

Journal Highlights

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

Ophthalmology

Infliximab for Refractory Noninfectious Uveitis

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Kruh et al. set out to establish whether infliximab is safe and effective for the treatment of refractory noninfectious uveitis. They found that the drug—a monoclonal antibody used in treating several chronic inflammatory diseases—induced a high rate of complete clinical remission in recalcitrant uveitis and was well tolerated by most patients.

In this retrospective, interventional, noncomparative cohort study, the researchers evaluated 88 patients from a single-center private practice. All of the patients had noninfectious uveitis that was resistant to other therapy, including corticosteroids and conventional immunomodulatory drugs. In addition, all of the patients had active inflammation at the time they were first infused with infliximab. The drug was administered at an initial dose of 4 to 6 mg/kg, with loading doses given at zero, two, and six weeks and maintenance doses given every four weeks until clinical remission was achieved. At that point, the interval between infusions was slowly lengthened in two-week increments.



Primary outcome measures included the rate of remission, time to remission, relapse rate, failure rate, and tolerance. Of the 88 patients, 72 (81.8 percent) achieved complete clinical remission while being treated with infliximab, and 33 patients (37.5 percent) were able to discontinue all other medications within 180 days of beginning infliximab therapy. The rate of continuing remission without relapse

was 84.7 percent at six months, 75.6 percent at one year, 56.4 percent at 18 months, and 53.4 percent at two years. Patients who relapsed typically did so when the infusion interval was lengthened; when this occurred, they were returned to a shorter interval. Thirty-two patients (36.4 percent)

experienced at least one side effect, and 17 (19.3 percent) discontinued therapy as a result.

One factor that affected remission and relapse was a patient's medication history. For instance, those who had previously taken mycophenolate or azathioprine had among the highest incidence rates of remission. Incidence of relapse was highest among patients with prior use of methotrexate and daclizumab.

The researchers noted that while their results require confirmation by a large multicenter study, continued

follow-up of their patient cohort is also necessary to fully determine the long-term effects of infliximab.

Predicting Retinal Detachment Risk After Open-Globe Injury

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Stryjewski et al. investigated the clinical factors associated with retinal detachment (RD) after open-globe trauma and developed a forecasting model for physicians to use when assessing patients' risk. They found that RD is common after open-globe trauma—although often not appearing until days or weeks after the initial traumatic event.

For this case-control study, the researchers reviewed the charts of 892 patients with 893 open-globe injuries. From these injuries, 255 eyes (29 percent) were ultimately diagnosed with RD. The remaining served as controls. Of the eyes that developed RD, 69 (27 percent) detached within 24 hours of primary open-globe repair, 119 (47 percent) detached within the first week, and 183 (72 percent) detached within the first month. Fourteen eyes (5 percent) experienced RD more than one year after the open-globe injury.

Compared with controls, patients who developed RD were more likely to have a zone III injury (defined as involving the sclera more than 5 mm posterior to the limbus). They also tended to be older, had a poorer me-

dian visual acuity, were less likely to have a visual acuity of at least 20/200, were more likely to have an afferent pupillary defect, and were more likely to have vitreous hemorrhage.

Using these and other clinical factors, the researchers created a multivariable logit model they call the Retinal Detachment after Open Globe Injury score. The score awards points based on three factors: the patient's visual acuity, the zone of injury, and the existence of vitreous hemorrhage at the time of presentation. On this scale, a patient with one point would have a 3 percent probability of developing an RD, while a patient with 7.5 points (the highest number) would have a 95 percent probability score.

Impact of Age-Related Retinal Nerve Fiber Layer and Macular Thicknesses on Glaucoma Evaluation

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Leung et al. examined normal age-related changes in the macular and circumpapillary retinal nerve fiber layers (RNFLs) and found that these changes should be taken into account when clinicians are evaluating disease progression in glaucoma patients—particularly when macular progression is being analyzed.

For this prospective, longitudinal study, the researchers evaluated 150 eyes of 90 glaucoma patients and 72 eyes of 40 individuals who did not have the disease. Imaging of the RNFL and macula was performed using optical coherence tomography (OCT) at four-month intervals for a mean of 45.8 months.

In evaluating those eyes without glaucoma, the researchers found that both RNFL and inner and outer macular thicknesses decreased with age. In the glaucoma group, before this normal rate of age-related loss was accounted for, rates of disease progression were substantial. Specifically, 75 eyes (50 percent) showed progression by measurement of ganglion cell and inner plexiform layer thickness; 75 eyes (50 percent) showed progression by inner retina layer thickness; 45 eyes

(30 percent) showed progression by the total macular thickness; 41 eyes (27.3 percent) showed progression by the circumpapillary RNFL thickness; and 15 eyes (10 percent) showed progression by the outer retina thickness. However, once normal age-related loss was taken into account, these rates of disease progression decreased across all parameters—to 14.7 percent, 20 percent, 16 percent, 26.7 percent, and 1.3 percent, respectively.

Thus, loss of macular thickness did not necessarily refer to disease progression, and accounting for age-related change was highly relevant to macular measurements. By contrast, the circumpapillary RNFL thickness showed only a slight reduction in the proportion of progressing eyes after accounting for this age-related change. In addition, these findings suggest that outer retina change is not typical in glaucoma.

American Journal of Ophthalmology

Corneal vs. Scleral Pneumatometry for Measuring IOP

November *AJO*

Kapamajian et al. evaluated scleral pneumatometry as an alternative method for measuring intraocular pressure (IOP)—especially in situations where corneal measurements are impractical—and found that this alternative correlated positively with corneal pneumatometry.

This prospective cross-sectional study included single eyes of 97 adult subjects aged 18 to 82 years recruited from the University of Illinois Eye and Ear Infirmary. Study measurements included corneal pneumatometry, scleral pneumatometry, axial length, spherical equivalent, and central corneal thickness. Main outcome measures were scleral IOP and corneal IOP.

Scleral pneumatometry was consistently higher than corneal pneumatometry and correlated positively with corneal pneumatometry, age, and spherical equivalent. The difference between scleral and corneal IOP correlated positively with scleral pneu-

matometry and spherical equivalent. Bland-Altman analysis for agreement between scleral and corneal pneumatometry measurements showed a mean difference of 8.08 mmHg, with the 95 percent limit of agreement between -3.47 and 19.64 mmHg.

Regression analysis yielded the following equation: corneal pneumatometry = 11.9 + (0.32 x scleral pneumatometry) - (0.05 x age). The authors noted that this model might allow for the conversion of scleral IOP measurements into conventional corneal values, thus making it more practical to add scleral measurements of IOP to routine tactile measurements in eyes implanted with keratoprostheses or in cases in which IOP measurements cannot be performed on the cornea.

AMD Candidate Genes and Their Distribution Among Racial/Ethnic Groups

November *AJO*

Using data from the Multi-Ethnic Study of Atherosclerosis, Klein et al. analyzed the relationships of select candidate genes associated with the prevalence of early age-related macular degeneration (AMD) in a cohort of Caucasians, African-Americans, Hispanics, and Chinese-Americans.

Specifically, the authors examined whether protective and deleterious alleles among 11 candidate genes for cardiovascular disease differ in their distributions among these groups and whether this might explain the higher prevalence of early AMD in Caucasians. They found that single nucleotide polymorphisms (SNPs) among the candidate genes only partially explained the variations in disease frequency among these groups.

This cross-sectional multicenter study included a total of 2,456 patients aged 45 to 84 years and combined genotype information with fundus photography. Twelve of 2,862 SNPs from 11 of 2,862 candidate genes for cardiovascular disease were selected for analysis based on screening. The

researchers used logistic regression models to test for association in case-control samples.

Early AMD was present in 4 percent of the total cohort and varied from 2.4 percent in African-Americans to 6 percent in Caucasians. In addition, the odds ratio for the entire cohort increased from 2.3 for one risk allele to 10 for four risk alleles in a joint effect analysis of *ARMS2* rs10490924 and *CFH* Y402H.

After adjusting for age, sex, ancestry-informative markers, study site, and smoking status, the researchers found that associations of several candidate genes with early AMD varied among the groups. However, differences in genotype frequencies were conflicting and not always significant; they thus did not fully explain the higher prevalence of early AMD in Caucasians compared with the other three groups, with the possible exception of the Chinese-American cohort. The researchers noted that the higher frequency of risk alleles for a number of SNPs in Chinese-Americans may, in part, be responsible for their disease frequency approaching that of Caucasians; for example, allele frequencies of most SNPs in the study, except for rs3754255 in *MTR*, were statistically significant between the two groups after adjusting for multiple testing.

Corneal Donor Graft Thickness in DSAEK

November *AJO*

Daoud et al. investigated the role of donor lenticule thickness in the outcome of Descemet stripping automated endothelial keratoplasty (DSAEK) surgery. They demonstrated that while DSAEK significantly improves best spectacle-corrected visual acuity (BSCVA), graft thickness may not play an important role in the final BSCVA, refractive error, or accuracy of intraocular pressure (IOP) measurement.

This retrospective chart review included 460 eyes that had undergone DSAEK surgery. They were separated into three groups based on the thick-

ness of the donor graft: less than 100 μm ($n = 67$ eyes), 100 to 150 μm ($n = 316$), and greater than 150 μm ($n = 77$). The researchers examined the three groups at six months after surgery for measurement of BSCVA, spherical equivalent, and IOP. All groups experienced significant improvement in BSCVA, mild hyperopic shift, and stability in IOP measurements. There were no significant differences in groups according to donor graft thicknesses with respect to change in BSCVA, hyperopic shift, or IOP measurement.

JAMA Ophthalmology

Relationship Between Dry Eye Symptoms and Pain Sensitivity

October *JAMA Ophthalmology*

Although dry eye disease is common, little is known about the factors that contribute to symptoms because of the poor correlation between symptoms and objective signs at the ocular surface. **Vehof et al.** explored how pain plays a role in patients' experience of dry eye disease and found that high pain sensitivity and low pain tolerance are associated with having pain symptoms of the disease, adding to previous associations of cell damage, severity of tear insufficiency, and psychological factors.

This population-based cross-sectional study included 1,635 female twin volunteers aged 20 to 83 years. The researchers categorized 438 (27 percent) volunteers as having dry eye disease based on possessing at least one of the following: a diagnosis of dry eye disease by a clinician, the prescription of artificial tears, or symptoms of dry eyes for at least three months.

Quantitative sensory testing using heat stimulus on the forearm was used on the entire study population to assess pain sensitivity (heat pain threshold) and pain tolerance (heat pain suprathreshold). The researchers found that women with dry eye disease showed a lower heat pain threshold and heat pain suprathresh-

old—and hence had higher pain sensitivity—than those without dry eye disease.

The authors concluded that management of dry eye disease symptoms is complex, and physicians need to consider the holistic picture, rather than simply treating ocular signs.

Analysis of the Choroid in Diabetic Retinopathy Using SD-OCT

October *JAMA Ophthalmology*

While diabetic retinopathy typically is characterized by retinal vascular pathology, such as microaneurysms or capillary nonperfusion, recent evidence suggests that choroidal angiopathy may coexist with retinal vascular abnormalities. To evaluate choroidal angiopathy in patients with diabetic retinopathy (DR), **Duker et al.** performed a retrospective review of 33 eyes of 33 patients with DR and 24 control subjects without any known eye pathology. They found that choroidal morphological features were indeed altered in patients with moderate to severe DR.

The researchers analyzed the morphological features and vascular layers of the choroid using spectral-domain optical coherence tomography (SD-OCT) from one-line raster scanning using two independent raters experienced in analyzing SD-OCT images. The chorioscleral interface had an irregular contour in eight of nine eyes with nonproliferative DR, nine of 10 eyes with proliferative DR, and 13 of 14 eyes with DME, compared with no irregular contours in the control eyes. The researchers also found that subfoveal choroidal thickness and subfoveal medium choroidal vessel layer and choriocapillaris layer thicknesses were significantly reduced in patients with proliferative DR and diabetic macular edema (DME).

Ophthalmology summaries are written by Jean Shaw and edited by John Kerrison, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. JAMA Ophthalmology summaries are written by the lead authors.

ROUNDUP OF OTHER JOURNALS

Melanopsin Antagonist: A Potential Target to Treat Migraine and Photophobia

Nature Chemical Biology
Published online Aug. 25, 2013

Melanopsin, expressed in a subset of retinal ganglion cells, mediates behavioral adaptation to ambient light and other nonimage-forming photic responses. This has raised the possibility that pharmacological manipulation of melanopsin can modulate several central nervous system responses, including photophobia, sleep, circadian rhythms, and neuroendocrine function. In this animal study, Jones et al. reported the discovery of opsinamide—a nonretinoid, first-in-class, highly specific compound that targets melanopsin—and found that this melanopsin antagonist effectively and reversibly suppressed nonvisual photoresponses without affecting overall rod and cone photoreceptor function.

The researchers screened 80,000 compounds and identified six that inhibited melanopsin photoactivation. Of these, two were selected for further study based on their druglike properties and their lack of interaction with rhodopsin—another biological pigment found in photoreceptor cells. The final candidate—opsinamide—proved superior in inhibiting both melanopsin-dependent photoresponses and behaviors in mice, including the pupillary light reflex and light aversion. This selectivity, the researchers noted, most likely arises from the primary amino acid sequence divergence between melanopsin and rod and cone opsins.

The researchers concluded that targeting melanopsin is a potential therapeutic strategy for treating such light-modulated disorders as migraines, photophobia, and sleep disturbances. In addition, the discovery of opsinamide might open the door to a related research strategy: identify-

ing new modulators of other opsins, including classical rhodopsin, to treat vision problems related to excessive activation of rhodopsin.

Femtosecond Laser Obviates Need for Viscosurgical Devices in Cataract Surgery

Journal of Refractive Surgery
Published online Aug. 23, 2013

Ophthalmic viscosurgical devices (OVDs) have become a standard tool in cataract surgery. Dick et al. reported, however, that the use of the femtosecond laser may render OVDs obsolete in many cases and described a technique for performing laser-assisted cataract surgery that does not require their application.

In this prospective case series of 23 eyes, the researchers used balanced salt solution instead of an OVD to stabilize the anterior chamber during lens and cortex aspiration. No intraoperative complications were observed. All patients achieved an increase in corrected distance visual acuity after surgery compared with baseline, and no decreases in visual acuity were observed one month later. Intraocular pressure (IOP) ranged from 7 to 23 mmHg before surgery, and no significant postoperative IOP increases were observed. In addition, corneal thickness measurements demonstrated no excessive postoperative swelling. Finally, the total amount of time for surgery and the amount of balanced salt solution used was comparable to that used during a standard cataract procedure.

The researchers noted that randomized clinical trials with a longer follow-up period and endothelial cell evaluations are needed to verify these early clinical findings. Nonetheless, they stated that OVD-free femtosecond laser-assisted cataract surgery appears to offer surgeons the ability to achieve clinical results comparable to those seen with standard cataract surgery using OVDs and phacoemulsification.

Cataract Surgery Outcome in Eyes With Keratoconus

British Journal of Ophthalmology
Published online Aug. 21, 2013

Watson et al. reviewed the refractive outcomes of cataract surgery in patients with keratoconus. They found that while the use of actual keratometry (K) values is a suitable option for eyes with mild and moderate keratoconus, a standard K value should be considered for eyes with severe keratoconus.

This retrospective review included the medical records of 64 patients (92 eyes) who underwent cataract surgery with implantation of an intraocular lens (IOL). Of these 92 eyes, 35 had mild keratoconus (mean K, less than 48 D), 40 had moderate disease (mean K, 48 to 55 D), and 17 had severe keratoconus (mean K, greater than 55 D).

Actual K values were used for IOL power calculation in all 75 eyes with mild or moderate disease, with a target refraction of approximately -1.0 D in mild keratoconus and -1.5 D in moderate disease. This resulted in a mean biometry prediction error (BPE) of 0.0 D and +0.3 D, respectively.

For the 17 eyes with severe disease, actual K values were used in eight eyes, with a mean target refraction of -5.4 D; this resulted in a mean BPE of +6.8 D. For the remaining nine eyes, when a standard K value of 43.25 D was used with a mean target refraction of -1.8 D, the mean BPE was +0.6 D.

The researchers noted one major limitation of the study—that in the absence of a validated protocol, the choice of measured or standard K values was left to the discretion of the surgeon. Nonetheless, they asserted that the data from the study will help clinicians improve surgical outcomes in patients with mild, moderate, and severe keratoconus.

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