**Journal Highlights**

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

**Ophthalmology**

**Meibomian Gland Dysfunction and Hypercholesterolemia**

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High cholesterol is a known risk factor for ischemic heart, cerebrovascular, and peripheral vascular disease. Previous studies have postulated that hypercholesterolemia (defined as total cholesterol of at least 200 mg/dL) also plays a role in the development of meibomian gland dysfunction (MGD). In this observational, case-control study, Pinna et al. investigated the correlation between MGD and hypercholesterolemia and found that patients with MGD had a significantly higher rate of hypercholesterolemia than age-matched controls who didn’t have the disease.

This study included 60 symptomatic MGD patients and 63 healthy controls, all of whom had no history of hypercholesterolemia and were between the ages of 18 and 54 years. The authors measured body mass index, fasting blood triglycerides, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), glucose, and creatinine. Main outcome measures included fasting blood levels of total cholesterol, LDL, and HDL.

MGD patients, mean total cholesterol, LDL, and HDL were 210.8, 127.6, and 61.6 mg/dL, respectively. In controls, these levels were 162.9, 94.2, and 52.5 mg/dL, respectively. All differences were statistically significant. Logistic regression analysis showed that MGD was indeed significantly associated with higher blood levels of total cholesterol, LDL, and HDL.

Because of the study’s relatively small sample size, the authors called for larger investigations into the relationship between MGD and increased blood cholesterol. At this stage, it is premature to advocate serum cholesterol screening for all MGD patients, they noted. However, if these findings are confirmed, MGD may become a marker of previously unknown hypercholesterolemia, and ophthalmologists may find themselves playing a larger role in the early detection of cardiovascular disease.

**Microbial Keratitis After Keratoprosthesis Implantation**

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In this retrospective, single-surgeon consecutive case series, Kim et al. identified the incidence of and risk factors for microbial keratitis after implantation of the Boston type 1 keratoprosthesis. They found that infectious keratitis developed in 13.6 percent of eyes, with similar rates of both culture-positive bacterial and fungal infection.

The authors collected data on ocular history, postoperative management, and surgical outcomes from 105 patients who had undergone a total of 125 keratoprosthesis procedures (110 eyes) with a Boston type 1 implant over an eight-year period. Twenty cases of infectious keratitis were diagnosed in 15 eyes (13.6 percent) of 15 patients (14.3 percent). Five eyes developed a second infiltrate that was distinctly different from the initial infiltrate in terms of location and date of diagnosis, with two infiltrates developing after the patient had a repeat prosthetic procedure.

The authors analyzed the roles of topical vancomycin use, topical steroid use, and contact lens wear. Although they found that these factors did not increase the risk of developing infectious keratitis, they did find an association between the prolonged use of vancomycin and an increased risk of fungal keratitis and infectious keratitis overall. They also found an association between persistent corneal epithelial defect formation and an increased risk...
of fungal keratitis and infectious keratitis overall.

According to the authors, these findings suggest the need for additional topical antimicrobial prophylaxis after keratoprosthesis implantation for patients at higher risk for infection, such as those with prolonged vancomycin use.

Micro- and Nonmicrovascular Causes of Ocular Motor Nerve Palsy

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Isolated third, fourth, and sixth cranial nerve palsies frequently occur as a result of presumed microvascular ischemia to the nerve. But in this prospective, multicenter, observational case series, Tamhankar et al. found a substantial number of other, nonmicrovascular causes as well, including neoplasm, giant cell arteritis, and brain stem infarction.

A total of 109 patients who were aged 50 years or older and had acute isolated ocular motor nerve palsy underwent magnetic resonance imaging of the brain and clinical assessment. Of these patients, 22 had cranial nerve III palsy, 25 had cranial nerve IV palsy, and 62 had cranial nerve VI palsy. The authors identified a microvascular cause in 91 patients, while 18 patients were diagnosed with nonmicrovascular palsy due to neoplasm, giant cell arteritis, and brain stem infarction.

In diagnosing glaucoma, the researchers used the same definition as that used in the Infant Aphakia Treatment Study: the presence of ocular hypertension plus either progressive optic disc cupping or buphthalmos. They found that nine eyes (14.5 percent) developed glaucoma, and an additional 16 eyes (25.8 percent) were diagnosed as glaucoma suspects during the follow-up period. Using the Kaplan-Meier method, the authors estimated that the probability that an eye would develop glaucoma or become a glaucoma suspect after surgery for congenital cataracts was 63 percent by the 10-year mark.

The authors concluded that long-term monitoring of patients following congenital cataract surgery is important because of the high risk of glaucoma development in these eyes.

Epiretinal Membranes After Cataract Surgery: Incidence and Progression

August AJO

Fong et al. assessed the incidence of eye-specific epiretinal membrane (ERM) three years following phacoemulsification surgery after eliminating potential detection bias attributable to preoperative cataract. They conducted this research as part of the Australian Prospective Cataract Surgery and Age-related Macular Degeneration Study.

Using retinal photographs taken one month postoperatively, the researchers found that ERM prevalence in this cohort study was 13.9 percent among 1,394 patients. Of those patients who had retinal photographs from both preoperative and one-month postoperative visits (n = 1,040), ERM was detected in 3.1 percent of patients during the preop visit and 14.8 percent of patients during the postop visit. The researchers reported that in 87 percent of eyes that were assessed as having ERM one month after cataract surgery, the condition had been missed in the preoperative assessment of their retinal images. Two-thirds of the preoperative images were poorly focused, and this contributed to the underdetection of the condition.

With regard to progression, the three-year cumulative incidence of ERM was 11.2 percent.

Multimodal Imaging of Optic Disc Drusen

August AJO

In a retrospective observational case series, Sato et al. examined optic nerve drusen with enhanced depth imaging optical coherence tomography (EDI-OCT), swept source OCT, and fundus autofluorescence.

The researchers evaluated 26 eyes of 15 patients. Of these 26 eyes, eight had visible optic disc drusen, and the remaining 18 had buried drusen on ophthalmoscopy. EDI-OCT and swept source OCT demonstrated the internal characteristics of the drusen and their relationship with the lamina cribrosa. The drusen were seen to be hyporeflective round or ovoid structures; in 12 eyes (46.2 percent), they contained hyperreflective foci. Most drusen were located immediately anterior to the lamina cribrosa.

The researchers also found that both the larger the drusen and the more areas of the optic canal occupied by drusen, the greater the associated retinal nerve fiber layer abnormalities. Both larger drusen and drusen with hyperreflective foci were correlated with a thinner nerve fiber layer thickness.
Comparison of Culture Techniques in Infectious Endophthalmitis
August AJO

Rachitskaya et al. compared the microbiological outcomes of two culture techniques—membrane filter system and blood culture bottles—in culturing diluted pars plana vitrectomy cassette vitreous. They found that the combination of the two techniques provides the highest number of positive culture outcomes.

In this retrospective comparative case series, the researchers studied 447 patients with 168 positive cultures obtained during a 10-year period, making this the largest study on the topic. Isolates were divided into three groups: those that had positive cultures with 1) both methods, 2) the membrane filter system only, and 3) the blood culture bottles only.

Of 168 total isolates, 123 (73 percent) were culture positive with both methods; of these, the most prevalent organisms were Staphylococcus epidermidis and yeast. Twenty-six (16 percent) isolates were culture positive with the membrane filter system only, with mold and Mycobacterium species being the most prevalent. Nineteen (11 percent) isolates were culture positive with the blood culture bottles only; of these, the most prevalent organisms were S. epidermidis and Propionibacterium species.

The researchers noted that the blood culture bottle method is technically easier to perform and represents a viable alternative to the more complex membrane filter system technique, particularly when a pars plana vitrectomy is being performed on an emergency basis after hours.

JAMA Ophthalmology

Review of Risk Factors and Genetics in Common Comitant Strabismus
July JAMA Ophthalmology

Manconchie et al. performed a systematic review of the literature to locate articles reporting environmental and genetic risk factors in common forms of comitant strabismus unassociated with neurological disorders and syndromes. They found that it was possible to characterize a population at high risk of developing the disorder.

The authors used an approach that included an adapted extraction and quality analysis tool to find prospective and retrospective case-control or population articles. After they assessed studies for content and quality, the authors included 41 articles in the analysis. Four key areas of interest were revealed: risk factor, twin, pedigree, and genetic studies. Because of the variability of study design, a descriptive analysis was performed.

The authors concluded that a high-risk population could be identified, and they characterized it as including 1) infants of mothers who smoked throughout pregnancy, 2) infants who were born prematurely and diagnosed with retinopathy of prematurity, 3) infants who had a low birth weight, even though they were not born prematurely, 4) infants with anisometropia, and 5) the presence of a family history of strabismus, particularly accommodative esotropia. Twin and pedigree studies highlighted the contribution of genetics to strabismus development, although only one common comitant strabismus locus, STBMSI, is currently known.

Additional understanding of the development of strabismus could help researchers discover additional genetic loci and high-risk populations, the authors concluded. Further identification and quantification of susceptibilities to strabismus would make a case for screening specific groups of children and would encourage prompt treatment, if warranted.

Novel Low-Vision Rehabilitation Program Boosts Cognitive Abilities
July JAMA Ophthalmology

Whitson et al. developed and tested a new low vision rehabilitation (LVR) program—known as Memory or Reasoning Enhanced Low Vision Rehabilitation (MORE-LVR)—for patients with mild cognitive deficits. They found that even patients with advanced age and significant comorbidity demonstrated improvements in objective and subjective measures of visual function and memory.

Key components of MORE-LVR include 1) repetitive training with a therapist twice weekly during a six-week period, 2) simplified training experience addressing no more than three self-selected goals in a minimally distracting environment, and 3) involvement of a companion (friend or family member).

Twelve patients with macular disease participated in a pilot program of MORE-LVR. None had dementia, but all exhibited deficits in memory or verbal fluency on a brief cognitive screening administered during their initial evaluation in a low vision clinic. The patients’ mean age was 84.5 years, and 75 percent were female.

At the end of the program, the participants demonstrated improved mean results on the National Eye Institute Visual Function Questionnaire-25 (VFQ-25) composite and near activities scores. They also did better on timed performance measures (such as writing a grocery list), on a measure of their satisfaction with their status of independence, and on an assessment of their logical memory. All of the patients and their companions reported progress toward at least one individualized goal; more than 70 percent reported progress toward all three personal goals.

The authors concluded that the MORE-LVR program can be feasibly incorporated in outpatient low vision clinics, although they noted that more research is needed to determine whether MORE-LVR is a superior and cost-effective alternative to standard LVR for persons with coexisting visual and cognitive impairments.

Ophthalmology summaries are written by Michael Mott 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.
Roudup of Other Journals

Genetic Variance and Risk of Age-Related Macular Degeneration
Nature Genetics
2013;45(7):813-817

In this study, van de Ven et al. explored the role of rare, highly penetrant genetic variants in age-related macular degeneration (AMD) and verified a previously reported hypothesis: Altered function of the serine protease factor I (FI) may increase disease risk. Specifically, they found direct evidence that a missense mutation in the CFI gene encoding a p.GLY119Arg substitution conferred a high risk of AMD and reduced the expression of FI.

The investigators sequenced CFI coding exons from the DNA of 84 unrelated patients with AMD and found two heterozygous variants in four cases. Three patients carried a p.Gly119Arg substitution; the fourth carried a p.Gly188Ala substitution. Neither of these variants was identified in 192 controls. The investigators then screened an additional 1,014 AMD patients and 711 controls specifically for the p.Gly119Arg substitution and identified the variant in 11 patients; it was again absent from controls. In addition, they genotyped 2,469 AMD patients and 3,035 controls from four independent studies; the variant was identified in six patients and one control. In total, the investigators identified the p.Gly119Arg variant in 20 of 3,567 AMD patients, versus only one of 3,937 controls.

Recombinant protein studies of individuals carrying the p.Gly119Arg variation and age-matched controls demonstrated that carriers had lower plasma FI concentrations. Additional in vivo testing on zebrafish embryos confirmed that the p.Gly119Arg substitution reduced FI activity and the ability to regulate vessel thickness and branching.

The investigators conclude that it is essential to understand the role of both common and highly penetrant, rare genetic variants in AMD before reliable predictive tests can be developed.

Sturge-Weber Syndrome, Port-Wine Stains, and Genetic Mutation
New England Journal of Medicine

Sturge-Weber syndrome is a congenital nevocutaneous disorder characterized by a port-wine stain of the face, intracranial calcifications, seizures, intellectual disability, and glaucoma, particularly when staining of both the upper and lower eyelids is involved. Previous studies have postulated that somatic mosaic mutations disrupting vascular development trigger the disorder and associated port-wine staining. In this study, Shirley et al. confirmed that, indeed, both are caused by a somatic activating mutation in the GNAQ gene.

The investigators performed whole-genome sequencing of DNA from six paired samples of both stained and visibly normal tissue from three patients with the disorder. They then tested for the presence of this somatic mosaic mutation in samples of both stained and visibly normal tissue from three patients with the disorder. They further analyzed the relationship between retinopathy and CV outcomes in 3,433 participants (mean age, 61 years) in the Action to Control Cardiovascular Risk in Diabetes trial. A subset of 2,856 patients was evaluated for progression of diabetic retinopathy at four years. Retinopathy was classified as none, mild, moderate, or severe, and worsening was classified as a less-than-two-step, two-to-three-step, or greater-than-three-step change.

Compared with the absence of retinopathy, the adjusted hazard ratios for CV outcomes rose from 1.49 in patients with mild retinopathy to 2.35 for severe retinopathy, demonstrating that more advanced forms of retinopathy at baseline predict a higher risk of serious CV outcomes. The investigators also found that the hazard of the primary CV outcome increased by 38 percent for every category of change in retinopathy severity. However, adding follow-up levels of hemoglobin A1c, systolic blood pressure, and lipids to their model (either individually or together) rendered the relationship between disease deterioration and CV outcomes nonsignificant. The authors concluded that easily measurable changes in the retina may help in identify patients whose CV risk is rising.