CME Monograph

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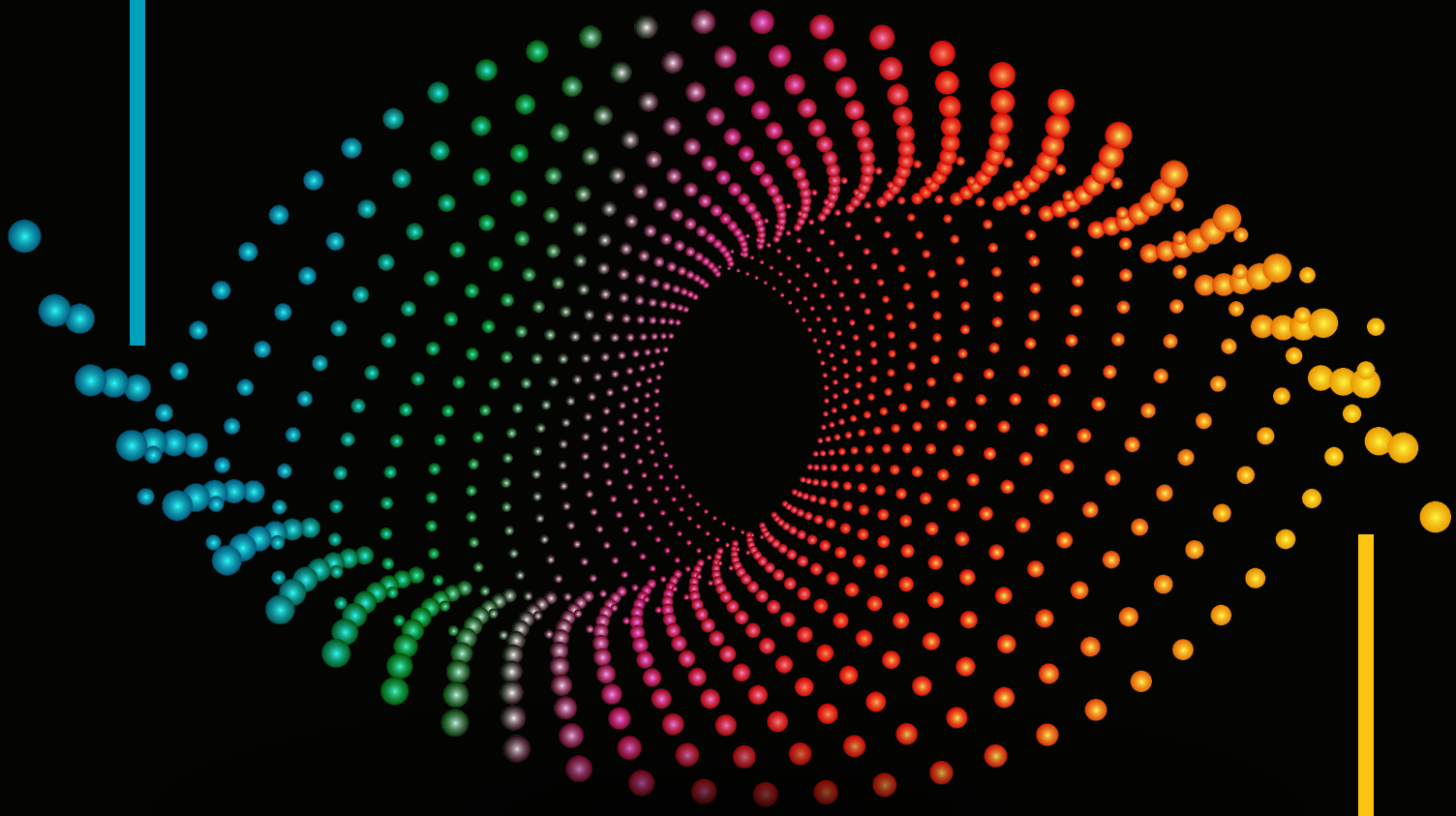
Glaucoma Management Strategies Across the Spectrum of Disease



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

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

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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 antihypertensive therapy to meet IOP goals throughout the day and night
- Develop individualized regimens for IOP control with multidrop 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

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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

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

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[1-3] but not in others.[4] 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.[5] 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)[6] and carbonic anhydrase inhibitors[7] provide IOP reduction during both the day and night; β-blockers[6] and α-adrenergic agonists[8] have little effect on IOP at night **(Figure 2)**.

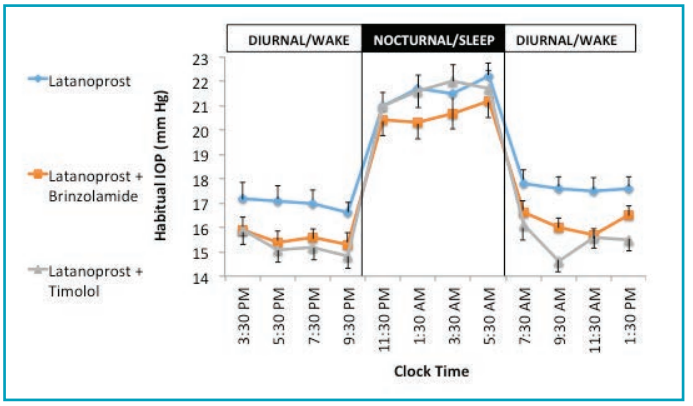

Figure 2. Topical carbonic anhydrase inhibitor vs β-blockers added to a prostaglandin analogue. The 24-hour intraocular pressure (IOP) curves demonstrate the IOP-lowering efficacy of carbonic anhydrase inhibitors, but not β-blockers, when used adjunctively to a prostaglandin analogue in 26 patients receiving latanoprost every evening for glaucoma.[7]

Another possible explanation for intermittent elevated IOP is subacute angle-closure glaucoma, which was deemed unlikely in this patient. Thin corneas can artifactually lower IOP measurements obtained by applanation tonometry and can give a false impression of IOP control. Thin corneas are a risk factor for glaucoma in ocular hypertensives[9] and for glaucoma progression.[10] In addition, artificially low IOP measurements can lull the eye care provider into believing the IOP is low when it really is not. This patient has very thin corneas: 492 and 500 µm. Although there is no reliable "correction factor" for IOP with thin or thick corneas, it can be safely said that this patient's IOPs are not in the low teens. However, considering that the initial untreated IOP was 28 mm Hg OU, the current IOPs represent a greater than 50% reduction in pressure, so the absolute number is less important when using a percent reduction rather than aiming for an absolute target number.

Poor adherence with medical therapy can also mimic good IOP control, especially if patients use their drops only in the few days preceding each office visit. Nonadherence is a significant problem in chronic glaucoma management. As many as 59% of patients with glaucoma may be noncompliant with therapy.[11] Further, ophthalmologists are poor at identifying noncompliant patients.[12] As a result, it can be difficult to distinguish between noncompliance or the lack of efficacy of therapy when high IOP is observed during an office visit.

Both low diastolic perfusion pressure and sleep apnea have been proposed as potential risk factors for glaucoma. Numerous epidemiologic studies have demonstrated a link between low diastolic perfusion pressure and the prevalence of glaucoma.[13-17] This may lead to chronic ischemia of the optic nerve head tissue. Similarly, a number of studies have identified a potential association between obstructive sleep apnea and glaucoma.[18,19] One potential mechanism to explain this association is the possibility of optic nerve hypoxia during apneic episodes.

When evaluating patients with progressive optic nerve changes despite low IOP, vigilance for nonglaucomatous causes of optic nerve disease must always be maintained. 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.[20] 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 pigmentary 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

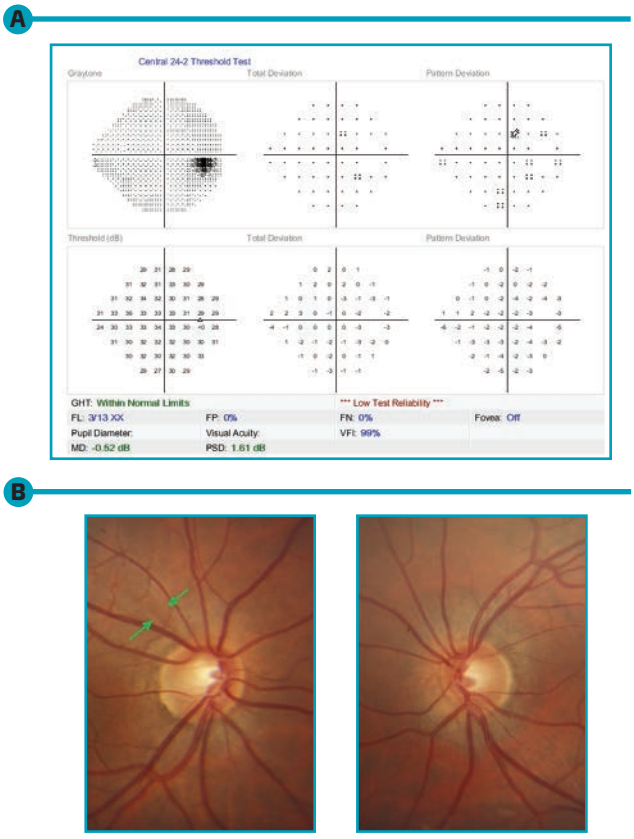

Figure 3. (A) Right visual field of the patient presented in Case 2. **(B)** Optic disc photographs of the same patient. Note the superior rim thinning in the right eye, which is associated with an early retinal nerve fiber layer bundle defect.

Images courtesy of Robert D. Fechtner, MD

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-blocker[25], 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 plugs[35] and an ocular surface ring impregnated with medication[36] 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. 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.

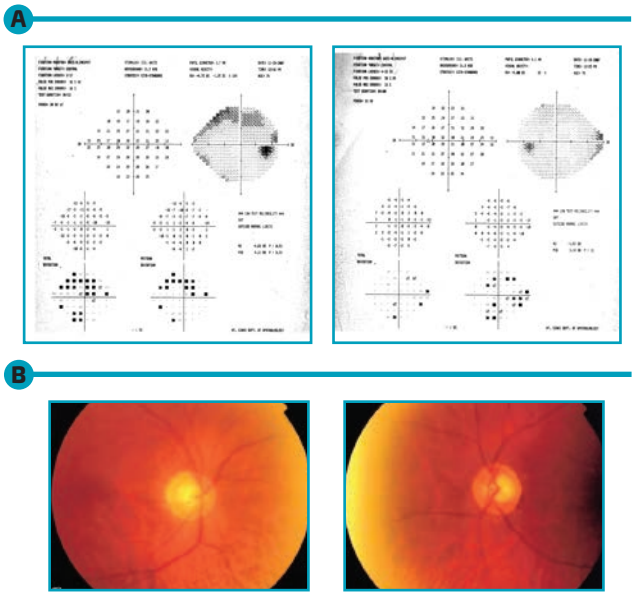

Figure 4. (A) Visual fields from the patient discussed in Case 3. **(B)** Optic nerve photographs from the same patient. Note the loss of inferior rim on the right optic nerve, with corresponding superior visual field loss.

Images courtesy of Janet B. Serle, MD

Initially, her latanoprost monotherapy was continued. Over the next 6 years, her IOP gradually rose above her target IOP, requiring additional medications. Her regimen now consisted of latanoprost in both eyes, timolol in both eyes, and brimonidine in the left eye. On this regimen, her IOP ranged from 10 to 19 mm Hg OU. Automated visual field testing became unreliable, and Goldmann perimetry was used. Goldmann fields demonstrated progressive loss of the inferior field in both eyes over the same 6-year period, which was confirmed with superior retinal nerve fiber layer thinning on serial optical coherence tomography imaging.

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.[38-40] To some extent, these 2 conditions—both being conditions that increase in prevalence with age[41,42]—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.[43,44] These changes are dose dependent, cumulative over time, and translate into clinical symptoms.[43,45]

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.[46] 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.[47,48]

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.[48-50] Factors not associated with IOP reduction by SLT include the type and severity of glaucoma, number and class of medications used, and previous trabeculoplasty.[49-51] Successful SLT can be safely and effectively repeated when the resulting IOP reduction wanes, which tends to be approximately 1 year on average,[52-57] and there is some evidence that repeat SLT following minimally effective SLT can also produce clinically significant IOP reductions.[58]

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.

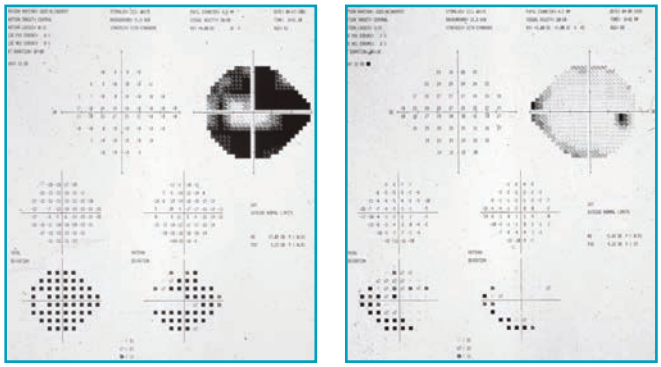

Figure 5. Right and left visual fields of the patient presented in Case 4. Note the marked asymmetry of visual field loss, which is worse in the left eye than in right eye.

Images courtesy of Steven J. Gedde, MD

The degree of optic disc cupping was consistent with the visual fields and confirmed very asymmetric glaucomatous damage.

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,[59] and historically has been the most commonly performed incisional procedure for glaucoma.[60] 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,[61,62] but at the cost of more hopotony[63] and bleb-related complications, including leaks and infections.[64]

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.[65]

The Tube Versus Trabeculectomy Study was a multicenter randomized clinical trial in which patients with prior ocular surgery (either cataract extraction or failed trabeculectomy) who required glaucoma surgery (with an IOP between 18 and 40 mm Hg, inclusive) were randomly assigned to undergo either

Table 1. Options for Incisional Glaucoma Surgery to Lower Intraocular Pressure

Glaucoma Surgery	Option
Traditional	Trabeculectomy
	Aqueous shunts
	Ex-PRESS implant
Nonpenetrating	Deep sclerectomy
	Viscocanalostomy
	Canaloplasty
Endoscopic photocoagulation	—
Minimally invasive glaucoma surgery	Ab interno trabeculectomy (Trabectome)
	Trabecular microbypass stent (iStent)
	Gonioscopy-assisted transluminal trabeculotomy
	Kahook dual blade
	CyPass microstent
	XEN gel stent

trabeculectomy with mitomycin C (0.4 mg/mL for 4 minutes) or tube shunt implantation (350-mm^2 Baerveldt glaucoma implant).[65] After 5 years of follow-up, both treatment groups had a comparable mean IOP and mean number of IOP-lowering medications. The rates of serious postoperative complications and vision loss were also similar between the tube and trabeculectomy groups. However, the 5-year cumulative probability of failure was 46.9% in the trabeculectomy group vs only 29.8% in the tube group (P = .002). Also, reoperations for glaucoma were necessary in 29% of eyes undergoing trabeculectomy vs 9% of eyes undergoing tube implantation (P = .025).

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.[66]

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.[67] 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.[1] 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.[2] 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,[3] exercise,[4] and accommodation.[5]

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.[6] 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.

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Ab interno trabeculectomy involves the removal of a strip of trabecular meshwork and Schlemm canal using an electrocautery hand piece inserted through a clear corneal incision. A meta-analysis of studies investigating this procedure reported a 31% reduction in IOP and a 66% average surgical success rate at 2 years postoperatively.[68]

The trabecular microbypass stent is a snorkel-shaped device made of heparin-coated titanium that is inserted into the Schlemm canal through the trabecular meshwork. It gained US Food and Drug Administration approval for use in conjunction with cataract extraction in patients with mild-to-moderate glaucoma[69] after randomized trials demonstrated greater reductions in IOP and medication use following combined surgery compared with cataract surgery alone.[70] Multiple stents may provide greater IOP reduction than a single stent.[71]

In addition to devices that shunt aqueous humor across the trabecular meshwork from the anterior chamber to the Schlemm canal, some newer devices are available that shunt aqueous humor from the anterior chamber to the subconjunctival space (the XEN gel stent) or to the suprachoroidal space (the CyPass microstent). The XEN gel stent is a permanent, collagen-derived gelatin tube that is inserted ab interno through the trabecular meshwork and sclera to exit into the subconjunctival space. The result is a filtering bleb with no conjunctival incision. The XEN gel implant—approved by the US Food and Drug Administration in November 2016[72]— has been shown in case series to reduce IOP to the mid-teens when inserted without an adjunctive antifibrotic agent, although needling procedures were required in up to 47% of patients.[73,74] The CyPass device combined with cataract surgery has been shown to lower IOP and medication use more than cataract surgery alone does.[75]

To recap the current case, the patient has a history of blebitis following trabeculectomy in the left eye and now requires a surgical glaucoma procedure in the right eye. Given this ocular history and the early stage of glaucoma in the right eye, a decision was made to proceed with implantation of a trabecular microbypass stent in combination with cataract extraction. This procedure resulted in visual acuity of 20/20, and IOP was well controlled at 14 mm Hg using only the dorzolamide/timolol fixed combination twice daily.

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

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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

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

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.

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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

4 3 2 1

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

1	2	3	4	5	6	7	8	9	10