

Journal Highlights

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

Ophthalmology

Impairments in Dark Adaptation in AMD Patients

October *Ophthalmology*

Flamendorf et al. investigated dark adaptation (DA) in patients with age-related macular degeneration (AMD). They found that impairment in DA was associated with a number of factors, including the presence of reticular pseudodrusen, greater severity of AMD, and decreased subfoveal choroidal thickness.

For this cross-sectional observational study, the researchers recruited 116 participants with AMD who were older than age 50 and had a best-corrected visual acuity (BCVA) of 20/100 or better in their study eye. Patients with advanced AMD in both eyes at baseline were excluded, as were those with any other active ocular or macular disease (e.g., glaucoma or diabetic retinopathy).

The investigators used a prototype of the AdaptDx dark adaptometer to measure DA via rod intercept time (RIT). Study eye imaging was graded for the presence of reticular pseudodrusen, and subfoveal choroidal thickness was measured manually on optical coherence tomography scans.

Increased RIT was associated with

greater AMD severity, increased age, poorer BCVA, pseudophakia, and decreasing subfoveal choroidal thickness. Moreover, patients with reticular pseudodrusen had a greater mean RIT than did those without pseudodrusen; this association held true across all AMD severity groups. This finding complements those from previous studies linking reticular pseudodrusen with rod dysfunction, the authors said.

Electronic Health Records: Financial Return and Effect on Productivity

October *Ophthalmology*



Wiggins et al. presented a detailed financial analysis of 1 practice's experience with the implementation of electronic health records (EHR). They found that their EHR program produced financial and operational benefits over a 5-year period.

At the time of this data capture (2007-2011), the practice had 11 ophthalmologists, 2 optometrists, and 3 locations in western North Carolina. All providers had been in practice for 3 or more years in the community and had full clinic schedules.

During the first month of implementation, patient load was reduced for 7 of the providers; after this, all schedules returned to baseline. During

the second, third, and fourth years, there were no schedule changes. However, during the fifth year, there was a net annual increase in productivity. The authors attribute this to greater familiarity with the EHR program and a greater proportion of returning patients, which decreased the amount of new data entry. They also note that the entire staff took the opportunity to examine workflow efficiency throughout the 5-year period, which led to reductions in staffing in the areas of medical records, transcription, billing, check-out, and appointment scheduling.

The authors point out that although their experience may not translate to other practices, their method of analyzing revenue and expenses may be helpful to those contemplating purchasing an EHR program.

Risk Factors, Outcomes for Multidrug-Resistant *Pseudomonas* Keratitis

October *Ophthalmology*

Vazirani et al. set out to identify risk factors for multidrug-resistant *Pseudomonas aeruginosa* (PA) keratitis and to report associated clinical characteristics and outcomes of infection.

For this retrospective case-control study, the researchers identified 90 episodes of PA keratitis that occurred from 2007 through 2014 at a tertiary care institution. Episodes of multidrug-resistant infections (n = 23) were

designated as cases; episodes of drug-sensitive infection ($n = 67$) served as controls. A number of potential risk factors were evaluated, including age and sex of patient, use of topical steroids or lubricant ointments, history of trauma or ocular surgery, and use of a bandage contact lens.

The authors found that the risk factors for multidrug-resistant PA keratitis are use of a lubricant ointment, presence of a compromised ocular surface, and use of a bandage contact lens. As expected, patients with the drug-resistant form of the infection had poorer outcomes than did those whose keratitis responded to treatment.

The authors recommend culturing all topical medications used by patients with drug-resistant keratitis; in addition, they state that culture of corneal scraping samples and antimicrobial drug sensitivity testing are essential in managing this infection. Antimicrobial susceptibility testing in vitro showed that colistin and imipenem are the most effective drugs against multidrug-resistant PA, but they are not available in ophthalmic formulations.

Intraoperative OCT in Children With Anterior Segment Anomalies

October *Ophthalmology*

Siebelmann et al. reported on their experience with intraoperative optical coherence tomography (OCT) in examining and performing surgery on infants and young children with anterior segment anomalies. They found that use of an operating microscope-mounted OCT device enabled visualization of all relevant anterior segment structures, even in patients with opaque corneas. With this technology, they were able to make diagnostic and therapeutic decisions that would not otherwise be possible; in particular, they were able to avoid unnecessary intraocular surgery in several patients.

This small case series involved 7 children with anterior segment abnormalities (4 corneal opacities, 1 brittle cornea, and 2 cataracts) who underwent either corneal or cataract surgery.

All examination and surgical procedures were performed under general anesthesia.

The authors said that intraoperative OCT was useful in allowing detailed examination of children, particularly those with a restricted view of the anterior chamber. It also permitted differentiation between corneal scars or keloids and Peters anomaly. Further, by providing ongoing monitoring during surgery, it facilitated timely treatment decisions in the OR.

The image quality was limited in 1 eye, which had dense corneal scar tissue, retrocorneally attached iris tissue, and no anterior chamber. The authors suggested that extending the imaging wavelengths to achieve deeper penetration might be helpful in such challenging cases.

American Journal of Ophthalmology

Disease Burden in the Treatment of Age-Related Macular Degeneration

October *AJO*

Prenner et al. performed a mixed-methods study using surveys, interviews, site visits, and time-and-motion observations to examine the burden that managing neovascular age-related macular degeneration (AMD) imposes on physicians, staff, patients, and caregivers.

The multicenter study was conducted from March 2011 through August 2012. First, the researchers conducted ethnographic research by means of site visits at 10 practices, where they “shadowed” AMD patients and conducted postobservational interviews with physicians and staff. They followed this phase with qualitative research involving in-depth interviews with a total of 30 AMD patients and caregivers. Finally, they conducted quantitative research through surveys of retina specialists who administered 50 or more anti-VEGF injections monthly (56 physicians completed records on 221 AMD patients) as well as surveys of 75 AMD patients.

The study found that neovascular AMD patients accounted for 20%

of the health care staff’s time per week, involving an average of 23 staff members. An average patient visit for neovascular AMD was 90 minutes. Patients reported that the average time associated with each visit was almost 12 hours, including preappointment preparation, travel, waiting time, treatment time, and postappointment recovery. Patients stated that caregivers took time away from work and personal activities to provide transportation to appointments.

Based on surveys and interviews of retina physicians and patients, the study quantitatively confirmed that neovascular AMD management imposes a substantial time burden on patients, caregivers, and practices. The authors suggested that additional support and/or reimbursement is needed for services required by patients and caregivers and provided by physicians.

Corneal Collagen Cross-linking for Progressive Corneal Ectasia

October *AJO*

In a study conducted in France, Poli et al. evaluated 6-year results of standardized epithelium-off corneal collagen cross-linking (CXL) for treatment of progressive corneal ectasia using a prospective consecutive, interventional case series. At 6 years, CXL had maintained long-term results in halting the progression of corneal ectasia, with significant improvement in corrected distance visual acuity and long-term stability of keratometry.

Thirty-six eyes of 25 consecutive patients with documented progressive primary or iatrogenic corneal ectasia underwent CXL following the Siena protocol. The main outcome measures at the endpoint, compared with baseline, were the following: uncorrected distance visual acuity, -0.08 ± 0.36 logMAR; corrected distance visual acuity, -0.14 ± 0.28 logMAR; topography-derived steep (K_{max} , $+0.11 \pm 1.70$ D) and flat (K_{min} , -0.25 ± 1.25 D) keratometry; central corneal thickness, -16.38 ± 37 μ m; IOP, $+1.0 \pm 2.3$ mm Hg; and endothelial cell density, $+31 \pm 400$ cells/mm². Bilateral macular optical

coherence tomography was performed at the endpoint visit. The mean follow-up was 66 months.

At 6 years, CXL had stabilized primary and iatrogenic corneal ectasia in 89% of the patients. In bilateral CXL, the progression of the first eye was highly predictive of the fellow eye's outcome. No cases of macular toxicity or severe adverse events were reported.

Retinal Toxicity From High-Dose Hydroxychloroquine

October *AJO*

Leung et al. report on the rapid onset of retinal toxicity in a series of oncology patients receiving a high-dose (1,000 mg daily) hydroxychloroquine regimen. This retrospective observational case study was conducted among patients who were part of a multicenter open-label, randomized controlled trial of hydroxychloroquine with or without erlotinib for advanced non-small cell lung cancer.

At most of the study centers, ophthalmic surveillance was performed using the FDA-recommended screening protocol, which included visual acuity testing, dilated fundus examination, Amsler grid testing, and color vision testing. However, at the Stanford University center, the following sensitive screening procedures were added at the discretion of the retinal physician: high-resolution spectral-domain optical coherence tomography (OCT), fundus autofluorescence (FAF) imaging, Humphrey visual field (HVF) testing, and multifocal electroretinography (mfERG).

Of the 7 patients at the Stanford site who had exposure of at least 6 months, 2 patients developed retinal toxicity (at 11 and 17 months of exposure). Damage was identified by OCT imaging, mfERG testing, and, in 1 case, HVF testing. FAF imaging remained normal. Neither patient had symptomatic visual acuity loss.

These cases suggest that high doses of hydroxychloroquine can initiate the development of retinal toxicity within 1 to 2 years. Although synergy with erlotinib is theoretically possible,

there are no prior reports of erlotinib-associated retinal toxicity despite more than a decade of use. The authors encouraged other investigators to incorporate modern, sensitive retinal screening techniques into their surveillance plans for future trials of high-dose hydroxychloroquine regimens.

Cataract Surgery Outcomes in Glaucomatous Eyes

October *AJO*

Turalba et al. compared visual acuity outcomes, vision-related quality of life, and complications related to cataract surgery in eyes with and without glaucoma, using a retrospective cohort study design. They found that eyes with glaucoma were more likely than those without glaucoma to experience cataract surgery complications.

Cataract surgery outcomes in eyes with glaucoma (cases) and without glaucoma (controls) from the Veterans Affairs Ophthalmic Surgical Outcomes Data Project were compared. The researchers identified 608 glaucoma cases and 4,306 controls who were undergoing planned cataract surgery. After adjustment for many factors, the glaucoma cases were more likely than the controls to have posterior capsular tear with vitrectomy and sulcus IOL placement during cataract surgery. Glaucoma cases were also more likely to have postoperative inflammation, prolonged elevated IOP, and additional surgery within 30 days.

Mean best-corrected visual acuity (BCVA) and Visual Function Questionnaire (VFQ) scores significantly improved after cataract surgery in both groups, but there were larger improvements in BCVA and VFQ composite scores in the controls than in the glaucoma cases. A postoperative BCVA of 20/40 or better was attained in 94% of control eyes and in 89% of glaucoma case eyes.

Eyes with glaucoma had a higher risk for complications related to cataract surgery, even when the researchers controlled for risk factors such as age, pseudoexfoliation, small pupils,

shallow anterior chamber depth, and prior ocular surgery. Glaucoma cases experienced more modest visual improvement compared with control eyes. Nevertheless, glaucoma patients still experienced substantial benefits in BCVA and vision-related quality-of-life outcomes after cataract extraction.

JAMA Ophthalmology

Cost-Related Medication Nonadherence and Cost Savings in Patients With Glaucoma

September *JAMA Ophthalmology*

Understanding factors that lead to nonadherence to glaucoma treatment is important in reducing glaucoma-related disability. **Blumberg et al.** evaluated how implementation of the Medicare Part D prescription drug benefit in 2006 affected cost-related nonadherence and cost-reduction strategies among Medicare beneficiaries with and without glaucoma. They also examined risk factors associated with such nonadherence.

This serial cross-sectional study used 2004-2009 Medicare Current Beneficiary Survey data linked with Medicare claims. Data extraction began in January 2014, and analyses were performed between September and November of 2014. Participants were all Medicare beneficiaries; they included patients with a glaucoma-related diagnosis in the year prior to the collection of the survey data, those with a nonglaucomatous ophthalmic diagnosis in the year prior to the collection of the survey data, and those without a recent eye care professional claim.

Between 2004 and 2009, the number of Medicare beneficiaries with glaucoma who reported taking smaller doses and skipping doses because of cost dropped from 9.4% and 8.2% to 2.7% ($p < .001$) and 2.8% ($p = .001$), respectively. However, failure to obtain prescriptions owing to cost did not improve significantly in the same period (3.4% in 2004 and 2.1% in 2009; $p = .12$). After implementation of Part D, there was a decrease in the percentage of glaucoma patients using

cost-reduction strategies, for example, price shopping (from 26.2% to 15.2%), purchasing outside the United States (from 6.9% to 1.3%), and spending less money on basic needs to save for medications (from 8.0% to 3.5%; $p < .001$ for all comparisons).

In a multivariate analysis, the main independent risk factors common to all cost-related nonadherence measures were female sex, younger age, lower income (<\$30,000), self-reported visual disability, and a smaller Lawton index (a measure of independence in activities of daily living).

The authors concluded that after the implementation of Part D, there was a decrease in the rate at which beneficiaries with glaucoma reported engaging in cost-saving measures. Although there was a decline in the rate of several cost-related nonadherence behaviors, patients reporting failure to fill prescriptions because of cost remained stable. The results suggest that efforts to improve cost-related nonadherence should focus on both financial hardship and medical therapy prioritization, particularly in certain high-risk sociodemographic groups.

Behavioral Intervention and Rates of Dilated Fundus Examination

September *JAMA Ophthalmology*

Data show that African-American individuals are at high risk of diabetes mellitus and diabetic retinopathy (DR) but have suboptimal rates of dilated fundus examinations (DFEs). Thus, Weiss et al. tested the efficacy of a program of behavioral activation for DR prevention on rates of DFEs in older African-American patients in a masked randomized clinical trial at 2 urban medical centers from Oct. 1, 2010, to May 31, 2014.

Participants included 206 African-American individuals aged 65 years and older with diabetes mellitus who had not obtained a DFE in the preceding 12 months. Participants were randomized either to behavioral activation for DR prevention or to supportive therapy (the control group). In this study, behavioral activation

was designed to provide education to patients, to help them identify and address health care barriers, and to promote goal setting to improve rates of DFEs. The primary outcome was medical documentation of a DFE at 6-month follow-up. Secondary outcomes included the Risk Perceptions and Risk Knowledge Survey of Diabetes Mellitus, Diabetes Self-Care Inventory, Patient Health Questionnaire 9, and National Eye Institute Visual Function Questionnaire 25 scores, as well as hemoglobin A_{1c} levels.

The results showed that more participants in the behavioral activation group (87.9%) had obtained a DFE compared with those in the supportive therapy group (34.1%) by the 6-month follow-up assessment ($p < .001$). Overall, participants in the behavioral activation group were 2.5 times more likely to obtain a DFE compared with those in the supportive therapy group (risk ratio, 2.58; $p < .001$). No short-term effect on secondary outcomes of hemoglobin A_{1c} levels, depression, or the Risk Perceptions and Risk Knowledge Survey of Diabetes Mellitus, or National Eye Institute Vision Function Questionnaire 25 composite scores was identified; however, both groups had improved adherence to diabetes mellitus self-care behaviors from baseline to 6-month follow-up.

The authors concluded that behavioral activation for DR prevention significantly increased rates of DFEs in older African-American individuals with diabetes mellitus, suggesting that behavioral interventions may have the potential to positively affect screening for DR in at-risk populations.

Elevated IOP After Intravitreal Triamcinolone Acetonide

September *JAMA Ophthalmology*

The Standard Care vs. Corticosteroid for Retinal Vein Occlusion (SCORE) Study showed that intravitreal triamcinolone acetonide (IVTA) is effective at reducing macular edema and improving visual acuity in participants with retinal vein occlusion (RVO). In this secondary analysis,

Aref et al. assessed the incidence, risk factors, and timing of IOP elevation after IVTA.

SCORE was a randomized clinical trial conducted between 2005 and 2009 at 75 sites, involving patients with macular edema secondary to RVO. In that trial, participants were randomized to standard care, 1 mg of IVTA, or 4 mg of IVTA and followed for a mean of 24.7 months.

In the current study, data from 616 of the 682 original SCORE patients were analyzed. Kaplan-Meier incidences of IOP elevation greater than 10 mm Hg from baseline at 36 months were 0.02, 0.09, and 0.45 in the standard care, 1-mg IVTA, and 4-mg IVTA groups, respectively. The rates of IOP-related events were higher for the 4-mg IVTA group compared with the other groups ($p \leq .001$ for main outcome measure). Younger age, 4-mg IVTA vs. 1-mg IVTA treatment, and higher baseline IOP were found to confer greater risk for IOP-related events ($p < .05$ for all). The median number of days elapsed from time of first injection to IOP elevation greater than 10 mm Hg from baseline was 34.0 and 52.5 days in participants treated with 1-mg and 4-mg IVTA, respectively.

These data indicate that IVTA therapy, particularly the 4-mg dose, is associated with an increased risk for IOP elevation and that IOP-related events may take several months from the time of first IVTA injection to occur. The authors urged clinicians to be mindful of the risk factors associated with IOP increase when they weigh the risks and benefits of IVTA therapy and also of the need for long-term follow-up of patients at risk for this complication.

Ophthalmology summaries are written by Jean Shaw and edited by Susan M. MacDonald, 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).

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