

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Ophthalmology Faculty: Diversity Needed

August 2021

Fairless et al. assessed the ethnic demographics of the faculty members in U.S. medical school departments. They found that ophthalmology departments have among the fewest minority faculty members (6.8%). In contrast, the obstetrics and gynecology sector has the most (15.7%).

For this study, the researchers analyzed data from the 2019 faculty roster of the Association of American Medical Colleges. The proportions of under-represented minority (URM) faculty, including chairs, were calculated for ophthalmology and 17 other clinical departments. In addition, the percentage of URM ophthalmology faculty was compared with the proportion of URM persons among graduates of medical schools and with the U.S. population at large. For this study, URM denoted persons who are Black, Hispanic/Latinx, Native American, Native Hawaiian, or Pacific Islander.

The dataset included nearly 158,000 faculty members. Of these, 3,060 were from ophthalmology departments. URM prevalence was significantly higher among all faculty combined (9.8%) than in the ophthalmology sector (6.8%). Moreover, ethnic diversity was lower for ophthalmology faculty than for graduating medical students or the overall U.S. population.

Of the 18 medical departments studied, ophthalmology had the third-lowest percentage of URM faculty; only radiology and orthopedics fell further behind. The difference between ophthalmology and other departments was statistically significant for 12 of the 18 comparisons.

To achieve parity with other clinical education programs and the diverse populations that physicians serve, work is needed to increase URM ophthalmology faculty, said the authors.

Which LPI Location Is Best?

August 2021

Laser peripheral iridotomy (LPI) is a common treatment for angle closure. However, consensus is lacking on the optimal location for iridotomy. Xu et al. looked at anatomic changes after LPI and developed statistical models to determine predictors of angle widening and angle opening. They found that angle widening was significantly greater when the LPI location was superior as opposed to temporal or nasal.

The study population included Chinese patients between 50 and 70 years (84% female), identified from the Zhongshan Angle Closure Prevention study. At baseline, all patients were



suspected of having primary angle closure, defined as inability to visualize pigmented trabecular meshwork in two or more quadrants on static gonioscopy. Each patient had LPI performed on one eye in the superior location (between 11 and 1 o'clock; n = 219) or the temporal or nasal location (at or below 10:30 or 1:30 o'clock, respectively; n = 235). OCT

imaging of the anterior segment and gonioscopy were performed at baseline and two weeks after LPI. One or two images per eye, oriented along the horizontal and/or vertical meridians, were analyzed with software that automatically segmented anterior segment structures and produced biometric measurements that corresponded to scleral spur markings. Thirteen biometric parameters that describe the anterior segment were explored.

The analyses showed significant differences in all biometric parameters from baseline to two weeks post-treatment ($p < .006$), except for iris thickness at 2,000 μm from the scleral spur. Residual signs of angle closure after LPI were evident in 120 eyes (26.4%). According to multivariate regression analyses, predictors of greater angle widening were superior LPI location, smaller angle-opening distance measured 750 μm from the scleral scar, and greater iris curvature. Predictors of insufficient widening were temporal and nasal LPI locations and smaller mean gonioscopy grades.

Based on these findings, the authors recommend that eye care providers consider the superior LPI location to optimize anatomic changes after LPI. Even so, they cautioned that long-term clinical outcomes and potential risks are unclear at this time.

Young Children Need Higher Atropine Doses

August 2021

Although low-dose atropine has shown promise for myopia control in children, the responses to treatment vary widely. In the Low-Concentration Atropine for Myopia Progression (LAMP) study, the spherical equivalent (SE) reductions over one year ranged from 27% to 67% for atropine concentrations of up to 0.05%. In a secondary analysis of LAMP data, Li et al. aimed to elucidate factors related to poor treatment response. They found that younger age predicts lower response, whereas baseline SE and parental myopia status did not affect the responses.

Of the original 438 children recruited for the LAMP study, 350 completed two years and were included in the follow-up study. Patients were categorized by age (4-6 years, 7-9 years, and 10-12 years) and were assigned randomly to receive atropine 0.05%, 0.025%, 0.01%, or placebo. In the second year, those initially given placebo received 0.05% atropine. Generalized estimating equations were used to evaluate potential predictors of change in SE and axial length (AL); these included age, gender, baseline refraction, parental myopia status, and other factors.

During both years of treatment, younger age was the only predictor of faster SE progression and AL elongation; the youngest group had the weakest treatment response. During the two-year period, myopia progression of 10-year-olds in the 0.01% group was similar to that of 8-year-olds in the 0.025% group and of 6-year-olds in the 0.05% group. For each younger-age year, the mean SE change was 0.14 D larger in the 0.05% group, 0.15 D larger in the 0.025% group, and 0.20 D larger in the 0.01% group. Although age and atropine concentration were significant

risk factors for SE progression and AL elongation, there was no interaction between the two, indicating that they influence myopia progression independently.

All concentrations of atropine were well tolerated, regardless of age. The mean accommodation amplitude decreased with age, but the mean changes in photopic pupil size were similar among treatment and age groups, as were the rates of photophobia and use of photochromic glasses. These results suggest that among the factors studied, age was the only predictor of response to atropine treatment. For children under 7 years of age, the highest concentration (0.05%) is required to attain efficacy similar to that of smaller doses in older children. (Also see *Clinical Update*, page 30.)

—Summaries by Lynda Seminara

Ophthalmology Glaucoma

Selected by Henry D. Jampel, MD, MPH

Marijuana, Glaucoma, and Social Media

July/August 2021

Jia et al. conducted an analysis of social media content on glaucoma and medical cannabis. They found robust support of cannabis for glaucoma patients, despite recommendations against its use by such organizations as the American Glaucoma Society and the Academy.

For this internet-based study, the researchers identified online information on Google, Facebook, and YouTube. The top 20 searches for Google and YouTube and the posts from the top nine patient-based glaucoma groups on Facebook were aggregated and analyzed. Each post, website, or video was evaluated for quality using Sandvik and risk scoring methodology. Additional analysis included whether the source was professional; these were further separated into ophthalmology/optometry and non-eye care sources.

The search resulted in an aggregate of 51 websites on Google, 126 posts from Facebook groups, and 37 videos on YouTube. Of note, the number of members in the Facebook support

groups ranged from 600 to more than 16,000. A significant portion of online material promoted cannabis use by glaucoma patients (24% of Google, 59% of YouTube, and 21% of Facebook results). Content from professional sources had a higher content quality score and a lower risk score and was less likely to support cannabis use. However, 11% and 27% of professional opinions on Google and YouTube, respectively, were pro-cannabis use. Upon further clarification, these professional opinions either were outdated, from non-eye care sources, or linked to cannabis organizations.

“It is important for physicians to be aware of the different platforms and opinions that are readily shared among patients,” the authors said, and they recommended directing patients to better-quality professional information on the topic. —Summary by Jean Shaw

Ophthalmology Retina

Selected by Andrew P. Schachar, MD

Changes in Treatment Paradigms and AMD Outcomes

August 2021

Schwartz et al. set out to describe treatment strategies for neovascular age-related macular degeneration (AMD) over a decade and determine their impact on visual outcomes. They found that, despite the evolution in treatment, patients continue to lose vision after the first year of anti-VEGF injections.

For this retrospective study, the researchers analyzed electronic health records from 27 National Health Service secondary care providers in the United Kingdom. Treatment-naive patients who received at least three intravitreal anti-VEGF injections in their first six months of follow-up were included. Those with a previous diagnosis of retinal vein occlusion, diabetic macular edema, or proliferative diabetic retinopathy were excluded. Eyes with at least three years of follow-up were grouped by years of treatment initiation, and three-year outcomes were compared between the groups.

A total of 13,705 patients (15,810 eyes) were included. All patients were

treated between September 2008 and December 2018, and 194,904 injections were provided. Visual acuity (VA) improved from baseline during the first year but dropped in the second and third years of treatment, a trend that did not change over time. Although an increasing proportion of patients retained functional VA and were able to continue driving as the decade progressed, this was linked to a trend of better baseline VA at start of treatment.

The data suggest that these results may be related to suboptimal treatment patterns, the researchers said. They noted that rethinking treatment strategies may be warranted, “possibly on a national level or through the introduction of longer-acting therapies.”

—Summary by Jean Shaw

Ophthalmology Science

Selected by Emily Y. Chew, MD

Choroidal Thickness and Systemic Health of Preterm Infants

June 2021

Michalak et al. used handheld OCT to analyze the impact of systemic health factors on choroidal thickness in preterm infants. They found that a thinner choroid in these infants may be related to a slower growth rate in the first weeks of life and the need for prolonged use of supplemental oxygen.

The researchers enrolled 118 preterm infants as part of the prospective, longitudinal BabySTEPS study. Both eyes of the infants were imaged with a handheld investigational swept-source OCT system at multiple time points during their stay in the intensive care nursery. Custom segmentation software was used to delineate the central 1 mm subfoveal choroidal thickness on OCT images. Errors in segmentation were manually corrected. Univariable and multivariable linear regression analyses were performed to evaluate factors associated with choroidal thickness. Maternal and infant clinical health data were collected. The main outcome was the association between infant health factors and choroidal thickness.

For this analysis, data were used

from 85 infants (170 eyes) at 36 ± 1 weeks postmenstrual age (PMA). Subfoveal choroidal thickness could be measured in 82 of the 85 infants (159 eyes). Mean choroidal thickness was $233 \pm 75 \mu\text{m}$. The infants' mean birth weight was 968 ± 271 g, and their mean gestational age was 28 ± 2 weeks.

The results showed that a thinner choroid is independently associated with slower postnatal growth velocity and the use of supplemental oxygen. In addition, a thinner choroid was associated with several other systemic health conditions, including baseline health metrics and cardiac and pulmonary abnormalities. Of these, the most common systemic factors were pulmonary and were related to the need for supplemental oxygen, which was the one statistically significant factor in the multivariable analyses.

As BabySTEPS is a longitudinal study, these children will be studied up to school age, with follow-up data on visual outcomes to be published at that time.

—Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Characteristics of Uveitis in Spondyloarthritis

August 2021

Spondyloarthritis denotes a spectrum of diseases with overlapping skeletal and extra-articular features. Although its most common extra-auricular sign is acute anterior uveitis (AAU), spondyloarthritis goes undiagnosed in nearly 40% of patients with uveitis. Bilge et al. looked at the frequency and features of AAU in a nationwide cohort of Turkish patients with spondyloarthritis of various subtypes. They found that radiographically observed damage and long duration of disease were linked to elevated uveitis risk.

The data source for this study was the TReasure registry, which includes detailed information on patients with inflammatory arthritis in regions throughout Turkey. The authors recorded data for patients with concurrent spondyloarthritis and uveitis, in-

cluding the timing of uveitis diagnosis, the number of attacks, and whether the involvement was unilateral or bilateral. History of uveitis was defined as AAU diagnosed by an ophthalmologist.

The study cohort included 4,297 patients; of these, 475 (11%) had experienced at least one episode of uveitis. Uveitis was more common in patients older than age 60 years ($p < .001$) and in those with a smoking history ($p = .004$), arthritis ($p < .001$), diagnostic delay ($p = .001$), disease lasting at least five years ($p < .001$), HLA-B27 positivity ($p < .001$), family history of spondyloarthritis ($p < .001$), or radiographic evidence of damage ($p < .001$). Uveitis was most prevalent in patients with ankylosing spondylitis and was less common in those with psoriasis or psoriatic arthritis.

Given these results, the authors recommend that eye care providers ask patients with uveitis about back pain and arthritis and refer them to a rheumatologist for a full spondyloarthritis workup. Collaboration between rheumatology and ophthalmology is crucial for optimal care of patients with uveitis, said the authors. To their knowledge, this study represents the largest cohort of patients with coexisting spondyloarthritis and uveitis.

Cluster of TASS Cases After Cataract Surgery

August 2021

Toxic anterior segment syndrome (TASS) is characterized by acute non-infectious inflammation of the anterior segment. Imamachi et al. reviewed seven cases (four patients) of TASS that occurred shortly after placement of the same type of IOL during cataract surgery. The procedures were performed by three surgeons at two facilities. The author stressed the importance of prompt diagnosis and treatment to preserve vision.

Among 162 eyes that received the Lentis Comfort/LS-313 MF15 IOL from July through November 2020, seven eyes (4.3%) displayed acute inflammation of the anterior chamber including fibrin formation within 15 days of uneventful surgery, which con-

sisted of cataract surgery alone (four eyes) or combined with minimally invasive glaucoma surgery (three eyes). During the same period, TASS did not occur with any other IOL model. The authors believe that this is the first study of TASS associated with the Lentis Comfort/LS-313 MF15 IOL. The seven incidents were reported to the lens manufacturer, who investigated the corresponding lens lots and found no deviations from the standard manufacturing protocol.

One patient was 60 years old; the others were in their 70s. Treatment of the inflammation and/or secondary angle closure (due to pupillary obstruction) varied by severity. For mild TASS cases, the authors recommend initial treatment of frequent instillation of a topical steroid (four to eight times daily), especially 0.1% dexamethasone. If this fails, a steroid can be injected.

In this series, one eye was treated conservatively with success, one eye required vitreous surgery, and another required Nd:YAG laser fibrin membranotomy. The fibrin membrane was removed in two eyes, and two others had anterior chamber washout. In all cases, the inflammation and angle closure responded to treatment, and there was no recurrence of fibrin or inflammation. However, the authors cautioned that TASS can cause irreversible corneal endothelial damage and other long-term sequelae.

—*Summaries by Lynda Seminara*

JAMA Ophthalmology

Selected and reviewed by Neil M. Bressler, MD, and Deputy Editors

Revised Estimate of VA Loss or Blindness in the United States

July 2021

Flaxman et al. set out to estimate the prevalence of visual acuity (VA) loss and blindness within the United States. They found that more than 7 million people are living with VA loss—and that, of this group, more than 1 million are living with blindness. They also found that a significant number of people with VA loss or blindness are younger than 40 years of age.

For this study, the researchers summarized data from the CDC's Vision and Eye Health Surveillance System, which includes information on visual difficulty or blindness from four national surveys. Using Bayesian meta-regression methods, they then stratified the data by location (U.S. state), age, sex, and ethnicity for the year 2017.

For all VA loss, the researchers estimated that 7.08 million people (95% uncertainty interval [UI], 6.32-7.89 million) live with VA loss (defined as best-corrected VA of 20/40 or worse). This corresponds to a crude prevalence rate of 2.17% (95% UI, 1.94% to 2.42%). By location, crude prevalence rates range from 1.35% in Maine to 3.59% in West Virginia.

In a second calculation, the researchers found that an estimated 1.08 million people (95% UI, 0.82-1.3) live with blindness (BCVA of 20/200 or worse). This corresponds to a crude prevalence rate of 0.33% (95% UI, .02% to .4%), with state-based findings ranging from a crude prevalence of 0.19% in Utah to 0.65% in West Virginia.

Unsurprisingly, rates of VA loss or blindness increase by age—but an estimated 1.62 million persons with VA loss are younger than 40 years, and 141,000 with blindness are younger than 40.

Overall, the estimated number of cases of VA loss or blindness in this study is 68.7% higher than the previous estimate from the Vision Problems in the United States (VPUS) study, although the estimate of blindness alone is lower. (*Also see related commentary by Emily Y. Chew, MD, in the same issue.*)

Link Between Visual Impairment and Depression

July 2021

Parravano et al. evaluated the prevalence of depression in patients with visual impairment who seek eye care. They found that 1 in 4 of these patients experience depression, making it a health problem in patients with such common eye diseases as age-related macular degeneration (AMD).

For this meta-analysis, the researcher evaluated 27 studies with a median sam-

ple size of 125 patients (range, 42-990 patients). All told, data on 6,992 patients (18 years or older) were included. The patients' mean age was 76 years, and the majority (60%) were female.

Although the studies adopted various definitions of visual impairment and used different tools to assess depression, the pooled analysis indicated that the prevalence of depression was high both in clinic-based studies and in those conducted in rehabilitation settings. Moreover, the prevalence did not vary by the extent of disease severity.

Thus, the researchers said, "the results of our review suggest the need for depression screening in patients attending eye clinics who are 65 years or older and have mild to severe visual loss, regardless of comorbidities."

In addition to this increased need for screening, the researchers noted that all eye care professionals need experience not only in recognizing the signs and symptoms of depression but also in determining which patients need to be referred for mental health treatment.

Protocol W: Two-Year Results in Diabetic Retinopathy

July 2021

In Protocol W of the DRCR Retinal Network, Maturi et al. investigated whether treatment with intravitreal aflibercept could prevent vision-threatening complications in eyes with moderate to severe nonproliferative diabetic retinopathy (NPDR). They found that aflibercept was more effective than sham in reducing the likelihood that a patient would develop PDR or center-involved diabetic macular edema (CI-DME). However, the mean change in visual acuity (VA) from baseline to the two-year mark was similar between the two groups.

For this study, the researchers enrolled 328 adults (399 eyes) with moderate to severe NPDR and no CI-DME. Participants' mean age was 57 years, and 57.6% were male. Baseline characteristics were balanced between treatment groups. Participants' eyes were randomly assigned to either sham injections (n = 199) or 2 mg

aflibercept (n = 200). Injections were given at baseline and at months 1, 2, and 4. After that, they were given every four months through year 2. Aflibercept injections were administered as needed if CI-DME developed or when eyes progressed to PDR.

At the two-year mark, preventive treatment with aflibercept resulted in a more than threefold reduction in CI-DME with decreased VA and a more than twofold reduction in new-onset PDR. Even so, 16.3% of aflibercept-treated eyes developed PDR or CI-DME with VA loss by two years. Moreover, VA was roughly equivalent between the two groups: The adjusted mean difference in VA between aflibercept and sham was 0.5 letters.

Protocol W is ongoing and is scheduled to be completed in 2022. (*Also see related commentary by Rajendra S. Apte, MD, PhD, and Christopher K. Hwang, MD, PhD, in the same issue.*)

—Summaries by Jean Shaw

OTHER JOURNALS

Selected by Prem S. Subramanian, MD, PhD

Targeted OCRL Modulation Reduces Steroid-Elevated IOP

Translational Vision Science & Technology

2021;10(6):10

Open-angle glaucoma can be induced by prolonged use of topical glucocorticoids and involves elevated intraocular pressure (IOP) with outflow resistance and abnormal trabecular meshwork (TM) function. Kowal et al. have used an optogenetic approach in TM to regulate 5-phosphatase (5ptase) OCRL, which contributes to regulating phosphatidylinositol 4,5-bisphosphate (PIP2). In a subsequent study, they applied this system with the intent of reversing compromised outflow in a steroid-induced murine model of ocular hypertension. They found that blue-light stimulation caused CRY2-OCRL-5ptase to translocate to plasma membrane and cilia in TM cells, which normalized IOP and outflow activity. Moreover, in cultured human TM cells, they noted that optogenetic stimulation

reduced the aberrant actin structures caused by dexamethasone.

For this study, the authors induced elevated IOP by subconjunctival injection of dexamethasone into wild-type mice. Following this, they injected adeno-associated viruses containing optogenetic modules of CRY2-OCRL-5ptase and CIBN-GFP into the anterior chamber. Four weeks after incubation, they measured IOP by tonometry and assessed outflow facility by perfusion analysis. In a separate evaluation of actin structures, they explored the effects of light stimulation on human TM cells exposed to dexamethasone.

As expected, the dexamethasone raised IOP and lowered outflow facility in the mice. Optogenetic constructs were expressed in the TM of mouse eyes, and light stimulation caused CRY2-OCRL-5ptase to translocate to the plasma membrane (CIBN-CAAX-GFP) and cilia (CIBN-SSTR3-GFP) of TM cells, which rescued the IOP and outflow facility. In human cells, the aberrant actin structures were minimized by optogenetic stimulation.

Subcellular targeting of inositol phosphatases to remove PIP2 is “a promising strategy to reverse defective TM function in steroid-induced ocular hypertension,” said the authors. Their findings support the hypothesis that cytoskeletal alterations and formation of cross-linked actin networks (CLANs) are responsible for the abnormal outflow facility and IOP observed in mice. They concluded that their study offers a new framework for a therapeutic approach based on signaling and emphasized the need to identify precise pathways that lead to formation of OCRL-dependent CLANs.

Intracameral Versus Topical Mydriasis

Journal of Cataract & Refractive Surgery

2021;47(5):570-578

Topical mydriatics for cataract surgery require advance preparation, and multiple instillations are needed during the procedure. In a phase 4 trial, Souki et al. compared eyedrops alone to a protocol including a mydri-

atic-anesthetic solution given intracamerally. They found that intracameral (IC) mydriasis resulted in better ocular surface integrity and higher satisfaction for patients and surgeons.

For this study, researchers enrolled 50 patients between the ages of 40 and 88 years who were slated for bilateral cataract surgery. The patients were assigned randomly to receive either topical drops or an IC mydriatic-anesthetic solution (Mydrane plus Fydrane) plus topical anesthetic drops in one eye for the first surgery. The other treatment was given to the fellow eye for the second surgery. Assessments were performed before surgery, immediately after surgery, at post-op day 1, and at post-op day 7. The primary endpoint was change from baseline in corneal and conjunctival surfaces. Secondary outcomes were epithelial alterations, point-spread function, ocular surface disease index (OSDI), tear film stability assessed by vision breakup time, adverse events (AEs), corrected distance visual acuity (CDVA), intraocular pressure (IOP), patient/investigator satisfaction, and surgery duration.

All eyes received pre-op topical anesthesia (one to two drops of oxybuprocaine chlorhydrate 0.4% + tetracaine chlorhydrate 0.1%). Control eyes also received one drop of tropicamide 1% and phenylephrine 10% at three 10-minute intervals beginning 30 minutes preoperatively, to achieve pupillary dilation. Those randomized to Mydrane/Fydrane received 0.2 mL of the solution, administered slowly into the anterior chamber, just after the first corneal incision.

Changes in corneal and conjunctival surfaces from baseline to day 1 did not differ significantly between treatments, but the Mydrane/Fydrane group had fewer epithelial alterations (p < .005), fewer folliculopapillary reactions (p < .05), shorter procedures (p < .001), less post-op discomfort (p < .05), and greater patient and provider satisfaction (p < .05). AEs were minimal in both groups. Outcomes for point-spread function, CDVA, IOP, and OSDI did not differ significantly but were better with Mydrane/Fydrane.

—Summaries by Lynda Seminara