

# Journal Highlights

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

### ***Ophthalmology***

#### **Predicting DME Response to Anti-VEGF Therapy**

July *Ophthalmology*

**S**ophie et al. investigated why visual outcomes vary in patients who receive intravitreal injections of ranibizumab for diabetic macular edema (DME). They found that certain factors at baseline—including good BCVA and the presence of submacular fluid—could be used to predict positive outcomes after 2 years of treatment.

This study involved post hoc analysis of patients who were enrolled in 2 randomized phase 3 studies, RISE and RIDE. All told, 502 patients received 0.3 or 0.5 mg of ranibizumab, and 257 patients received sham treatment. Macular laser was used at the discretion of the investigator starting at month 3. At the 24-month primary endpoint, 15.2% of the sham-treated patients had gained 15 or more letters compared with 39.2% of the 0.3-mg ranibizumab group and 42.5% of the 0.5-mg ranibizumab group.

The researchers found that ranibizumab-treated patients were more likely to achieve a final BCVA of 20/40 or better if they were male and had

submacular fluid and good BCVA at baseline. Ranibizumab-treated patients were less likely to achieve this outcome, however, if they had cardiovascular disease at baseline or had previously undergone panretinal photocoagulation.

As for sham-treated patients, a final BCVA of 20/40 or better was correlated with good BCVA at baseline, mild foveal thickening, and hard exudates within 2 disc areas of the fovea. This outcome was less likely in patients who had renal disease.



#### **Smoking Linked to Uveitis**

July *Ophthalmology*

**I**n this population-based case-control study, Yuen et al. implicated cigarette smoking as a risk factor for uveitis.

The researchers examined electronic health records from Kaiser Permanente Hawaii dating back 2 years and identified 100 cases of uveitis. For controls, they randomly selected 522 patients from the general Kaiser Hawaii population and 528 patients from the Kaiser Hawaii ophthalmology clinic.

Current smokers had 1.63 and 2.33 times greater odds of developing uveitis compared with those who had never smoked in the general and ophthalmology control groups, respectively. The association was even stron-

ger with noninfectious uveitis, which yielded odds ratios of 2.10 and 2.96 in the same respective control populations. The majority of uveitis cases were anterior (n = 86) and noninfectious (n = 80) in nature. Intermediate and posterior uveitis accounted for 3 and 11 cases, respectively.

The researchers concluded that further investigation into the pathologic mechanisms that underlie the association between smoking and uveitis are necessary to establish causality.

#### **CMV Retinitis, AIDS, and Survival**

July *Ophthalmology*

**W**hat is the impact of modern combination antiretroviral therapy on long-term outcomes of patients with cytomegalovirus (CMV) retinitis and AIDS? Jabs et al. found that prolonged survival was possible if immune recovery was achieved. In addition, rates of ocular complications and vision loss were substantially lower than those observed before this era of therapy.

For this prospective cohort study, the researchers evaluated 479 patients who were diagnosed with CMV retinitis after 1996. Nearly all (98.1%) had received antiretroviral therapy at one time, either before enrollment or during follow-up.

Affected patients who experienced immune recovery as a result of antiretroviral therapy had an estimated

median survival of 27.0 years; in comparison, those with no immune recovery had an estimated median survival of 13.5 months. Framing the impact on survival in another way, the researchers stated that 75% of those with immune recovery would be alive more than 10 years after diagnosis of CMV retinitis, while less than 10% of those with no immune recovery would be alive 5 years after diagnosis.

They also found that the rates of bilateral visual impairment and blindness did not differ by immune recovery status and remained relatively low 10 years after diagnosis of CMV retinitis. At 5 years after diagnosis, the rates of visual impairment and blindness were 9.5% and 3.2%, respectively. At the 10-year mark, these rates increased to 11.2% and 5.7%.

### Progression From Ocular to Generalized Myasthenia Gravis

July *Ophthalmology*

**N**agia et al. calculated the rate of conversion from ocular to generalized myasthenia gravis and found it was lower than what has previously been reported. They also noted that a subset of patients continued progressing to the systemic form 2 years after the initial onset of ocular symptoms, making continued follow-up a necessity.

For this retrospective analysis, the researchers reviewed the charts of 158 patients who were diagnosed with myasthenia gravis between 1993 and 2012 and divided them into 2 subgroups: those treated with immunosuppressant drugs ( $n = 76$ ) and those who did not undergo such treatment ( $n = 82$ ). Two-thirds of all patients were male, and symptom onset occurred at a median age of 61.5 years. Median follow-up was 60.5 months.

The overall conversion rate to generalized myasthenia gravis was 20.9%, significantly lower than previously reported rates of 50% to 64%. At 2 years, generalized disease had developed in 10.5% of patients treated with immunosuppressants and 18.3% of nontreated patients. Median time for dis-

ease conversion was 20 months in the nontreated group and 24 months in the immunosuppressant group. Conversion occurred after 2 years of ocular symptom onset in 30% of patients.

The researchers noted that, as with any retrospective chart review, this study did have limitations, including a small sample size, heterogeneity of treatment, and nonstandardized evaluation criteria.

### *American Journal of Ophthalmology*

#### Effects of Dry Eye Therapies on Ocular Surface Disease

July *AJO*

**M**oore et al. evaluated the effectiveness of artificial tears and corticosteroids for mitigating the ocular surface response to low-humidity environments. They found that corticosteroid eyedrops did indeed diminish the adverse effects of low humidity, likely due to the suppression of stress-activated inflammatory pathways.

The researchers enrolled 20 patients with aqueous-deficient dry eye. These patients were first exposed to a 90-minute low-humidity environment and then directed to use artificial tears for 2 weeks prior to a second low-humidity exposure. Next, they used 0.1% dexamethasone for 2 additional weeks before they were exposed a third and final time. Digital polymerase chain reaction was performed to measure HLA-DR RNA transcripts in conjunctival cells taken by impression cytology at each visit.

The researchers found significantly less corneal and conjunctival epitheliopathy as well as decreased HLA-DR transcripts after use of dexamethasone compared with artificial tears. Patients also reported significantly less eye irritation during the low-humidity exposure following dexamethasone.

The researchers cautioned that extended use of corticosteroids is not indicated and that other anti-inflammatory therapies with activity against stress-activated pathways may also prove to be effective.

### Endophthalmitis After Intravitreal Injections

July *AJO*

**D**ossarps et al. reported the incidence and characteristics of endophthalmitis following intravitreal injections of anti-VEGF agents and corticosteroids. They found that although the incidence of presumed endophthalmitis following injections was low, the overall prognosis was poor.

For this retrospective, multicenter case series, the researchers investigated a total of 316,576 intravitreal injections from 25 French ophthalmic centers. For each center, the number of intravitreal injections was determined using billing codes, and the injection protocol was recorded.

During the study period, the researchers found 65 cases of presumed endophthalmitis, giving an overall incidence of 0.021%. The median number of days from injection to presentation was 4 days, and the most common symptom was vision loss. Bacterial identification was achieved in 43% of patients, and the most frequent pathogens were gram-positive bacteria (91%), including coagulase-negative *Staphylococcus* in 78%. A majority of patients had worse visual acuity after 3 months of follow-up compared with acuity prior to endophthalmitis.

### Influence of Age on Corneal Astigmatism Following Cataract Surgery

July *AJO*

**H**ayashi et al. investigated the relationship between long-term changes in corneal astigmatism following cataract surgery and age at the time of the procedure. They found that astigmatic changes did not differ significantly due to age and were comparable to changes in eyes that did not undergo surgery.

In this retrospective cohort study, a total of 437 eyes underwent phacoemulsification with a 4.1-mm horizontal corneoscleral incision. For controls, 600 eyes without surgery were divided into 4 age groups: 60 years of age or

younger, 61 to 65 years, 66 to 70 years, and 71 years or older. The researchers then compared the corneal astigmatic change between 1) baseline and 5 years, 2) 5 and 10 years, and 3) baseline and 10 years among the different age groups and between eyes with and without surgery.

Corneal astigmatic change, expressed as x and y coordinates, showed an against-the-rule shift of 0.2 to 0.4 D during the 10-year span in all age groups of both the surgery and control eyes. The researchers also found that the mean x and y coordinates did not differ significantly among the age groups in either surgery or control eyes.

They concluded that further studies are necessary to determine corneal astigmatic change more than 10 years following cataract surgery.

### **JAMA Ophthalmology**

#### **Google Glass During Scleral Buckling Surgery**

June *JAMA Ophthalmology*

**R**ahimy and Garg detailed their intraoperative experience with using Google Glass to record scleral buckling surgery. They found that the device's ability to transmit exactly what the surgeon sees—and in real time—holds promise for surgical teaching in the coming years.

The researchers used Google Glass to record all steps of the scleral buckling procedure, including conjunctival peritomy, rectus muscle isolation, administration of the sub-Tenon block, external drainage of subretinal fluid, and anterior chamber paracentesis with intravitreal gas tamponade injection. To protect patient privacy, they deactivated the device's connection to the Internet while it was being charged and deleted any multimedia that automatically synced to Google's backup servers during the surgical procedure.

The researchers found that the still images and video clips provided adequate details for viewers who were not present during the surgery to recognize the salient steps of the procedure. The

simultaneous audio recordings obtained from the video were also clear and audible upon playback. Several factors, however, limited the optimal image and video quality. For example, the bright illumination provided by the high-intensity overhead OR lamps occasionally overexposed the areas of interest. In addition, the absence of a flash resulted in decreased image quality in low-lighting environments. Finally, the camera's wide-angle lens, combined with the lack of any zoom capabilities, led to a decreased size of the operative field.

#### **Electronic Health Record System Implementation**

June *JAMA Ophthalmology*

**I**n a retrospective case-control study, Singh et al. examined the clinical and economic impact of implementing an electronic health record (EHR) system in a large multispecialty ophthalmic practice. They did not identify any differences in revenue or productivity following EHR conversion, nor did the EHR incentive payments fully offset the costs of implementation.

The researchers compared total revenue, total visit volume, revenue per visit, coding volumes, and the number of diagnostic tests and procedures performed at the Cole Eye Institute for pre- and post-EHR time periods. They also evaluated the total cost of EHR implementation and the expected return in EHR incentive payments.

A total of 28,161 patient encounters were identified between April 1, 2011, and April 5, 2013 (13,969 in the pre-EHR period and 14,191 in the post-EHR period). The researchers identified no changes in total net fiscal revenue, patient volume, revenue per visit volume, and volume of billable diagnostic tests and procedures after EHR implementation. They also found that overall use of Eye codes declined (−15.7%), while the use of E&M codes increased (14.7%).

Total capital and personnel costs for implementation amounted to \$1,571,864 and \$1,514,334, respectively, and the researchers expected to receive

\$983,103 from meaningful use attestation by 2016. They concluded that the progress of EHRs should be further monitored to ensure long-term stability in operating revenue and volume.

#### **Prediction of Juvenile-Onset Myopia**

June *JAMA Ophthalmology*

**A**s part of the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study, Zadnik et al. investigated multiple predictors for myopia onset in school-age children and found cycloplegic spherical equivalent refractive error to be the best single predictor of future myopia.

This study was conducted at 5 clinical sites from Sept. 1, 1989, through May 22, 2010, and included data from 4,512 ethnically diverse, school-age children from grades 1 through 8. The researchers defined myopia onset as follows: −0.75 D or more of myopia in each principal meridian of the right eye as measured by cycloplegic autorefraction during any visit after baseline until grade 8. They then evaluated risk factors using odds ratios from discrete time survival analysis, the area under the curve, and cross-validation.

A total of 414 children became myopic from grades 2 through 8 (ages 7 through 13 years). Of the 13 predictive factors evaluated, 10 were associated with the risk for myopia onset. Of these 10 factors, 8 retained their association in multivariate models: spherical equivalent refractive error at baseline, parental myopia, axial length, corneal power, crystalline lens power, ratio of accommodative convergence to accommodation, horizontal/vertical astigmatism magnitude, and visual activity. The researchers found that a less hyperopic/more myopic baseline refractive error was consistently associated with risk of myopia onset in multivariate models, while near work, time outdoors, and having myopic parents were not. Spherical equivalent refractive error was the best predictive factor, performing as well as all other factors combined, with an area under the curve ranging from 0.87 to 0.93.

## ROUNDUP OF OTHER JOURNALS

### Closing Cutaneous Surgical Wounds

*JAMA Dermatology*

Published online April 15, 2015

What's the optimal way to close a cutaneous surgical wound? **Custis et al.** evaluated the use of adhesive strips along with dermal suturing and found that the strips neither improved cosmetic outcomes nor reduced scar width.

The researchers enrolled 48 patients who were scheduled for dermatology procedures, the majority of which involved Mohs surgery for skin lesions. All wounds were at least 3 cm and closed using subcuticular buried vertical mattress sutures. Adhesive strips were applied to a randomized half-section of each wound.

At the 3-month mark, 45 patients were available for evaluation. No significant differences were observed between wound half-sections in terms of scar appearance and width as well as vascularity, pigmentation, thickness, relief, pliability, and surface area. One case of wound dehiscence was noted at a site where adhesive strips were used, while 2 cases occurred at sites that did not receive the strips.

The researchers concluded that, given the low cost of adhesive strips and the small amount of time needed to employ them, further studies should be undertaken.

### Preventing Corneal Graft Failure

*American Journal of Transplantation*

Published online April 14, 2015

Why do corneal allografts—especially second or third grafts—fail? **Paunicka et al.** investigated this question in an animal model of penetrating keratoplasty (PK). They found that the answer lies in the transplantation procedure itself, which nullifies immune privilege when corneal nerves are severed in the graft bed. Moreover, they noted that when PK is performed in one eye, immune privi-

lege is eliminated in the fellow eye.

Using mice, the researchers found that 50% of the initial corneal transplants survived, while 100% of the subsequent grafts in the fellow eyes underwent rejection. They determined that when corneal nerves are severed during surgery, substance P (a neuropeptide) is secreted in both eyes, thus disabling the regulatory T cells that are required for graft survival. However, the researchers were able to restore immune privilege and promote graft survival by administering a substance P antagonist.

In an accompanying editorial, **Blanco and Saban** noted that the cornea is an intriguing model site for exploring how the nervous and immune systems interface, as it is arguably the most densely innervated site in mammals. As to why the unilateral severing of corneal nerves triggers a bilateral burst in substance P, they hypothesized that the burst has a pathogenic effect on the long-lived macrophages that reside proximal to nerves.

### Severe Dry Eye and Neuropathic Pain

*British Journal of Ophthalmology*

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**G**alor et al. set out to determine whether dry eye could be linked to self-reported symptoms of neuropathic ocular pain (NOP). They found that NOP features are common in patients with dry eye and that these features correlate with the severity and persistence of dry eye symptoms.

For this cohort study, the researchers evaluated 102 men seen at a Veterans Affairs eye clinic. The patients underwent a baseline exam consisting of a dry eye questionnaire and an ocular surface evaluation. They were reevaluated 2 years later. NOP was considered present if a patient reported 1) eye pain that was “hot burning,” 2) symptoms of allodynia to light and/or change in temperature, and/or 3) symptoms of hyperalgesia to wind.

In all, 70 patients reported at least mild symptoms of dry eye during both evaluations, and 53 of these reported 1 or more symptoms of NOP—with 21 describing 1 NOP feature, 20 describing 2 features, 8 describing 3 features, and 4 describing all 4 features. The presence of any NOP feature was associated with significantly higher dry eye symptom scores at either examination.

The researchers acknowledged that self-reported assessments of pain are not as precise as direct assays of nerve conduction. Nonetheless, they noted that patients who have dry eye symptoms and report NOP may be candidates for multimodal therapy that focuses on protecting the ocular surface.

*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 is written by Jean Shaw and edited by Deepak P. Edward, MD.*

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