The Future of Glaucoma: Perspectives for Optometry

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Our increased understanding of glaucoma risk factors and clinical markers, coupled with advances in imaging techniques, provide valuable insights for the development of novel therapies to treat this debilitating condition.

Glaucoma is characterized by a disruption of fluid dynamics in the anterior chamber of the eye that translates to hemodynamic and biomechanical changes at the lamina cribrosa of the optic nerve, resulting in irreversible visual impairment. Increased intraocular pressure (IOP) is the most important risk factor in the progression of glaucoma; however, the disease is complex in its etiology, as evidenced by the fact that reduced IOP does not always stop disease progression.

**RISK FACTORS**

Glaucoma is recognized as a neurodegenerative disease in which the accelerated loss of retinal ganglion cells (RGC) and their axons is a significant clinical feature. RGCs do not have the capacity to regenerate following an insult, which renders them susceptible to apoptosis. While the precise pathogenesis of glaucoma remains unclear, repetitive insult to the RGC axons, particularly at the level of the lamina cribrosa, may play a role. Primary open-angle glaucoma (POAG), which includes normal tension glaucoma (NTG), have mechanical and hemodynamic risk factors, both of which contribute to ischemic insult in the optic nerve.

Mechanical risk factors involve an altered structural relationship between the sclera and lamina cribrosa. This causes disruption of the translaminar pressure dynamics and vascular perfusion of the optic nerve. This can be further exacerbated by hemodynamic risk factors including arterial stiffness/arteriosclerosis, antihypertensive medication, exaggerated nocturnal hypotension, low ocular perfusion pressure (OPP), and autonomic dysregulation. All of these risk factors can translate to reduced health of the lamina cribrosa capillary bed and thus impaired perfusion of the optic nerve.

The management of glaucoma in patients with underlying systemic hypertension can be complex. Early-stage, untreated, systemic hypertension may be protective against glaucoma due to the associated increased capillary flow in the optic nerve. Conversely, treatment for systemic hypertension may lead to low blood pressure and decreased capillary perfusion of the optic nerve. Adequate monitoring of therapy for both systemic and ocular hypertension is important in the management of glaucoma and may include administering systemic hypertension medication in the morning rather than at night in view of normal nocturnal elevations of IOP.

**ASSESSING GLAUCOMA**

The three essential techniques used to diagnose and measure the progression of glaucoma are tonometry (to assess IOP), imaging (to assess the optic nerve and nerve fiber layer), and perimetry (to assess visual field). These techniques are powerful for assessing glaucoma when...
used in combination, particularly when measures are repeated and a full clinical picture is developed. Yet, no test in isolation is completely reliable. Lowered IOP does not translate to complete cessation of glaucomatous progression; nerve fiber defects and optic nerve abnormality can be caused by conditions other than glaucoma; and 25% to 35% of RGCs may be lost before any repeatable visual field defect can be detected using the clinical standard automated perimetry (SAP).  

Since OPP is the difference between mean arterial blood pressure and IOP, both of which fluctuate throughout the day, monitoring OPP is far from simple. Devices such as the Triggerfish® Sensor (Sensimed, Lausanne, Switzerland), a contact lens with sensors that capture spontaneous circumferential changes in the cornea/sclera, are a valuable step toward measuring nocturnal and 24 hour IOP, estimating 24 hour OPP, and potentially better managing glaucoma. However, there are limitations to the application of this device, such as the potential for the lens to adhere too tightly to the cornea and the prohibitively high cost of the device.

**STRUCTURAL BIOMARKERS**

There is increasing focus among researchers to find biomarkers of disease and its progression. A biomarker (biological marker) is a cellular, biochemical, or molecular alteration that is measurable in tissues, cells, or fluids; these indicate normal or pathologic processes. Equally important are surrogate markers, which are laboratory measurements or clinical signs used as a substitute for a clinically meaningful endpoint to predict the effect of therapy. Of all the potential biomarkers and surrogate markers for glaucoma, structural alterations/signs are closest to clinical application. Significant advances have been made in the application of imaging techniques for visualizing and quantifying structural aspects of the retina and optic nerve and thus identifying damage. One such tool is spectral domain optical coherence tomography (SD-OCT), which can provide anatomical quantification of the retinal nerve fiber layer (RNFL), ganglion cell layer, macula, and optic nerve. Another approach is to provide a single structural/functional metric of pathology by combining an estimate of RGC counts obtained from OCT with those obtained from SAP. Detection of Apoptosing Retinal Cells (DARC) is also a promising methodology for assessing RGC apoptosis in early-stage glaucoma. This technique provides real-time in vivo imaging of apoptotic RGCs via a non-radioactive method, allowing direct microscopic observation of cellular processes in the retina and the potential to evaluate neuroprotective agents in glaucoma.

Clinical psychophysics is an exciting area of research in which simulator-based visual field tests are being used to extend the dynamic range of measuring visual function in patients with glaucoma. These simulator-based methods are able to capture the impact of common ocular diseases, such as glaucoma, on driving ability and safety.

**BIOCHEMICAL MARKERS**

Genome-wide association studies (GWAS) are becoming powerful tools for identifying molecular markers associated with complex diseases such as glaucoma. While single genetic markers have been found for some of the congenital glaucomas, multiple markers are more likely to be implicated in POAG; yet these genetic markers have yet to be identified. The ultimate aim is for there to be...
a commercially available test based on tears/blood samples or mouth/nasal swabs to act as a biomarker of glaucoma onset, progression, and therapeutic response.

**DRUG TREATMENTS**

The immediate goal for treating glaucoma is to reduce IOP and modify fluid production and/or drainage. Fluid drainage occurs via two pathways: the trabecular meshwork (the predominant pathway) and the uveoscleral pathway (Figure 1). The QD prostaglandin analogues (latanoprost, travoprost, bimatoprost), typically used as first-line therapy, act by increasing aqueous outflow via the uveoscleral pathway. They have an advantage over the BID beta-blockers (timolol, levobunolol, betaxolol), which decrease aqueous fluid production but must be avoided in patients with asthma, heart failure, poor circulation, or depression. Prostaglandin analogues also have an advantage over the QID cholinomimetics (pilocarpine, carbochol), which increase aqueous drainage through the trabecular meshwork by acting on ciliary and sphincter pupillae muscles but often incur problems with focussing and light adaptation due to pupil constriction. The alpha2 agonists (brimonidine, apraclonidine) reduce formation of aqueous humor and may enhance outflow.

Latanoprostene bunod (LBN; Bausch+Lomb) is an NO-donating prostaglandin F2α analog designed to take advantage of the fact that approximately 70% of aqueous outflow occurs via the trabecular meshwork. LBN appears to be effective in increasing trabecular meshwork outflow by potentially targeting the nitric oxide (NO) pathway. Following exposure to esterases in the ocular environment, LBN is rapidly metabolized into latanoprost acid, a prostaglandin analog, and butanediol mononitrate, a NO-donating moiety, both of which exert the effect of lowering IOP.9,10 FDA approval for LBN is anticipated by the end of 2016.

The biotech company Inotek is investigating the safety and efficacy of trabodenoson, an adenosine mimetic that targets the A1 receptor to restore trabecular meshwork function. Trabodenoson upregulates proteases to clear proteins in the outflow pathway of the meshwork so it may better act as a conduit for aqueous outflow and lower IOP.9

Delivery devices are being designed to deliver drug for long periods of time (3-6 months) to address the issue of patient compliance with pharmacological medications. For example, Duraterm® is a biodegradable sustained-release implant placed in the subconjunctival space of the eye via a minimally invasive procedure.

Other therapies under investigation include the angiotensin converting enzyme inhibitors ramiprilat, enalaprilat, fosinopril, and perindopril (traditionally used in systemic hypertension but potentially effective in reducing ocular hypertension) and the acetylcholinesterase inhibitors, which induce miosis in the eye and lower IOP.9,10

**NEUROPROTECTION**

A number of other pharmacological approaches aim to provide neuroprotection to the RGC and optic nerve to attenuate active disease. The cellular kinase inhibitors have potential to confer neuroprotective properties, improve ocular blood perfusion, and reduce IOP due to their important role in several cellular events such as cell proliferation and migration, cytoskeletal organization, and apoptosis. Such investigative molecules include myosin light chain kinase inhibitor, tyrosine kinase inhibitor, cell cyclin-dependent kinase inhibitor, Rho-kinase inhibitors, protein kinase C inhibitor, integrin linked kinase inhibitor, integrin linked kinase inhibitor, LIM-kinase 2 inhibitor, dual leucine zipper kinase inhibitor, JNK inhibitors and ion channel blockers/inhibitors.8,12

There is increasing interest in the use of neurotrophic signaling peptides—such as nerve growth factor, brain-derived growth factor, and ciliary neurotrophic factor—for the treatment of glaucoma due to their fundamental role in the normal development and survival of neurons. IOP elevation has been reported to obstruct the transport of brain-derived neurotrophic factors that nourish RGCs and induce apoptosis. One challenge associated with neurotrophic factors in the treatment of glaucoma is their ubiquitous nature, the potential multiple pathways they may influence in a cell, and their non-specific activity.13

**SURGICAL APPROACHES**

With the growing sophistication of IOP-lowering and neuroprotective pharmacotherapies, glaucoma treatment is increasingly shifting away from invasive surgical approaches. Nonetheless, these techniques are valuable for patients who are recalcitrant to pharmacologic therapy. The less invasive procedures of argon or selective laser trabeculoplasty (ALT and SLT, respectively) are performed by applying energy in the trabecular meshwork to stimulate more effective fluid drainage and lower IOP. The more invasive technique of trabeculectomy, in which a drainage channel directs fluid to a tiny flap (bleb) created in the sclera in order to facilitate aqueous outflow, has been the mainstay of glaucoma surgery. The significant adverse effects observed with the invasive surgical procedures, coupled with their inability to maintain optimal IOP long-term, has led to increasing focus on the development of minimally invasive glaucoma (MIG) devices. The FDA-approved Trabectome (NeoMedix Corporation, Tustin, CA), is designed to ablate a strip of tissue from...
the trabecular meshwork and Schlemm’s canal to facilitate aqueous outflow. Newer-generation MIG devices are inserted via corneal incision and facilitate aqueous fluid flow through various mechanisms such as dilating Schlemm’s canal or providing a scaffold of multiple flow channels. The iStent Trabecular Micro Bypass device (Glaukos, Laguna Hills, CA), which is FDA approved, the iStent Inject (Glaukos), and the Hydrus Micro Stent (Ivantis Inc, Irvine, CA) all utilize the trabecular meshwork pathway, while the Gold Micro Shunt (SOLX Corp, Waltham, MA), Aqua Shunt (Opka Health Inc, Miami, FL), and CyPass suprachoroidal shunt (Transend Medical, Menlo Park, CA) utilize the uveoscleral pathway. MIGs have an excellent safety profile; however, their efficacy is modest compared to the clinical standard of trabeculectomy and current drainage devices. As a result, they may be used for mild to moderate glaucoma or in cases where early, less invasive intervention is indicated.14

THE FUTURE

Overall, the current IOP-lowering therapies offer safe and effective outcomes in approximately 80% of compliant patients, providing adequate lifetime management of glaucoma. Still, there is significant room for improvement and a number of unmet needs, including: more sensitive devices to monitor changes in ocular hypertension in a safe, effective, patient-compliant manner and provide real time, continuous generation of data; more sophisticated drug-delivery options for pharmacological agents that provide optimal outcomes and enhance patient compliance; surgical devices to lower IOP that require less intervention and confer long-term success with minimal complications; and therapeutic approaches that confer neuroprotection and neuroregeneration to address the underlying disease.

Many of these unmet needs are being addressed through the identification of biomarkers, novel pharmacological approaches, and surgical advances, as discussed above. Other approaches currently under investigation include advanced drug-delivery devices, gene-delivery systems, and stem cell therapies. Advanced drug-delivery devices, such as slow-release nanoparticles and drug-impregnated inserts, aim to reduce dosing frequency for patients and enhance medication compliance. Due to their size, nanoparticles have the potential to increase drug penetration at the target site and enhance bioactivity, with fewer drug administrations at lower doses compared to conventional eye drops.8

Viral and non-viral vector gene-delivery systems target specific tissues involved in the pathogenesis of glaucoma, namely the trabecular meshwork, ciliary body, ciliary epithelium, Müller cells, and retinal ganglion cells.8 This approach involves modifying DNA and messenger RNA using small interfering or microRNAs (RNAi).11 There are potential limitations in using viral vectors as a glaucoma target; at present, only moderate efficacy can be achieved over long periods of time, and optimal efficacy is observed generally in diseases in which a pathogenic protein is implicit, which is not necessarily the case with a multifactorial disease like glaucoma. Other areas of gene-delivery research include the use of implantation devices containing genetically modified human cells to secrete trophic factors; and trans-orbital alternating current stimulation, which upregulates IGF-1 by Müller cells for visual restoration following optic nerve damage.15

One of the most exciting areas of glaucoma research is the development of stem cell therapies to confer neuroregeneration and restore vision already lost through glaucomatous optic neuropathy. By directing mouse and human stem cells along specific developmental paths to differentiate into a variety of ocular cell types (such as retinal pigment epithelial cells, trabecular meshwork cells, or ganglion cells), this research offers the potential to replace cells damaged by the glaucoma disease process with functional ones. In addition, these pluripotent cells have the potential to secrete neuroprotective factors, which are critical for the maintenance and survival of neurons in the optic nerve.16

However, developing stem cell therapies continues to be challenging. Transplantation of RGCs requires transplanted axons to navigate the nerve fiber layer, optic disc, optic nerve, and chiasm; traverse long distances to reach appropriate target tissues; and connect with appropriate higher-order neurons to achieve vision. All of this must take place in an adult, glaucomatous environment quite dissimilar to that of the developing eye.16

CONCLUSION

There has never been a more exciting time in glaucoma research. A number of experimental technologies have the potential to not only address the symptoms but also modify the underlying disease process. At present, there are challenges in establishing neuroprotective or disease-modifying drugs for glaucoma due to the lack of validated biomarkers for disease progression and requirement for long-term trials of large patient cohorts to identify changes in functional neuroprotective endpoints.17 However, continued collaboration between scientists, clinical experts in glaucoma, and pharmaceutical and medical device companies is helping to develop new ways of measuring and managing this complex and common disease.

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REFERENCES

4. John Flanagan, OD, PhD, DSc (hon), FBOptom, FAAO, is Dean and Professor of Optometry and Vision Science in the School of Optometry at the University of California-Berkeley. Dr. Flanagan is on the advisory board for Alcon, Allergan, and Inotek Pharmaceuticals. Medical Writer, Caroline M. Markey, PhD, of Markey Medical Consulting Pty Ltd, assisted in the preparation of this manuscript.

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Glaucoma, by definition, is a progressive optic neuropathy. Clinicians and patients must work together to prevent visual loss; the goal being to retard functional loss to a rate similar to that caused by natural aging. Monitoring the optic nerve and visual field helps illuminate individual rates and patterns of glaucoma progression and responses to treatment and sets the stage for vision-preserving care.

**WHAT TO MONITOR**

It is important to distinguish between a risk factor for progression and actual progression. For example, intraocular pressure (IOP)—a well-known determinant of glaucoma progression—is a single risk factor and not the disease itself. In fact, despite being the only therapeutic target for medical anti-glaucoma treatment at present, IOP is a poor marker for glaucoma. This is evidenced by the fact that many patients without IOP elevation have glaucoma (normotensive glaucoma) and many others have ocular hypertension but never develop glaucoma (glaucoma suspect). Still, individuals with ocular hypertension are prophylactically treated with IOP-lowering agents when the risk for conversion to glaucoma is significant.

Other risk factors—including hysteresis (corneal rigidity), low blood pressure, and low ocular perfusion pressure—may also play a role in the development of glaucoma. Ocular perfusion pressure, a measure of blood flow to the optic nerve, is grossly calculated by subtracting the highest IOP from diastolic blood pressure; thus, low blood pressure is a risk factor for glaucoma, similar to higher IOP.

IOP, IOP fluctuation, and ocular perfusion pressure, however, are not indicators of damage or glaucoma; they are indicators of risk for developing glaucoma and/or progression. Glaucoma progression, on the other hand, requires evaluating: 1) structure, which is indicated by nerve head appearance, macular thickness, and retina nerve fiber layer (RNFL) thickness; and 2) function, which is monitored by perimetry. Structural change is monitored by optical coherence tomography (OCT); functional change is monitored by visual field testing (VFT).

**MONITORING STRUCTURE**

**Rationale**

In the natural history of glaucoma, the most common scenario is for the optic nerve/RNFL to show damage before visual fields are affected. In fact, patients with mild to moderate glaucoma may not only be asymptomatic (patients typically have no idea that they have glaucoma or that it might be getting worse), but mild to moderate glaucoma may also be imperceptible on VFT. This structure/function dichotomy is part of a strong rationale for using optic nerve/RNFL imaging to monitor glaucoma early and regularly in the course of the disease.

Documenting and following disease progression with OCT also provides a means for communicating with patients about their disease. Since vision loss is not present in patients with an early diagnosis of glaucoma, information regarding glaucoma and its progression can feel rather abstract to patients; a lack of tangible evidence may undermine patient motivation to comply with daily treatment. Retinal images can often provide a more concrete impression than words and descriptions alone, helping patients appreciate more fully the reality of their disease.
Evolving Technology

Prior to the development of OCT, fundus photography was used to detect changes in the optic nerve over time. Photography, however, is limited by low sensitivity for detecting subtle changes and a high degree of subjectivity in image interpretation. Over the past 10 years, OCT has emerged as the modality of choice for retinal imaging and is now routinely performed in the evaluation of patients with glaucoma.

OCT is used to detect progression in glaucoma by quantifying RNFL thickness (Figure 1). It is important to recognize that up to one-third of the RNFL thickness may be lost before a value falls below the “normal” range; serial evaluations are necessary to detect values that are drifting downward (by at least 5 microns between measurements), indicating progression.

OCT Floor Effect

As mentioned, OCT is currently the most sensitive modality for following glaucoma-related change early in the disease process, and it remains so until the RNFL degrades to its thinnest state. At that point—known as the “floor effect”—repeated OCT images will yield the same low RNFL thickness of 50 to 55 microns compared to a baseline thickness of about 105 to 110 microns in its healthy state. The OCT floor effect reveals that there is a limited amount of RNFL tissue; the remaining 50 microns must be alert for images of low quality and those taken under a weak signal (a low signal-to-noise ratio) so that they are not incorporated into the final average, creating a false impression of progression.

MONITORING FUNCTION

Even though OCT is newer, more “high tech,” more patient friendly, and less labor intensive to administer, it is not a substitute for VFT (also known as perimetry). Function correlates most directly with current patient status, as it reflects their visual experience in the world. Information gained through VFT complements that gained through OCT and should be the principle monitoring method among patients with moderate to advanced disease.

According to the American Optometric Association Preferred Practice Guidelines, VFT should be performed at least yearly for all glaucoma patients and glaucoma suspects. However, VFT may erroneously be falling out of favor. A study by Stein and coworkers evaluating managed care database reimbursement claims from optometrists and ophthalmologists for glaucoma patients revealed a drop in VFT and a marked increase in OCT claims (suggesting reduced and increased usage, respectively) over the past 10 years.

How VFT Works

VFT assesses patients’ visual sensitivity to light directed at locations in their central visual field (the central 24 to 30 degrees) while they are looking straight ahead. Testing the peripheral visual field (beyond 30 degrees) is not commonly done, as it is less precise.

Advances in VFT technology have improved sensitivity and specificity of results and reduced inter-test and inter-technician variability. The latest
VFT software provides a clean backdrop against which true progression-related change can be observed, akin to noise-cancelling headphones. Incorporated in the software is a database derived from glaucoma patients who underwent repeated VFT testing over a short period in a multicenter trial; observed changes are designated as inter-test variability or “noise.” With automated VFT, results are filtered through the database, and any matching, location-specific “frequencies” are neutralized, leaving only those changes likely to indicate real progression. Results are reported as “possible” or “likely” change, with “likely” carrying a high specificity for a progression event. In addition to event analysis, both VFT and OCT provide trend analyses, or quantification of overall change over a course of time. The visual field index (VFI) is used to track changes over time. The VFI is a summary measure of the visual field based upon pattern standard deviation maps. Thus, changes in media opacities such as cataracts should not produce a worsening trend analysis. A baseline of 100% represents a full visual field; a reduced VFI (for example, 70% or less) is an indication that a change has occurred, and often at this point the individual may perceive something amiss in their vision. A worsening visual field trend analysis is one of the indications for clinicians to reassess the therapeutic course.

There have also been advances in recent years to improve the ability of VFT to detect early functional loss. One shift has been to use the 10-2 test pattern, in which 55 test locations over 10 degrees of field are measured at 2-degree intervals, instead of the traditional 24-2 test pattern, which has test locations marked at 6-degree intervals. The theory behind this change is that fewer defects go undetected with the 10-2 test pattern because the locations are closer (Figure 2).

Front-loading
Formerly, conventional wisdom held that digital imaging and VFT should be performed once yearly upon diagnosis of glaucoma. With the recognition that about 10% of patients progress rapidly and that at least five data points were needed for the analyzing software to detect a trend of statistically significant progression, the recommendation changed to five tests at 6-month intervals over the first 2 years of care (ie, at 6, 12, 18, and 24 months following initial testing). By front-loading the testing in this way, rapid progressors can be identified; and patients who are not progressing can be reduced to once-yearly testing.

Risk factors for progression—including higher IOP, lower ocular perfusion pressure, family history of glaucoma, degree of damage, status of each eye, and advanced age—must also be considered when determining how frequently to monitor. Higher-risk patients may benefit from more frequent monitoring.

Variable Patterns
Glaucoma progression is not always linear. A patient who is stable for 2 years, for example, may begin to experience progression during the third year. Therefore, it is good practice to stay vigilant for change.

I see newly diagnosed glaucoma patients every 3 months for the first 2 years, performing VFT and imaging at every other visit. At 2 years, if their disease is mild to moderate in severity as well as stable, I will reduce visits to every 4 months and perform VFT and imaging once per year. Patients with lower ocular perfusion pressure, greater damage, lower hysteresis values, or a disk hemorrhage will be monitored more closely. If a patient’s glaucoma progresses, I will increase imaging or VFT twice per year until the disease stabilizes.

GLAUCOMA SUSPECTS
Glaucoma suspects have one or more risk factors but no test results (either structural or functional) definitive for glaucoma. They often fall into one of two categories: ocular hypertensives with normal visual fields, normal appearance of the optic nerve, and normal RNFL thickness; or those with suspicious optic nerve appearance.

Glaucoma suspects should be followed carefully with imaging and VFT on a yearly basis for any changes. Any change that is detected must always be confirmed by additional testing before a diagnosis is made.

Looking Ahead
Currently, structure and function are evaluated separately. It may be, however, that subtle changes on both imaging and VFT that do not meet the threshold of significance on one device alone might do so if the two technologies were integrated. In the not-too-distant future, such combined analysis technology using advanced mathematics such as neural networks should become available, which would increase the sensitivity and precision over current technology. This is different from having a combined printout that includes the results in one location.

In addition, OCT technology is continuing to improve, with higher speeds and greater resolution, which should improve detection of RNFL loss and other changes at an earlier point in time.

Conclusion
Both OCT and VFT are essential for monitoring glaucoma patients and suspects over time. Early detection of progression is critical for appropriate and timely management of this chronic condition.

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References

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1. Which of the following factors may confound the accuracy of OCT readings?
   A. Inadequate technician training
   B. Low signal-to-noise ratio
   C. Poor quality images that are not deleted
   D. Any of the above may contribute to inaccuracies

2. Which statement is correct regarding surgical options for the treatment of glaucoma?
   A. Trabeculectomy has an excellent long-term efficacy and safety profile
   B. MIGs have yet to be FDA-approved as a surgical treatment for glaucoma
   C. MIGs are designed to minimize the disruption of ocular anatomy and postoperative inflammation
   D. MIGs facilitate aqueous outflow via only the trabecular meshwork/Schlemm’s canal pathway

3. According to insurance claims data analyzed by Stein and colleagues, clinicians are using VFT:
   A. At increasing frequency
   B. At decreasing frequency
   C. With improper technique
   D. None of the above were shown in Stein’s research

4. Which of the following statements is accurate regarding biomarkers of glaucoma?
   A. Functional endpoints are far more valuable than structural endpoints
   B. GWAS are providing important insights into genetic markers of glaucoma
   C. Commercial tools are available to assess a patient’s risk for developing glaucoma
   D. Novel electrophysiologic techniques for assessing glaucoma include OCT, DARC, and PERG

5. Which of the following are risk factors for developing glaucoma?
   A. Thinning of the nerve fiber layer
   B. Arteriosclerosis
   C. Systemic hypotension
   D. All of the above

6. Glaucoma suspects should undergo VFT and OCT at least:
   A. Once every three months
   B. Once every four months
   C. Once every six months
   D. Once yearly

7. Which statement is correct regarding pharmacologic therapies for treating glaucoma?
   A. Prostaglandin analogues are no longer the first-line therapy for treating glaucoma
   B. Latanoprostene bunod increases aqueous flow via the uveoscleral channel by targeting the nitric oxide pathway
   C. Cellular kinase inhibitors have limited neuroprotective properties
   D. Viral vectors have been FDA approved for the treatment of POAG

8. Based on current research directions, which of the following are potential therapies for the treatment of glaucoma?
   A. Viral vectors
   B. Stem cells
   C. Neurotrophic factors
   D. All of the above

9. Which of the following is NOT an indication of glaucoma progression?
   A. Increasing IOP
   B. Decreasing retinal nerve fiber layer thickness
   C. Visual field loss by event analysis
   D. Visual field loss by trend analysis

10. Which of the following is NOT true regarding current VFT technology?
    A. It accounts for testing-related visual field variability
    B. It distinguishes possible vs likely progression
    C. It is inferior to OCT for detecting progression
    D. It is painless and noninvasive


