al. conducted the first head-to-head comparison of intravitreal aflibercept and laser photocoagulation in patients with diabetic macular edema (DME). The researchers found that aflibercept, which blocks VEGF, outperformed laser in both functional and anatomic outcomes.

This investigation comprised two double-masked, randomized phase 3 trials known by the acronyms VISTA<sup>DME</sup> and VIVID<sup>DME</sup>. The VISTA study randomized 466 patients in the United States, while the VIVID study included 406 patients in Europe, Japan, and Australia. Both studies included patients with type 1 and type 2 dia-

betes, and all patients had DME with central involvement. Those patients randomized to aflibercept received the drug either every four or every eight weeks (after five initial monthly doses).

The main outcome measure was the change from baseline in best-corrected visual acuity (BCVA). Secondary outcomes included the proportion of eyes that gained 15 or more letters from baseline and the mean change in central retinal thickness from baseline.

At one year, mean BCVA gains in the VISTA study were 12.5 letters for those treated every four weeks with aflibercept, 10.7 letters for those treated every eight weeks with aflibercept, and 0.2 letters for those treated with laser. In the VIVID study, the aflibercept four-week and eight-week treatment groups experienced gains of 10.5 and 10.7 letters, respectively, while those in the laser group experienced gains of 1.2 letters.

The researchers found that the number of eyes gaining 15 or more letters was similar for both studies: in VISTA, 41.6 percent of the four-week aflibercept group, 31.1 percent of the eight-week aflibercept group, and 7.8 percent of the laser group; and in VIVID, 32.4 percent, 33.3 percent, and 9.1 percent, respectively. Mean reductions in central retinal thickness in VISTA were 185.9 and 182.1  $\mu\text{m}$  for the four- and eight-week aflibercept groups, respectively, versus 73.3  $\mu\text{m}$  for the laser group; in VIVID, mean reductions were 195.0 and 192.4  $\mu\text{m}$  versus 66.2  $\mu\text{m}$ .

Overall incidences of adverse events, including thromboembolic events, were similar across all treatment groups.

### *American Journal of Ophthalmology*

#### Correlation of Visual Acuity and Subfoveal Choroidal Thickness

October *AJO*

**S**hao et al. of the 2011 Beijing Eye Study examined the association between best-corrected visual acuity (BCVA) and subfoveal choroidal

thickness. They found that better visual acuity was strongly associated with thicker subfoveal choroid, independent of additional factors such as age, axial length, level of education, and major ocular disease.

The researchers included 3,468 participants over the age of 50. Each underwent an ophthalmologic examination, including spectral-domain optical coherence tomography with enhanced depth imaging for measurement of choroidal thickness. Choroidal measurements were available for 3,233 (93 percent).

Better BCVA was significantly associated with thicker subfoveal choroid in general, and a thickness of more than 30  $\mu\text{m}$  in particular, after adjusting for younger age, higher level of education, taller body stature, higher body mass index, axial length shorter than 26 mm, and absence of glaucoma, diabetic retinopathy, and late-stage age-related macular degeneration. In a reverse manner, thicker subfoveal choroid was associated with better BCVA after adjusting for younger age, male sex, longer axial length, and higher corneal curvature radius.

The researchers noted that because the study included only participants 50 years of age or older, these results may not be generalizable to other age groups.

#### Long-Term Safety and Efficacy of Excimer Laser Photorefractive Keratectomy

October *AJO*

**O**'Brart et al. investigated the long-term efficacy and safety of photorefractive keratectomy (PRK) and found a slight but significant increase in myopic spherical equivalent refractive error (SEQ) after PRK, particularly in those patients under 40 at the time of treatment and in women. The procedure was safe, with no long-term sight-threatening complications and with improvements in corrected distance visual acuity and corneal transparency with time.

For this observational case series, the researchers included a study popu-

lation of 42 patients (42 eyes) who had undergone PRK 20 years previously as part of a randomized trial. All patients had received corrections of  $-3$  or  $-6$  D with either 5- or 6-mm optical zones or a multizone treatment. The mean preoperative SEQ was  $-5.13$  D. Outcome measures included visual acuity, refractive error, and corneal topography.

During the 20-year span, there was an increase in mean myopic SEQ of  $-0.54$  D. In patients who were younger than 40 years at the time of correction, this increase was  $-0.92$  D, with an accompanying increase in variance; and in those who were older than 40 years, the increase was  $-0.08$  D. Female and male patients experienced mean SEQ increases of  $-0.69$  and  $-0.26$  D, respectively.

The efficacy index (postoperative uncorrected visual acuity/preoperative corrected distance visual acuity [CDVA]) and safety index (postoperative CDVA/preoperative CDVA) were 0.49 and 0.97, respectively, at 20 years. Corrected distance visual acuity improved during this time span. In addition, the researchers found that 93 percent of corneas were clear at 20 years. There was also an improvement in haze scores, while corneal power remained unchanged throughout.

### Inflammation After Intravitreal Injection of Aflibercept

October *AJO*

**G**oldberg et al. reported the presenting features and clinical outcomes in patients with noninfectious inflammation after intravitreal aflibercept injection. The researchers found that the inflammation typically presents without pain, conjunctival injection, or hypopyon, and it responds to topical steroid therapy. Visual outcomes were also generally favorable, although the return to baseline acuity often took many weeks.

In this noncomparative, consecutive case series, the researchers reviewed medical records of those patients in a Boston-area retina service who presented with noninfectious in-

flammation after intravitreal aflibercept injection between November 2011 and June 2013. Twenty patients with postinjection inflammation were identified in 5,356 aflibercept injections. On average, they had received six prior injections.

All patients presented with decreased vision one to 13 days after injection. Three noted pain, while two had conjunctival injection and one had a hypopyon. Only one patient—the first to present with inflammation in this series—received an intravitreal tap and injection of antibiotics. All patients were managed with frequent topical steroids and were followed closely for signs of improvement.

Preinjection visual acuity was regained in all but one patient. Four patients were subsequently rechallenged with aflibercept, and one developed inflammation again after five additional aflibercept injections.

### Incidence of Neovascular Subtypes in Neovascular AMD

October *AJO*

**N**eovascular lesions in age-related macular degeneration (AMD) are most commonly graded by fluorescein angiography (FA). In this retrospective cohort study, Jung et al. determined the frequency of neovascularization subtypes using FA alone versus FA combined with optical coherence tomography (OCT). They found that the multimodal approach increased the sensitivity for detecting type 3 (intraretinal) and mixed neovascular lesions.

The researchers included 232 patients (266 eyes) with newly diagnosed neovascular AMD who underwent intravitreal anti-VEGF therapy between October 2005 and December 2012. Mean age was 86.3 years. Sixty-eight percent of patients were women, and 95 percent of patients were Caucasian. Two independent graders classified the baseline lesions using FA alone and FA plus OCT, and the researchers compared the frequency of lesion subtypes detected by both methods.

The distribution of neovascular

subtypes using FA alone was 50 percent occult choroidal neovascularization (CNV), 12 percent classic CNV, 29 percent retinal angiomatous proliferation lesions, and 10 percent mixed CNV. Based on anatomic classification using both FA and OCT, 40 percent of lesions were type 1 (sub-retinal pigment epithelium), 9 percent type 2 (subretinal), 34 percent type 3 (intraretinal), and 17 percent mixed neovascularization.

Overall, there was good agreement between FA and the anatomic classification ( $\kappa = 0.65$ , where a value of 1 represents perfect agreement). When looking at each subtype individually, the researchers found a significant increase in type 3 and mixed lesions and a decrease in type 1 with the anatomic classification. The overall incidence of pure classic or type 2 lesions was low in both methods.

### *JAMA Ophthalmology*

#### Telemedicine Diagnosis of Cytomegalovirus Retinitis by Nonophthalmologists

September *JAMA Ophthalmology*

**T**elemedicine holds the potential to increase the number of people screened for cytomegalovirus (CMV) retinitis, but it is unclear whether staff other than ophthalmologists should be responsible for interpreting fundus photographs captured in a telemedicine program. Yen et al. evaluated the accuracy of nonophthalmologist photographic graders in diagnosing CMV retinitis via digital fundus photographs and found that the sensitivity and specificity of their remote diagnosis was variable, including a level of accuracy comparable to that of CMV retinitis experts.

For this study, 15 nonexpert graders each evaluated 182 mosaic retinal images taken of the eyes of patients with acquired immunodeficiency syndrome. Graders diagnosed each image as CMV retinitis present, CMV retinitis absent, or unknown. These results were compared with those of an indirect ophthalmoscopic examination

by an experienced onsite ophthalmologist as well as with the consensus grade given by a panel of CMV retinitis experts.

Relative to examination by onsite ophthalmologists, the sensitivity of remote CMV retinitis diagnosis by nonexpert graders ranged from 64.0 percent to 95.5 percent, and the specificity ranged from 65.6 percent to 92.5 percent. Agreement between nonexpert graders and the panel of expert graders was high: The mean sensitivity and specificity values of nonexpert diagnosis using expert consensus as the reference standard were 93.2 percent and 88.4 percent, respectively. Mean intrarater reliability also was high.

Regardless of these findings, the researchers cautioned that more intensive training and periodic evaluations would be required if nonexperts are to be used in clinical practice in such a manner.

### Effect of Disease Stage on Progression of Hydroxychloroquine Retinopathy

September *JAMA Ophthalmology*

Hydroxychloroquine sulfate retinopathy can progress after the drug is stopped. However, it is not clear how this relates to the stage of retinopathy or whether early screening with current imaging technology can prevent visual loss. **Marmor and Hu** determined the relationship between progression of retinopathy and the severity of disease and assessed the value of early screening for the toxic effects of hydroxychloroquine. They found that in patients with hydroxychloroquine retinopathy involving the retinal pigment epithelium, optical coherence tomography (OCT) revealed progressive damage at least three years after the drug was discontinued, including loss of foveal thickness and cone structure.

Clinical findings in 11 patients with hydroxychloroquine retinopathy were monitored with repeated anatomical and functional examinations for 13 to 40 months after the drug was stopped. Toxic effects were categorized as early

(patchy parafoveal damage shown on field or objective testing), moderate (a 50-100 percent parafoveal ring of OCT thinning but intact retinal pigment epithelium), and severe (visible bull's-eye damage).

Among the study participants, visual acuity and visual fields showed no consistent change. Fundus autofluorescence showed little or no change except in severe cases in which the bull's-eye damage expanded progressively. OCT cross sections showed little visible change in early and moderate cases, but in severe cases, it showed progressive foveal thinning (approximately 7  $\mu\text{m}$  per year) and loss of the ellipsoid zone (in the range of 100  $\mu\text{m}$  per year). The measurements also showed some foveal thinning (approximately 4  $\mu\text{m}$  per year) and deepening of parafoveal loss in moderate cases, but the breadth of the ellipsoid zone remained constant in both early and moderate cases. A few cases suggested ellipsoid zone improvement.

The researchers concluded that early recognition of hydroxychloroquine toxic effects before any fundus changes are visible could minimize progression and risk of visual loss.

### Management of Epiphora After Dacryocystorhinostomy

September *JAMA Ophthalmology*

Approximately 5 to 10 percent of patients continue to experience persistent epiphora following an anatomically successful dacryocystorhinostomy (DCR) for nasolacrimal duct obstruction or stenosis. **Shams et al.** investigated the management and success rate of this so-called functional failure of DCR and found that functional epiphora following DCR appears to be uncommon. Although benefits can be achieved in most patients with intubation or eyelid tightening, more than one procedure is often required.

Among the 65 patients included in this retrospective case series, epiphora recurred a mean of 8.9 months after primary DCR. Fifty-eight patients had evidence of a patent ostium, and all were patent on lacrimal irrigation.

Epiphora was reported immediately following DCR in 21 patients, and within six weeks after removal of the stent in 20 patients. Late recurrence (more than 12 months after DCR) developed in 24 patients. In 10 cases, participants declined any treatment following DCR. The remainder underwent a mean of 1.3 interventions during a mean of 23 to 41 months after primary DCR, after which 47 patients had a successful outcome—the eight who failed to improve declined further intervention. Thirty-nine patients underwent intubation with a silicone stent with a 54 percent success rate.

The researchers called for further prospective randomized studies to assess the long-term success of other specific interventions.

*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).*



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Check out "ABC in Effective Ophthalmic Publishing,"

which gives an inside look at the editorial processes at peer-reviewed journals and describes author habits that help speed publication.

Attendees will also learn about:

- the basics of a well-written article,
- the role and preparation of case reports,
- plagiarism and citations, and
- the impact factor and its role as a marker for journal ranking.

**When:** Sunday, Oct. 19, 10:15 a.m.-12:30 p.m. **Where:** Room N136.

**Access:** Academy Plus course pass.

