Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

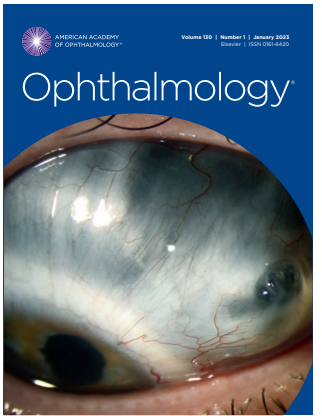
Selected by Russell N. Van Gelder, MD, PhD

Risk of *Acanthamoeba* Keratitis in Contact Lens Users

January 2023

Acanthamoeba keratitis (AK) is a vision-threatening condition that occurs mainly in contact lens (CL) wearers whose eyes are healthy. **Carnt et al.** conducted a case-control study to compare AK rates between wearers of single-use daily disposable (DD) lenses and reusable daily wear (DW) lenses. They also explored risk factors for AK among DD lens users. They found a higher risk of AK in the DW group, and they identified several modifiable factors that can decrease this risk, including removing lenses before showering.

The case and control participants of the study were recruited from an emergency ophthalmology department that serves South-East England. All wore DD or DW lenses. Those in the case group (n = 83) presented with keratitis, and those in the control group (n = 122) had a disorder thought to be unrelated to CL wear. Patients in both groups received a 48-item questionnaire, and the case group was given 15 additional questions. Domains included demographics, history of CL wear, disinfection solutions, environment of CL use, and frequency of eye care. Responses were compiled and analyzed. Outcomes of interest were independent risk factors and the population-attributable risk percentage (PAR%) for AK.



Among the study population, 24% of the case group and 54% of the controls used DD lenses; the others wore DW lenses. Multivariable analyses, adjusted for potential confounders, showed that AK risk was higher with reusable soft DW lenses (OR, 3.84) and rigid gas-permeable DW lenses (OR, 4.56) than with DD lenses. Among DD users with AK, several modifiable risk factors were identified: lower frequency of professional follow-up visits (OR, 10.12), showering with lenses in place (OR, 3.29), reusing lenses (OR, 5.41), and wearing them overnight (OR, 3.93). PAR% findings demonstrated that 30% to 62% of AK cases could be prevented by switching to DD lenses.

Although AK risk is about threefold higher with DW lenses, this can be lowered by improving CL hygiene and increasing the frequency of follow-up care, as noted in this study. Given that AK accounts for half of the severe keratitis cases in CL users, these safety measures are expected to benefit public health, said the authors, who emphasized the importance of identifying modifiable risk factors for AK. "Unlike bacterial keratitis in CL users, 90% of cases are associated with avoidable risks." The data may encourage more CL wearers to switch to DD lenses and avoid lens reuse, overnight wear, or contamination by water. They believe that manufacturers could help to improve safety by including clear risk-avoidance information on CL packaging.

Factors Linked to Keratoplasty for Fuchs

January 2023

In recent years, endothelial keratoplasty (EK) has eclipsed penetrating keratoplasty (PK) as the preferred treatment for Fuchs endothelial corneal dystrophy (FECD). Previous work by **Heckenlaible et al.** showed that among Medicare members, White patients were twice as likely as Black patients to receive surgery for FECD. In a newer study, the same investigators mined a large Medicare database, spanning 10 years of claims, and found that men were more likely than women to undergo either type of keratoplasty and that White patients were more likely than others to undergo PK but not EK. The odds of receiving PK were higher for patients with concurrent diabetic retinopathy (DR) or glaucoma.

The recent study was retrospective in nature and included Medicare beneficiaries (≥65 years) who received an FECD diagnosis from 2011 through 2019 and had not been treated previously for the disease. To determine demographic and medical factors associated with EK and PK, the investigators used a multivariate logistic regression

model that included age, race/ethnicity, sex, geographic location, comorbidities, surgery history, and socioeconomic status. Kaplan-Meier survival curves were generated to establish the rate of EK after cataract and various types of ocular surgery, including complex and other anterior segment procedures.

Among the relevant Medicare population (N = 719,066), 31,372 (4.4%) had EK and 2,426 (.3%) had PK. According to multivariable analysis, female sex lowered the likelihood of EK and PK (adjusted OR [aOR], .83 and .84, respectively). Factors that raised the odds of either EK or PK were Western U.S. residence versus Southern residence (aOR, 1.33 and 1.25, respectively) and history of complex or other anterior segment surgery (aOR, 1.62 and 5.52, respectively). Relative to White patients, Blacks (aOR, 0.76), Asians and Pacific Islanders (aOR, 0.54), and Hispanics/Latinos (aOR, 0.62) were less likely to have EK and more likely to have PK (aOR, 1.32, 1.46, and 1.62, respectively). One year after cataract surgery, the overall probability of EK was 1.3%; by eight years, it increased to 2.3%. Among patients with complex or other surgery of the anterior segment, the EK rate was 3.3% at one year and 5.6% at eight years. Comorbidities that reduced EK likelihood were DR, age-related macular degeneration, macular hole, and epiretinal membrane, likely due to the low potential for visual improvement, said the authors. PK was more common in patients with comorbid DR or glaucoma.

Although complex ocular anatomy may be a key driver for PK, a link to race and ethnicity persists. Findings of this study "may be useful when counseling patients about rates of EK after cataract or complex surgeries," said the authors, and "may inform future efforts to increase diversity in clinical trial recruitment for FECD."

Extra OCT Scans May Be Needed to Determine Glaucoma Progression Rate

January 2023

Thickness of the peripapillary retinal nerve fiber layer (RNFL) as measured by OCT is a common metric to assess glaucoma progression and guide treatment, but how many scans are needed to accurately establish the progression rate? **Bradley et al.** set out to answer this question, with the goal of providing evidence-based guidelines for practitioners. In their large cohort of adults with confirmed or suspected glaucoma, they found that increasing the number of scans obtained in a two-year period from three to seven could boost accuracy by 20% or more.

For this descriptive simulation study, the researchers included 12,150 eyes (7,392 adults) who were suspected or confirmed to have glaucoma and received follow-up at Wilmer Eye Institute during a nine-year period. Each eye had at least five measurements of RNFL thickness by Cirrus OCT, with signal strength of six or higher. Linear regression was applied to measure rates of RNFL worsening for average RNFL thickness and for each of the four quadrants.

Simulations were used to estimate the accuracy of detecting worsening, defined as the proportion of patients for whom the true rate of RNFL worsening was at or below different criterion rates of worsening when the OCT-measured rate was also at or below the same rates. Two measurement strategies were used: evenly spaced (equal time intervals between measurements) and clustered (approximately 50% of measurements obtained at each period's end point). Main outcome measures were the 75th percentile (moderate) and the 90th percentile (rapid) rates of RNFL worsening for average RNFL thickness, as well as accuracy of the diagnosed worsening at both rates.

The mean RNFL thickness at baseline was 87.50 µm, and the mean interval between measurements was 390 days. The 75th and 90th percentile rates of worsening for average RNFL thickness were –1.09 µm/year and –2.35 µm/year, respectively.

The simulations demonstrated that, for the average measurement frequency in the study population (approximately three OCT scans within two years), the diagnosis of moderate and rapid RNFL worsening was accurate for only 47% and 40%, respectively. According to the analysis, achieving accuracy of at least 60% would require seven scans. Accuracy of 70% would require 14 scans for moderate-rate progression and 16 scans for rapid-rate progression. The clustered-measurement strategy was more accurate.

The authors suggest using a clustered-measurement strategy when practical, with multiple scans obtained at each visit. They emphasized that OCT scans take little time and are patient-friendly. They recommend further research to define the best approach for obtaining clustered OCT measurements. To their knowledge, the currently available OCT software does not permit inclusion of clustered measurements in linear regression models of RNFL progression.

—Summaries by Lynda Seminara

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Assessing Photoreceptor Status in Pegcetacoplan-Treated Patients With AI

January 2023

Riedl et al. used spectral-domain OCT (SD-OCT) and artificial intelligence–based algorithms to assess the ability of intravitreal pegcetacoplan to inhibit photoreceptor (PR) loss and thinning in geographic atrophy (GA). They found that this strategy enabled them to report the condition of PRs with high precision, including both PR loss and thinning.

For this post hoc analysis of 246 patients (246 eyes), the researchers evaluated 12-month data from the FILLY trial, which investigated the safety and efficacy of pegcetacoplan, which inhibits complement component 3 (C3), for the treatment of GA. They limited this follow-up investigation to only those eyes imaged using the Spectralis OCT (161 eyes of 161 participants), using scans acquired at baseline and at months 2, 6, and 12.

The difference in the change of the area of PR loss was compared among the trial's cohorts (monthly treatment,

bimonthly treatment, and sham injections), along with the change in PR thickness adjacent to the GA borders and the entire 20-degree scanning area. The main outcome measures were the area of PR loss, PR thickness, and ratio of PR loss to retinal pigment epithelium (RPE) loss.

All told, 31,556 B-scans of 644 SD-OCT volumes were evaluated with a convolutional neural network that delineated the PR layer on each B-scan. Of the 162 participants, 52 had received monthly pegcetacoplan injections, 54 were given bimonthly injections, and 56 served as controls.

The results of the analysis showed statistically significant less growth in the area of PR loss in the monthly treatment group than in controls at all time points. In addition, PR thinning was significantly reduced under monthly treatment than with sham injections within the GA junctional zone as well as throughout the 20-degree scanning area. Finally, the analysis found a trend toward greater inhibition of PR loss than RPE loss in those who were actively treated.

In their discussion, the authors note that the results provide "objective proof of principle that complement inhibition can indeed preserve PRs as the major correlate of retinal function." They also pointed out that automated quantification of PR loss and/or maintenance, using OCT images, is a fast and accurate method of monitoring patient progression.

—Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Printed Materials Provided at ED Discharge Boost Follow-Up Rates

January 2023

Studies have shown wide-ranging rates of compliance to follow-up care after emergency department (ED) visits, and it is difficult to predict which patients won't comply. Furthermore, data on follow-up after ophthalmic-related ED visits are lacking. **Dong et al.** looked at factors that may discourage follow-up care and tested an intervention aimed at improving compliance. Their protocol, which included written materials, led to significantly better compliance rates.

This prospective study included an intervention group and historical controls. Follow-up care was defined as presentation to the ophthalmology clinic of Jamaica Hospital (New York City) within six weeks of an ED visit at the same hospital.

Patients in the intervention group (n = 199) received verbal instructions, written instructions, and follow-up telephone calls. If they did not take action, a letter was mailed to their home. Those in the control group (n = 763) received verbal instructions only. The main outcome measure was the difference in overall follow-up rates between the study cohorts. Other outcomes were follow-up rates for demographic subsets. The authors developed a diagnostic classification system for their study, with risk of adverse outcomes ranked from lowest (class I) to highest (class V).

Results of the data analysis showed that follow-up was significantly more common in the intervention group (68.8% vs. 42.9% in the control group; $p < .001$). Significant improvement also occurred in most demographic subgroups. Exceptions included young adults (18-29 years of age), patients with diagnosis severity class III, patients without insurance, those with hospital financial aid, and patients with unknown employment status. The strongest predictors of obtaining follow-up were having health insurance, having class IV disease severity, and receiving the intervention.

Of note, control participants with class V severity also were unlikely to pursue follow-up care. This was surprising, the authors noted, as these patients have the greatest risk for loss of vision and loss of life.

Moreover, there are sight- and life-threatening conditions that have only mild symptoms, further emphasizing the importance of timely follow-up. It may be possible to boost follow-up rates for the least-compliant patients by targeting and tailoring efforts to them, said the authors.

Standalone Phacoemulsification Lowers IOP Significantly

January 2023

Rothman et al. analyzed IRIS Registry data to determine the real-world IOP changes produced by standalone phacoemulsification. They compared the data with baseline IOP values for the same eyes and for phakic fellow eyes (controls) that subsequently underwent cataract removal. They found that eyes with and without glaucoma that received the standalone surgery had significantly lower IOP in the 90-day postoperative period relative to baseline and fellow-eye IOP.

This retrospective cohort study included 1,334,868 patients in the IRIS Registry. Of these, 336,060 had glaucoma. All patients received standalone phacoemulsification in one eye, and their fellow eye later underwent cataract surgery. Mean daily IOP values were obtained and compared for surgical and control eyes from post-op day 1 to day 90. A generalized linear model was applied to determine when the postoperative daily mean IOP stabilized, which represented the final mean IOP. This IOP value was compared with baseline IOP.

Shortly after surgery, mean IOP spiked initially. However, by postoperative day 13, the daily mean IOP was significantly lower for surgically treated eyes ($p < .001$ vs. controls), which persisted through 90 days postoperatively. The mean final IOP of eyes that had surgery was 1.55 mm Hg lower than their baseline value, representing a reduction of 7.79%. After the standalone procedure, final IOP was 1.91 mm Hg lower for glaucomatous eyes (8.89% reduction) and 1.37 mm Hg lower for eyes without glaucoma (7.24% reduction). Regardless of glaucoma status, nearly all eyes treated surgically had a significant IOP decline ($p < .0001$); the exception was eyes with uveitic glaucoma ($p = .0016$).

Despite the limitations of retrospective research, this study provides meaningful evidence of the IOP-low-

ering effect of standalone phacoemulsification, said the authors, which was more pronounced in eyes with glaucoma, ocular hypertension, primary angle closure, and pseudoexfoliation.

—Summaries by Lynda Seminara

JAMA Ophthalmology

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

When Patients Use Google to Find an Eye Doctor

December 2022

What happens when potential patients conduct a Google search for "eye doctor near me"? **Soares et al.** examined this issue and found that, in most counties in the United States, ophthalmologists are underrepresented in the search results.

For this cross-sectional study, the researchers used a Google application programming interface to search the phrase "eye doctor near me" from the centroid of every county in the United States. They then used CMS data to estimate the real number of ophthalmologists and optometrists in each county. The primary outcome was the mean proportion of ophthalmologists listed by the Google search as compared with the real proportion of ophthalmologists.

A total of 2,955 counties from all 50 states and two territories were included. The national Google proportion of ophthalmologists was 28.91%, which was less than their real proportion (37.58%). Ophthalmologists were underrepresented in 33 of the 52 states and territories (67.3%).

To counteract this imbalance, the researchers recommend that ophthalmologists actively pursue search engine optimization (SEO) marketing techniques to boost their online presence. As they point out, when it comes to physician websites and online patient education material, "Great content alone is no longer the determining factor for being featured in internet searches. The proper SEO keywords need to be embedded within the content." *(Also see related commentary by Jayanth Sridhar, MD, in the same issue.)*

IOP Variations and RNFL Thinning in OAG

December 2022

Nishida et al. set out to investigate the association of mean IOP and IOP variability with the rate of retinal nerve fiber layer (RNFL) thinning over time in patients with open-angle glaucoma (OAG). They found that IOP variability was independently associated with structural change in these patients, even after adjustment for mean IOP.

For this retrospective analysis, the researchers evaluated 508 patients (815 eyes) who had participated in two longitudinal studies and had at least four visits and two years of follow-up with OCT and IOP measurements. The patients' mean age was 65.5 years (SD, 11 years), and the majority were female (55.1%) and White (55.3%). Of the 815 eyes, 564 had perimetric and 251 had preperimetric glaucoma. A linear mixed-effect model was used to investigate the association of IOP parameters with the rates of RNFL thinning. Dominance analysis was performed to determine the relative importance of the IOP parameters. Eyes were categorized into groups (fast, medium, and slow progressor) according to their rate of RNFL thinning.

During follow-up (mean, 6.3 years), mean IOP was 14.8 mm Hg, peak IOP was 18.8 mm Hg, IOP fluctuation was 2.4 mm Hg, and IOP range was 7.4 mm Hg. All IOP measurements were highest for the fast progressor group. With regard to RNFL change, the mean rate was –.67 per year (95% CI, –.73 to –.60)—and in multivariable models adjusted for mean IOP and other confounding factors, a faster annual rate of RNFL thinning was associated with a higher SD of IOP. Among the portion of change that could be attributed to IOP measurements, IOP fluctuation had a greater impact than did mean IOP.

In their discussion, the authors note several limitations of this analysis—for instance, they did not exclude patients who showed signs of disease progression and may have received glaucoma-lowering drugs. Nonetheless, they suggest that the addition of IOP variations to mean IOP measurements may have clinical utility. *(Also see related commentary by Paul F. Palmberg, MD, PhD, in the same issue.)*

Social Determinants of Health and Visual Impairment

December 2022

Which social determinants of health (SDOH) are associated with severe visual impairment (VI) in the United States? **Besagar et al.** investigated this question and found multiple social disparities and barriers to health care access.

For this quality improvement study, the researchers used cross-sectional data for 2019 and 2020 from the Behavioral Risk Factor Surveillance System (BRFSS), an annual telephone survey conducted by the CDC. The main outcome was severe VI associated with factors such as race/ethnicity, household income, education level, and employment status.

From January 2019 to December 2020, 820,226 people (53.07% female) participated in the BRFSS survey. Of these, 42,412 (5.17%) self-identified as being blind or having "serious difficulty" seeing, even while wearing glasses.

For the demographic factors analysis, the researchers evaluated 77.3% of the total surveyed participants (n = 633,866). The results were as follows:

- **Race/ethnicity.** Compared with Whites, non-Hispanic individuals, who served as the reference value (OR, 1), the risk of severe VI was highest for Hispanic, Native American, Black, and multiracial individuals (ORs, 1.65, 1.63, 1.50, and 1.33, respectively).
- **Income.** Household income less than $35,000 per year was associated with greater odds of severe VI, while income of $50,000 or more was associated with decreased odds. Those with the lowest annual income (<$10,000) had an OR of 1.70, while those with the highest income (>$75,000) had an OR of .59.
- **Education.** Those who did not complete high school had an OR of 1.50, versus .73 for those who completed college or a technical school.
- **Employment status.** Those who re-

ported not working for a year or more, being retired, or being unable to work also had greater odds of severe VI; the ORs for these participants were 1.78, 2.03, and 2.90, respectively.

- **Access to care.** For the analysis of health care access factors, the researchers evaluated 90% of the total surveyed participants (n = 734,614). The results of this analysis indicated that lack of health care coverage was associated with a greater likelihood of severe VI (OR, 1.22). Those who had needed care in the last 12 months but who could not afford it also had greater odds of severe VI (OR, 1.62). *(Also see related commentary by Patrice M. Hicks, PhD, MPH; Maria A. Woodward, MD, MS; and Paula Anne Newman-Casey, MD, MS, in the same issue.)*

—Summaries by Jean Shaw

Other Journals

Selected by Prem S. Subramanian, MD, PhD

Potential Biomarkers of Ischemic Stroke

Translational Vision Science & Technology
2022;11(10):21

There is mounting evidence that the microvascular damage associated with small vessel disease is a major cause of ischemic stroke, but the resolution of neuroimaging techniques may not allow for direct visualization of minor changes. Little is known about the relationship between ischemic stroke and abnormal OCT angiography (OCTA) findings in the setting of machine learning. **Duan et al.** combined OCTA and machine learning to quantitatively assess retinal microvasculature of the superficial and deep capillary plexuses. In particular, they explored geometric changes of the retinal microvasculature and the foveal avascular zone (FAZ) in patients with ischemic stroke. Their findings suggest that the FAZ axis ratio and FAZ circularity of the deep capillary plexus may be potential biomarkers of ischemic stroke. Moreover, OCTA depicted distinct patterns of damage in the retinal microvascular and macular morphology for the common subtypes of ischemic stroke.

For this study, the researchers evaluated 33 patients who experienced ischemic stroke (14 nonlacunar infarctions, 19 lacunar infarctions) and 27 control participants.

Based on OCTA, three vascular parameters were extracted and analyzed for the superficial and deep capillary plexuses: vascular area density, vascular fractal dimension, and vascular orientation distribution. In addition, four FAZ-related parameters were assessed for the same plexuses: area, roundness, axis ratio, and circularity. Regression analysis was performed, and odds ratios were determined.

According to multivariate logistic regression analysis, factors independently linked to ischemic stroke were poor BCVA (OR, .21), high FAZ axis ratio of the deep capillary plexus (OR, 2.77), and low FAZ circularity of the deep capillary plexus (OR, .36). Low vascular orientation distribution of the superficial capillary plexus correlated strongly with lacunar infarction. However, no other parameter had a significant relationship to ischemic stroke or to either subtype.

"Our study adds to the knowledge of the retinal microvasculature and FAZ in ischemic stroke and its subtypes," said the authors. Their findings suggest that FAZ axis ratio and FAZ circularity of the deep capillary plexus may serve as potential biomarkers of ischemic stroke.

Tackling Pediatric Visual Impairment Requires Extra Vigilance

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Children who are blind or otherwise visually impaired are at risk for poor health, low education, low socioeconomic status, and adverse psychosocial outcomes. Data on vision-impairing conditions affecting children are lacking for many countries, and there are disparities in the definitions of avoidable, preventable, and treatable blinding disorders. **Solebo et al.** set out to address the information gap and quantify the current burden of avoidable childhood visual impairment (VI) in the United Kingdom. They found that about 30% of children have a disorder that is considered treatable or preventable.

The investigation, known as the British Childhood Visual Impairment and Blindness Study 2 (BCVIS2), is a national prospective longitudinal study of pediatric patients with a new diagnosis of vision worse than 0.48 logMAR in both eyes. Outcome measures were the proportion of participants with an avoidable disorder, defined as "treatable" (isolated disorder for which readily available effective interventions can improve vision or halt visual loss) or "potentially preventable" (isolated disorder with interventions proven to reduce disease incidence). Treatable conditions included cataract, glaucoma, tumors of the visual pathway, and retinopathy of prematurity (ROP). Potentially preventable disorders included eye injury, congenital infections, autosomal inherited disorders with an established family history, and hypoxic-ischemic encephalopathy in the absence of a coexisting cause of unavoidable blindness.

Among the 784 children in BCVIS2, 313 had moderate VI, and 471 had severe VI. Of those with purely isolated causes of VI, 132 had disorders that were potentially preventable, including hypoxic-ischemic encephalopathy (n = 64) and autosomal inherited disorders (n = 46). Another 99 children had treatable conditions; the most common were cataract (n = 42), ROP (n = 27), and glaucoma (n = 21).

The World Health Organization has developed supranational guidance for community- and hospital-based eye and vision care, but uptake of the strategies to prevent and treat key blinding disorders in children varies throughout the world, reflecting transitions in health care that accompany economic changes.

Although many high-income nations have substantially improved efforts to address childhood VI in recent decades, greater vigilance is needed to ensure effective implementation of prevention and treatment programs, said the authors.

—Summaries by Lynda Seminara