Medical Therapy for Intraocular Pressure Reduction

L. Jay Katz, MD

Intraocular pressure reduction is the single most important therapeutic intervention in glaucoma. A stepwise approach to managing pressure—potentially including medical, laser, surgical, and lifestyle measures—should be tailored to the patient and based on the most current understanding of what is effective.

The importance of identifying glaucoma early in its course and treating effectively cannot be overstated. Several large National Eye Institute-sponsored multicenter clinical trials have demonstrated the value of aggressively lowering intraocular pressure (IOP); indeed, IOP lowering is the sole therapeutic intervention available to clinicians for lowering intraocular pressure (IOP); indeed, IOP lowering is the sole therapeutic intervention available to clinicians for maintaining glaucoma patients’ vision over an extended period of time.1,2 In my experience, a stepwise approach that moves patients as rapidly as necessary through staged increments of increasing medical therapy (starting with a single agent, then multi-drug regimens, if needed), laser trabeculoplasty, and on to glaucoma surgery, serves patients well and provides the greatest likelihood of preventing or minimizing progression.

IDENTIFYING PATIENTS

Identifying individuals who will benefit from anti-glaucoma therapy requires a high and consistently maintained index of suspicion from practitioners on the front line of care, typically primary care and comprehensive eyecare providers. The annual comprehensive eye examination is the perfect opportunity to discuss glaucoma risk with patients and look for signs of disease, most importantly, elevated IOP and an abnormal-appearing optic nerve or iridocorneal angle.

Patients with abnormalities should undergo structural (eg, quantitative analysis of the retinal nerve fiber layer by optical coherence tomography [OCT]) and functional (eg, visual field) testing. Referral to a glaucoma specialist may be useful at any point in the workup or management.

PATIENT HISTORY

Thorough history taking is essential for successful patient management and includes ocular history, family history (including glaucoma severity and visual outcome, where relevant), medical and surgical history, and medication history (including both ocular and systemic medications as well as tolerability issues).3 Patients who have a first-degree relative with proven primary open angle glaucoma (POAG) have between a 2- and 9-fold greater risk of developing the disease compared to individuals without an affected family member.4,5

Topics in Glaucoma is jointly sponsored by Candeo Clinical/Science Communications, LLC, and the University of Florida College of Medicine. This publication is administered by an independent editorial board and supported by an unrestricted educational grant from Bausch + Lomb, Inc. Copyright 2015 Candeo Clinical/Science Communications, LLC. All rights reserved. Neither the University of Florida nor Candeo Clinical/Science Communications, LLC, assumes any responsibility for injury or damage to persons or property arising from the use of information or ideas contained in this publication.

COURSE DIRECTOR
Anup Kubal, MD
University of Florida
Gainesville, FL, USA

EDITORS
Paul Kaufman, MD, is a professor of ocular pharmacology and department chair emeritus in the department of ophthalmology and visual sciences at the University of Wisconsin-Madison School of Medicine and Public Health.
Robert Noecker, MD, is an assistant clinical professor of ophthalmology at the Yale University School of Medicine and clinical professor of surgery at the Frank Netter School of Medicine of Quinnipiac University. He practices at Ophthalmic Consultants of Connecticut.
Rohit Varma, MD, MPH, is director of the USC Eye Institute, chair of the department of ophthalmology, and professor of ophthalmology and preventive medicine at the Keck School of Medicine at the University of Southern California.

TARGET AUDIENCE
This educational activity is intended for ophthalmologists and ophthalmologists in residency or fellowship training.

LEARNING OBJECTIVES
Upon completion of this activity, participants will be able to:
1. Create a staged management plan for patients with glaucoma.
2. List steps to take in the event that target IOP is not maintained.
3. Describe structural and functional bases of aqueous humor formation and outflow.
4. Use aqueous humor pathophysiology to interpret ocular hypertension and the mechanisms of action of current pharmacological therapies for glaucoma.

See INSIDE for:
Aqueous Humor Dynamics, Intraocular Pressure, and Glaucoma
by W. Daniel Stamer, PhD

To obtain CME credit for this activity, go to http://cme.ufl.edu/ed/self-study/tig/

Supported by an unrestricted educational grant from Bausch + Lomb, Inc.
To obtain CME credit for this activity, go to http://cme.ufl.edu/ed/self-study/tig/

Unfortunately, due to part in low public awareness of glaucoma, patients may be unaware of the presence of glaucoma in their families, or, if aware, may underestimate or downplay its importance.

It is often estimated that half the glaucoma population is unaware of their condition, so clinicians need to use every means at their disposal to screen for glaucoma suspects. This underscores the relevance of knowing about a possible genetic predisposition for glaucoma whenever possible. Patients with a positive family history should receive appropriate counseling and work up to identify or rule out additional risk factors and possible glaucomatous changes.

EARLY DIAGNOSIS

One of the tragedies of glaucoma—and a key point in the argument for aggressive pre-symptomatic screening—is that patients who present with symptoms typically do so late in the course of disease. The hallmark symptom of glaucoma is gradual asymmetric peripheral visual loss, which is difficult for patients to perceive since, with both eyes open, the better eye compensates for the more affected one. When patients do finally present, they may complain that the top or peripheral visual field of one eye appears smudged or gray or absent, and that they only noticed it after a sudden need to close the other eye.

Some patients may be more forthcoming about their experiences, if the doctor gives them the opportunity to do so. A study of patient-physician communication in glaucoma clinics revealed that over 90% of the questions doctors asked their patients were closed-ended (eg, “can you see well at night?”) rather than open-ended (“tell me how you see at night”), and key pieces of information were frequently missed. Taking a moment to include open-ended questions invites the patient to reveal more of their history and can uncover potentially useful clues to early disease.

TARGET IOP

Nearly all patients with POAG are prescribed medical therapy to lower IOP and reduce the risk for vision loss. A typical exception might be a very elderly patient with a short life expectancy and early stage asymptomatic and slowly progressing glaucoma who elects, after counseling, to forego treatment. The goal of therapy for patients with POAG, as stated by the American Academy of Ophthalmology consensus panel, is “to maintain the IOP in a range at which a patient is likely to remain stable or at which worsening of glaucoma will be

OFF-LABEL USE STATEMENT

This activity has been designed and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCMEd) through the joint sponsorship of the University of Florida College of Medicine and Candoc Clinical Science Communications, LLC. The University of Florida College of Medicine is accredited by the ACCMed to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

The University of Florida College of Medicine designates this educational activity for a maximum of 1.0 AMA PRA Category 1 Credit™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

FACULTY AND DISCLOSURE STATEMENTS

Paul Kaufman, MD (Faculty Advisor), is a professor of ophthalmology and professor of biomedical engineering at Duke University, Durham, NC. He receives grant support from the National Eye Institute, Research to Prevent Blindness Foundation, Allergan, and Bausch + Lomb. His research is primarily focused on the development of new treatments for glaucoma.

Robert Noecker, MD (Faculty Advisor), is an assistant clinical professor of ophthalmology at the Yale University School of Medicine and the professor of surgery at the Frank Netter School of Medicine of Quinnipiac University, and he practices at Ophthalmic Consultants of Connecticut. He states that he has been on the speakers bureau for Allergan, Aerie Pharmaceuticals, and Glaukos.

L. Jay Katz, MD, is director of the Glaucoma Service at Wills Eye Institute, Philadelphia, Pennsylvania. Dr. Katz has received research support from Allergan, Aerie Pharmaceuticals, Bausch + Lomb, and Malt Therapeutics. He has been a consultant for Allergan, Alcon, and Glaukos, and he has been the spokescor for Allergan and Glaukos. He is also a consultant for Aerie Pharmaceuticals.

Daniel Stamer, PhD, is a consultant for pharmaceutical and medical device companies, and he has received research support from the National Eye Institute, Research to Prevent Blindness Foundation, Allergan, and Bausch + Lomb. His research is primarily focused on the development of new treatments for glaucoma.

DISCLAIMER

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and professional development. The information presented in this activity is not meant to serve as a guideline for patient care. Procedures, medications, and other courses of diagnosis and treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patients’ conditions and possible contraindications or dangers in use, applicable manufacturer’s product information, and comparison with recommendations of other authorities.

COMMERCIAL SUPPORTERS

This activity is supported by an unrestricted educational grant from Bausch + Lomb, Inc.
To obtain CME credit for this activity, go to http://cme.ufl.edu/ed/self-study/tig/

ALTERNATIVE FIRST-LINE AGENTS

In select patients for whom neither a PGA nor a beta-blocker is indicated, an alpha-agonist or carbonic anhydrase inhibitor may be used as initial therapy. Both have good efficacy (15% to 25% IOP reduction) but require dosing two to three times a day. Alpha agonists have been associated with toxic blepharconjunctivitis, fatigue, lethargy, and hypotension in some patients; side effects of topical carbonic anhydrase inhibitors include metallic taste, allergic conjunctivitis, and corneal edema.³

Pilocarpine, a parasympathomimetic, was at one point widely used to lower IOP but has fallen out of favor because it requires four times a day dosing and has been associated with cataract development and dimming vision. However, pilocarpine or another parasympathomimetic may be appropriate for an occasional pseudophakic patient who is not a candidate for or is intolerant to more commonly prescribed agents.

COMBINATION MEDICATIONS

Roughly half of glaucoma patients require more than one topical antihypertensive agent to achieve target IOP. When choosing a combination regimen, the prospect of greater IOP reduction must be balanced with the potential for increased side effects, costs, and inconvenience to the patient. While cost and convenience may seem like minor issues compared to blindness from glaucoma, it’s worth remembering that if patients stop using their medication for any reason, the efficacy of the prescribed drug(s) becomes a moot point. Good communication with patients is key to uncovering resolvable tolerability and access issues. Fixed combination ophthalmic formulations help reduce the burden of multiple bottles and doses for patients who need more than one medication.

At present, three fixed combination topical anti-glaucoma medications are available in the US: timolol and brimonidine (a beta-blocker and alpha-agonist combination); timolol and dorzolamide (beta-blocking and carbonic anhydrase inhibitor); and, the newest addition, brimonidine and brinzolamide combination (alpha-agonist and carbonic anhydrase inhibitor). Dosing frequency is twice or three times daily depending on the drug.

LASER TRABECULOPLASTY

Laser trabeculoplasty is typically reserved for patients who, for whatever reason, have not been successful on medical therapy. But laser trabeculoplasty can be considered first-line therapy for patients who prefer not to take drugs or who have physical disabilities, such as arthritis or dementia, that limit their ability to use topical medical therapy.

Several studies have looked at laser trabeculoplasty as first-line therapy for the management of glaucoma. The Glaucoma Laser Trial, a large prospec-
tive randomized study conducted in the 1980s and 1990s showed that initial therapy with argon laser trabeculoplasty was at least as effective at preserving visual field and optic disc health, and more effective in reducing IOP, than timolol among previously untreated POAG patients. Studies have shown that selective laser trabeculoplasty with a SLT laser was comparable to medical therapy as first-line treatment for reducing IOP.

LIFESTYLE ADJUNCTS

Many patients are enthusiastic about incorporating lifestyle changes in their treatment plans as adjuncts in lowering IOP. When we look at the research to date, healthy diet and dynamic exercise are worth recommending, and, along with medication compliance, can empower patients to play an active role in their well-being. In the 1990s, Passo and coworkers showed in a prospective trial that previously sedentary patients who began exercise regularly experienced significant drops in their IOP.

FOLLOW-UP

The length of the follow-up interval between visits to assess glaucoma status, including optic nerve and visual field assessments, depends upon several variables: whether target IOP has been achieved, duration of IOP stability, and progression of disease. Therapeutic intensity and stage of disease might also be factored in. For example, a patient with early disease who has been stable on a single agent for at least 6 months may need to be seen every 6 months. On the opposite end of the spectrum, a monocular patient who requires multiple medications and barely achieves target pressure requires more frequent follow-up—perhaps every 2 to 3 months.

CONCLUSION

An increasing range of options is available for the medical management of glaucoma. Being methodical but efficient in one’s approach and staying attuned to compliance issues can help patients achieve their goals and maintain vision.

L. J. Katz, MD, is director of the Glaucoma Service at Wills Eye Institute, Philadelphia, Pennsylvania. Dr. Katz has received grant and research support from Allergan, Aerie Pharmaceuticals, Bausch + Lomb, and Mati Therapeutics. He has been a consultant for Allergan, Alcon, and Glaukos, and has been on the speakers bureau for Allergan and Glaukos. Dr. Katz is also a stock shareholder for Mati Therapeutics, Aerie Pharmaceuticals, and Glaukos. This manuscript was prepared with the assistance of medical writer Noelle Lake, MD.

REFERENCES


Aqueous Humor Dynamics, Intraocular Pressure, and Glaucoma

W. Daniel Stamer, PhD

Intraocular pressure, the only modifiable risk factor for glaucoma, is a direct reflection of the dynamics of aqueous humor circulation. Altered aqueous humor dynamics not only underlie the pathogenesis of ocular hypertension and progression in glaucoma, but also hold the key to developing new IOP-lowering therapies.

Glaucoma is a group of progressive optic neuropathies that share a distinct pattern of permanent vision loss resulting from degeneration of optic nerve axons and the death of retinal ganglion cells. For most forms of glaucoma, intraocular pressure (IOP) is an important risk factor and a major contributor to disease progression.

The risk of developing glaucomatous optic nerve damage increases exponentially with increasing IOP. Compared to an eye with an IOP ≤ 15 mm Hg, the risk of glaucomatous dam-
Aqueous humor is actively secreted by the epithelium of the ciliary processes. This epithelium consists of two cell layers: a non-pigmented layer that is in contact with the aqueous humor in the posterior chamber and a pigmented layer that is in contact with the ciliary stroma. With their apical surfaces juxtaposed, the pigmented and non-pigmented epithelial cells work together to move solutes, predominantly sodium chloride and sodium bicarbonate, from the stroma of the ciliary body into the posterior chamber. This active transport of solutes creates a local osmotic gradient across the ciliary epithelium, and this drives water into the eye.

Regulation of aqueous production is complicated and impacted by a variety of factors. Subject to a circadian rhythm, aqueous humor flow in humans peaks during the day and falls by half at night. And aging is accompanied by a steady decline in aqueous production. A variety of hormones and neuropeptides modulate the secretion of aqueous humor, but their mechanisms of action, while not entirely known, act to impact transporters and ion channels in the epithelial bilayer.

For example, several classes of antihypertensive agents produce their effect by limiting ion movement. The carbonic anhydrase inhibitors suppress aqueous humor formation by inhibiting carbonic anhydrase, a critical enzyme involved in the movement of solutes, such as sodium bicarbonate, in the pigmented ciliary epithelium. Beta-blockers (β-adrenergic receptor antagonists) and alpha-2 receptor agonists act through different adrenergic receptors to reduce production of cyclic adenosine monophosphate (cAMP), which is known to modify channel and transporter activity, increasing aqueous secretion.

AQUEOUS HUMOR OUTFLOW

Aqueous fluid leaves the eye via two outflow routes that begin at the irido-ocular angle. The conventional or "trabecular meshwork" pathway, composed of the trabecular meshwork, Schlemm’s canal, collector channels and episcleral veins, is the primary route and accounts for 70% to 90% of aqueous outflow in humans. The remaining 10% to 30% of aqueous drainage occurs through the uveoscleral pathway, which consists of the uveal meshwork, the anterior face of the ciliary muscle, and the spaces between the longitudinal muscle fibers, which empty into the supraciliary and suprachoroidal spaces. In human eyes, an age-related reduction occurs in both trabecular meshwork and uveoscleral flow, most likely due to age-related changes, such as presbyopia, decreased cellularity, and increased extracellular deposition that produces physical blockage of the conventional tract.

IOP increases associated with most forms of glaucoma are the result of impaired aqueous outflow rather than overabundant aqueous formation. The cause of this outflow impairment varies depending on the type of glaucoma. For most forms of congenital glaucoma, developmental defects in the outflow pathway are the problem; in the case of pigmentary or pseudoexfoliative glaucoma, it is a clogged trabecular meshwork. In primary open-angle glaucoma (POAG), the most common form of the disease, no discernible morphological abnormalities in the conventional outflow pathway are visible, suggesting defects at the molecular level are responsible for elevated IOP.

To obtain CME credit for this activity, go to http://cme.ufl.edu/ed/self-study/tig/
Prostaglandin analogs, a relatively new class of glaucoma agents, lower IOP by increasing aqueous outflow, especially outflow through the uveoscleral pathway. Multiple mechanisms contribute to their IOP-lowering effect, the dominant one appears to be stimulation of metalloproteinases and degradation of extracellular matrix within the ciliary muscle and trabecular meshwork.\textsuperscript{11}

OUTFLOW RESISTANCE AND IOP

IOP is determined primarily by resistance to aqueous humor outflow, the bulk of which is localized to the conventional pathway, and more specifically to the juxtacanalicular portion of the trabecular meshwork and the inner wall of Schlemm’s canal.\textsuperscript{7,12} The pressure gradient force resulting from the difference between IOP and the episcleral venous pressure drives drainage of the aqueous through the conventional route. Varying outflow resistance or facility (the reciprocal of resistance) has substantial effects on IOP. When resistance increases, facility decreases and IOP rises. The uveoscleral pathway, in contrast, is less pressure-dependent—normal IOP variations have little effect on aqueous outflow through this route.

The precise source of trabecular outflow resistance, however, has not been identified. None of the tissues in the vicinity of the juxtacanalicular region—the trabecular meshwork cells and their extracellular matrix or the inner wall of Schlemm’s canal—is able to account by itself for the measured total resistance. It has recently been proposed, based on evidence from pharmacologic studies, that the trabecular meshwork and Schlemm’s canal cells interact synergistically to generate resistance through a hydrodynamic effect known as “funneling.”\textsuperscript{13}

In principal, the trabecular meshwork functions as a filter, while the juxtacanalicular region (including the inner wall of Schlemm’s canal) acts like a resistor. Except for pressure-dependent pore sites, the inner wall of the canal, a continuous endothelial cellular layer, is relatively impermeable. The aqueous humor filtered through the juxtacanalicular connective tissue must converge or “funnel” to pass through the pores of the inner wall, a mechanism that increases hydraulic resistance in the juxtacanalicular tissue. For this funneling effect to occur, trabecular meshwork cells and the inner wall must be coupled physically and hydrodynamically.

Trabecular outflow resistance is regulated by a large and still-growing number of autocrine and paracrine mediators.\textsuperscript{7} These endogenous, local mediators affect the conventional pathway resistance to a varying degree, in either direction (increase or decrease). They fall into several major categories, including bioactive lipids (eg, lysophospholipids, prostaglandins, cannabinoids), cytokines (eg, TGF-beta, bone morphogenetic protein, Wnt, IL-1, TNF\textalpha{}), nucleotides (ATP/adenosine), and gases (nitric oxide).

PATHOLOGICAL RESISTANCE IN GLAUCOMA

The juxtacanalicular region is not only where most outflow resistance occurs in the normal eye but also the site of extra resistance that results in impaired aqueous humor outflow and elevated pressure in glaucoma.\textsuperscript{12}

Thus far, no clear consensus exists on the pathological basis for the extra resistance in POAG. One of the early discoveries was that there were fewer cells in the trabecular meshwork in POAG eyes.\textsuperscript{14} Recent research findings suggest that the extracellular matrix plays a key role in the regulation of aqueous outflow, and changes in the quality and quantity of the extracellular matrix in the juxtacanalicular region of the trabecular meshwork are responsible for increased outflow resistance in glaucoma.\textsuperscript{15} Indeed, the juxtacanalicular tissue appears to be more fibrotic, and TM and SC cells stiffer, in glaucoma patients, most likely the result of pathological changes in the interaction between cytoskeleton and extracellular matrix. This makes intuitive sense—a stiffer tissue should, in all likelihood, be more resistive to fluid flow.

IOP HOMEOSTASIS: THE CONCEPT

Various factors, including time of day, activity level, and fluid intake, can affect IOP. Yet, ocular pressure is maintained within a rather narrow range over a lifetime in the majority of the population. This rigorous control of IOP suggests that robust homeostatic mechanisms are at work in a healthy eye to keep IOP within suitable, physiological ranges.\textsuperscript{16} Researchers have shown that the trabecular meshwork and/or Schlemm’s canal inner wall cells can sense IOP imbalances and restore IOP to acceptable levels by adjusting the aqueous humor outflow resistance.\textsuperscript{16} Key molecular aspects of this IOP homeostatic process still await elucidation, however a couple of critical signaling molecules, adenosine and nitric oxide, appear important.

Presumably, sustained IOP elevations cause mechanical stretch or dis-
tortion of the cells and extracellular matrix, which in turn respond by initiating a complex extracellular matrix turnover process and/or relaxation of cells. Ultimately, restoration of extracellular matrix components and cellular tone leads to modification of outflow resistance and, accordingly, corrective adjustment of IOP.

In glaucoma, compromise to or loss of IOP homeostatic capability may occur due to inadequate IOP sensing or ineffective resistance adjustment. Consequently, IOP becomes abnormally high, triggering glaucomatous neuronal damage. This theory may explain why glaucoma is most typically a disease of older people—the IOP homeostatic capacity, like other self-stabilizing systems in the human body, deteriorates with age.

**IMPLICATIONS FOR GLAUCOMA THERAPEUTICS**

Although many of the pathologies responsible for elevated pressures associated with glaucoma are located in the pressure-sensitive, trabecular meshwork outflow pathway, no currently approved pharmacological therapy targets this part of the system. This might be one important reason why many glaucoma patients cannot achieve sufficient IOP reduction with current drugs. In the past decade, drug development has been focused on the conventional outflow pathway and is making substantial progress: several classes of drugs associated with glaucoma are now being evaluated in clinical trials.17 Rhokinase inhibitors target the trabecular meshwork cells to enhance aqueous outflow. By reducing the contractile tone of cytoskeleton, they reduce stiffness of the tissue and thus outflow resistance. Nitric oxide donors also relax tissue through the cytoskeletal systems. Adenosine receptor agonists potentially work through multiple mechanisms, but their main effect is increased degradation of the extracellular matrix.

As previously noted, different types of glaucoma may have different etiologies. One ultimate goal for development of conventional outflow drugs is to specifically target the pathologies associated with each type of glaucoma. Agents that treat pigment dispersion syndrome or pseudoexfoliation glaucoma, for example, should act by mechanisms different from the mechanisms employed by agents to treat steroid-induced glaucoma or POAG. Given multiple types of conventional outflow drugs in development, it may eventually be possible for clinicians to personalize treatment for a particular patient, depending on what kind of glaucoma the patient has.

Ideally, future drugs will be available in sustained delivery dosage forms, such as an implant or a patch. By eliminating the need to take daily drops, more patients could benefit from better pressure control.

One component that contributes to outflow resistance but has largely been ignored in glaucoma research and drug development is distal resistance, the smaller portion of outflow resistance (about 25%) that occurs beyond Schlemm’s canal, in the episcleral venous plexus. Episcleral venous pressure contributes to IOP and is theoretically the lowest attainable IOP from therapies targeting the trabecular meshwork. We have limited understanding about this distal-most part of the trabecular outflow system, but potentially it can be targeted to lower IOP and may prove to have a role in glaucoma therapy.

W. Daniel Stamer, PhD, is Joseph A. C. Wadsworth professor of ophthalmology and professor of biomedical engineering at Duke University, Durham, NC. He receives grant support from the National Eye Institute, Research to Prevent Blindness Foundation, Allegan, Aerie Pharmaceuticals, Ironwood Pharmaceuticals, and Novartis. He is also a consultant for Aerie Pharmaceuticals. Medical writer Ying Guo, MBBS, PhD, assisted in the preparation of this article.

**REFERENCES**

## EXAMINATION ANSWER SHEET  TOPICS IN GLAUCOMA — ISSUE 2

This CME program is sponsored by the University of Florida College of Medicine and supported by an unrestricted educational grant from Bausch + Lomb, Inc. **DIRECTIONS:** Select the one best answer to each question in the exam (Questions 1–10) and in the evaluation (Questions 11–16) below by circling one letter for each answer. Participants must score at least 80% on the questions and complete the entire Evaluation section on the form below. The University of Florida College of Medicine designates this activity for a maximum of 1.0 AMA PRA Category 1 Credit™. There is no fee to participate in this activity. You can take the test online at [http://cme.ufl.edu/self-study/tig/](http://cme.ufl.edu/self-study/tig/).  

To obtain CME credit for this activity, go to [http://cme.ufl.edu/ed/self-study/tig/](http://cme.ufl.edu/ed/self-study/tig/)

### 1. Which of the following lowers IOP by decreasing aqueous humor formation?  
   A. beta-adrenergic receptor antagonists  
   B. alpha-2 receptor agonists  
   C. Carbonic anhydrase inhibitors  
   D. All of the above

### 2. Which class of IOP-lowering drugs is contraindicated in patients with 2nd degree heart block?  
   A. Alpha adrenergic receptor agonists  
   B. Beta-blockers  
   C. PGAs  
   D. Carbonic anhydrase inhibitors

### 3. Having a high index of suspicion for POAG is important because:  
   A. The disease can produce significant eye pain  
   B. The disease is an early indicator of serious systemic illness  
   C. Early symptoms are hard to detect  
   D. All of the above

### 4. Which of the following statements about the conventional aqueous outflow pathway is FALSE?  
   A. It is the primary route for drainage of aqueous humor  
   B. It is the primary site where pathologies responsible for elevated IOP in glaucoma occur  
   C. It is the primary target of current pharmaco logical therapies for glaucoma  
   D. It is IOP dependent

### 5. In humans, the majority of the resistance to the aqueous humor outflow is localized to:  
   A. Juxtacanalicular tissue  
   B. Uveoscleral tract  
   C. Episcleral veins  
   D. Uveal meshwork

### 6. Approximately what proportion of glaucoma patients need more than one medication to achieve target IOP?  
   A. 50%  
   B. 15%  
   C. 5%  
   D. 0.5%

### 7. Which of the following is NOT an effective first-line intervention for patients with POAG?  
   A. Topical PGA  
   B. Systemic beta-blocker  
   C. Selective laser trabeculoplasty  
   D. Argon laser trabeculoplasty

### 8. Prostaglandin analogs lower IOP mainly by:  
   A. Inhibiting aqueous humor secretion  
   B. Increasing trabecular meshwork outflow  
   C. Enhancing uveoscleral outflow  
   D. Reducing episcleral venous pressure

### 9. How much does an individual’s risk of developing POAG increase if the individual has a first degree relative with POAG?  
   A. Approximately 5%  
   B. Approximately 1% per year after age 50  
   C. None, the risk is virtually unchanged  
   D. Somewhere between 2-fold and 9-fold

### 10. Which of the following statements about aqueous humor formation is FALSE?  
   A. It occurs at the ciliary processes  
   B. It fluctuates diurnally  
   C. It decreases with age  
   D. It increases in glaucoma patients

### EVALUATION:  
1=Poor 2=Fair 3=Satisfactory 4=Good 5=Outstanding

**Objective 1:**  
11. Extent to which the activity met the identified:  
   A. 1 2 3 4 5  
   B. 1 2 3 4 5  
   C. 1 2 3 4 5  
   D. 1 2 3 4 5

**Objective 2:**  
12. Rate the overall effectiveness of how the activity:  
   A. Related to my practice:  
   B. Will influence how I practice:  
   C. Will help me improve patient care:  
   D. Stimulated my intellectual curiosity:  
   E. Overall quality of material:  
   F. Overall met my expectations:  
   G. Avoided commercial bias/influence:  
   1 2 3 4 5

**Organizational/Institutional Evaluation:**  
13. Will the information presented cause you to make any changes in your practice?  
   A. Yes  
   B. No

**Address Line 1:**  
14. If yes, please describe:  
   ____________________________________________________________

**Address Line 2:**  
15. How committed are you to making these changes?  
   A. 1 2 3 4 5

**Address Line 3:**  
16. Are future activities on this topic important to you?  
   A. Yes  
   B. No

---

If you wish to receive credit for this activity, please fill in the following information. Retain a copy for your records.

**PLEASE PRINT CLEARLY**

**FIRST NAME**  
**LAST NAME**  
**DEGREE**

**ORGANIZATION/INSTITUTE**

**ADDRESS LINE 1**

**ADDRESS LINE 2**

**CITY**  
**STATE**  
**ZIP**

**PHONE**  
**FAX**

**E-MAIL ADDRESS**