

Journal Highlights

NEW FINDINGS FROM *OPHTHALMOLOGY*, *AJO*, AND *ARCHIVES*

Ophthalmology

Age-Related Macular Degeneration and Variations in the *ARMS2* Gene

Ophthalmology

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Chakravarthy et al. demonstrated a strong association between all severity stages of age-related macular degeneration (AMD) and variation in the age-related maculopathy susceptibility 2 (*ARMS2*) gene. They also confirmed a significant gene–environment interaction with cigarette smoking.

In this population-based European Eye Study, the authors classified 4,750 participants aged 65 years and older into five mutually exclusive AMD severity stages ranging from no AMD to late AMD. They also gathered smoking history and noted whether participants were non-smokers, former smokers, or current smokers. Early AMD was present in 36.4 percent of participants and late AMD in 3.3 percent. Data on both genotype and AMD were available for 4,276 participants. The odds ratios for associations between AMD stage and *ARMS2* increased monotonically with more severe stages of early AMD. Compared with persons with no AMD, carriers of the TT genotype for

the single-nucleotide polymorphism rs10490924 in *ARMS2* had a 10-fold increase in risk of late AMD. In addition, interactions between rs10490924 in *ARMS2* and smoking status were significant.

Retinoblastoma and Simulating Lesions

Ophthalmology

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Shields et al. investigated the types and frequency of ocular conditions that simulate retinoblastoma. The most common simulating lesions were Coats disease, persistent fetal vasculature, vitreous hemorrhage, ocular toxocariasis, familial exudative vitreoretinopathy, rhegmatogenous retinal detachment, coloboma, astrocytic hamartoma, combined hamartoma of retina and retinal pigment epithelium, and endophthalmitis. The authors pointed out that their team was able to recognize these pseudoretinoblastomas quickly and manage the various conditions.

This retrospective case series involved 2,775 patients referred for management of retinoblastoma; 2,171 patients had confirmed retinoblastoma, and 604 patients had simulating lesions. In the pseudoretinoblastoma cohort, the mean patient age at presen-

tation was 4 years. Simulating lesions differed based on age at presentation. Children younger than 1 year were most likely to have persistent fetal vasculature (49 percent), Coats disease (20 percent), or vitreous hemorrhage (7 percent); those 1 to 2 years of age were most likely to have Coats disease (58 percent), persistent fetal vasculature (11 percent), or vitreous hemorrhage (5 percent); those 2 to 5 years of age were most likely to have Coats disease (61 percent), toxocariasis (8 percent), or persistent fetal vasculature (7 percent); and those older than 5 years were most likely to have Coats disease (57 percent), toxocariasis (8 percent), or familial exudative vitreoretinopathy (6 percent).

Given these findings, the authors recommended that when clinicians identify a possible retinoblastoma case, they should consult with a retinoblastoma specialist before planning a treatment strategy.

Myopic Eyes Less Likely to Have AMD and Diabetic Retinopathy

Ophthalmology

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Pan et al. investigated the relationship of myopia and axial length with major age-related eye diseases, including AMD, diabetic retinopathy (DR), age-related cataract, and primary open-angle glaucoma (POAG). They found that myopic eyes are less



likely to have AMD and DR but more likely to have nuclear cataract, posterior subcapsular cataract, and POAG.

This population-based study involved 3,400 Indians aged 40 to 84 years living in Singapore. The authors found that myopic eyes were less likely to have AMD or DR compared with emmetropic eyes and that each millimeter increase in axial length was associated with a lower prevalence of AMD. On the other hand, myopic eyes were more likely to have nuclear and posterior subcapsular cataract (but not cortical cataract) and POAG, with each millimeter increase in axial length being associated with a higher prevalence of posterior subcapsular cataract and POAG.

The authors concluded that their findings have key clinical and public health implications—especially given the emerging myopia epidemic worldwide. They called for additional cohort studies to confirm these findings.

Factors Impacting Selection of Ophthalmology Residency Program

Ophthalmology

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Which factors are important to applicants in choosing an ophthalmology residency program? According to a cross-sectional survey by **Yousuf et al.**, educational and interpersonal factors are more important than geographic factors. They also found that future career plans and demographic factors play a significant role in the decision. Reasons for applicants to rank a program lower than others included a poor interview experience, perception of low resident morale, and program or institutional instability.

Participants anonymously completed a 25-item questionnaire after the submission of their residency rank lists. A multiple-choice format and ordinal scale were used to query applicants on demographics, career plans, and the importance of factors related to program characteristics. One question allowed for a written response to identify additional factors that caused

the applicant to rank a program lower than other programs. The response rate was 37 percent (218 out of 595). The three most important factors impacting rank lists were resident–faculty relationships, clinical and surgical volume, and diversity of training. Female and ethnic minority applicants placed greater importance on the diversity of faculty and residents. Applicants planning a post-residency fellowship or academic career placed greater importance on opportunities for resident research and a program's prestige.

American Journal of Ophthalmology

Capillary Hemangioma of the Eyelid Treated With Systemic Propranolol

January's *AJO*

Vassallo et al. assessed the efficacy and safety of systemic propranolol for infantile capillary hemangiomas of the eyelid. The authors found that four months of treatment led to complete regression of lesions in patients younger than 1 year. They also noted that treatment might be considered in patients older than 5 years for reducing astigmatism and for aesthetic purposes.

For this prospective, interventional case series, the authors included seven male and seven female patients (mean age, 20.8 months) who had eyelid infantile capillary hemangiomas and were at risk for developing amblyopia. Maximum length of treatment was four months; mean length of treatment was 2.5 months. Mean follow-up was 10.6 months. Propranolol was suspended in case of collateral effects or when complete regression of lesions was achieved.

Capillary hemangiomas involved the upper eyelid in 10 cases and the lower eyelid in four cases. The authors stopped treatment in one patient because of hypotension and in another because of allergy. Ten patients younger than 1 year demonstrated complete regression. Two patients older than 5 years demonstrated significant although incomplete regression. In four cases, amblyogenic astigmatism was

present and decreased from 1.25 D before treatment to 0.25 D after treatment. The authors observed no regrowth and no major collateral effects.

AMD Treatment With Ranibizumab and Reasons for Discontinuation

January's *AJO*

In this retrospective, single-center chart review, **Falk et al.** evaluated four-year treatment results of ranibizumab for AMD. The authors found that a slight decline in visual acuity occurred over time and that different responder groups could be identified within the first two years of treatment.

The study included 855 patients with AMD who were treated with ranibizumab during a four-year period. Of those, 456 patients were still receiving treatment at the end of the period, whereas 399 patients had discontinued treatment. Mean follow-up was 23.3 months. Overall treatment results showed a significant decrease in vision from 53.2 Early Treatment Diabetic Retinopathy Study letters to 50.5 letters. The reason for discontinuing treatment in 181 patients was no signs of disease activity, whereas 113 patients were judged to be untreatable. Thirty-six patients did not want to receive further injections, and 69 patients declined further treatment for various other reasons.

The authors also identified three groups of responders: bad or nonresponders (15 percent of patients), good responders (approximately 21 percent of patients), and regular responders (approximately 64 percent of patients). The first two groups were identified within the first two years of treatment, whereas the third group required continuous monitoring and treatment for a longer period of time.

Tumor Necrosis Factor α Antagonists and the Risk of Optic Neuritis

January's *AJO*

In this population-based cohort study, **Winthrop et al.** evaluated the incidence of optic neuritis (ON) in

patients using tumor necrosis factor α (TNF) antagonists for various autoimmune inflammatory diseases, including rheumatoid arthritis, psoriasis, ankylosing spondylitis, and inflammatory bowel disease. They found that ON is rare in such patients and is no more likely to occur than in patients who start nonbiologic immunosuppressive therapies.

This population-based cohort study included 61,227 inflammatory disease patients who were new users of either anti-TNF agents (etanercept, infliximab, or adalimumab) or nonbiologic disease-modifying antirheumatic drugs (DMARDs). The investigators used validated algorithms to identify ON cases occurring after onset of new drug exposure and then calculated and compared ON incidence rates between exposure groups.

The investigators found three ON cases among new anti-TNF users; these cases occurred a median of 123 days after first use. The DMARD comparison group demonstrated no ON cases. For anti-TNF users, the crude incidence rate of ON across all disease indications was 10.4 cases per 100,000 person-years. In a sensitivity analysis considering current *or* past anti-TNF or DMARD use, the investigators identified a total of six ON cases: three among anti-TNF users and three among DMARD users. Crude ON rates were similar between both groups.

Antibiotic Resistance in Patients Undergoing Cataract Surgery

January's *AJO*

Hsu et al. investigated the antibiotic susceptibility profiles and spectra of conjunctival flora in patients undergoing cataract surgery. Coagulase-negative staphylococci (CNS) were the most commonly isolated organisms, while gentamicin had the highest overall antibacterial susceptibility. A surprisingly large proportion of different CNS strains from the same eye harbored different antibiotic susceptibility profiles.

For this prospective study, the authors obtained conjunctival cultures

from patients undergoing cataract surgery. This was done on the day of surgery prior to instillation of any ophthalmic medications. Isolates and antibiotic susceptibility profiles were identified using standard microbiological techniques.

A total of 183 eyes were cultured, yielding 225 isolates. Twenty-seven eyes (15 percent) showed no growth. CNS were the most commonly isolated organisms (74.8 percent). Sixty-four percent of these CNS isolates were sensitive to ciprofloxacin; 30 percent were resistant to more than three classes of antibiotics, and 47 percent were resistant to oxacillin. Among eyes with multiple CNS strains, 41 percent had different antibiotic susceptibility profiles, even though the strains were the same species.

The authors concluded that their cohort harbored organisms with similar rates of antibiotic resistance as elsewhere in the United States, including oxacillin resistance; however, the rate of fluoroquinolone resistance was less than in other reports. These regional findings should prompt further dialogue regarding perioperative antibiotic choice for cataract surgery.

Archives of Ophthalmology

OCT Imaging of Subretinal Pigment Epithelium Lipid

December's *Archives*

In this retrospective, observational case series, Mukkamala et al. described the “onion sign,” an optical coherence tomography (OCT) finding of layered hyperreflective bands beneath the retinal pigment epithelium believed to represent lipid within a vascularized pigment epithelial detachment. They found that this novel sign is usually associated with chronic exudation from type 1 neovascularization in patients with AMD. And since the “onion sign” colocalizes to areas of exudation that are known to be composed of lipoprotein, these bands may represent layers of precipitated lipid in the subretinal pigment epithelium space.

The authors reviewed clinical histories of 20 patients (22 eyes) with the “onion sign” and analyzed data obtained from OCT, color and red-free (RF) photographs, near-infrared reflectance (nIR), fundus autofluorescence (FAF), and blue-light FAF (bFAF). Mean patient age was 76 years. Snellen BCVA ranged from 20/25 to counting fingers. Two patients had bilateral involvement, and three of 17 eyes had multifocal “onion signs” in the same eye. All eyes had AMD with type 1 neovascularization. In all patients, the “onion sign” correlated with areas of yellow-gray exudates that appeared bright on RF and nIR imaging. No specific FAF or bFAF pattern was identified.

The authors noted that this is the first report of lipid detected in the subretinal pigment epithelium space on clinical examination.

Continuous Monitoring of IOP Patterns With Contact Lens Sensors

December's *Archives*

As part of an FDA trial, Mansouri et al. evaluated the safety, tolerability, and pattern reproducibility of the Sensimed Triggerfish contact lens sensor. The investigators reported that 24-hour intraocular pressure (IOP) patterns obtained with the device demonstrated fair to good reproducibility in the short term.

Forty patients with suspected or established glaucoma participated in two 24-hour monitoring sessions at a one-week interval using the contact lens sensor. The investigators did not control for daily activities and sleep behavior.

The most common adverse events were conjunctival hyperemia (80 percent) and blurred vision (82 percent). The majority of adverse events were classified as mild, and the mean resolution time was less than 24 hours following sensor removal. The device was well tolerated. Patients also noted a significant tendency for better comfort during the second session.

To assess the degree of similarity of individual patient patterns between

the two sessions, the authors computed Pearson correlation between parallel time points in both sessions. Despite the uncontrolled ambulatory nature of this study, they reported an overall correlation of 0.59, which indicates fair to good correlation. There was also higher agreement between specific periods, especially the transition from a state of wakefulness to the first two hours of sleep.

Grading Eyebrow Expansion Associated With Thyroid-Associated Orbitopathy

December's *Archives*

In patients with thyroid-associated orbitopathy, the eyebrow region thickens, leading to accentuation of the glabellar folds and a rounded lateral bulge between the brow and

temporal fossa.

Savar et al. reported on the photographic evidence of eyebrow expansion in patients with this condition and established a consistent grading key through the use of standardized photographs. They found that tissue expansion is indeed a common manifestation of thyroid-associated orbitopathy and that comparison of photographs taken before (premorbid) and after disease onset (morbid) is a useful means to identify and characterize the extent of brow involvement.

In this retrospective cohort study, the investigators reviewed photographs of 75 patients (150 eyes) taken before and after diagnosis of thyroid eye disease. Six independent, masked observers then used a standardized grading scale to assign each brow a grade of 0

to 4, corresponding to increasing severity of tissue expansion. The average grade was 0.3 for premorbid and 1.1 for morbid eyes.

Intraclass correlation coefficients demonstrated a high degree of consistency, and morbid photographs showed a higher degree of correlation than premorbid photographs. Coefficients for the premorbid photographs were 0.705 and 0.632 for the right and left eye, respectively; coefficients for the morbid photographs were 0.921 and 0.916, respectively.

Ophthalmology summaries are written by Lori Baker Schena, EdD, and edited by John Kerrison, MD. American Journal of Ophthalmology summaries are edited by Thomas J. Liesegang, MD. Archives of Ophthalmology summaries are written by the lead authors.

ROUNDUP OF OTHER JOURNALS

Low Vision App for Patients With AMD

British Journal of Ophthalmology

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In the letters section, Walker describes a new iPad app designed to function as a low vision aid for individuals with AMD. The app, named the MD_evReader, aims to improve reading by enhancing the eccentric viewing technique via dynamic text presentation. Eccentric viewing is a strategy adopted by individuals with AMD that involves using the relatively preserved peripheral region of the retina in order to see. This technique requires the reader to look away from the focus of interest and suppress the tendency to make eye movements.

The MD_evReader app scrolls the text on the iPad one line at a time right to left, mimicking the ticker-tape format used on the bottom of television news programs. Users keep their eyes focused on a visible marker that can be positioned anywhere on the screen to match their preferred location. This helps ensure that a steady eye position is maintained. The user can also control the scrolling speed.

LASIK With Femtosecond Laser Not Detrimental to Endothelial Health

Journal of Cataract and Refractive Surgery

Published online Oct. 16, 2012

Klinger et al. compared the differences in endothelial cell density and morphology between eyes with LASIK flaps created via femtosecond laser and mechanical keratome. They found that the additional energy delivered to the cornea with a femtosecond laser was not detrimental to endothelial health.

The investigators randomized one eye of each patient to flap creation by femtosecond laser and the other to mechanical microkeratome. They then analyzed central endothelial images, and found that five years after LASIK, corneal endothelial changes in the flap created with a femtosecond laser were similar to those made with a mechanical microkeratome. There were no significant differences in the endothelial cell density or coefficient of variation of cell area at any examination. The mean annual rate of corneal endothelial cell loss was 0.1 percent for both treatments.

Photoactivated Riboflavin Treatment of Infectious Keratitis

Journal of Refractive Surgery

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Price et al. evaluated corneal collagen cross-linking with photoactivated riboflavin as an adjunct treatment for infectious keratitis. They found that this approach was generally safe and was most effective when the infection depth was limited; it was also more effective in bacterial infections than in fungal infections.

This study included 40 patients aged 14 to 86 years with infectious keratitis. They were treated with riboflavin 0.1 percent solution for 30 minutes and were then exposed to 365-nm UVA light for 15 to 45 minutes while riboflavin was being instilled.

The authors pointed out that a longer duration of UVA exposure or different type of radiation might result in deeper penetration and more effective treatment of resistant organisms.

Roundup of Other Journals is written by Lori Baker Schena, EdD, and edited by Deepak P. Edward, MD.