

OPTOMETRIC CLINICAL PRACTICE GUIDELINE

Care of the Patient with **Open Angle Glaucoma**



OPTOMETRY: THE PRIMARY EYE CARE PROFESSION

Doctors of optometry are independent primary health care providers who examine, diagnose, treat, and manage diseases and disorders of the visual system, the eye, and associated structures as well as diagnose related systemic conditions.

Optometrists provide more than two-thirds of the primary eye care services in the United States. They are more widely distributed geographically than other eye care providers and are readily accessible for the delivery of eye and vision care services. There are approximately 36,000 full-time-equivalent doctors of optometry currently in practice in the United States. Optometrists practice in more than 6,500 communities across the United States, serving as the sole primary eye care providers in more than 3,500 communities.

The mission of the profession of optometry is to fulfill the vision and eye care needs of the public through clinical care, research, and education, all of which enhance the quality of life.



OPTOMETRIC CLINICAL PRACTICE GUIDELINE CARE OF THE PATIENT WITH OPEN ANGLE GLAUCOMA

Reference Guide for Clinicians

Murray Fingeret, O.D., Principal Author

Prepared by the American Optometric Association Original Consensus
Panel on Care of the Patient with Open Angle Glaucoma:

Gary L. Mancil, O.D., Principal Author
Ian L. Bailey, O.D., M.S.
Kenneth E. Brookman, O.D., Ph.D., M.P.H.
J. Bart Campbell, O.D.
Michael H. Cho, O.D.
Alfred A. Rosenbloom, M.A., O.D., D.O.S.
James E. Sheedy, O.D., Ph.D.

Revised by: Murray Fingeret, O.D.
December 2010

Reviewed by the AOA Clinical Guidelines Coordinating Committee:

David A. Heath, O.D., Ed.M., Chair
Diane T. Adamczyk, O.D.
John F. Amos, O.D., M.S.
Brian E. Mathie, O.D.
Stephen C. Miller, O.D.

Approved by the AOA Board of Trustees, March 20, 1998.
Reviewed 2001, 2006, revised 2010.

© American Optometric Association, 2011
243 N. Lindbergh Blvd., St. Louis, MO 63141-7881

NOTE: Clinicians should not rely on the Clinical Guideline alone for patient care and management. Refer to the listed references and other sources for a more detailed analysis and discussion of research and patient care information. The information in the Guideline is current as of the date of publication. It will be reviewed periodically and revised as needed.

TABLE OF CONTENTS

INTRODUCTION	1
I. STATEMENT OF THE PROBLEM	3
A. Description and Classification of Open Angle Glaucoma	3
1. Primary Open Angle Glaucoma	4
2. Secondary Open Angle Glaucoma	6
B. Epidemiology of Open Angle Glaucoma	8
1. Incidence and Prevalence	8
a. Primary Open Angle Glaucoma	8
b. Secondary Open Angle Glaucoma	9
2. Risk Factors	11
a. General	11
b. Ocular	12
c. Nonocular	15
d. Ocular Hypertension	16
C. Clinical Background of Open Angle Glaucoma	16
1. Natural History	16
2. Common Signs, Symptoms, and Complications	18
3. Early Detection and Prevention	18
II. CARE PROCESS	23
A. Diagnosis of Primary Open Angle Glaucoma	23
1. Initial Glaucoma Evaluation	23
a. Patient History	23
b. Ocular Examination	24
c. Supplemental Testing	32
2. Follow-up Glaucoma Evaluation	33
B. Diagnosis of Secondary Open Angle Glaucoma	36
1. Pigmentary Glaucoma	36
2. Pseudoexfoliation Glaucoma	37
C. Management of Open Angle Glaucoma	39
1. Basis for Treatment	39
2. Available Treatment Options	44
a. Medical (Pharmaceutical) Treatment	44
b. Laser Trabeculoplasty	55
c. Surgery	60
d. Alternative Treatment Strategies	62

e. Treatment of Pigmentary Glaucoma	63
f. Treatment of Pseudoexfoliation Glaucoma	64
3. Patient Education	64
4. Prognosis and Follow-up	66
a. Frequency of Follow-up	67
b. Therapy Modification	67
c. Effectiveness of Treatment	68
d. Prognosis after Treatment of Secondary Open Angle Glaucoma	74
5. Management of Patients with Severe, Irreversible Vision Loss	75
CONCLUSION	79
III. REFERENCES	81
IV. APPENDIX	149
Figure 1: Potential Components of an Initial Glaucoma Evaluation	149
Figure 2: Optometric Management of the Patient with Primary Open Angle Glaucoma: A Brief Flowchart	150
Figure 3: Frequency and Composition of Evaluation and Management Visits for Open Angle Glaucoma	151
Figure 4: ICD-10-CM Classification of Open Angle Glaucoma	153
Abbreviations of Commonly Used Terms	157
Glossary	161

INTRODUCTION

Optometrists, through their clinical education, training, experience, and broad geographic distribution, have the means to provide effective primary eye and vision care for a significant portion of the American public and are often the first health care practitioners to diagnose glaucoma.

This Optometric Clinical Practice Guideline for the Care of the Patient with Open Angle Glaucoma is designed to provide optometrists with appropriate examination and treatment protocols to reduce the risk of visual disability from primary open angle glaucoma through timely diagnosis, treatment, patient education, and, when necessary, referral for consultation with or treatment by another health care provider. This Guideline will assist optometrists in achieving the following goals:

- Identify patients at risk of developing open angle glaucoma
- Accurately diagnose open angle glaucoma
- Improve the quality of care rendered to patients with open angle glaucoma
- Minimize the damaging effects of open angle glaucoma
- Preserve the gains obtained through treatment
- Inform and educate patients and other health care practitioners about the visual complications, risk factors, treatment options, and adverse reactions to treatments associated with open angle glaucoma.



I. STATEMENT OF THE PROBLEM

Glaucoma is not a single clinical entity but a group of ocular diseases with various causes that ultimately are associated with a progressive optic neuropathy leading to loss of vision function. About 8.4 million persons worldwide are bilaterally blind as a result of glaucoma (4,472,083 open angle glaucoma (OAG) and 3,936,241 angle closure glaucoma (ACG)), making it the second leading cause of bilateral blindness. The number of persons with open angle glaucoma in the United States, estimated at 2.2 million in 2004, is expected to rise as the population ages, to 3.36 million by 2020.² An estimated 130,000 Americans are blind from glaucoma.³ It is the third most common cause of blindness in the United States.⁴⁻⁷

The Baltimore Eye Survey estimated the prevalence of glaucomatous blindness to be 1.7 per 1,000 in the general population, of which more than 75 percent was due to primary open angle glaucoma (POAG).⁶ Over 11 percent of all blindness and 8 percent of all visual impairment may be due to glaucoma.⁸ POAG is 6.6–6.8 times more prevalent and accounts for about 19 percent of all blindness among African Americans, compared with 6 percent of blindness in Caucasians.^{5,6} On average, it begins 10 years earlier in African Americans than in Caucasians. The Los Angeles Latino Eye Study (LALES) has shown that older Latinos' risk of developing open angle glaucoma (OAG) is comparable to that for African Americans, starting at the age of 60.⁹ Information on the prevalence of blindness from glaucoma is inadequate because of the lack of a standardized definition of blindness across studies, and because not all blind people are included in blindness registries.^{8,10} Therefore, these estimates may be 2–3 times less than the true prevalence.⁵ Periodic comprehensive eye examination is the most cost-effective approach to detecting glaucoma in a high-risk population.

A. Description and Classification of Open Angle Glaucoma

Glaucoma can be classified as primary when it is not related to another underlying condition. Secondary glaucoma results from another ocular or systemic disease, trauma, or the use of certain drugs. The glaucomas can also be classified, on the basis of anatomy of the anterior chamber

4 Open Angle Glaucoma

angle of the eye, as either OAG or angle closure glaucoma (ACG).¹¹ This Clinical Practice Guideline focuses on OAG (see Appendix Figure 4 for ICD-10-CM classification of OAG).

1. Primary Open Angle Glaucoma

POAG is a chronic, progressive disease that most often presents with characteristic optic nerve (ON) damage, retinal nerve fiber layer (NFL) defects, and subsequent visual field (VF) loss. OAG occurs primarily in adults and is generally bilateral, but not always symmetrical, in its presentation. The majority of persons with POAG have elevated intraocular pressure (IOP). Although 21 mm Hg is considered the upper limit of statistically normal IOP, at least one-sixth of patients with POAG have IOP levels below 21 mm Hg, which is considered statistically normal in the 95th percentile range.^{4,12-14} Moreover, some whose IOP levels are statistically abnormal (>21 mm Hg) have no evidence of ON damage or loss of vision function, a condition known as ocular hypertension (OH). OAG in which the IOP is below a certain level, typically 21 mm Hg, is known as normal tension glaucoma (NTG). Historically, this has also been referred to as "low tension glaucoma" (LTG).

The elevated IOP observed in the classic presentation of POAG usually results from decreased outflow of aqueous fluid from the eye. Though not well understood, this elevation in IOP is thought to be due to resistance within the trabecular meshwork. It may be attributable to acceleration and exaggeration of normal aging changes in the anterior chamber angle, iris, and ciliary body tissues of the eye.¹⁵⁻¹⁷ These changes include loss of trabecular endothelial cells, increased pigment accumulation within these endothelial cells, thickening or fusion of the trabecular lamellae, thickening of the scleral spur, increased extracellular plaque material in the anterior chamber angle, and loss of ability of the endothelial cells lining Schlemm's canal to form giant vacuoles.¹⁸

The etiology of glaucoma has been described as mechanical or vascular. The mechanical process involves compression of the axons due to elevated IOP. The vascular process includes events in which reduced blood flow to the posterior pole leads to damage. Whether mechanical or

vascular, or both, compromise of the ganglion cell axons at the level of the lamina cribrosa leads to apoptosis or genetically programmed cell death.¹⁹⁻²¹ Cellular damage activates proteins that control at least two key genes, one that inhibits apoptosis (bcl-2) and one that promotes cell death (bax).²¹ These genes, in turn, affect a cascade of cellular events that result in the death of ganglion cells.

At least two stimuli appear to activate the process of ganglion cell apoptosis in glaucoma: neurotrophin deprivation²² and glutamate toxicity.²³ Blockage of retrograde axonal transport prevents the normal movement of neurotrophic factors from the brain to the ganglion cell body.¹⁹ These peptides normally bind to the cell surface receptors of the ganglion cells and stimulate molecular events that affect essential functions of cell metabolism. Disruption of axonal transport compromises the ganglion cell and stimulates apoptosis at normal IOP; elevated IOP increases this response.

Müller cells play a critical role in maintaining transport systems in the retina,²⁴ by keeping the normal excitatory protein glutamate at low levels.²⁵ In response to hypoxia or ischemia as a result of high IOP, ganglion cells' primary response is excessive production of glutamate, which overrides Müller cell control. The resulting high levels of glutamate overstimulate N-methyl-D-aspartate receptors, leading to a cascade of molecular events that result in apoptosis.²⁵⁻²⁷ Calcium channels in the ganglion cell membrane open up, causing an overload of calcium,²⁵ which activates the enzyme nitric oxide synthase, leading to the formation of excessive levels of nitric oxide, and, finally, cell death.²⁸⁻²⁹

Excitotoxicity, a process in which neurons are stimulated to death, involves mainly glutamate, although other excitatory amino acids may participate.^{25,30,31} Investigators have discovered increased levels of nitric oxide in the optic nerve head (ONH)³² and elevated levels of glutamate in the vitreous²⁶ of patients with POAG. Although lowering IOP may remove the primary mechanical or vascular insult to the ganglion cell axons of the retina, destruction of the surrounding tissue (secondary axonal degeneration) proceeds because of the creation of an excitotoxic environment,³³⁻³⁵ and the result is continuing apoptosis. This

excitotoxicity may help explain why some glaucoma patients continue to show damage even after reduction of IOP to a level expected to control the disease process.

2. Secondary Open Angle Glaucoma

The cause of secondary OAG can be any of a variety of substances that mechanically block the outflow of aqueous through the trabecular meshwork, resulting in elevated IOP. These substances include pigment, exfoliation material, and red blood cells. Secondary OAG can also result from alterations in the structure and function of the trabecular meshwork, due to insults such as trauma, inflammation, and ischemia.¹¹

Two conditions frequently contribute to the development of secondary OAG.

- **Pigmentary dispersion syndrome (PDS).** A condition in which pigment is released from the back surface of the iris and is deposited onto structures in the anterior and posterior chambers of the eye, PDS causes the development of pigmentary glaucoma (PG) in some persons.

PDS occurs when the posterior iris rubs against the zonules of the lens or the ciliary processes, mechanically damaging the pigment epithelium of the iris and releasing pigment.³⁶ The concept of reverse pupillary block has been proposed to explain the anatomic abnormalities that lead to iris concavity, which can result in PDS.^{37,38} Reverse pupillary block may occur momentarily during each lid blink.³⁹ A concave iris configuration similar to that in PDS can also be induced by accommodation.⁴⁰

A correlation between pigment release and elevated IOP with worsening glaucoma has been reported in patients who have PDS and PG.⁴¹ It has been proposed that the trabecular endothelium phagocytizes the pigment and damages the cells, possibly via cellular toxicity, and causes them to drop off the trabecular lamellae. The denuded trabeculae no longer function properly and possibly collapse, obstructing aqueous outflow.⁴²

Not everyone with excess pigment in the trabecular meshwork develops glaucoma. Dense pigmentation of the trabecular meshwork can exist for as long as 20 years without IOP elevation or abnormal outflow.⁴³ When pigment is released into the anterior chamber, other events ensue. Eyes that develop elevated IOP have difficulty managing the excess pigment load. PG may also be due to congenital abnormality of the anterior chamber,⁴⁴ and it can exist as a variant of POAG.⁴⁵

- **Pseudoexfoliation syndrome (PES).** The presence of “flaky” or “dandruff-like” grayish-white exfoliative material in the anterior and posterior chambers of the eye,^{46,47} and in the conjunctiva and orbit,^{48,49} is called pseudoexfoliation syndrome. This material accumulates on the ciliary epithelium, zonules, lens, posterior iris epithelium, intrastromal iris blood vessels,⁵⁰ anterior chamber angle, and corneal endothelium.⁵¹

Exfoliative deposits are associated with degeneration of the ciliary epithelium, zonules (zonular dehiscence and lens subluxation),⁵² and posterior iris epithelium (pigment dispersion, poor pupil dilation, posterior synechiae).^{51,53} The actual source of the fibrillogranular pseudoexfoliative material, which is similar to amyloid in composition,⁵⁴ appears to be various basement membranes of the eye,^{55,56} including the lens capsule.⁵⁷ PES may represent abnormal basement membrane production at multiple sites by aging epithelial cells,⁵⁶ or it may be linked to microfibrils in the elastic elements of connective tissue.⁵⁸

Persons with PES have a higher prevalence of OAG than those without PES.^{46,47} Elevated IOP in pseudoexfoliation glaucoma (PEG) probably occurs because of direct mechanical blockage of aqueous outflow from the anterior chamber by pseudoexfoliative material⁵⁹⁻⁶³ and pigment granules, or because of dysfunction of the trabecular endothelium⁵⁶ or high aqueous protein levels.⁶⁴ Some persons with PES maintain normal IOP, despite massive deposits in the trabecular meshwork,⁶⁵ possibly as a result of

decreased aqueous production secondary to degeneration of the ciliary epithelium.⁵¹

B. Epidemiology of Open Angle Glaucoma

1. Incidence and Prevalence

a. Primary Open Angle Glaucoma

An estimated 2.22 million Americans have OAG,² although at least half of all cases may be undiagnosed.⁶⁶ Seven times more prevalent than ACG in western populations,⁶⁷ POAG accounts for approximately 70 percent of all adult glaucoma cases.⁸ One-fourth of all cases of OAG in America are African American.⁶⁸ Various estimates as 0.8–3.0 percent for Caucasians,^{12,13,67,69-74} the prevalence of POAG in persons over age 40 was 1.7 percent for Caucasians and 5.6 percent for African Americans in the Baltimore Eye Survey.⁶⁷

The LALES showed the prevalence of OAG for Latinos to be 4.74 percent and that of ocular hypertension (OH), 3.56 percent. The prevalence of both OAG and OH was higher in older Latinos, with no gender relationships. Latinos' risk for OAG increases significantly with age. The prevalence of OAG in Latinos is similar to the prevalence in African American among groups of persons ages 60 and older.⁹

The Framingham Eye Study calculated the prevalence of POAG in people ages 52–85 years as 1.65 percent.⁴ When VF testing was added to the screening of a subset of Framingham subjects, the prevalence of POAG rose to 2.1 percent.⁷⁵ While various studies show that the prevalence of cases with high IOP and VF defects is consistently between 0.3 and 0.4 percent,⁸ the prevalence of NTG ranges from 0.05 to 0.79 percent.^{4,13,76,77}

The existing data are inadequate for determination of the precise incidence of glaucoma,^{8,10} and estimates vary. Five-year incidence rates for Caucasians, calculated using pooled data, translate to 40–60 cases per 100,000 persons per year at the age of 55 years and 200–220 cases per 100,000 per year at age 75.^{68,78} Pooling data on African Americans

results in estimates 4 times higher at age 55 (263 per 100,000 per year) and twice as high at age 75 (541 per 100,000).⁶⁸ A similarly high incidence among blacks was confirmed by direct observation in the Barbados Eye Study.⁷⁹ Because the prevalence of many glaucomas is strongly related to age, the growth of the elderly population will dramatically increase the incidence of the disease and the absolute number of persons with glaucoma who will need care in the future.

The Baltimore Eye Survey found that 7–8 percent of people over the age of 40 have IOP above 21 mm Hg on a single tonometric reading. Using the 1990 census, the survey provided support for the estimate that 7–8 million Americans over the age of 40 have OH.^{13,76,77} An estimated 0.5–1.0 percent of persons with OH develop evidence of ON damage per year⁸⁰; however, the majority of those with OH will probably not develop glaucoma.^{4,12,13,81} The Ocular Hypertension Treatment Study (OHTS) has shown that, while this estimate may be correct, new modeling based upon an assessment of risk factors enables prediction of which individuals are at greatest risk for converting to glaucoma. In fact, risk assessment shows that some individuals may have risks as great as 10 percent per year for converting to glaucoma.^{82–85}

b. Secondary Open Angle Glaucoma

- **Pigmentary dispersion syndrome.** PDS occurs in about 2.5 percent of adult Caucasians in the United States.⁸⁶ It occurs less commonly in African Americans and Asians. About 20–60 percent of persons with PDS develop OH; 25–50 percent, PG.^{86,87} Pigmentary glaucoma constitutes about 4.4 percent of all glaucomas^{86,88} and 1–2.5 percent of OAGs.⁸⁶ PDS is usually bilateral and affects persons at younger ages than POAG (30–50 years).^{88–90} Its occurrence is most common in Caucasian males with myopia.^{87–89} In fact, about 90 percent of individuals with PDS are myopic.⁹¹ PDS may have an autosomal-dominant, multifactorial basis, suggesting the importance of family history.^{88,92,93} At least one genetic locus has been identified for PDS.⁹⁴

- **Pseudoexfoliation syndrome.** The prevalence of pseudoexfoliation syndrome varies widely throughout the world,⁹⁵ with estimates ranging from about 1.6 to 2.3 percent in persons over age 50 in the United States.^{96,97} The prevalence of PES with subsequent PEG increases with age, and these conditions most commonly occur between the ages of 60 and 80.^{96,97} PES is 2–3 times more common in women than in men,^{97–99} and its prevalence is much lower in African Americans than in Caucasians.^{96,100} Family studies are investigating several putative sites on chromosome 2 for genetics related to PES.¹⁰¹

PES has been reported to be unilateral at initial diagnosis in 50–70 percent of cases,^{97–99,102} a prevalence that may be overstated due to inadequate evaluation.¹⁰² Unilateral PES may actually occur at a younger age as a precursor to the involvement of both eyes.^{59,969} In 13–15 percent of cases of unilateral PES, involvement of the other eye is discovered during 10–15 years of follow-up.^{60,103} Thus, it appears that unilateral PES is rare, but more often asymmetric at a subclinical level.¹⁰³

PES is a definite risk factor for OH and OAG.^{59,98,99} Initial screening has found OH in 22–30 percent of individuals with PES.^{59,104} OH develops in about 10 percent of persons who had PES and normal IOP at initial diagnosis. The cumulative probability of developing OH is 5.3 percent in 5 years and 15.4 percent in 10 years.⁹⁹ The prevalence of PES in a glaucoma population ranges from 1.6 to 28 percent in the United States.^{60,96,100,105,106} Among persons with PES, 30–60 percent reportedly develop OAG.^{96,104} The Early Manifest Glaucoma Trial (EMGT) showed that after a mean follow-up of 8.7 years, 55.1 percent of individuals with PES and OH developed OAG, compared with 27.6 percent who had OH only. The glaucoma conversion ratio was twice as high when other factors were matched for individuals with PES and OH.¹⁰⁷

2. Risk Factors

a. General

- **Age.** Age is a major risk factor for the development of glaucoma. The prevalence of glaucoma is 4–10 times higher in the older age groups than in persons in their forties.^{4,13,67} In the Collaborative Glaucoma Study, the incidence of VF loss from glaucoma rose with age, from 0.7 percent in persons under the age of 40 years to 4.8 percent in persons age 60 and over. Damage to the ON from glaucoma is uncommon before the age of 50 in Caucasians, but it appears to occur at least a decade earlier in African Americans.¹⁰⁸
- **Race.** Race is another major risk factor for POAG. African Americans develop the disease earlier, do not respond as well to treatment, are more likely to require surgery, and have a higher prevalence of blindness from glaucoma than Caucasians.^{67,109-112} The age-adjusted prevalence of POAG was 4.3 times greater in African Americans than in Caucasians in the Baltimore Eye Survey.⁶⁷ Studies in St. Lucia¹¹³ and Barbados¹¹⁴ found POAG in 7–16 percent of blacks over age 40. Although the prevalence of NTG has been reported to be high in Asians,¹¹⁵ this rate may be influenced by the accuracy of tonometry in this ethnic group.¹¹⁶ Older Latinos' risks of developing OAG are comparable to those of African Americans, starting at the age of 60 years.⁹
- **Family History.** The etiology of glaucoma most likely involves multifactorial or polygenic inheritance mechanisms.¹¹⁷⁻¹²² Studies have suggested that 13–25 percent of patients with glaucoma have positive family histories for the disease.¹²³⁻¹²⁶ In close relatives of persons with POAG, the prevalence is 3–6 times that of the general public,¹¹⁷ and the incidence of the disease in first-degree relatives is 3–5 times the rate in the general population.^{119,120} The 22 percent lifetime risk for glaucoma in relatives of patients with glaucoma is almost 10 times that of controls.¹²⁷ The risk may be greater in siblings than in parents or children.^{126,127} A family history of glaucoma places a person with OH at greater risk of developing the disease.^{128,129} Ocular characteristics associated

with glaucoma, including IOP^{122,130} and the cup-to-disc (C/D) ratio,¹³¹ have been associated with moderate familial risk.

Mutations in transcription factor genes are responsible for developmental disorders associated with glaucoma.¹³² Although POAG is not an obvious developmental problem, the finding that adult-onset glaucoma results from mutations in the same genes that cause developmental defects such as juvenile glaucoma supports such a relationship.¹³³ Many forms of POAG probably result from a combination of mutations in more than one gene.^{133,134} Among at least six major genes for glaucoma that have been localized,¹³³ certain mutations have a higher incidence in specific types of OAG.¹³⁵

POAG is not likely inherited as a single gene but rather as a complex trait. More than 30 mutations of the myocilin (MYOC/TIGR) gene have been associated with POAG in different ethnic populations throughout the world.¹³⁶ A myocilin gene mutation may be present in 3–5 percent of patients with OAG.^{137,138} The presence of myocilin in the ON axons and lamina cribrosa astrocytes suggests that the trabecular meshwork might not be the only target for abnormal myocilin GLC1A-linked OAG.¹³⁶ Eventually, glaucoma treatment may involve inhibiting the expression of this gene. At present, genetic counseling usually includes providing information about the risks for persons whose close relatives have glaucoma.¹¹⁷

There is no conclusive evidence that gender is a risk factor for glaucoma.^{10,139}

b. Ocular

- **Intraocular pressure (IOP).** IOP has a strong, direct relationship with the prevalence and long-term risk for glaucoma.^{8,10,125,140} For persons with IOP above 21 mm Hg, the risk of developing glaucoma is 16 times the risk for persons with IOP below 16 mm Hg.^{4,14} Moreover, the percentage of eyes developing VF defects after 5 years is 6.7 percent for those with IOP over 20 mm Hg,

compared with 1.5 percent of eyes with IOP below 20 mm Hg.¹⁰⁸ Even in NTG, the higher the pressure, the greater the risk.^{141,142} Asymmetric levels of IOP in individual pairs of eyes correlate with asymmetric damage to the ON.^{141,142} Lowering the IOP reduces the risk for ON damage.¹⁴³

Long-term studies have consistently shown that a large percentage of persons with statistically elevated IOP (>21 mm Hg) do not develop glaucoma,^{4,12,13,76,77, 80,108,144,145} while many persons with glaucoma have IOP well within the statistically normal range.^{4,13,14,81} Population-based studies have demonstrated that one-tenth or fewer of those with elevated IOP suffer VF loss when monitored over several years.^{4,12,13,76} The incidence of glaucoma among persons with OH is at most 1 percent per year.^{80,144,145} One-third to one-half of persons with glaucoma have IOP at or below 20 mm Hg at initial diagnosis.^{4,12,13,76,108}

The Barbados Eye Study showed a relationship between baseline IOP and the development of glaucoma. Among persons who developed glaucoma, 46 percent had baseline IOPs exceeding 21 mm Hg. The risk for OAG increased by 12 percent for each 1 mm Hg increase in IOP. The incidence of OAG increased from 1.8 percent for persons with baseline IOP less than 17 mm Hg to 22.3 percent for those with baseline IOP exceeding 25 mm Hg.¹⁴⁶

Several studies have addressed the question of which IOP measurement is most important—mean IOP, highest IOP measurement, or IOP fluctuation. Mean IOP has consistently been associated with the development of glaucoma, while the data related to fluctuation of IOP in relation to true IOP are conflicting.¹⁴⁷⁻¹⁴⁹

- **Corneal thickness.** The OHTS showed a relationship between corneal thickness and the development of OAG. Thin corneas were at a greater risk of developing glaucoma (hazard ratio [HR], 1.71 for each 40 μ m change in cornea thickness).⁸³ African Americans had thinner corneas, and a thin cornea influenced the accuracy of tonometry measurement.¹⁵⁰ The OHTS also showed

that, although for individuals with OH the risk of developing OAG is approximately 1 percent per year, those with increased central corneal thickness (CCT) may have a much higher risk.⁸³ Evaluation of each individual for key risk factors—age, IOP, vertical C/D ratio, VF status, and CCT—will provide a better idea of who is at a higher risk for OAG.

- **Visual field loss.** In the Malmo Ocular Hypertension Study to evaluate the importance of baseline risk factors for development of glaucomatous VF loss in patients with high-risk OH, the investigators randomized 90 patients to topical timolol or placebo treatment and observed them prospectively for up to 10 years. Eligibility criteria were elevated IOP, open angles, and normal VFs plus at least one extra risk factor (suspect disc or known disc hemorrhage; positive family history of glaucoma, PES, or PDS; diabetes; or mean IOP \geq 27 mm Hg). The researchers evaluated the risk factors as well as the mean baseline IOP and IOP fluctuation, sex, age, and blood pressure as predictors for development of reproducible glaucomatous VF loss. In addition to the prospective data, they retrieved post-study data from patients' records, extending maximum follow-up to 17 years. Thirty-seven patients developed glaucomatous VF loss. Of all factors included in the analysis, those emerging as significant risks were disc appearance, older age, and higher IOP. Suspect disc appearance increased the risk approximately threefold (HR, 2.90; 95% CI, 1.34–6.30). The hazard ratio was 1.05 (95% CI, 1.03–1.09) per year of age, while mean baseline IOP increased the risk in patients by 14 percent per mm Hg (95% CI, 1.01–1.28). Patients with OH were at higher risk of developing glaucomatous VF loss in the presence of suspect discs, high IOP, and older age.¹⁵¹

Various optic nerve (ON) characteristics can be considered clinically as both risk factors and criteria for the detection and assessment of the progression of glaucoma. These features relate to the size and shape of the optic cup, the thickness and uniformity of the neuroretinal rim,^{140,152-154} and the symmetry of the optic cups.¹⁵⁵

Though potentially subject to selection bias, several studies have demonstrated, after adjustment for age, a twofold to fivefold higher prevalence of POAG in patients with myopia.^{128,156,157}

c. Nonocular

- **Diabetes mellitus.** The association of diabetes mellitus with the development of both elevated IOP and POAG has been controversial.¹³⁹ Several studies lend support to a higher prevalence of OH¹⁵⁸ and POAG¹⁵⁹⁻¹⁶⁵ in persons with diabetes, for whom the relative risk for POAG ranges from 1.6 to 4.7.^{128,166,167} Others have found no relationship, or that the presence of diabetes even has a protective effect against the development of OH or POAG.^{83,108,125,129,140,158,166, 168-170}
- **Vasospasm.** Vasospasm is one possible mechanism for, or as a factor contributing to, ON damage in glaucoma.^{171,172} This theory is supported by evidence of an association of NTG with migraine headaches and Raynaud's syndrome.¹⁷³ The literature is equivocal on an association between systemic hypertension and POAG.^{10,125,140,158,166,167,169,174} The Baltimore Eye Survey suggested the complexity of the relationship between POAG and systemic blood pressure.¹⁷⁵ Patient age and the duration of the hypertension modified the effect of systemic blood pressure on POAG. Lower perfusion pressure (BP-IOP) was significantly associated with an increased prevalence of POAG. Low systemic blood pressure,^{176,177} including the nocturnal dip,^{176,178,179} also may pose a risk for NTG and OAG. The EMGT and the Barbados Eye Study revealed a relationship between lower systolic perfusion pressure and the development or progression of OAG.^{180,181}
- **Perfusion pressure ratio.** A study using full-field perfusion analysis of scanning laser Doppler flowmetry images to compare ONH and peripapillary retinal blood flow in eyes with OAG and OH with normal eyes showed an association between reduced blood flow and OAG. Neuroretinal rim flow values showed a significant inverse correlation with C/D ratio ($P = 0.001$). Mean neuroretinal rim blood flow was significantly higher in the 10 OH

patients whose C/D ratios were under 0.4 (350 ± 184 au) than in the 10 OH patients who had higher C/D ratios (203 ± 79 au; $P = 0.039$). Conversely, peripapillary retinal blood flow did not correlate significantly with any clinical parameter. Blood flow in the ONH was significantly lower in the OAG patients than in the OH patients and normal volunteers. The authors found no significant differences in ONH blood flow between patients with OH and normal volunteers, and peripapillary retinal blood flow did not differ significantly across groups. The inverse correlation of neuroretinal rim blood flow and increased C/D ratio was significant. Patients with OH who had higher C/D ratios demonstrated significantly lower rim blood flow than those whose C/D ratios were lower, suggesting the importance of reducing rim perfusion in persons with high-risk OH before the manifestation of VF defects.¹⁸²

d. Ocular Hypertension

When the criterion for OH is 20 mm Hg or higher, the prevalence of OH increases with age, from less than 5 percent of persons under age 40 to 20 percent or more of persons over age 70.^{4,14,76,77} Age-controlled data analysis has shown a higher prevalence of OH in African Americans than in Caucasians.¹⁰⁹

The general, ocular, and nonocular risk factors for POAG are summarized in Table 1.

C. Clinical Background of Open Angle Glaucoma

1. Natural History

ON damage in glaucoma has traditionally been attributed to the tissue's inability to continue to tolerate a certain IOP. Initially, the axons of the ganglion cells of the retina are destroyed at the level of the lamina cribrosa scleralis.¹⁸³⁻¹⁸⁵ There are two theories concerning how this specific damage occurs. One stresses the reduction in blood flow to the axons¹⁸⁶; the other is based more on mechanical damage as the axons pass through the lamina cribrosa scleralis.^{184,187} The premise for both

Table 1
Risk Factors for Primary Open Angle Glaucoma

General	Ocular	Nonocular
Age	Elevated or asymmetric levels of IOP	Diabetes
Race	Diffuse or focal enlargement of cup	mellitus
Family history	portion of optic nerve	Vasospasm
	Diffuse or focal narrowing of neuro-retinal rim	Perfusion pressure ratio
	Asymmetry of cup-to-disc ratios >0.2	
	Myopia	
	Central corneal thickness	
	Visual field status (pattern standard deviation)	

hypotheses involves abnormality—either abnormal IOP or the axons' abnormal susceptibility to damage when the IOP is "normal."

Untreated or inadequately treated glaucoma will progress to the point that loss of visual function results in disability or blindness.^{188,189} Once glaucomatous damage has occurred in one eye, the risk for damage in the other eye increases.¹⁹⁰ The rate of progression varies significantly, depending on the IOP, the ON's susceptibility to damage, and the severity of the disease. Untreated glaucoma may cause blindness in 3–15 years, depending on the IOP.¹⁸⁹

There is great variability in the susceptibility of the ON to glaucomatous damage. Some persons with relatively low IOP (NTG) incur ON damage, while others with rather high IOP (OH) never show such damage. Even with the most sensitive clinical test available, the earliest unequivocal indication of loss of function may not be detectable until at least one-fifth of the ganglion cell axons of the retina have been destroyed and there is a uniform 5-decibel (dB) decrease in threshold across the entire VF.¹⁹¹ The authors of a study showing a 25 percent loss

of retinal ganglion cells in patients for whom threshold automated perimetry revealed a 5-dB loss of retinal sensitivity concluded that at least a 25–35 percent loss of ganglion cells is associated with typical clinical criteria for detecting abnormalities.¹⁹²

2. Common Signs, Symptoms, and Complications

Patients in the mild or moderate stages of OAG seldom have symptoms or complaints. When the disease progresses to the severe stage, some patients may present with symptoms or complaints related to restricted VF or reduced vision. Glaucoma patients' more common symptoms, complications, and complaints are associated with the side effects, inconvenience, and cost of medications to treat the disease.

3. Early Detection and Prevention

There is no scientific evidence of any method of preventing OAG, nor is there any absolute way to predict who will develop the disease later in life.⁸ The presence of certain ocular, systemic, and general risk factors increases the probability that a person will develop glaucoma. Among these risk factors, only IOP can be altered.⁸

Large population screenings seem ideal for detecting diseases, such as OAG, that have a high prevalence, cause vision disability, and are asymptomatic. Moreover, patients can benefit from early treatment.^{143,193,194} Unfortunately, techniques to screen for glaucoma lack the sensitivity or specificity to be effective, due to significant overlap in affected and unaffected individuals' results on key clinical tests.^{139,193-196} Even screening protocols using multivariate predictive models do not adequately distinguish between persons affected and unaffected by glaucoma.¹⁹⁴ Glaucoma screening procedures may include, but are not limited to:

- **Tonometry.** Measurement of IOP is not a reliable screening procedure for detecting glaucoma.^{194,197,198} No level of IOP provides the necessary balance between sensitivity and specificity.¹⁹⁴ Moreover, as many as one-half of persons with glaucoma may have IOPs below 22 mm Hg at screening,^{4,13,67,108}

and most with elevated IOPs do not have, and may never develop, glaucoma.^{4,80,144,145}

The EMGT showed that increased IOP fluctuation was not an independent factor for the progression of glaucoma. The median follow-up time was 8 years (range, 0.1–11.1 years) with 68 percent of the patients progressing. Follow-up of IOP and IOP fluctuation in the same time-dependent model showed that mean IOP was a significant risk factor for progression (HR, 1.11; 95% CI, 1.06–1.17; $P < 0.0001$). IOP fluctuation was not related to progression (HR, 1.00; 95% CI, 0.81–1.24; $P = 0.999$). EMGT results confirm that elevated IOP is a strong factor for glaucoma progression: The HR increased by 11 percent for every 1 mm Hg of increase in IOP. IOP fluctuation was not an independent risk factor for the progression of glaucoma, a finding that conflicts with earlier reports. One explanation for the discrepancy is that the EMGT analyses did not include postprogression IOP values, which would be biased toward larger fluctuations because of more intensive treatment.¹⁴⁸

- **Optic nerve assessment.** Despite pronounced ON cupping in eyes that eventually develop glaucoma, the clinical finding of a 0.6 C/D ratio has only about a 60 percent (41%–77%) sensitivity for predicting which cases of OH will convert to the disease.^{199–201} There is no cutoff value for the C/D ratio that would change this conclusion.¹⁹⁴ Determining the C/D ratio by direct ophthalmoscopy is even less precise, due to intraobserver and interobserver variability.^{4,199,202} The evidence suggests even greater variability in assessment of the notching or width of the neuroretinal rim.¹⁹⁹ The topography of the ON and configuration of the neuroretinal rim may be more sensitive and specific than the C/D ratio in the detection of glaucoma.²⁰³

The preferred method of assessing the ON and evaluating the cup and neuroretinal rim tissue is to use a fundus lens and biomicroscope to obtain a dilated-pupil stereoscopic view of the ON. Using optical coherence tomography (OCT) parameters to facilitate identification of glaucomatous damage and evaluation of

differences between normal eyes, eyes with OH, and those with glaucoma, research showed that mean retinal NFL thickness around the disc and superior and inferior retinal NFL thicknesses were significantly less in glaucomatous eyes than in eyes with OH or in normal eyes ($P < 0.001$). Rim parameter values were significantly lower in glaucomatous eyes than in normal ($P < 0.001$) and OH eyes ($P = 0.01$). C/D ratios were significantly higher in glaucomatous eyes than in OHT ($P < 0.001$) and normal ($P < 0.001$) eyes. The differences between normal and OH eyes were significant for seven disc parameters. There were no differences across groups for parameters describing retinal NFL asymmetry between the eyes. The average ratio of change (AROC) curves representing the average rate of change of the other NFL and disk parameters ranged from 0.741 to 0.85. Results obtained using the Stratus OCT differed significantly for almost all NFL and disc parameters, thus clearly discriminating between glaucomatous and normal eyes. Although the authors found significant differences between ON parameters in normal and OH eyes, there were no differences between their retinal NFL parameters.²⁰⁴

Evaluation of OCT findings for the detection of early glaucoma showed that one eye from each of 50 normal persons, 42 glaucoma suspects (GS), and 59 patients with early glaucoma diagnosed on the basis of VF defect (EGVF) met the following VF criteria: VF mean deviation at least -6.00 dB, age ≥ 40 years, spherical refractive error ≤ 5 diopters (D), astigmatism ≤ 3 D, and visual acuity $\geq 20/30$. Average nerve fiber layer thicknesses (NFLT) were 128.4 ± 15.4 , 102.0 ± 25.4 , and 86.5 ± 31.5 μm in normal, GS, and EGVF eyes, respectively. Normal eyes were different from eyes in both glaucoma groups ($P < 0.001$); NFLT in the superior quadrant and at the 11 o'clock position had the highest area under the receiver operating characteristic curve (0.840 and 0.933) in the GS and EGVF groups ($P = 0.03$). The sensitivity of OCT for detection of glaucoma was 71 percent for the GS group and 85 percent for the EGVF group, with specificity fixed at 90 percent. Although the OCT discriminates well between normal

eyes and those with early perimetric glaucoma, its performance is less adequate in eyes with suspicious discs and normal VFs.²⁰⁵

- **Photography.** Stereoscopic fundus photography is useful for evaluating the ON, because it reduces observer variability in assessment of the C/D ratio¹⁹⁹. However, stereoscopic fundus photography assessment of the horizontal or vertical C/D ratio, or of the narrowest neuroretinal rim width, does not achieve a sensitivity-specificity balance adequate for screening.¹⁹⁴ Photography may be of value in assessing the NFL,²⁰³ except that media changes common in the age groups screened for glaucoma diminish the quality of the photographs.¹⁹³ The sensitivity and specificity of NFL assessment are highest when the photographs are of high quality.^{207,208}
- **Perimetry.** The use of automated perimeters for mass screenings has not been practical because of the size and cost of most modern instruments.¹⁹³ In the past, perimetry results from mass screenings were quite variable.²⁰⁹ For example, use of the Henson perimeter test yielded a very high number of false-positive findings for glaucoma in the Beaver Dam Eye Study.⁷⁰

Frequency doubling technology (FDT) perimetry has proven effective in screening for glaucoma. The Glaucoma Advisory Committee of Prevent Blindness America has determined that a VF test to screen for glaucoma should have 95 percent specificity, compared with standard automated perimetry, and 85 percent sensitivity for moderate to advanced VF loss.^{210,211}

The sensitivity and specificity of FDT vary, depending on the mode of testing (screening vs. thresholding)^{210,211} and the severity of the disease in the population being tested. For moderate and advanced glaucoma, FDT has sensitivity²¹² and specificity values above 90 percent for detecting glaucomatous VF loss.^{210,211, 213-216} FDT sensitivity in the detection of early glaucomatous damage has been lower and more variable between studies.^{210,211,213,216}

FDT perimetry has demonstrated better patient reliability,²¹⁷ less intratest and intertest variability,²¹⁸ and results that are comparable to or better than standard automated perimetry for the detection of glaucoma.^{213,217} It appears that FDT can facilitate diagnosis and grading of the extent of glaucoma.²¹⁹

Despite the availability of new technologies for NFL assessment, three-dimensional imaging of the ON, and VF testing, periodic comprehensive eye examination may be the most cost-effective way to detect glaucoma in a high-risk population.

A relevant question is whether glaucomatous damage occurs first to the structure of the eye (ON/NFL) or to its function (as assessed by perimetry). A study seeking age-related structural and functional changes used pattern electroretinogram (PERG), perimetry, and retinal tomography to examine 34 normal subjects and 40 patients with glaucoma and found little difference, depending upon the scale of the test used. The unit of differential light sensitivity (DLS) in perimetry is the decibel. The investigators recorded transient and steady-state PERGs and measured peak-to-trough amplitude. Then they correlated the PERG amplitudes with decibel and 1/Lambert DLS for the central 18 degrees of the VF and with neuroretinal rim area in the temporal part of the optic disc. Examination of the correlation between variables by linear and quadratic regression analysis revealed a curvilinear relationship between decibel DLS and both PERG amplitude and neuroretinal rim area, as well as a linear relationship between 1/Lambert DLS and PERG amplitude and neuroretinal rim area. These findings support the hypothesis that there is no ganglion cell functional reserve but rather a continuous structure-function relationship, and that the impression of a functional reserve results from the logarithmic (decibel) scaling of the VF.²²⁰

II. CARE PROCESS

This Guideline describes the optometric care provided to a patient with POAG. The components of patient care described are not intended to be all-inclusive. Professional judgment and individual patient symptoms and findings may have significant impact on the nature, extent, and course of services provided. Some components of care may be delegated.

A. Diagnosis of Primary Open Angle Glaucoma

Although POAG is not a curable disease, early diagnosis and adequate treatment are effective in reducing or preventing further ON damage.^{143,153,221} The difficulty of distinguishing between eyes without glaucoma and eyes with early or subtle glaucoma is widely acknowledged.²²² Furthermore, there is no unanimous opinion on what constitutes the first signs of damage in glaucoma.²²³

1. Initial Glaucoma Evaluation

The initial glaucoma evaluation may include the tests and procedures of a comprehensive adult eye and vision examination,* in addition to some procedures specific to the differential diagnosis of glaucoma (see Appendix Figure 1).²²⁴ Proper management of glaucoma requires longitudinal evaluation of established baseline data for important clinical parameters.²²⁵

a. Patient History

The patient history should include a thorough analysis of all general, familial, ocular, and nonocular risk factors for the various types of glaucoma. A complete medical history, including current medication and known medicine intolerance and allergies, is essential.

*Refer to the Optometric Clinical Practice Guideline on Comprehensive Adult Eye and Vision Examination.

24 Open Angle Glaucoma

b. Ocular Examination

Evaluation of a patient suspected of having OAG may include, but is not limited to, the following:

- **Visual acuity (VA).** Best corrected distance or near visual acuity, or both, should be measured as one indicator of the integrity of the central vision system.
- Careful evaluation of the pupils should be performed to reveal the presence of a relative afferent defect.²²⁶
- **Biomicroscopy.** Assessment of the cornea and structures of the anterior and posterior chambers, both before and after pupillary dilation, should be conducted to evaluate anomalies or abnormalities that could cause or contribute to a secondary increase in IOP. The anterior chamber depth should be estimated.
- **Tonometry.** Measurement of the IOP should precede pupillary dilation and gonioscopy. The instrument used, as well as the time of day at examination, should be recorded. Multiple measurements in each eye (serial tonometry) at various times of the day may help to evaluate diurnal variability.²²⁷ Attention should be directed toward differences between the IOPs of the two eyes¹⁴² and changes in pressure over time.²²⁸ IOP tends to rise when a person lies down at bedtime (assumes a supine position), and it continues to rise during the nocturnal hours, irrespective of the decline in aqueous production during this period. IOP tends to peak around 5:30 a.m., just before awakening. Approximately 6 percent of IOP spikes occur outside traditional office hours.²²⁹
- **Pachymetry.** Measurement of the CCT with a pachymeter is indicated as part of the evaluation of the patient with glaucoma or the glaucoma suspect. The examiner should perform pachymetry on each eye, taking three or more measurements and using the mean of these measurements for each eye. IOP measurement by Goldmann applanation tonometry (GAT) assumes an average CCT of 520 μm .²³⁰ Meta-analysis of values reported in the literature

indicates that “normal” individuals have a significant variation in CCT ($0.535 \pm 0.031 \mu\text{m}$),²³¹ which could influence the accuracy of this measurement. Research has indicated that the average corneal thickness is closer to $545 \mu\text{m}$. In fact, cannulation studies have indicated that a 10 percent change in CCT can result in a mean change in IOP (measured by GAT) of 1–3.5 mm Hg.^{232,233} A thick cornea may influence IOP measurement with non-contact tonometry more than with GAT.²³⁴

One study evaluated whether patients with glaucoma with asymmetric CCT demonstrated greater VF loss in their thinner CCT eye than in their thicker CCT eye.²³⁵ Of the 52 subjects who met all criteria for study inclusion, the mean Advanced Glaucoma Intervention Study (AGIS)²³⁶ score was significantly higher in thinner CCT eyes than in thicker CCT eyes. Subjects with higher AGIS scores for their thinner CCT eyes outnumbered subjects with higher AGIS scores in their thicker CCT eyes, with the differences approaching statistical significance for the full sample ($P = 0.06$) and achieving significance when the analysis was limited to subjects with CCT asymmetry of at least $15 \mu\text{m}$ ($P = 0.001$). Multivariate logistic regression analysis identified thinner CCT as the primary risk factor associated with higher AGIS scores in subjects with CCT asymmetry $\geq 15 \mu\text{m}$. These results correspond to prior reports implicating CCT as an independent risk factor for glaucomatous VF loss. When significant CCT asymmetry is present in patients with glaucoma, the thinner CCT eye is at greater risk for more advanced VF loss.²³⁵

The objective of another study, conducted in subjects whose mean corneal thickness was $540 \mu\text{m}$, was to determine the correlation of CCT to Goldmann applanation tonometry and dynamic contour tonometry (DCT, PASCAL) findings, and to glaucoma stage as assessed by C/D ratio. The corneal thickness values were lowest for African Americans and NTG patients ($518 \mu\text{m}$ and $522 \mu\text{m}$, respectively); their central corneas were significantly thinner than those of Caucasians ($549 \mu\text{m}$) and subjects with OH ($564 \mu\text{m}$). IOP assessed by GAT was significantly correlated with CCT (sample correlation coefficient $[r] = 0.068$, $P < 0.001$), whereas

PASCAL was not significantly associated with CCT ($r < 0.001$, $P = 0.997$). There was a significant correlation ($r = 0.13$, $P < 0.001$) between increased IOP and the large ocular pulse amplitudes predominantly found in ocular hypertensive patients. The investigators also detected a significant negative correlation between C/D ratio and CCT ($r = 0.102$, $P < 0.001$). Thin central corneas are more likely to exist in patients whose glaucoma is at an advanced stage and among persons with NTG as well as persons of black African ancestry. Underestimation of IOP by GAT could be a causative factor for this finding.²³⁷

To evaluate the association between NTG and CCT, researchers studied 56 eyes in 56 subjects with NTG and 84 eyes in a group of 84 subjects with no VF loss. They found a significantly thicker mean CCT for the group with no VF loss, compared with those for all three groups with glaucomatous VF loss (NTG). Multivariate regression analysis revealed a robust, independent, association between CCT and the presence of NTG-related VF loss. Conversely, there was no relationship between CCT and the severity of NTG-related VF loss. In eyes characterized by statistically normal IOP (measured by GAT), there was a significant relationship between CCT and the presence, but not the severity, of glaucomatous VF loss.²³⁸

Many studies have demonstrated above-average CCT in some individuals classified as having OH²³⁹⁻²⁴⁸ and below-average CCT in some patients diagnosed with NTG.^{240,241,244-247,249} On the basis of CCT, two studies reclassified 35 percent and 56 percent of cases of OH and 44 percent and 36 percent of those with NTG, respectively.^{241,245} One study has recommended CCT measurement as a way to avoid overdiagnosis of OH patients with thick corneas and underdiagnosis of those with thin corneas. African Americans may have thinner central corneas than Caucasians, potentially resulting in underestimation of their actual IOPs.²⁵⁰ Similarly, a decrease in CCT following in situ keratomileusis could result in underestimation of actual IOP.^{251,252}

- **Gonioscopy.** Careful evaluation of the anterior chamber angle is essential for differentiating between open angle and closed angle glaucomas, and for distinguishing primary glaucoma from secondary glaucomas.
- **Optic nerve assessment.** Examination of the ON requires procedures that provide stereoscopic visualization with adequate magnification, through a dilated pupil if clinically appropriate. Use of a biomicroscope with an ancillary lens is the preferred procedure. A lens of 60, 66, or 78 D, or a fundus contact lens, enables the best stereopsis. Evaluation of the ON includes ruling out other potential causes of ON atrophy and other tissue abnormalities that might result in VF loss similar to that caused by glaucoma, especially in glaucoma suspects with IOP below 21 mm Hg.

A stepwise process is often used to assess the optic disc and retinal nerve fiber layer in evaluating whether glaucomatous damage is present. This stepwise process includes assessing the optic disc for size, the health of the neuroretinal rim using the “ISNT” rule, and whether disc hemorrhages, peripapillary atrophy, or NFL defects are present. The ISNT rule states that in a healthy optic disc, the location of the thickest rim tissue is *inferior*, followed by *superior*, then *nasal*; the thinnest rim tissue is in the *temporal* quadrant. The significance of assessing for optic disc size is that a large disc will have a large C/D ratio, which may be natural for this disc size. A small disc rarely has a large cup; when present, it may be a sign of damage. The converse is also true in that, in the presence of a small disc, a low C/D ratio may be associated with glaucomatous damage.²⁵³ The mean disk area varies depending upon race with larger disk size associated with individuals of African descent.²⁵⁴ The average disc size is approximately 1.96–2.42 mm², depending upon the study.^{255,256}

A study to evaluate whether the ISNT rule can differentiate normal from glaucomatous eyes enrolled 66 subjects (33 black, 33 white) with normal eyes and 43 subjects (15 black, 28 white) with OAG. The ISNT rule was intact for 52 (79%) of the normal eyes and 12

(28%) glaucomatous eyes ($P < 0.001$). Multiple logistic regression analysis yielded an odds ratio of 6.04 (95% CI, 1.74–20.95) for glaucoma associated with violation of the ISNT rule, after adjustment for age. Race was not a confounder of this association. The ISNT rule is useful in differentiating normal from glaucomatous optic nerves and is unaffected by race.²⁵³

Imaging of the ON and the retinal NFL has received increasing attention in the diagnosis and treatment of glaucoma. Among ON and retinal NFL imaging devices, which provide quantitative information, no single instrument outperforms any other in distinguishing subjects with glaucoma from healthy control subjects. Still, imaging does provide useful clinical information for evaluation with data from other components of the glaucoma examination.²⁵⁸

Users of confocal scanning laser tomography (CSLT) have concentrated on the early identification of patients with glaucoma. The most beneficial application of this technology may be in the detection and monitoring of subtle changes in ON tissue over time.²⁵⁹ Because of significant physiological variation of the ONH within the normal population, it is difficult, even with an ideal imaging system, to identify early glaucoma accurately in a single session.²⁵⁹

The advantages of CSLT include the ability to obtain images without pupil dilation,²⁶⁰ the use of low-intensity light, and real-time imaging. The major disadvantage is the dependence of measurements on the operator’s subjective definition of a reference plane. Inflection-point analysis may help to alleviate this problem.²⁶¹

Despite the tendency with CSLT to overestimate the neuroretinal rim and to underestimate the C/D ratio,²⁶² studies have shown that the parameters generated by this technology are adequate for discrimination between normal ONHs and those of patients with OH²⁵⁷ and early glaucoma.^{263,264} CSLT has a sensitivity of 89

percent and a specificity of 84 percent for differentiating between normal eyes and those with early glaucomatous VF defects.²⁶⁵

Longitudinal studies using CSLT have found that for various parameters measured over time, there are significant differences between OH and glaucoma patients with progressive VF loss and those with stable fields.^{266,267}

Optical coherence tomography (OCT) also allows the assessment of the ON in glaucoma. The advantages of OCT are similar to those of CSLT, although the reference plane is generated by the instrument, subject to operator inspection.

- **Nerve fiber layer assessment.** The procedure for evaluating the integrity of the NFL is similar to that described for evaluating the ON. The NFL is best visualized using digital photography or stereophotographic techniques with red-free illumination and high-resolution black and white film.^{207,208,268} Serial NFL examination is more sensitive than color ON evaluation in detecting the eyes' conversion from OH to POAG. In one study, a minority of the eyes (about 20%) with OH that converted to glaucoma over a 5-year period showed changes in the ON, while about 50 percent showed developing or worsening atrophy of the NFL.¹⁹⁸ In another study, 60 percent of eyes with OH that converted to POAG had NFL defects at least 6 years before VF loss, and 88 percent had NFL defects at the time of the initial VF loss.²⁶⁹

Technology for assessing the NFL in detecting and monitoring the progression of glaucoma has benefited from significant advances. Studies have investigated the capabilities of scanning laser polarimetry,²⁷⁰⁻²⁷² OCT,²⁷³⁻²⁷⁷ and scanning laser ophthalmoscopy^{278,279} in distinguishing normal and OH eyes from those with POAG,^{271,272,274-279} as well as the reproducibility of results obtained with these instruments.^{270,273} The study results are encouraging with respect to accurate measurement of NFL thickness, but whether these instruments have the sensitivity and specificity to detect the onset and the progression of glaucomatous damage remains to be determined.²⁷⁷ The correlations between VF

indices and peripapillary NFL thickness have been weak,^{276,278,279} and the distribution of parameters measured by these techniques in normal eyes overlaps measurements made in eyes with OH or both OH and POAG, thereby reducing the sensitivity and the specificity of these tests.^{271,272}

- **Peripapillary area assessment.** Atrophy of the peripapillary area (PPA) occurs more frequently in eyes with glaucoma than in those with OH or in normal eyes.²⁸⁰⁻²⁸⁸ IOP may not significantly affect the extent of PPA atrophy,^{281,286,289,290} but atrophy in both zone alpha (peripheral to zone beta) and zone beta (bordering the optic nerve head) is significantly more extensive in eyes with glaucoma.^{284,287} Zone beta atrophy occurs significantly more often in persons with glaucoma than in normal individuals,^{282-284,286,287} yet the measurement of zone beta may be of limited usefulness in the detection or follow-up of glaucoma.^{280,282,291}

There is a correlation between the loci of peripapillary atrophy and ON and VF damage.^{281-283,287,292,293} In the normal eye, peripapillary atrophy is more extensive and more frequently located in the temporal horizontal sector.^{282,284}

The value of following the changes in PPA atrophy in glaucoma suspects or individuals with glaucoma has not been well established.^{291,294} Some studies have found a correlation between the progression of PPA atrophy and the progression of both POAG^{287,294,295} and NTG.^{286,296} Others have found no significant difference between the prevalence of PPA atrophy in eyes with progressive glaucoma and those with nonprogressive OH.^{200,280,291}

In a study of 978 eyes in 511 Caucasian subjects, investigators followed 548 eyes with OAG (194, NTG), 289 with OH, and 141 without ON disease for 4.5 ± 2.4 years (median, 3.8 years; range: 1.5–9.8 years). After average follow-up of nearly 4 years, they detected enlargement of the peripapillary zone beta in 16 eyes (1.6% of the 978), including 15 eyes (2.7%) with OAG and 1 (0.3%) with OH, but there was no zone beta enlargement in the normal eyes. After excluding eyes with a myopic refractive error

exceeding -3 D, they found zone beta enlargement significantly more often in eyes with progressive glaucoma (5/81 or 6.2%) than in eyes with nonprogressive glaucoma (3/354 or 0.8%; $P < 0.001$). Peripapillary atrophy (zone beta) increased in relatively few eyes with chronic OAG. In the refractive range above -3 D, zone beta enlargement occurred significantly more often ($P < 0.001$) in progressive glaucoma than in nonprogressive glaucoma. In view of its low frequency, enlargement of zone beta may not be very useful as a marker for glaucoma progression.²⁹⁷

- **Fundus photography.** As a means of improving accurate clinical diagnosis and follow-up,²⁹⁸ stereoscopic fundus photography through a dilated pupil is preferable. Qualitative evaluation of the structural features of the ON, NFL, and surrounding PPA, and of function (VF parameters) by direct observation and the assessment of photographs may offer more diagnostic precision than quantitative evaluation (e.g., digital imaging analysis) in determining the presence of structural glaucomatous damage^{203,299} at the stage of early VF loss.

Evidence that optic disc hemorrhages were detected more frequently by evaluation of digital pictures of the retina than by assessment of the ON,³⁰⁰ suggests that photographic documentation every 2 years is appropriate for establishing the baseline appearance of the ON, NFL, and the peripapillary layer, and that stereoscopic photography is indicated each time the ON or NFL changes in glaucoma suspects over time.²⁹⁸

- **Visual fields.** Measurement of threshold levels in areas of the VF likely to be affected by glaucomatous damage should be made by perimetry through a pupil of adequate size.³⁰¹ The results of perimetry should be compared with the reference values from an age-matched control population and evaluated with respect to the probability of abnormal (glaucomatous) findings.³⁰² The clinician should consider factors that can influence interpretation of the findings, including the patient's learning curve.³⁰³

c. Supplemental Testing

Other procedures may be used to detect the earliest loss of visual function from glaucoma. Although measurement of color vision,³⁰⁴⁻³⁰⁶ contrast sensitivity, and dark adaptation, in addition to pattern electroretinograms and visual evoked potentials, have been thoroughly studied, none has proven ability to distinguish glaucoma suspects from individuals with POAG.³⁰⁷ Tonography³⁰⁸ and provocative testing³⁰⁹ are of little value in the diagnosis of OAG, due to their poor sensitivity and specificity.⁷

Short-wavelength automated perimetry (SWAP) may be useful in evaluating early or subtle diseases of the ON and retina.³¹⁰ A technique with which to isolate the blue color (short-wavelength) vision mechanism, SWAP appears to uncover loss of visual function earlier in the disease process than traditional white-on-white automated perimetry.³¹¹⁻³¹⁴ SWAP facilitates prediction of future defects that white-on-white perimetry will eventually detect.^{310,311,313,315} The VF defects found with SWAP are larger and progress more rapidly than those localized with white-on-white automated perimetry.^{311,313}

SWAP results, which may be predictive of which eyes with early glaucomatous VF loss are most likely to progress,³¹¹ correlate with structural changes in the ON^{316,317} and the NFL.³¹⁴ Moreover, an association between the prevalence of defects localized with SWAP and other risk factors is predictive of the development of glaucoma in patients with OH.^{312,315} Of clinical concern, however, are the longer duration of testing and the fluctuation of patient responses that may occur with the use of SWAP.

Threshold frequency doubling technology (FDT) perimetry may detect visual function loss when the standard white on white visual field is full. The changes can also be correlated with ON and NFL losses and are predictive of the development of glaucoma in patients with OH.³¹⁸

2. Follow-up Glaucoma Evaluation

Because the earliest detection of glaucoma may require clinical observation of very subtle changes in the appearance of the ON, NFL, PPA, or VF over several years, repeated evaluation, even within a 1-year period, may be needed for a definitive diagnosis.²⁰⁰ Continual changes in any one of these parameters may facilitate the first clinical recognition of the earliest stages of glaucoma.³¹⁹

The person with one or more risk factors, who has a higher probability of developing POAG, needs more frequent evaluation to rule out the presence of the earliest clinical signs of glaucoma. This evaluation should be done at least yearly in the absence of complicating factors, but perhaps more often, depending on the person's relative risk of developing glaucoma. Follow-up evaluations are based on tests and procedures similar to those in the initial glaucoma evaluation. Less comprehensive follow-up examinations may be useful in assessing specific clinical parameters in glaucoma suspects.

Follow-up evaluation of the patient with diagnosed OAG is similar to the procedure used to make the initial diagnosis of the disease. Patients need to be assessed in the first 1–2 years after diagnosis to ascertain whether the condition is stable or progressing. In approximately 10 percent of newly diagnosed patients, the OAG progresses rapidly, and such persons need to have their treatment regimen adjusted. Progression can only be discovered by performing optic disc evaluation, imaging, and perimetry at least yearly and in many cases more often.¹⁸⁰ Tests may include, but are not limited to the following assessments:^{224,320}

- **Patient history.** In addition to a review of risk factors, the history should focus on changes in the patient's medical status or medications, side effects or adverse reactions to therapy, and compliance with prescribed therapy.³²⁰
- **Visual acuity.** Various forms of treatment for glaucoma as well as advanced stages of the disease can affect visual acuity.

- **Blood pressure and pulse.** Adrenergic agonists and beta-adrenergic-blocking agents can adversely affect blood pressure and heart rate.
- **Biomicroscopy.** Examination of the lids, conjunctiva, cornea, and anterior and posterior chambers is needed to detect adverse reactions to therapy or signs of the development of secondary glaucoma.
- **Tonometry.** Diurnal IOP curves and IOP measurements with the patient in the supine position³²¹ may be needed for certain glaucoma patients, especially those with NTG.^{322,323}
- **Gonioscopy.** To rule out the development of an angle closure component in the glaucoma, gonioscopy should be repeated periodically. This examination is more frequently needed in follow-up of patients on miotic therapy or in those who show changes in IOP.
- **Optic nerve assessment.** Stereoscopic examination of the ON, NFL, and PPA through a dilated pupil should be performed at least once per year, but may be needed more frequently in cases of advanced glaucoma.²⁹⁹ Sequential stereoscopic photography or imaging technology can be valuable in detecting subtle changes in the ON or NFL.²⁰³ Visible damage to the ON can occur early in the disease process, before detectable VF loss.^{152,324} Once VF defects have been established, sequential perimetry may be a more sensitive indicator of progressive glaucomatous damage.³²⁴
- **Nerve fiber layer assessment.** Assessment of the NFL is similar to ON assessment but uses red-free illumination. The NFL can also be assessed with digital photography and imaging. In the early stages of glaucoma, estimation of structural abnormalities from serial NFL photographs may be more sensitive than assessment of the ON.²⁰⁰

- **Fundus photography.** When the patient's condition is unstable, stereophotography through a dilated pupil can be useful. Digital imaging analysis may be a valuable alternative.
- **Automated perimetry.** Threshold perimetry should be performed at least once per year; more frequent testing may be needed for cases of unstable or advanced glaucoma. Comparison of repeated threshold perimetry results and statistical analyses are required to detect the most subtle VF changes due to glaucoma.³²⁵ Three to five perimetric tests may be needed to show the progression of VF loss in glaucoma.³²⁶
- **Supplemental testing.** Other tests that may be performed to detect the progression of vision loss include color vision, SWAP, FDT perimetry, and contrast sensitivity.

Whether glaucomatous damage is first observed with VFs or in the ONH assessment is an important issue addressed by the OHTS researchers, who evaluated the association between change from baseline in the ONH and the VF during follow-up of OH participants. Forty-one eyes reached an endpoint by both VF and optic disc criteria; 40 eyes reached only a VF endpoint, and 87 reached only an optic disc endpoint. Times to reach isolated disc or field endpoints were similar. VF endpoints were more likely ($P < 0.0001$) in eyes that showed any of the following ONH features: ONH hemorrhage, thinning of the optic disc rim, or enlargement of the horizontal C/D ratio. Optic disc endpoints were more likely ($P < 0.0001$) when eyes showed these VF features: evidence of a nasal step or a partial arcuate VF defect, or an increase in the pattern standard deviation (PSD). The VF and the optic disc must be monitored with equal diligence, because either may show the first evidence of glaucomatous damage. ONH changes based on stereophotographic observation (rim thinning, hemorrhage, or a slight increase in C/D ratio) and VF changes (evidence of a nasal step/partial arcuate defect or an increase in PSD) suggest increased risk of developing glaucoma. Confirmation of such subtle findings should be sought through repeat testing and correlation with other clinical results.³²⁷

The Confocal Scanning Laser Ophthalmoscopy (CSLO) Ancillary Study to the OHTS evaluated whether optic disc topographic measurements are associated with the development of POAG in persons with OH. Included in the CSLO study were 865 eyes from 438 participants who had good-quality baseline images. Univariate and multivariate proportional hazards models were used in evaluating each baseline CSLO parameter to determine its association with the development of POAG. Forty-one eyes from 36 CSLO ancillary study participants developed POAG. Several baseline topographic optic disc measurements were significantly associated with the development of POAG in both univariate and multivariate analyses, including larger C/D ratio, mean cup depth, mean height contour, cup volume, reference plane height, and smaller rim area, rim area to disc area, and rim volume.³²⁸

In the CLSO Ancillary Study, classification as “outside normal limits” by the Heidelberg Retina Tomograph classification and the Moorfields Regression Analysis classifications (overall, global, temporal inferior, nasal inferior, and superior temporal regions) was significantly associated with the development of POAG. Within the follow-up period of this analysis, the positive predictive value of CSLO indexes ranged from 14 percent (Heidelberg Retina Tomograph classification and Moorfields Regression Analysis overall classification) to 40 percent for Moorfields Regression Analysis temporal superior classification. Several baseline topographic optic disc measurements, alone or in combination with baseline clinical and demographic factors, were significantly associated with the development of POAG among OHTS participants.³²⁸

B. Diagnosis of Secondary Open Angle Glaucoma

1. Pigmentary Glaucoma

Differential diagnosis of pigmentary glaucoma involves the same clinical approach as the comprehensive initial and follow-up evaluations of a person who is suspect for POAG. PG is often diagnosed at an earlier age in men than in women, and men require more aggressive medical and surgical therapy.^{87,329}

The clinical presentation of pigmentary dispersion syndrome with associated PG includes:

- Spoke-like transillumination defects in the midperiphery of the iris⁴⁵
- Pigment on the anterior surface of the iris, often as concentric rings within the furrows of the iris⁸⁹
- Pigment in the anterior and posterior chambers, and possibly Krukenberg's spindles on the corneal endothelium³³⁰
- A dense, homogeneously pigmented trabecular meshwork, especially posteriorly^{89,90,331}
- An open, deep anterior chamber angle with possible posterior bowing (concavity) of the iris^{36,91}
- Rise of the IOP to rather high levels, with dramatic fluctuation^{331,332}
- Pigment release resulting from pupillary dilation³³³ or strenuous exercise,³³⁴ which requires assessment of the IOP after dilation.

2. Pseudoexfoliation Glaucoma

Differential diagnosis of PEG involves the same clinical approach as the initial and follow-up evaluations of persons who are suspect for POAG, with special attention to biomicroscopy and gonioscopy. The evolution from first pigmentary and lens changes to full-scale PES may require 5–10 years.³³⁵ The clinical presentation of PES with associated PEG includes:

- Distribution of pseudoexfoliative material on the pupillary margin of the iris and on the surface of the lens, as a central translucent disc with curled edges surrounded by an annular clear zone

- A peripheral granular zone on the anterior surface of the lens, best viewed through a dilated pupil^{46,47}
- Transillumination defects in the iris near the pupil and pigmentation of the trabecular meshwork^{46,47}; pigment granules that may form a whorled pattern over the sphincter muscle on the surface of the iris³³⁶
- Depigmentation of pupillary ruff
- Poor pupillary response to topical mydriatic agents
- Accelerated cataract formation.

Biomicroscopy performed through a dilated pupil can increase the ability to diagnose PES.³³⁷ Pigment may be dispersed from the pigment epithelium of the iris near the pupil, caused by rubbing of the iris on the roughened surface of the lens. This rubbing can result in depigmentation of the pupillary ruff, giving it a moth-eaten appearance.³³⁸

The pigmentation of the trabecular meshwork in PES differs from that in PDS. It is patchy, lacks homogeneity, and may be located in the superior angle and anterior to Schwalbe's line.^{60,105} Pupillary dilation can cause pigment dispersion,^{61,62} resulting in a spike in IOP⁶¹ that necessitates postdilation tonometry.³³⁹ Increased trabecular pigmentation may precede the appearance of pseudoexfoliative material on the surface of the lens, even though this material is present in the conjunctiva.⁶³

IOP can be extremely high in PEG, which has a more serious clinical course than POAG and greater propensity for VF loss at the time of diagnosis.³⁴⁰ Among newly diagnosed cases of PEG, 69 percent are unilateral, compared with 46 percent of POAG cases.³⁴¹

The Malmo Ocular Hypertension Study compared glaucoma conversion rates in patients with OH with and without pseudoexfoliation. A population-based glaucoma screening of elderly citizens of Malmo, Sweden, conducted between 1992 and 1997, had yielded participants for the EMGT. The Malmo investigators re-examined and compared EMGT

subjects with pseudoexfoliation and control EMGT subjects without pseudoexfoliation, matched for age, gender, and IOP of 24–32 mm Hg. The investigators performed computerized VF tests to identify persons with manifest glaucoma and measured visual acuity, refraction, IOP, and CCT. After a mean 8.7 years (range, 6.3–11.4), 54 of 98 patients (55.1%) with pseudoexfoliation at the baseline examination and 27 of 98 patients (27.6%) without pseudoexfoliation had developed glaucoma. The glaucoma conversion rate was twice as high in patients with OH and pseudoexfoliation as in control patients matched for IOP, age, and gender (risk ratio, 2.0; $P < 0.0001$). Thus, pseudoexfoliation is a strong independent risk factor for glaucoma in patients with OH.¹⁰⁷

C. Management of Open Angle Glaucoma

Treatment and management of POAG involves patient education, continuity of care, compliance with therapy, communication with patients' physicians, and possibly comanagement with a glaucoma specialist (see Appendix Figure 2).

1. Basis for Treatment

The fundamental rationale for the treatment of glaucoma is that abnormal IOP plays a major role in the development of glaucomatous optic neuropathy. Although high IOP is certainly not the only factor contributing to ON damage, it is the only risk factor that can be clinically modified.³⁴² Medically lowering IOP in patients with OH may reduce the incidence of glaucoma.¹⁴³ In at least two-thirds of patients with high-tension glaucoma, marked lowering of the IOP stops progression of the disease.³⁴²⁻³⁴⁶ Even in NTG patients, the IOP level is a risk factor related to the degree of glaucomatous damage.^{141,142,347,348}

The OHTS showed that topical OH medication is effective in delaying or preventing the onset of OAG in patients with elevated IOP. The investigators randomized a total of 1,636 participants with no evidence of glaucomatous damage, aged 40–80 years and with IOP of 24–32 mm Hg in one eye and 21–32 mm Hg in the other eye, to either observation or treatment with commercially available topical ocular hypotensive medication. The goal in the medication group was to reduce the IOP by

at least 20 percent and to reach IOP of 24 mm Hg or less. During the course of the study, the mean reduction in IOP in the medication group was 22.5 (SD \pm 9.9) percent. The IOP declined by 4.0 (\pm 11.6) percent in the observation group. At 60 months, the cumulative probability of developing POAG was 4.4 percent for the medication group and 9.5 percent for the observation group (HR, 0.40; 95% CI, 0.27–0.59; $P < 0.0001$). There was little evidence of increased systemic or ocular risk associated with ocular hypotensive medication. Topical ocular hypotensive medication was effective in delaying or preventing the onset of POAG in individuals with elevated IOP. Although these results do not imply that all patients with borderline or elevated IOP should receive medication, clinicians should consider initiating treatment in persons with OH who are at moderate or high risk for developing POAG.⁸²

The OHTS also compared the results in white and black Americans when their OH was managed. Of the 1,636 OHTS participants randomized, 408 self-identified as African American. The primary outcome was the development of reproducible VF abnormality and/or reproducible optic disc deterioration attributable to POAG. Among the African American subjects, 17 (8.4%) of 203 in the medicated group developed POAG during the study (median follow-up, 78 months), compared with 33 (16.1%) of 205 subjects in the observation group (HR, 0.50; 95% CI, 0.28–0.90; $P = 0.02$). The investigators concluded that topical ocular hypotensive therapy is effective in delaying or preventing the onset of POAG in African Americans who have OH.³⁴⁹

To develop a risk model that would enable identification of which individuals have the greatest chance of developing glaucoma within 5 years in the presence of OH, the OHTS and European Glaucoma Prevention Study (EGPS) groups identified a set of risk factors that included elevated IOP, thin cornea, increased vertical C/D ratio, VF status using pattern standard deviation (PSD), and age. They validated their model using data from the Diagnostic Innovations in Glaucoma Study (DIGS).⁸⁴ OHTS/EGPS data also facilitated development of a risk model with which to predict which individuals are also at the greatest risk of converting from OH to OAG.⁸⁵

The EMGT compared immediate therapy with no therapy to reduce IOP in newly detected OAG and showed that therapy to reduce IOP is effective in preventing progressive damage.⁸²

The Advanced Glaucoma Intervention Study (AGIS)²³⁶ demonstrated that sustaining IOP below 18 mm Hg and averaging 12.3 mm Hg resulted in little change in VF over a period of 6–8 years. Although these results support prior studies showing the benefit of a significant IOP reduction in patients with advanced glaucoma,^{343-345,350-354} a significant reduction in IOP does not necessarily protect the eye of a patient with advanced glaucoma from future VF loss.^{342,355,358} It does appear that glaucoma patients with higher peak IOP,^{34,356,359-364} and with wide variability (fluctuation) in IOP,^{34,236,342,351,356,359,361-363,365-367} are more susceptible to progressive VF loss.

The objective of treating glaucoma by lowering IOP is to prevent additional damage to the ON, thus preserving remaining visual function.^{7,34,200} This objective must be achieved in the safest and most effective manner for each individual, while minimizing the impact of treatment on the patient's vision, health, and quality of life (see Table 2).

To achieve the goal of treatment, the clinician should establish a “target pressure” for each patient and document it in the patient’s medical record. This target is the range of IOPs below which additional damage to the ON is unlikely over the patient's lifetime. In general, the target pressure should be 30–50 percent lower than the pretreatment level³⁶⁸; it cannot simply be “normal” pressure, because some patients with glaucomatous damage have baseline IOPs that are similar to those of normal eyes.³⁶⁹ Because the IOPs of patients with thin corneas may have been underestimated, their target pressures may need readjustment over time when progressive damage is detected.

In estimating the initial target pressure, the clinician can use knowledge about the existing damage to the ON, the degree of VF loss, and the patient’s age and highest IOP, along with clinical experience (see Table 3).³⁷⁰

Table 2

**Suggestions for the Medical Management
of Primary Open Angle Glaucoma and Ocular Hypertension***

1. Determine whether therapy is indicated for either OH or OAG. For OH, this may include performing a risk assessment analysis.
2. Rule out any secondary forms of glaucoma that may affect the therapy or prognosis.
3. Determine appropriate target pressure and readjust when necessary.
4. Use the fewest medications in the lowest concentrations needed to achieve the target pressure.
5. When the treatment is ineffective, initially substitute, rather than add, medication.
6. Continually stress, with the patient, the need for treatment compliance.
7. Make the treatment regimen as convenient for the patient as possible.
8. Teach the patient the correct method of instilling eyedrops.
9. Write down the treatment regimen for the patient, including time of day, number of drops, and color of bottle cap.
10. Communicate with the patient's family doctor.
11. Always ask the patient about changes in medical history and any side effects or adverse reactions to medications.
12. Continually educate the patient about risks and prognosis of the disease and side effects and adverse reactions of medications.

*Modified from Stamper RL, Lieberman MF, Drake MV. Becker-Shaffer's diagnosis and therapy of the glaucomas, 7th ed. St. Louis: Mosby, Inc., 1999:422.

Table 3
Clinical Stages of Primary Open Angle Glaucoma

Mild	ON	Mild concentric narrowing or partial localized narrowing of the neuroretinal rim; disc hemorrhage; cup/disc asymmetry
	NFL	Less bright reflex; fine striations to texture; large retinal blood vessels clear; medium retinal blood vessels less blurred; small retinal blood vessels blurred
	VF	Isolated paracentral scotomas; partial arcuate or nasal step; damage limited to one hemifield with fewer than 25% of points involved, mean deviation (MD) less than -6 dB
Moderate	ON	Moderate concentric narrowing of the neuroretinal rim; increase in the area of central disc pallor; a complete localized notch or loss of the neuroretinal rim in one quadrant; undermining of vessels
	NFL	Minimal brightness to reflex; no texture; large, medium, and small retinal blood vessels clear ¹
	VF	Partial or full arcuate scotoma in at least one hemifield; damage may involve both hemifields; fixation should not be involved; mean deviation between -6 and -12 dB
Severe	ON	Complete absence of the neuroretinal rim in at least three quadrants; bayoneting of vessels; markedly increased area of central disc pallor
	NFL	Reflex dark; no texture; large, medium, and small retinal blood vessels clear ²
	VF	Advanced loss in both hemifields; 5°–10° central island of vision; MD worse than -12 dB, fixation may be involved

¹As described by Quigley HA, Reacher M, Katz J, et al. Quantitative grading of nerve fiber layer photographs. *Ophthalmology* 1993; 100:1800-7.

²As described by Quigley HA, Dunkelberger BS, Green WR. Retinal ganglion cell atrophy correlated with automated perimetry in human eyes with glaucoma. *Am J Ophthalmol* 1989; 107:453-64.

44 Open Angle Glaucoma

When the initial target pressure is not reached, the clinician should reassess patient compliance, the treatment regimen, or the range of the target pressure, always keeping in mind the goal of therapy.

2. Available Treatment Options

Traditionally, glaucoma treatment has begun with pharmacological intervention, proceeding to laser therapy and surgery when necessary.³⁷¹ Though designed to maximize the benefit of treatment while minimizing risk to the patient, the pharmacological approach has been challenged as less effective than the other sequences of therapy.³⁷²⁻³⁷⁴ Some glaucoma patients may require all three treatment options, and, because glaucoma is a chronic, progressive disease with no known cure, all treatments should be made available to each patient.

In the choice of a specific form of treatment or the decision to alter or provide additional therapy, the overriding consideration must be the risk or benefit to the patient. All forms of treatment for glaucoma have potential side effects or complications.³⁷⁵⁻³⁷⁷ The clinician must evaluate the possible impact of the treatment from a social, psychological, financial, and convenience standpoint.

a. Medical (Pharmaceutical) Treatment*

The treatment of OAG includes the use of topical or orally administered agents that enhance aqueous outflow or reduce aqueous production or both (see Table 4).^{375,376,378}

- **Prostaglandin analogs.** Latanoprost 0.005% is a synthetic prodrug of prostaglandin F_{2α} that lowers IOP by 27–35 percent when given once a day.³⁷⁸⁻³⁸² Its 24-hour efficacy³⁸³ makes latanoprost equal to³⁸² or more effective^{380,384,385} than timolol maleate 0.5% in lowering IOP. Latanoprost may be more

*Every effort has been made to ensure that the drug dosage recommendations are accurate at the time of Guideline publication. However, as treatment recommendations change, due to continuing research and clinical experience, clinicians should verify drug dosage schedules on product information sheets and current scientific literature.

Table 4
Pharmacological Agents for Management
of Primary Open Angle Glaucoma

Prostaglandin analogs	Bimatoprost Latanoprost Travoprost
Alpha2-adrenergic agonists	Nonselective Epinephrine Dipivefrin Selective Apraclonidine Brimonidine
Beta-blocking agents*	Nonselective Carteolol Levobunolol Metipranolol Timolol Selective Betaxolol
Carbonic anhydrase inhibitors	Systemic, oral Acetazolamide, injection or sustained release Dichlorphenamide Methazolamide Topical Dorzolamide Brinzolamide
Cholinergic agonists—miotics	Pilocarpine, solution or gel Carbachol
Combination agents	Timolol-dorzolamide Timolol-brimonidine

*Systemic beta-blocking agents may influence IOP.

effective when administered in the evening,^{379, 383-386} and there appears to be no development of tachyphylaxis.³⁸⁰ Latanoprost has been approved for use in individuals with OAG or OH.

It enhances pulsatile ocular perfusion,^{387,388} and is effective in lowering IOP³⁸⁹ and increasing ocular perfusion pressure³⁹⁰ in NTG. It is additive with dipivefrin,³⁹¹ acetazolamide,³⁹² brimonidine, dorzolamide,³⁹³ and timolol.^{379, 383,394}

A study to determine the proportion of patients with POAG or OH who do not respond to latanoprost therapy included 340 consecutive patients with a new diagnosis of POAG or OH, or previously treated only with a beta-blocker (after an appropriate washout period). All were treated with latanoprost for 1 month and then divided into three groups on the basis of the reduction in IOP: nonresponders (<15% reduction), responders (≥15% but <30%), and high responders (≥30%). Only nonresponders entered a randomized crossover study to investigate the efficacy of timolol, brimonidine, and pilocarpine. IOP at baseline was 24.1 ± 1.4 , and after 1 month's latanoprost therapy, it was 16.9 ± 2.4 mm Hg, a mean 29.9 ± 4.2 percent reduction in IOP. Nonresponders accounted for 4.1 percent of the patients; high responders, 41.2 percent. The nonresponders showed a statistically significant reduction in IOP after brimonidine treatment ($P = 0.05$), whereas the reduction after timolol and pilocarpine treatment was clinically relevant but not statistically significant. This multicenter prospective study found that only 14 of 340 patients did not respond to latanoprost. In the crossover trial on nonresponders, IOP reduction reached statistical significance only after brimonidine, but the small number in the study reduced its statistical power.³⁹⁵

Bimatoprost 0.03% is a synthetic prostamide similar in mode of action and effectiveness to latanoprost. It reduces IOP up to 33 percent.³⁹⁶

Travoprost 0.004% is an FP-class prostaglandin agonist similar in mode of action and effectiveness to latanoprost. It reduces IOP up to 33 percent. U.S. Food and Drug Administration (FDA) Phase II and Phase III studies indicate that travoprost has a potentially higher effectiveness than other active agents in lowering IOP in African Americans.³⁹⁷

The adverse reactions^{380,382,384,385,398-400} and contraindications^{400,403-405} for bimatoprost, latanoprost, and travoprost are listed in Table 5. Eyelash changes include increases in number, length, thickness, curvature, and pigmentation.³⁹⁸ Patients who use PGs immediately following cataract surgery may benefit from concurrent use of a topical nonsteroidal anti-inflammatory eye drop to prevent anterior uveitis and minimize the development of cystoid macular edema.⁴⁰⁰

The docosanoid unoprostone isopropyl is a derivative of docosahexaenoic acid that lowers IOP. An aqueous solution of 0.15% unoprostone isopropyl has been approved by the FDA as adjunct therapy for the treatment of mild to moderate glaucoma. Studies have shown that unoprostone isopropyl 0.12% used twice daily lowers IOP in OH and POAG by 11–23 percent.^{381,406,407} In some studies the efficacy of unoprostone 0.12% was statistically equal to that of timolol 0.5% in controlling diurnal IOP levels⁴⁰⁸ for 1 month to 1 year.^{407,409-411} Unoprostone is also additive to timolol.⁴¹² In NTG, unoprostone reduced IOP by 11 percent⁴¹³; however, unoprostone is not as effective an ocular hypotensive agent as latanoprost.^{381,414} Unoprostone is no longer available in the United States. Table 5 lists adverse reactions^{406,408,410,415} and contraindications for unoprostone isopropyl. Changes in iris pigmentation were reported in one case.⁴¹⁶

- **Epinephrine compounds.** Epinephrine drops (0.25%–2%) are instilled in the eye twice per day. An epinephrine prodrug, dipivefrin, is available in a 0.1% concentration. Due to greater penetration of the cornea,⁴¹⁷ the lower concentration of dipivefrin is equivalent in effectiveness to a 1%–2% concentration of epinephrine.⁴¹⁸ In general, epinephrine compounds are not as effective as other categories of drugs in lowering IOP in glaucoma patients; thus, the frequency of using them to treat glaucoma has decreased to rare.

Because of its efficacy and reduced potential for ocular and systemic side effects,³⁷⁸ dipivefrin is the drug of choice among

Table 5
Major Adverse Reactions and Contraindications
of Pharmaceutical Agents Used in Treatment of Glaucoma

Pharmaceutical Agent	Adverse Reactions	Contraindications
Prostaglandin Analogs	<i>Ocular:</i> Blurred vision Stinging, burning Hyperemia Foreign body sensation Itching Increased iris pigmentation ¹ Eyelash changes Punctate epithelial keratitis Cystoid macular edema Iritis Herpes simplex keratitis <i>Systemic:</i> Headaches Upper respiratory tract symptoms	<i>Ocular:</i> History of uveitis, CME, herpes simplex, keratitis, complicated cataract surgery <i>Systemic:</i> None
Epinephrine ²	<i>Ocular:</i> Stinging, burning Mydriasis Allergic sensitivity Pigment deposits Cystoid macular edema Increased IOP <i>Systemic:</i> Increased blood pressure Increased heart rate Severe headaches	<i>Ocular:</i> Aphakia/pseudophakia Narrow angles <i>Systemic:</i> Systemic hypertension Heart disease Hyperthyroidism Diabetes mellitus Certain medications

¹Changes in iris pigmentation were reported in one case with unoprostone isopropyl.

²Adverse ocular reactions and contraindications are fewer with dipivefrin than with epinephrine.

Table 5 (cont.)

Pharmaceutical Agent	Adverse Reactions	Contraindications
Alpha2-adrenergic agonists	<i>Ocular:</i> Allergic sensitivity ³ Minimal mydriasis ³ Lid retraction ³ Conjunctival vasoconstriction ³ Stinging, burning Foreign body sensation Hyperemia Conjunctival follicles <i>Systemic:</i> Gastrointestinal discomfort Taste abnormalities Headache Fatigue/drowsiness Oral dryness	<i>Ocular:</i> None <i>Systemic:</i> None
Topical beta-blockers	<i>Ocular:</i> Stinging, burning Superficial punctate keratitis Allergic sensitivity Decreased corneal sensitivity Uveitis ⁵ <i>Systemic:</i> COPD ⁶ Systemic hypotension Bradycardia Diabetes mellitus Myasthenia gravis Certain medications	<i>Ocular:</i> Narrow angles <i>Systemic:</i> Chronic obstructive pulmonary disease Systemic hypotension Bradycardia Diabetes mellitus Myasthenia gravis Certain medications

³Adverse ocular reactions are less common with brimonidine.⁴May be less severe with betaxolol.⁵Metipranolol.

Table 5 (cont.)

Pharmaceutical Agent	Adverse Reactions	Contraindications
Oral carbonic anhydrase inhibitors	<i>Ocular:</i> None <i>Systemic:</i> Malaise Depression, confusion Metallic taste Anorexia Diarrhea Paresthesias Kidney stones Metabolic acidosis Blood dyscrasias	<i>Ocular:</i> None <i>Systemic:</i> History of kidney stones Liver disease Sulfonamide allergy Cardiac disease Addison's disease Renal disease Severe chronic obstructive pulmonary disease
Topical carbonic anhydrase inhibitors	<i>Ocular:</i> Stinging, burning Allergic sensitivity Blurred vision Superficial punctate keratitis Corneal edema <i>Systemic:</i> Altered taste	<i>Ocular:</i> Corneal endothelium compromise <i>Systemic:</i> Sulfonamide allergy
Pilocarpine	<i>Ocular:</i> Stinging, irritation Ciliary spasms (myopia) Miosis (vision) Pupillary block Retinal detachment <i>Systemic:</i> Headache, pain Sweating Vomiting, diarrhea Salivation Bradycardia Arrhythmia Dyspnea	<i>Ocular:</i> History of retinal detachment Severe myopia Cataracts Inflammation/infection Aphakia/pseudophakia <i>Systemic:</i> Asthma Ulcers Bladder dysfunction Parkinson's disease

epinephrine drops in the treatment of glaucoma.⁴¹⁹ Table 5 presents adverse reactions and contraindications for epinephrine compounds.^{375,378,420,421}

- **Alpha2-adrenergic agonists.** As a single topical agent, the alpha2-adrenergic agonist apraclonidine can lower IOP in patients with OH or POAG. In a 1% concentration, it is useful for controlling or preventing the acute spike in IOP that may occur after argon laser trabeculoplasty (ALT) and other anterior segment laser procedures.⁴²² By lowering IOP about 25 percent, apraclonidine is also effective in minimizing precipitous IOP increases after cycloplegia in patients with POAG.⁴²³ Apraclonidine also can decrease significant IOP elevations in glaucomatous eyes undergoing trabeculectomy combined with extracapsular cataract surgery.⁴²⁴

Apraclonidine 0.5% is approved for short-term adjunctive use in POAG patients on maximally tolerated medical therapy, requiring additional reduction in IOP. For patients in this category, the mean reduction in IOP has been 2.4 mm Hg, with a maximum reduction of 6 mm Hg⁴²⁵ for up to 90 days. Some eyes may not benefit from this additional treatment, however.

Used 3 times per day, 0.5% apraclonidine lowers IOP to the same degree as 0.5% timolol used twice per day.⁴²⁶ In 17–22 percent of patients, it also has an additive effect with topical timolol maleate in lowering IOP,⁴²⁷ and it may be valuable for use in patients resistant to further reduction in IOP. Long-term use of apraclonidine may be limited, due to allergic reactions (in at least 15% of patients),⁴²⁸ tachyphylaxis,⁴²⁵ and marked reduction in conjunctival oxygen tension, probably as a result of vasoconstriction.⁴²⁸ Table 5 lists adverse reactions to apraclonidine.^{425,426,428,429}

Brimonidine is an alpha2-adrenergic agonist with 23–32 times more selectivity than apraclonidine for alpha-2 receptors.⁴³⁰ In a 0.2% solution, brimonidine reduces IOP about 23–27 percent,^{431,432} with no apparent tachyphylaxis.⁴³³ Brimonidine is also available in

0.1% and 0.15% concentrations. When used twice a day, it is more effective than betaxolol⁴³⁴ and similar in effect to timolol maleate, although not at the trough measurement.^{433,435–438} As monotherapy, brimonidine is less effective than latanoprost.⁴³⁹

Brimonidine is additive with timolol^{440,441} and latanoprost,⁴³⁹ and it can be used as combination or replacement therapy.⁴³¹ Like apraclonidine, brimonidine can be used to prevent IOP spikes after ALT.⁴⁴¹

The neuroprotective effect of brimonidine in animal models is not clearly understood.^{442–444} One possible mechanism is the inhibition of extracellular glutamate accumulation in the retina in response to ischemic stress.⁴⁴⁵ Brimonidine has no effect on retrobulbar⁴⁴⁶ or retinal⁴⁴⁷ blood flow, blood lipids,⁴³³ heart rate,^{433,435,437,438} or pulmonary function.^{434,435,437} Table 5 lists the adverse reactions and contraindications for brimonidine,^{394,432,433,435,438–449} which appears to elicit a lower incidence of ocular allergic reactions than apraclonidine.^{432,433,438}

- **Beta-blocking drugs.** Topical beta-blockers are either nonselective (i.e., blocking both beta-1 and beta-2 receptors) or selective (blocking beta-1 receptors).^{375,378} Timolol (maleate, hemihydrate, preservative-free, or gum-based), carteolol, levobunolol, metipranolol, and betaxolol (suspension) are unique beta-blocker preparations for treating glaucoma. The doses of beta-blockers used in treating glaucoma range from 0.25% to 1.0%, usually instilled 1–2 times per day.⁴⁵⁰

The selective beta-blocker betaxolol may cause fewer pulmonary and cardiovascular side effects,⁴⁵¹ but it is less effective in lowering IOP than the nonselective beta-blockers timolol, carteolol, levobunolol, and metipranolol.⁴⁵² Betaxolol may have a neuroprotective effect, by altering ion channels in retinal ganglion cells, resulting in a decreased influx of calcium.^{453,454} Betaxolol does not increase retinal or retrobulbar blood flow.⁴⁵⁵ Table 5 lists adverse reactions and contraindications for beta-adrenergic blocking agents.^{375,378,456}

- **Carbonic anhydrase inhibitors (CAIs).** The administration of CAIs depends upon the drug and the severity of the glaucoma. One CAI, acetazolamide, is available for injection and in sustained-release capsules (Sequels®).⁴⁵⁷ CAIs usually lower IOP by about 20–40 percent.⁴⁵⁷ The most effective doses are 500 mg of acetazolamide Sequels®⁴⁵⁸ 1–2 times per day and 50 mg of methazolamide 2–3 times per day.⁴⁵⁹

Though effective in significantly lowering IOP, CAIs are poorly tolerated. The best-tolerated CAIs are acetazolamide Sequels® and methazolamide tablets,⁴⁶⁰ which produce fewer kidney stones.⁴⁶¹ There is no evidence that routine blood testing will help predict or prevent possible blood dyscrasias, which can result from CAI treatment.^{462,463} Table 5 lists CAIs' adverse reactions and contraindications for their use.^{378,458,460–463}

Topical CAIs approved for the treatment of glaucoma include several thienothiopyran-2-sulfonamides. Studies of dorzolamide hydrochloride ophthalmic solution, which has approval for use in patients with OH and OAG, in a 2% concentration, applied 3 times per day, lowers IOP 3–5 mm Hg for 1 year. As adjunctive therapy, dorzolamide is approximately equivalent to 2% pilocarpine in further lowering IOP.⁴⁶⁴

Brinzolamide (1% solution) is a topical CAI that is equal to dorzolamide 2% (3 times daily) in lowering IOP,^{465–467} but not quite equal to 0.5% timolol maleate.^{467,468} The IOP-lowering effect of brinzolamide appears to be the same, whether used 2 or 3 times per day.^{468,469} Both brinzolamide^{470–472} and dorzolamide,^{394,440,464,472} applied twice daily, have additive effects when used with timolol.

Brinzolamide increases ONH blood flow in animals, without affecting systemic blood pressure or heart rate.⁴⁷³ In humans, dorzolamide accelerates blood velocity in the superficial vessels of the retina and the ONH, but it does not affect retrobulbar hemodynamics.⁴⁷⁴ Dorzolamide also has a positive effect on perimacular circulation,⁴⁷⁵ and on ocular pulse amplitude (an estimate of choroidal perfusion).⁴⁷⁶

Patients have found brinzolamide more comfortable to use than dorzolamide.^{465–467,477–479} Adverse reactions^{469,471,477} and contraindications for using topical CAIs are presented in Table 5.

- **Miotic agents.** Pilocarpine is the miotic drug most often used in treating POAG. It is instilled topically, generally 4 times per day, in doses ranging from 1.0% to 4%; the duration of action is at least 6 hours. Higher dosages may be considered for use in darkly pigmented individuals.⁴⁸⁰ Pilocarpine also is available in a 4% gel preparation. Table 5 lists adverse reactions and contraindications for the use of pilocarpine.^{375,378,481}
- **Combination medications.** Studies support the rationale for combining separate topical glaucoma medications into a single formulation to decrease the number of applications per day, thereby increasing compliance. After 3 months' use, a combination drug consisting of 2% dorzolamide and 0.5% timolol maleate was more effective in decreasing IOP (28% vs. 33%) than monotherapy with either dorzolamide or timolol (reductions of 15%–20% and 22%, respectively).⁴⁸³ The combination drug was equally as effective as both components, given concomitantly, except in the early morning and afternoon, for up to 12 months.⁴⁸³ The net effect of this combination drug was a 3–4 mm Hg reduction in IOP below the baseline IOP with 0.5% timolol.⁴⁸⁴ The adverse effects and contraindications of this combination drug are similar to those for the component drugs (Table 5).

On the other hand, the combined therapy of timolol and dorzolamide, twice daily, was less effective than the prostaglandin analog latanoprost, given once daily, in lowering IOP (17.9% vs. 23.2%, respectively) for up to 3 months.⁴⁸⁵

Another fixed combination agent is comprised of 0.2% brimonidine tartrate and 0.5% timolol maleate. In two identical 12-month, randomized, double-masked multicenter trials involving patients with OH or OAG, 385 patients received twice-daily treatment with fixed brimonidine-timolol, 382 patients received thrice-daily 0.2% brimonidine tartrate, and 392 patients received

twice-daily 0.5% timolol maleate. Decreases from baseline IOPs during 12-month follow-up were 4.4–7.6 mm Hg with fixed brimonidine-timolol, 2.7–5.5 mm Hg with brimonidine alone, and 3.9–6.2 mm Hg with timolol alone. The mean IOP reductions were significantly greater with fixed brimonidine-timolol than with timolol at all times measured ($P \leq 0.002$) and significantly greater than brimonidine at 8 a.m., 10 a.m., and 3 p.m. ($P < 0.001$) but not at 5 p.m. The incidence of treatment-related adverse events in the fixed-combination group was lower than that in the brimonidine group ($P = 0.006$) but higher than that in the timolol group ($P < 0.001$). The rates of discontinuation of treatment for adverse events were 14.3 percent with the fixed combination, 30.6 percent with brimonidine, and 5.1 percent with timolol.⁴⁸⁶

Other combination drugs have been or are being developed and await approval by the FDA for use in the United States.

b. Laser Trabeculoplasty

Laser trabeculoplasty is commonly used when topical medication(s) have failed to achieve the target IOP, when progression requires further IOP reduction, when side effects have reduced the use of certain medications, or when the patient is unable to instill medications. The long-term benefits of laser trabeculoplasty for the treatment of glaucoma remain controversial,⁴⁸⁷ because its effectiveness diminishes over time.⁴⁸⁷⁻⁴⁹¹

The two forms of laser trabeculoplasty are argon and selective. Argon laser trabeculoplasty (ALT) involves placing from 50 to 100 laser burns (50-micron size, 0.1 seconds in duration, at 500- to 1,000-MW power) around 180° or 360° of the anterior one-third of the trabecular meshwork. This procedure is adequate to produce a visible tissue response.^{377,492} Laser trabeculoplasty has also been successful when performed with krypton, Nd:YAG, and diode lasers.^{493,494} Selective laser trabeculoplasty (SLT) uses a q-switched 532-nm Nd:YAG laser for selectively targeting pigmented trabecular meshwork cells without causing coagulative damage to the meshwork structure or to nonpigmented cells.⁴⁹⁵

Although its mechanism of action is not well understood, several theories have been proposed to explain how laser trabeculoplasty increases the rate of aqueous outflow.³⁷⁷ One theory attributes the increase in aqueous outflow to the formation of microscars causing tissue retraction around the trabecular lamellae, thereby pulling the meshwork open between the scars.⁴⁹⁶ Other possibilities include changes in the physiology of the trabecular endothelial cells that effect an increase in either their phagocytic activity or their number.^{497,498}

Possible complications of laser trabeculoplasty include an increase in IOP within hours of the procedure⁴⁹⁹⁻⁵⁰¹ and inflammation, which may lead to the formation of peripheral anterior synechiae.⁵⁰¹⁻⁵⁰³ A rise in IOP immediately after laser trabeculoplasty can be reduced by antiglaucoma medications such as apraclonidine.⁵⁰⁴ Long-term scarring of the anterior chamber angle by laser trabeculoplasty may result in a delayed rise in IOP.^{505,506} Table 6 provides recommendations for the postoperative management of patients following laser trabeculoplasty. Both ALT and SLT lose their effectiveness over time, such that 5 years after trabeculoplasty glaucoma is controlled in only 50 percent of patients. Subsequent ALT procedures yield reduced effectiveness and duration; thus, more than two sessions per individual eye is rarely indicated.⁵⁰⁷

Theoretically, SLT is repeatable, given its mechanism of action and its capability of targeting pigmented cells only, thus leaving much of the trabecular meshwork undamaged. However, there is no evidence to support repeated use of SLT. In the absence of such data, SLT is used interchangeably with ALT, because, although SLT is less destructive to trabecular cells, the two procedures offer similar IOP reduction.⁵⁰⁸

In a study of 100 eyes (61 patients) to determine the efficacy and safety of SLT as an initial treatment for newly diagnosed OAG, and to elucidate the role of SLT as adjunctive therapy, the investigators assigned 74 eyes newly diagnosed with OAG or OH to the primary treatment (SLT) group and 26 eyes to the control treatment (latanoprost), according to patient choice. They conducted follow-up of both groups at 1, 3, 6, and 12 months. A second treatment group of patients was included to determine SLT's efficacy in patients intolerant of medical therapy or with prior

Table 6
General Guidelines for Postoperative Management
of Patients Following Argon Laser Trabeculoplasty*

1 Hour Postoperative

- Measure IOP and evaluate with biomicroscope.
- If IOP is normal, re-evaluate patient 1–2 weeks later.
- If IOP is elevated or other conditions occur, provide appropriate treatment.

1–2 Weeks Postoperative

- Measure IOP (full effect of treatment may not be apparent for 6–8 weeks).
- Check for ocular inflammation.
- Check for compliance with use of medication.

4–8 Weeks Postoperative

- Measure IOP (which should be below pretreatment level, if procedure has been successful).

* Follow-up schedule should be modified if complications occur, or if the glaucoma is severe.

unsuccessful SLT, with or without previous ALT. The average absolute and percent IOP reductions for the primary treatment group were 8.3 mm Hg (31.0%), compared with 7.7 mm Hg (30.6%) for the control group ($P = 0.208$ and $P = 0.879$, respectively). Based on 20 percent pressure reduction, the responder rates were 83 and 84 percent for the primary and control groups, respectively. There was no difference in the degree to which SLT lowered IOP on the basis of angle pigmentation. The investigators observed a modest contralateral effect in the untreated fellow eyes of patients undergoing SLT. The study showed that SLT and latanoprost were equally effective in reducing IOP in newly diagnosed OAG and OH over 12 months, independent of angle pigmentation. The

efficacy of nonsteroidal anti-inflammatory therapy was similar to that of steroids after laser therapy.⁵⁰⁹

A prospective clinical trial in England also evaluated SLT, comparing SLT (532-nm Nd:YAG laser) with latanoprost 0.005% for the control of IOP in OH and OAG. The investigators randomized 167 patients (one eye each) with either OH or OAG to 90, 180, or 360 degrees of SLT or latanoprost 0.005% at night and evaluated them at 1 hour, 1 day, 1 week, and at 1, 3, 6, and 12 months. The mean follow-up interval was 10.3 months (range, 1–12 months). Early transient complications such as postoperative ocular pain, uveitis, and a 1-hour IOP spike occurred in a number of eyes after receiving SLT. The patients reported pain more frequently following 360-degree treatment than following 90-degree treatments ($P < 0.001$). Success rates, defined in terms of at least 20 percent and at least 30 percent IOP reduction from baseline measurements, with no additional antiglaucomatous interventions, were better with latanoprost than with SLT treatments of 90 degrees ($P < 0.001$) and 180 degrees ($P < 0.02$). Differences between success rates for latanoprost and SLT of 360 degrees did not reach statistical significance ($P < 0.5$).⁵¹⁰

Success rates in this SLT/latanoprost study were greater with 180 degrees and 360 degrees compared with 90 degrees of SLT ($P < 0.05$): 82 percent of the eyes receiving 360 degrees of SLT achieved a 20 percent or greater IOP reduction, and 59 percent exceeded a 30 percent reduction from baseline IOP. Although the success rates were better with 360 degrees than with 180 degrees of SLT treatment, the differences did not reach statistical significance. There were no differences with regard to age, sex, race, pretreatment IOP, OH versus OAG, laser power settings, or total laser energy delivered between eyes that responded with IOP reductions of more than 20 percent and more than 30 percent, and those that did not respond to 180- and 360-degree SLT treatments. Success rates were higher with latanoprost 0.005% at night than with 90 and 180 degrees of SLT, suggesting that at 90 degrees, SLT is generally not effective. On the other hand, 360 degrees appears effective for SLT; approximately 60 percent of eyes achieved an IOP reduction of 30% or more. Transient anterior uveitis with associated ocular discomfort is not unusual in the first few days after SLT. The investigators reported

encountering no late complications causing ocular morbidity after SLT.⁵¹⁰

The use of laser trabeculoplasty is contraindicated in patients with corneal edema or opacities that prevent a clear view of the anterior chamber angle,³⁷⁷ in those who have post-traumatic or uveitic secondary glaucomas, and in situations requiring a large decrease in IOP.⁴⁹¹

To evaluate which sequence of surgical therapies works best in treating medically uncontrolled glaucoma, the AGIS included 451 eyes in 332 black patients and 325 eyes in 249 white patients with glaucoma that did not respond to medication alone. After random assignment, the eyes received treatment with one to two sequences of ALT or ATT or TAT. When an intervention failed, the study offered second and third treatments. The patients were observed every 6 months (range of total potential follow-up, 8 years 4 months–13 years) to determine the percentages of eyes having moderate losses of VF and VA. Race-treatment interactions were significant for VF and VA losses, the two main outcome measures; therefore, results of treatment sequence differences were presented by race.⁵¹¹

Among the AGIS black patients, the average percentage of eyes with VF loss was less following the ATT sequence than the TAT sequence (difference not statistically significant at any visit). Conversely, in white patients after 18 months, the average percentage of eyes with VF loss was less following the TAT sequence, and the difference increased to statistical significance in years 8–10. For both black and white patients, the average percentage of eyes with VA loss was less following the ATT sequence, a difference that was statistically significant throughout 10 follow-up years for black patients but for only follow-up year 1 for white patients. In both black and white patients, average IOP reductions were greater following the TAT sequence, although the TAT-ATT difference was substantially greater in white patients. First-intervention failure rates were substantially lower for trabeculectomy than for trabeculoplasty in both black and white patients.⁵¹¹

The AGIS 10-year cumulative incidence of unilateral VF impairment comparable to legal blindness was modest in the eyes of both black (ATT

11.9%, TAT 18.5%) and white (ATT 9.9%, TAT 7.3%) patients. Both trabeculoplasty sequences lowered IOP in black and white patients with medically uncontrolled glaucoma, but long-term VF outcomes were better for the ATT sequence in black patients and better for the TAT sequence in white patients.⁵¹¹

c. Surgery

Surgical intervention is indicated for many patients with moderate or advanced glaucoma, to lower the IOP into the target range.⁵¹²⁻⁵¹⁴ It is usually the third option in the management of glaucoma, when medical therapy and laser trabeculoplasty do not achieve optimal IOP levels for various reasons. Surgery is also indicated when glaucomatous damage continues to progress and the patient has exhausted medical and other options. Some clinical situations require significant early IOP reduction, and in such cases, surgical intervention is the treatment of choice. Filtration surgery usually results in a dramatic and stable reduction in IOP.^{346,352,376} Although long-term control of IOP is often achieved via filtration surgery, many patients must remain on medications and may require additional filtration or other surgery.

Filtration surgical procedures create alternative pathways for the outflow of aqueous. Among filtering procedures to lower IOP are thermal sclerostomy, posterior or anterior lip sclerectomy, trephination, and trabeculectomy.³⁷⁷ In the most commonly performed filtration procedure, trabeculectomy, the surgeon creates a guarded flap within the sclera to allow aqueous humor to bypass the trabecular meshwork and be absorbed through a bleb created on the external part of the eye. Cyclodestructive procedures, which damage the ciliary body and thereby decrease aqueous production, are less commonly used³⁷⁷

New surgical techniques for OAG include several types of non-penetrating deep sclerectomy (NPDS): Canaloplasty, the Aquaflow® collagen wick (CW), and viscocanalostomy (VC).⁵¹⁵⁻⁵¹⁷ These procedures involve unroofing Schlemm's canal, bypassing the juxtacanalicular tissue, creating a window for aqueous outflow in Descemet's membrane, and maintaining patency of the intrascleral space.⁵¹⁵⁻⁵¹⁷ Canaloplasty incorporates an additional step, the use of a

microcatheter to dilate Schlemm's canal circumferentially and the injection of a viscoelastic agent to reopen it. Glaucoma drainage devices (GDDs) are in common use, especially after filtration surgery failure. GDDs include setons and valves such as Molteno and Baerveldt implants and Ahmed valves.

The advantages of various NPDS techniques are their lack of penetration of the anterior chamber, less use of antimetabolites, less postoperative hypotony, rapid recovery of visual acuity, fewer filtration blebs (VC), less bleb fibrosis (CW),^{515,518,519} and, in general, fewer complications than with trabeculectomy.^{506,520} The disadvantages of NPDS are the procedures' difficulty and length,⁵¹⁸ lower success rates than trabeculectomy,^{518,521,522} less IOP reduction than trabeculectomy, and the need for postoperative ancillary procedures to maintain control of IOP.

Short-term complications from filtration surgery include the development of shallow anterior chambers, hypotony, choroidal detachment, uveitis, blebitis, hyphema, suprachoroidal hemorrhages,^{371,377,523} and loss of a remaining small island of central vision.⁵²⁴ Long-term complications include corneal edema, infection, leaking or failure from fibrosis of the subconjunctival bleb, cataract formation, and endophthalmitis.^{377,524-528} Filtration surgery is contraindicated in eyes that are already blind and in patients with severe systemic medical problems.³⁷⁷

Postoperative subconjunctival scarring, a common problem after filtration surgery, causes the IOP to return to pretreatment levels. Antifibrotic agents, used either during or after surgery to prevent or reduce scar formation, include mitomycin and 5-fluorouracil. Injection of the human monoclonal antibody CAT-152 is under investigation as a means of neutralizing a cytokine growth factor (TGF- β_2) to influence wound healing following trabeculectomy. A 1-year clinical trial of trabeculectomy demonstrated no unusual complications and a diffuse, non-cystic, non-vascular bleb, as well as a trend toward lower IOP.⁵²⁹

Complications from NPDS include perforation of Descemet's membrane,⁵³⁰ iris plugging, hyphema, and encapsulated blebs.^{521,531} Although filtration blebs are not supposed to develop with VC,

subconjunctival microcysts or blebs have occurred in one-third⁵²¹ to one-half of reported cases.^{517,531}

d. Alternative Treatment Strategies

Several clinical trials have evaluated ALT^{373,501,532,533} and filtration surgery³⁷²⁻³⁷⁴ as initial (primary) treatments for POAG. The multicenter, randomized Glaucoma Laser Trial (GLT) and the GLT Follow-up Study evaluated the efficacy and safety of ALT as an alternative to topical medication for the initial treatment of POAG.⁵⁰¹ The GLT investigators reported that eyes treated initially with ALT had lower (1.2 mm Hg) IOP, better (0.6 dB) VF, better ON status, and fewer days of medication than their fellow eyes that received topical medication initially and through 9 years of follow-up.⁵⁰¹ Other investigators have questioned the GLT research design, including assessment of the crossover effect of timolol, and interpreted the initial results more cautiously.⁵³⁴

Patients receiving laser therapy as the primary form of treatment face a greater than 50 percent chance of requiring medications to control glaucoma within 2 years. VF deterioration has accounted for nearly twice as many medication step changes in laser-treated eyes as in non-laser-treated eyes.^{501,535}

A 2-year prospective, randomized study compared ALT with pilocarpine as the initial treatment in patients with OAG. Especially in the case of PEG, ALT was more effective than pilocarpine in decreasing IOP and preserving the ONH and VF in high-tension glaucoma.⁵³⁶⁻⁵³⁸

When a study performed in the United Kingdom compared filtration surgery to medical therapy for the initial treatment of glaucoma, the surgical group showed better IOP control and less VF deterioration than the medically treated group (success rates, 98% vs. 80%, respectively) after a minimum 4 years follow-up.³⁷³ Initial filtration surgery resulted in a mean IOP of 13.3 mm Hg, compared with 16.8 mm Hg for patients on medical therapy and 17.8 mm Hg for those receiving laser therapy (success rate, 60%) as the initial treatment. The success rate for primary trabeculectomy (98%) was higher than that for surgery (79%) following medical treatment.⁵³⁹

The Collaborative Initial Glaucoma Treatment Study, a randomized, controlled clinical trial, was designed to determine whether patients with newly diagnosed OAG are best managed by the conventional approach of topical medications or by immediate filtration surgery. The results show that medications often can reduce IOP to near surgically reduced levels with similar 5-year functional results.⁵⁴⁰ Interim results reported at 4+ years revealed similar VF status for the medically and surgically treated groups, while vision loss related to cataract formation was greater in the surgical group.⁵⁴¹

e. Treatment of Pigmentary Glaucoma

The goals and approaches to the treatment and management of PG are similar to those for POAG.^{331,332} Their medical management involves the use of similar drug regimens. Prostaglandin analogs are often the agents of choice, due to their efficacy and safety profiles. They increase outflow from the eye, which has a theoretic advantage for treating PG. While miotic drugs also provide improved aqueous outflow, they may also benefit the eye by decreasing the area of contact between the posterior surface of the iris and the lens zonules.^{331,332} However, young people do not tolerate miotic agents well,³⁸³ and these drugs may increase the risk for retinal detachment in patients with PDS or PG.^{87,88,542}

Thorough examination of the peripheral retina is required before instituting miotic therapy. Although the initial results of ALT in PG are often good, the failure rate may be greater and it may occur more quickly than in POAG.⁵⁴³ In the case of PG, younger patients seem to respond better to ALT than older patients.⁵⁴⁴ Argon laser iridoplasty⁵⁴⁵ and laser peripheral iridotomy⁵⁴⁶ are also being evaluated for the treatment of PG. Reverse pupil block is the proposed mechanism for the development of PG, and laser iridotomy is believed to break this block by equalizing the pressure between the anterior and posterior chambers. This theory has led to the proposal that iridotomy be accepted as a modality for the treatment of PG. However, there is no evidence that this surgical approach is superior to the use of medications.⁵⁴⁷

f. Treatment of Pseudoexfoliation Glaucoma

The goals and approach to the treatment and management of PEG are similar to those for POAG. Patients with PES may respond less favorably to timolol and other ocular hypotensive agents.⁵⁴⁸ The IOP levels in PEG are often higher and seem more difficult to manage than in POAG.^{340,549-554} ON and VF damage tends to be greater in patients with PEG than in those with POAG.^{361,555} ALT is particularly effective early in the course of PEG⁵⁵⁶; however, the failure rate may be greater, and occur more quickly, than in POAG.^{557,558} The results of filtration surgery in patients with PEG are similar to results in patients with POAG, but complications may occur more often.⁵⁵⁹ ALT and filtration surgery are used earlier and more often in PEG than in POAG.^{549,555}

3. Patient Education

The proper management of glaucoma requires full compliance by the patient.^{320,560,561} Patient acceptance of medical treatment for glaucoma is often poor, however, because the therapy, which must continue throughout life, is expensive and inconvenient (requiring multiple applications per day), and often has unwanted side effects.^{320,560} Inasmuch as the disease is basically asymptomatic, patients often choose not to comply with the prescribed therapy.⁵⁶²⁻⁵⁶⁴

One-fourth to one-half of glaucoma patients do not take their medications properly.^{565,566} A study of advanced POAG showed that the disease progressed in 50 percent of the patients with poor compliance but remained stable in 90 percent of compliant patients.³⁵¹ Patient education regarding the benefits and risks of the treatment and proper use of medications is critical to ensure maximum compliance.^{320,560,561,567} Continual reinforcement of the seriousness of the disease and the importance of following the therapy regimen is essential. Patient participation in developing the treatment plan can help overcome the social and psychological barriers that often arise.⁵⁶⁸

When initiating treatment for glaucoma or modifying the therapy, it may be appropriate for the clinician to conduct a uniocular trial, except with beta-blocking agents, due to their crossover effect^{320,560,561} (which can be

reduced by the use of nasolacrimal occlusion or punctal plugs). This uniocular trial can help determine the likelihood of treatment effectiveness and indicate potential side effects or adverse reactions. Still, the use of a uniocular trial is controversial, and some have questioned whether a drug's response in one eye accurately predicts the response in the other eye.⁵⁶⁹ The patient should be well educated regarding all possible side effects of the medications prescribed. The clinician should inform the patient that nasolacrimal occlusion by lid closure or digital pressure can significantly reduce systemic absorption of topically applied drugs, thereby reducing the potential for side effects.^{320,560,561,567}

A retrospective cohort study examined health insurance claims data involving 3,623 cases of newly diagnosed and treated glaucoma and 1,677 cases of suspect glaucoma. For each of these two diagnostic groups, the investigators calculated the duration of continuous treatment with the initially prescribed medication (persistence) and the prevalence of use of the initial medication at various time points (adherence). They included four classes of drugs: beta-blockers, alpha-adrenergic agonists, carbonic anhydrase inhibitors, and prostaglandin analogs.⁵⁷⁰

The study showed that nearly half of the individuals who had filled glaucoma prescriptions discontinued all topical ocular hypotensive therapy within 6 months, and just 37 percent of these individuals had refilled their initial medication 3 years after the first dispensing. Hazard ratios for the discontinuation of prostaglandins compared with beta-blockers were 0.40 (95% CI, 0.35–0.44) for diagnosed patients and 0.44 (95% CI, 0.37–0.52) for persons with suspect glaucoma. Prostaglandins showed a similar advantage in adherence. Furthermore, patients with diagnosed glaucoma were more likely to adhere to therapy than patients with suspect glaucoma (relative risk, 1.11; 95% CI, 1.05–1.18). Persistence and adherence were substantially better with prostaglandins than with other classes of drugs.⁵⁷⁰

4. Prognosis and Follow-up

After the initiation of treatment for OH and glaucoma, follow-up examinations are required to monitor the stability of the IOP, ON, and VF, as well as patient compliance with the therapy, the presence of side effects associated with the treatment, and the effectiveness of patient education. Follow-up also provides an opportunity to reconfirm the diagnosis.³¹⁴ The management of glaucoma is a fluid, dynamic situation in which side effects may occur at a later time; the IOP, ON, or VF may change over the course of a patient's lifetime of therapy. Determining whether the disease is progressing may be clinically challenging, due to the difficulty, in some patients, of distinguishing subtle structural or functional changes representing normal fluctuation from changes caused by progressive glaucomatous damage.⁵⁷¹

IOP response to medical therapy also may vary on the basis of corneal thickness—specifically, thick corneas, which constitute a particular risk factor. Addressing the question of whether CCT correlates with measured IOP response to topical ocular hypotensive medication, the OHTS investigators used Goldmann applanation tonometry to measure IOP and ultrasonic pachymetry to measure CCT. They examined the following indicators of IOP response to topical ocular hypotensive medication: (1) IOP after an initial 4- to 6-week one-eyed therapeutic trial of a nonselective beta-blocker (549 patients) and a prostaglandin analog (201 patients); (2) the mean IOP response during 12–60 months of follow-up among 689 of the medication participants; (3) the percentage of follow-up visits at which both eyes met the treatment goal; (4) the total number of different medications prescribed to reach the treatment goal; and (5) the total number of different medications prescribed, multiplied by the number of months that each medication was prescribed. CCT was inversely related to the IOP response after the initial one-eyed therapeutic trial and during 12–60 months' follow-up ($P < 0.05$). Mean CCT did not correlate with the number of different medications prescribed during follow-up, or with total medication months, or with the percentage of visits at which the IOP target was met. The study participants with thicker corneas had smaller measured IOP responses to ocular hypotensive medication than those with normal or thin corneas.⁵⁷²

a. Frequency of Follow-up

The frequency of follow-up evaluation of a glaucoma patient under active treatment depends upon the IOP level^{342,343,345,360,364} and the stability and severity of the disease^{342,345,512} (see Appendix Figure 3). “Stability” refers to the status of IOP, ON, and VF. The higher the IOP or the more severe the glaucoma, the more frequently the patient needs to be evaluated.⁵⁷³ Every patient diagnosed with glaucoma should be seen at least every 6 months. A dilated-pupil fundus examination and threshold perimetry should be performed at least once per year. The recommended frequencies for follow-up of patients with glaucoma are as follows:

- **OH and stable mild-stage disease:** Every 3–6 months, depending on the duration of IOP control.
- **Stable moderate-stage disease:** Every 2–4 months, depending on the duration of stability and the IOP.
- **Stable severe disease:** Every 1–3 months, depending on the duration of stability and the IOP.
- **Recently established stability:** Every 1–3 months, depending on both the severity of the disease and the IOP.
- **Unstable disease:** Cases in which IOP, ON, or VF is unstable require adjustment of therapy, which could involve weekly or biweekly follow-up for a brief period or until stability is achieved.

The frequency of follow-up care after laser trabeculoplasty (see Table 6) involves monitoring IOP immediately (within several hours) and monitoring both IOP and signs of ocular inflammation at 1–2 weeks and 4–8 weeks postoperatively.³⁷⁷

b. Therapy Modification

Unstable glaucoma requires re-evaluation of the treatment regimen, including reassessment of the patient's target pressure.^{320,560} The need to

modify the therapy can arise from the IOP's being too high or from its being above the target pressure, as well as from lack of full compliance, the development of side effects from the treatment, contraindications to the treatment, or progressive damage, as evidenced by deterioration in either the status of the ON or the VFs, despite maintenance of the target IOP. The target IOP represents an educated guess as to what pressure should control the condition; only by periodically monitoring the ON and VFs can the clinician be sure that the glaucomatous condition is controlled. The discovery of changes is an indication that the target IOP needs to be reduced.

Any adjustments to glaucoma therapy must be weighed against the potential benefit or risk to the patient. The use of uniocular trials at the time of modification of medical therapy may be considered but are not mandatory.³²⁰ Following modification of therapy, the clinician needs to see the patient more frequently until stability in the progression of the disease has been re-established.

In a study to compare the efficacy and safety of timolol maleate 0.5% versus brinzolamide 1%, each added to travoprost 0.004%, in patients with OH or POAG, the 97 patients on brinzolamide had a baseline diurnal IOP of 21.5 ± 2.2 mm Hg and the 95 on timolol maleate had 21.3 ± 2.5 mm Hg. The diurnal mean IOP at week 12 was 18.1 ± 2.7 mm Hg for the brinzolamide group and 18.1 ± 3.0 mm Hg for the timolol group ($P = 0.96$). The investigators found no statistical difference between treatment groups in the absolute level of pressure, or in the reduction in IOP from baseline, at any point in time or for the diurnal curve ($P > 0.05$). Nor was there a significant difference between groups for any adverse event ($P > 0.05$). The most common side effect was conjunctival hyperemia in 15 of 97 ($P > 0.05$) patients on brinzolamide and 6 of 95 (6%) patients on timolol ($P = 0.06$). The results showed that in the presence of travoprost, the safety and efficacy of brinzolamide and timolol maleate are similar.⁵⁷⁴

c. Effectiveness of Treatment

The lack of consensus on a clear definition of progression of the disease hinders interpretation of the effectiveness of treatment for glaucoma.^{8,362}

The rate of VF loss in POAG is usually slow.⁵⁷⁵ Patients who are diagnosed with early glaucoma and receive appropriate treatment may not reach end-stage disease status for many years.^{192,576}

A prospective study showed that one-third of eyes with either POAG or NTG deteriorated during an average follow-up of 9 years. The rate of vision loss was 3 percent per year for patients in both POAG and NTG groups.⁵⁷⁶ Although the rate of deterioration in that study represented a mean deviation of less than 0.7 dB per year,⁵⁷⁶ other investigators have found higher rates of deterioration (mean deviation, approximately 1–5 dB per year).^{34,577,578} Various studies have shown worsening of VFs in patients with POAG ranges from 25 to 80 percent (average, about 50%) over 5 years.^{34,340,342,345,346,356,357,360,372,554,578-583} Factors associated with progression were treatment and follow-up IOP, age, bilaterality, exfoliation, and the presence of disc hemorrhages. Also predictive of risk for progression of glaucoma were thinner corneas, lower systolic blood pressure, lower systolic perfusion pressure (blood pressure minus IOP), and history of cardiovascular disease.¹⁸⁰

A few clinical studies have addressed the effectiveness of medical therapy for glaucoma.^{8,143,343} At least 40 percent of glaucoma patients respond immediately and consistently to medication.⁵⁸⁴ The GLT demonstrated, however, that after 2 years only 30 percent of medically treated glaucoma was controlled by a single beta-blocker.⁵²¹ About 40 percent of patients treated with prostaglandin analogs require additional medications and/or surgery to maintain control of glaucoma. Approximately three-fourths of the eyes under medical therapy have shown progression of the disease when followed for up to 10 years.^{340,580,581}

The rates at which patients experience VF deterioration vary⁵⁷ and often are associated with age.^{575,577} The progression of both early and advanced glaucoma is more likely when the IOP is higher and when there is greater fluctuation of IOP during therapy.^{512,513} In one study, medically treated patients with IOPs below 16 mm Hg had rates of progressive VF loss ranging from zero (early glaucoma) to 33 percent (advanced glaucoma), while the rates of progression for treated patients with higher IOPs (>20 mm Hg) ranged from 20 to 100 percent.³⁶⁰ Thus,

many treated glaucoma patients whose IOP is in the “normal” range do show progression of the disease.^{223,340}

The EMGT illustrated that 15 percent of newly diagnosed mild glaucomas will progress rapidly, showing VF losses that exceed 1 dB per year.¹⁸⁰ This subgroup of patients needs to be identified, and, per the EMGT recommendation, VF testing needs to be performed on a 6-month basis for the first 2 years after diagnosis. Statistical tools such as regression analysis (e.g., the Glaucoma Progression Analysis program) are useful in VF monitoring. When the glaucoma has been identified as stable, yearly VF testing is appropriate.¹⁸⁰

When AGIS data were used to investigate the risk factors associated with progression of VF loss, the mean (\pm standard deviation, SD) follow-up time and baseline AGIS scores were 7.4 (\pm 1.7) and 7.7 (\pm 4.4) years, respectively. Progression of VF loss was detected in 30 percent of eyes ($n = 151$). Factors associated with increased odds of progression of VF loss were older age at the initial intervention ($P = 0.0012$; odds ratio [OR], 1.30; 95% CI, 1.11–1.50), larger IOP fluctuation ($P = 0.0013$; OR, 1.31; 95% CI, 1.12–1.54), increasing number of glaucoma interventions ($P = 0.01$; OR, 1.74; 95% CI, 1.14–2.64), and longer follow-up ($P = 0.02$; OR, 1.19; 95% CI, 1.03–1.38). Repeated regression analysis for eyes with and without a history of cataract extraction revealed that IOP fluctuation was the only variable consistently associated with progression of VF loss. Both increasing age and greater IOP fluctuation increased the odds of the progression of VF loss by 30 percent for each 5-year increment in age and 1-mm Hg increase in IOP fluctuation. The investigators consistently observed higher risk conferred by IOP fluctuation in eyes with and without a history of cataract extraction.⁵⁸⁵

In a study addressing the issue of blindness associated with glaucoma, the investigators focused on how many patients with treated glaucoma or OH go blind and which factors are associated with blindness. Retrospective evaluation of data pertaining to 106 consecutive patients (at diagnosis, 39 with POAG, 27 with PEG, 40 with OH) revealed that at their most recent visits, 17 (16%; 95% CI, 9–23) were visually handicapped; 13 (14%) were bilaterally blind. Glaucoma was the cause of blindness in one or both eyes in 16 patients (15%; 95% CI, 8–22) and

in both eyes in 6 patients (6%; 95% CI, 1–10). Analysis of only one eye of each patient showed a cumulative incidence of glaucoma-caused blindness of 6 percent (95% CI, 2–11) at 5 years, 9 percent (95% CI, 4–15) at 10 years, and 15 percent (95% CI, 9–23) at 15 years. Factors associated with increased occurrence of blindness attributable to glaucoma were advanced stage of glaucoma at diagnosis, IOP fluctuation during treatment, the presence of exfoliation syndrome, and poor patient compliance. Neither a positive family history of glaucoma nor vascular causes of death had had any effect on visual outcome. The study's reported risk of going blind from glaucoma in both eyes was 6 percent.⁵⁸⁶

Comparison of the success rates of ALT across various studies is difficult because of differences in the variables affecting outcomes. These variables include patient selection, technique, and the criteria for defining a successful outcome.⁴⁹¹ When ALT is performed as adjunct therapy following the use of one or more topical drugs, about 85 percent of eyes show a clinically significant reduction in IOP (6–9 mm Hg) within the first month following the procedure.^{502,503,587}

After 1 year, the reported rate of success in controlling the IOP with ALT is about 80 percent.^{487,489-491} After the first year, this rate declines about 5–15 percent per year.^{487-489,535,588,589} In general, IOP is successfully controlled in about one-half of patients 5 years after ALT^{488,489,590} and in one-tenth^{481,583} to one-third⁴⁸³ of patients 10 years after ALT. Repeated ALT has a lower success rate and a higher risk.⁵⁹¹ SLT appears to be equivalent to ALT in lowering IOP.⁵⁹²⁻⁵⁹⁴ Patients who previously failed to improve with ALT may have a greater reduction in IOP when treated with SLT.^{532,534}

One study reported that ALT achieved successful control of glaucoma in 77 percent of eyes in a predominantly African American population after mean follow-up of 2 years.⁵⁹⁵ After 5 years' extended follow-up, the overall success rate for the same population was 46 percent. ALT was more successful in the Caucasian patients than in the African Americans (65% and 32%, respectively).⁴⁹⁰ Other studies have found no racial differences in success rates for ALT.

In most cases, drug therapy must continue following ALT^{487,490}; only infrequently (25% of cases) can medication be reduced from pre-laser levels.^{587,596} The risk of failure to control the progression of glaucoma with ALT is higher in younger patients,^{504,597} when pretreatment IOP is very high, and when glaucoma is more severe.^{488,490}

Various types of filtration surgery to control glaucomatous damage have had success rates of about 75–95 percent in previously unoperated eyes.^{371,597} Postoperative medical therapy is needed in 15–50 percent of these patients.⁵⁹⁹⁻⁶⁰² The risk of permanent vision loss due to surgery is about 5 percent.³⁶⁹ Second-filtration procedures have a much lower success rate (36%).^{603,604} The use of intraoperative⁶⁰⁵ and postoperative⁶⁰⁶ antimetabolites, such as 5-fluorouracil (5-FU) and mitomycin, has improved the success rates for both initial and repeat filtration surgery.

Eyes that have undergone filtration surgery are twice as likely as those treated medically to have no further progression of glaucomatous damage.^{343,345,582} Surgically treated patients on postoperative steroids have achieved a mean postsurgical IOP of 13.2 mm Hg with a 6 percent rate of progression of VF after 5 years,³⁴⁴ and a mean IOP of 13.1 with a 17 percent rate of progression after 10 years.³⁵³ Although 15 mm Hg may be considered a target pressure following filtration surgery,³¹³ long-term follow-up has demonstrated progressive VF loss following filtration surgery in 18–40 percent of patients with POAG, despite having IOPs in the normal range.^{342,343,345,357,358,362,364,366,526,598,601,603,607}

Filtration procedures are less successful in African Americans, in patients with neovascular or uveitic glaucoma, in children, in patients who have had cataract surgery, and in those whose eyes have undergone previous filtration surgery.³⁷⁷ In research focusing on the sequence of treatment modalities, the AGIS investigators found racial differences in the progression of advanced glaucoma. The TAT sequence resulted in a greater reduction of IOP than the ATT sequence. For African Americans, the ATT sequence resulted in a lower rate of VF loss; for Caucasians, ATT was more effective during the first 15 months of follow-up, but thereafter the TAT sequence resulted in less progression of VF loss.⁶⁰²

With outcomes slightly less favorable than those for trabeculectomy, collagen wick NPDS has helped to reduce IOPs to the lower to middle teens^{517,518}; however, the NPDS success rate may or may not be higher with CW.⁵¹⁸ CW resulted in an average IOP of 14.1 mm Hg after 6 months as well as a decrease in the number of topical medications required for control of IOP.⁵¹⁵ Other studies have shown a decline in success rate with CW over time, and a greater success with the addition of postoperative antiglaucoma medications.^{518,522} Postoperative outcomes are also positively influenced (15%–41%) by injections of 5-FU (25%) or goniotomy with a Nd:YAG laser.^{519,522}

Viscocalostomy (VC) has reportedly been successful in reducing IOP below 22 mm Hg in black Africans whose IOP was previously uncontrolled⁶⁰⁹; however, no other investigators have achieved the 85 percent success rate reported for this procedure.^{521,531} VC does not result in as low a postoperative IOP as trabeculectomy,⁴⁶⁹ and VC success rates are higher when topical antiglaucoma medications are used postoperatively.^{521,531} A prospective study comparing VC with trabeculectomy in Caucasians who had no history of surgery reported success rates of 50 percent with trabeculectomy, and zero with VC at 6 months postsurgery. Success was defined as achieving IOP between 7 and 20 mm Hg without medication.⁶¹⁰

The high rates of progression of glaucoma in patients under treatment, especially the 50–75 percent using only topical medications, indicate the need to select target pressures that are, in general, no higher than 20 mm Hg for early glaucoma patients, but between 14 and 18 mm Hg for those with advanced glaucoma.^{343,345,351,352,355,360,367,501,582,610,611} A 30 percent reduction in pretreatment IOP is usually an effective goal for early glaucomas.^{345,347,348,353,372,612} In the AGIS, an IOP of 18 mm Hg or lower at every follow-up visit, averaging 12.3 mm Hg for 6–8 years, resulted in little change in the VF.²³⁶ Still, this study was not designed to evaluate the concept of target pressures; post hoc analysis revealed the 12.3 mm Hg IOP outcome. When appropriate target pressures are achieved and maintained, filtration surgery and medical therapy are equally effective in preserving the structure and functional integrity of the eye with OAG.⁶¹¹ Target pressures need adjustment on an individual basis,

depending on age, cumulative risk for the progression of glaucoma, and the severity of the disease.

Whereas in NTG the IOP is always below 21 mm Hg, aggressive medical or early surgical intervention is often required to achieve and maintain an appropriately low target pressure.^{513,514,612} It appears that lowering the IOP to 10–12 mm Hg can slow the progression of VF loss in NTG.^{506,512,613–616} The Collaborative Normal-Tension Glaucoma Study demonstrated that reducing IOP by at least 30 percent results in a slower rate of VF loss,^{347,348} a finding that was reconfirmed after follow-up periods of 5⁶¹⁷ and 10⁶¹⁸ years. Almost 60 percent of patients with NTG can maintain a 30 percent reduction in IOP with topical medication or ALT treatment or both.³⁶⁸ Nevertheless, even after lowering IOP by 30 percent, the disease continued to progress in 12 percent of eyes with NTG.³⁴⁷ The study of NTG also showed that NTG is either slow or nonprogressive in nature: About 65 percent of untreated eyes showed no progression of the disease over 4 years,⁶¹⁹ and about half of the eyes showed no change over 5–7 years.³⁴⁷ In eyes that did have progressive disease, the changes occurred slowly, and there was a great variation in their rate of deterioration.^{347,348,620}

d. Prognosis after Treatment of Secondary Open Angle Glaucoma

- **Pigmentary glaucoma.** A prospective study of 110 eyes with PDS or PG followed for an average of 27 months showed 61 percent remaining stable, 36 percent with progressing glaucoma, and 3 percent improving.⁴¹ About one-half of persons with PG eventually require laser or surgical treatment.⁸⁷ Patients with PG respond well to ALT, but in contrast to those with POAG, younger patients with PG appear to respond to ALT better than those who are older.⁵⁴⁴ Chronic injury from the accumulation of pigment in the trabecular meshwork may make some patients with PG more resistant to the ameliorating effect of ALT.⁴⁹² A higher percentage of patients with PG than with POAG, especially men,^{87,88} require surgery.

In some patients there appears to be an improvement or arrest of PG with increasing age, due to natural pupillary miosis and an

increase in axial thickness of the lens, which pushes the iris off the zonules.^{35,329,621} More often, however, the severity of PG increases with age, especially in patients who have increasing iris transillumination and increasing pigmentation of the cornea or lens.⁸⁷

- **Pseudoexfoliation glaucoma.** Eyes with PEG often manifest with higher IOP,¹⁰⁵ more rapid VF loss,⁵⁵⁰ and poorer response to medical therapy than those with POAG.⁵⁵¹⁻⁵⁵³ Though often successful initially, medical treatment of PEG is not very satisfactory over the long term.⁵⁴⁹ One study³⁴⁰ found similar rates of VF deterioration (70%–80%) in POAG and PEG patients after mean follow-up of 10.2 and 9.1 years, respectively. Treatment consisting of ALT^{544,586} and filtration surgery^{549,622-625} with supplemental medical therapy is at the very least as effective for PEG as for POAG. The fact that eyes with PEG may fail at a faster rate than those with POAG after both initial and consecutive ALT treatments mandates close postoperative surveillance.⁶²⁵ The reported success rates for trabeculectomy as a primary procedure are 79 percent at 3 years and 64 percent at 5 years in patients receiving medication for PEG.⁶²⁴

5. Management of Patients with Severe, Irreversible Vision Loss

Patients with POAG may suffer permanent vision loss. In such cases, consultation with an optometrist who has advanced training or clinical experience in vision rehabilitation is advisable. To reduce the debilitating effects of vision loss from POAG, patients should be evaluated to determine their potential to benefit from comprehensive low vision rehabilitation,* which includes the use of specialized optical devices and training. A task-oriented evaluation may include but is not limited to:

- Expanded patient history and needs assessment
- Evaluation of ocular health

*Refer to the AOA's Optometric Clinical Practice Guideline on Care of the Patient with Visual Impairment (Low Vision Rehabilitation).

- Low vision assessment of visual acuity (including eccentric viewing)
- Low vision refraction
- Binocular function assessment
- Supplemental testing, including perimetry, contrast sensitivity, and color vision
- Response to optical and electronic optical enhancement devices
- Response to selective absorption filters.

Once appropriate optical requirements have been determined, the clinician should educate and train the patient in methods of improving visual function with and without optical devices. The patient should be encouraged to use prescription optical and electronic optical enhancement devices for work, home, and social activities.

The goal of low vision rehabilitation is to reduce the effects of ocular morbidity and enhance the quality of life. In addition to optical intervention, the evaluation should include the need for non-optical devices, special lighting, posture aids, contrast enhancement, enlarged print, and non-visual methods or devices when appropriate. These devices, which significantly enhance the rehabilitative process, may be needed to complement the use of optical and electronic optical enhancement devices.

When indicated, the optometrist should recommend blind rehabilitation; occupational, vocational, and independent living counseling services; and psychosocial consultation. Patients should be informed of other resources, including agencies that register and provide services and advocacy for individuals who are legally blind or have significant visual impairment. These agencies can provide information regarding large-print and talking books, independent travel aids, and other devices geared to improve patients' quality of life and their ability to function in their own households.

The optometrist should provide written documentation of the patient's status regarding legal blindness for state and federal (Internal Revenue Service) tax requirements. Local and national support groups for significantly visually impaired persons assist many patients in coping

with the anxiety and concerns of vision loss. Such groups also provide information about resources to help patients function safely and productively in their environment.



CONCLUSION

Primary open angle glaucoma is one of the leading causes of blindness, especially in older and African American populations. Some persons who develop glaucoma have relatively low IOP, while others with rather high IOPs never show ON damage (OH). Untreated or inadequately treated glaucoma will progress to vision loss. Glaucoma cannot be prevented, but adequate treatment can reduce the rate and extent of additional damage.

Although it appears that large population screenings would greatly assist in the early detection and, in turn, the early treatment of glaucoma, traditional screening tests and procedures lack adequate specificity and sensitivity. A comprehensive eye examination is essential for the earliest possible diagnosis of POAG. Periodic evaluation of a glaucoma suspect is required to detect subtle ON, NFL, PPA, and VF changes that may precede the overt clinical signs of the disease.

Controversy exists about the relationship between the level of IOP and progressive damage from glaucoma. Lowering IOP appears to reduce the incidence of glaucoma and its progression in both POAG and NTG patients. The treatment of POAG usually begins with the use of one and then multiple topical medications. As achievement of the target pressure becomes clinically more difficult with advancing disease, medical treatment is usually followed by laser trabeculoplasty and then filtration surgery.

Coordination of the patient's care, which is essential to increasing the probability of success, involves communication with the patient's family doctor, consultation with a glaucoma specialist as appropriate, patient education regarding the disease, proper patient instruction, and diligence to ensure maximum patient compliance with the therapeutic regimen. Management of a glaucoma patient requires periodic comprehensive eye examinations, the frequency of which will vary, depending on the severity and stability of the disease.

The effectiveness of the treatment of POAG depends on the specific modality and varies significantly between studies. The majority of

POAG patients with maximally tolerated medical therapy will show progression of the disease within 10 years of initial treatment. This rate of progression can be reduced with reduction of the IOP. In only about one-half of cases is glaucoma adequately controlled 5 years after ALT; no more than one-third after 10 years. Filtration surgery in a previously unoperated eye with POAG has a high initial success rate. Target IOPs for maintaining stability during the treatment of POAG need to be adjusted on an individual basis, depending on patient age, cumulative risk for progression of the disease, and severity of the glaucoma.



III. REFERENCES

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 2006; 90:262-7.
2. Friedman DS, Wolfs RC, O'Colmain BJ; Eye Diseases Prevalence Research Group. Prevalence of open-angle glaucoma in the United States. *Arch Ophthalmol* 2004; 122:532-8.
3. Congdon N, O'Colmain B, Klaver CC; Eye Diseases Prevalence Research Group. Causes and prevalence of visual impairment among adults in the United States. *Arch Ophthalmol* 2004; 122:477-85.
4. Leibowitz HM, Krueger DE, Maunier LR, et al. The Framingham Eye Study monograph: An ophthalmological and epidemiological study of cataracts, glaucoma, diabetic retinopathy, macular degeneration, and visual acuity in a general population of 2631 adults, 1973-1975. *Surv Ophthalmol* 1980; 24(suppl):335-610.
5. Kahn HA, Moorehead HB. Statistics on blindness in the model reporting areas, 1969-1970. DHEW publication no. (NIH) 73-427. Washington, DC: US Government Printing Office, 1973.
6. Sommer A, Tielsch JM, Katz J, et al. Racial differences in the cause-specific prevalence of blindness in East Baltimore. *N Engl J Med* 1991; 325:1412-7.
7. Hiller R, Kahn HA. Blindness from glaucoma. *Am J Ophthalmol* 1975; 80:62-9.
8. Leske MC, Rosenthal J. The epidemiologic aspects of open-angle glaucoma. *Am J Epidemiol* 1979; 109:250-72.
9. Varma R, Ying-Lai M, Francis BA, et al. Prevalence of open-angle glaucoma and ocular hypertension in Latinos. *Ophthalmology* 111: 1439-48, 2004.

10. Tielsch JM. The epidemiology of primary open angle glaucoma. *Ophthalmol Clin North Am* 1991; 4:649-57.
11. Lewis TL. Definition and classification of glaucomas. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw-Hill, 2001:3-5.
12. Bengtsson B. The prevalence of glaucoma. *Br J Ophthalmol* 1981; 65:46-9.
13. Hollows FC, Graham PA. Intraocular pressure, glaucoma, and glaucoma suspects in a defined population. *Br J Ophthalmol* 1966; 50:570-86.
14. Sommer A, Tielsch JM, Katz J, et al. Relationship between intraocular pressure and primary open angle glaucoma among black and white Americans. The Baltimore Eye Survey. *Arch Ophthalmol* 1991; 109:1090-5.
15. Alvarado J, Murphy C, Juster R. Trabecular meshwork cellularity in primary open-angle glaucoma and nonglaucomatous normals. *Ophthalmology* 1984; 91:564-79.
16. Grierson I, Calthorpe CM. Characteristics of meshwork cells and age changes in the outflow system of the eye: their relevance to primary open-angle glaucoma. In: Mills KB, ed. *Glaucoma*. Proc 4th Symp Northern Eye Inst, Manchester, UK: 1988:12-31.
17. Grierson I. What is open angle glaucoma? *Eye* 1987; 1:15-28.
18. Lewis TL, Chronister CL. Etiology and pathophysiology of primary open-angle glaucoma. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw Hill, 2001:63-80.
19. Quigley HA, Nickells RW, Pease ME, et al. Retinal ganglion cell death in experimental monkey glaucoma and axotomy occurs by apoptosis. *Invest Ophthalmol Vis Sci* 1995; 36:774-86.

References 83

20. Kerrigan LA, Zack DJ, Quigley HA, et al. TUNEL-positive ganglion cells in human primary open-angle glaucoma. *Arch Ophthalmol* 1997; 115:1031-5.
21. Nickells RW. Retinal ganglion cell death in glaucoma: the how, the why, and the maybe. *J Glaucoma* 1996; 5:345-56.
22. Mey J, Thanos S. Intravitreal injection of neurotrophic factor support the survival of axotomized retinal ganglion cells in adult rats in vivo. *Brain Res* 1993; 602:304-17.
23. Olney JW. Glutamate-induced retinal degeneration in neonatal mice: electron microscopy of the acutely evolving lesion. *J Neuropath Exp Neurol* 1969; 28:455-74.
24. Pow DV, Barnett NL, Penfold P. Are neuronal transporters relevant in retinal glutamate homeostasis? *Neurochem Int* 2000; 37:191-8.
25. Sucher NJ, Lipton SA, Dreyer EB. Molecular basis of glutamate toxicity in retinal ganglion cells. *Vision Res* 1997; 37:3483-93.
26. Dreyer EB, Zurakowski D, Schumer RA, et al. Elevated glutamate in the vitreous body of humans and monkeys with glaucoma. *Arch Ophthalmol* 1996; 114:299-305.
27. Hahn JS, Aizenman E, Lipton SA. Central mammalian neurons normally resistant to glutamate toxicity are made sensitive by elevated extracellular Ca^{2+} : toxicity is blocked by the N-methyl-D-aspartate antagonist MK-801. *Proc Natl Acad Sci USA* 1988; 85:6556-60.
28. Dawson VL, Dawson TM, Bartley DA, et al. Mechanisms of nitric oxide-mediated neurotoxicity in primary brain cultures. *J Neurosci* 1993; 13:2651-61.
29. Dawson TM, Dawson VL. Nitric oxide: actions and pathological roles. *Neuroscientist* 1994; 1:9-20.

84 Open Angle Glaucoma

30. Azuma N, Kawamura M, Kohsaka S. Morphological and immunohistochemical studies on degenerative changes of the retina and the optic nerve in neonatal rats injected with monosodium-L-glutamate. *Nippon Ganka Gakkai Zasshi* 1983; 93:72-9.
31. Vorwerk CK, Lipton SA, Zurakowski D, et al. Chronic low dose glutamate is toxic to retinal ganglion cells; toxicity blocked by memantine. *Invest Ophthalmol Vis Sci* 1996; 37:1618-24.
32. Neufeld AA, Hernandez MR, Gonzalez M. Nitric oxide synthase in the human glaucomatous optic nerve head. *Arch Ophthalmol* 1997; 115:497-503.
33. Cockburn DM. Does reduction of intraocular pressure (IOP) prevent visual field loss in glaucoma? *Am J Optom Physiol Opt* 1983; 60:703-11.
34. O'Brien C, Schwartz B, Takamoto T, Wu DC. Intraocular pressure and the rate of visual field loss in chronic open-angle glaucoma. *Am J Ophthalmol* 1991; 111:491-500.
35. Levkovitch-Verbin H, Quigley HA, Kerrigan-Baumrind LA, et al. Optic nerve transection in monkeys may result in secondary degeneration of retinal ganglion cells. *Invest Ophthalmol Vis Sci* 2001; 42:975-82.
36. Campbell DG. Pigmentary dispersion and glaucoma. A new theory. *Arch Ophthalmol* 1979; 97:1667-72.
37. Campbell DG, Schertzer RM. Pathophysiology of pigment dispersion syndrome and pigmentary glaucoma. *Curr Opin Ophthalmol* 1995; 6:96-101.
38. Karickhoff JR. Reverse pupillary block in pigmentary glaucoma: followup and new developments. *Ophthalmic Surg* 1993; 24:562-3.

References 85

39. Campbell DG. Iridotomy, blinking and pigmentary glaucoma. *J Glaucoma* 1993; 2:44-9.
40. Pavlin CJ, Macken P, Trope GE, et al. Accommodation and iridotomy in the pigment dispersion syndrome. *Ophthalmic Surg Lasers* 1996; 27:113-20.
41. Richter R, Richardson TM, Grant WM. Pigmentary dispersion syndrome and pigmentary glaucoma: a prospective study of the natural history. *Arch Ophthalmol* 1986; 104:211-5.
42. Richardson TM, Hutchinson BT, Grant WM. The outflow tract in pigmentary glaucoma: a light and electron microscopic study. *Arch Ophthalmol* 1977; 95:1015-25.
43. Epstein DL. Pigment dispersion and pigmentary glaucoma. In: Chandler PA, Grant WM, eds. *Glaucoma*. Philadelphia: Lea & Febiger 1979:122-9.
44. Jerndal T. Goniodysgenesis and pigmentary glaucoma. *Acta Ophthalmol* 1969; 47:424-9.
45. Donaldson DD. Transillumination of the iris. *Trans Am Ophthalmol Soc* 1974; 62:89-106.
46. Sugar HS. Pigmentary glaucoma and the glaucoma associated with exfoliation-pseudoexfoliation syndrome: update. Robert N Shaffer lecture. *Ophthalmology* 1984; 91:307-10.
47. Sugar HS. The pseudoexfoliation syndrome. *Metab Pediatr Syst Ophthalmol* 1982; 6:227-35.
48. Ringvold A. On the occurrence of pseudo-exfoliation material in the extrabulbar tissue from patients with pseudo-exfoliation syndrome of the eye. *Acta Ophthalmol* 1973; 51:411-8.
49. Speakman JS, Ghosh M. The conjunctiva in senile lens exfoliation. *Arch Ophthalmol* 1976; 94:1757-9.

86 Open Angle Glaucoma

50. Konstas AG, Marshall GE, Camerson SA, Lee W. Morphology of iris vasculopathy in exfoliation glaucoma. *Acta Ophthalmol (Copenh)* 1993; 71:751-9.
51. Morrison JC, Green WR. Light microscopy of the exfoliation syndrome. *Acta Ophthalmol (Copenh)* 1988; 184(suppl):5-27.
52. Schlötzer-Schrehardt U, Naumann GO. A histopathologic study of zonular instability in pseudoexfoliation syndrome. *Am J Ophthalmol* 1994; 118:730-43.
53. Asano N, Schlötzer-Schrehardt U, Naumann GOH. A histopathologic study of iris changes in pseudoexfoliation syndrome. *Ophthalmology* 1995; 102:1279-90.
54. Ringvold A, Husby G. Pseudo-exfoliation material—an amyloid-like substance. *Exp Eye Res* 1973; 17:289-99.
55. Dark AJ, Streeten BW, Cornwall CC. Pseudoexfoliative disease of the lens: a study in electron microscopy and histochemistry. *Br J Ophthalmol* 1977; 61:462-72.
56. Eagle RC Jr, Font RL, Fine BS. The basement membrane exfoliation syndrome. *Arch Ophthalmol* 1979; 97:510-5.
57. Davanger M. The pseudo-exfoliation syndrome: a scanning electron microscopy study. I. The anterior lens surface. *Acta Ophthalmol* 1975; 53:809-20.
58. Streeten BW, Dark AJ, Barnes CW. Pseudoexfoliative material and oxytalan fibers. *Exp Eye Res* 1984; 38:523-31.
59. Aasved H. Intraocular pressure in eyes with and without fibrillogluthia epitheliocapsularis. *Acta Ophthalmol* 1971; 49:601-10.
60. Roth M, Epstein DL. Exfoliation syndrome. *Am J Ophthalmol* 1980; 89:477-81.

References 87

61. Krause U, Helve J, Forsius H. Pseudoexfoliation of the lens capsule and liberation of pigment. *Acta Ophthalmol* 1973; 51:39-46.
62. Mapstone R. Pigment release. *Br J Ophthalmol* 1981; 65:258-63.
63. Prince AM, Streeten BW, Ritch R, et al. Preclinical diagnosis of pseudoexfoliation syndrome. *Arch Ophthalmol* 1987; 105:1076-82.
64. Vesti E, Kivelä T. Exfoliation syndrome and exfoliation glaucoma. *Prog Ret Eye Res* 2000; 19:345-68.
65. Benedikt O, Roll P. The trabecular meshwork of a non-glaucomatous eye with the exfoliation syndrome. *Virchows Archiv A* 1979; 384:347-55.
66. Prevent Blindness America. Vision problems in the U.S. Schaumburg, IL: PBA, 1994.
67. Tielsch JM, Sommer A, Katz J, et al. Racial variations in the prevalence of primary open-angle glaucoma. The Baltimore Eye Survey. *JAMA* 1991; 266:369-74.
68. Quigley HA, Vitale S. Models of open-angle glaucoma incidence and prevalence in the United States. *Invest Ophthalmol Vis Sci* 1997; 38:83-91.
69. Dielemans I, Vingerling JR, Wolfs RC, et al. The prevalence of primary open-angle glaucoma in a population-based study in The Netherlands. The Rotterdam Study. *Ophthalmology* 1994; 101:1851-5.
70. Klein BE, Klein R, Sponsel WE, et al. Prevalence of glaucoma. The Beaver Dam Eye Study. *Ophthalmology* 1992; 99:1499-504.
71. Leske MC. The epidemiology of open-angle glaucoma: a review. *Am J Epidemiol* 1983; 118:166-91.

88 Open Angle Glaucoma

72. Mitchell P, Smith W, Attebo K, Healey PR. Prevalence of open-angle glaucoma in Australia. The Blue Mountains Eye Study. *Ophthalmology* 1996; 103:1661-9.
73. Wensor MD, McCarty CA, Stanislavsky YL, et al. The prevalence of glaucoma in the Melbourne Visual Impairment Project. *Ophthalmology* 1998; 105:733-9.
74. Wolfs RC, Borger PH, Ramrattan RS, et al. Changing views on open-angle glaucoma: definitions and prevalences—the Rotterdam Study. *Invest Ophthalmol Vis Sci* 2000; 41:3309-21.
75. Kahn HA, Milton RC. Alternative definitions of open-angle glaucoma. Effect on prevalence and associations in the Framingham Eye Study. *Arch Ophthalmol* 1980; 98:2172-7.
76. Bankes JL, Perkins ES, Tsolakis S, Wright JE. Bedford glaucoma survey. *Br Med J* 1968; 1:791-6.
77. Armaly MF. On the distribution of applanation pressure and arcuate scotoma. In: Paterson G, Miller SJH, Paterson GD, eds. *Drug mechanisms in glaucoma*. Boston: Little, Brown, & Co, 1966:167-89.
78. Podgor MJ, Leske MC, Ederer F. Incidence estimates for lens changes, macular changes, open-angle glaucoma, and diabetic retinopathy. *Am J Epidemiol* 1983; 118:206-12.
79. Leske MC, Connell AMS, Wu SY, et al. Incidence of open-angle glaucoma: the Barbados Eye Study. The Barbados Eye Studies Group. *Arch Ophthalmol* 2001; 119:89-95.
80. Kitazawa Y, Horie T, Aoki S, et al. Untreated ocular hypertension. A long-term prospective study. *Arch Ophthalmol* 1977; 95:1180-4.
81. Sommer A. Intraocular pressure and glaucoma. *Am J Ophthalmol* 1989; 107:186-8.

References 89

82. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002; 120:701-13.
83. Gordon MO, Beiser JA, Brandt JD, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:714-20.
84. Medeiros FA, Weinreb RN, Sample PA, et al. Validation of a predictive model to estimate the risk of conversion from ocular hypertension to glaucoma. *Arch Ophthalmol* 2005; 123:1351-60.
85. Ocular Hypertension Treatment Study Group, European Glaucoma Prevention Study Group, Gordon MO, Torri V, Miglior S, et al. Validated prediction model for the development of primary open-angle glaucoma in individuals with ocular hypertension. *Ophthalmology* 2007; 114:10-9.
86. Ritch R, Steinberger D, Leibmann JM. Prevalence of pigment dispersion syndrome in a population undergoing glaucoma screening. *Am J Ophthalmol* 1993; 115:707-10.
87. Farrar SM, Shields MB, Miller KN, Stoup CM. Risk factors for the development and severity of glaucoma in the pigment dispersion syndrome. *Am J Ophthalmol* 1989; 108:223-9.
88. Scheie HG, Cameron JD. Pigment dispersion syndrome: a clinical study. *Br J Ophthalmol* 1981; 65:264-9.
89. Sugar HS. Pigmentary glaucoma. A 25-year review. *Am J Ophthalmol* 1966; 62:499-507.
90. Sugar HS, Barbour FA. Pigmentary glaucoma: a rare clinical entity. *Am J Ophthalmol* 1949; 32:90-2.

90 Open Angle Glaucoma

91. Davidson JA, Brubaker RF, Ilstrup DM. Dimensions of the anterior chamber in pigment dispersion syndrome. *Arch Ophthalmol* 1983; 101:81-3.
92. Mandelkorn RM, Hoffman ME, Olander KW, et al. Inheritance and the pigmentary dispersion syndrome. *Ophthalmic Paediatr Genet* 1985; 6:85-91.
93. McDermott JA, Ritch R, Berger A, Wang RF. Familial occurrence of pigmentary dispersion syndrome. *Invest Ophthalmol Vis Sci* 1987; 28(suppl):136.
94. Andersen KL, Pralea AM, DelBono EA, et al. Localization of the gene for pigment dispersion syndrome to chromosome 7q35-36. *Arch Ophthalmol* 1997; 115:384-8.
95. Dell WM. The epidemiology of the pseudo-exfoliation syndrome. *J Am Optom Assoc* 1985; 56:113-9.
96. Cashwell LF Jr, Shields MB. Exfoliation syndrome. Prevalence in a southeastern United States population. *Arch Ophthalmol* 1988; 106:335-6.
97. Hiller R, Sperduto RD, Krueger DE. Pseudoexfoliation, intraocular pressure, and senile lens changes in a population based survey. *Arch Ophthalmol* 1982; 100:1080-2.
98. Kozart DM, Yanoff M. Intraocular pressure status in 100 consecutive patients with exfoliation syndrome. *Ophthalmology* 1982; 89:214-8.
99. Henry JC, Krupin T, Schmitt M, et al. Long-term follow-up of pseudoexfoliation and the development of elevated intraocular pressure. *Ophthalmology* 1987; 94:545-52.
100. Ball SF. Exfoliation prevalence in the glaucoma population of South Louisiana. *Acta Ophthalmol* 1988; 66(suppl 184):93-8.

References 91

101. Sotirova V, Irkec M, Percin EF, et al., and the PEX Molecular Study Group. Molecular genetic study of families with pseudoexfoliation syndrome suggests two putative loci on 2p14-2cen and 2q35-36 regions. *Invest Ophthalmol Vis Sci* 1999; 40(suppl):512.
102. Mizuno K, Muroi S. Cycloscopy of pseudoexfoliation. *Am J Ophthalmol* 1979; 87:513-8.
103. Layden WE, Shaffer RN. Exfoliation syndrome. *Am J Ophthalmol* 1974; 78:835-41.
104. Kivelä T, Hietanen J, Uusitalo M. Autopsy analysis of clinically unilateral exfoliation syndrome. *Invest Ophthalmol Vis Sci* 1997; 38:2008-15.
105. Ringvold A, Bilka S, Elsås T. The middle-Norway eye-screening study: II. Prevalence of simple and capsular glaucoma. *Acta Ophthalmol* 1991; 69:273-80.
106. Horven I. Exfoliation syndrome: incidence and prognosis of glaucoma capsulare in Massachusetts. *Arch Ophthalmol* 1966; 76:505-11.
107. Grodum K, Heijl A, Bengtsson B. Risk of Glaucoma in Ocular Hypertension with and without Pseudoexfoliation. *Ophthalmology* 112; 386-3390, 2005
108. Armaly MF, Krueger DE, Maunder L, et al. Biostatistical analysis of the collaborative glaucoma study. I. Summary report of the risk factors for glaucomatous visual-field defects. *Arch Ophthalmol* 1980; 98:2163-71.
109. Coulehan JL, Helzlsouer KJ, Rogers KD, Brown SI. Racial differences in intraocular tension and glaucoma surgery. *Am J Epidemiol* 1980; 111:759-68.

92 Open Angle Glaucoma

110. Martin MJ, Sommer A, Gold EB, Diamond EL. Race and primary open-angle glaucoma. *Am J Ophthalmol* 1985; 99:383-7.
111. Wilensky JT, Gandhi N, Pan T. Racial influences in open-angle glaucoma. *Ann Ophthalmol* 1978; 10:1398-402.
112. Wilson R, Richardson TM, Hertzmark E, Grant WM. Race as a risk factor for progressive glaucomatous damage. *Ann Ophthalmol* 1985; 17:653-9.
113. Mason RP, Kosoko O, Wilson MR, et al. National Survey of the Prevalence and Risk Factors of Glaucoma in St. Lucia, West Indies. Part I: Prevalence findings. *Ophthalmology* 1989; 96:1363-8.
114. Leske MC, Connell AM, Schachat AP, Hyman L, and the Barbados Eye Study Group. The Barbados Eye Study. Prevalence of open angle glaucoma. *Arch Ophthalmol* 1994; 112:821-9.
115. Shiose Y. Prevalence and clinical aspects of low tension glaucoma. In: Henkind P, ed. *Acta XXIV Int Cong of Ophthalmol*. Philadelphia: JB Lippincott, 1983:587-91.
116. Foster PJ, Wong JS, Wong E, et al. Accuracy of clinical estimates of intraocular pressure in Chinese eyes. *Ophthalmology* 2000; 107:1816-21.
117. Netland PA, Wiggs JL, Dreyer EB. Inheritance of glaucoma and genetic counseling of glaucoma patients. *Int Ophthalmol Clin* 1993; 33:101-20.
118. Teikari JM. Genetic factors in open-angle (simple and capsular) glaucoma: a population-based twin study. *Acta Ophthalmol* 1987; 65:715-20.
119. Miller SJ. Genetics of glaucoma and family studies. *Trans Ophthalmol Soc UK* 1978; 98:290-2.

References 93

120. Rosenthal AR, Perkins ES. Family studies in glaucoma. *Br J Ophthalmol* 1985; 69:664-7.
121. Perkins ES. Family studies in glaucoma. *Br J Ophthalmol* 1974; 58:529-35.
122. Armaly MF, Monstavičius BF, Sayegh RE. Ocular pressure and aqueous outflow in siblings. *Arch Ophthalmol* 1968; 80:354-60.
123. Becker B, Kolker AE, Roth FD. Glaucoma family study. *Am J Ophthalmol* 1969; 50:557-67.
124. Kellerman L, Posner A. The value of heredity in detection and study of glaucoma. *Am J Ophthalmol* 1955; 40:681-5.
125. Leske MC, Connell AM, Wu SY, et al. Risk factors for open-angle glaucoma. The Barbados Eye Study. *Arch Ophthalmol* 1995; 113:918-24.
126. Tielsch JM, Katz J, Sommer A, et al. Family history and the risk of primary open angle glaucoma. The Baltimore Eye Study. *Arch Ophthalmol* 1994; 112:69-73.
127. Wolfs RC, Klaver CC, Ramrattan RS, et al. Genetic risk of primary open-angle glaucoma. Population-based familial aggregation study. *Arch Ophthalmol* 1998; 116:1640-5.
128. Wilson MR, Hertzmark E, Walker AM, et al. A case-control study of risk factors in open angle glaucoma. *Arch Ophthalmol* 1987; 105:1066-71.
129. Seddon JM, Schwartz B, Flowerdew G. Case-control study of ocular hypertension. *Arch Ophthalmol* 1983; 101:891-4.
130. Levene RZ, Workman PL, Broder SW, Hirschhorn K. Heritability of ocular pressure in normal and suspect ranges. *Arch Ophthalmol* 1970; 84:730-4.

94 Open Angle Glaucoma

131. Armaly MF. Genetic determination of cup/disc ratio of the optic nerve. *Arch Ophthalmol* 1967; 78:35-43.
132. Craig JE, Mackey DA. Glaucoma genetics: Where are we? Where will we go? *Curr Opin Ophthalmol* 1999; 10:126-34.
133. Wirtz MK, Samples JR, Rust K, et al. GLC1F, a new primary open-angle glaucoma locus, maps to 7q35-q36. *Arch Ophthalmol* 1999; 117:237-41.
134. Damji KF, Bains HS, Stefansson E, et al. Is pseudoexfoliation syndrome inherited? A review of genetic and nongenetic factors and a new observation. *Ophthalmic Genet* 1998; 19:175-85.
135. Stoilova D, Child A, Tritan OC, et al. Localization of locuses (GLC1B) for adult-onset primary open angle glaucoma to the 2cen-q13 region. *Genomics* 1996; 36:142-50.
136. Budde WM. Heredity in primary open-angle glaucoma. *Curr Opin Ophthalmol* 2000; 11:101-6.
137. Stone EM, Fingert JH, Alwand WL, et al. Identification of a gene that causes primary open angle glaucoma. *Science* 1997; 275:668-70.
138. Fingert JH, Heon E, Liebmann JM, et al. Analysis of myocilin mutations in 1,703 glaucoma patients from five different populations. *Hum Mol Genet* 1999; 8:899-905.
139. Tielsch JM. The epidemiology and control of open angle glaucoma: a population-based perspective. *Annu Rev Public Health* 1996; 17:121-36.
140. Quigley HA, Enger C, Katz J, et al. Risk factors for the development of glaucomatous visual field loss in ocular hypertension. *Arch Ophthalmol* 1994; 112:644-9.

References 95

141. Cartwright MJ, Anderson DR. Correlation of asymmetric damage with asymmetric intraocular pressure in normal-tension glaucoma (low-tension glaucoma). *Arch Ophthalmol* 1988; 106:898-900.
142. Crichton A, Drance SM, Douglas GR, Schulzer M. Unequal intraocular pressure and its relation to asymmetric visual field defects in low-tension glaucoma. *Ophthalmology* 1989; 96:1312-4.
143. Kass MA, Gordon MO, Hoff MR, et al. Topical timolol administration reduces the incidence of glaucomatous damage in ocular hypertensive individuals. A randomized double-masked, long-term clinical trial. *Arch Ophthalmol* 1989; 107:1590-8.
144. Armaly MF. Ocular pressure and visual fields. A ten-year follow-up study. *Arch Ophthalmol* 1969; 81:25-40.
145. Perkins ES. The Bedford Glaucoma Survey. I. Long-term follow-up of borderline cases. *Br J Ophthalmol* 1973; 57:179-85.
146. Nemesure B, Honkanen R, Hennis A, et al. Incident open angle glaucoma and intraocular pressure. *Ophthalmology* 114: 1810-1815, 2007.
147. Asrani S, Zeimer R, Wilensky J, et al. Large diurnal fluctuations in intraocular pressure are an independent risk factor in patients with glaucoma. *J Glaucoma*. 2000; 9:134-42.
148. Bengtsson B, Leske MC, Hyman L, et al. Fluctuation of intraocular pressure and glaucoma progression in the early manifest glaucoma trial. *Ophthalmology* 2007; 114:205-9.
149. Medeiros FA, Weinreb RN, Zangwill LM, et al. Long-term intraocular pressure fluctuations and risk of conversion from ocular hypertension to glaucoma. *Ophthalmology* 2008; 115:934-40. Epub 2007 Oct 15.

96 Open Angle Glaucoma

150. Brandt JD, Beiser JA, Kass MA, et al. Central corneal thickness in the Ocular Hypertension Treatment Study. *Ophthalmology* 108: 1779-88; 2001.
151. Bengtsson B, Heijl A. A long-term prospective study of risk factors for glaucomatous visual field loss in patients with ocular hypertension. *J Glaucoma* 2005; 142:135-8.
152. Pederson JE, Anderson DR. The mode of progressive disc cupping in ocular hypertension and glaucoma. *Arch Ophthalmol* 1980; 98:490-5.
153. Read RM, Spaeth GL. The practical clinical appraisal of the optic disc in glaucoma: the natural history of cup progression and some specific disc-field correlations. *Trans Am Acad Ophthalmol Otolaryngol* 1974; 78:255-74.
154. Sommer A, Pollack I, Maumenee AE. Optic disc parameters and onset of glaucomatous field loss. I. Methods and progressive changes in disc morphology. *Arch Ophthalmol* 1979; 97:1444-8.
155. Yablonski ME, Zimmerman TJ, Kass MA, Becker B. Prognostic significance of optic disc cupping in ocular hypertensive patients. *Am J Ophthalmol* 1980; 89:585-92.
156. Perkins ES, Phelps CD. Open angle glaucoma, ocular hypertension, low-tension glaucoma, and refraction. *Arch Ophthalmol* 1982; 100:1464-7.
157. Mitchell P, Hourihan F, Sanbach J, Wang JJ. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. *Ophthalmology* 1999; 106:2010-15.
158. Kahn HA, Leibowitz HM, Ganley JP, et al. The Framingham Eye Study. II. Association of ophthalmic pathology with single variables previously measured in the Framingham Heart Study. *Am J Epidemiol* 1977; 106:33-41.

References 97

159. Becker B. Diabetes mellitus and primary open-angle glaucoma: The XXVII Edward Jackson Memorial Lecture. *Am J Ophthalmol* 1971; 71:1-16.
160. Clark CV, Mapstone R. The prevalence of diabetes mellitus in the family history of patients with primary glaucoma. *Doc Ophthalmol* 1986; 62:161-3.
161. Dielemans I, deJong PT, Stolk R, et al. Primary open-angle glaucoma, intraocular pressure, and diabetes mellitus in the general elderly population. The Rotterdam Study. *Ophthalmology* 1996; 103:1271-5.
162. Klein BE, Klein R, Moss SE. Intraocular pressure in diabetic persons. *Ophthalmology* 1984; 91:1356-60.
163. Klein BE, Klein R, Jensen SC. Open-angle glaucoma and older-onset diabetes. The Beaver Dam Eye Study. *Ophthalmology* 1994; 101:1173-7.
164. Mitchell P, Smith W, Chey T, Healey PR. Open-angle glaucoma and diabetes: the Blue Mountains Eye Study, Australia. *Ophthalmology* 1997; 104:712-8.
165. Reynolds DC. Relative risk factors in chronic open angle glaucoma: an epidemiological study. *Am J Optom Physiol Optics* 1997; 54:116-20.
166. Katz J, Sommer A. Risk factors for primary open angle glaucoma. *Am J Prev Med* 1988; 4:110-4.
167. Morgan RW, Drance SM. Chronic open-angle glaucoma and ocular hypertension. An epidemiological study. *Br J Ophthalmol* 1975; 59:211-5.
168. Armaly MF, Baloglou PJ. Diabetes mellitus and the eye. II. Intraocular pressure and aqueous outflow facility. *Arch Ophthalmol* 1967; 77:493-502.

98 Open Angle Glaucoma

169. Christiansson J. Intraocular pressure in diabetes mellitus. *Acta Ophthalmol (Copenh)* 1961; 39:155-67.
170. Tielsch JM, Katz J, Quigley HA, et al. Diabetes, intraocular pressure, and primary open-angle glaucoma in the Baltimore Eye Survey. *Ophthalmology* 1995; 102:48-53.
171. Drance SM, Douglas GR, Wijsman K, et al. Response of blood flow to warm and cold in normal and low-tension glaucoma patients. *Am J Ophthalmol* 1988; 105:35-9.
172. Gasser P. Ocular vasospasm: a risk factor in the pathogenesis of low-tension glaucoma. *Int Ophthalmol* 1989; 13:281-90.
173. Phelps CD, Corbett JJ. Migraine and low-tension glaucoma. A case-control study. *Invest Ophthalmol Vis Sci* 1985; 26:1105-8.
174. Leske MC, Podgor MJ. Intraocular pressure, cardiovascular risk variables, and visual field defects. *Am J Epidemiol* 1983; 118:280-7.
175. Tielsch JM, Katz J, Quigley HA, et al. Hypertension, perfusion pressure and primary open angle glaucoma: a population-based assessment. *Arch Ophthalmol* 1995; 113:216-21.
176. Ishida K, Yamamoto T, Kitazawa Y. Clinical factors associated with progression of normal-tension glaucoma. *J Glaucoma* 1998; 7:372-7.
177. Drance SM, Sweeney VP, Morgan RW, Feldman F. Studies of factors involved in the production of low tension glaucoma. *Arch Ophthalmol* 1973; 89:457-65.
178. Meyer JH, Brandi-Dohrn J, Funk J. Twenty-four hour blood pressure monitoring in normal tension glaucoma. *Br J Ophthalmol* 1996; 80:864-7.

References 99

179. Graham SL, Drance SM, Wijsman K, et al. Ambulatory blood pressure monitoring in glaucoma. The nocturnal dip. *Ophthalmology* 1995; 102:61-9.
180. Leske MC, Heijl A, Hyman L, et al. Predictors of long-term progression in the Early Manifest Glaucoma Trial. *Ophthalmology* 2007; 114:1965-72.
181. Leske MC, Wu SY, Hennis A, et al. BESS Study Group. Risk factors for incident open angle glaucoma. *Ophthalmology* 2008; 115:85-93. Epub 2007 Jul 16.
182. Hafez AS, Bizzarro RL, Lesk MR. Evaluation of optic nerve head and peripapillary retinal blood flow in glaucoma patients, ocular hypertensives, and normal subjects. *Am J Ophthalmol* 2003; 136:1022-31.
183. Quigley HA. Reappraisal of the mechanism of glaucomatous optic nerve damage. *Eye* 1987; 1:318-22.
184. Quigley HA, Hohman RM, Addicks EM, et al. Morphologic changes in the lamina cribrosa correlated with neural loss in open-angle glaucoma. *Am J Ophthalmol* 1983; 95:673-91.
185. Quigley HA. The pathogenesis of optic nerve damage in glaucoma. Symposium on the laser in ophthalmology and glaucoma update. *Trans New Orleans Acad Ophthalmol* 1985;111-28.
186. Hayreh SS. The pathogenesis of optic nerve lesions in glaucoma. Symposium: the optic disc in glaucoma. *Trans Am Acad Ophthalmol Otolaryngol* 1976; 81:197-213.
187. Zeimer RC, Ogura Y. The relationship between glaucomatous damage and optic nerve head mechanical compliance. *Arch Ophthalmol* 1989; 107:1232-4.

100 Open Angle Glaucoma

188. Palmberg P. The rationale and effectiveness of glaucoma therapy. Distributed at the Ann Meeting Am Glaucoma Soc, Miami, FL, Dec 1988.
189. Jay JL, Murdoch JR. The rate of visual field loss in untreated primary open angle glaucoma. *Br J Ophthalmol* 1993; 77:176-8.
190. Kass MA, Kolker AE, Becker B. Prognostic factors in glaucomatous visual field loss. *Arch Ophthalmol* 1976; 94:1274-6.
191. Quigley HA, Dunkelberger BS, Green WR. Retinal ganglion cell atrophy correlated with automated perimetry in human eyes with glaucoma. *Am J Ophthalmol* 1989; 107:453-64.
192. Kerrigan-Baumrind LA, Quigley HA, Pease, ME, et al. Number of ganglion cells in glaucoma eyes compared with threshold visual field tests in the same persons. *Invest Ophthalmol Vis Sci* 2000; 41:741-8.
193. Tielsch JM. Screening for glaucoma continuing dilemma. *Proc New Orleans Acad Ophthalmol* 1991; 40:1-11.
194. Tielsch JM, Katz J, Singh K, et al. A population-based evaluation of glaucoma screening. The Baltimore Eye Survey. *Am J Epidemiol* 1991; 134:1102-10.
195. Levi L, Schwartz B. Glaucoma screening in the health care setting. *Surv Ophthalmol* 1983; 28:164-74.
196. Gottlieb LK, Schwartz B, Pauker SG. Glaucoma screening. A cost-effectiveness analysis. *Surv Ophthalmol* 1983; 28:206-26.
197. Eddy DM, Sanders LE, Eddy JF. The value of screening for glaucoma with tonometry. *Surv Ophthalmol* 1983; 28:194-205.

198. Power EJ, Wagner JL, Duffy BM. Screening for open-angle glaucoma in the elderly. Washington, DC: Office of Technology Assessment, Congress of the United States, 1988.
199. Tielsch JM, Katz J, Quigley HA, et al. Intraobserver and interobserver agreement in measurement of optic disc characteristics. *Ophthalmology* 1988; 95:350-6.
200. Quigley HA, Katz J, Derick RJ, et al. An evaluation of optic disc and nerve fiber layer examinations in monitoring progression of early glaucoma damage. *Ophthalmology* 1992; 99:19-28.
201. Motolko M, Drance SM. Features of the optic disc in preglaucomatous eyes. *Arch Ophthalmol* 1981; 99:1992-4.
202. Lichter PR. Variability of expert observers in evaluating the optic disc. *Trans Am Ophthalmol Soc* 1976; 74:532-72.
203. O'Connor DJ, Zeyen T, Caprioli J. Comparisons of methods to detect glaucomatous optic nerve damage. *Ophthalmology* 1993; 100:1498-503.
204. Anton A, Moreno-Montanes J, Blazquez F, et al. Usefulness of optical coherence tomography parameters of the optic disc and the retinal nerve fiber layer to differentiate glaucomatous, ocular hypertensive, and normal eyes. *J Glaucoma* 2007; 16:1-8.
205. Nouri-Mahdavi K, Hoffman D, Tannenbaum DP. Identifying early glaucoma with optical coherence tomography. *Am J Ophthalmol* 2004; 137:228-35.
206. Komulainen R, Tuulonen A, Airaksinen PJ. The follow-up of patients screened for glaucoma with non-mydriatic fundus photography. *Int Ophthalmol* 1992; 16:165-9.
207. Airaksinen PJ, Drance SM, Douglas GR, et al. Diffuse and localized nerve fiber loss in glaucoma. *Am J Ophthalmol* 1984; 98:566-71.

208. Sommer A, Quigley HA, Robin AL, et al. Evaluation of nerve fiber layer assessment. *Arch Ophthalmol* 1984; 102:1766-71.
209. Keltner JL, Johnson CA. Mass visual field screening in a driving population. *Ophthalmology* 1980; 87:785-92.
210. Burnstein Y, Ellish NJ, Magbalon M, Higginbotham EJ. Comparison of frequency doubling perimetry with Humphrey visual field analysis in a glaucoma practice. *Am J Ophthalmol* 2000; 129:328-33.
211. Quigley HA. Identification of glaucoma-related visual field abnormality with the screening protocol of frequency doubling technology. *Am J Ophthalmol* 1998; 125:819-29.
212. Khong JJ, Dimitrov PN, Orth B, et al. Can the specificity of the FDT for glaucoma be improved by confirming abnormal results? *J Glaucoma* 2001; 10:199-202.
213. Cello KE, Nelson-Quigg JM, Johnson CA. Frequency doubling technology perimetry for detection of glaucomatous visual field loss. *Am J Ophthalmol* 2000; 129:314-22.
214. Johnson CA, Cioffi GA, Van Buskirk EM. Evaluation of two screening tests for frequency doubling technology perimetry. The Hague, the Netherlands: Kugler; 1999.
215. Johnson CA, Samuels SJ. Screening for glaucomatous visual field loss with frequency-doubling perimetry. *Invest Ophthalmol Vis Sci* 1997; 38:413-25.
216. Tribble JR, Schultz RO, Robinson JC, Rothe TL. Accuracy of glaucoma detection with frequency-doubling perimetry. *Am J Ophthalmol* 2000; 129:740-5.
217. Cioffi GA, Mansberger S, Spry P, et al. Frequency doubling perimetry and the detection of eye disease in the community. *Trans Am Ophthalmol Soc* 2000; 98:195-202.

218. Spry PG, Johnson CA, McKendrick AM, Turpin A. Variability components of standard automated perimetry and frequency-doubling technology perimetry. *Invest Ophthalmol Vis Sci* 2001; 42:1404-10.
219. Sponsel WE, Arango S, Trigo Y, Mensah J. Clinical classification of glaucomatous visual field loss by frequency doubling perimetry. *Am J Ophthalmol* 1998; 125:830-6.
220. Garway-Heath DF, Holder GE, Fitzke FW, Hitchings RA. Relationship between electrophysiological, psychophysical, and anatomical measurements in glaucoma. *Invest Ophthalmol Vis Sci* 2002; 43:2213-20.
221. Epstein DL, Krug JH Jr, Hertzmark E, et al. A long-term clinical trial of timolol versus no treatment in the management of glaucoma suspects. *Ophthalmology* 1989; 96:1460-7.
222. Douglas GR. Diagnostic concepts in open-angle glaucoma. *Curr Opin Ophthalmol* 1992; 3:162-9.
223. Greve EL. The effect of treatment on progression of glaucoma (summary). *Surv Ophthalmol* 1989; 33(suppl):431-3.
224. Casser L. Examining the patient: glaucoma detection, diagnosis, and evaluation. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*. Norwalk, CT: Appleton & Lange, 1993:83-106.
225. Lewis TL. An approach to the diagnosis of glaucoma. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw Hill, 2001:295-309.
226. Kohn AN, Moss AP, Podos SM. Relative afferent pupillary defect in glaucoma without characteristic field loss. *Arch Ophthalmol* 1979; 97:294-6.
227. Kitazawa Y, Horie T. Diurnal variation of intraocular pressure and its significance in the medical treatment of open-angle glaucoma.

- In: Krieglstein GK, Leydhecker W, eds. *Glaucoma update*. New York: Springer, 1979:169-76.
228. Schwartz B, Talusan AG. Spontaneous trends in ocular pressure in untreated ocular hypertension. *Arch Ophthalmol* 1980; 98:105-11.
229. Mosaed S, Liu JH, Weinreb RN. Correlation between office and peak nocturnal intraocular pressures in healthy subjects and glaucoma patients. *Arch Ophthalmology* 2005; 139:320-4.
230. Goldmann H. Applanation tonometry. In: Newell FW, ed. *Glaucoma transactions of the second conference*. New York: Josiah Macy Jr. Foundation. 1957:167-220.
231. Doughty MJ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measures: a review and meta-analysis approach. *Surv Ophthalmol* 2000; 44:367-408.
232. Ehlers N, Bramsen T, Sperling S. Applanation tonometry and central corneal thickness. *Acta Ophthalmol (Copenh)* 1974; 53:34-43.
233. Whitacre MM, Stein RA, Hassanein K. The effect of corneal thickness on applanation tonometry. *Am J Ophthalmol* 1993; 115:592-6.
234. Matsumoto T, Makino H, Uozato H, et al. The influence of corneal thickness and curvature on the difference between intraocular pressure measurements obtained with a non-contact tonometer and those with a Goldmann applanation tonometer. *Jpn J Ophthalmol* 2000; 44:691.
235. Sullivan-Mee M, Gentry JM, Qualls C. Relationship between asymmetric central corneal thickness and glaucomatous visual field loss within the same patient. *Optom Vis Sci* 2006; 83:516-9.
236. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular

- pressure and visual field deterioration. *Am J Ophthalmol* 2000; 130:429-40.
237. Kniestedt C, Lin S, Choe J et al. Correlation between intraocular pressure, central corneal thickness, stage of glaucoma, and demographic patient data: prospective analysis of biophysical parameters in tertiary glaucoma practice populations. *J Glaucoma* 2006; 15:91-7.
 238. Sullivan-Mee M, Halverson KD, Saxon MC, et al. Central corneal thickness and normal tension glaucoma: a cross-sectional study. *Optometry* 2006; 77:134-40.
 239. Argus WA. Ocular hypertension and central corneal thickness. *Ophthalmology* 1995; 102:1810-2.
 240. Bechmann M, Thiel MJ, Roesen B, et al. Central corneal thickness determined with optical coherence tomography in various types of glaucoma. *Br J Ophthalmol* 2000; 84:1233-7.
 241. Copt RP, Thomas R, Mermound A. Corneal thickness in ocular hypertension, primary open-angle glaucoma, normal tension glaucoma. *Arch Ophthalmol* 1999; 117:14-6.
 242. Herman DC, Hodge DO, Bourne WM. Increased corneal thickness in patients with ocular hypertension. *Arch Ophthalmol* 2001; 119:334-6.
 243. Herndon LW, Choudhri SA, Cox T, et al. Central corneal thickness in normal, glaucomatous, and ocular hypertensive eyes. *Arch Ophthalmol* 1997; 115:1137-41.
 244. Monrad Y, Sharon E, Hefetz L, Nemet P. Corneal thickness and curvature in normal-tension glaucoma. *Am J Ophthalmol* 1998; 125:164-8.

245. Shah S, Chatterjee A, Mathai M, et al. Relationship between corneal thickness and measured intraocular pressure in a general ophthalmology clinic. *Ophthalmology* 1999; 106:2154-60.
246. Singh RP, Goldberg I, Graham SL, et al. Central corneal thickness, tonometry, and ocular dimensions in glaucoma and ocular hypertension. *J Glaucoma* 2001; 10:206-10.
247. Ventura AC, Bohnke M, Mojon DS. Central corneal thickness measurements in patients with normal tension glaucoma, primary open angle glaucoma, pseudoexfoliation glaucoma, or ocular hypertension. *Br J Ophthalmol* 2001; 85:792-5.
248. Wolfs RC, Klaver CC, Vingerling JR, et al. Distribution of central corneal thickness and its association with intraocular pressure. The Rotterdam Study. *Am J Ophthalmol* 1997; 123:767-72.
249. Emara BY, Tingey DP, Probst LE, Motolko MA. Central corneal thickness in low-tension glaucoma. *Can J Ophthalmol* 1999; 34:319-24.
250. La Rosa FA, Gross RL, Orengo-Nania S. Central corneal thickness of Caucasians and African Americans in glaucomatous and nonglaucomatous populations. *Arch Ophthalmol* 2001; 119:23-7.
251. Abbasoglu OE, Bowman WR, Cavanagh DH, McCulley JP. Reliability of intraocular pressure measurements after myopic excimer photorefractive keratectomy. *Ophthalmology* 1998; 105:2193-6.
252. Emara B, Probst LE, Tingey DP, et al. Correlation of intraocular pressure and central corneal thickness in normal myopic eyes and after laser in situ keratomileusis. *J Cataract Refract Surg* 1998; 24:1320-5.

253. Fingeret M, Meideros FA, Susanna R, Weinreb RN. Five rules to evaluate the optic disc and retinal nerve fiber layer in glaucoma. *Optometry* 2005; 76: 661-6.
254. Girkin CA, McGwin G Jr, Xie A, Deleon-Ortega J. Differences in optic disc topography between black and white normal subjects. *Ophthalmology* 2005; 112: 33-9.
255. Ramrattan RS, Wolfs RC, Jonas JB, et al. Determinants of optic disc characteristics in a general population. The Rotterdam Study. *Ophthalmology* 1999; 106:1588-96.
256. Huynh SC, Wang XY, Rochtchina E, et al. Distribution of optic disc parameters measured by OCT: findings in a population-based study of six-year-old Australian children. *Invest Ophthalmol Visual Sci* 2006; 47:3276-85.
257. Harizman N, Oliveira C, Chiang A, et al. The ISNT rule and differentiation of normal from glaucomatous eyes. *Arch Ophthalmol* 2006; 124:1579-83.
258. Lin SC, Singh K, Jampel HD, et al. Optic nerve head and retinal nerve fiber layer analysis. A report from the American Academy of Ophthalmology 2007; 114:1937-49.
259. Flanagan JG. Imaging of the optic nerve and nerve fiber layer in glaucoma. In: Lewis TL, Fingeret M, eds. *Primary care of glaucomas*, 2nd ed. New York, NY: McGraw-Hill, 2001:187-200.
260. Zangwill L, Irak I, Berry CC, et al. Effect of cataract and pupil size on image quality with confocal scanning laser ophthalmoscopy. *Arch Ophthalmol* 1997; 115:983-90.
261. Yan DB, Flanagan JG, Farra T, et al. Study of regional deformation of the optic nerve head using scanning laser tomography. *Curr Eye Res* 1998; 17:903-16.

262. Zangwill L, Shakiba S, Caprioli J, Weinreb RN. Agreement between clinicians and a confocal scanning laser ophthalmoscope in estimating cup/disc ratios. *Am J Ophthalmol* 1995; 119:415-21.
263. Zangwill LM, Van Horn S, Lima MD, et al. Optic nerve head topography in ocular hypertensive eyes using confocal scanning laser ophthalmoscopy. *Am J Ophthalmol* 1996; 37:2393-401.
264. Wollstein G, Garway-Heath DF, Hitchings RA. Identification of early glaucoma cases with the scanning laser ophthalmoscope. *Ophthalmology* 1998; 105:1157-63.
265. Mikelberg FS, Parfitt CM, Swindale NV, et al. Ability of the Heidelberg retina tomograph to detect early glaucomatous visual field loss. *J Glaucoma* 1995; 4:242-7.
266. Kamal DS, Viswanathan AC, Garway-Heath DF, et al. Detection of optic disc change with the Heidelberg retina tomograph before confirmed visual field change in ocular hypertensives converting to early glaucoma. *Br J Ophthalmol* 1999; 83:290-4.
267. Farra T, Flanagan JG, Trope GE. The detection of glaucomatous progression using scanning laser tomography. *Invest Ophthalmol Vis Sci* 1999; 39(suppl):389.
268. Litwak AB. Evaluation of the retinal nerve fiber layer in glaucoma. *J Am Optom Assoc* 1990; 61:390-7.
269. Sommer A, Katz J, Quigley HA, et al. Clinically detectable nerve fiber layer atrophy precedes the onset of glaucomatous field loss. *Arch Ophthalmol* 1991; 109:77-83.
270. Colen TP, Tjon-Fo-Sang MJ, et al. Reproducibility of measurements with the nerve fiber layer analyzer (NfA/GDx). *J Glaucoma* 2000; 9:363-70.

271. Tjon-Fo-Sang MJ, Lemij HG. The sensitivity and specificity of nerve fiber layer measurements in glaucoma as determined with scanning laser polarimetry. *Am J Ophthalmol* 1997; 123:62-9.
272. Weinreb RN, Zangwill L, Berry CC, et al. Detection of glaucoma with scanning laser polarimetry. *Arch Ophthalmol* 1998; 116:1583-9.
273. Blumenthal EZ, Williams JM, Weinreb RN, et al. Reproducibility of nerve fiber layer thickness measurements by use of optical coherence tomography. *Ophthalmology* 2000; 107:2278-82.
274. Mistlberger A, Liebmann JM, Greenfield DS, et al. Heidelberg retina tomography and optical coherence tomography in normal, ocular-hypertensive, and glaucomatous eyes. *Ophthalmology* 1999; 106:2027-32.
275. Pons ME, Ishikawa H, Gurses-Ozden R, et al. Assessment of retinal nerve fiber layer internal reflectivity in eyes with and without glaucoma using optical coherence tomography. *Arch Ophthalmol* 2000; 118:1044-7.
276. Schuman JS, Hee MR, Puliafito CA. Quantification of nerve fiber layer thickness in normal and glaucomatous eyes using optical coherence tomography. *Arch Ophthalmol* 1995; 113:586-96.
277. Zangwill LM, Williams J, Berry CC, et al. A comparison of optical coherence tomography and retinal nerve fiber layer photography for detection of nerve fiber layer damage in glaucoma. *Ophthalmology* 2000; 107:1309-15.
278. Tsai CS, Zangwill L, Sample PA, et al. Correlation of peripapillary retinal height and visual field in glaucoma and normal subjects. *J Glaucoma* 1995; 4:110-3.
279. Weinreb RN, Shakiba S, Sample PA, et al. Association between quantitative nerve fiber layer measurements and visual field loss in glaucoma. *Am J Ophthalmol* 1995; 120:732-8.

280. Airaksinen PJ, Juvala PA, Tuulonen A, et al. Change of peripapillary atrophy in glaucoma. In: Krieglstein GK, ed. *Glaucoma update III*. Berlin; New York: Springer-Verlag, 1987; 97-102.
281. Anderson DR. Correlation of the peripapillary anatomy with the disc damage and field abnormalities in glaucoma. In: Greve EL, Heijl A, eds. *Fifth International Visual Field Symposium, 1982*. The Hague: Dr W Junk, 1983; 1-10 (Doc Ophthalmol Proc Ser; 35).
282. Jonas JB, Fernandez MC, Naumann GO. Glaucomatous parapapillary atrophy. Occurrence and correlations. *Arch Ophthalmol* 1992; 110:214-22.
283. Jonas JB, Naumann GO. Parapapillary chorioretinal atrophy in normal and glaucoma eyes. II. Correlations. *Invest Ophthalmol Vis Sci* 1989; 30:919-26.
284. Jonas JB, Nguyen XN, Gusek GC, Naumann GO. Parapapillary chorioretinal atrophy in normal and glaucoma eyes. I. Morphometric data. *Invest Ophthalmol Vis Sci* 1989; 30:908-18.
285. Primose J. Early signs of the glaucomatous disc. *Br J Ophthalmol* 1971; 55:820-5.
286. Tezel G, Kass MA, Kolker AE, Wax MB. Comparative optic disc analysis in normal pressure glaucoma, primary open-angle glaucoma, and ocular hypertension. *Ophthalmology* 1996; 103:2105-13.
287. Uhm KB, Lee DY, Kim JT, Hong C. Peripapillary atrophy in normal and primary open-angle glaucoma. *Korean J Ophthalmol* 1998; 12:37-50.
288. Wilensky JT, Kolker AE. Peripapillary changes in glaucoma. *Am J Ophthalmol* 1976; 81:341-5.

References 111

289. Buus DR, Anderson DR. Peripapillary crescents and halos in normal-tension glaucoma and ocular hypertension. *Ophthalmology* 1989; 96:16-9.
290. Jonas JB, Xu L. Parapapillary chorioretinal atrophy in normal-pressure glaucoma. *Am J Ophthalmol* 1993; 115:501-5.
291. Tuulonen A, Jonas JB, Välimäki S, et al. Interobserver variation in the measurements of peripapillary atrophy in glaucoma. *Ophthalmology* 1996; 103:535-41.
292. Heijl A, Samander C. Peripapillary atrophy and glaucomatous visual field defects. *Doc Ophthalmol* 1985; 42:403.
293. Park KH, Tomita G, Liou SY, Kitazawa Y. Correlation between peripapillary atrophy and optic nerve damage in normal-tension glaucoma. *Ophthalmology* 1996; 103:1899-906.
294. Uchida H, Ugurlu S, Caprioli J. Increasing peripapillary atrophy is associated with progressive glaucoma. *Ophthalmology* 1998; 105:1541-5.
295. Rockwood EJ, Anderson DR. Acquired peripapillary changes and progression in glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1988; 226:510-5.
296. Araie M, Sekine M, Suzuki Y, Koseki N. Factors contributing to the progression of visual field damage in eyes with normal-tension glaucoma. *Ophthalmology* 1994; 101:1440-4.
297. Budde WM, Jonas JB. Enlargement of parapapillary atrophy in follow-up of chronic open-angle glaucoma. *Am J Ophthalmol* 2004; 137:646-54.
298. Tuulonen A, Lehtola P, Airaksinen PJ. Nerve fiber layer defects with normal visual fields. Do normal optic disc and normal visual

112 Open Angle Glaucoma

- field indicate absence of glaucomatous abnormality? *Ophthalmology* 1993; 100:587-97.
299. Caprioli J. Discrimination between normal and glaucomatous eyes. *Invest Ophthalmol Vis Sci* 1992; 33:153-9.
300. Budenz DL, Anderson DR, Feuer MS, et al. Detection and prognostic significance of optic disc hemorrhages during the Ocular Hypertension Treatment Study. *Ophthalmology* 2006; 113:2137-43.
301. Heijl A, Drance SM, Douglas GR. Automated perimetry (COMPETER). Ability to detect early glaucomatous field defects. *Arch Ophthalmol* 1980; 98:1560-3.
302. Heijl A, Lindgren G, Olsson J. A package for the statistical analysis of visual fields. *Doc Ophthalmol Proc Ser* 1987; 49:153-68.
303. Heijl A, Lindgren G, Olsson J. The effect of perimetric experience in normal subjects. *Arch Ophthalmol* 1989; 107:81-6.
304. Adams AJ, Rodic R, Husted R, Stamper R. Spectral sensitivity and color discrimination changes in glaucoma and glaucoma-suspect patients. *Invest Ophthalmol Vis Sci* 1982; 23:516-24.
305. Lakowski R, Drance SM. Acquired dyschromatopsias: the earliest functional losses in glaucoma. *Doc Ophthalmol Proc Ser* 1979; 19:159-65.
306. Airaksinen PJ, Lakowski R, Drance SM, Prince M. Color vision and retinal nerve fiber layer in early glaucoma. *Am J Ophthalmol* 1986; 101:208-13.
307. Israeloff CB. Psychophysical and electrophysiological testing in glaucoma. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*. Norwalk, CT: Appleton & Lange, 1993:197-208.

References 113

308. Fisher RF. Value of tonometry and tonography in the diagnosis of glaucoma. *Br J Ophthalmol* 1972; 56:200-4.
309. Rasmussen KE, Jorgenson HA. Diagnostic value of the water-drinking test in the early detection of simple glaucoma. *Acta Ophthalmol* 1976; 54:160-6.
310. Johnson CA, Adams AJ, Casson EJ, Brandt JD. Progression of early glaucomatous visual field loss as detected by blue-on-yellow and standard white-on-white automated perimetry. *Arch Ophthalmol* 1993; 111:651-6.
311. Johnson CA, Adams AJ, Casson EJ, Brandt JD. Blue-on-yellow perimetry can predict the development of glaucomatous visual field loss. *Arch Ophthalmol* 1993; 111:645-50.
312. Johnson CA, Brandt JD, Khong AM, Adams AJ. Short-wavelength automated perimetry in low-, medium-, and high-risk ocular hypertensive eyes. Initial baseline results. *Arch Ophthalmol* 1995; 113:70-6.
313. Sample PA, Weinreb RN. Progressive color visual field loss in glaucoma. *Invest Ophthalmol Vis Sci* 1992; 33:2068-71.
314. Teesalu P, Airaksinen PJ, Tuulonen A. Blue-on-yellow visual field and retinal nerve fiber layer in ocular hypertension and glaucoma. *Ophthalmology* 1998; 105:2077-81.
315. Sample PA, Taylor JD, Martinez GA, et al. Short-wavelength color visual fields in glaucoma suspects at risk. *Am J Ophthalmol* 1993; 115:225-33.
316. Teesalu P, Vihanninjoki K, Airaksinen PJ, et al. Correlation of blue-on-yellow visual fields with scanning confocal laser optic disc measurements. *Invest Ophthalmol Vis Sci* 1997; 38:2452-9.

114 Open Angle Glaucoma

317. Yamagishi N, Anton A, Sample PA, et al. Mapping structural damage of the optic disk to visual field defects in glaucoma. *Am J Ophthalmol* 1997; 123:667-76.
318. Kim TW, Zangwill LM, Bowd C. Retinal nerve fiber layer damage as assessed by optical coherence tomography in eyes with a visual field defect detected by frequency doubling technology perimetry but not by standard automated perimetry. *Ophthalmology* 2007; 114:1053-7.
319. Anderson DR. Discussion of "nerve fiber layer defects with normal visual fields. Do normal optic disc and normal visual field indicate absence of glaucomatous abnormality?" *Ophthalmology* 1993; 100:597-8.
320. Fingeret M. Medical management of glaucoma. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw Hill, 2001:333-63.
321. Hyams SW, Frankel A, Keroub C, et al. Postural changes in intraocular pressure with particular reference to low tension glaucoma. *Glaucoma* 1984; 6:178-81.
322. Hatsuda TA. Low-tension glaucoma. *Folia Ophthalmol Jpn* 1977; 28:244-9.
323. Hoskins HD, Kass MA. Primary open-angle glaucoma. In: *Becker-Shaffer's diagnosis and therapy of the glaucomas*, 7th ed. St. Louis: Mosby, Inc., 1999:286-316.
324. Zeyen TG, Caprioli J. Progression of disc and field damage in early glaucoma. *Arch Ophthalmol* 1993; 111:62-5.
325. Heijl A, Lindgren G, Lindgren A, et al. Extended empirical statistical package for evaluation of single and multiple field in glaucoma: Statpac 2. In: Mills RP, Heijl A, eds. *Perimetry update 1990/91*. Amsterdam: Kugler, 1991:303-15.

326. Hoskins HD. Does computerized perimetry offer practical advances in choice of therapy in the glaucoma patient? *Eye* 1992; 6:43-6.
327. Keltner JL, Johnson CA, Anderson DR, et al. The association between glaucomatous visual fields and optic nerve head features in the Ocular Hypertension Treatment Study. *Ophthalmology* 2006; 113:1603-12.
328. Zangwill LM, Weinreb RN, Beiser JA, et al. Baseline topographic optic disc measurements are associated with the development of primary open-angle glaucoma: the Confocal Scanning Laser Ophthalmoscopy Ancillary Study to the Ocular Hypertension Treatment Study. *Arch Ophthalmol* 2005; 123:1188-97.
329. Speakman JS. Pigmentary dispersion. *Br J Ophthalmol* 1981; 65:249-51.
330. Becker B, Podos SM. Krukenberg's spindles and primary open-angle glaucoma. *Arch Ophthalmol* 1966; 76:635-9.
331. Farrar SM, Shields MB. Current concepts in pigmentary glaucoma. *Surv Ophthalmol* 1993; 37:233-52.
332. Fingeret M, Thimons JJ. Common secondary glaucomas. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw Hill, 2001:461-75.
333. Kristensen P. Mydriasis-induced pigment liberation in the anterior chamber associated with acute rise in intraocular pressure in open-angle glaucoma. *Acta Ophthalmol* 1965; 43:714-24.
334. Schenker HI, Luntz MH, Kels B, Podos SM. Exercise-induced increase of intraocular pressure in the pigmentary dispersion syndrome. *Am J Ophthalmol* 1980; 89:598-600.

335. Jerndal T. Open angle glaucoma and the pseudo-exfoliation syndrome. In: *Glaucoma*, vol II. Cairns JE, ed. London: Grune & Stratton, 1986:661-7.
336. Prince AM, Ritch R. Clinical signs of pseudoexfoliation syndrome. *Ophthalmology* 1986; 93:803-7.
337. Aasved H. Mass screening for fibrillographia epitheliocapsularis, so-called senile exfoliation or pseudoexfoliation of the anterior lens capsule. *Acta Ophthalmol* 1971; 49:334-43.
338. Aasved H. Incidence of defects in the pigmented pupillary ruff in eyes with and without fibrillographia epitheliocapsularis. *Acta Ophthalmol* 1973; 51:710-5.
339. Cavallerano AA, Alexander LJ. The secondary glaucomas. In: Classé JG, ed. *Optometry clinics*, vol 1. Norwalk, CT: Appleton & Lange, 1991:127-64.
340. Pohjanpelto P. Long-term prognosis of visual field in glaucoma simplex and glaucoma capsulare. *Acta Ophthalmol* 1985; 63:418-23.
341. Tarkkanen A. Pseudoexfoliation of the lens capsule. *Acta Ophthalmol Copenh* 1962; 40(suppl 71):1-98.
342. Kidd MN, O'Connor M. Progression of field loss after trabeculectomy: a five-year follow-up. *Br J Ophthalmol* 1985; 69:827-31.
343. Odberg T. Visual field prognosis in advanced glaucoma. *Acta Ophthalmol* 1987; 65(suppl 182):27-9.
344. Roth SM, Spaeth GL, Starita RJ, et al. The effects of postoperative corticosteroids on trabeculectomy and the clinical course of glaucoma: five year follow-up study. *Ophthalmic Surg* 1991; 22:724-9.

345. Kolker AE. Visual prognosis in advanced glaucoma: a comparison of medical and surgical therapy for retention of vision in 101 eyes with advanced glaucomas. *Trans Am Ophthalmol Soc* 1977; 75:539-55.
346. Leydhecker W, Gramer E. Long-term studies of visual field changes by means of computerized perimetry (Octopus 201) in eyes with glaucomatous field defects after normalization of the intra-ocular pressure. *Int Ophthalmol* 1989; 13:113-7.
347. Collaborative Normal-Tension Glaucoma Study Group. Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma with patients with therapeutically reduced intraocular pressures. *Am J Ophthalmol* 1998; 126:487-97.
348. Collaborative Normal-Tension Glaucoma Study Group. The effectiveness of intraocular pressure reduction in the treatment of normal-tension glaucoma. *Am J Ophthalmol* 1998; 126:498-505.
349. Higginbotham EJ, Gordon MO, Beiser JA, et al. The Ocular Hypertension Treatment Study: topical medication delays or prevents primary open-angle glaucoma in African American individuals. *Arch Ophthalmol* 2004; 122:813-20.
350. Odberg T. Visual field prognosis in early glaucoma. A long-term clinical follow-up. *Acta Ophthalmol* 1993; 71:721-6.
351. Vogel R, Crick RP, Shipley M, et al. Association between intraocular pressure and loss of visual field in chronic simple glaucoma. *Br J Ophthalmol* 1990; 74:3-6.
352. Mao LK, Stewart WC, Shields MB. Correlation between intraocular pressure control and progressive glaucomatous damage in primary open-angle glaucoma. *Am J Ophthalmol* 1991; 111:51-5.

353. Bergeå B, Bodin L, Svedbergh B. Impact of intraocular pressure regulation on visual fields in open-angle glaucoma. *Ophthalmology* 1999; 106:997-1005.
354. Chauhan BC, Drance SM. The relationship between intraocular pressure and visual field progression in glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1992; 230:521-6.
355. Weber J, Koll W, Krieglstein GK. Intraocular pressure and visual field decay in chronic glaucoma. *Ger J Ophthalmol* 1993; 2:165-9.
356. Martínez-Belló C, Chauhan BC, Nicolela MT, et al. Intraocular pressure and progression of glaucomatous visual field loss. *Am J Ophthalmol* 2000; 129:302-8.
357. Schulzer M, Mikelberg FS, Drance SM. Some observations on the relation between intraocular pressure reduction and the progression of glaucomatous visual loss. *Br J Ophthalmol* 1987; 71:486-8.
358. Stewart WC, Kolker AE, Sharpe ED, et al. Factors associated with long-term progression or stability in primary open-angle glaucoma. *Am J Ophthalmol* 2000; 130:274-9.
359. Rollins DF, Drance SM. Five-year follow-up of trabeculectomy in the management of chronic open angle glaucoma. *New Orleans Acad Ophthalmol Symposium on Glaucoma* 1991:295-300.
360. Stewart WC, Chorak RP, Hunt HH, Sethuraman G. Factors associated with visual loss in patients with advanced glaucomatous changes in the optic nerve head. *Am J Ophthalmol* 1993; 116:176-81.
361. Quigley HA, Maumenee AE. Long-term follow-up of treated open-angle glaucoma. *Am J Ophthalmol* 1979; 87:519-25.
362. Araujo A, Spaeth GL, Roth SM, Starita RJ. A ten-year follow-up on prospective, randomized trial of postoperative corticosteroids after trabeculectomy. *Ophthalmology* 1995; 102:1753-9.

- 363. Spaeth GL. The effect of change in intraocular pressure on the natural history of glaucoma: lowering intraocular pressure in glaucoma can result in improvement of visual fields. *Trans Ophthalmol Soc UK* 1985; 104:256-64.
- 364. Werner EB, Drance SM, Schulzer M. Trabeculectomy and the progression of glaucomatous visual field loss. *Arch Ophthalmol* 1977; 95:1374-7.
- 365. Popovic V, Sjostrand J. Long-term outcome following trabeculectomy. II. Visual field survival. *Acta Ophthalmol (Copenh)* 1991; 69:305-9.
- 366. Greve EL, Dake CL. Four-year follow-up of a glaucoma operation. Prospective study of the double flap Scheie. *Int Ophthalmol* 1979; 1:139-45.
- 367. Zeimer RC, Wilensky JT, Gieser DK, Viana MAG. Association between intraocular pressure peaks and progression of visual field loss. *Ophthalmology* 1991; 98:64-9.
- 368. Schulzer M. Intraocular pressure reduction in normal-tension glaucoma patients. *Ophthalmology* 1992; 99:1468-70.
- 369. Quigley HA. Open-angle glaucoma. *N Engl J Med* 1993; 328:1097-106.
- 370. Jampel HD. Target pressure in glaucoma therapy. *J Glaucoma* 1997; 6:133-8.
- 371. Quigley HA. A reevaluation of glaucoma management. *Int Ophthalmol Clin* 1984; 24:1-11.
- 372. Jay JL, Allan D. The benefit of early trabeculectomy versus conventional management in primary open angle glaucoma relative to severity of disease. *Eye* 1989; 3:528-35.

- 373. Migdal CS, Hitchings RA. Control of chronic simple glaucoma with primary medical, surgical and laser treatment. *Trans Ophthalmol Soc UK* 1986; 105:653-6.
- 374. Smith RJ. The enigma of primary open-angle glaucoma. The Lang lecture 1986. *Trans Ophthalmol Soc UK* 1986; 105:618-33.
- 375. Bartlett JD, Jaanus SD. Ocular hypotensive drugs. In: Bartlett JD, Jaanus SD, eds. *Clinical ocular pharmacology*, 4th ed. Boston: Butterworth-Heinemann, 2001:167-204.
- 376. Burnham TH. Agents for glaucoma. In: Burnham TH, Wickersham RM, Schweain SL, et al. *Drug facts and comparisons (pocket version)*. St. Louis: Facts and Comparisons, Wolters Kluwer Co, 2003:1061-75.
- 377. Werner EB. Tertiary glaucoma surgical procedures. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw Hill, 2001:411-7.
- 378. Erickson K, Schroeder A. Pharmacology of antiglaucoma medications. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw Hill, 2001:313-32.
- 379. Alm A, Widengard I, Kjellgren D. Latanoprost administered once daily caused a maintained reduction of intraocular pressure in glaucoma patients treated concomitantly with timolol. *Br J Ophthalmol* 1995; 79:12-6.
- 380. Camras CB and the United States Latanoprost Study Group. Comparison of latanoprost and timolol in patients with ocular hypertension and glaucoma: a six-month, masked, multi-center trial in the United States. *Ophthalmology* 1996; 103:138-47.
- 381. Susanna R, Giampani J Jr, Borges AS, et al. A double-masked, randomized clinical trial comparing latanoprost with unoprostone in patients with open-angle glaucoma or ocular hypertension. *Ophthalmology* 2001; 108:259-63.

382. Watson P, Stjernschantz J, the Latanoprost Study Group. A six-month, randomized double-masked study comparing latanoprost with timolol in open-angle glaucoma and ocular hypertension. *Ophthalmology* 1996; 103:126-37.
383. Rácz P, Ruzsonyi M, Nagy ZT, et al. Around-the-clock intraocular pressure reduction with once-daily application of latanoprost by itself or in combination with timolol. *Arch Ophthalmol* 1996; 114:268-73.
384. Alm A, Stjernschantz J, the Scandinavian Latanoprost Study Group. Effects on intraocular pressure and side effects of 0.005% latanoprost applied once daily, evening or morning. *Ophthalmology* 1995; 102:1743-52.
385. Mishima HK, Masuda K, Kitazawa Y, et al. A comparison of latanoprost and timolol in primary open-angle glaucoma and ocular hypertension. A 12-week study. *Arch Ophthalmol* 1996; 114:929-32.
386. Konstas AG, Maltezos AC, Gandi S, et al. Comparison of 24-hour intraocular pressure reduction with two dosing regimens of latanoprost and timolol maleate in patients with primary open-angle glaucoma. *Am J Ophthalmol* 1999; 128:15-20.
387. McKibbin M, Menage MJ. The effect of once-daily latanoprost on intraocular pressure and pulsatile ocular blood flow in normal tension glaucoma. *Eye* 1999; 13:31-4.
388. Sponsel WE, Mensah J, Kiel JW, et al. Effects of latanoprost and timolol-XE on hydrodynamics in the normal eye. *Am J Ophthalmol* 2000; 130:151-9.
389. Rulo AH, Greve EL, Geijssen HC, Hoyng PF. Reduction of intraocular pressure with treatment of latanoprost once daily in patients with normal-pressure glaucoma. *Ophthalmology* 1996; 103:1276-82.

390. Drance SM, Crichton A, Mills RP. Comparison of the effect of latanoprost 0.005% and timolol 0.5% on the calculated ocular perfusion pressure in patients with normal-tension glaucoma. *Am J Ophthalmol* 1998; 125:585-92.
391. Alm A, Widengard I, Mepea O. Combination of latanoprost with dipivefrin in patients with open-angle glaucoma or ocular hypertension. Presented at the 27th International Congress of Ophthalmology, Toronto, Canada, 1994.
392. Hoyng PF, Rulo A, Greve E, et al. The additive intraocular pressure-lowering effect of latanoprost in combined therapy with other ocular hypotensive agents. *Surv Ophthalmol* 1997; 41(suppl 2):S93-8.
393. Vanlandingham BD, Brubaker RF. Combined effect of dorzolamide and latanoprost on the rate of aqueous humor flow. *Am J Ophthalmol* 1998; 126:191-6.
394. Stewart WC, Sharpe ED, Day DG, et al. Comparison of the efficacy and safety of latanoprost 0.005% compared to brimonidine 0.2% or dorzolamide 2% when added to a topical beta-adrenergic blocker in patients with primary open-angle glaucoma or ocular hypertension. *J Ocul Pharmacol Ther* 2000; 16:251-9.
395. Rossetti L, Gandolfi S, Traverso C, et al. An evaluation of the rate of nonresponders to latanoprost therapy. *J Glaucoma* 2006; 15:238-43.
396. Laibovitz RA, VanDenburgh AM, Felix C, et al. Comparison of the ocular hypotensive lipid AGN 192024 with timolol. Dosing, efficacy and safety evaluation of a novel compound for glaucoma management. *Arch Ophthalmol* 2001; 119:994-1000.
397. Netland PA, Landry T, Sullivan EK, et al, and the Travoprost Study Group. Travoprost compared with latanoprost and timolol

in patients with open-angle glaucoma or ocular hypertension. *Am J Ophthalmol* 2001; 132:472-84.

398. Johnstone MA. Hypertrichosis and increased pigmentation of eye lashes and adjacent hair in the region of the ipsilateral eyelids of patients treated with unilateral topical latanoprost. *Am J Ophthalmol* 1997; 124:544-7.
399. Fechtner RD, Khouri AS, Zimmerman TJ, et al. Anterior uveitis associated with latanoprost. *Am J Ophthalmol* 1998; 126:37-41.
400. Miyake K, Ota I, Maekubo K, et al. Latanoprost accelerates disruption of the blood-aqueous barrier in the incidence of angiographic cystoid macular edema in early postoperative pseudophakias. *Arch Ophthalmol* 1999; 117:34-40.
401. Rowe JA, Hattenhauer MG, Herman DC. Adverse side effects with latanoprost. *Am J Ophthalmol* 1997; 124:683-5.
402. Wistrand PJ, Stjernschantz J, Olsson K. The incidence and time-course of latanoprost-induced iridial pigmentation as a function of eye color. *Surv Ophthalmol* 1997; 41(suppl 2):S129-38.
403. Dios Castro E, Maquet Dusart JA. Latanoprost-associated recurrent herpes simplex keratitis. *Arch Soc Esp Oftalmol* 2000; 75:775-8.
404. Hoyng PF, Rulo AH, Greve EL, et al. Fluorescein angiographic evaluation of the effect of latanoprost treatment on blood-retinal barrier integrity: a review of studies conducted on pseudophakic glaucoma patients and on phakic and aphakic monkeys. *Surv Ophthalmol* 1997; 41(suppl 2):S83-8.
405. Wand M, Gilbert CM, Liesegang TJ. Latanoprost and herpes simplex keratitis. *Am J Ophthalmol* 1999; 127:602-4.
406. Azuma I, Masuda K, Kitazawa Y, et al. Phase II double-masked dose-determination study of UF-021 ophthalmic solution in

primary open-angle glaucoma and ocular hypertension. *Folia Ophthalmol Jpn* 1992; 43:1425-31.

407. Azuma I, Masuda K, Kitazawa Y, et al. Double-masked comparative study of UF-021 and timolol ophthalmic solutions in patients with primary open-angle glaucoma or ocular hypertension. *Jpn J Ophthalmol* 1993; 37:514-25.
408. Stewart WC, Stewart JA, Kapik BM. The effects of unoprostone isopropyl 0.12% and timolol maleate 0.5% on diurnal intraocular pressure. *J Glaucoma* 1998; 7:388-94.
409. Nordmann JP, Rouland JF, Mertz BP. A comparison of the intraocular pressure-lowering effect of 0.5% timolol maleate and the docosanoid derivative of a PGF₂ alpha metabolite, 0.12% unoprostone, in subjects with chronic open-angle glaucoma or ocular hypertension. *Curr Med Res Opin* 1999; 15:87-93.
410. Yamamoto T, Kitazawa Y, Azuma I, Masuda K. Clinical evaluation of UF-201 (Rescula®; isopropyl unoprostone). *Surv Ophthalmol* 1997; 41(suppl 2):S99-103.
411. Takase M, Murao M, Koyano S, Okita M. Ocular effects of topical instillation of UF-021 ophthalmic solution in healthy volunteers. *Nippon Ganka Gakkai Zasshi* 1992; 96:1261-7.
412. Nakamatsu T, Okinami S, Oono S. The ocular hypotensive effect of concomitantly applied isopropyl unoprostone and timolol. *J Eye* 1996; 13:439-41.
413. Fujimori C, Yamabayashi S, Hosoda M, et al. The clinical evaluation of UF-201, a new prostaglandin related compound, in low tension glaucoma patients. *Nippon Ganka Gakkai Zasshi* 1993; 97:1231-5.
414. Tsukamoto H, Yokoyama T, Okada K, et al. Substituting latanoprost (Xalatan) for isopropyl unoprostone (Rescula) in

- monotherapy and combination therapy. *Acta Ophthalmol Scand* 2000; 78:604-5.
415. Toshino A, Okamoto S, Shimamura I, et al. The mechanism of corneal epithelial disorder induced by prostaglandin F2 alpha isopropyl unoprostone. *Nippon Ganka Gakkai Zasshi* 1998; 102:101-5.
 416. Yamamoto T, Kitazawa Y. Iris-color change developed after topical isopropyl unoprostone treatment. *J Glaucoma* 1997; 6:430-2.
 417. Mandell AI, Stentz F, Kitabchi AE. Dipivalyl epinephrine: a new pro-drug in the treatment of glaucoma. *Ophthalmology* 1978; 85:268-75.
 418. Kaback MB, Podos SM, Harbin TS Jr, et al. The effects of dipivalyl epinephrine on the eye. *Am J Ophthalmol* 1976; 81:768-72.
 419. Anderson JA. Systemic absorption of topical ocularly applied epinephrine and dipivefrin. *Arch Ophthalmol* 1980; 98:350-3.
 420. Kolker AE, Becker B. Epinephrine maculopathy. *Arch Ophthalmol* 1968; 79:552-62.
 421. Podos SM, Ritch R. Epinephrine as the initial therapy in selected cases of ocular hypertension. *Surv Ophthalmol* 1980; 25:188-94.
 422. Robin AL, Pollack IP, House B, Enger C. Effects of ALO 2145 on intraocular pressure following argon laser trabeculoplasty. *Arch Ophthalmol* 1987; 105:646-50.
 423. Hill RA, Minckler DS, Lee M, et al. Apraclonidine prophylaxis for postcycloplegic intraocular pressure spikes. *Ophthalmology* 1991; 98:1083-6.

424. Robin AL. Effect of topical apraclonidine on the frequency of intraocular pressure elevation after combined extracapsular cataract extraction and trabeculectomy. *Ophthalmology* 1993; 100:628-33.
425. Lish AJ, Camras CB, Podos SM. Effect of apraclonidine on intraocular pressure in glaucoma patients receiving maximally tolerated medications. *J Glaucoma* 1992; 1:19-22.
426. Nagasubramanian S, Hitchings RA, Demailly P, et al. Comparison of apraclonidine and timolol in chronic open-angle glaucoma. A three-month study. *Ophthalmology* 1993; 100:1318-23.
427. Morrison JC, Robin AL. Adjunctive glaucoma therapy. A comparison of apraclonidine to dipivefrin when added to timolol maleate. *Ophthalmology* 1989; 96:3-7.
428. Serdahl C, Galustian J, Lewis RA. The effects of apraclonidine on conjunctival oxygen tension. *Arch Ophthalmol* 1989; 107:1777-9.
429. Robin AL. Short-term effects of unilateral 1 percent apraclonidine therapy. *Arch Ophthalmol* 1988; 106:912-5.
430. Burke J, Schwartz M. Preclinical evaluation of brimonidine. *Surv Ophthalmol* 1996; 41(suppl 1):S9-18.
431. Lee DA, Gornbein J, Abrams C. The effectiveness and safety of brimonidine as mono-combination, or replacement therapy for patients with primary open-angle glaucoma or ocular hypertension: a post hoc analysis of an open-label community trial. *Glaucoma Trial Study Group. J Ocul Pharmacol Ther* 2000; 16:3-18.
432. Walters TR. Development and use of brimonidine in treating acute and chronic elevations of intraocular pressure: a review of safety, efficacy, dose response and dosing studies. *Surv Ophthalmol* 1996; 41(suppl 1):S19-26.
433. Schuman JS, Horwitz B, Choplin NT, et al. A 1-year study of brimonidine twice daily in glaucoma and ocular hypertension. A

- controlled, randomized, multicenter clinical trial. *Arch Ophthalmol* 1997; 115:847-52.
434. Serle JB and the Brimonidine Study Group III. A comparison of the safety and efficacy of twice daily brimonidine 0.2% versus betaxolol 0.25% in subjects with elevated intraocular pressure. *Surv Ophthalmol* 1996; 41(suppl 1):S39-47.
 435. Javitt JC, Schiffman RM. Clinical success and quality of life with brimonidine 0.2% or timolol 0.5% used twice daily in glaucoma or ocular hypertension: a randomized clinical trial. Brimonidine Outcomes Study Group I. *J Glaucoma* 2000; 9:224-34.
 436. LeBlanc RP for the Brimonidine Study Group. Twelve-month results of an ongoing randomized trial comparing brimonidine tartrate 0.2% and timolol 0.5% given twice daily in patients with glaucoma or ocular hypertension. *Ophthalmology* 1998; 105:1960-7.
 437. Nordlund JR, Pasquale LR, Robin AL, et al. The cardiovascular, pulmonary and ocular hypotensive effects of 0.2% brimonidine. *Arch Ophthalmol* 1995; 113:77-83.
 438. Schuman JS. Clinical experience with brimonidine 0.2% and timolol 0.5% in glaucoma and ocular hypertension. *Surv Ophthalmol* 1996; 41(suppl 1):S27-37.
 439. Stewart WC, Day DG, Stewart JA, et al. Therapeutic success of latanoprost 0.005% compared to brimonidine 0.2% in patients with open-angle glaucoma or ocular hypertension. *J Ocul Pharmacol Ther* 2000; 16:557-64.
 440. Mehta NH, Simmons ST, the Alphagan/Trusopt Study Group. The safety and efficacy of brimonidine and dorzolamide as concomitant therapy in primary open angle glaucoma and ocular hypertension. *Invest Ophthalmol Vis Sci* 1998; 39(suppl):481.

441. Barnebey HS, Robin AL, Zimmerman TJ, et al. The effect of brimonidine in decreasing elevations in intraocular pressure after laser trabeculoplasty. *Ophthalmology* 1993; 100:1083-8.
442. Yoles E, Müller S, Schwartz M. Injury-induced secondary degeneration of rat optic nerve can be attenuated by α -adrenoceptor agonists AGN191103 and brimonidine. *Invest Ophthalmol Vis Sci* 1996; 37(suppl):114.
443. Yoles E, Wheeler LA, Schwartz M. Alpha2-adrenoceptor agonists are neuroprotective in a rat model of optic nerve degeneration. *Invest Ophthalmol Vis Sci* 1999; 40:65-73.
444. Levkovitch-Verbin H, Harris-Cerruti C, Groner Y, et al. RGC death in mice after optic nerve crush injury: oxidative stress and neuroprotection. *Invest Ophthalmol Vis Sci* 2000; 41:4169-74.
445. Donello JE, Padillo EU, Webster ML, et al. Alpha2-adrenoceptor agonists inhibit vitreal glutamate and aspartate accumulation and preserve retinal function after transient ischemia. *J Pharmacol Exp Ther* 2001; 296:216-23.
446. Lachkar Y, Migdal C, Dhanjil S. Effect of brimonidine tartrate on ocular hemodynamic measurements. *Arch Ophthalmol* 1998; 116:1591-4.
447. Carlsson AM, Chauhan BC, Lee AA, LeBlanc RP. The effect of brimonidine tartrate on retinal blood flow in patients with ocular hypertension. *Am J Ophthalmol* 2000; 129:297-301.
448. Byles DB, Frith P, Salmon JF. Anterior uveitis as a side effect of topical brimonidine. *Am J Ophthalmol* 2000; 130:287-91.
449. Williams GC, Orengo-Nania S, Gross RL. Incidence of brimonidine allergy in patients previously allergic to apraclonidine. *J Glaucoma* 2000; 9:235-8.

450. Yalon M, Urinowsky E, Rothkoff L, et al. Frequency of timolol administration. *Am J Ophthalmol* 1981; 92:526-9.
451. van Buskirk EM, Weinreb RN, Berry DP, et al. Betaxolol in patients with glaucoma and asthma. *Am J Ophthalmol* 1986; 101:531-4.
452. Allen RC, Hertzmark E, Walker AM, Epstein DL. A double-masked comparison of betaxolol vs timolol in treatment of open-angle glaucoma. *Am J Ophthalmol* 1986; 101:535-41.
453. Osborne NN, Cazevieuille C, Carvalho AL, et al. In vivo and in vitro experiments show that betaxolol is a retinal neuroprotective agent. *Brain Res* 1997; 751:113-23.
454. Hirooka K, Kelly ME, Baldrige WH, Barnes S. Suppressive actions of betaxolol on ionic currents in retinal ganglion cells may explain its neuroprotective effects. *Exp Eye Res* 2000; 70:611-21.
455. Harris A, Arend O, Chung HS, et al. A comparative study of betaxolol and dorzolamide effect on ocular circulation in normal-tension glaucoma patients. *Ophthalmology* 2000; 107:430-4.
456. Wilson RP, Spaeth GL, Poryzees E. The place of timolol in the practice of ophthalmology. *Ophthalmology* 1980; 87:451-4.
457. Maren TH. A comparison between topical and oral sulfonamides in treatment of elevated ocular pressure in man. *Invest Ophthalmol Vis Sci* 1992; 33(suppl):1246.
458. Epstein DL, Grant WM. Carbonic anhydrase inhibitor side effects: serum chemical analysis. *Arch Ophthalmol* 1977; 95:1378-82.
459. Stone RA, Zimmerman TJ, Shin DH, et al. Low-dose methazolamide and intraocular pressure. *Am J Ophthalmol* 1977; 83:674-9.

460. Lichter PR, Newman LP, Wheeler NC, Beall OV. Patient tolerance to carbonic anhydrase inhibitors. *Am J Ophthalmol* 1978; 85:495-502.
461. Wisch N, Fischbein FI, Siegel R, et al. Aplastic anemia resulting from the use of carbonic anhydrase inhibitors. *Am J Ophthalmol* 1973; 75:130-2.
462. Zimran A, Beutler E. Can the risk of acetazolamide-induced aplastic anemia be decreased by periodic monitoring of blood cell count? *Am J Ophthalmol* 1987; 104:654-8.
463. Mogk LG, Cyrlin MN. Blood dyscrasias and carbonic anhydrase inhibitors. *Ophthalmology* 1988; 95:768-71.
464. Laibovitz R, Boyle J, Snyder E, et al. Dorzolamide versus pilocarpine as adjunctive therapies to timolol: a comparison of patient preference and impact on daily life. *Clin Ther* 1996; 18:821-32.
465. Barnebey H, Kwok SY. Patient's acceptance of a switch from dorzolamide to brinzolamide for the treatment of glaucoma in a clinical practice setting. *Clin Ther* 2000; 22:1204-12.
466. Sall K and the Brinzolamide Primary Therapy Study Group. The efficacy and safety of brinzolamide 1% ophthalmic suspension (Azopt) as a primary therapy in patients with open-angle glaucoma or ocular hypertension. *Surv Ophthalmol* 2000; 44(suppl 2):S155-62.
467. Silver LH and the Brinzolamide Primary Therapy Study Group. Clinical efficacy and safety of brinzolamide (Azopt), a new topical carbonic anhydrase inhibitor for primary open-angle glaucoma and ocular hypertension. *Am J Ophthalmol* 1998; 126:400-8.
468. March WF, Ochsner KI, and the Brimonidine Long-Term Therapy Study Group. The long-term safety and efficacy of brinzolamide

- 1.0% (Azopt) in patients with primary open-angle glaucoma or ocular hypertension. *Am J Ophthalmol* 2000; 129:136-43.
469. Silver LH and the Brinzolamide Dose-Response Study Group. Dose-response evaluation of the ocular hypotensive effect of brinzolamide ophthalmic suspension (Azopt). *Surv Ophthalmol* 2000; 44(suppl 2):S147-53.
470. Nardin G. Activity of the topical CAI MK-507 bid when added to timolol bid. *Invest Ophthalmol Vis Sci* 1991; 32(suppl):989-95.
471. Shin D and the Brinzolamide Adjunctive Therapy Study Group. Adjunctive therapy with brinzolamide 1% ophthalmic suspension (Azopt) in patients with open-angle glaucoma or ocular hypertension maintained on timolol therapy. *Surv Ophthalmol* 2000; 44(suppl):S163-8.
472. Strahlman ER, Vogel R, Tipping R, Clineschmidt CM. The use of dorzolamide and pilocarpine as adjunctive therapy to timolol in patients with elevated intraocular pressure: the Dorzolamide Additivity Study Group. *Ophthalmology* 1996; 103:1283-93.
473. Barnes GE, Li B, Dean T, Chandler ML. Increased optic nerve head blood flow after 1 week of twice daily topical brinzolamide treatment in Dutch-belted rabbits. *Surv Ophthalmol* 2000; 44(suppl 2):S131-40.
474. Harris A, Arend O, Arend S, Martin B. Effects of topical dorzolamide on retinal and retro-bulbar hemodynamics. *Acta Ophthalmol Scand* 1996; 74:569-72.
475. Kavanagh JT, Yasaga E, Sponsel WE, et al. Does dorzolamide 2% protect against hyperventilation-induced depression of perimacular circulation? *Invest Ophthalmol Vis Sci* 1996; 37(suppl):269.
476. Schmidt KG, Von Rückmann AV, Pillunat LE. Topical carbonic anhydrase inhibition increases ocular pulse amplitude in high

- tension primary open-angle glaucoma. *Br J Ophthalmol* 1998; 82:758-62.
477. Silver LH and the Brinzolamide Comfort Study Group. The ocular comfort of brinzolamide 1% ophthalmic suspension compared to dorzolamide 2% ophthalmic solution: results from two multicenter comfort studies. *Surv Ophthalmol* 2000; 44(suppl 2):S141-5.
478. Donohue EK, Wilensky JT. Trusopt, a topical carbonic anhydrase inhibitor. *J Glaucoma* 1996; 5:68-74.
479. Stewart R and the Brinzolamide Comfort Study Group. The ocular comfort of TID-dosed brinzolamide 1% compared to TID-dosed dorzolamide 2% in patients with primary open-angle glaucoma or ocular hypertension. *Invest Ophthalmol Vis Sci* 1997; 38 (suppl):559.
480. Abramson DH, Chang S, Coleman J. Pilocarpine therapy in glaucoma: effects on anterior chamber depth and lens thickness in patients receiving long-term therapy. *Arch Ophthalmol* 1976; 94:914-8.
481. Zimmerman TJ. Pilocarpine. *Ophthalmology* 1981; 88:85-8.
482. Boyle JE, Ghosh K, Gieser DK, et al. and the Dorzolamide - Timolol Study Group. A randomized trial comparing the dorzolamide-timolol combination given twice daily to monotherapy with timolol and dorzolamide. *Ophthalmology* 1998; 105:1945-51.
483. Strohmaier K, Snyder E, DuBiner H, et al. The efficacy and safety of the dorzolamide-timolol combination versus the concomitant administration of its components. *Ophthalmology* 1998; 105:1936-44.
484. Clineschmidt CM, Williams RD, Snyder E, et al., and the Dorzolamide-Timolol Combination Study Group. A randomized trial in patients inadequately controlled with timolol alone

- comparing the dorzolamide-timolol combination to monotherapy with timolol or dorzolamide. *Ophthalmology* 1998; 105:1952-9.
485. Polo V, Larrosa JM, Gomez ML, et al. Latanoprost versus combined therapy with timolol plus dorzolamide: IOP-lowering effect in open-angle glaucoma. *Acta Ophthalmol Scand* 2001; 79:6-9.
 486. Sherwood MB, Craven ER, Chou C, et al. Twice-daily 0.2% brimonidine-0.5% timolol fixed-combination therapy vs monotherapy with timolol or brimonidine in patients with glaucoma or ocular hypertension: a 12-month randomized trial. *Arch Ophthalmol* 2006; 124:1230-8.
 487. Baez K, Spaeth GL. Argon laser trabeculoplasty controls one third of patients with progressive, uncontrolled open-angle glaucoma for five years. *Trans Am Ophthalmol Soc* 1991; 84:47-58.
 488. Moulin F, Le Mer Y, Haut J. Five-year results of the first 159 consecutive phakic chronic open-angle glaucomas treated by argon laser trabeculoplasty. *Ophthalmologica* 1991; 202:3-9.
 489. Shingleton BJ, Richter CU, Dharma SK. Long-term efficacy of argon laser trabeculoplasty. A 10-year follow-up study. *Ophthalmology* 1993; 100:1324-9.
 490. Schwartz AL, Love DC, Schwartz MA. Long-term follow-up of argon laser trabeculoplasty for uncontrolled open-angle glaucoma. *Arch Ophthalmol* 1985; 103:1482-4.
 491. Wise JB. Ten year results of laser trabeculoplasty. Does the laser avoid glaucoma surgery or merely defer it? *Eye* 1987; 1:45-50.
 492. Reiss GR, Wilensky JT, Higginbotham EJ. Laser trabeculoplasty. *Surv Ophthalmol* 1991; 35:407-28.

493. Moriarty AP, McHugh JD, Ffytche TJ, et al. Long-term follow-up of diode laser trabeculoplasty for primary open-angle glaucoma and ocular hypertension. *Ophthalmology* 1993; 100:1614-8.
494. Chung PY, Schuman JS, Netland PA, et al. Five-year results of a randomized, prospective, clinical trial of diode vs. argon laser trabeculoplasty for open-angle glaucoma. *Am J Ophthalmol* 1998; 126:185-90.
495. Latina MA, Park C. Selective targeting of trabecular meshwork cells: in vitro studies at pulsed and CW laser interactions. *Exp Eye Res* 1995; 60:359-71.
496. Wise JB. Glaucoma treatment by trabecular tightening with the argon laser. *Int Ophthalmol Clin* 1981; 21:69-78.
497. van Buskirk EM, Pond V, Rosenquist RC, Acott TS. Argon laser trabeculoplasty. Studies of mechanism of action. *Ophthalmology* 1984; 91:1005-10.
498. Bylsma SS, Samples JR, Acott TS, Van Burskirk EM. Trabecular cell division after argon laser trabeculoplasty. *Arch Ophthalmol* 1988; 106:544-7.
499. Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial. I. Acute effects of argon laser trabeculoplasty on intraocular pressure. *Arch Ophthalmol* 1989; 107:1135-42.
500. Krupin T, Kolker AE, Kass MA, Becker B. Intraocular pressure the day of argon laser trabeculoplasty in primary open-angle glaucoma. *Ophthalmology* 1984; 91:361-5.
501. Glaucoma Laser Trial Research Group. The Glaucoma Laser Trial (GLT) and Glaucoma Laser Trial Followup Study: 7. Results. *Am J Ophthalmol* 1995; 120:718-31.

502. Schwartz AL, Whitten ME, Bleiman B, Martin D. Argon laser trabeculoplasty in uncontrolled phakic open-angle glaucoma. *Ophthalmology* 1981; 88:203-12.
503. Wilensky JT, Jampol LM. Laser therapy for open angle glaucoma. *Ophthalmology* 1981; 88:213-7.
504. Robin AL. Argon laser trabeculoplasty medical therapy to prevent the intraocular pressure rise associated with argon laser trabeculoplasty. *Ophthalmic Surg* 1991; 22:31-7.
505. Wilensky JT, Weinreb RN. Early and late failures of argon laser trabeculoplasty. *Arch Ophthalmol* 1983; 101:895-7.
506. Hoskins HD Jr, Hetherington J Jr, Minckler DS, et al. Complications of laser trabeculoplasty. *Ophthalmology* 1983; 90:796-9.
507. Damji KF, Bovell AM, Wodge WG, et al. Selective laser trabeculoplasty versus argon laser trabeculoplasty: results from a 1-year randomized clinical trial. *Br J Ophthalmol* 2006; 90:1490-4.
508. Girkin CA. Selective vs. argon laser trabeculoplasty: controversy in evolution. *Am J Ophthalmol* 2007; 144:120-1.
509. McIlraith I, Strasfeld M, Colev G, Hutnik CM. Selective laser trabeculoplasty as initial and adjunctive treatment for open-angle glaucoma. *J Glaucoma* 2006; 15:124-30.
510. Nagar M, Ogunyomade A, O'Brart DP, et al. A randomised, prospective study comparing selective laser trabeculoplasty with latanoprost for the control of intraocular pressure in ocular hypertension and open angle glaucoma. *Br J Ophthalmol* 2005; 89:1413-7.
511. Ederer F, Gaasterland DA, Dally LG, et al. The Advanced Glaucoma Intervention Study (AGIS): 13. Comparison of

- treatment outcomes within race: 10-year results. *Ophthalmology* 2004; 111:651-64.
512. Chandler PA. Long-term results in glaucoma therapy. *Am J Ophthalmol* 1960; 49:221-46.
513. Abedin S, Simmons RJ, Grant WM. Progressive low-tension glaucoma. Treatment to stop glaucomatous cupping and field loss when these progress despite normal intraocular pressure. *Ophthalmology* 1982; 89:1-6.
514. de Jong N, Greve EL, Hoyng PF, et al. Results of a filtering procedure in low-tension glaucoma. *Int Ophthalmol* 1989; 13:131-8.
515. Bylsma S. Nonpenetrating deep sclerectomy: collagen implant and viscocanalostomy procedures. *Int Ophthalmol Clin* 1999; 39:103-19.
516. Crandall AS. Nonpenetrating filtering procedures: viscocanalostomy and collagen wick. *Semin Ophthalmol* 1999; 14:189-95.
517. Mermoud A. Sinusotomy and deep sclerectomy. *Eye* 2000; 14:531-5.
518. Demailly P, Lavat P, Kretz G, Jeanteur-Lunel MN. Non-penetrating deep sclerectomy (NPDS) with or without collagen device (CD) in primary open-angle glaucoma: middle-term retrospective study. *Int Ophthalmol* 1996-1997; 20:131-40.
519. Sanchez E, Schnyder CC, Sickenberg M, et al. Deep sclerotomy: results with and without collagen implant. *Int Ophthalmol* 1996-1997; 20:157-62.
520. Chiou AG, Mermoud A, Jewelewicz DA. Post-operative inflammation following deep sclerectomy with collagen implants

- versus standard trabeculectomy. Graefes Arch Clin Exp Ophthalmol 1998; 236:593-6.
521. Carassa RG, Bettin P, Fiori M, et al. Viscocanalostomy versus trabeculectomy: a 12 month randomized prospective trial. Invest Ophthalmol Vis Sci 2000; 41(suppl):744.
522. Karlen M, Sanchez E, Schnyder CC, et al. Deep sclerectomy with collagen implant: medium term results. Br J Ophthalmol 1999; 83:6-11.
523. Sharir M, Zimmerman TJ. Initial treatment of glaucoma: medical therapy. Surv Ophthalmol 1993; 37:299-304.
524. Lichter PR, Ravin JG. Risk of sudden visual loss after glaucoma surgery. Am J Ophthalmol 1974; 78:1009-13.
525. Mills KB. Trabeculectomy: a retrospective long-term follow-up of 444 cases. Br J Ophthalmol 1981; 65:790-5.
526. D'Ermo F, Bonomi L, Doro D. A critical analysis of the long-term results of trabeculectomy. Am J Ophthalmol 1979; 88:829-35.
527. Katz LJ, Cantor LB, Spaeth GL. Complications of surgery in glaucoma, early and late bacterial endophthalmitis following glaucoma filtering surgery. Ophthalmology 1985; 92:959-63.
528. Hitchings RA, Grierson I. Clinico-pathological correlation in eyes with failed fistulizing surgery. Trans Ophthalmol Soc UK 1983; 103:84-8.
529. Siriwardena PT, Khaw ML, Donaldson AJ, et al. A randomized placebo-controlled trial of human anti-TGFB₂ monoclonal antibody (CAT-152): a new modulator of wound healing following trabeculectomy. Invest Ophthalmol Vis Sci 2000; 41(suppl):744.

530. Unlu K, Aksunger A. Descemet membrane detachment after viscocanalostomy. Am J Ophthalmol 2000; 130:833-4.
531. Drusedau MU, von Wolff K, Bull H, von Barsewisch B. Viscocanalostomy for primary open-angle glaucoma. The Gross Pankow experience. J Cataract Refract Surg 2000; 26:1367-73.
532. Tuulonen A. Laser trabeculoplasty as primary therapy in chronic open angle glaucoma. Acta Ophthalmol (Copenh) 1984; 62:150-5.
533. Tuulonen A, Kopponen J, Alanko HI, Airaksinen PJ. Laser trabeculectomy versus medication treatment as primary therapy for glaucoma. Acta Ophthalmol (Copenh) 1989; 67:275-80.
534. van Buskirk EM. The laser step in early glaucoma therapy. Am J Ophthalmol 1991; 112:87-90.
535. Lichter PR. Practice implications of the glaucoma laser trial. Ophthalmology 1990; 97:1401-2.
536. Bergeå B, Bodin L, Svedbergh B. Primary argon laser trabeculoplasty vs pilocarpine. II. Long-term effects on intraocular pressure and facility of outflow. Study design and additional therapy. Acta Ophthalmol (Copenh) 1994; 72:145-54.
537. Bergeå B, Bodin L, Svedbergh B. Primary argon laser trabeculoplasty vs pilocarpine. III. Long-term effects on visual fields. Acta Ophthalmol Scand 1995; 73:207-15.
538. Bergeå B, Bodin L, Svedbergh B. Primary argon laser trabeculoplasty vs pilocarpine. IV. Long-term effects on optic nerve head. Acta Ophthalmol Scand 1995; 73:216-21.
539. Lavin MJ, Wormald RP, Migdal CS, Hitchings RA. The influence of prior therapy on the success of trabeculectomy. Arch Ophthalmol 1990; 108:1543-8.

- 540. Lichter PR, Musch DC, Gillespie BW, et al. Interim clinical outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medications or surgery. *Ophthalmology* 2001; 108:1943-53.
- 541. Feinrer L, Piltz-Seymour JR. Collaborative Initial Glaucoma Treatment Study Group. Collaborative Initial Glaucoma Treatment Study: a summary of results to date. *Curr Opin Ophthalmol* 2003; 14:106-11.
- 542. Migliazzi CV, Shaffer RN, Nykin R, Magee S. Long-term analysis of pigmentary dispersion syndrome and pigmentary glaucoma. *Ophthalmology* 1986; 93:1528-36.
- 543. Liebmann JM, Ritch R. Pigment dispersion syndrome and pigmentary glaucoma. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw-Hill, 2001:429-41.
- 544. Ritch R, Liebermann J, Robin A, et al. Argon laser trabeculoplasty in pigmentary glaucoma. *Ophthalmology* 1993; 100:909-13.
- 545. Walker JD. A suggested role for argon laser iridoplasty in management of pigmentary glaucoma. *Ophthalmic Surg* 1986; 17:762-3.
- 546. Karickhoff JR. Pigmentary dispersion syndrome and pigmentary glaucoma: a new mechanism concept, a new treatment, and a new technique. *Ophthalmic Surg* 1992; 23:269-77.
- 547. Reistad CE, Shields MB, Campbell DG, et al. American Glaucoma Society Pigmentary Glaucoma Iridotomy Study Group. The influence of peripheral iridotomy on the intraocular pressure course in patients with pigmentary glaucoma. *J Glaucoma* 2005; 14:255-9.

- 548. Aasved H, Seland JH, Slagvold JE. Timolol maleate in the treatment of open-angle glaucoma. *Acta Ophthalmol (Copenh)* 1979; 57:700-8.
- 549. Brooks AM, Gillies WE. The presentation and prognosis of glaucoma in pseudoexfoliation of the lens capsule. *Ophthalmology* 1988; 95:271-6.
- 550. Lindblom B, Thornburn W. Prevalence of visual field defects due to capsular and simple glaucoma in Halsingland, Sweden. *Acta Ophthalmol (Copenh)* 1982; 60:353-61.
- 551. Tarkkanen A. Treatment of chronic open angle glaucoma associated with pseudoexfoliation. *Acta Ophthalmol (Copenh)* 1965; 43:514-23.
- 552. Airaksinen PJ. The long-term hypotensive effect of timolol maleate compared with the effect of pilocarpine in simple and capsular glaucoma. *Acta Ophthalmol (Copenh)* 1979; 57:425-34.
- 553. Blika S, Saunte E. Timolol maleate in the treatment of glaucoma simplex and glaucoma capsulare. A three-year follow-up study. *Acta Ophthalmol (Copenh)* 1982; 60:967-76.
- 554. Olivius E, Thornburn W. Prognosis of glaucoma simplex and glaucoma capsulare: a comparative study. *Acta Ophthalmol (Copenh)* 1978; 56:921-34.
- 555. Aasved H. The frequency of optic nerve damage and surgical treatment in chronic simple glaucoma and capsular glaucoma. *Arch Ophthalmol (Copenh)* 1971; 49:589-600.
- 556. Ritch R, Podos SM. Laser trabeculoplasty in secondary glaucomas. In: Jakobiec FA, Sigelman J, eds. *Advanced techniques in ocular surgery*. Philadelphia: Saunders, 1984:124-34.

- 557. Spaeth GL, Baez KA. Argon laser trabeculoplasty controls one third of cases of progressive, uncontrolled, open angle glaucoma for 5 years. *Arch Ophthalmol* 1992; 110:491-4.
- 558. Threlkeld AB, Hertzmark E, Sturm RT, et al. Comparative study of the efficacy of argon laser trabeculoplasty for exfoliation and primary open-angle glaucoma. *J Glaucoma* 1996; 5:311-6.
- 559. Ritch R, Liebmann JM. Exfoliation syndrome and exfoliation glaucoma. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw-Hill, 2001:443-59.
- 560. Bartlett JD, Jaanus SD. Medical management of the glaucomas. In: Bartlett JD, Jaanus SD, eds. *Clinical ocular pharmacology*, 4th ed. Boston: Butterworth-Heinemann, 2001:831-91.
- 561. Stamper RL, Lieberman MF, Drake MV. Medical treatment of glaucoma: general principles. In: *Becker-Shaffer's diagnosis and therapy of the glaucomas*, 7th ed. St. Louis: Mosby, Inc., 1999:414-32.
- 562. Bloch S, Rosenthal AR, Friedman L, Caldarolla P. Patient compliance in glaucoma. *Br J Ophthalmol* 1977; 61:531-4.
- 563. Vincent P. Patient viewpoints of glaucoma therapy. *Sight Saving Rev* 1973(winter):213-21.
- 564. Friedman DR, Quigley HA, Gelb L, et al. Using pharmacy claims data to study adherence to glaucoma medications: methodology and findings of the Glaucoma Adherence and Persistency Study (GAPS). *Invest Ophthalmol Vis Sci* 2007; 48:5052-7.
- 565. Kass MA, Gordon M, Morley RE Jr, et al. Compliance with topical timolol treatment. *Am J Ophthalmol* 1987; 103:188-93.
- 566. Kass MA, Meltzer DW, Gordon M, et al. Compliance with topical pilocarpine treatment. *Am J Ophthalmol* 1986; 101:515-23.

- 567. MacKean JM, Elkington AR. Compliance with treatment of patients with chronic open-angle glaucoma. *Br J Ophthalmol* 1983; 67:46-9.
- 568. Spaeth GL. Visual loss in a glaucoma clinic. I. Sociologic considerations. *Invest Ophthalmol* 1970; 9:73-82.
- 569. Realini T, Vickers WR. Symmetry of fellow-eye intraocular pressure responses to topical glaucoma medications. *Ophthalmology* 2005; 112:599-602.
- 570. Nordstrom BL, Friedman DS, Mozaffari E, et al. Persistence and adherence with topical glaucoma therapy. *Am J Ophthalmol* 2005; 140:598-606.
- 571. Heijl A, Lindgren G, Olsson J. Normal variability of static perimetric threshold values across the central visual field. *Arch Ophthalmol* 1987; 105:1544-9.
- 572. Brandt JD, Beiser JA, Gordon MO, Kass MA. Central corneal thickness and measured IOP response to topical ocular hypotensive medication in the Ocular Hypertension Treatment Study. *Am J Ophthalmol* 2004; 138:717-22.
- 573. Richardson KT. Medical control of glaucomas. *Br J Ophthalmol* 1972; 56:272-7.
- 574. Hollo G, Chiselita D, Petkova N, et al. The efficacy and safety of timolol maleate versus brinzolamide each given twice daily added to travoprost in patients with ocular hypertension or primary open-angle glaucoma. *Eur J Ophthalmol* 2006; 16:816-23.
- 575. Quigley HA, Tielsch JM, Katz J, Sommer A. Rate of progression in open-angle glaucoma estimated from cross-sectional prevalence of visual field damage. *Am J Ophthalmol* 1996; 122:355-63.

- 576. Rasker MT, van den Enden A, Bakker D, Hoyng PF. Rate of visual field loss in progressive glaucoma. *Arch Ophthalmol* 2000; 118:481-8.
- 577. Katz J, Gilbert D, Quigley HA, Sommer A. Estimating progression of visual field loss in glaucoma. *Ophthalmology* 1997; 104:1017-25.
- 578. Smith SD, Katz J, Quigley HA. Analysis of progressive change in automated visual fields in glaucoma. *Invest Ophthalmol Vis Sci* 1996; 37:1419-28.
- 579. Nouredin BN, Poinosawmy D, Fietzke FW, Hitchings RA. Regression analysis of visual field progression in low tension glaucoma. *Br J Ophthalmol* 1991; 75:493-5.
- 580. Hart WM Jr, Becker B. The onset and evolution of glaucomatous visual field defects. *Ophthalmology* 1982; 89:268-79.
- 581. Mikelberg FS, Schulzer M, Drance SM, Lau W. The rate of progression of scotomas in glaucoma. *Am J Ophthalmol* 1986; 101:1-6.
- 582. Chumbley LC, Brubaker RF. Low-tension glaucoma. *Am J Ophthalmol* 1976; 81:761-7.
- 583. Shirakashi M, Iwata K, Sawaguchi S, et al. Intraocular pressure-dependent progression of visual field loss in advanced primary open-angle glaucoma: a 15-year follow-up. *Ophthalmologica* 1993; 207:1-5.
- 584. Watson PG, Grierson I. The place of trabeculectomy in the treatment of glaucoma. *Ophthalmology* 1981; 88:175-96.
- 585. Nouri-Mahdavi K, Hoffman D, Coleman AL, et al. Predictive factors for glaucomatous visual field progression in the Advanced Glaucoma Intervention Study. *Ophthalmology* 2004; 111:1627-35.

- 586. Forsman E, Kivela T, Vesti E. Lifetime visual disability in open-angle glaucoma and ocular hypertension. *J Glaucoma* 2007; 16:313-9.
- 587. Thomas JV, Simmons RJ, Belcher CD 3rd. Argon laser trabeculoplasty in the presurgical glaucoma patient. *Ophthalmology* 1982; 89:187-97.
- 588. Wickham MG, Worthen DM. Argon laser trabeculoplasty: long-term followup. *Ophthalmology* 1979; 86:495-503.
- 589. Ustundag C, Diestelhorst M. Efficacy of argon laser trabeculoplasty: 3-year preliminary results of a prospective placebo-controlled study. *Graefes Arch Clin Exp Ophthalmol* 1997; 235:354-8.
- 590. Moulin F, Haut J. Argon laser trabeculoplasty. Results over 10 years. *J Fr Ophtalmol* 1994; 17:93-8.
- 591. Richter CU, Shingleton BJ, Bellows AR, et al. Retreatment with argon laser trabeculoplasty. *Ophthalmology* 1987; 94:1085-9.
- 592. Damji KF, Shah KC, Bains KS, et al. Selective laser trabeculoplasty. V. Argon laser trabeculoplasty: a prospective randomized clinical trial. *Br J Ophthalmol* 1999; 83:718-22.
- 593. Kajiya S, Hayakawa K, Sawaguchi S. Clinical results of selective laser trabeculoplasty. *Jpn J Ophthalmol* 2000; 44:574-5.
- 594. Latina MA, Sibayan SA, Shin DH, et al. Q-switched 532 nm Nd:YAG laser trabeculoplasty (selective laser trabeculoplasty): a multicenter, pilot, clinical study. *Ophthalmology* 1998; 105:2082-8.
- 595. Schwartz AL, Kopelman J. Four-year experience with argon laser trabecular surgery in uncontrolled open-angle glaucoma. *Ophthalmology* 1983; 90:771-80.

596. Pollack IP, Robin AL, Sax H. The effect of argon laser trabeculoplasty on the medical control of primary open-angle glaucoma. *Ophthalmology* 1983; 90:785-9.
597. Safran MJ, Robin AL, Pollack IP. Argon laser trabeculoplasty in younger patients with primary open-angle glaucoma. *Am J Ophthalmol* 1984; 97:292-5.
598. Nouri-Mahdavi K, Brigatti L, Weitzman M, Caprioli J. Outcomes of trabeculectomy for primary open-angle glaucoma. *Ophthalmology* 1995; 102:1760-9.
599. Watson PG, Grierson I. Early trabeculectomy in the treatment of chronic open-angle glaucoma in relationship to histological changes. *Int Ophthalmol Clin* 1984; 24:13-32.
600. Tornqvist G, Drolsum LK. Trabeculectomies: a long-term study. *Acta Ophthalmol (Copenh)* 1991; 69:450-4.
601. Jerndal T, Lundstrom M. 330 trabeculectomies: a long time study (3-5½ years). *Acta Ophthalmol (Copenh)* 1980; 58:947-56.
602. Robinson DI, Lertsumitkul S, Billson FA, Robinson LP. Long-term intraocular pressure control by trabeculectomy: a ten-year life table. *Aust NZ J Ophthalmol* 1993; 21:79-85.
603. Inaba Z. Long-term results of trabeculectomy in Japanese: an analysis by life-table method. *Jpn J Ophthalmol* 1982; 26:361-73.
604. Shirato S, Kitazawa Y, Mishima S. A critical analysis of the trabeculectomy results in a prospective follow-up design. *Jpn J Ophthalmol* 1982; 26:468-80.
605. Palmer SS. Mitomycin as adjunct chemotherapy with trabeculectomy. *Ophthalmology* 1991; 98:317-21.
606. The Fluorouracil Filtering Surgery Study Group. Fluorouracil Filtering Surgery Study. One year follow-up. *Am J Ophthalmol* 1989; 108:625-35.

607. Vesti E, Raitta C. A review of the outcome of trabeculectomy in open-angle glaucoma. *Ophthalmic Surg Lasers* 1997; 28:128-32.
608. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 4. Comparison of treatment outcomes within race. *Ophthalmology* 1998; 105:1146-64.
609. Stegmann R, Pienaar A, Miller D. Viscocanalostomy for open-angle glaucoma in black African patients. *J Cataract Refract Surg* 1999; 25:316-22.
610. Jonescu-Cuypers C, Jacobi P, Konen W, Krieglstein G. Primary viscocanalostomy versus trabeculectomy in white patients with open-angle glaucoma. A randomized clinical trial. *Ophthalmology* 2001; 108:254-8.
611. Stewart WC, Sine CS, LoPresto C. Surgical versus medical management of chronic open-angle glaucoma. *Am J Ophthalmol* 1996; 122:767-74.
612. Gillies WE, Dallison IW, Brooks AM. Long-term results with argon laser trabeculoplasty. *Aust NZ J Ophthalmol* 1994; 22:39-43.
613. Katz LJ, Spaeth GL, Cantor LB, et al. Reversible optic disk cupping and visual field improvement in adults with glaucoma. *Am J Ophthalmol* 1989; 107:485-92.
614. Daugeliene L, Yamamoto T, Kitazawa Y. Effect of trabeculectomy of visual field in progressive normal-tension glaucoma. *Jpn J Ophthalmol* 1998; 42:286-92.
615. Hagiwara Y, Yamamoto T, Kitazawa Y. The effect of mitomycin C trabeculectomy on the progression of visual field defects in normal-tension glaucoma. *Graefes Arch Clin Exp Ophthalmol* 2000; 238:232-6.
616. Koseki N, Araie M, Shirato S, Yamamoto S. Effect of trabeculectomy on visual field performance in central 30° field in

progressive normal tension glaucoma. *Ophthalmology* 1997; 104:197-201.

617. Hitchings RA, Wu J, Poinoosawmy D, McNaught A. Surgery for normal tension glaucoma. *Br J Ophthalmol* 1995; 79:402-6.
618. Pecori Giraldi J, De Benedetti G, Santarelli S, et al. Normal tension glaucoma: a ten-year follow-up. *Acta Ophthalmol Scand suppl* 1997; 224:17-8.
619. Shirai H, Sakuma T, Sogano S, Kitazawa Y. Visual field change and risk factors for progression of visual field damage in low tension glaucoma. *Nippon Ganka Gakkai Zasshi* 1992; 96:352-8.
620. Anderson DR, Drance SM, Schulzer M. Collaborative Normal-Tension Glaucoma Study Group. Natural history of normal-tension glaucoma. *Ophthalmology* 2001; 108:247-53.
621. Ritch R. Pigmentary glaucoma: a self-limited entity? *Ann Ophthalmol* 1983; 15:115-6.
622. Jerndal T, Kriisa V. Results of trabeculectomy for pseudoexfoliative glaucoma. A study of 52 cases. *Br J Ophthalmol* 1974; 58:927-30.
623. Raitta C. Filtering surgery in capsular glaucoma. *Acta Ophthalmol Suppl* 1988; 184:148-9.
624. Tanihara H, Negi A, Akimoto M, et al. Surgical effects of trabeculotomy ab externo on adult eyes with primary open angle glaucoma and pseudoexfoliation syndrome. *Arch Ophthalmol* 1993; 111:1653-61.
625. Higginbotham EJ, Richardson TM. Response of exfoliation glaucoma to laser trabeculoplasty. *Br J Ophthalmol* 1986; 70:837-9.

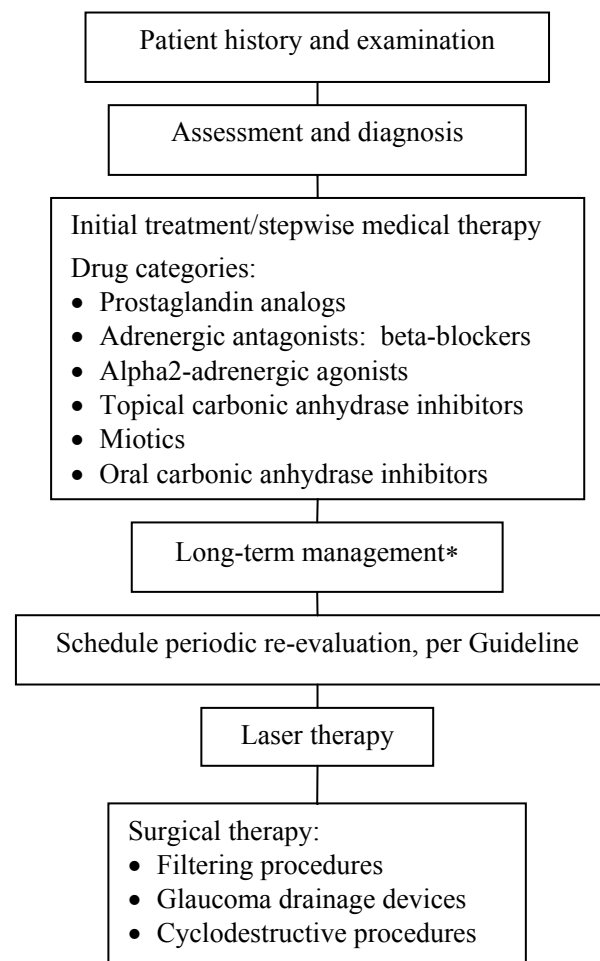


IV. APPENDIX

Figure 1
Potential Components of an Initial Glaucoma Evaluation

1. **Patient History**
Ocular and systemic risk factors and medical history
2. **Visual Acuity**
Corrected and uncorrected visual acuity
3. **Pupil Assessment**
Relative afferent pupillary defect
4. **Biomicroscopy**
Evaluation of anterior and posterior ocular segment
5. **Applanation Tonometry**
Diurnal variability
Symmetry
6. **Central Corneal Thickness Measurement**
7. **Gonioscopy**
Open or closed angle
Primary or secondary glaucoma
8. **Assessment of Optic Nerve**
Stereoscopic evaluation through a dilated pupil
Tomography
9. **Assessment of Nerve Fiber Layer**
Stereoscopic evaluation through a dilated pupil
Evaluation with red-free illumination
Confocal scanning laser polarimetry, optical coherence tomography, confocal scanning laser ophthalmoscopy
10. **Assessment of Peripapillary Area**
11. **Fundus Stereophotography**
Photodocumentation of optic nerve and nerve fiber layer
12. **Visual Fields**
Standard automated perimetry
Frequency doubling perimetry
Short wavelength automated perimetry

Figure 2
Optometric Management of the Patient with Primary Open Angle Glaucoma: A Brief Flowchart



*Long-term management of POAG involves patient education, continuity of care, compliance with therapy, communication with patients' physicians, and possibly comanagement with a glaucoma specialist.

Figure
Frequency and Composition of Evaluation

Type of Patient, Stage of Disease	Examination Frequency	Tonometry	Gonioscopy
New glaucoma patient or new glaucoma suspect	Weekly or biweekly to achieve target pressure	Multiple readings may be needed to establish baseline	Standard classification and documentation at initial visit
Glaucoma suspect	6-12 months, depending on level of risk	Multiple readings may be needed to establish baseline	Annually
Stable, mild	3-6 months	Every visit	Annually
Stable, moderate	2-4 months	Every visit	Annually
Stable, severe	1-3 months	Every visit	Annually
Unstable, IOP poorly controlled; ON or VF progressing	Weekly or biweekly until stability is established	Every visit	Initial visit and each time other clinical findings warrant reassessment
Stability recently established	1-3 months	Every visit; re-establish baseline	Depends on severity of the glaucoma

¹Confocal scanning laser imaging, confocal scanning laser polarimetry, and optical coherence tomography are all recommended annually in glaucoma suspect patients and those with mild to moderate disease who can respond to standard testing. Tests may be performed up to 2 times per year for patients with unstable borderline control and other

3
and Management Visits for Open Angle Glaucoma

ON/NFL Assessment	Stereoscopic ON, NFL, PPA; Documentation CSLI ¹	Perimetry ²	Management Plan
Dilate; optic nerve documentation at initial visit	As part of initial glaucoma evaluation	Repeat to establish baseline	Prepare problem list with treatment plan
Dilate every year	Annual	Annual	Review
Dilate every year at least	Annual	Annual	Review
Dilate every year at last	Annual	6-12 months, depending on prior data	Review
Dilate every year at least	Annual; CSLI ³	4-8 months, depending on prior data	Review
Dilate at initial visit and each time other clinical findings warrant reassessment	Annual or each time ON or NFL changes	4-6 weeks or as needed to establish new baselines	Formulate new plan until stable
Dilate every year	Annual or each time ON or NFL changes	Depends on severity of the disease	Review

glaucoma risk factors in whom visual fields or tonometry cannot be assessed.

²Threshold automated perimetry is recommended.

³These tests may not be useful for monitoring stable-severe or end-stage disease.

Figure 4
ICD–10–CM Classification of Open Angle Glaucoma

Glaucoma	365
<i>Excludes:</i> blind hypertensive eye [absolute glaucoma] (360.42) congenital glaucoma (743.20-743.22)	
Borderline glaucoma [glaucoma suspect]	365.0
Preglaucoma, unspecified	365.00
Open angle with borderline findings	365.01
Open angle with: borderline intraocular pressure cupping of optic discs	
Anatomical narrow angle	365.02
Steroid responders	365.03
Ocular hypertension	365.04
Open-angle glaucoma	365.1
Open-angle glaucoma, unspecified	365.10
Wide-angle glaucoma NOS (no other specifications)	
Primary open-angle glaucoma	365.11
Chronic simple glaucoma	
Low tension glaucoma	365.12
Pigmentary glaucoma	365.13
Glaucoma of childhood	365.14
Infantile or juvenile glaucoma	
Residual stage of open angle glaucoma	365.15
Corticosteroid-induced glaucoma	365.3
Glaucomatous stage	365.31
Residual stage	365.32

Glaucoma associated with disorders of the lens	365.5
Phacolytic glaucoma	365.51
<i>Use additional code for associated hypermature cataract (366.18)</i>	
Pseudoexfoliation glaucoma	365.52
<i>Use additional code for associated pseudoexfoliation of capsule (366.11)</i>	
Glaucoma associated with other lens disorders	365.59
<i>Use additional code for associated disorder, as: dislocation of lens (379.33–379.34) spherophakia (743.36)</i>	
Glaucoma associated with other ocular disorders	365.6
Glaucoma associated with unspecified ocular disorder	365.60
Glaucoma associated with ocular inflammations	365.62
<i>Use additional code for associated disorder, as: glaucomatocyclitic crises (364.22) iridocyclitis (364.0-364.3)</i>	
Glaucoma associated with vascular disorders	365.63
<i>Use additional code for associated disorder, as: central retinal vein occlusion (362.35) hyphema (364.41)</i>	
Glaucoma associated with tumors or cysts	365.64
<i>Use additional code for associated disorder, as: benign neoplasm (224.0-224.9) epithelial downgrowth (364.61) malignant neoplasm (190.0-190.9)</i>	
Glaucoma associated with ocular trauma	365.65
<i>Use additional code for associated condition, as: contusion of globe (921.3) recession of chamber angle (364.77)</i>	

Other specified forms of glaucoma	365.8
Hypersecretion glaucoma	365.81
Glaucoma with increased episcleral venous pressure	365.82
Other specified glaucoma	365.89
Unspecified glaucoma	365.9



Abbreviations of Commonly Used Terms

ACG	Angle closure glaucoma
AGIS	Advanced Glaucoma Intervention Study
ALT	Argon laser trabeculoplasty
AROC	Average rate of change
ATT	ALT-trabeculectomy-trabeculectomy
CAI	Carbonic anhydrase inhibitor
CCT	Central corneal thickness
C/D	Cup-to-disc ratio
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CSLT	Confocal scanning laser tomography
CW	Collagen wick
D	Diopter
dB	Decibel
DCT	Dynamic contour tonometry
EMGT	Early Manifest Glaucoma Trial
FDA	Food and Drug Administration
FDT	Frequency doubling technology

GAT	Goldmann applanation tonometry
GLT	Glaucoma Laser Trial
HR	Hazard ratio
IOP	Intraocular pressure
NEI	National Eye Institute of the National Institutes of Health
NFL	Nerve fiber layer
NPDS	Non-penetrating deep sclerectomy
NTG	Normal tension glaucoma
OAG	Open angle glaucoma
OCT	Optical coherence tomography
OH	Ocular hypertension
OHTS	Ocular Hypertension Treatment Study
ON	Optic nerve
ONH	Optic nerve head
PDS	Pigmentary dispersion syndrome
PEG	Pseudoexfoliation glaucoma
PERG	Pattern electroretinogram
PES	Pseudoexfoliation syndrome
PG	Pigmentary glaucoma

POAG	Primary open angle glaucoma
PPA	Peripapillary area
PSD	Pattern standard deviation
RNFL	Retinal nerve fiber layer
SWAP	Short-wavelength automated perimetry
TAT	Trabeculectomy-ALT-trabeculectomy
TIGR	Trabecular meshwork-induced glucocorticoid response protein
VC	Viscocanalostomy
VF	Visual field



Glossary

Afferent pupillary defect A defect of the pupillary reflex characterized by less constriction of both pupils when the affected eye is stimulated by light relative to that occurring when the unaffected eye is stimulated, as with the swinging flashlight test. The defect is also known as the Marcus Gunn pupil.

Anterior chamber The space in the eye, filled with aqueous humor, bordered anteriorly by the cornea and a small portion of the sclera and posteriorly by a small portion of the ciliary body, the iris, and that portion of the lens which presents through the pupil.

Apoptosis The programmed death of cells controlled by genetic expression from within the cell, which can be activated by a variety of physiological signals or cellular injuries.

Argon laser trabeculoplasty Perforation of the trabecular meshwork of the angle of the anterior chamber by an argon laser beam to facilitate aqueous humor outflow for the treatment of glaucoma.

Aqueous humor The clear, watery fluid that fills the anterior and posterior chambers of the eye.

Biomicroscopy Examination of ocular tissue, using a bright focal source of light with a slit of variable width and height and a binocular microscope with variable magnification.

Confocal scanning laser ophthalmoscopy The recording of two-dimensional sectional images for the evaluation of ocular tissue, using a confocal laser imaging system displayed digitally in real time.

Confocal scanning laser tomography The recording of a series of images along the axial axis of the eye enabling the three-dimensional reconstruction of the topography of the surface of the specific tissue under examination, using a confocal laser imaging system.

Confocal scanning laser polarimetry The measurement of the birefringent properties of the retinal nerve fiber layer, allowing indirect measurement of NFL thickness. The measurements are compared against a normative database.

Cup-to-disc ratio The ratio of the diameter of the area of excavation of the surface of the optic disc to that of the diameter of the optic disc in any given meridian, often either the horizontal or vertical meridian.

Excitotoxicity The stimulation of neurons to death by excessive levels of excitatory neurotransmitters.

Filtration surgery Surgical procedures (e.g., thermal sclerostomy, posterior or anterior lip sclerectomy, trephination, trabeculectomy) used to create an alternative pathway for the outflow of aqueous humor to lower intraocular pressure.

Fundus photography The use of a camera with optics and an illumination system that permits photographing the fundus of the eye.

Genetic mutation The alteration of DNA sequencing by changes in the genome.

Glaucoma A group of ocular diseases with various causes that ultimately are associated with progressive optic neuropathy leading to loss of visual function. Glaucoma is often associated with abnormally increased intraocular pressure.

Gonioscopy A diagnostic procedure to examine the angle of the anterior chamber in which a specialized corneal contact lens and a biomicroscope are used.

Intraocular pressure The pressure within the eye relative to the constant formation and drainage of the aqueous humor.

Multifactorial inheritance The determination of phenotype by multiple genetic and environmental factors, each making a small contribution.

Myocilin A protein believed to be associated with POAG, found both extraocularly and in the trabecular meshwork, optic nerve, retina, cornea, iris, ciliary body, and sclera.

Nerve fiber layer The layer of the retina that comprises unmyelinated axons of retinal ganglion cells.

Neuroprotection The use of pharmacological agents, genetic alteration, and other means to attenuate a destructive cellular environment, thereby protecting neurons from secondary degeneration caused by a variety of primary insults (ischemia/hypoxia, stroke, trauma, degeneration).

Neuroretinal rim The tissue between the optic cup and disc margins.

Nocturnal dip The decrease in systemic blood pressure during sleep.

Optical coherence tomography A noncontact, noninvasive imaging technique used to obtain high-resolution cross-sectional images of the retina. It is analogous to ultrasound B-scan imaging, except that it uses light rather than sound waves. OCT is used to measure the retinal nerve fiber layer thickness as well as optic nerve head and macula parameters.

Optic nerve The cranial nerve (N II) that carries visual impulses from the retina to the brain.

Pachymetry Measurement of the thickness of the cornea, usually done with an ultrasonic tool.

Perimetry Determination of the extent of the visual field for various types and intensities of stimuli for the purpose of diagnosing and localizing disturbances in the visual pathway.

Peripapillary area Tissue surrounding the optic nerve head.

Polygenic The traits or diseases caused by the impact of many genes, each with a small additive effect on phenotype.

Posterior chamber The space in the eye delimited by the posterior surface of the iris, the ciliary processes, and the valleys between them, the zonule of Zinn, and the anterior surface of the crystalline lens. It includes the canal of Hanover, the canal of Petit, and the retrolental space of Berger.

Pulsatile ocular blood flow The indirect assessment of choroidal blood flow by estimating the influx of blood into the eye during cardiac systole from an evaluation of the continuous IOP pulse wave.

Refraction Clinically, the determination of the refractive errors of an eye, or eyes (e.g., myopia, hyperopia, astigmatism, anisometropia).

Reverse pupillary block The blockage of the movement of aqueous humor from the posterior to the anterior chamber due to a concave anatomical configuration of the iris.

Selective laser trabeculoplasty The use of a q-switched Nd:YAG laser to selectively destroy pigmented cells in the trabecular meshwork without causing coagulative necrosis.

Short-wavelength automated perimetry A form of automated perimetry that isolates the blue cone mechanism of the visual system by utilizing a two-color incremental thresholding technique consisting of a large blue target on a bright yellow background.

Tonometry A procedure for measurement of the pressure within the eye. Clinically, tonometry measures the intraocular tension.

Trabecular meshwork The meshwork of connective tissue located between the canal of Schlemm and the anterior chamber and involved in drainage of aqueous humor from the eye.

Trabeculectomy Surgical removal of a portion of the trabecular meshwork to facilitate aqueous humor outflow in glaucoma.

Visual acuity The clearness of vision that depends on the sharpness of the retinal image and the integrity of the retinal and visual pathway. It is

expressed as the angle subtended at the anterior focal point of the eye by the detail of the letter or symbol recognized.

Visual field The area or extent of space visible to an eye in a given position.

Sources:

Grosvenor TP. Primary care optometry. Part I. Anomalies of refraction and binocular vision, 4th ed. Woburn, MA: Butterworth-Heinemann, 2002.

Hofstetter HW, Griffin JR, Berman MS, Everson RW. Dictionary of visual science and related clinical terms, 5th ed. Boston, MA: Butterworth-Heinemann, 2000.

Millodot M. Dictionary of optometry and visual science. Boston, MA: Butterworth-Heinemann, 1997.

Vaughan D, Asbury T, Riordan-Eva P. General ophthalmology, 15th ed. Stamford, CT: Appleton & Lange, 1999:419-22.

