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Glaucoma 2021

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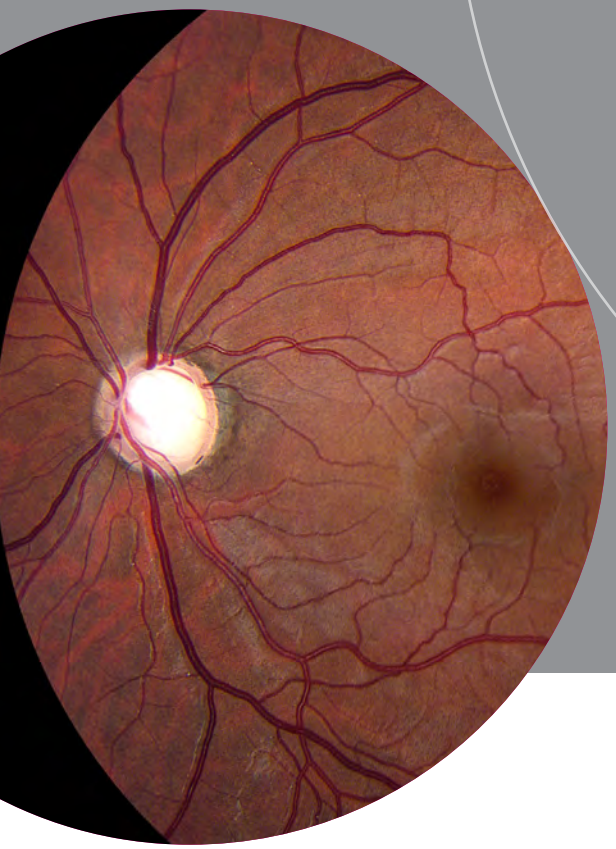

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INDICATIONS AND USAGE

Rhopressa® (netarsudil ophthalmic solution) 0.02% is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION

DOSAGE AND ADMINISTRATION

The recommended dosage is one drop in the affected eye(s) once daily in the evening.

WARNINGS AND PRECAUTIONS

Bacterial Keratitis: There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Contact Lenses: Contact lenses should be removed prior to instillation of Rhopressa® and may be reinserted 15 minutes following its administration.

ADVERSE REACTIONS

The most common ocular adverse reaction observed in controlled clinical studies with Rhopressa® dosed once daily was conjunctival hyperemia, reported in 53% of patients. Six percent of patients discontinued therapy due to conjunctival hyperemia. Other common (approximately 20%) adverse reactions were: corneal verticillata, instillation site pain, and conjunctival hemorrhage. Instillation site erythema, corneal staining, blurred vision, increased lacrimation, erythema of eyelid, and reduced visual acuity were reported in 5-10% of patients.

The corneal verticillata seen in Rhopressa®-treated patients were first noted at 4 weeks of daily dosing. This reaction did not result in any apparent visual functional changes. Most corneal verticillata resolved upon discontinuation of treatment.

Please see full Prescribing Information for Rhopressa® at Rhopressa.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

ONCE-DAILY rhopressa® (netarsudil ophthalmic solution) 0.02%

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Please refer to Brief Summary on the reverse side.

IOP, intraocular pressure; PGA, prostaglandin analog.

ONCE-DAILY
rhopressa®
(netarsudil ophthalmic solution) 0.02%

BRIEF SUMMARY

Consult the full Prescribing Information for complete product information.

INDICATIONS AND USAGE

Rhopressa® (netarsudil ophthalmic solution) 0.02% is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION

The recommended dosage is one drop in the affected eye(s) once daily in the evening.

If one dose is missed, treatment should continue with the next dose in the evening. Twice a day dosing is not well tolerated and is not recommended. If Rhopressa® is to be used concomitantly with other topical ophthalmic drug products to lower IOP, administer each drug product at least 5 minutes apart.

WARNINGS AND PRECAUTIONS

Bacterial Keratitis

There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been previously contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Use with Contact Lenses

Rhopressa® contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to instillation of Rhopressa® and may be reinserted 15 minutes following its administration.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

The most common ocular adverse reaction observed in controlled clinical studies with Rhopressa® dosed once daily was conjunctival hyperemia which was reported in 53% of patients. Six percent of patients discontinued therapy due to conjunctival hyperemia. Other common (approximately 20%) ocular adverse reactions reported were: corneal verticillata, instillation site pain, and conjunctival hemorrhage. Instillation site erythema, corneal staining, blurred vision, increased lacrimation, erythema of eyelid, and reduced visual acuity were reported in 5-10% of patients.

Corneal Verticillata

Corneal verticillata occurred in approximately 20% of the patients in controlled clinical studies. The corneal verticillata seen in Rhopressa®-treated patients were first noted at 4 weeks of daily dosing. This reaction did not result in any apparent visual functional changes in patients. Most corneal verticillata resolved upon discontinuation of treatment.

For additional information, please refer to full Prescribing Information at Rhopressa.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-1088.

Manufactured for: Aerie Pharmaceuticals, Inc., Irvine, CA 92614, U.S.A.

U.S. Patent Nos.: 8,450,344; 8,394,826; 9,096,569; 9,415,043; 9,931,336; 10,174,017

References: 1. Rhopressa® (netarsudil ophthalmic solution) 0.02% Prescribing Information. Aerie Pharmaceuticals, Inc., 2019. **2.** Data on file. Aerie Pharmaceuticals, Inc.

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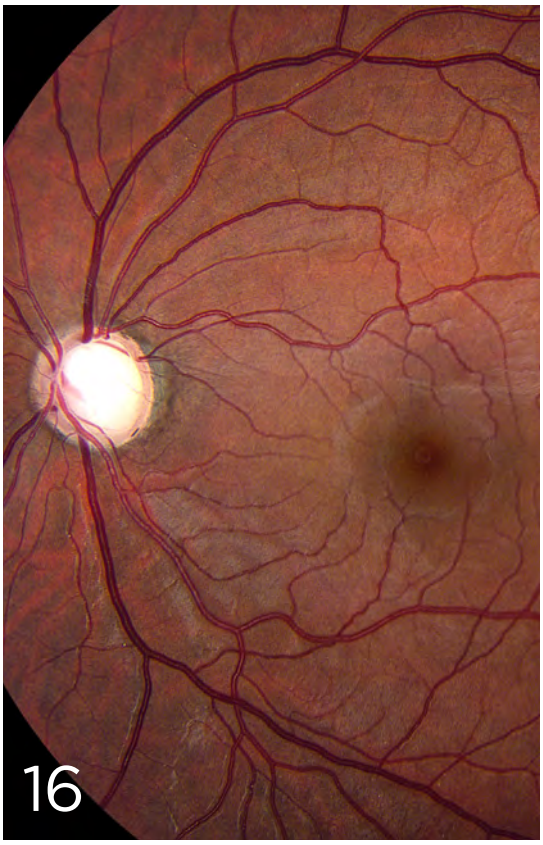

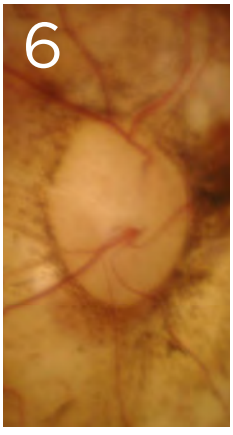

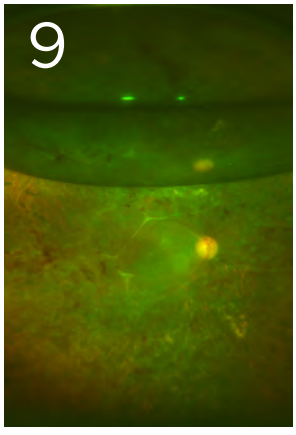

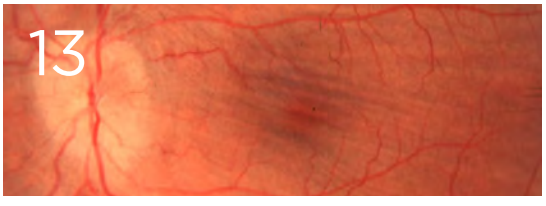

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REPRINTS FOR
GLAUCOMA SUBSPECIALTY DAY
AT AAO 2021

COVER PHOTOGRAPH
Jason S. Calhoun, COA

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How to Spot Glaucoma in the Myopic Patient

By 2050, about half the world's population will have myopia.[1] "In some parts of the world, these rates are already approaching 90%," said Sarwat Salim, MD, FACS, at the New England Eye Center in Boston. Compounding these troubling statistics are population-based studies that show a 2- to 4-fold increased prevalence of glaucoma in myopic eyes, she said, with an even stronger association for those with moderate-to-high myopia.

This lends urgency to the task of identifying myopic patients who are most at risk for developing glaucoma, but there isn't a simple solution for doing so. The structural and functional defects in myopic eyes are difficult to distinguish from those caused by glaucoma, said Dr. Salim. "What's most important is to focus on various risk factors for glaucoma and get baseline ancillary tests, such as OCTs, visual fields, and disc photos; to be aware of clinical features of both myopic and glaucomatous optic nerves; and to follow these patients longitudinally."

Why Does Myopia Increase Glaucoma Risk?

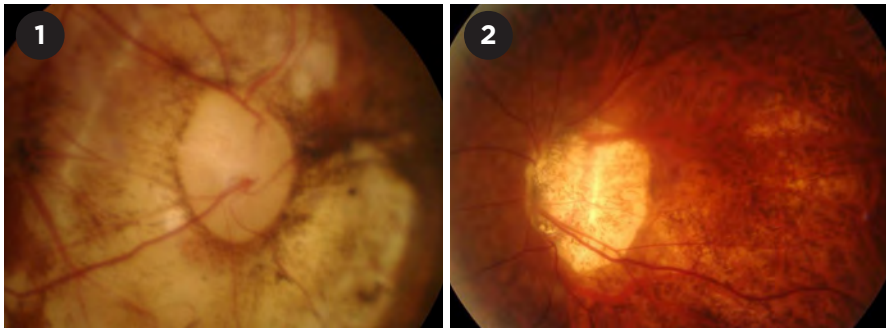
"We don't have a good understanding of the connection between myopia and glaucoma, and this is an area of active research," said Dr. Salim. It is believed that the myopic eye's structural abnormalities, mainly those related to laminar collagen fibers, increase the risk of developing glaucoma, she said.

For instance, axial length can be greater than 25.5 mm in moderate-to-high myopia, versus 23 mm in normal eyes, she said, and this elongation causes stretching and thinning of the lamina cribrosa and thinning and weakening of the sclera. These structural changes, combined with morphological changes of the optic nerve, make these patients' optic nerves more susceptible to damage related to intraocular pressure (IOP) elevation.

IOP and myopia. The Singapore Epidemiology of Eye Diseases study found that IOP and myopia may act synergistically on the development of primary open-angle glaucoma (POAG).[2] The authors looked at varying levels of IOP and severity of myopia—comparing one group without myopia to another with moderate-to-high myopia. "Those with moderate-to-high myopia and IOP of 20 mm Hg or greater were four times more likely to develop POAG," said Dr. Salim.

IOP and axial length. The Singapore researchers also looked at the correlation between IOP and axial length. Eyes with high IOP and axial length greater than 25.5 mm were 16 times more likely to develop POAG when compared with those with shorter axial length and lower IOP. "That's clinically important information. As we care for patients, we should pay attention not only to refractive status and the level of myopia, but also to axial length, which can be easily measured in clinics and can provide invaluable information for future glaucoma monitoring and therapeutic decisions," Dr. Salim said.

Ethnicity. Because of a higher rate of myopia in Asians, the detection of glaucoma is especially important in these populations, said Kyoko Ohno-Matsui, MD, PhD, at Tokyo Medical and Dental University's Advanced Clinical Center for Myopia. Researchers haven't yet



DISC ABNORMALITIES. *Potential optic disc changes seen in myopic patients include: (1) an acquired megalodisc and (2) an extremely tilted disc.*

Kyoko Ohno-Matsui, MD, PhD

Originally published in May 2021

BY ANNIE STUART, CONTRIBUTING WRITER, INTERVIEWING **SHAN LIN, MD, KYOKO OHNO-MATSUI, MD, PHD,** AND **SARWAT SALIM, MD, FACS.**

confirmed, however, that race is a risk factor for glaucoma in high myopes, said Shan Lin, MD, at the Glaucoma Center of San Francisco.

Additional concerns. "A significant risk factor for developing glaucoma, including in highly myopic patients, is a family history of glaucoma," he said. "In individuals with moderate-to-high myopia, glaucoma can develop earlier than in regular POAG—often in young or middle adulthood. And the risk appears relatively high, even with borderline IOP, around 20 or 21 mm Hg."

A less well-known risk for myopic glaucoma is Flammer syndrome, a vascular dysregulation more common in women and Asians, said Dr. Lin. In addition to myopia, symptoms of this syndrome may include cold hands and feet, systemic hypotension, low body mass index, decreased thirst, difficulty falling asleep, migraines, tendonitis, and increased sensitivity to pain, odors, and certain drugs.[3] "Migraines," he pointed out, "are a well-known risk factor for normal tension glaucoma."

Structural and Functional Assessments

Interpreting glaucomatous changes in highly myopic eyes is particularly difficult, especially in those with pathologic myopia, where there's myopic maculopathy and posterior staphyloma, said Dr. Ohno-Matsui.

Multiple challenges. In high myopes, "fundus features can be difficult to observe because the optic disc is severely tilted and deformed," she said. "And a coexisting large conus and lesions of myopic maculopathy can make it more challenging to use the Humphrey field analyzer." Generalized retinal thinning can also complicate quantitative assessment of the nerve fiber layer defect (NFLD) or ganglion cell complex (GCC) on OCT, she said.

"Swept-source OCT centered on the optic disc can detect optic disc pits and conus pits that may relate to the development of glaucomatous visual field defects in patients with pathologic myopia," she said. "However, we basically rely on Goldman perimetry for detecting visual field defects in eyes with pathologic myopia."

To Treat or Not to Treat?

"Deciding who to treat is a challenge for me as a clinician," said Dr. Salim. "I pay attention to many pieces of the puzzle. In addition to the severity of myopia, I consider the age and race of the patient, the family history of glaucoma, the baseline IOP, and the axial length. All these factors play a role in my decision-making."

In patients with pathologic myopia, glaucoma develops at a younger age than it does in nonmyopes, said Dr. Ohno-Matsui. "These patients can go completely blind in their productive years. I recommend early treatment if I suspect glaucoma."

Dr. Lin usually treats patients at the first visit if the optic nerve and visual field findings appear consistent with glaucoma. "But if visual fields are normal, I will likely categorize them as a glaucoma suspect and follow them over time," he said. "The biggest dilemma occurs when pressures are in the normal range, but the patient has features—especially optic nerve characteristics—that are consistent with glaucoma. That can put clinicians on the fence about whether or not to treat the patient. It all comes down to being hypervigilant, having a thorough understanding of how these patients can present, and following them closely over time."

Myopic optic nerves. It's critical to know the characteristics of myopic and glaucomatous changes to the optic nerve—and to remember that there can be an overlap between the two, said Dr. Salim. She noted that compared with glaucomatous optic nerves, myopic optic nerves tend to be larger, with a disc area greater than 3.25 mm^2. In addition, they are vertically elongated with an oval shape, which can cause a tilt in the optic nerves that obscures both the temporal and nasal rims. They also have very shallow diffuse cupping, an increased incidence and extent of beta zone peripapillary atrophy, and a decreased retinal nerve fiber layer (RNFL) thickness.

OCT strategies. "We need to interpret OCT findings very carefully," said Dr. Salim. "To begin with, high myopes have decreased average RNFL at baseline, which may also have an atypical distribution. RNFL bundles can shift temporally, which can cause thinning in nasal sectors and thickening in temporal quadrants, complicating assessment for glaucoma."

It's also important to pay attention to the size of the optic nerves and peripapillary atrophy on OCT printouts, she said. "In myopic eyes with significant peripapillary atrophy, the circle centered around the optic nerve for RNFL measurements can overlap the atrophy, leading to erroneous measurements" and inaccurate interpretation.

Normative databases. Overall, OCT has not been particularly reliable for detection of glaucoma in people with moderate-to-high myopia, because these patients are not well represented in the normative reference database, said Dr. Salim. The optic disc and nerve tissue is so abnormal in these patients, said Dr. Lin, that this database may cause you to misclassify them—either by categorizing them as patients who do not have glaucoma or, conversely, by attributing their damage to glaucoma when it is more related to myopia.

But researchers are now developing normative databases for people with myopia, Dr. Lin said. He also noted that a Korean group found that using a myopic-specific database helped to discern areas of defect in eyes with myopic glaucoma when applying OCT color probability codes.[4] The Nidek OCT machine has a myopic-specific database for detecting NFLD and GCC for low-to-moderate myopia, added Dr. Ohno-Matsui. "But using this database to assess the thickness of RNFL or GCC may not be useful for highly and pathologically myopic eyes."

Optic disc stereophotography. In general, optic disc photos are no longer routinely done, said Dr. Salim. "But for this particular patient population, I find them extremely valuable, especially since OCT may not be reliable. These photos provide a more objective assessment and are useful for longitudinal follow-up to see if any new and subtle structural changes [attributable to glaucoma] are taking place."

Visual field defects in myopia. Although visual fields play a major role in evaluating eyes at risk for glaucoma, clinicians must be aware that many visual field defects can occur with myopia alone. These may include a large blind spot, nasal step, arcuate defect, or paracentral defect, said Dr. Salim. "These visual defects in myopia occur in patterns that are similar to those in glaucoma, but they may be unrelated to it."

In one study, nearly 80% of myopic patients without glaucoma had visual field defects. More than 15% had nasal step and about 28% had paracentral defects.[5] "Arcuate scotomas, which may correspond to thin or nonexistent rim tissues at the inferior and superior poles of myopic optic nerves, occurred in 35.5%," Dr. Salim said.

Another study followed 16 Chinese men who had either glaucoma or were glaucoma suspects, 14 of whom had had baseline visual fields.[6] "After seven years of follow-up, none had progression of optic nerve or visual field defects, irrespective of their IOP reduction," said Dr. Salim. The takeaway message? The defects might have been due to myopia, not glaucoma, she said, cautioning that, at times, myopic eyes may be at risk of being overtreated for glaucoma.

Visual field strategies. In highly myopic eyes, macular lesions impair central vision, which causes poor fixation during a functional evaluation, said Dr. Ohno-Matsui. Microperimetry may overcome this problem, as clinicians can assess the retinal sensitivity at the point they would like to measure, she said. "Goldmann perimetry taken by a skilled technician is the best strategy for detecting characteristic visual field defects in myopic glaucoma. I highly recommend that patients with high or pathologic myopia have Goldmann perimetry at least once a year to avoid underdiagnosis of glaucoma. However, in highly myopic eyes without large conus or myopic macular atrophy, the Humphrey field analyzer may be an option, too."

Dr. Lin advises getting visual fields more than once a year—as often as every three to six months. "It's imperative that we follow these patients closely because progression of glaucoma can sometimes be rapid." He has had myopic patients in their 20s, 30s, and 40s with severe visual field defects who had a confirmed diagnosis of glaucoma. However, he emphasized that it's important not to dismiss the possibility that defects can be attributed to high myopia alone.

To help differentiate between the two, Dr. Lin recommended alternating between 24-2 or 30-2 visual fields and 10-2 visual fields. The latter provides a more closely spaced mapping of the central 10 degrees, thus helping clinicians spot any small defects in central vision at an earlier stage.

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Dr. Lin is co–research director at the Glaucoma Center of San Francisco. *Relevant financial disclosures: None.*
Dr. Ohno-Matsui is professor and chairperson of ophthalmology and visual science at Tokyo Medical and Dental University (TMDU) in Tokyo, Japan. She is also chief of the Advanced Clinical Center for Myopia at TMDU. *Relevant financial disclosures: None.*
Dr. Salim is professor of ophthalmology, vice chair of clinical and academic affairs, and director of the glaucoma service at the New England Eye Center, Tufts University School of Medicine, in Boston. *Relevant financial disclosures: None.*
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Cataract, Cornea, and Retina Surgeries: Strategies to Manage Postoperative IOP Events

Elevated intraocular pressure (IOP) is not uncommon after ocular surgeries—from phacoemulsification to keratoplasty to vitrectomy. For most eyes, moderate spikes are often transient and don't pose a significant threat to long-term visual health. However, extremely high IOP or IOP elevation in patients with certain preexisting conditions, such as optic nerve damage, can significantly threaten vision following an otherwise successful surgery.

To complicate matters, ophthalmologists aren't always able to predict which patients will experience a spike. That's why it's valuable to know how to both minimize the risk of IOP elevation and address high pressure after it occurs.

Cataract: Vexing Viscoelastic

Elevated IOP is the most frequent complication that requires treatment following phacoemulsification, said Ahmad A. Aref, MD, MBA, at the University of Illinois in Chicago. And its most common cause is retained viscoelastic material, which inhibits aqueous outflow through the trabecular meshwork. The surgeon should therefore be aggressive in removing as much viscoelastic as possible before completing the procedure, he said.

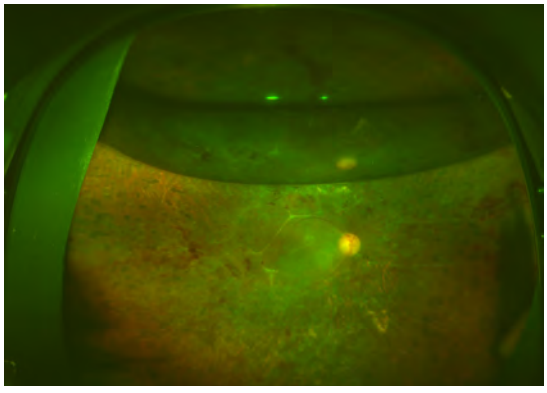
Dr. Aref also relies on two pharmacological interventions to preemptively manage the possibility of post-op IOP spikes in certain cases.

Acetazolamide. Cataract surgeons who administer oral acetazolamide for IOP control commonly do so right after completing surgery, said Dr. Aref. Recent research, however, shows that acetazolamide's effects are superior when given to the patient *prior* to surgery.[1]

"These results changed my practice patterns," said Dr. Aref. "Instead of using the acetazolamide as a post-op treatment in higher-risk eyes, I'm now administering one hour before and seeing fewer IOP events for one to 24 hours after surgery."

Despite that success, Dr. Aref doesn't use acetazolamide in every case. He typically uses it only for patients with advanced preexisting glaucoma or those who have a known outflow obstruction. This is because, in addition to a host of potential systemic side effects, the medication can, in rare instances, induce acute bilateral angle-closure glaucoma with choroidal detachment, he said.

Acetylcholine. Dr. Aref saves his second pharmacological intervention for surgeries that require manipulation of the iris or other complex anterior segment procedures. Injected during the cataract procedure, intracameral acetylcholine is a miotic that pulls the iris away from the trabecular meshwork, improving outflow and helping to decrease IOP. And it's safe to use in combination with acetazolamide. However, acetylcholine also comes with some risk that may limit routine use. In rare cases, for example, acetylcholine injections have resulted in aqueous misdirection, which can cause a postoperative angle closure event and uncontrolled IOP, said Dr. Aref.



TAMPONADE. *Post-op eye after 25-gauge vitrectomy and C_3F_8 gas to repair traction retinal detachment due to proliferative diabetic retinopathy.*

Burping the wound. If a pressure spike is evident on the first postoperative day and the patient is deemed to be at risk for secondary complications, Dr. Aref moves on to "burping" the wound. "With a sterile cotton tip applicator, I apply direct pressure next to the corneal paracentesis site to release the remnant viscoelastic and aqueous from inside the eye," he said. "This decompression

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BY MICHAEL MOTT, CONTRIBUTING WRITER, INTERVIEWING **AHMAD A. AREF, MD, MBA; ALEKSANDRA V. RACHITSKAYA, MD;** AND **ELIZABETH YEU, MD.**

is immediate and can be performed repeatedly on an as-needed basis."

In some cases, a short course of topical IOP-lowering agents may also be indicated in order to keep the pressure controlled over the first postoperative week, he said.

Cornea: Taming Glaucoma

Keratoplasty procedures can induce elevated IOP—which in turn can accelerate graft failure and endothelial cell loss, said Elizabeth Yeu, MD, at Virginia Eye Consultants in Norfolk, Virginia. In addition, management of corneal disease typically requires a long course of anti-inflammatory steroids, which can cause elevated IOP, she said. "As a result, cornea surgeons create a lot of secondary glaucoma."

Pre-op. When candidates for lamellar transplantation present with very poorly controlled IOP, Dr. Yeu refers them to a glaucoma specialist to stabilize that pressure.

Immediately post-op. Cornea surgery can cause IOP spikes even in relatively healthy eyes. What should you watch for during the immediate post-op period?

Viscoelastic. The typical culprit in IOP rise after a full-thickness PK is the leftover viscoelastic that's used to maintain adequate separation between the transplanted cornea and the iris and lens, said Dr. Yeu. "As in cataract surgery, this material increases the risk of blocking the trabecular meshwork." An IOP spike can be treated shortly after surgery, by burping out some of the viscoelastic between two sutures at the graft-host junction, she said.

> "Instead of using the acetazolamide as a post-op treatment in higher-risk eyes, I'm now administering one hour *before* and seeing fewer IOP events for one to 24 hours after surgery." —*Dr. Aref*

Bubble-induced IOP elevation. For lamellar endothelial keratoplasty, increased post-op pressure is often due to the introduction of gas in the anterior chamber that helps hold the graft tightly to the posterior stroma of the host. Although a large gas bubble minimizes the risk of graft detachment, overfilling the chamber can prevent aqueous from entering the anterior chamber, resulting in a pupillary block.

To prevent pupillary block, cornea surgeons have traditionally used a peripheral iridotomy (PI) inferiorly, around the 6-o'clock position, said Dr. Yeu. But she cautioned that the PI can be rendered useless if the bubble occludes the iridotomy opening. "I'll use more than one PI to give the patient two shots at the goal," said Dr. Yeu. "That way, when they do sit upright following the keratoplasty, the gas elevates and the aqueous can travel through multiple sites." In addition, she dilates the patient at the end of the surgery with a few drops of atropine 1%.

She advised that patients be sent home with instructions to avoid activity and to lie face up for much of the first 24 to 48 hours to help the graft adhere. However, if a patient experiences acute signs of pupillary block—including worsening headache, nausea, or vomiting—they should sit or stand upright to make sure the intraocular bubble can rise above the PI site and/or the inferior pupillary margin. For severe, unremitting symptoms, they should be seen emergently, she said.

Late post-op. Typically, a signficant volume of the gas will have dissipated one week post-op. Any remaining IOP elevation is likely a response to the prescribed steroids, said Dr. Yeu.

To address this issue, she includes topical medications, including beta blockers and adrenergic agonists. Dr. Yeu avoids topical and oral carbonic anhydrase inhibitors because they may stun the active sodium pumps within the endothelium (which can reduce graft adhesion). She also avoids prostaglandin analogs because of their proinflammatory qualities.

If postkeratoplasty glaucoma does not respond adequately to medication, selective laser trabeculoplasty or more traditional glaucoma treatment might be necessary, she said. But, she added, the risk of corneal graft failure increases significantly when any hardware, like a tube shunt, is placed in the anterior chamber.

For patients who require glaucoma surgery up to four weeks after keratoplasty, Dr. Yeu always asks that subsequent eye care teams perform a pachymetry at every visit to identify any corneal thickness changes that might indicate early graft rejection. "I also want the patient back in my chair afterward," she said, "because, at this point, it's still a very vulnerable cornea and any surgery can beat up the ocular surface."

Retina: Buckles, Gas, and Oil

Acute increases in postoperative IOP can also occur during or after some vitreoretinal procedures. In most cases, the spikes can be managed with oral or topical pressure-lowering medications. In more complex patients, however, additional surgery might be required.

Scleral buckling. "Initial placement of a scleral buckle can cause increased IOP intraoperatively," said Aleksandra V. Rachitskaya, MD, at the Cleveland Clinic in Ohio. She said that the retina surgeon should always check for optic nerve pulsation when using a buckle. After tightening the band, visible pulsation indicates that IOP is on the higher side. The absence of pulsation can signify that either perfusion is normal or the pressure is elevated. "To distinguish between the two scenarios, we usually take a cotton tip applicator and press on the eye," said Dr. Rachitskaya. "If the additional pressure results in pulsations, we know that the IOP was normal." Anterior chamber tap might be used to decrease the pressure if indicated, she said.

After repair of a retinal detachment, scleral buckling surgery can impair venous drainage from the vortex veins. "A high scleral buckle, for example, can lead to congestion and swelling of the ciliary body," said Dr. Rachitskaya. "This forward rotation of the ciliary body can also shift the lens-iris diaphragm forward, resulting in a shallow anterior chamber or even angle closure."

Typically, mildly elevated IOP following scleral buckling resolves within weeks, said Dr. Rachitskaya. If not, additional medical treatment includes cycloplegics,

corticosteroids, and oral or topical pressure-lowering medications. She cautions that performing traditional glaucoma surgery on these eyes can be difficult due to the excessive scarring caused by the original buckle surgery.

Vitrectomy. IOP rise associated with vitrectomy largely stems from the use of sulfur hexafluoride (SF_6) and perfluoropropane (C_3F_8) gases as well as silicone oil. Although these tamponade agents are necessary for successful retinal reattachment, there are several caveats, said Dr. Rachitskaya.

SF_6 and C_3F_8 gas. Unlike silicone oil, gas at 100% concentration is highly expansive. "Determining the appropriate gas concentration is extremely important," said Dr. Rachitskaya. "I make it a habit of verbally confirming with my team the gas that is being used before mixing it myself. My go-to is 20% SF_6 and 14% C_3F_8."

Most IOP elevation following vitrectomy surgery is benign and the result of gas overfill. This can be remedied by topical pressure-lowering drops or oral carbonic anhydrase inhibitors as well as aspiration of a small amount of gas via a pars plana tap, if needed, she said. However, she added, in more serious cases of uncontrolled IOP stemming from incorrect gas concentration, there should be no delay in surgically replacing the gas tamponade, as prolonged elevation can cause permanent perfusion issues and optic nerve damage.

Patient warning. Since intraocular gas can expand with changes in atmospheric pressure, patients should abstain from air travel or exposure to significant changes in altitude until the bubble resorbs. Patients should also avoid postoperative exposure to nitrous oxide gas until resorption. The gas is highly soluble and quickly diffuses into the intraocular bubble, which can dangerously expand and lead to permanent vision loss, said Dr. Rachitskaya. As a result, it's common practice to place a bracelet on patients' arms indicating that they recently received vitrectomy surgery in case they need to undergo any subsequent surgery with general anesthesia.

Silicone oil. An oil tamponade doesn't expand like its gas counterpart, but oil overfill is still possible, said Dr. Rachitskaya. When issues do arise, they're typically seen in aphakic patients. "Without a lens to keep back the silicone oil, pupillary block can occur," said Dr. Rachitskaya. "To prevent this, I perform a prophylactic peripheral iridotomy in the 6-o'clock position intraoperatively. Because the oil floats, blockage of an iridotomy can occur if you choose a more superior position."

In more challenging retinal surgeries, including in patients with refractory glaucoma or with complete synechial angle closure, glaucoma surgery may be necessary—which raises an important point, said Dr. Rachitskaya. "Post-op IOP events often occur in complex patients requiring multiple treatments that span subspecialties. So regardless of expertise, all ophthalmologists should be aware of how common ocular surgeries can induce elevated pressure."

1 Hayashi K et al. *Ophthalmology*. 2017;124(5):701-708.

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For full disclosures, see this article at aao.org/eyenet.

SUBSPECIALTY DAY
Subspecialty Day is Friday, Nov. 12, and Saturday, Nov. 13.

Friday: Retina (day 1), Glaucoma, Neuro-Ophthalmology, Ocular Oncology and Pathology, Pediatric Ophthalmology, and Refractive Surgery. **Saturday:** Retina (day 2), Cornea, Oculofacial Plastic Surgery.

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Management of Hypotony After Glaucoma Surgery

Ocular hypotony is an uncommon but potentially vision-threatening event defined as either an intraocular pressure (IOP) that is 3 standard deviations below normal (<6.5 mm Hg) or an IOP low enough to cause visual impairment. This condition often manifests in the form of hypotony maculopathy (Fig. 1), corneal edema, astigmatism, choroidal effusion, and/or accelerated cataract formation. Treatment is typically reserved for patients with visual impairment and is often not required for those with asymptomatic "statistical" hypotony.

Etiology. Hypotony has numerous possible etiologies, which can be broadly classified in two groups: decreased aqueous production or increased aqueous outflow. Hypotony related to decreased aqueous production can be caused by ischemia of the ciliary body, uveitis, and tractional ciliary body detachment. Hypotony related to increased outflow can result from cyclodialysis clefts, retinal detachment, and iatrogenic causes such as glaucoma filtering surgeries, among others. Thus, management is specific to the etiology and relies on a detailed ocular history and exam.

Glaucoma surgery. Hypotony associated with glaucoma surgery is the most common etiology. The reported incidence of clinical hypotony ranges from 1% to 31% following filtering glaucoma surgery.[1,2] The most frequent causes of postsurgical hypotony are, in order, bleb leak, post-trabeculectomy overfiltration, use of glaucoma drainage devices, and iatrogenic cyclodialysis cleft formation.

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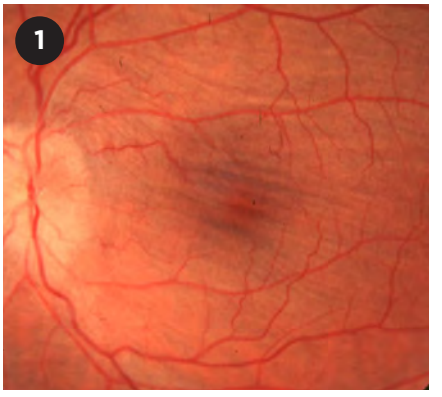
BY **JOEL KOVOOR, BS, JOSEPH F. PANARELLI, MD,** AND **ANNA T. DO, MD.**
EDITED BY BENNIE H. JENG, MD.

Bleb Leak

Pathophysiology and background. Bleb leaks are primarily caused by poor conjunctival integrity. Early bleb leaks (days to weeks after trabeculectomy) are often the result of inadvertent buttonhole tears or conjunctival retraction, whereas late bleb leaks (months to years after trabeculectomy) most commonly occur when focal, thin, avascular blebs erode or rupture. Antifibrotics such as mitomycin C and 5-fluorouracil are well-documented risk factors for late bleb leaks and must be used judiciously. Diagnosis of bleb leakage is typically confirmed with the Seidel test.

Management: early leak. The management approach to an early bleb leak depends largely on the extent of leakage. In cases of hypotony with a small amount of leakage, deep anterior chamber, and minimal change in visual acuity, various conservative measures can be used. These include steroid taper to allow for healing, aqueous humor suppressants to slow the rate of leakage, and/or soft bandage contacts with antibiotics to tamponade the leak and prevent infection. If these efforts fail, autologous blood injection and cyanoacrylate or fibrin glue have been shown to help, but outcomes are variable.



HYPOTONY MACULOPATHY. *Chorioretinal macular folds characteristic of hypotony maculopathy are seen on this fundus photograph and can be detected on vertical optical coherence tomography scans.*

In the more urgent cases—those with shallow anterior chambers and worse visual symptoms—resuturing of the wound with or without resuturing of the underlying scleral flap should be considered. Using compression sutures to wall off the leaking area is an alternative; however, adding sutures may lead to scarring and limit the bleb flow in the future.

Management: late leak. Management of late leaks depends on the severity of the condition; the conservative measures described for early leaks may be tried when appropriate. However, late leaks often require surgical intervention such as conjunctival advancement. One method involves

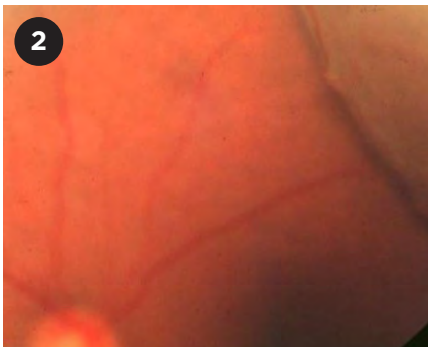
advancement of healthy conjunctiva over a denuded bleb after stripping the overlying epithelium. In another method, the bleb is entirely excised before conjunctival advancement, but this technique is associated with a higher rate of bleb failure and a greater need for glaucoma medications.[1]

If there is not enough viable conjunctiva surrounding the bleb for advancement, a free autologous graft from another site in the same eye or from the fellow eye can be used. Success in treating bleb leak or hypotony with conjunctival grafts has been reported to be 75.8%.[2] As an alternative, amniotic membrane can be used, but it may have slightly lower rates of long-term graft survival compared with standard conjunctival advancement.[3]

Overfiltering Bleb

Pathophysiology and background. An overfiltering bleb allows too much aqueous humor to pass through the bleb. Overfiltration can be caused by a loose scleral flap or insufficient inflammatory response at the surgical site, both of which reduce outflow resistance. Patients with overfiltering blebs typically present several years after glaucoma surgery and may be completely asymptomatic or have decreased vision or other signs of hypotony. On examination, the bleb will appear enlarged, elevated, and extended tangentially as well as posteriorly, with no evidence of leakage on Seidel test—even with gentle digital pressure.

Management. As with early bleb leaks, management typically starts with conservative methods, including steroid taper, aqueous humor suppressants, and autologous blood injection. In cases of overfiltration with shallow anterior chambers, cycloplegics (e.g., atropine or cyclopentolate) can be used to deepen the anterior chamber. Medical treatment with a cycloplegic agent will shift the lens-iris diaphragm posteriorly, which will help restart or increase ciliary body aqueous production. These medications can help resolve hypotony in mild to moderate cases of overfiltration, but patients should be warned that their vision may be affected by limited accommodation.



CHOROIDAL EFFUSIONS. *Fundus photograph of peripheral choroidal effusion secondary to hypotony following a trabeculectomy with mitomycin C.*

In chronic cases of overfiltration refractory to conservative treatment, surgical techniques such as conjunctival compression sutures can be employed. Compared with more invasive techniques such as direct transconjunctival scleral flap resuturing, compression sutures can easily be removed at the slit lamp to titrate the flow and have the advantage of not piercing the scleral flap itself. According to one retrospective study, conjunctival compression sutures had a 64.4% success rate for total resolution of hypotony at six months.[4] Conjunctival advancement and suturing with Vicryl sutures with or without scleral cauterization can also be used to induce additional scarring and reduce overfiltration.

Scleral flap resuturing is another technique, and it can be performed through an open or a transconjunctival approach. In the more traditional open approach, the overlying conjunctiva is reopened and the exposed scleral flap is resutured directly.

In the transconjunctival approach, sutures are passed radially through intact conjunctiva, the scleral flap, and then the adjacent sclera and knotted tightly over the conjunctiva. This technique has the advantage of not reopening the conjunctiva.

If first-line surgical management fails, bleb excision with scleral or pericardial graft can be used with conjunctival advancement.

Glaucoma Drainage Implants

Pathophysiology and background. Glaucoma drainage implants reduce IOP by shunting aqueous humor from the anterior chamber to an equatorial endplate placed in the subconjunctival space. These devices are typically indicated for patients in whom trabeculectomy was unsuccessful or those at high risk of trabeculectomy failure.

Two of the most commonly used drainage implant variants are the Ahmed Glaucoma Valve (AGV) and the Baerveldt Glaucoma Implant (BGI), which are primarily differentiated by the presence of a flow-restricting valve in the AGV. Valveless devices such as BGI are more liable to cause hypotony and require a temporary tube ligature to control IOP until the endplate is encapsulated. Although the incidence of persistent hypotony is greater for the BGI than for the AGV, the absolute rate of hypotony is fairly low: approximately 0.4% and 4.5% for the AGV and BGI, respectively.[5] The most common causes of hypotony with glaucoma drainage implants are insufficient endplate encapsulation and reduced production of aqueous humor secondary to postoperative inflammation.

Management. Conservative treatment starts with watchful waiting in cases of transient hypotony without evidence of excessive anterior chamber shallowing or symptomatic vision loss. IOP will often rise as the endplate naturally encapsulates or as postoperative inflammation resolves. Intracameral injection of a cohesive viscoelastic may also be used to help stabilize the eye and allow more time for encapsulation. If hypotony persists, the tube can be ligated with absorbable or nonabsorbable suture to halt outflow. Nonabsorbable sutures can be released in the office by laser transconjunctival ligature lysis as needed for IOP control.

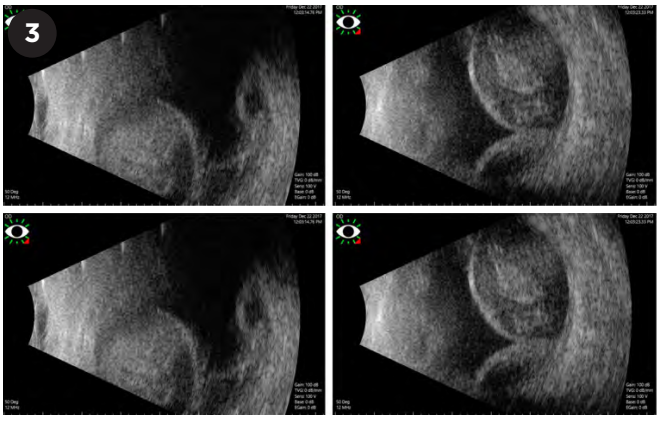
Intraluminal stenting, which involves running a suture segment through the tube lumen, can also be employed to increase resistance by reducing the total cross-sectional area of the tube. This technique can be performed through an ab interno or ab externo approach and has the advantage of easily being removed if IOP becomes too high.[6]

Ultimately, if hypotony after glaucoma surgery persists, the drainage implant can be removed.

P.A. Sidoti, MD/J. Panarelli, MD

Cyclodialysis Cleft

Pathophysiology and background. A cyclodialysis cleft occurs when the ciliary body is detached from the scleral spur, creating an abnormal pathway between the anterior chamber and suprachoroidal space. Although a cyclodialysis cleft is usually the result of blunt trauma to the eye, it can also be caused iatrogenically during any intraocular surgery that involves manipulation of the anterior chamber and angle structures. Minimally invasive angle procedures such as goniotomy with the Kahook Dual Blade (New World Medical) or Trabectome (MST), gonioscopy-assisted transluminal trabeculotomy, and insertion of an iStent (Glaukos) or Hydrus Microstent (Ivantis) are at higher risk of cyclodialysis cleft than other surgeries.



HEMORRHAGIC EFFUSION. *B-scan imaging demonstrating large hemorrhagic effusions with low to medium internal reflectivity characteristic of a partially liquefied clot.*

Many clefts resolve spontaneously, but those that persist require urgent attention to prevent development of further visual deficits. Clefts can be visualized on gonioscopy, ultrasound biomicroscopy, and anterior segment optical coherence tomography.

Management. Cycloplegics can be used as a first step in conservative treatment of small cyclodialysis clefts. These medications work by relaxing the ciliary body, allowing the detached muscle fibers to realign with the scleral spur.

If this does not resolve the cleft, treatment can be escalated to argon photocoagulation, transscleral cyclophotocoagulation, or cryotherapy to promote inflammation at the detachment site, thereby inducing adhesion to seal the cleft. This treatment can be repeated multiple times and has shown good success for smaller clefts (less than 3 clock-hours).[7]

Direct cyclopexy can be employed for large clefts (3 to 6 clock-hours) or those that failed to close with the preceding measures. Although many techniques have been described for cyclopexy, the most common method involves creating a full-thickness scleral flap to access the ciliary body and using mattress sutures to attach it directly to the undersurface of the sclera. Other techniques include employing a partial or shelved limbal-scleral flap. Long-term results are promising, with one study reporting 100% resolution of IOP for 12 patients who underwent direct cyclopexy with a double lamellar scleral flap.[8]

Related Complication: Choroidal Effusions

Pathophysiology and background. Choroidal effusions are a common and clinically relevant complication of hypotony after glaucoma surgery (Fig. 2). They can present in serous or hemorrhagic form. In serous effusions, low IOP reduces the hydrostatic pressure opposing choroidal vessels, allowing transudative fluid accumulation, whereas rupture of those same vessels will result in a hemorrhagic effusion. Because it may be difficult to differentiate between the two on clinical examination, an ultrasound B-scan should be performed (Fig. 3). Small peripheral effusions are usually asymptomatic, whereas large effusions may extend posteriorly into the macula or may displace the lens-iris diaphragm, leading to decreased vision.

Management. Conservative treatment starts with medical management targeted toward the specific etiology of hypotony. This approach includes treatments such as cycloplegic drops, steroid taper, or bandage contact lenses.

However, for cases in which persistent or large effusions are accompanied by symptomatic vision loss or a flat anterior chamber, surgical drainage is indicated. Choroidal effusion drainage is approached by quadrant and can be repeated if recurrent.

Conclusion

Glaucoma surgical procedures are the most common cause of ocular hypotony, which can occur as a result of bleb leak or overfiltration, use of glaucoma drainage implants, or iatrogenic cyclodialysis cleft. This rare complication may be asymptomatic or lead to visual loss. Asymptomatic patients with adequate anterior chamber depth may be observed. Hypotony that causes a shallow anterior chamber or visual symptoms is managed according to the etiology and severity, with treatments ranging from medical therapy with aqueous suppressants or cycloplegics to surgical interventions including conjunctival advancement, compression sutures, tube ligation, and flap suturing as appropriate.

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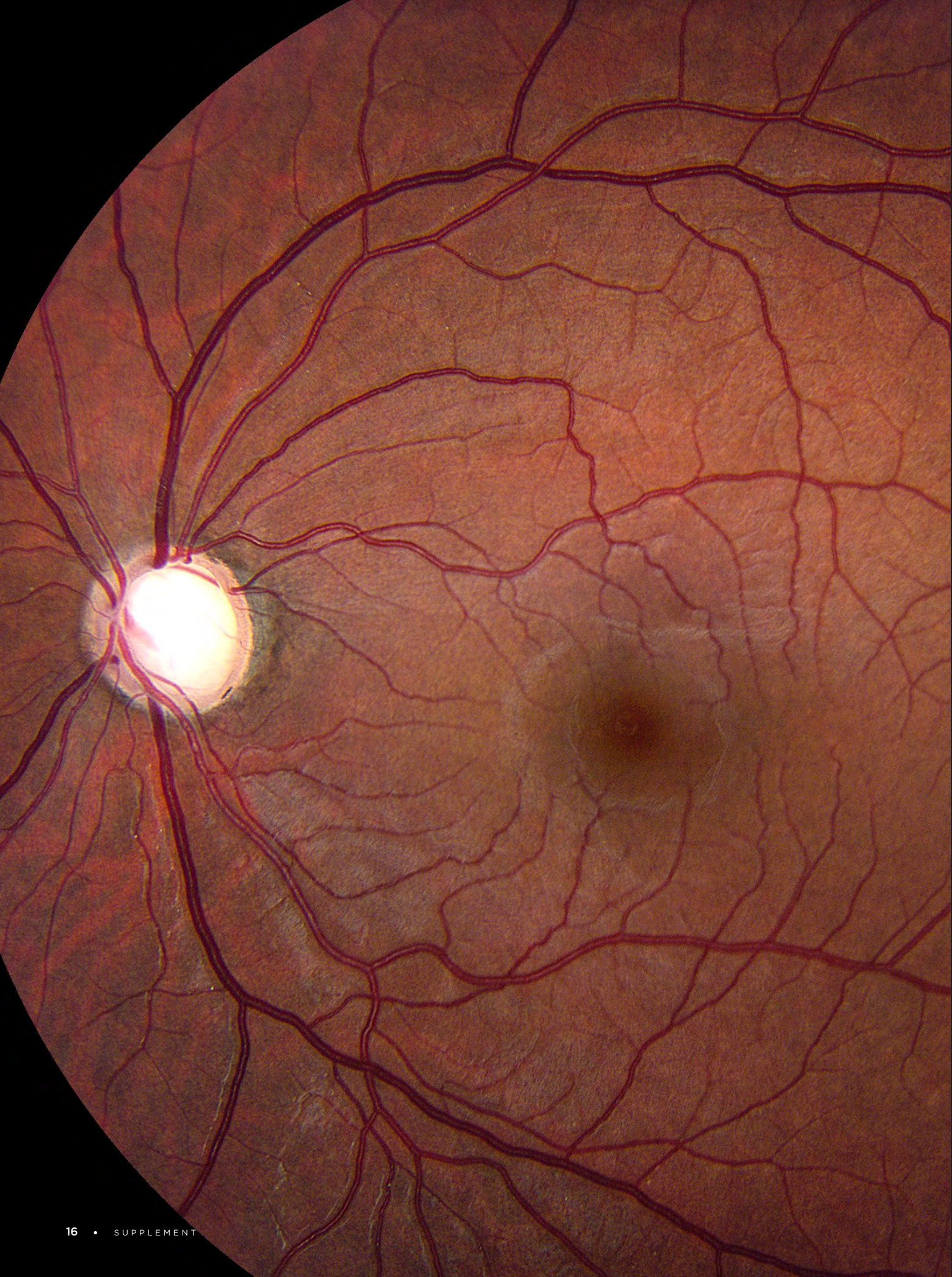
See disclosure key, page 5.

J. Panarelli, MD



Tackling Health Care Disparities

Disparities in patient care are present throughout medicine. An overview of how these inequities play out in the care of patients with glaucoma.

By Lori Baker-Schena, MBA, EdD, Contributing Writer

THIS PAST YEAR, LEON W. HERNDON Jr., MD, spent countless hours on Zoom calls discussing what the twin crises of COVID-19 and racial injustice laid bare—the glaring disparities in eye care delivery and research among underrepresented minority groups.

Glaucoma specialists like Dr. Herndon are well aware of the social determinants of health. After all, research has shown that primary open-angle glaucoma (POAG) is six times more prevalent among Blacks than in age-matched Whites, with Blacks exhibiting more severe disease that is resistant to intervention and results in higher rates of blindness.[1]

Toll on Patients' Vision

While the genetic underpinnings of glaucoma continue to be studied, the relationship between socioeconomic status, ethnicity, access to eye care, and reduced quality of life also play a role in glaucoma development and disease severity. And in a March 2021 keynote talk to the International Agency for the Prevention of Blindness, Dr. Herndon noted that this web of intersecting factors is taking a direct toll on patients' vision.

OUTSIZED IMPACT. *The likelihood of developing POAG—and experiencing its complications—is higher in Black patients.*

Jason S. Calhoun, COA

"I am not a social sciences researcher, but I have lived my entire life witnessing inequities in health care," said Dr. Herndon, at Duke University Eye Center in Durham, North Carolina. "There is so much information that many ophthalmologists are not aware of. If we as a profession are to make an impact, we must be aware of the problems, educate ourselves, and be open to change."

One Step Forward, Two Steps Back?

Three decades ago, when Eydie Miller-Ellis, MD, was a resident at the University of Pennsylvania in Philadelphia, she became interested in glaucoma after witnessing patient after patient fall through the cracks of the health care system.

"A lack of follow-up, marginal patient education, and low treatment compliance was resulting in needless vision loss in individuals with glaucoma," Dr. Miller-Ellis said. "Glaucoma is the No. 1 cause of preventable blindness, disproportionately affecting individuals of African descent—and glaucoma runs in my family. I thought glaucoma is where I could make the biggest difference."

Ongoing economic fallout. Thirty years later, while Dr. Miller-Ellis has seen great progress in treatment, disparities in glaucoma care have actually become worse, as even more patients are not able to access—or have become lost in—the health care system, or have needed to sacrifice their health in general because of a lack of a societal safety net.

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Role of insurance coverage. "While the Affordable Care Act has tried to close the coverage gaps, extensive access challenges still exist," Dr. Miller-Ellis said. "Patients in underserved communities are less able to navigate the current insurance system, which prevents them from receiving the health care they need."

For example, the insurance authorization process for medications and procedures often places barriers between the physician and their glaucoma patients. "In some offices, the situation is so difficult that the staff give up trying, and the patient suffers," Dr. Miller-Ellis said.

She also argues in favor of universal, basic health care insurance: "Individuals should not have to choose between paying rent and paying for their health care and medications."

Impact of COVID. During the pandemic, Blacks and Hispanics have been more likely to visit the emergency room for—or be hospitalized with—SARS-CoV-2.[2,3] And once sick, they were more likely to die of COVID than were Whites.[4] The pandemic also had a significant impact on socioeconomic measures of well-being, such as employment rates (see "The Statistics Tell the Story").

Despite the abrupt and severe impact of the pandemic, "we didn't get this way overnight," Dr. Herndon said. "We cannot solve these inequities without taking into consideration the structural racism rooted in our society. It is going to take a lot of awareness, education, and empathy."

Disparities in Delivering Care

As Dr. Herndon noted, the social determinants of health have deep and complex roots.[5,6] For instance, the systemic disinvestment in segregated neighborhoods has resulted in under-resourced medical facilities. In turn, this pattern of disinvestment makes it difficult to attract experienced primary care providers—which, in turn, impacts patient access to and utilization of health care.[6]

Who gets tested? In the age of big data, individual utilization of health care resources is becoming easier to ascertain. For example, Dr. Miller-Ellis pointed out, data can show whether a patient with a diagnosis code for glaucoma is receiving the appropriate diagnostic tests.

"Research has demonstrated that minority populations do not receive all of the testing they need, as opposed to majority populations," Dr. Miller-Ellis said, citing study findings indicating large disparities in the receipt of glaucoma care between Medicaid enrollees and patients with commercial insurance.[7] For this study, researchers followed 21,766 patients with newly diagnosed open-angle glaucoma (OAG) enrolled in Medicaid or a large U.S. managed care network. The results showed that patients with Medicaid insurance were less likely to receive glaucoma testing in the 15 months following initial diagnosis than those in the managed care program.

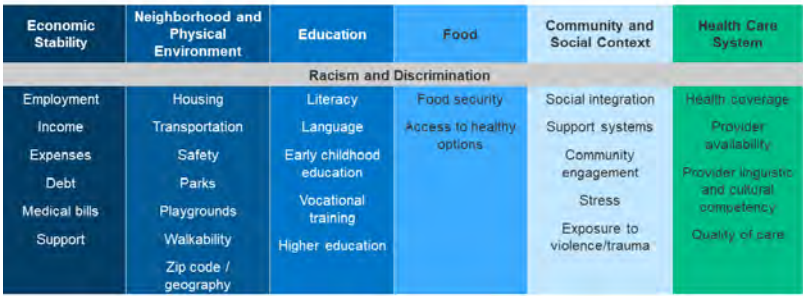
Additionally, nearly half (49%) of all OAG patients with Medicaid insurance had no record of any glaucoma testing in the first 15 months following the initial diagnosis, while only 1 in 5 (21%) with commercial health insurance had no record of any glaucoma testing. Moreover, the odds of receiving no glaucoma testing in patients with Medicaid coverage, when compared with those with commercial coverage, were 198% higher for Whites, 291% higher for Blacks, and 167% higher for Hispanics.

"Even within the Medicaid group, all of whom have lower socioeconomic status, Black patients with a blinding eye disease are less likely to be adequately followed than their majority population counterparts," Dr. Miller-Ellis said.

How can compliance be encouraged? Compliance in glaucoma treatment is essential. "Yet if someone has a complicated life, it is harder to keep up with treatment maintenance," Dr. Miller-Ellis said. "If your home situation is unstable or chaotic, it is more difficult to care for your own health issues."

This scenario is exacerbated in women, who often are caretakers for children and aging parents. That's because caretakers tend to neglect themselves, Dr. Miller-Ellis noted. In addition, people who are economically disadvantaged have a hierarchy of concerns, including securing food and shelter, so eye care

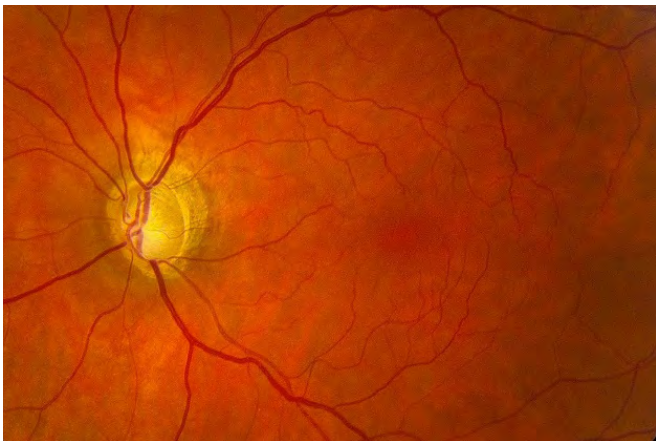
Factors That Drive Health Outcomes



OVERLAPPING CHALLENGES. *Determinants of health outcomes include myriad social and economic factors. SOURCE: Adapted from the Kaiser Family Foundation.*

may not even be on their list. "These factors greatly impact whether patients can return for follow-up visits," Dr. Miller-Ellis said. "And it takes many office visits to get a glaucoma patient under control."

Educating patients. Getting patients to buy into using daily eyedrops and sticking with their treatment plan involves health literacy and education, Dr. Miller-Ellis said. "As physicians, we are charged with having to communicate with our patients in ways they can understand. Since many of my patients are visual learners, I provide written instructions that are clear so that key directions can be easily followed."



TOLL ON VISION. *The likelihood of glaucoma complications is higher in minority populations.*

Choosing treatment. Issues of compliance also may prompt a clinician to recommend surgery instead of medication. "I advocate early intervention with laser trabeculoplasty or incisional glaucoma surgery to lessen the long-term challenges with medication compliance," Dr. Miller-Ellis said.

Disparities in Research

One of the major burdens facing marginalized people with debilitating eye conditions is the lack of relevant research.

Who gets studied? Glaucoma serves as a key example of this, as most research has been conducted in Whites. This leads to huge gaps in understanding and clinical care, Dr. Herndon said. He quoted Liu et al.: "To tackle the elevated burden of eye disease facing marginalized communities, we need to promise and fulfill our commitment to increase racial and ethnic inclusion in clinical trials. Without addressing this important issue, we risk perpetuating rather than resolving current health disparities."[8]

Focus on genetics. Janey L. Wiggs, MD, PhD, at Harvard Medical School in Boston, noted that the majority of genetic studies in glaucoma have been in Whites who are of European ancestry. "When you think about the translatability of genetic information from glaucoma research to clinical care, the patients who are going to benefit the most from genetic studies are White because of the nature of the data."

She added, "Historically, information from genetic investigation of individuals of African ancestry has been missed, which limits the diagnostic and therapeutic applications. To help gain more insight into glaucoma, we need more research on large populations of African ancestry, and this is a crucial step for the field."

Dr. Wiggs noted that these disparities are seen throughout medicine, as many genetic studies have primarily been conducted in White populations. She cited the use of polygenic risk scores derived from genome-wide association studies (GWASs) to assess disease risk. "These risk scores are beginning to be used in diseases with complex inheritance such as glaucoma for risk stratification and treatment consideration."

"However," she added, "currently these polygenic risk scores have been primarily tested using White patients. This is because the studies that generated the scores were mainly performed in Caucasian individuals. We cannot yet predict if these scores have any relevant predictability in African ancestry populations, and we need more research to determine whether these scores are transferable to individuals of African ancestry."

Promising shift in direction. Research inequities are beginning to be addressed, however, as efforts by the following research groups indicate:

Genetics of Glaucoma in People of African Descent Consortium. This group performed a GWAS of African-ancestry populations for POAG.[9] The study discovered a genetic variant in the *APBB2* gene associated with a higher risk of POAG, and the genetic association was discovered only in individuals of African ancestry.

International Glaucoma Genetics Consortium. This group recently published a study showing that many glaucoma genetic risk factors have similar effects on disease risk in people of European Caucasian, African, and Asian ancestry.[10]

"This study, which identified risk loci contributing to the development of POAG across ethnic groups, is an advance over prior POAG GWAS studies that have mainly focused on individuals from a single ancestry group," Dr. Wiggs said. "However, it is important to note that further research in ethnic groups not currently well represented in genetic research is needed."

University of Pennsylvania. Penn researchers

have been investigating the genetics of glaucoma in Blacks through the POAAGG (Primary Open-Angle African American Glaucoma Genetics) study.[11] "Our study has recruited more than 10,200 African Americans from the city of Philadelphia," Dr. Miller-Ellis said.

Community outreach was an essential part of this study. The researchers partnered with community leaders to spread the word about the study and glaucoma risk. "We also offered free glaucoma screenings at our institute," Dr. Miller-Ellis said. "These efforts allowed us to collect full phenotypic information on more than 90% of glaucoma patients."

In addition, Penn researchers performed a GWAS on cases and controls in this population, as well as whole-exome sequencing in collaboration with Regeneron Genetics Center. "Thus far, we have identified a novel variant on chromosome 11 near the *TRIM66* gene,[12] as well as several genes associated with POAG-related quantitative traits," she said. "These results confirm that POAG is a heterogeneous disease characterized by distinct phenotypes. Our long-term goals are to define the genetic subtypes of POAG and to develop more targeted diagnostic and therapeutic interventions for this most affected population."

The Statistics Tell the Story

Evidence of social and health inequities to consider:

Median household assets. In 2011, these figures were $110,500 for White, $7,683 for Hispanic, and $6,314 for Black households.[1]

Unemployment. In March 2020, the unemployment rate was 6.8% among Blacks, 6% among Hispanics, and 3.9% among Whites. The next month, these percentages skyrocketed to 16.7% for Blacks, 18.9% for Hispanics, and 14.1% for Whites. By March 2021, these rates improved to 9.6% for Blacks, 7.9% for Hispanics, and 5.4% for Whites.[2]

Life expectancy at birth. In 2014, Whites could expect to live to age 79, versus age 82 for Hispanics and 74 for Blacks.[1] But the pandemic could be expected to reduce U.S. life expectancy in 2020 by 0.68 years for Whites, 2.10 years for Blacks, and 3.05 years for Hispanics.[3]

Heart disease and mortality. In 2014, the age-adjusted mortality related to heart disease—the No. 1 cause of death in the United States—per 100,000 population was 166 for Whites, 116 for Hispanics, and 206 for Blacks.[1]

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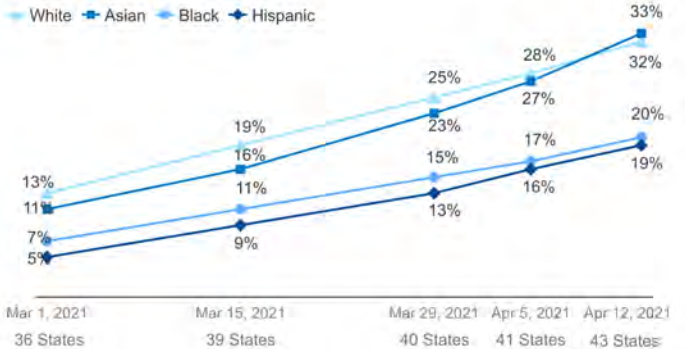
COVID-19 Vaccination Rates



WHO'S VACCINATED? *Estimate of vaccination rates by ethnicity, from March 1 to April 12, 2021, based on publicly available data on state websites. SOURCE: Adapted from the Kaiser Family Foundation.*

An Often-Overlooked Factor

Dr. Herndon noted that a key factor contributing to health care disparities is the lack of diversity in the physician workforce. (*EyeNet* will cover this topic later this year.)

"There is strong evidence that communication in racially discordant medical interactions is usually less productive and positive in content and tone than in racially concordant interactions," Dr. Herndon said. "A variety of studies have shown that racial discordance leads to less relationship building, less health information exchange, and less treatment planning."

This discordance can be traced to the low percentage of members of minority groups in the physician workforce, Dr. Herndon noted. For instance, he said, "In 2015, only 2.5% of practicing ophthalmologists were Black. Our numbers are not improving, yet for the health of the patient it is essential that providers reflect the community they serve."

To address these inequities, ophthalmology as a profession must focus on creating a pipeline of underrepresented minority groups to enter the field. Role models are a key component of these efforts. Dr. Herndon recalled his own experience as a medical student when he reached out to Dr. Miller-Ellis, who was at the University of North Carolina, Chapel Hill, at the time.

"Here was someone who looked like me doing ophthalmology,"

Dr. Herndon said. "Dr. Miller-Ellis was such an inspiration and gave me the confidence to pursue a career in ophthalmology. We need more role models who can inspire young medical students of color to pursue the field of ophthalmology." (See "Academy Resources.")

Moving Forward

Dr. Miller-Ellis noted that the University of Pennsylvania, under the leadership of Eve J. Higginbotham, SM, MD, ML, has been at the forefront of change (see "What's in a Word?" online with this article at aao.org/eyenet).

"While diversity, health disparities, and inclusion have been discussed for years, the events of 2020 have put these issues at the forefront," Dr. Miller-Ellis said. "We are finally seeing a real commitment from the government, health providers, and insurers to move these initiatives forward—working on inclusion in bench research and clinical trials while addressing disparities in health care."

She added, "Sometimes it takes a disaster to see the holes in the safety net, and the COVID-19 pandemic showed how a lot of people—particularly those from minority communities—are falling disproportionately through those holes. However, if we as a society can address issues facing the most disadvantaged of people, it will help everyone. Diverse ideas make organizations better. We need to keep moving forward."

ACADEMY RESOURCES

For more information, see the following:

Web page. Information on health care disparities and diversity, equity, and inclusion (DEI), including two related task forces, is available at aao.org/diversity-equity-and-inclusion.

Mentoring. Three years ago, the Academy, in partnership with the American Academy of University Professors, launched the Minority Ophthalmology Mentoring program. See aao.org/minority-mentoring.

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MORE ONLINE. For suggested reading and a conversation with Dr. Higginbotham, see this article at aao.org/eyenet.

Meet the Experts

Leon W. Herndon Jr., MD Professor of ophthalmology and chief of the glaucoma division at Duke University Eye Center in Durham, N.C. *Financial disclosures: None.*

Eve J. Higginbotham, SM, MD, ML Vice Dean for Inclusion and Diversity at the University of Pennsylvania's Perelman School of Medicine in Philadelphia. She is also a senior fellow at the Leonard Davis Institute for Health Economics and professor of ophthalmology at the University of Pennsylvania as well as Vice Chair of the Ocular Hypertension Treatment Study. *Financial disclosures: NEI: S.*

Eydie Miller-Ellis, MD Professor of clinical ophthalmology and Vice Chair for Faculty Affairs and Diversity for the Scheie Eye Institute at the University of Pennsylvania's Perelman School of Medicine in Philadelphia. She also serves as the chief of glaucoma service and director of the glaucoma fellowship program at the Scheie Eye Institute and director of glaucoma at the Philadelphia Veterans Administration Medical Center. *Financial disclosures: Aerie: C; Allergan: C; NIH: S.*

Janey L. Wiggs, MD, PhD Paul Austin Chandler Professor of Ophthalmology and the Vice Chair for Clinical Research in Ophthalmology at Harvard Medical School in Boston. She also directs the genetic testing laboratory at Massachusetts Eye and Ear and is codirector of the Ocular Genomics Institute and the Glaucoma Center of Excellence. *Financial disclosures: Aerpio: C,S; Allergan: C; Editas: C; Maze: C; NIH: S; Regenxbio: C.*

See disclosure key, page 5.

AMERICAN ACADEMY
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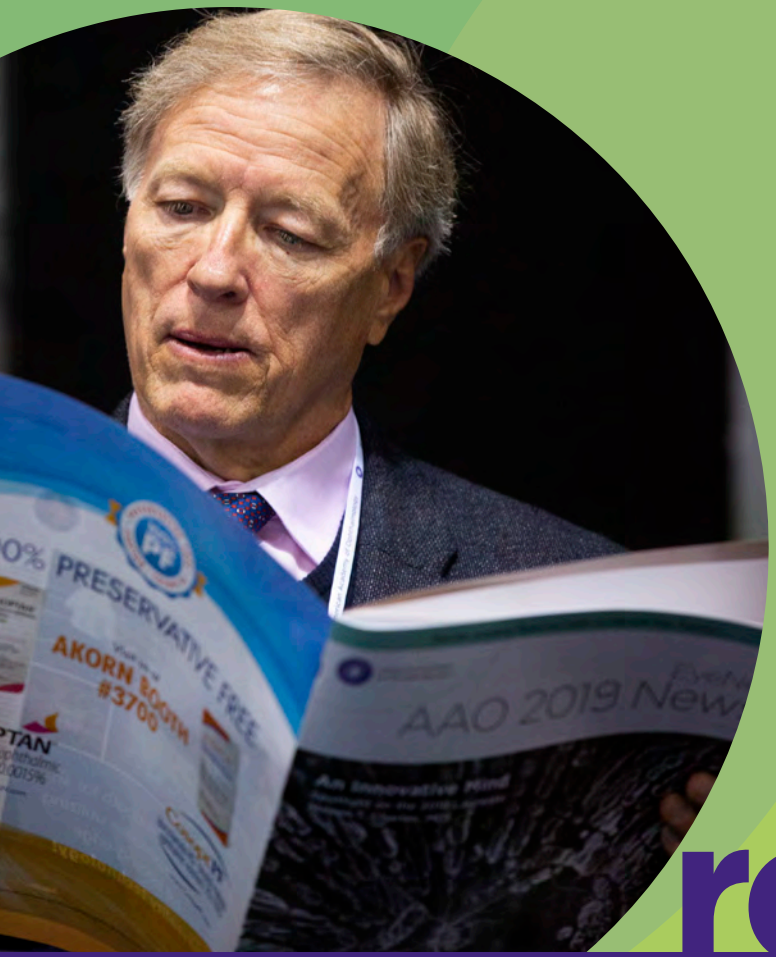
AAO 2021

Don't Miss *EyeNet*'s Ongoing Meeting Coverage

Find out what's new at AAO 2021 and Subspecialty Day.



MONTHLY PREVIEWS
Destination AAO 2021: Deadlines, quick tips, and sneak peeks in the June-November issues of *EyeNet® Magazine*.

THE MEETING NEWSPAPER
AAO 2021 News: Subspecialty Day recommendations, named lecture previews, and more.

MAP AND LISTINGS *Exhibitor Guide:* Must-know exhibitor information.

BREAKING NEWS *AAO 2021 Daily:* Meeting news emailed nightly from New Orleans.

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ONCE-DAILY

rocklatan®

(netarsudil and latanoprost ophthalmic solution) 0.02%/0.005%

BRIEF SUMMARY
Consult the full Prescribing Information for complete product information.

INDICATIONS AND USAGE
Rocklatan® (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005% is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION
The recommended dosage is one drop in the affected eye(s) once daily in the evening.

If one dose is missed, treatment should continue with the next dose in the evening. The dosage of Rocklatan® should not exceed once daily. Rocklatan® may be used concomitantly with other topical ophthalmic drug products to lower IOP. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Pigmentation
Rocklatan® contains latanoprost which has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as latanoprost is administered.

The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Beyond 5 years the effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with Rocklatan® can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes
Rocklatan® contains latanoprost which may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation
Rocklatan® contains latanoprost which should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation because it may exacerbate inflammation.

Macular Edema
Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost. Rocklatan® should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Herpetic Keratitis
Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. Rocklatan® should be used with caution in patients with a history of herpetic keratitis. Rocklatan® should be avoided in cases of active herpes simplex keratitis because it may exacerbate inflammation.

Bacterial Keratitis
There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Use with Contact Lenses
Contact lenses should be removed prior to the administration of Rocklatan® and may be reinserted 15 minutes after administration.

ADVERSE REACTIONS
Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Rocklatan®
The most common ocular adverse reaction observed in controlled clinical studies with Rocklatan® was conjunctival hyperemia which was reported in 59% of patients. Five percent of patients discontinued therapy due to conjunctival hyperemia. Other common ocular adverse reactions reported were instillation site pain (20%), corneal verticillata (15%), and conjunctival hemorrhage (11%). Eye pruritus, visual acuity reduced, increased lacrimation, instillation site discomfort, and blurred vision were reported in 5-8% of patients.

Other adverse reactions that have been reported with the individual components and not listed above include:

Netarsudil 0.02%
Instillation site erythema, corneal staining, increased lacrimation and erythema of eyelid.

Latanoprost 0.005%
Foreign body sensation, punctate keratitis, burning and stinging, itching, increased pigmentation of the iris, excessive tearing, eyelid discomfort, dry eye, eye pain, eyelid margin crusting, erythema of the eyelid, upper respiratory tract infection/nasopharyngitis/influenza, photophobia, eyelid edema, myalgia/arthralgia/back pain, and rash/allergic reactions.

DRUG INTERACTIONS
In vitro drug interaction studies have shown that precipitation can occur when eye drops containing thimerosal are mixed with Rocklatan®. If such drugs are used, they should be administered at least five (5) minutes apart.

The combined use of two or more prostaglandins or prostaglandin analogs including latanoprost ophthalmic solution 0.005% is not recommended. It has been shown that administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical elevations in IOP.

For additional information, refer to the full Prescribing Information at Rocklatan.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Manufactured for: Aerie Pharmaceuticals, Inc., Irvine, CA 92614, U.S.A.

U.S. Patent Nos.: 8,450,344; 8,394,826; 9,096,569; 9,415,043; 9,931,336; 9,993,470; 10,174,017; 10,532,993; 10,588,901

References: 1. Rocklatan® (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005% Prescribing Information. Aerie Pharmaceuticals, Inc., 2020. **2.** Asrani S, Bacharach J, Holland E, et al. Fixed-dose combination of netarsudil and latanoprost in ocular hypertension and open-angle glaucoma: pooled efficacy/safety analysis of phase 3 MERCURY-1 AND -2. *Adv Ther.* 2020;37(4):1620-1631.

Powerful IOP reduction in a single bottle

ONE DROP POWER

Only Rocklatan® demonstrated superior efficacy over latanoprost at all time points[1,2]

INDICATIONS AND USAGE

Rocklatan® (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005% is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION

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CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

- Increased **pigmentation** of the iris, periorbital tissue (eyelid), and eyelashes can occur. Iris pigmentation likely to be permanent.
- Gradual **change to eyelashes** may include increased length, thickness, number, and misdirected growth of lashes. Usually reversible upon discontinuation of treatment.
- Use with caution in patients with a history of **intraocular inflammation** (iritis/uveitis). Should generally not be used in patients with active intraocular inflammation.
- **Macular edema**, including cystoid macular edema, has been reported with latanoprost. Use with caution in aphakic patients, pseudophakic patients with a torn posterior lens capsule, or patients with known risk factors for macular edema.
- Use with caution in patients with a history of **herpetic keratitis**. Avoid use in cases of active herpes simplex keratitis.
- **Bacterial keratitis** has been reported with multiple-dose containers of topical ophthalmic products inadvertently contaminated by patients.
- Remove **contact lenses** prior to administration and reinsert 15 minutes after administration.

ADVERSE REACTIONS

The most common ocular adverse reactions were conjunctival hyperemia (59%), with 5% of patients discontinuing therapy for this reason, instillation site pain (20%), corneal verticillata (15%), and conjunctival hemorrhage (11%). Eye pruritus, visual acuity reduced, increased lacrimation, instillation site discomfort, and blurred vision were reported in 5-8% of patients.

Please see full Prescribing Information for Rocklatan® at Rocklatan.com

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Visit Rocklatan.com to learn more about this innovative IOP-lowering treatment

Please refer to Brief Summary on the reverse side.

IOP, intraocular pressure.

ONCE-DAILY rocklatan® (netarsudil and latanoprost ophthalmic solution) 0.02%/0.005%