GLAUCOMA

CyPass Update: IOP Effect Seen, Cell Loss Noted

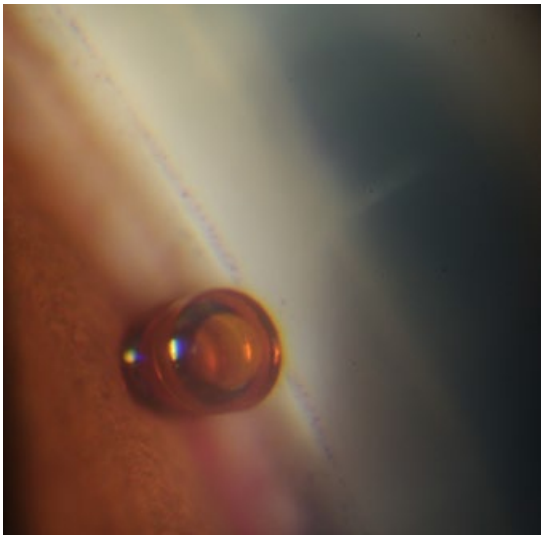
FIVE YEARS OF PATIENT FOLLOW-UP has confirmed that late endothelial cell loss occurs in mild to moderate open-angle glaucoma (OAG) patients implanted with the CyPass supraciliary microstent, combined with cataract surgery. But the remaining cells continued to keep the corneas clear, and the microstent reduced intraocular pressure (IOP) throughout the study.[1,2]

Alcon withdrew the CyPass from the market in August 2018, and the FDA later issued a class 1 recall. These steps were triggered by earlier monitoring results, which suggested that CyPass-treated eyes had accelerated cell loss at four and five years after surgery.

Recent findings. COMPASS XT investigators reported a mean decrease in endothelial cell density (ECD) of 20.4% in the CyPass eyes at five years after the combined surgery, compared to a mean 10.1% drop in the phacoemulsification-only control eyes.

This contrasted with the results at two years, when there was no difference in mean ECD between the two groups, said Jonathan H. Lass, MD, at Case Western Reserve University and University Hospitals Eye Institute in Cleveland.

"This is going to alert cornea and glaucoma specialists to be looking more closely at these patients over the long term. And then if they see signs of endothelial cell loss, such as the development of localized or diffuse striae and/or corneal edema, to do specular microscopy to evaluate the eyes further," Dr. Lass said. "I would also refer clinicians to the ASCRS consensus statement regarding management."[3]



George R. Reiss, MD

IN PLACE. *A well-positioned CyPass in the supraciliary space with distal opening in front of the trabecular meshwork.*

Other five-year outcomes with the CyPass device were positive, said principal investigator George R. Reiss, MD, at Eye Physicians and Surgeons of Arizona, in Glendale and Scottsdale. The device was "well tolerated in the majority of patients," he noted. "As compared with phacoemulsification alone, the group with CyPass had better pressure reduction and was more likely to be off medications."

At five years, the mean reduction in IOP was slightly greater in the microstent cohort (8.4 mm Hg; 95% confidence interval [CI]: 7.8-8.9) than in the control group (8.0 mm Hg; 95% CI: 6.8-9.2), the investigators reported. (However, the study was not powered sufficiently to evaluate effectiveness with statistical significance.)

Adverse events were few, and there were no serious device-related adverse events. Three of the eyes had transient focal corneal edema in the region of the microstent at 33, 55, and 60 months, but no persistent corneal edema occurred in any eyes, the researchers reported.

Innate resilience? Previous studies of other causes of endothelial damage have shown that the endothelium is resilient, and this possibly explains why the corneas of patients who had received the CyPass remained healthy despite localized cell loss, Dr. Lass said.

"The issue is not the absolute endothelial cell density so much as it is the rapidity of the damage occurring. Because, even at low cell counts, the remaining cells—if given the chance—have the ability to adapt," Dr. Lass said. "They get larger, change shape and size, increase the number of pump sites on their lateral margin, and migrate over to mitigate the damage. That's probably what's happening here, but further studies are needed."

Looking ahead. CyPass was originally approved for mild to moderate glaucoma, but it might be more appropriate for use in more severe glaucoma cases in which surgical IOP reduction without bleb formation is desired, the COMPASS XT investigators suggested.

"Hopefully the device will make its way back into the market," Dr. Reiss

said. "Many glaucoma specialists miss this supraciliary stenting option."

—Linda Roach

1 Reiss G et al. *Am J Ophthalmol.* Published online Aug. 1, 2019.
2 Lass JH et al. *Am J Ophthalmol.* Published online Aug. 1, 2019.
3 Rhee D et al. Preliminary ASCRS CyPass Withdrawal Consensus Statement. https://ascrs.org/CyPass_Statement. Accessed on Sept. 18, 2019.
Relevant financial disclosures—Dr. Lass: Alcon: S; Transcend Medical: S. Dr. Reiss: Aerie: L; Alcon: C,L,S; Allergan: C,S; Bausch Medical: L; Glaukos: L; Santen/InnFocus: C,S.

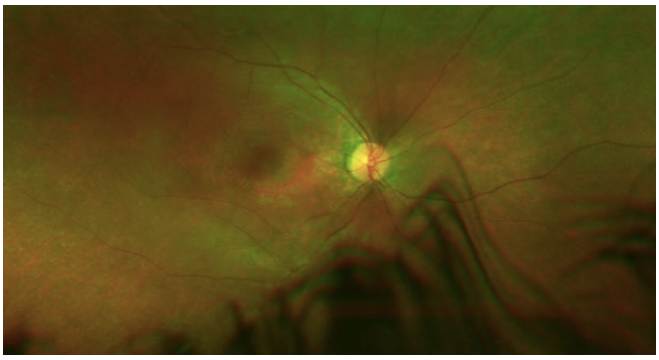
PEDIATRICS

Genetic Dx in Kids: Knowledge Needed

MANY EARLY-ONSET OCULAR DIS-orders are genetic, yet pediatric ophthalmologists lack a solid understanding of genetic disorders and how to approach them, according to a survey conducted by the American Association for Pediatric Ophthalmology and Strabismus (AAPOS) Genetic Eye Disease Task Force.[1]

"No one can know everything," conceded task force chair Arlene V. Drack, MD, at the University of Iowa in Iowa City. "But pediatric ophthalmologists should be able to recognize a disorder as potentially genetic and either pursue a workup or refer to the appropriate subspecialist."

The 16-question survey, which was emailed to 1,489 AAPOS members, focused on physicians' ability to understand and use genetic tests and to counsel patients. While most respondents (93%) reported caring for children with genetic eye disorders on a weekly basis, nearly half (48%) reported no understanding of genetic testing modalities. A majority (81%) described themselves as "a little or not at all comfortable" explaining genetic test results



EARLY DX. *Nystagmus in an infant, along with visual loss, should raise suspicion for Leber congenital amaurosis (shown here). An FDA-approved therapy is now available for selected cases.*

NEURO-OPHTHALMOLOGY

Visual Signs May Herald Parkinson Disease

MAYO CLINIC RESEARCHERS HAVE FOUND THAT visual abnormalities are among the most frequent nonmotor symptoms in the early stages of Parkinson disease (PD).[1] In some cases, visual symptoms could indicate PD onset before more specific physical signs and symptoms develop. They may even predict disease progression.

"Parkinson can affect almost any part of the visual system, including subtle changes in the retina, ocular motor function, and cortical visual processing," said John J. Chen, MD, PhD, at the Mayo Clinic in Rochester, Minnesota.

The early signs. In a literature review, Dr. Chen and his colleagues described the ophthalmic abnormalities that can be seen in PD and outlined how dopaminergic therapy can influence these symptoms. For instance, they noted that impairments in color vision and contrast sensitivity in PD patients may be related to the loss of dopaminergic neurons in the retina.

"These visual manifestations are important to recognize because some of them will be symptomatic in our patients, while others may end up being a prodromal symptom that can help with the PD diagnosis," Dr. Chen said.

Prodromal clues? The prodromal visual manifestations of PD are "the most exciting part of the study," he said. "Some of these may precede the development of PD and could possibly be used as a biomarker to predict or follow progression."

To that end, Dr. Chen is conducting a pilot study to explore the use of optical coherence tomography in patients with REM (rapid eye movement) sleep behavior disorder, which is strongly associated with a risk for conversion to PD.[2]

Clinical implications. Most ophthalmologists know that patients with PD often have dry eye from poor blink rate and may also have some ocular motility abnormalities, Dr. Chen said. But PD can cause other visual abnormalities that often go unrecognized—not only impaired color vision and contrast sensitivity but also problems with stereopsis, saccades, and smooth pursuit eye movements. Patients may even develop visual hallucinations.

"These are important to identify," Dr. Chen said, "because these symptoms can be explained to the patient" as part of the disease process. Moreover, he said, "they may even lead to a diagnosis of unrecognized PD" in some cases.

—Miriam Karmel

1 Turcano P et al. *J Neurol.* 2019;266(9):2103-2111.
2 Postuma RB, Berg D. *Nat Rev Neurol.* 2016; 12(11):622-634.
Relevant financial disclosures—Dr. Chen: None.

to patients. Of those who order testing, 90% work with a genetic counselor.

The good news: Most respondents appeared eager to learn more about testing modalities, citing interest in continuing education.

Missed diagnoses? Despite two email reminders, the survey response rate was only 18%. The researchers suspect that the nonresponders may think they don't see patients with genetic disorders, so a survey about genetic eye disease does not apply to them. But, said cochair Virginia Miraldi Utz, MD, at the University of Cincinnati, "most likely, they are seeing at least one genetic eye disease patient a week, but they may not realize that the underlying cause of that patient's problem is genetic."

What you don't know . . . Most pediatric ophthalmologists have not been trained to do genetic testing for congenital/infantile nystagmus, infantile/juvenile cataracts, pediatric glaucoma, and congenital malformations. And this is occurring at a time when novel gene-based diagnostic strategies[2] and therapies continue to emerge.

"It is not common for children to have serious eye disorders," Dr. Drack said. Thus, when such disorders present, she urged ophthalmologists to have a high level of suspicion for a genetic cause. "We won't find what we don't look for." —*Miriam Karmel*

1 Drack AV et al. *J AAPOS.* Published online June 21, 2019.

2 Gillespie RL et al. *Ophthalmology.* 2016;123(1): 217-220.

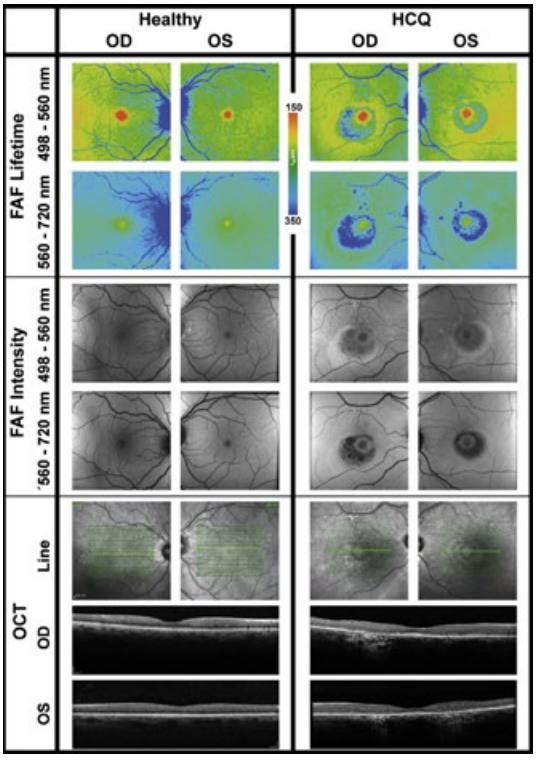
Relevant financial disclosures—Drs. Drack and Utz: None.

RETINA

FLIO May Help in Screening for HCQ Toxicity

CAN A NOVEL IMAGING TECHNOLOGY reveal retinal damage earlier than currently available imaging modalities? Researchers have yet to prove that it can, but they are pursuing leads that fluorescence lifetime imaging ophthalmoscopy (FLIO) may be useful for detection of hydroxychloroquine (HCQ; Plaquenil) toxicity in a retina that appears otherwise healthy.[1]

"FLIO is a novel technology that is not yet widely known, but it has already revealed disease-related patterns for age-related macular degeneration and other retinal conditions," said Lydia Sauer, MD, at the John A. Moran Eye Center in Salt Lake City, Utah. "We believe that it has great potential to enhance the diagnosis of retinal diseases by detecting metabolic changes in the retina, before overt damage occurs." Other imaging modalities, including optical coherence tomography (OCT), describe changes only after retinal damage is manifest.



COMPARISON. *Fundus autofluorescence lifetime and intensity images, as well as OCT imaging, from a healthy subject and a patient with severe HCQ toxicity.*

What FLIO may tell us. This noninvasive imaging technology measures the span of time that naturally occurring retinal fluorophores glow, following excitation with a laser pulse. This is known as the autofluorescence lifetime.

Dr. Sauer and her colleagues harnessed FLIO to measure retinal toxicity from HCQ, which is well-known for its ability to cause retinal damage.

Study specifics. The researchers used a modified Spectralis OCT (Heidelberg Engineering) to measure fluorescence lifetimes in 58 patients. Of these, 12 had definite HCQ toxicity; eight were clinically normal and considered at low risk, as they had been on HCQ for less than five years; 16 were clinically normal but considered high risk, as they had been on the drug for more than five years; and 22 were age-matched healthy controls.

All of the patients with definite HCQ toxicity showed significantly prolonged FLIO lifetimes in regions of damage. Of the clinically normal patients, nine of the 16 in the high-risk HCQ group (56%) and two of the eight in the low-risk group (25%) showed prolonged autofluorescence lifetimes in a pattern suspicious for HCQ toxicity. No such patterns were observed in the healthy controls.

Next steps. Dr. Sauer stressed that researchers are unsure about the metabolic and structural origins of the altered FLIO lifetimes. Thus, they plan to monitor their cohort of "suspicious" patients to determine whether FLIO findings suggestive of HCQ toxicity evolve to overt damage visible with established imaging modalities, she said. "This would prove our hypothesis and may allow us to change individual treatments based on FLIO findings to preserve eyesight." —*Miriam Karmel*

1 Sauer L et al. *Ophthalmol Retina.* Published online May 2, 2019.

Relevant financial disclosures—Dr. Sauer: Novartis: C; Tesseract: C. Heidelberg Engineering provided nonfinancial support.

See the financial disclosure key, page 8. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.