REVIEW ARTICLE

GLAUCOMA: A REVIEW FOR THE FAMILY PHYSICIAN

E. Hunter Harrison, OMS-III[1]; Leonid Skorin Jr., DO, OD, MS, FAAO, FAOCO[2]

[1]VCOM-Carolinas, Spartanburg, SC
[2]Mayo Clinic Health System, Albert Lea, MN

KEYWORDS:

Angle-closure glaucoma

Glaucoma

Intraocular pressure

Normal tension glaucoma

Primary open-angle glaucoma

Retinal nerve fiber layer

Glaucoma is an insidious disease process that causes damage to the optic nerve head and retinal nerve fiber layer, resulting in progressive vision loss. Multiple factors play a role in its pathophysiology, but intraocular pressure is a significant yet modifiable risk factor and therefore is targeted by all current treatment modalities. Its high prevalence and potential for irreversible damage necessitate an understanding of the condition by primary care physicians, who will undoubtedly be managing conditions and medications that can influence glaucomatous progression. This article will explore the pathophysiologic basis of glaucoma, discuss some of the common subtypes and highlight important clinical considerations.

INTRODUCTION

Glaucoma is one of the foremost causes of vision loss globally, with a staggering 111.8 million people worldwide projected to be affected by it in 2040.[1] In the United States, glaucoma is second only to cataracts among the leading causes of vision loss.[2,3] Unlike cataracts, the damage incurred from glaucoma is irreversible and cannot be improved with surgery, although surgery may limit further damage. Given the indolent nature of the disease, there is often substantial damage present before a patient is aware of vision changes. The retinal nerve fiber layer (RNFL) may be 28%–50% damaged before a visual field defect is documented.[4,5] Therefore, timely diagnosis and treatment are imperative.

Although there are various forms of glaucoma, they are unified and defined by characteristic changes to the optic nerve head (ONH) and RNFL.[6] Such changes clinically manifest as a gradual reduction in peripheral vision, which can progress to central vision loss in severe cases. Due to the multifactorial nature of the disease, its pathogenesis is influenced by a myriad of common conditions, medications and other risk factors. As family physicians are often the ones managing these conditions and medications, they play a vital role in caring for glaucoma patients. In addition to being familiar with factors that hasten glaucomatous progression, it is in the patient's best interest for physicians to remain cognizant of systemic effects of various glaucoma medications and their potential impact on comorbidities.

CORRESPONDENCE:
Leonid Skorin Jr., DO, OD, MS, FAAO, FAOCO | skorin.leonid@mayo.edu

 Print ISSN: 1877-573X
DOI: doi:10.33181/13063

CLASSIC PRESENTATION

In the most common type of glaucoma—primary open-angle glaucoma—the disease course is slowly progressive and painless. Patients undergo a gradual reduction in peripheral vision bilaterally that is usually imperceptible until later stages. In the primary care setting, this may be detected during a patient's physical exam by testing confrontation visual fields. Central vision is often preserved, thus visual acuity (as measured with a Snellen chart) may appear to be unchanged. Patients frequently have elevated intraocular pressure, although this is not a prerequisite feature for the diagnosis of glaucoma. On fundoscopic exam, one should expect to see pathological cupping of the optic disc, characterized by an increased cup-to-disc ratio.[6]

PATHOPHYSIOLOGY

Despite significant advances in the understanding and treatment of glaucoma, its pathophysiology has yet to be fully elucidated. This has given rise to several theories, two of which have received more attention than others: the mechanical theory, which pertains to deformation of retinal nerve fibers as they traverse the lamina cribrosa, and the vascular theory, which pertains to alterations in optic nerve blood supply. It is probable that both scenarios play a role in the disease process, together inducing apoptosis of retinal ganglion cells by disrupting axoplasmic transport of nutrients and waste as well as by causing ischemia.[7,8] An important, well-established contributor is elevated intraocular pressure (IOP). IOP is dependent upon the dynamics of aqueous humor in the eye.[9]

Within the posterior chamber of the eye, the ciliary body produces aqueous humor, a fluid that nourishes avascular structures (eg, lens and cornea) and contributes to the structural integrity of the eye.[9] Under normal conditions, aqueous humor flows from the posterior chamber to the anterior chamber via the pupil, eventually reaching the iridocorneal angle. From here, 90% of aqueous humor traverses the trabecular meshwork to reach Schlemm's canal, where episcleral veins return the fluid to circulation. The remaining aqueous exits the eye primarily through the uveoscleral pathway, aided by the venous system of the ciliary body, choroid and sclera.[6] Secretion and outflow of aqueous humor are modulated through various autonomic receptors and structural factors, ultimately striking a balance that determines IOP. If there is a disturbance in secretion exceeding outflow, the resultant elevation in IOP can predispose the ciliary body to glaucomatous damage.

During fundoscopic examination, glaucomatous damage is evidenced by an increased cup-to-disc ratio that continues to increase as more nerve fibers are lost (Figure 1). Peripapillary atrophy may be noted adjacent to the optic disc (Figure 1). As shown in Figure 2, a healthy optic nerve is characterized by a normal cup-to-disc ratio. In glaucoma patients, additional features that may be present include disc hemorrhages, bayoneting of vessels and notching of the neuro-retinal rim (Figure 3).[6] A disc hemorrhage, also known as a Drance hemorrhage, is suggestive of inadequate IOP control or disease progression when seen in a glaucoma patient.[9]

FIGURE 1:

Increased cup-to-disc ratio with adjacent peripapillary atrophy (arrow)

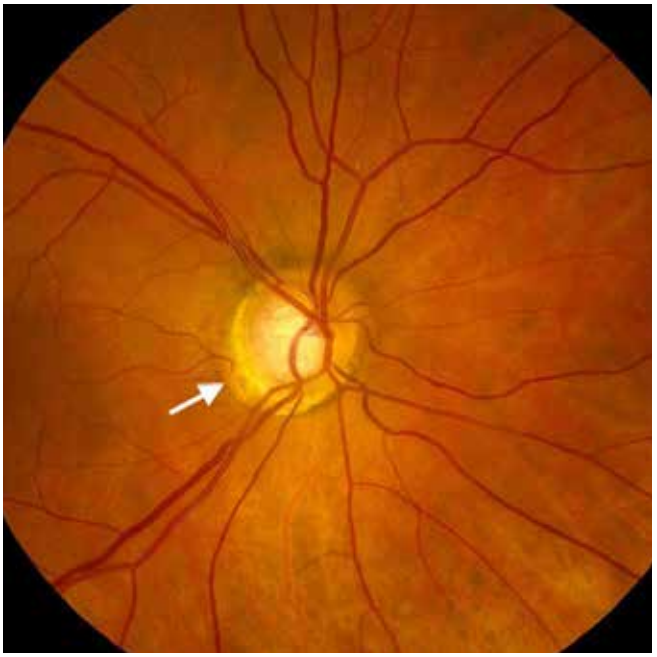


FIGURE 2:

Healthy optic nerve with a normal cup-to-disc ratio

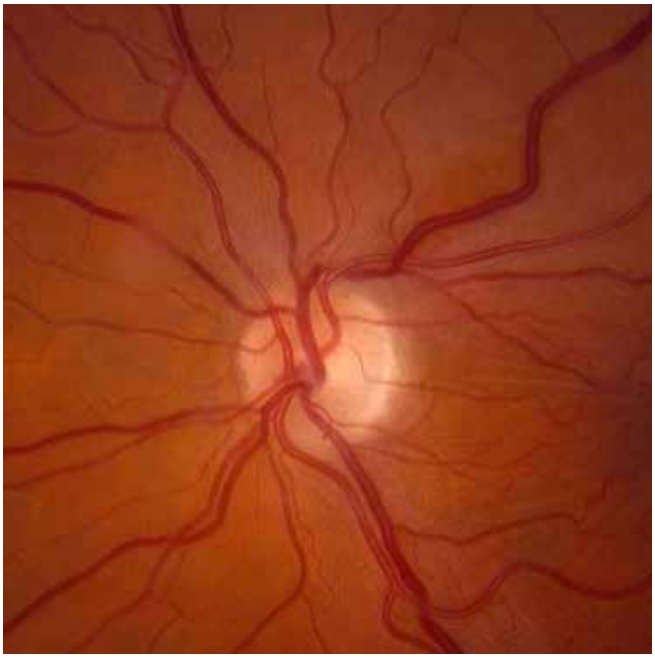
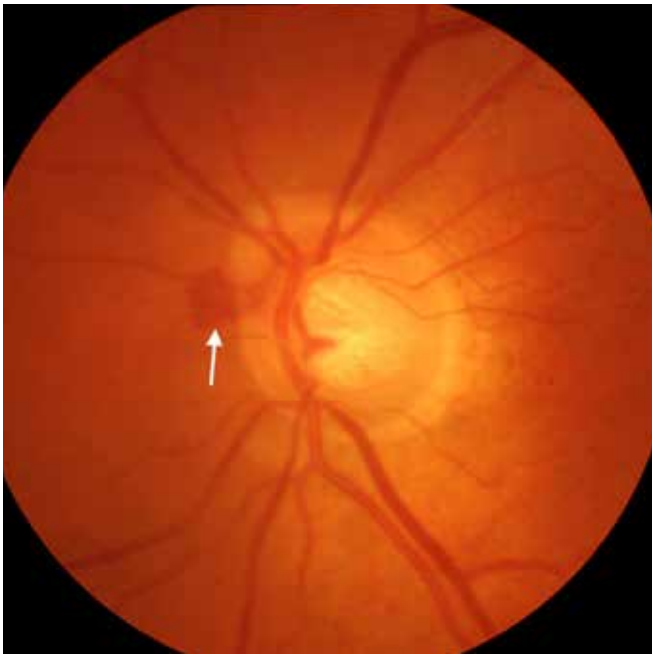


FIGURE 3:

Disc hemorrhage, also known as a Drance hemorrhage (arrow)

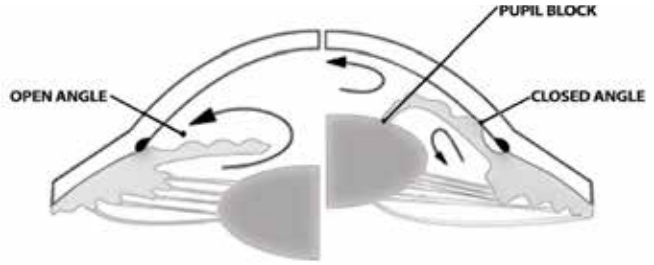


COMMON TYPES

Glaucoma may be broadly categorized as open-angle glaucoma or angle-closure glaucoma, depending upon the openness of the iridocorneal angle (Figure 4). Further distinction may be made if the process is determined to be idiopathic (primary) or attributable to an identifiable etiology (secondary).[10]

FIGURE 4:

Aqueous flow from posterior to anterior chambers. The cross-section on the right depicts the pupillary block mechanism of angle closure. Reproduced with permission from *The Indian Optician*, September–October 2016.



Primary open-angle glaucoma (POAG) is the most common form of glaucoma in the United States.[11] Some estimate the number of Americans with POAG may increase from 52.7 million in 2020 to 79.8 million in 2040.[1] As the name suggests, the iridocorneal angle in the anterior chamber appears open; however, aqueous outflow is nonetheless impeded by debris that obstructs the trabecular meshwork. As intraocular pressure rises due to impaired drainage, damage to the optic nerve ensues.

Beyond elevated IOP, there are additional risk factors that should alert the primary care physician to patients who may be asymptomatic but at higher risk of developing POAG. Advanced age is a well-established risk factor, particularly beyond the fifth decade of life.[9,12] Race plays a role, as prevalence is roughly three times higher in African American and Hispanic patients than in white patients.[13] Family history is another factor, given that first-degree relatives of those with POAG are much more likely to be affected.[14–16] The multifactorial nature of the disease is supported by the fact that only about 5% of POAG cases display Mendelian inheritance, most commonly in association with MYOC gene variants.[17] This gene encodes myocilin, and mutations cause accumulation of the protein within cells of the trabecular meshwork, compromising its function as a drainage pathway.[18]

Although data does not currently support widespread screening, Medicare and Medicaid cover annual glaucoma evaluations for diabetics, patients with a family history of glaucoma, African Americans aged 50 years or older, and Hispanics aged 65 or older.[19,20] Such evaluations should involve IOP measurement, ophthalmoscopy and visual field testing.

Normal tension glaucoma (NTG) is a less common form of glaucoma and may be considered a variant of POAG. Although there is substantial overlap between the two, NTG is distinguished by glaucomatous damage that occurs at a normal IOP within the range of 11–21 mm Hg.[6] This lends credence to the idea that other IOP-independent mechanisms—particularly structural or vascular anomalies—contribute to the pathogenesis. Despite this fact, reducing IOP has shown efficacy in treating NTG and remains a cornerstone of therapy.

Anatomic variation may partially explain why some eyes are seemingly less tolerant of normal IOP. For example, larger eye size or a larger optic disc can amplify the mechanical strain incurred from a given pressure within the eye.[21] Central corneal thickness is lower in NTG patients than in POAG patients.[22] This can result in underestimation of IOP, as a thin cornea exerts less resistance against a tonometer tip. It is also possible that a thin cornea corresponds to a thin lamina cribrosa—another finding seen in patients with NTG.[9,23]

Adequate control of certain comorbidities may help attenuate NTG, as several conditions lead to reduced ocular blood flow and predispose the ONH to injury. Vascular dysregulation occurring in Raynaud's phenomenon or migraine is more common with NTG than with POAG.[24,25] In obstructive sleep apnea (OSA), transient hypoxemia results in vasospasm that predisposes the ONH to ischemic injury.[26] OSA has been noted in patients with NTG.[26] Evidence suggests that continuous positive airway pressure is a useful adjunct to conventional glaucoma therapy in such cases.[27,28]

Primary angle-closure glaucoma (PACG) differs from POAG and NTG in that it involves a narrow iridocorneal angle with the peripheral iris impeding aqueous outflow. Although POAG is more common, PACG accounts for a larger amount of glaucoma-related blindness.[29] The most common mechanism—pupillary block—occurs when aqueous cannot flow around the lens and through the pupil, forming a pressure gradient that causes the iris to billow forward and obstruct the anterior chamber angle.[6] The non–pupillary block mechanism usually involves an abnormally thick peripheral iris that blocks aqueous drainage. Demographic features that predispose individuals to PACG include advanced age; female sex; and being of Vietnamese, Chinese, Inuit or Pakistani descent.[30]

In most cases, the disease follows a chronic course like that of POAG.[6] Symptomatic attacks of acute angle closure can be precipitated by factors that induce pupillary dilation (eg, watching a movie in a darkened room). These patients may present to their primary care provider with ocular pain, blurred vision, nausea, vomiting and headache. In such cases, examination often reveals a markedly elevated IOP (ie, 50–80 mm Hg); a tense globe; and a mid-dilated, poorly reactive pupil.[6] Immediate referral and prompt reduction of IOP are crucial to prevent blindness. Administration of topical and oral medication is performed to quickly lower IOP and alleviate pain.[30] Definitive treatment is obtained with a laser iridotomy, which involves forming a small hole in the iris with a laser and allowing aqueous to bypass the obstruction and maintain outflow. Laser iridotomy is also performed prophylactically in the other eye because roughly half of these patients may experience an attack in the fellow eye within five years.[30]

MANAGEMENT

Management of glaucoma is based upon two primary goals: preservation of vision and maintenance of quality of life. Patients should see an ophthalmologist regularly for fundoscopic examination and diagnostic assessments, such as visual field testing (Figure 5) and optical coherence tomography (Figure 6), which help monitor disease progression. By comparing current with previous visits, these assessments help determine if glaucoma is well-controlled.

FIGURE 5:

Superior arcuate visual field defect of the right eye as detected by automated perimetry.

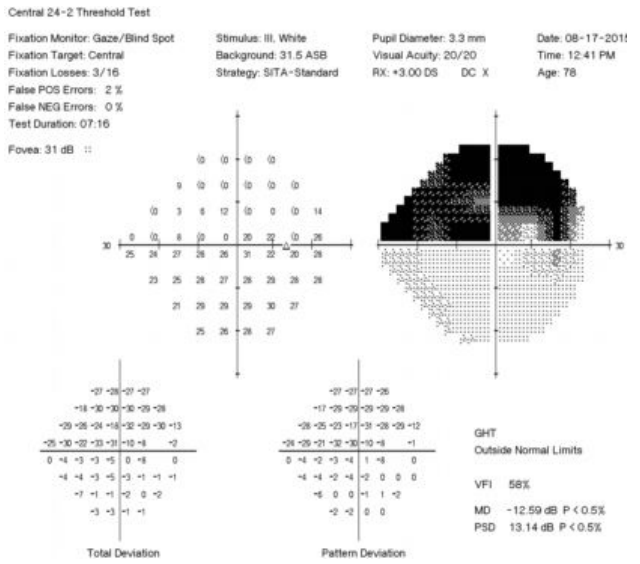
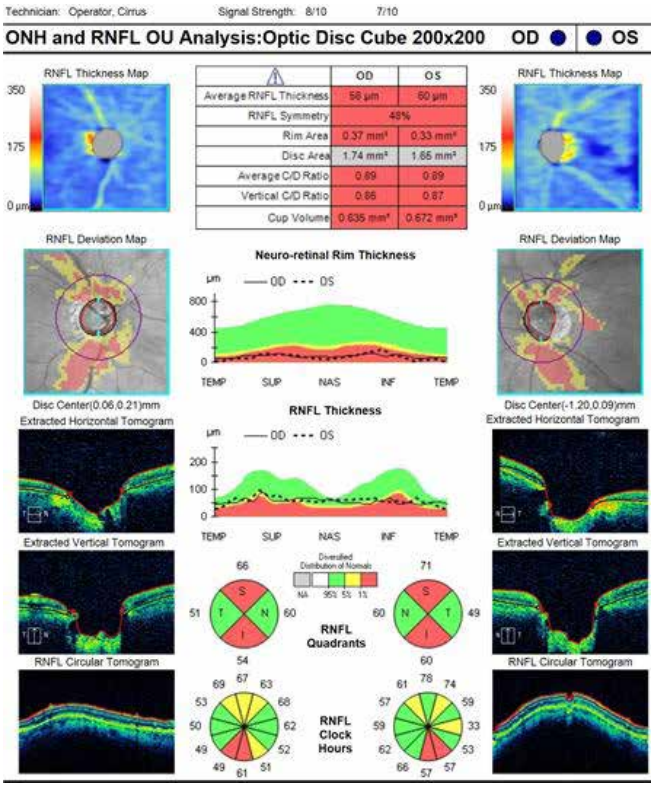


FIGURE 6:

Optical coherence tomography that depicts thinning of the retinal nerve fiber layer (RNFL). RNFL quadrants/clock hours indicate thinning in red color. Green color indicates stable RNFL. Yellow color indicates borderline changes.



TREATMENT

Topical prostaglandin analogues are typically used as first-line agents due to their once-daily dosing and few systemic adverse effects. These agents reduce IOP primarily by enhancing aqueous outflow via the uveoscleral pathway.[31] Examples include latanoprost, travoprost and bimatoprost. Patients often remember them by their turquoise-colored cap. The most common adverse effects with this class are local and include conjunctival hyperemia, eyelash growth, irreversible darkening of the iris, and periorbital fat loss.[31] Less commonly, prostaglandin analogues may precipitate migraines in some patients.[32]

Topical beta-blockers are also commonly used, but their adverse effect profile can be problematic for many patients. These agents reduce IOP by decreasing aqueous humor production.[33] Examples include timolol and levobunolol. These have a yellow-colored cap. Most notably, beta blockers can cause bronchospasm and should be avoided in patients with existing pulmonary disease. Cardiovascular effects may include bradycardia, heart block and hypotension. Hypotension may be of particular concern in the elderly because it may further increase their risk of falls.[9] Less common effects include exacerbation of Raynaud's phenomenon, reduced exercise tolerance, sexual dysfunction, depression, dyslipidemia and reversible alopecia.[33] Advising patients to keep their eyes closed for a few minutes after eyedrop administration or performing manual nasolacrimal occlusion can help limit systemic absorption.

Topical alpha-2 agonists, such as brimonidine, lower IOP by reducing aqueous production and by increasing uveoscleral outflow.[34] Additionally, some evidence suggests a neuroprotective effect on retinal ganglion cells.[34] These agents typically have a purple-colored cap. Ocular irritation is a local adverse effect that is sometimes observed. Systemically, however, alpha-2 agonists are known to cause fatigue, xerostomia and worsened vascular insufficiency.[6] These agents are contraindicated in patients under 2 years old because of their potential to cause central nervous system depression and apnea.[11,34] If a patient with Parkinson's disease or depression has been prescribed a monoamine oxidase inhibitor, concurrent use of an alpha-2 agonist can precipitate hypertensive crisis.[6]

Carbonic anhydrase inhibitors (CAIs) come in topical and oral forms, both of which inhibit aqueous production.[6] Topical CAIs, which have an orange-colored cap, include dorzolamide and brinzolamide. An oral CAI, such as acetazolamide, is used when a rapid reduction in IOP is needed, as in acute angle-closure glaucoma. Systemic effects are more common with oral formulations and include hypokalemia, paresthesia, Stevens-Johnson syndrome and bone marrow suppression.[6] Although evidence is primarily limited to case reports, topical dorzolamide has been associated with thrombocytopenia and nephrolithiasis in some patients.[35,36]

Miotics, such as pilocarpine, are cholinergic agonists primarily used in the management of acute angle closure, although they can also be used in POAG. Pilocarpine has a green-colored cap. By inducing pupillary constriction and ciliary muscle contraction, miotics open the anterior chamber angle to promote aqueous

outflow.[33] Patients may complain of blurry vision (particularly at night) or brow ache after use.[9] Rarely, cholinergic agonism may result in bradycardia, diarrhea, urinary frequency and increased sweating.[33]

Topical rho kinase inhibitors are a new class of glaucoma medication. Netarsudil has been shown to reduce IOP by facilitating outflow through the trabecular meshwork, reducing episcleral venous pressure and decreasing aqueous production.[37] Netarsudil is available with a white-colored cap. Adverse effects seem to be primarily local, with conjunctival hyperemia being the most commonly reported problem.[37] Less commonly, patients may develop small conjunctival hemorrhages or cornea verticillata (whorl-like opacities).[37]

Although described as stand-alone classes, several combined preparations are available for the treatment of glaucoma. In certain circumstances, laser or surgical modalities may be warranted. Some options include laser trabeculoplasty, cycloablation, trabeculectomy, minimally invasive glaucoma surgery and placement of drainage shunts.[6] Despite the variety of procedures available, the goal of each intervention is a reduction in IOP.

ADDITIONAL CONSIDERATIONS

In addition to the demographic factors and medical conditions previously discussed, certain systemic medications pose the risk of worsening glaucomatous progression. Patients requiring long-term corticosteroid therapy should undergo evaluation by an ophthalmologist, as these drugs can increase IOP and predispose some patients to glaucoma. These individuals are considered steroid responders, and they often have a first-degree relative with POAG.[38] This risk is magnified by high potency, long duration of use and proximity of administration to the eye. Recent studies have also identified prolonged use of oral contraceptives as a potential risk factor for glaucoma.[39,40]

Medications with anticholinergic effects can dilate the pupil and precipitate acute angle closure in patients with narrow angles. It is inadvisable to prescribe antimuscarinics—such as ipratropium for chronic obstructive pulmonary disease, scopolamine for motion sickness or oxybutynin for overactive bladder—for these patients. Other drugs that can exacerbate PACG include antihistamines, tricyclic antidepressants, selective serotonin/norepinephrine reuptake inhibitors and topiramate (Table 1).[41,42] As this can potentially result in blindness, family physicians should be vigilant in the event that a patient on one of these medications presents with symptoms of acute angle closure. These agents are mostly problematic in those susceptible to pupillary block; therefore, patients that have undergone laser iridotomy should be able to take these drugs without precipitating angle closure.

TABLE 1:

Commonly prescribed medications that may exacerbate glaucoma.

Common medications that may exacerbate glaucoma
Antidepressants
Citalopram, Fluoxetine, Duloxetine, Imipramine, Paroxetine
Antihistamines and Antiemetics
Hydroxyzine, Promethazine, Scopolamine
Antimuscarinic bronchodilators
Ipratropium, Tiotropium
Antispasmodics
Oxybutynin, Tolterodine
Other
Corticosteroids, Topiramate

CONCLUSION

Glaucoma is a slowly progressive disease with various subtypes and etiologies, each resulting in gradual vision loss as the optic nerve head and retinal nerve fiber layer are damaged. One should be suspicious of glaucoma when patients with risk factors (eg, family history or advanced age) complain of impaired peripheral vision. In such cases, further evaluation by an ophthalmologist can establish the diagnosis and allow initiation of the appropriate therapy. Family physicians play a crucial role in minimizing vision loss, as they can encourage adherence to anti-glaucoma regimens as well as recognize conditions or medications that can exacerbate glaucoma.

AUTHOR DISCLOSURE(S)

No relevant financial affiliations or conflicts of interest. If the authors used any personal details or images of patients or research subjects, written permission or consent from the patient has been obtained. This work was not supported by any outside funding.

REFERENCES

1. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040. *Ophthalmology*. 2014;121(11):2081–2090. doi:10.1016/j.ophtha.2014.05.013
2. National Eye Institute. Glaucoma data and statistics. Updated July 17, 2019. Accessed January 31, 2021. https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/glaucoma-data-and-statistics
3. National Eye Institute. Cataract data and statistics. Updated July 17, 2019. Accessed January 31, 2021. https://www.nei.nih.gov/learn-about-eye-health/resources-for-health-educators/eye-health-data-and-statistics/cataract-data-and-statistics
4. Medeiros FA, Lisboa R, Weinreb RN, Liebmann JM, Girkin C, Zangwill LM. Retinal ganglion cell count estimates associated with early development of visual field defects in glaucoma. *Ophthalmology*. 2013;120(4):736–744. doi:10.1016/j.ophtha.2012.09.039
5. Quigley HA, Addicks EM, Green WR. Optic nerve damage in human glaucoma: III. Quantitative correlation of nerve fiber loss and visual

field defect in glaucoma, ischemic neuropathy, papilledema, and toxic neuropathy. *Arch Ophthalmol*. 1982;100(1):135–146. doi:10.1001/archopht.1982.01030030137016

6. Salmon JF. Glaucoma. In: Salmon JF. *Kanski's Clinical Ophthalmology: A Systematic Approach*. 9th ed. Elsevier; 2020:346–421.
7. Davis BM, Crawley L, Pahlitzsch M, Javaid F, Cordeiro MF. Glaucoma: the retina and beyond. *Acta Neuropathol*. 2016;132:807–826. doi:10.1007/s00401-016-1609-2
8. Nickells RW. The cell and molecular biology of glaucoma: mechanisms of retinal ganglion cell death. *Invest Ophthalmol Vis Sci*. 2012;53(5):2476–2481. doi:10.1167/iovs.12-9483h
9. Skorin L, Blanco D, Goemann L. Glaucoma: a primary care review with a focus on medication management. *Consultant*. 2017;57(6):336–341.
10. National Eye Institute. Types of glaucoma. Updated December 22, 2020. Accessed February 6, 2021. https://www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/glaucoma/types-glaucoma
11. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. *JAMA*. 2014;311(18):1901–1911. doi:10.1001/jama.2014.3192
12. Le A, Mukesh BN, McCarty CA, Taylor HR. Risk factors associated with the incidence of open-angle glaucoma: the Visual Impairment Project. *Invest Ophthalmol Vis Sci*. 2003;44(9):3783–3789. doi:10.1167/iovs.03-0077
13. Gedde SJ, Vinod K, Wright MM, *et al*. Primary open-angle glaucoma preferred practice pattern®. *Ophthalmology*. 2020;128(1):71–150. doi:10.1016/j.ophtha.2020.10.022
14. Doshi V, Ying-Lai M, Azen SP, *et al*. Sociodemographic, family history, and lifestyle risk factors for open-angle glaucoma and ocular hypertension. The Los Angeles Latino Eye Study. *Ophthalmology*. 2008;115(4):639–647. doi:10.1016/j.ophtha.2007.05.032
15. Wolfs RCW, Klaver CCW, Ramrattan RS, *et al*. Genetic risk of primary open-angle glaucoma: population-based familial aggregation study. *Arch Ophthalmol*. 1998;116(12):1640–1645. doi:10.1001/archopht.116.12.1640
16. Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt JC. Family history and risk of primary open angle glaucoma: the Baltimore Eye Survey. *Arch Ophthalmol*. 1994;112(1):69–73. doi:10.1001/archopht.1994.01090130079022
17. Stein JD, Khawaja AP, Weizer JS. Glaucoma in adults—screening, diagnosis, and management: a review. *JAMA*. 2021;325(2):164–174. doi:10.1001/jama.2020.21899
18. Kwon YH, Fingert JH, Kuehn MH, Alward WLM. Primary open-angle glaucoma. *N Engl J Med*. 2009;360(11):1113–1124. doi:10.1056/NEJMra0804630
19. Burr JM, Mowatt G, Hernandez R, *et al*. The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and economic evaluation. *Health Technol Assess* 2007;11(41):iii-iv,ix-x,1–190. doi:10.3310/hta11410
20. Centers for Medicare and Medicaid Services. Your Medicare coverage: glaucoma tests. https://www.medicare.gov/coverage/glaucoma-tests
21. Quigley HA. Glaucoma. *Lancet*. 2011;377(9774):1367–1377. doi:10.1016/S0140-6736(10)61423-7
22. Shetgar AC, Mulimani MB. The central corneal thickness in normal tension glaucoma, primary open angle glaucoma and ocular hypertension. *J Clin Diagn Res*. 2013;7(6):1063–1067. doi:10.7860/JCDR/2013/4292.3022
23. Lopilly Park HY, Jeon SH, Park CK. Enhanced depth imaging detects lamina cribrosa thickness differences in normal tension glaucoma and primary open-angle glaucoma. *Ophthalmology*. 2012;119(1):10–20. doi:10.1016/j.ophtha.2011.07.033
24. Gramer G, Weber BHF, Gramer E. Migraine and vasospasm in glaucoma: age-related evaluation of 2027 patients with glaucoma or ocular hypertension. *Invest Ophthalmol Vis Sci*. 2015;56(13):7999–8007. doi:10.1167/iovs.15-17274
25. Mallick J, Devi L, Malik PK, Mallick J. Update on normal tension glaucoma. *J Ophthalmic Vis Res*. 2016;11(2):204–208. doi:10.4103/2008-322X.183914
26. Bilgin G. Normal-tension glaucoma and obstructive sleep apnea syndrome: a prospective study. *BMC Ophthalmol*. 2014;14(27). doi:10.1186/1471-2415-14-27
27. Kremmer S, Niederdräing N, Ayertey HD, Steuhl KP, Selbach JM. Obstructive sleep apnea syndrome, normal tension glaucoma, and nCPAP therapy—a short note. *Sleep*. 2003;26(2):161–162. doi:10.1093/sleep/26.2.161
28. Himori N, Ogawa H, Ichinose M, Nakazawa T. CPAP therapy reduces oxidative stress in patients with glaucoma and OSAS and improves the visual field. *Graefes Arch Clin Exp Ophthalmol*. 2020;258:939–941. doi:10.1007/s00417-019-04483-z
29. Jonas JB, Aung T, Bourne RR, Bron AM, Ritch R, Panda-Jonas S. Glaucoma. *Lancet*. 2017;390(10108):2183–2193. doi:10.1016/S0140-6736(17)31469-1
30. Gedde SJ, Chen PP, Muir KW, et al. Primary angle-closure disease preferred practice pattern®. *Ophthalmology*. 2020;128(1):30–70. doi:10.1016/j.ophtha.2020.10.021
31. Alm A, Grierson I, Shields MB. Side effects associated with prostaglandin analog therapy. *Surv Ophthalmol*. 2008;53(1):S93–105. doi:10.1016/j.survophthal.2008.08.004
32. Weston BC. Migraine headache associated with latanoprost. *Arch Ophthalmol*. 2001;119(2):300–301. PMID:11176999
33. Hoyng PF, van Beek LM. Pharmacological therapy for glaucoma: a review. *Drugs*. 2000;59(3):411–434. doi:10.2165/00003495-200059030-00003
34. Arthur S, Cantor LB. Update on the role of alpha-agonists in glaucoma management. *Exp Eye Res*. 2011;93(3):271–283. doi:10.1016/j.exer.2011.04.002
35. Martin XD, Danese M. Dorzolamide-induced immune thrombocytopenia: a case report and literature review. *J Glaucoma*. 2001;10(2):133–135. doi:10.1097/00061198-200104000-00011
36. Carlsen J, Durcan J, Zabriskie N, Swartz M, Crandall A. Nephrolithiasis with dorzolamide. *Arch Ophthalmol*. 1999;117(8):1087–1088. doi:10.1001/archopht.117.8.1087
37. Tanna AP, Johnson M. Rho kinase inhibitors as a novel treatment for glaucoma and ocular hypertension. *Ophthalmology*. 2018;125(11):1741–1756. doi:10.1016/j.ophtha.2018.04.040
38. Phulke S, Kaushik S, Kaur S, Pandav SS. Steroid-induced glaucoma: an avoidable irreversible blindness. *J Curr Glaucoma Pract*. 2017;11(2):67–72. doi:10.5005/jp-journals-l0028-1226
39. Wang YE, Kakigi C, Barbosa D, *et al*. Oral contraceptive use and prevalence of self-reported glaucoma or ocular hypertension in the United States. *Ophthalmology*. 2016;123(4):729–736. doi:10.1016/j.ophtha.2015.11.029
40. Pasquale L, Kang J. Female reproductive factors and primary open-angle glaucoma in the Nurses' Health Study. *Eye*. 2011;25:633–641. doi:10.1038/eye.2011.34

41. Ah-Kee EY, Egong E, Shafi A, Lim LT, Yim JL. A review of drug-induced acute angle closure glaucoma for non-ophthalmologists. *Qatar Med J*. 2015;2015(1):6. doi:10.5339/qmj.2015.6

42. Lachkar Y, Bouassida W. Drug-induced acute angle closure glaucoma. *Curr Opin Ophthalmol*. 2007;18(2):129–133. doi:10.1097/ICU.0b013e32808738d5

CALENDAR OF EVENTS

JANUARY 13–16, 2022
Midwinter Osteopathic Family Practice Conference
Iowa Chapter ACOFP
Des Moines, IA
acofp-ia.org

JANUARY 20–23, 2022
Winter Family Medicine Update
Michigan Association of Osteopathic Family Physicians
Boyne Falls, MI
maofp.org

JANUARY 27–30, 2022
Winter Family Medicine Update
Missouri Society of the American College of Osteopathic Family Physicians
Columbia, MO
msacofp.org

FEBRUARY 11–13, 2022
ACOFP Faculty Development and Program Directors' Workshop
American College of Osteopathic Family Physicians
Virtual
acofp.org

FEBRUARY 12–13, 2022
MOA 2022 Midwinter Symposium
Maine Osteopathic Association
Portland, ME & Virtual
mainedo.org

FEBRUARY 19, 2022
2022 Annual Winter CME Conference
North Carolina Society of the American College of Osteopathic Family Physicians
Lillington, NC
nc-acofp.org

MARCH 16, 2022
ACOFP Congress of Delegates
American College of Osteopathic Family Physicians
Dallas, TX
acofp.org

MARCH 17–20, 2022
ACOFP 59th Annual Convention & Scientific Seminars
American College of Osteopathic Family Physicians
Dallas, TX
acofp.org

MARCH 30 – APRIL 2, 2022
AOMA 100th Annual Convention
Arizona Osteopathic Medical Association
Scottsdale, Arizona
azosteo.org