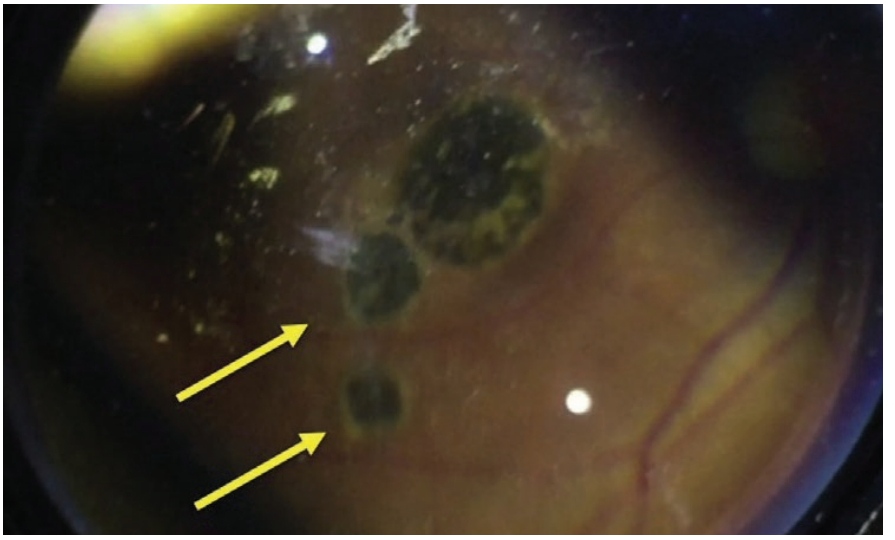


EVD UVEITIS. *Fundus photo using a 28-diopter condensing lens and an iPhone shows chorioretinal scarring with characteristic hyperpigmented scars with hypopigmented halo (yellow arrows) in an EVD survivor with posterior uveitis. Similar lesions were observed in the retinal periphery.*

Visual Loss in Ebola Survivors

THOUGH EBOLA VIRUS DISEASE (EVD) killed more than 11,000 people in western Africa in 2014-2015, thousands of others survived the infection. And survivors are at high risk for developing vision loss from uveitis in the months after their recovery from acute disease, researchers have concluded.

Wide range of ocular findings. Ophthalmic examinations of 96 Ebola survivors who had sought help for vision problems at a specially established clinic in Monrovia, Liberia, showed that 21 patients (22%) had uveitis (26 affected eyes), and 3 patients (4 eyes) had optic neuropathy.[1] The researchers noted that their report was the first detailed characterization of an EVD-associated uveitis phenotype and its association with impaired visual acuity.

"The wide spectrum of findings was really interesting, in that patients ranged from [having] anterior uveitis to panuveitis. In addition, optic neuropathy was observed. We also saw patients who had chorioretinal scarring, sometimes within the macula, unfortunately," said coauthor Jessica Shantha, MD, fellow in uveitis at the F.I. Proctor Foundation, University of California, San Francisco. "Nearly 40% of patients who developed eye disease had severe vision impairment by World Health Organization criteria—that is, 20/400 or worse vision."

Dr. Shantha and Emory University uveitis specialist Steven Yeh, MD, were among the visiting physicians who responded to reports of ocular problems among Ebola survivors by helping to establish an eye clinic at the Eternal Love Winning Africa (ELWA) Hospital in Monrovia.

Clinical exams of the 96 patients during the clinic's first month of operation showed the following:

- **Symptoms.** Blurry vision and photophobia were the most common symptoms, found in 76% and 68% of clinic patients, respectively. Other common symptoms were tearing (62%), pain (56%), floaters (47%), and redness (43%).
- **Eye conditions.** Among those presenting to the clinic, 35 (36.5%) had apparently normal ocular exams. In addition, a number of patients were found to have non–EVD-associated eye disease, including cataract, refractive error, dry eye, glaucoma, and retinal detachment.
- **Visual acuity (VA).** Eyes with EVD-associated uveitis had significantly worse vision than did those without uveitis. Of the eyes with uveitis, 38.5% were blind (defined as VA 20/400 or worse). However, 54% of uveitic eyes had VA of 20/70 or better.
- **Uveitis subtypes.** Posterior uveitis was the most common form (57%), followed by panuveitis (29%). Active Ebola virus was found in 6 eyes, all of which had been diagnosed with panuveitis.
- **Exam findings.** Eyes with uveitis were significantly more likely than those without uveitis to have anterior chamber cells ($p = .01$), keratic precipitates ($p = .01$), posterior synechiae ($p < .001$), and chorioretinal scars ($p < .001$).

Caring for survivors. Overall, the study demonstrates the importance of ophthalmic care for patients who contract Ebola, said Dr. Yeh, who is the M. Louise Simpson Associate Professor of Ophthalmology at Emory University. "Ebola survivors should be evaluated, at the very least, shortly after they leave the Ebola Treatment Unit setting," he said.

However, because ophthalmic care

Shantha JG et al. *Ophthalmology.* Published online, Dec. 1, 2016.

is scarce in the countries of western Africa, he and other visiting ophthalmologists have been teaching health care workers to perform screening exams, he said. "Eye care nurses trained in the slit-lamp examination are also very capable of evaluating patients for uveitis," he said.

Theories of Ebola eye disease. Many mysteries remain about when and how Ebola affects the eye, Dr. Yeh said. For instance, an earlier study in Sierra Leone found an association between uveitis and 2 factors observed in the disease's acute phase: a greater concentration of Ebola virus in patients' blood samples, and red/injected eyes at the time of diagnosis.[2]

"One hypothesis is that a higher viral load enables Ebola to enter the eye, establish viral persistence, and later lead to uveitis. Red/injected eyes could be a sign of conjunctival hyperemia or subconjunctival hemorrhage, which is frequently seen as a manifestation of acute EVD. Alternatively, red/injected eyes could also be a sign of acute uveitis at the time of EVD diagnosis. However, this link requires further study," Dr. Yeh said. *—Linda Roach*

1 Shantha JG et al. *Ophthalmology*. 2017;124(2):170-177.
2 Mattia JG et al. *Lancet Infect Dis*. 2016;16(3):331-338.

Relevant financial disclosures—Dr. Shantha: None. Dr. Yeh: None.

DIABETES IN YOUTH

DR Screening: Time to Rethink Guidelines?

YOUNG PEOPLE WITH DIABETES mellitus (DM) are at considerable risk for diabetic retinopathy (DR), according to researchers who looked at the incidence and risk factors for developing DR among youth with DM.[1] These findings, which have implications for screening guidelines, challenge the perception that DR is very uncommon in youth.

Higher-than-expected rates of DR. The study included 2,240 youths with type 1 DM (T1DM) and 1,768 youths with type 2 DM (T2DM). All were 21 years or younger at the time of initial enrollment in a large U.S. managed care network. Overall, 578 (14.4%) received a DR diagnosis.

"We were surprised to find that, overall, more than 1 in 5 youths with type 1 diabetes and 7% of the youths with type 2 diabetes received a diagnosis of DR during the time they were monitored in the health plan," said Sophia Y. Wang, MD, lead author on the study and resident physician at the University of Michigan Department of Ophthalmology and Visual Sciences. "Youth with DM can indeed develop DR, and thus it is worthwhile for them to periodically undergo screening by an eye care professional."

Delayed diagnosis. Many patients received a DR diagnosis before the recommended time for screening. Current Academy guidelines recommend starting screening for DR 5 years after T1DM onset. In this group of patients, 25% would have had a delayed DR di-

RETINA RISK FACTORS

Oral Anticoagulants & Intraocular Hemorrhage

USING DATA FROM THE WORLD HEALTH ORGANIZATION (WHO) VigiBase—the largest drug safety database in the world—Canadian researchers have found a linkage between intraocular hemorrhage and warfarin and new oral anticoagulants (NOACs). The researchers' disproportionality analysis of data spanning from 1968 to 2015 revealed a strong signal for the number of intraocular bleeding events with the use of either warfarin or NOACs compared with the risk of intraocular bleeding reported for all other drugs.[1]

"This strong signal warrants a large epidemiologic study to better quantify the risk and adjust for confounders," said coauthor Mahyar Etminan, PharmD, MSc, assistant professor of ophthalmology at the University of British Columbia in Vancouver.

Reported cases. The researchers identified 80 cases of vitreous, choroidal, or retinal hemorrhage with warfarin and 156 cases with NOACs, including rivaroxaban, dabigatran, and apixaban. The strongest linkage was seen between warfarin and choroidal hemorrhage, likely due to that drug's longer history of use, which resulted in more reports of hemorrhage, said Dr. Etminan. However, rivaroxaban had the highest association with retinal and vitreous hemorrhage, even though it has been available for a shorter time than warfarin or dabigatran. According to the authors, the small number of apixaban cases made it more difficult to draw strong conclusions about its level of risk.

Spotlight on NOACs. There aren't clear guidelines on how to manage NOACs in patients who require ocular surgeries, said Dr. Etminan, but this study begins to fill in some of the knowledge gaps. And future epidemiologic studies can help shed further light on the magnitude of bleeding risks with each type of NOAC and with specific types of ocular surgery, he added.

"In the meantime, I think the results of our study are compelling enough that ophthalmologists should carefully assess a patient's risk of bleeding before conducting ocular surgery on patients using NOACs." This is particularly important given the growing popularity of NOACs and given the challenges in reversing their effects, he said, which—unlike warfarin—lack a validated antidote. *—Annie Stuart*

1 Talany G et al. *Eye*. 2016;doi:10.1038/eye.2016.265.

Relevant financial disclosures—Dr. Etminan: None.

agnosis if screening began at that time. Even according to stringent 3- to 5-year guidelines recommended by some other professional societies, an initial DR diagnosis would have been delayed in 18% of cases. (Existing guidelines for youth with T2DM are the same as for adults, to screen for DR at the time of the initial T2DM diagnosis.)

Among the other key findings:

- Young people with T1DM developed DR faster than those with T2DM. At the 6-year follow-up, 27.6% of T1DM patients were diagnosed with DR, compared with 8.6% with T2DM. At 8 years, the numbers rose to 30% and 10.3%, respectively.
- For every 1-point increase in hemoglobin A_{1c}, the risk for DR increased by 20% for youth with T1DM and by 30% for those with T2DM.
- Males with T2DM had a 122% higher risk for DR compared with females. In contrast, sex was not a risk factor in T1DM cases.
- Income mattered with T2DM. Youth in households in the highest net worth category (≥$500,000) had a 52% decreased risk of DR versus those in households in the lowest category (<$25,000).

Clinical implications. The study underscores the importance of referring youth with DM to an eye care provider at least as often as current guidelines suggest, said Dr. Wang. While further research is needed to determine the ideal timing for screening, she said professional societies might want to consider the adequacy of their guidelines. "It may be that a subset of patients who are at very high risk for developing DR require very early and frequent monitoring, while for many others the existing guidelines are completely adequate."

What's next? The researchers plan to study whether youth with DM are undergoing DR screening according to existing guidelines and whether socioeconomic factors affect guideline adherence.

For now, Dr. Wang urges doctors to consider the importance of periodic screening by an eye care professional in this patient population, keeping in mind that young people with diabetes are at risk for DR. —*Miriam Karmel*

1 Wang SY et al. *Ophthalmology*. Published online Dec. 1, 2016.

Relevant financial disclosures—Dr. Wang: None.

GLAUCOMA DRUGS

Intracameral Implant Lowers IOP as Well as Eyedrops

A BIODEGRADABLE SUSTAINED-release drug implant for glaucoma treatment proved as effective as topical drops at the 6-month mark of a 2-year clinical trial.[1] Bimatoprost SR was well tolerated and provided rapid, sustained reduction of intraocular pressure (IOP) in patients with mild to moderate visual field loss.

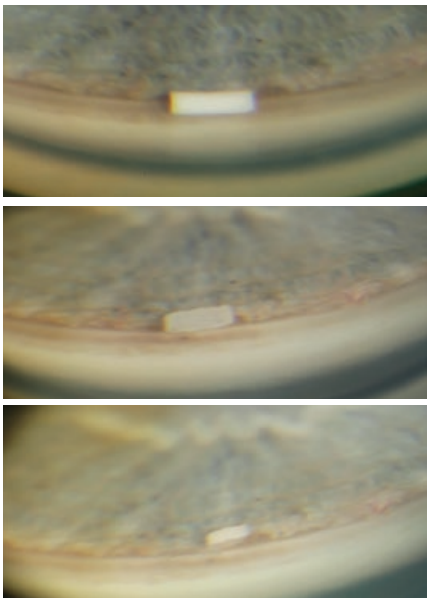
The implant was developed to address poor adherence, which is endemic in glaucoma. "Applying drops is not only challenging for many patients, leading to poor compliance, but requires higher doses to get through the cornea," said Richard A. Lewis, MD, at Sacramento Eye Consultants.

"The implant is fundamentally the same as the Ozurdex [dexamethasone] implant used for posterior segment disease," Dr. Lewis said. In both cases, the active drug is slowly eluted over time through the Novadur (Allergan) biodegradable polymer platform.

The study. In this phase 1/2 study, 75 open-angle glaucoma patients received varying doses of Bimatoprost SR intracamerally in the study eye. The fellow eye received topical bimatoprost 0.03% once daily. Among the findings:

- IOP reduction was observed in implant eyes as early as day 1 and at all subsequent visits through month 6.
- Through week 16, mean IOP reduction from baseline ranged from 7.2 to 9.5 mm Hg depending on dosing, compared with 8.4 mm Hg in topically treated eyes.

Safety. More than half (52.0%) the study eyes experienced adverse events (typically conjunctival hyperemia), compared with 30.7% of fellow eyes. But study eye events mostly occurred within 2 days of the injection procedure and were transient.



IMPLANT IN PLACE. *Gonioscopic photographs of a 10 µg bimatoprost sustained-release implant in the anterior chamber of the eye of a patient with open-angle glaucoma at (top) 2 weeks, (center) 9 months, and (bottom) 12 months after injection.*

Later-onset conjunctival hyperemia occurred more often in topically treated eyes (17.3%) compared with implanted eyes (6.7%).

Patient-reported outcomes. The high level of patient satisfaction surprised Dr. Lewis. At week 12, nearly 80% said they would likely have another implant procedure. The implant lasts 4 to 6 months.

"This is the beginning of a new era in drug delivery for many diseases," Dr. Lewis said. "Implants optimized for specific diseases will allow better treatment as well as better compliance."

—*Miriam Karmel*

1 Lewis RA et al. *Am J Ophthalmol.* 2017;175: 137-147.

Relevant financial disclosures—Dr. Lewis: Aerie: E (part time); Alcon: C; Allergan: C; AVS: C; Glaukos: C; Ivantis: C. This study was sponsored by Allergan plc, maker of Novadur.

See the financial disclosure key, page 10. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.