

Journal Highlights



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AVAILABLE

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

Ophthalmology

Tear Fluid Production Increases in Meibomian Gland Loss

May *Ophthalmology*

Arita et al. set out to investigate the role of homeostasis in the tear film by evaluating tear film parameters and meibomian gland features and function in patients with and without dry eye. They found that an increase in tear fluid production appears to compensate for the loss of meibomian glands in patients with meibomian gland dysfunction (MGD).

For this cross-sectional, observational case series, the researchers evaluated one eye of each participant in the following groups: 41 patients with dry eye, 70 patients with MGD, 17 patients with both dry eye and MGD, and 70 control participants with neither condition. (Of note, all of the patients with dry eye had non-Sjögren syndrome aqueous deficiency.) All study participants were female.

Tear fluid secretion, as reflected by Schirmer's test value, increased markedly in the MGD patients according to the extent of meibomian gland loss, the researchers found. This change did not occur in the dry eye patients with aqueous deficiency nor in the

control group, which suggests that tear secretion increases to compensate for a deficiency of the oily layer, thereby improving tear film stability.

Bevacizumab vs. Laser for ROP

May *Ophthalmology*

Hwang et al. evaluated the effectiveness and major complications associated with two treatments for type 1 retinopathy of prematurity (ROP): intravitreal injections of bevacizumab and panretinal photocoagulation (PRP). They found that both are effective options for treating type 1 ROP.

For this retrospective case series, the researchers evaluated 28 patients (54 eyes) who had been treated between 2008 and 2012. Main outcome measures were recurrence rate, complication rate, and refractive error.

A total of 11 patients (22 eyes) received bevacizumab; of these, 16 eyes had zone 1 ROP and six had posterior zone 2 ROP. Of the 17 patients (32 eyes) who were treated with PRP, five eyes had zone 1 ROP and 27 eyes had posterior zone 2 ROP.

Over five years, ROP recurred in three of the bevacizumab eyes and in one PRP eye. None of the bevacizumab-treated eyes developed retinal detachment or macular ectopia, while

one PRP-treated eye developed retinal detachment, and five PRP-treated eyes developed macular ectopia.

Finally, intravitreal bevacizumab was associated with lower myopia than PRP, with a mean spherical equivalent at the last refraction of -2.4 D for bevacizumab-treated eyes and -5.3 D for PRP-treated eyes. However, given the relative novelty of bevacizumab as a treatment for ROP, longer follow-up is needed to confirm this finding, the researchers said.

AREDS Report: Lens Opacity Changes and Risk of Progression

May *Ophthalmology*

In a report from the Age-Related Eye Disease Study (AREDS) Research Group, Indaram et al. investigated whether the two-year change in lens opacity severity on the AREDS lens-grading scale predicts progression to cataract surgery or loss of visual acuity (VA) by five years. They found that this is indeed the case, making these early changes potential surrogate end points in follow-up studies.

For this report, the researchers analyzed 3,466 AREDS participants (6,054 eyes). Main outcome measures were progression of lens opacities at two years, cataract surgery, and VA loss of two or more lines at five years.

Even a modest progression of opacities (a worsening of 1 or more units for nuclear cataract or a 5 percent or more



increase in opacity grade for cortical or posterior subcapsular cataract) at two years increased the likelihood of cataract surgery by five years, the researchers found. Similarly, the same modest changes by the five-year mark also increased the risk of progression to cataract surgery by the 10-year mark, they reported.

Increased severity of nuclear and posterior subcapsular opacities was predictive of a loss of two or more lines of VA by the five-year follow-up. The results with cortical opacities were less consistent.

RVO Linked to Increased Stroke Risk

June *Ophthalmology*

In a nationwide longitudinal study in Korea, Rim et al. evaluated the risk of stroke following retinal vein occlusion (RVO). They found that RVO was significantly associated with stroke development, particularly in younger patients.

For this study, the researchers randomly selected 1,025,340 subjects from a database of more than 46 million residents of Korea. Within that group, they identified 1,031 patients with RVO and then randomly selected a comparison group consisting of 5,074 socioeconomically and demographically matched individuals.

During an eight-year follow-up period, stroke developed in 173 (16.8 percent) of the RVO patients and in 543 (10.7 percent) of the comparison group. The most common subtype of stroke was ischemic, occurring in 145 (14.1 percent) of the RVO patients and in 438 (8.6 percent) of the comparison group. Hypertension, diabetes, and chronic kidney disease—all of which were more common in the RVO group—were linked to an increased risk of stroke.

Both hypertension and RVO were more closely associated with stroke in younger adults (those below 50 years of age) than in older cohorts, the researchers found, and they flagged this finding as one that warrants close attention from clinicians caring for patients with RVO.

American Journal of Ophthalmology

One-Year Results of Aflibercept Treatment of AMD

May *AJO*

Oishi et al. conducted a prospective, nonrandomized, interventional case-series study to evaluate the efficacy of aflibercept treatment in three subtypes of age-related macular degeneration (AMD). They also assessed predictive factors for visual outcome.

A total of 98 patients with AMD were recruited from a clinic at Kyoto University in Japan. Of these, 46 had typical AMD, 42 had polypoidal choroidal vasculopathy (PCV), and 10 had retinal angiomatous proliferation (RAP). Patients received aflibercept injections monthly for three months, followed by once every two months for eight months. The logMAR acuity at 12 months and improvement of vision from baseline were compared among patients with PCV, RAP, and typical AMD. Overall mean logMAR improved from 0.36 to 0.21 in 12 months.

While there was no difference in visual improvement between typical AMD and PCV, final logMAR was better in PCV (0.32 ± 0.09 vs. 0.08 ± 0.04 , $p = .016$). The authors also assessed polypoidal lesions in 39 PCV patients who had follow-up angiography and found that polyps regressed in 27 cases (69 percent).

Multiple regression analysis showed that the factors associated with better visual outcome with aflibercept were the presence of external limiting membrane, a smaller greatest linear dimension, and the presence of polypoidal lesions.

Effect of Pupil Dilation on Biometry

May *AJO*

Adler et al. conducted a prospective observational case-series study to evaluate the effect of pupil dilation on biometric measurements and intraocular lens (IOL) power calculation with the IOLMaster. They concluded that pupil dilation has no clinically

significant impact on IOLMaster measurements.

Two consecutive optical biometry measurements, before and after pupil dilation, were obtained using the IOLMaster on 318 eyes of 214 patients prior to cataract surgery. The parameters compared were axial length, corneal power, cylinder, and the corresponding IOL power, which was calculated using the SRK/T formula. The study found no statistically significant difference before and after dilation in axial length, corneal power, or calculated IOL power. There was, however, a statistically significant difference in cylinder measurements.

Risk Factors for Progressive Myopia With Atropine Therapy

May *AJO*

In the Atropine for the Treatment of Myopia Study, a small group of children experienced myopic progression despite therapy. Loh et al. sought to determine the factors that contributed to such progression.

In this cohort study, 200 of 400 children were randomized to receive atropine 1 percent in one eye only. Children were followed up with cycloplegic autorefractometry every four months over two years. Children whose myopia worsened by more than 0.5 D in the atropine-treated eye at one year were classified as progressors. Among the 182 children still in the study at one year, 22 (12 percent) were progressors. Univariate analysis suggested that these children tended to be younger, to have higher myopic spherical equivalent at baseline, and to have two myopic parents. In children classified as nonprogressors, myopic progression at one year was less in the atropine-treated eye than in the untreated fellow eye; in contrast, among progressors, the myopic change was more similar between treated and untreated eyes.

Regression analysis showed that the risk of being a progressor was 40 percent lower with each year of increased age, 43 percent lower for every 1 D less in myopia at baseline, and 59 percent

lower for every 1 D less in myopic change in the untreated eyes over the first year.

JAMA Ophthalmology

Retinal Nerve Fiber Layer Loss and Quality of Life in Glaucoma

April *JAMA Ophthalmology*

To better characterize the relationship between structural changes and disease disability, Gracitelli et al. examined the correlation between rates of retinal nerve fiber layer (RNFL) loss and longitudinal changes in quality of life in glaucoma. Their observational cohort study included 130 patients (260 eyes) with glaucoma who were followed for a mean (SD) of 3.5 (0.7) years.

At baseline, all patients had repeatable visual field defects on standard automated perimetry (SAP). The 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) was administered annually, and spectral-domain optical coherence tomography and SAP were performed at six-month intervals. A joint model was used to investigate the association between change in NEI VFQ-25 Rasch-calibrated scores and change in RNFL thickness, adjusting for confounding socioeconomic and clinical variables.

Progressive binocular RNFL thickness loss was associated with worsening of NEI VFQ-25 scores over time. In a multivariable model adjusting for baseline disease severity and the rate of change in binocular SAP sensitivity, each 1 $\mu\text{m}/\text{year}$ loss of RNFL thickness was associated with a decrease of 1.3 units (95 percent CI, 1.02-1.56) per year in NEI VFQ-25 scores ($p < .001$). After adjustment for the contribution from SAP, 26 percent (95 percent CI, 12-39) of the variability of change in NEI VFQ-25 scores was associated uniquely with change in binocular RNFL thickness.

The authors concluded that progressive binocular RNFL thickness loss is associated with longitudinal loss in quality of life, even after adjustment for progressive visual field loss. These

findings suggest that rates of binocular RNFL change are valid markers for the degree of neural loss in glaucoma and have a strong relationship with glaucoma-associated disability.

Assessment of Online Patient Education Materials

April *JAMA Ophthalmology*

Patients are increasingly using the Internet to obtain medical information. Huang et al. assessed the reading levels of patient education materials (PEMs) available on ophthalmologic association websites to see if they conform to the fourth- to sixth-grade reading level recommended by the American Medical Association and National Institutes of Health. PEMs from major ophthalmology websites were downloaded from June 1, 2014, through June 30, 2014, and assessed for level of readability using 10 scales. Text from each article was pasted into Microsoft Word. These documents were analyzed using the software Readability Studio professional edition for Windows.

A total of 339 online PEMs from seven ophthalmologic associations were assessed. The mean Flesch Reading Ease score was 40.7 (range, 17.0-51.0), which is defined as difficult. The mean readability grade levels on the other nine scales were as follows: 10.4 to 12.6 for the Flesch-Kincaid Grade Level; 12.9 to 17.7 for the Simple Measure of Gobbledygook test; 11.4 to 15.8 for the Coleman-Liau Index; 12.4 to 18.7 for the Gunning Fog Index; 8.2 to 16.0 for the New Fog Count; 11.2 to 16.0 for the New Dale-Chall Readability Formula; 10.9 to 12.5 for the FORCAST scale; 11.0 to 17.0 for the Raygor Readability Estimate Graph; and 12.0 to 17.0 for the Fry Readability Graph.

The authors concluded that online PEMs on major ophthalmologic association websites are written well above the recommended reading level and that consideration should be given to revision of these materials to allow greater comprehension among a wider audience.

Changes in Microperimetry and Low Luminance VA in AMD

April *JAMA Ophthalmology*

Wu et al. investigated whether microperimetry and low luminance visual acuity (LLVA) could serve as sensitive measures of disease activity in intermediate-stage age-related macular degeneration.

Their prospective longitudinal study included 49 participants with AMD (41 with intermediate-stage AMD and eight with nonfoveal geographic atrophy due to AMD) and 10 control participants at a research clinic from May 1, 2012, to Dec. 31, 2013. Participants underwent microperimetry examinations in one eye during a 12-month period (at six-month intervals for participants with AMD and at baseline and 12 months for control participants). Best-corrected visual acuity (BCVA) and LLVA were measured at baseline and at 12 months in all participants. Side-by-side comparisons of color fundus photographs from the initial and final visit were used to assess the pathological features of intermediate-stage AMD and to grade each participant's status as worsened, stable, or improved.

A reduction in mean microperimetric point-wise sensitivity was identified at 12 months compared with the baseline in eyes with intermediate-stage AMD graded as stable (-0.31 dB; $p = .003$) or worsened (-0.42 dB; $p < .001$). An increase in mean point-wise sensitivity was identified in eyes graded as improved (1.13 dB; $p < .001$). A reduction in mean pointwise sensitivity was identified in eyes with nonfoveal geographic atrophy at both six months (-1.41 dB; $p < .001$) and 12 months compared with the baseline (-2.56 dB; $p < .001$). Among the control participants, no change in mean pointwise sensitivity was detected over the 12-month period (-0.11 dB; $p = .34$). In all groups, no changes in BCVA or LLVA were identified over the 12-month period ($p \geq .07$).

The authors concluded that in eyes with intermediate-stage AMD, microperimetry detected subtle changes in

visual function over a 12-month period that were not identified on VA measures. This technique warrants further study as a way to assess efficacy of new treatments for intermediate-stage

AMD, potentially allowing a shorter follow-up period.

Ophthalmology summaries are written by Jean Shaw and edited by Susan M. MacDon-

ald, 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

Genetics of Exfoliation Syndrome: New Locus Identified

Nature Genetics

Published online Feb. 23, 2015

To better understand the etiology of exfoliation syndrome (XFS), Aung et al. conducted a genome-wide association study. They found a significant association between a new locus—the first one identified outside of *LOXLI*—and increased susceptibility to XFS.

The new locus is *CACNA1A* rs4926244; it emerged in the initial analysis of 1,484 cases of XFS and 1,188 controls, all of whom were of Japanese ancestry. The results were verified in an additional analysis of 6,901 cases and 20,727 controls from 17 countries. Overall, the results suggest that risk for XFS increases by approximately 1.6-fold for each copy of the minor G allele.

Given the lack of information on *CACNA1A* expression in the eye, the researchers examined the mRNA and protein expression profiles of this gene in a variety of human ocular tissues and cell lines. They found mRNA expression in all of the ocular tissues they examined, with the exception of the optic nerve head. Distribution of *CACNA1A* was similar, whether or not the patient had XFS.

GATT for Primary Congenital and Juvenile Open-Angle Glaucomas

British Journal of Ophthalmology

Published online Feb. 12, 2015

How safe and effective is gonioscopy-assisted transluminal trabeculotomy (GATT), a minimally invasive and conjunctiva-sparing procedure, for treating primary con-

genital glaucoma (PCG) and juvenile open-angle glaucoma (JOAG)? Grover et al. evaluated the ab interno procedure in this setting and found that it can be used successfully to treat PCG and JOAG.

For this retrospective chart review, the researchers evaluated 10 patients (14 eyes) who had undergone GATT and had been followed for at least 12 months (range, 12–33 months). At the time of treatment, patients' ages ranged from 17 months to 30 years.

The only complication that occurred during or after surgery was early postoperative hyphema in five eyes (36 percent); this cleared by one month in all eyes. The mean intraocular pressure dropped from 27.3 mmHg to 14.8 mmHg, and the mean number of medications required dropped from 2.6 to 0.86. In addition, all patients were examined by gonioscopy after the third month following GATT surgery; at that time, all of the eyes had an open trabecular shelf in more than 180 degrees of the angle.

The authors state that GATT has two primary advantages: 1) Unlike the traditional ab externo approach, it does not involve extensive conjunctival dissection or an invasive scleral flap; and 2) unlike goniotomy, it opens 360 degrees of the angle. However, they acknowledge that the procedure requires a surgical learning curve.

Optic Neuritis and Presence of Selected Autoantibodies

JAMA Neurology

2015;72(2):187-193

Martinez-Hernandez et al. investigated the frequency of selected autoantibodies in patients with isolated optic neuropathy (ON). They

found that the presence of antibodies to aquaporin 4 (AQP4) has diagnostic and prognostic value, but the significance of antibodies to myelin-oligodendrocyte glycoprotein (MOG) and the glycine receptor $\alpha 1$ subunit (GlyR) remains unclear at this time.

For this retrospective case-control study, the researchers evaluated 51 patients with ON and 142 patients who served as controls. Of the control group, 30 individuals were healthy, 48 had neuromyelitis optica (NMO), and 64 had multiple sclerosis (MS). No clinical or magnetic resonance imaging findings outside the optic nerve were available for the ON patients.

Serum antibodies were detected in 23 (45 percent) of the ON patients, including MOG in 10 patients, AQP4 in six, and GlyR in seven (concurrent with MOG in three ON patients and with AQP4 in one patient). Those with AQP4 antibodies had a worse visual outcome, while those with MOG had a better outcome, similar to that of seronegative patients.

Antibody levels in the control group varied widely: 1) Of the 48 patients with NMO, 37 (77 percent) had AQP4 antibodies, four (8 percent) had MOG antibodies, two (4 percent) had AQP4 antibodies concurrent with MOG antibodies, and five (10 percent) were seronegative. None had GlyR antibodies. 2) Of the 64 patients with MS, five (8 percent) had GlyR antibodies, and none had AQP4 or MOG antibodies. 3) All of the 30 healthy individuals were seronegative.

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



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