Glaucoma Management Strategies
Across the Spectrum of Disease

Original Release: April 1, 2017
Last Review: March 14, 2017
Expiration: April 30, 2018

This continuing medical education activity is jointly provided by New York Eye and Ear Infirmary of Mount Sinai and MedEdicus LLC.

This continuing medical education activity captures content from a CME symposium held on October 17, 2016, in Chicago, Illinois.

Faculty
Donald L. Budenz, MD, MPH (Chair)
Robert D. Fechtner, MD
Steven J. Gedde, MD
Janet B. Serle, MD

Distributed with EyeNet
LEARNING METHOD AND MEDIUM
This educational activity consists of a supplement and ten (10) study questions. The participant should, in order, read the learning objectives contained at the beginning of this supplement, read the supplement, answer all questions in the post test, and complete the Activity Evaluation/Credit Request form. To receive credit for this activity, please follow the instructions provided on the post test and Activity Evaluation/Credit Request Form. This educational activity should take a maximum of 1.5 hours to complete.

CONTENT SOURCE
This continuing medical education (CME) activity captures content from a CME symposium held on October 17, 2016, in Chicago, Illinois.

ACTIVITY DESCRIPTION
Managing individual cases of patients with glaucoma is complicated by the increasing number of medical and surgical interventions. Moreover, the approach to glaucoma therapy is frequently dictated by the severity of the disease. Eyes with higher intraocular pressure (IOP) or more advanced optic nerve damage and/or visual field loss will typically be managed more aggressively than those with lower IOP or earlier-stage disease. The purpose of this case-based activity is to update ophthalmologists on current information on diagnostic testing, medical management, and surgical interventions that can help slow the rate of progression and prevent vision loss from glaucoma.

TARGET AUDIENCE
This educational activity is intended for ophthalmologists.

LEARNING OBJECTIVES
Upon completion of this activity, participants will be better able to:
- Select appropriate ocular hypotensive therapy to meet IOP goals throughout the day and night
- Develop individualized regimens for IOP control with multodrop or fixed-combination therapy
- Describe effective IOP-lowering strategies, including patient counseling, in patients with ocular surface disorders
- Evaluate surgical procedures for patients requiring IOP-lowering interventions

ACCREDITATION STATEMENT
This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCMCE) through the joint providership of New York Eye and Ear Infirmary of Mount Sinai and MedEdicus LLC. The New York Eye and Ear Infirmary of Mount Sinai is accredited by the ACCME to provide continuing medical education for physicians. In July 2013, the Accreditation Council for Continuing Medical Education (ACCMCE) through the joint providership of New York Eye and Ear Infirmary of Mount Sinai and MedEdicus LLC named New York Eye and Ear Infirmary of Mount Sinai “Accreditation with Commendation,” for six years as a provider of continuing medical education for physicians, the highest accreditation status awarded by the ACCME.

AMA CREDIT DESIGNATION STATEMENT
The New York Eye and Ear Infirmary of Mount Sinai designates this enduring material for a maximum of 1.5 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

GRANTOR STATEMENT
This continuing medical education activity is supported through unrestricted educational grants from Alcon and Allergan.

DISCLOSURE POLICY STATEMENT
It is the policy of New York Eye and Ear Infirmary of Mount Sinai that the faculty and anyone in a position to control activity content disclose any real or apparent conflicts of interest relating to the topics of this educational activity, and also disclose discussions of unlabeled/unapproved uses of drugs or devices during their presentation(s). New York Eye and Ear Infirmary of Mount Sinai has established policies in place that will identify and resolve all conflicts of interest prior to this educational activity. Full disclosure of faculty/planners and their commercial relationships, if any, follows.

DISCLOSURES
Donald L. Budenz, MD, MPH, had a financial agreement or affiliation during the past year with the following commercial interests in the form of Consultant/Advisory Board: Alcon, ForSight VISIONS, Iovations Inc, Contracted Research: Abbott Medical Optics, Alcon, ForSight VISIONS, and New World Medical, Inc. Robert D. Fechtner, MD, had a financial agreement or affiliation during the past year with the following commercial interests in the form of Consultant/Advisory Board: Alcon, Bausch & Lomb Incorporated, ForSight VISIONS, Glaucus Corporation, and Santen Pharmaceutical Co, Ltd, Contracted Research: Alcon, and Allergan. Steven J. Gedde, MD, has no relevant commercial relationships to disclose.

Janet B. Serle, MD, had a financial agreement or affiliation during the past year with the following commercial interests in the form of Consultant/Advisory Board: Aerie Pharmaceuticals, Inc, and Velos Pharmaceuticals, Inc. Thomas Panarelli, MD, had a financial agreement or affiliation during the past year with the following commercial interests in the form of Consultant/Advisory Board: Aerie Pharmaceuticals, Inc, and Allergan.

EDITORIAL SUPPORT DISCLOSURES
Tong Reali, MD, MPH, had a financial agreement or affiliation during the past year with the following commercial interests in the form of Consultant/Advisory Board: Alcon, Bausch & Lomb Incorporated, and Inotek Pharmaceuticals Corporation. Contracted Research: Alcon, and F. Hoffmann-La Roche Ltd.

DIANE McCARTIE, PHD, CYNTHIA TORNALUYG, RD, MBA, CHCP, KIMBERLY CORBIN, CHCP, BARBARA AUBEL, and Michelle Ong have no relevant commercial relationships to disclose.

DISCLOSURE ATTESTATION
The contributing physicians listed above have attested to the following:
1) that the relationships/affiliations noted will not bias or otherwise influence their involvement in this activity,
2) that the practice recommendations given relevant to the companies with whom they have relationships/affiliations will be supported by the best available evidence or, absent evidence, will be consistent with generally accepted medical practice, and
3) that all reasonable clinical alternatives will be discussed when making practice recommendations.

OFF-LABEL DISCUSSION
This CME activity includes discussion of unlabeled and/or investigative uses of drugs. Please refer to the official prescribing information for each drug discussed in this activity for FDA-approved dosing, indications, and warnings.

FOR DIGITAL EDITIONS
System Requirements:
- If you are viewing this activity online, please ensure the computer you are using meets the following requirements:
  • Operating System: Windows or Macintosh
  • Media Viewing Requirements: Flash Player or Adobe Reader
  • Supported Browsers: Microsoft Internet Explorer, Firefox, Google Chrome, Safari, and Opera
  • A good Internet connection

NEW YORK EYE AND EAR INFIRMARY OF MOUNT SINAI PRIVACY & CONFIDENTIALITY POLICIES
http://www.nyee.edu/health-professionals/cme/enduring-activities

CME PROVIDER CONTACT INFORMATION
For questions about this activity, call 212-977-4383.

TO OBTAIN AMA PRA CATEGORY 1 CREDIT™
To obtain AMA PRA Category 1 Credit™ for this activity, read the material in its entirety and consult referenced sources as necessary. Complete the evaluation form along with the post test answer box within this supplement. Remove the Activity Evaluation/Credit Request page from the printed supplement or print the Activity Evaluation/Credit Request page from the Digital Edition. Return via mail to Kim Corbin, Director, ICME, New York Eye and Ear Infirmary of Mount Sinai, 645 Madison Avenue, 17th Floor, New York, NY 10022 or fax to (212) 353-5703. Your certificate will be mailed to the address you provide on the Activity Evaluation/Credit Request form. Please allow 3 weeks for Activity Evaluation/Credit Request forms to be processed. There are no fees for participating in and receiving CME credit for this activity.

Alternatively, we offer instant certificate processing and support Green CME. Please take this post test and evaluation online by going to https://tungurl.com/glaucomasp eag or. Upon passing, you will receive your certificate immediately. You must score 70% or higher to receive credit for this activity, and may take the test up to 2 times. Upon registering and successfully completing the post test, your certificate will be mailed online and you can print it or file it.

DISCLAIMER
The views and opinions expressed in this educational activity are those of the faculty and do not necessary represent the views of New York Eye and Ear Infirmary of Mount Sinai, MedEdicus LLC, Alcon, Allergan, EyeNet, or the American Academy of Ophthalmology.

This CME activity is copyrighted to MedEdicus LLC ©2017. All rights reserved.
Glaucoma Management Strategies
Across the Spectrum of Disease

INTRODUCTION

The approach to glaucoma therapy is frequently dictated by the severity of the disease. Eyes with higher intraocular pressure (IOP) or more advanced optic nerve damage and/or visual field loss will typically be managed more aggressively than those with lower IOP or earlier-stage disease. In this case-based educational activity, a panel of glaucoma specialists share insights for glaucoma management at different stages in the spectrum of glaucoma severity. These insights will include current information on diagnostic testing, medical management, and surgical interventions that can help slow the rate of progression and prevent vision loss from glaucoma.

—Donald L. Budenz, MD, MPH, Program Chair

CASE 1. PROGRESSION WITH LOW INTRAOCULAR PRESSURE
FROM THE CASE FILES OF DONALD L. BUDENZ, MD, MPH

A 57-year-old man with established primary open-angle glaucoma (POAG) was referred for evaluation of recent progression in the right eye. His peak pretreatment IOP was 28 mm Hg in both eyes. He is currently using travoprost and a dorzolamide/timolol fixed combination, and has previously undergone selective laser trabeculoplasty (SLT) in both eyes. He is allergic to brimonidine. On treatment, his IOP has consistently been in the 10- to 13-mm Hg range.

On examination, his visual acuity is 20/20 in both eyes. He has thin corneas, measuring 492 and 500 μm in the right and left eye, respectively. His angles are open. His IOP is 10 mm Hg in the right eye and 11 mm Hg in the left eye. Figure 1 shows his optic nerves and visual fields. The right optic nerve demonstrates clear progression when comparing disc photographs from 2010 to 2014, whereas the left nerve has remained stable. The right visual field also shows progression.

This patient has definite glaucoma progression in the right eye despite significant and consistent IOP reduction in excess of 50% from untreated baseline. Issues to consider in the setting of glaucoma progression at low IOP include:

• Diurnal IOP fluctuations
• Nighttime IOP elevation
• Poor compliance
• Thin corneas masking elevated IOP
• Intermittent angle-closure glaucoma
• Low blood pressure/Low perfusion pressure
• Sleep apnea
• Neuro-ophthalmic diseases
• IOP still not low enough

For the patient described above, the most likely scenario is intermittently high IOP. Intraocular pressure fluctuations have been shown to be associated with glaucoma progression in some studies but not in others. Assessing diurnal IOP can reveal pressure spikes during the day; however, this patient underwent a 12-hour diurnal curve that showed a peak IOP of only 16 mm Hg. Nighttime IOP peaks, which typically occur while the patient is prone and asleep, are clearly more difficult to assess. Because of the technical difficulties of obtaining nighttime IOP measurements in most patients, therapies that provide consistent 24-hour IOP control should be selected. Of the various classes of IOP-lowering medications available, only the prostaglandin analogues (PGAs) and carbonic anhydrase inhibitors provide IOP reduction during both the day and night; β-blockers and α-adrenergic agonists have little effect on IOP at night (Figure 2).

Figure 1. (A) Right and left optic nerves of the patient presented in Case 1, which were photographed in 2010 and 2014, showing thinning of the neuroretinal rim in the right eye in the interim. (B) Visual field of the patient’s right eye demonstrating progression over time.

Images courtesy of Donald L. Budenz, MD, MPH
Glaucoma is the most common optic neuropathy, but a host of other entities—related to ischemia, inflammation, masses, and other etiologies—can cause progressive optic nerve damage. In general, patients with the following characteristics should be considered for neuroimaging to rule out nonglaucomatous processes:

- Optic disc pallor > cupping
- Visual field defects out of proportion to cupping
- Bitemporal, homonymous, or vertically aligned visual field defects
- Early loss of central visual acuity
- Early dyschromatopsia
- Afferent pupillary defect without asymmetric cupping

Finally, the possibility that the patient in Case 1 is experiencing progressive IOP-mediated glaucomatous optic neuropathy even at this low IOP level cannot be ruled out. When all of the other possible explanations described previously have been ruled out, the appropriate next step is to lower IOP even further. A study of patients with progressive normal-tension glaucoma treated with trabeculectomy demonstrated that lowering IOP from an average of 13.1 mm Hg to 8.5 mm Hg halted progression in 87% of eyes. Approximately 40% of these patients developed postoperative hypotony (IOP ≤ 5 mm Hg), but only 7% developed hypotony maculopathy. Thus, although IOP reduction to single digits may be beneficial in halting progression, it does come with the potential for adverse events.

The patient underwent trabeculectomy with mitomycin C in the right eye, achieved IOP levels consistently in the 8- to 11-mm Hg range, and demonstrated no further structural or functional progression over the next several years.

**CASE 2. SELECTING ADJUNCTIVE THERAPY WHEN MONOTHERAPY FAILS**

**FROM THE CASE FILES OF ROBERT D. FECHTNER, MD**

A 43-year-old white man with previously diagnosed open-angle glaucoma and high myopia presents for a second opinion. His peak untreated IOPs are 30 and 24 mm Hg in the right and left eye, respectively. He is currently using latanoprost once daily in the right eye only. He is young and appropriately concerned about going blind and wants to be sure his disease is being well managed.

On examination, his visual acuity is 20/20 in both eyes, with correction of -7D for the right eye and -5D for the left eye. His anterior segment examination is remarkable only for faint peripheral radial slit-like transillumination defects, which are more prominent in the right eye than in the left eye. No Krukenberg spindle is seen in either eye. His IOP is 23 mm Hg in the right eye and 19 mm Hg in the left eye, and pachymetry is 545 and 552 μm, respectively. Gonioscopy revealed wide open angles, with 4+ pigment in the right trabecular meshwork and 3+ pigment in the left, and no iris backbowing (see Sidebar: Role of Iridotomy for Pigment Dispersion Syndrome). Figure 3 shows his optic nerves and visual fields.

Overall, a case of pigment dispersion syndrome with early pigmented glaucoma in the right eye, evidenced by early neuroretinal rim loss and possibly an early retinal nerve fiber layer defect, was suspected. Given that latanoprost monotherapy in the right eye had lowered IOP from a
pretreatment peak of 30 mm Hg to 23 mm Hg, nearly a 25% reduction, the patient’s current regimen was continued with routine follow-up. Over the next 2 years, the patient’s IOP ranged from 19 to 24 mm Hg in the right eye and from 16 to 20 mm Hg in the left eye. But within 2 years, his visual field in the right eye developed a reproducible inferior nasal step, which was indicative of progression. Target pressure was revised to the low to mid-teens, and adjunctive therapy was considered to achieve the lower target IOP.

Selecting adjunctive therapy to prostaglandins represents a significant clinical challenge. Single-agent options include a β-blocker, a carbonic anhydrase inhibitor, or an α-adrenergic agonist. In numerous clinical trials evaluating the additivity of these agents to PGAs, the typical effect is an additional IOP reduction of 2 to 4 mm Hg.21-24

In this patient, the goal is to lower his IOP from the low 20s to the mid-teens. A single-agent adjunct is unlikely to accomplish this, and multiple adjunct medications may be required. Historically, medications have been added 1 at a time to assess their individual contributions to both efficacy and safety. In the modern glaucoma pharmacology era, a number of fixed combinations of the common adjunctive medications are available. The dorzolamide/timolol fixed-combination formulation is still labeled for use only in patients inadequately controlled on a β-blocker25, but is commonly used off-label without going through the β-blocker step. The timolol/brimonidine and brinzolamide/brimonidine fixed-combination formulations are labeled for and used as first-line or first adjunctive therapy. When added to prostaglandins, these multidrug combinations typically deliver an additional IOP reduction of 5 to 6 mm Hg.26,27 A fixed combination as first adjunct to the patient’s latanoprost therapy is the most realistic next step. Fixed combinations have several additional benefits over concomitant dosing,28,29 including a reduction in exposure to excipient ingredients, such as preservatives, elimination of the washout effect that arises when consecutive drops are instilled too closely together in time, and elimination of 1 copayment for patients with prescription drug coverage. Disadvantages of fixed combinations include the inability to titrate the dosage of the individual components as well as cost; for patients without prescription drug coverage, the unfixed combination of generic drugs may be less expensive than the branded fixed combination.28,29

Another option is SLT, which has been shown to lower IOP by the same amount as a PGA.30,31 The added benefit of SLT is elimination of concerns regarding adherence to medical therapy. This is relevant because studies have demonstrated that the addition of a second medication to the glaucoma treatment regimen often results in reduced adherence.32,33 With pigmentary glaucoma, lowering the power to prevent damage to the densely pigmented trabecular meshwork and staging the procedure in two 180° sessions to minimize the risk of IOP spikes improves patient outcomes.34

Several novel drug delivery systems that may also have a positive effect on adherence are in the pipeline. These include punctal plugs35 and an ocular surface ring impregnated with medication36 and injectable devices that elute medication over time.37 The role of these devices, which come with disadvantages, such as cost and safety issues, will become clearer as they become available in the marketplace.

CASE 3. MANAGING GLAUCOMA IN A PATIENT WITH COEXISTING OCULAR SURFACE DISEASE
FROM THE CASE FILES OF JANET B. SERLE, MD

A 70-year-old white woman initially presented with a 3-year history of open-angle glaucoma managed with latanoprost monotherapy in both eyes. Her peak IOP on treatment was 24 mm Hg in each eye. Her medical history was remarkable only for a right hip replacement. On examination, her visual acuity with a moderate hyperopic correction was 20/30+ in the right eye and 20/20- in the left eye. Her corneal thickness was normal at 568 and 574 μm, respectively. Intraocular pressure was 19 mm Hg in each eye. Her medical history was remarkable only for a right hip replacement. Anterior segment examination revealed no evidence of secondary open-angle glaucoma, and gonioscopy revealed open angles, with moderate trabecular meshwork pigmentation in both eyes. Figure 4 shows her optic nerves and visual fields.
and function. These changes are dose dependent, changes in conjunctival cell membrane permeability, anatomy, preservative benzalkonium chloride (BAK)—is associated with research has demonstrated that chronic exposure to excipient relationship between the 2 is likely. A significant body of number of patients with glaucoma. However, a causal symptoms of OSD. To some extent, these 2 conditions—Ocular surface disease (OSD) commonly coexists in patients with glaucoma. Three clinical studies, both using the Ocular Surface Disease Index to detect symptoms of OSD, found that 50% to 60% of patients with glaucoma are also troubled by superficial punctate keratopathy in both eyes.

Seven years after the initial presentation, she developed what she described as “foggy vision” in both eyes, which was worse in the right eye. She reported difficulty with near-sighted tasks, such as writing checks. At this time, her visual acuity was 20/40 in both eyes at distance, but at near, her acuity was J16 in the right eye and J10 in the left. Examination revealed mild superficial punctate keratopathy in both eyes.

Ocular surface disease (OSD) commonly coexists in patients with glaucoma. Three clinical studies, both using the Ocular Surface Disease Index to detect symptoms of OSD, found that 50% to 60% of patients with glaucoma are also troubled by symptoms of OSD. To some extent, these 2 conditions—both being conditions that increase in prevalence with age—would be expected to occur coincidentally in a number of patients with glaucoma. However, a causal relationship between the 2 is likely. A significant body of research has demonstrated that chronic exposure to excipient ingredients in glaucoma medications—particularly the preservative benzalkonium chloride (BAK)—is associated with changes in conjunctival cell membrane permeability, anatomy, and function. These changes are dose dependent, cumulative over time, and translate into clinical symptoms.

Topical glaucoma medications preserved with BAK have been associated with a 3-fold higher risk of developing symptoms of OSD compared with medications without BAK. Alternative preservatives that efficiently oxidize microbes have been developed, such as SofZia and Purite, with significantly fewer effects on ocular surface cells compared with BAK.

At this time, this patient’s IOP-lowering regimen was transitioned to formulations that were either preservative free or BAK free, and preservative-free artificial tears were added. A consultation with a cornea specialist led to the initiation of topical cyclosporine therapy and the placement of bilateral punctal plugs, with some modest improvement in symptoms. She also underwent cataract surgery in the right eye, all with minimal improvement in visual acuity, which continued to fluctuate in the range of 20/30 to 20/100.

Over the next few months, her ocular surface symptoms became severe enough that she became nonadherent with her IOP medications because of their effects on her vision and symptoms. She then underwent SLT in the right eye, with no appreciable effect on IOP. Not everyone responds well to SLT; however, there are positive predictive factors for IOP reduction, including a higher baseline IOP, central corneal thickness < 555 μm, and response to SLT in the fellow eye. Factors not associated with IOP reduction by SLT include the type and severity of glaucoma, number and class of medications used, and previous trabecuoplasty. Successful SLT can be safely and effectively repeated when the resulting IOP reduction wanes, which tends to be approximately 1 year on average, and there is some evidence that repeat SLT following minimally effective SLT can also produce clinically significant IOP reductions.

After a discussion with the patient regarding the risks and benefits of continuing topical medical therapy, attempting repeat SLT in the right eye (and initial SLT in the left eye), or proceeding to incisional surgery, the patient underwent bilateral trabeculectomy with mitomycin C augmentation. This achieved an IOP of 7 to 8 mm Hg in the right eye and approximately 14 mm Hg in the left eye and substantial subjective and measured improvement in visual acuity in both eyes.

CASE 4. SELECTING THE CORRECT PROCEDURE WHEN GLAUCOMA SURGERY IS NECESSARY

FROM THE CASE FILES OF STEVEN J. GEDDE, MD

A 72-year-old woman was referred for evaluation of uncontrolled POAG in her right eye. She was using latanoprost once daily, brimonidine twice daily, and dorzolamide/timolol fixed combination twice daily, all in the right eye. Both eyes had previously undergone SLT, and the left eye had previously undergone a trabeculectomy with mitomycin C, which was complicated by postoperative blebitis that was successfully managed without vision loss.

On examination, her visual acuity was 20/30 in both eyes. Her IOP was 25 mm Hg in the right eye and 7 mm Hg in the left eye. She had 2-3+ nuclear sclerotic cataracts in both eyes. Her angles were wide open. Figure 5 shows her optic nerves and visual fields.
Trabeculectomy had produced an IOP in the high single-digit range, which is desirable for this stage of disease. However, her postoperative course was complicated by a bleb-related infection, a potentially blinding adverse event associated with filtration surgery. Her right eye now has uncontrolled POAG, despite maximal medical therapy and SLT treatment. This eye requires surgical intervention to lower IOP and prevent the level of visual field loss that has occurred in the left eye.

Not so long ago, surgical options were generally limited to trabeculectomy or tube-shunt implantation. In recent years, however, numerous novel procedures have been developed to lower IOP in glaucomatous eyes (Table 1).

Modern trabeculectomy was first described in 1968, and historically has been the most commonly performed incisional procedure for glaucoma. Trabeculectomy consists of a scleral fistula to allow drainage of aqueous humor into the subconjunctival space, creating a filtering bleb. Antifibrotic agents, such as 5-fluorouracil and mitomycin C, are routinely used as adjuncts to modulate wound healing. Antifibrotics have been shown to significantly enhance surgical success, but at the cost of more hopotony and bleb-related complications, including leaks and infections.

Tube-shunt implantation is an alternative to trabeculectomy, in which a silicone tube shunts aqueous humor from the anterior chamber to a reservoir, or end plate, placed subconjunctivally in the equatorial region of the globe. Various designs have been introduced that generally fall within 2 categories: those that have an internal flow restriction component (such as the Ahmed and Krupin implants) and those that do not (such as the Baerveldt and Molteno implants). Traditionally, these devices have been reserved for eyes at high risk for filtration failure or as a second procedure following trabeculectomy failure, but in recent years, the use of tube-shunt surgery has been expanding. This trend has been supported by the Tube Versus Trabeculectomy Study.

The Ex-PRESS mini shunt represents a hybrid of trabeculectomy. The small stainless steel tube is inserted through a needle sclerotomy under a scleral flap and functions as a trans-scleral shunt for aqueous humor from the anterior chamber into the subconjunctival bleb. In a prospective, randomized comparison with trabeculectomy, the Ex-PRESS implantation procedure produced comparable IOP reduction, glaucoma medication use, and overall success rates, with fewer complications and faster visual recovery, compared with trabeculectomy.

An array of minimally invasive glaucoma surgeries have been developed in recent years (Table 1). These procedures share a number of characteristics, including an ab interno approach, minimal trauma to ocular tissues, modest efficacy, excellent safety, and rapid postoperative recovery. They are frequently performed in combination with cataract surgery, and their popularity is growing, in part because their ease of performance has encouraged cataract and glaucoma surgeons to adopt them as add-on procedures for patients with coexistent cataracts and glaucoma. Given their efficacy and safety profiles, they are best used in patients with early disease who do not require low levels of IOP.
Role of Iridotomy for Pigment Dispersion Syndrome

Pigmentary glaucoma (PG) represents one of the most common causes of secondary open-angle glaucoma. Pigment dispersion syndrome (PDS)—the precursor to pigmentary glaucoma—was first reported by Sugar and Barbour in 1949. Clinically, PDS is characterized by radial slit-like transillumination defects of the iris, pigment deposition on the corneal endothelium (called the Krukenberg spindle), a heavily pigmented trabecular meshwork, and backbowing of the iris. A classic paper by Campbell in 1979 described the pathophysiology of PDS. Iris backbowing leads to chafing of the posterior surface of the iris against the zonules, resulting in sloughing of the iris pigment epithelium, which produces the classic iris transillumination defects and pigment dispersion throughout the anterior chamber. When the pigment load in the meshwork is sufficient to impede the outflow of aqueous humor, intraocular pressure begins to rise, and glaucomatous optic neuropathy can ensue.

The cause of iris backbowing—which presumably precipitates the sequence of events leading to PDS and to PG—is unclear. The condition is more common in patients with high myopia, whose larger eyes may have larger, floppier irises. The iris in these eyes may act as a 1-way valve, allowing aqueous humor to move from the posterior to anterior chambers, creating a reverse pupillary block configuration. Maintenance of this reverse pupillary block configuration can be attained by blinking, exercise, and accommodation.

Strategies to flatten the iris have been employed in the treatment of PDS and PG. Miotics such as pilocarpine have been proposed to pull the iris forward and interrupt the iris-zonule contact, but most patients with PDS are young and myopic and tend to tolerate miotics poorly.

Iridotomy has also been proposed as a means to flatten the iris. As in the setting of angle closure—in which the iris is bowed forward because of pupillary block—laser iridotomy in PDS could equalize pressure across the iris diaphragm and correct the reverse pupillary block.

Studies evaluating the clinical effectiveness of laser iridotomy in the setting of PDS and PG have been mixed. A meta-analysis of the best studies concluded that there was insufficient evidence to support the recommendation of iridotomy in eyes with PDS/PG. The authors did point out, however, that additional research is needed to identify the optimal timing of the intervention because several studies considered in their analysis included only patients with manifest PG or those with PDS and elevated intraocular pressure, in whom the therapeutic window for halting pigment dispersion and protecting the meshwork from damage may have already passed.

References

Key Take-Home Messages
- Consideration should be given to using BAK-free or preservative-free eye drops earlier in the course of disease in patients with ocular surface disease.
- Ocular surface disease occurs in more than 50% of patients with glaucoma because of a combination of reduced tear secretion with aging and the effects of medication and excipients on the surface of the eye.
References (continued)


CME Post Test Questions

To obtain AMA PRA Category 1 Credit™ for this activity, complete the CME Post Test by writing the best answer to each question in the Answer Box located on the Activity Evaluation/Credit Request form on the following page. Alternatively, you can complete the CME Post Test online at https://tinyurl.com/glaucomaspectrum.

See detailed instructions at To Obtain AMA PRA Category 1 Credit™ on page 2.

1. At what time of day is IOP typically the highest in patients with glaucoma?
   a. 6 AM to 12 PM
   b. 12 PM to 6 PM
   c. 6 PM to 12 AM
   d. 12 AM to 6 AM

2. Which classes of glaucoma medications lower IOP at night?
   a. β-blockers and α-adrenergic agonists
   b. PGAs and topical carbonic anhydrase inhibitors
   c. PGAs and β-blockers
   d. PGAs and α-adrenergic agonists

3. One plausible mechanism by which both low ocular perfusion pressure and obstructive sleep apnea can increase the risk of glaucoma is by:
   a. Mechanical stress on the lamina cribrosa
   b. Raising intraocular pressure
   c. Reducing aqueous outflow at night
   d. Causing ischemia to the optic nerve head

4. The addition of a β-blocker, a carbonic anhydrase inhibitor, or an α-adrenergic agonist to a PGA will result in an average incremental IOP reduction of:
   a. 1 to 2 mm Hg
   b. 2 to 4 mm Hg
   c. 5 to 6 mm Hg
   d. 8 to 10 mm Hg

5. Considerations in the differential diagnosis of normal-tension glaucoma include which of the following?
   a. Diurnal IOP spikes seen during office hours
   b. Good adherence with glaucoma therapy
   c. Afferent pupillary defect with asymmetric cupping
   d. Sleep apnea

6. Which of the following topical treatments for patients with moderate OSD result in improved Ocular Surface Disease Index scores?
   a. BAK-preserved drops
   b. BAK-free drops
   c. Preservative-free drops
   d. Both preservative-free and BAK-free drops

7. What percentage of patients on glaucoma medications have symptoms of OSD?
   a. ≤ 20%
   b. 21% to 40%
   c. 50% to 60%
   d. > 60%

8. Neuroimaging should be considered for a patient with glaucoma and:
   a. Cupping exceeding pallor
   b. Intact central visual acuity
   c. Visual field defects respecting the vertical meridian
   d. Afferent pupillary defect with asymmetric cupping

9. Which of the following is a typical characteristic of minimally invasive glaucoma surgery procedures?
   a. Ab interno approach
   b. Poor safety profile
   c. Significant trauma to tissue
   d. IOP reduction to low teens

10. In the Tube Versus Trabeculectomy Study, the rate of which of the following was significantly higher in the tube group compared with the trabeculectomy group?
    a. Reoperation for glaucoma
    b. Serious complications
    c. Surgical success
    d. Vision loss
Activity Evaluation/Credit Request

Glaucoma Management Strategies Across the Spectrum of Disease

To receive AMA PRA Category 1 Credit™, you must complete this Evaluation form and the Post Test. Record your answers to the Post Test in the Answer Box located below. Mail or Fax this completed page to New York Eye and Ear Infirmary of Mount Sinai—ICME, 485 Madison Avenue, 17th Floor, New York, NY 10022 (Fax: 212-353-5703). Your comments help us to determine the extent to which this educational activity has met its stated objectives, assess future educational needs, and create timely and pertinent future activities. Please provide all the requested information below. This ensures that your certificate is filled out correctly and is mailed to the proper address. It also enables us to contact you about future CME activities. Please print clearly or type. Illegible submissions cannot be processed.

PARTICIPANT INFORMATION (Please Print)  ☐ Home  ☐ Office
Last Name ___________________________ First Name ___________________________
Specialty ___________________________ Degree ☐ MD ☐ DO ☐ OD ☐ PharmD ☐ RPh ☐ NP ☐ RN ☐ PA ☐ Other ___________________________
Institution ______________________________________________________________________________________________________
Street Address ____________________________________________________________
City ___________________________ State ___________ ZIP Code ___________ Country ______________________
E-mail ______________________________________________________________________ Phone ___________________________ Fax ___________________________

Please note: We do not sell or share e-mail addresses. They are used strictly for conducting post-activity follow-up surveys to assess the impact of this educational activity on your practice.

Learner Disclosure: To ensure compliance with the US Centers for Medicare and Medicaid Services regarding gifts to physicians, New York Eye and Ear Infirmary of Mount Sinai Institute for CME requires that you disclose whether or not you have any financial, referral, and/or other relationship with our institution. CME certificates cannot be awarded unless you answer this question. For additional information, please call NYEE ICME at 212-979-4383. Thank you.

☐ Yes  ☐ No I and/or my family member have a financial relationship with New York Eye and Ear Infirmary of Mount Sinai and/or refer Medicare/Medicaid patients to it.

☐ I certify that I have participated in the entire activity and claim 1.5 AMA PRA Category 1 Credits™.

Signature Required ___________________________ Date Completed ___________________________

OUTCOMES MEASUREMENT

☐ Yes  ☐ No Did you perceive any commercial bias in any part of this activity? IMPORTANT! If you answered “Yes,” we urge you to be specific about where the bias occurred so we can address the perceived bias with the contributor and/or in the subject matter in future activities.

Circle the number that best reflects your opinion on the degree to which the following learning objectives were met:
5 = Strongly Agree  4 = Agree  3 = Neutral  2 = Disagree  1 = Strongly Disagree

Upon completion of this activity, I am better able to:

• Select appropriate ocular antihypertensive therapy to meet IOP goals throughout the day and night  5  4  3  2  1
• Develop individualized regimens for IOP control with multidrop or fixed-combination therapy  5  4  3  2  1
• Describe effective IOP-lowering strategies, including patient counseling, in patients with ocular surface disorders  5  4  3  2  1
• Evaluate surgical procedures for patients requiring IOP-lowering interventions  5  4  3  2  1

1. Please list one or more things, if any, you learned from participating in this educational activity that you did not already know.

2. As a result of the knowledge gained in this educational activity, how likely are you to implement changes in your practice?
4 = definitely will implement changes  3 = likely will implement changes  2 = likely will not implement any changes  1 = definitely will not make any changes

Please describe the change(s) you plan to make:

3. Related to what you learned in this activity, what barriers to implementing these changes or achieving better patient outcomes do you face?

4. Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced for you through participation in this activity.
☐ Patient Care  ☐ Practice-Based Learning and Improvement  ☐ Professionalism
☐ Medical Knowledge  ☐ Interpersonal and Communication Skills  ☐ Systems-Based Practice

5. What other topics would you like to see covered in future CME programs?

ADDITIONAL COMMENTS

POST TEST ANSWER BOX

<table>
<thead>
<tr>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>