

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.

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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

First Edition Originally Prepared by (and Second Edition Reviewed by)
the American Optometric Association Consensus Panel on Care of the
Patient with Open Angle Glaucoma:

Thomas L. Lewis, O.D., Ph.D., Author
Howard S. Barnebey, M.D. (1st Edition)
Jimmy D. Bartlett, O.D.
Allen J. Blume, O.D.
Murray Fingeret, O.D.
Peter A. Lalle, O.D.
Daryl F. Mann, O.D.

Assisted by:

Sigrid Mueller, O.D.
Kelly S. Shintani, O.D.

Reviewed by the AOA Clinical Guidelines Coordinating Committee:

John C. Townsend, O.D., Chair (2nd Edition)
John F. Amos, O.D., M.S. (1st and 2nd Editions)
Barry Barresi, O.D., Ph.D. (1st Edition)
Kerry L. Beebe, O.D. (1st Edition)
Jerry Cavallerano, O.D., Ph.D. (1st Edition)
John Lahr, O.D. (1st Edition)
W. Howard McAlister, O.D., M.P.H. (2nd Edition)
Stephen C. Miller, O.D. (2nd Edition)
David Mills, O.D. (1st Edition)

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Refer to the listed references and other sources
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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, 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 6.7 million persons worldwide are blind as a result of glaucoma, making it the second leading cause of bilateral blindness.¹ An estimated 130,000 Americans are blind from glaucoma,¹ making it the third most common cause of blindness in the United States.²⁻⁵

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).⁴ Over 11 percent of all blindness and 8 percent of all visual impairment may be due to glaucoma.⁶ 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.^{3,4} On average, it begins 10 years earlier in African Americans than in Caucasians.

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.^{6,7} Therefore, these estimates may be 2–3 times less than the true prevalence.³ 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 angle of the eye, as either open angle glaucoma (OAG) or angle closure glaucoma (ACG).⁸ This Clinical Practice Guideline focuses on OAG (see Appendix Figure 4 for ICD-9-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, 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.^{2,9-11} 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 typically below a certain level, typically 21 mm Hg, is known as low tension or normal tension glaucoma (NTG).

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 may be due to acceleration and exaggeration of normal aging changes in the anterior chamber angle, iris, and ciliary body tissues of the eye.¹²⁻¹⁴ 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.¹⁵

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.¹⁶⁻¹⁸ Cellular damage activates proteins that control at least two key genes, one that inhibits apoptosis (bcl-2) and one that promotes cell death (bax).¹⁸ These genes, in turn, affect a cascade of cellular events that result in the death of ganglion cells.

At least two key stimuli appear to activate the process of ganglion cell apoptosis in glaucoma: neurotrophin deprivation¹⁹ and glutamate toxicity.²⁰ Blockage of retrograde axonal transport prevents the normal

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movement of neurotrophic factors from the brain to the ganglion cell body.¹⁶ 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, but elevated IOP increases this response.

Müller cells play a critical role in maintaining transport systems in the retina,²¹ by keeping the normal excitatory protein glutamate at low levels.²² 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.²²⁻²⁴ Calcium channels in the ganglion cell membrane open up, causing an overload of calcium,²² which activates the enzyme nitric oxide synthase, leading to the formation of excessive levels of nitric oxide, and, finally, cell death.^{25,26}

Excitotoxicity, a process in which neurons are stimulated to death, involves mainly glutamate, although other excitatory amino acids may participate.^{22,27,28} Investigators have recently discovered increased levels of nitric oxide²⁹ in the optic nerve head (ONH) and elevated levels of glutamate in the vitreous²³ 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,³⁰⁻³² and the result is continuing apoptosis. This helps to explain why some glaucoma patients continue to show tissue damage, even after IOP is reduced to a level that would be expected to control the disease process.

2. Secondary Open Angle Glaucoma

Secondary open angle glaucoma can be caused by any of a variety of substances that mechanically block the outflow of aqueous through the anterior chamber angle, resulting in an elevation of IOP. These substances include pigment, exfoliation material, and red blood cells.

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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.⁸

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 zonules of the lens or the ciliary processes, mechanically damaging the pigment epithelium of the iris and releasing pigment.³³ The concept of reverse pupillary block has been proposed to explain the anatomic abnormalities that lead to iris concavity, which can result in PDS.^{34,35} Reverse pupillary block may occur momentarily during each lid blink.³⁶ A concave iris configuration similar to that in PDS can also be induced by accommodation.³⁷

A correlation between pigment release and elevated IOP with worsening of glaucoma has been reported in patients who have PDS and PG.³⁸ 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 collapse, obstructing aqueous outflow.³⁹

Not everyone with a lot of 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.⁴⁰ PG may also be due to congenital abnormality of the anterior chamber⁴¹ or exist as a variant of POAG.⁴²

Pseudoexfoliation syndrome (PES). The presence of “flaky” or “dandruff-like” grayish-white exfoliative material in the anterior and posterior chambers of the eye,^{43,44} and in the conjunctiva and orbit,^{45,46} is called pseudoexfoliation syndrome. This material accumulates on the

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ciliary epithelium, zonules, lens, posterior iris epithelium, intrastromal iris blood vessels,⁴⁷ anterior chamber angle, and corneal endothelium.⁴⁸

Exfoliative deposits are associated with degeneration of the ciliary epithelium, zonules (zonular dehiscence and lens subluxation),⁴⁹ and posterior iris epithelium (pigment dispersion, poor pupil dilation, posterior synechiae).^{48,50} The actual source of the fibrillo-granular pseudoexfoliative material, which is amyloid-like in composition,⁵¹ appears to be various basement membranes of the eye,^{52,53} including the lens capsule.⁵⁴ PES may represent abnormal basement membrane production at multiple sites by aging epithelial cells,⁵³ or it may be linked to microfibrils in the elastic elements of connective tissue.⁵⁵

Persons with PES have a higher prevalence of OAG than those without PES.^{43,44} Elevated IOP in pseudoexfoliation glaucoma (PEG) probably occurs because of direct mechanical blockage of aqueous outflow from the anterior chamber by pseudoexfoliative material⁵⁶⁻⁶⁰ and pigment granules, or because of dysfunction of the trabecular endothelium⁵³ or high aqueous protein levels.⁶¹ Some persons with PES maintain normal IOP, despite massive deposits in the trabecular meshwork,⁶² possibly because of decreased aqueous production secondary to degeneration of the ciliary epithelium.⁴⁸

B. Epidemiology of Open Angle Glaucoma

1. Prevalence and Incidence

a. Primary Open Angle Glaucoma

An estimated 2.5 million Americans have open angle glaucoma,¹ although at least half of all cases may be undiagnosed.⁶³ Seven times more prevalent than ACG,⁶⁴ POAG accounts for approximately 70 percent of all adult glaucoma cases.⁶ One-fourth of all cases of OAG in America are African American.¹ Various estimates as 0.8–3.0 percent for Caucasians,^{9,10,64-70} 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.⁶⁴

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The Framingham Eye Study calculated the prevalence of POAG in people ages 52–85 years as 1.65 percent.² When VF testing was added to the screening of a subset of Framingham subjects, the prevalence of POAG rose to 2.1 percent.⁷¹ While various studies show that the prevalence of cases with high IOP and VF defects is consistently between 0.3 and 0.4 percent,⁶ the prevalence of NTG ranges from 0.05 to 0.79 percent.^{2,10,72,73}

The existing data are inadequate for determination of the precise incidence of glaucoma,^{6,7} 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.^{1,74} Pooling data on blacks 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).¹ A similarly high incidence among blacks was confirmed by direct observation in the Barbados Eye Study.⁷⁵ 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 suggested that 7–8 percent of people over the age of 40 have IOP above 21 mm Hg on a single tonometric reading. The 1991 census provides support for the estimate that 7–8 million Americans over the age of 40 have OH.^{10,72,73} Approximately 0.5–1.0 percent of persons with OH develop evidence of ON damage per year,⁷⁶ however, the majority of those with OH will probably not develop glaucoma.^{2,9,10,77}

b. Secondary Open Angle Glaucoma

Pigmentary dispersion syndrome occurs in about 2.5 percent of adult Caucasians in the United States.⁷⁸ It rarely occurs in African Americans and Asians. About 20–60 percent of persons with PDS develop OH; 25–50 percent, PG.^{78,79} Pigmentary glaucoma constitutes about 4.4 percent of all glaucomas^{78,80} and 1–2.5 percent of OAGs.⁷⁸ PDS is usually bilateral and affects persons at younger ages than POAG (30–50

years).⁸⁰⁻⁸² Its occurrence is most common in Caucasian males with myopia.⁷⁹⁻⁸¹ In fact, about 90 percent of individuals with PDS are myopic.⁸³ PDS may have an autosomal-dominant, multifactorial basis, suggesting the importance of family history.^{80,84,85} At least one genetic locus has been identified for PDS.⁸⁶

The prevalence of pseudoexfoliation syndrome varies widely throughout the world,⁸⁷ ranging from about 1.6 to 2.3 percent in persons over age 50 in the United States.^{88,89} The prevalence of PES with subsequent pseudoexfoliation glaucoma increases with age, and these conditions most commonly occur between the ages of 60 and 80.^{88,89} PES is 2–3 times more common in women than in men,⁸⁹⁻⁹¹ and its prevalence in African Americans is much lower than in Caucasians.^{88,92} Through family studies, several putative sites on chromosome 2 are being investigated for genetic mutations related to PES.⁹³

PES has been reported to be unilateral at initial diagnosis in 50–70 percent of cases,^{89-91,94} a prevalence that may be overstated due to inadequate evaluation.⁹⁴ Unilateral PES may actually occur at a younger age and serve as a precursor to bilateral involvement.^{56,91} In 13–15 percent of cases of unilateral PES, involvement of the other eye is discovered during 10–15 years of followup.^{57,95} Thus, it appears that unilateral PES is rarely unilateral, but, rather, asymmetric at a subclinical level.⁹⁵

PES is a definite risk factor for OH and OAG.^{56,90,91} On initial screening, OH is found in 22–30 percent of individuals with PES.^{56,96} 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.⁹¹ The prevalence of PES in a glaucoma population ranges from 1.6 to 28 percent in the United States.^{57,88,92,97,98} Thirty to sixty percent of individuals with PES have been reported to develop OAG.^{88,96}

2. Risk Factors

a. General

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.^{2,10,64} 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.⁹⁹

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.^{64,100-103} The age-adjusted prevalence of POAG was 4.3 times greater in African Americans than in Caucasians in the Baltimore Eye Survey.⁶⁴ Studies in St. Lucia¹⁰⁴ and Barbados¹⁰⁵ found POAG in 7–16 percent of blacks over age 40. Although the prevalence of NTG has been reported to be high in Asians,¹⁰⁶ this rate may be influenced by the accuracy of tonometry in this ethnic group.¹⁰⁷

The etiology of glaucoma most likely involves multifactorial or polygenic inheritance mechanisms.¹⁰⁸⁻¹¹³ Studies have suggested that 13–25 percent of patients with glaucoma may have family histories positive for the disease.¹¹⁴⁻¹¹⁷ In close relatives of persons with POAG, the prevalence is 3–6 times that of the general public,¹⁰⁸ and the incidence of the disease in first-degree relatives is 3–5 times that found in the general population.^{110,111} The 22 percent lifetime risk for glaucoma found in relatives of patients with glaucoma is almost 10 times that of controls.¹¹⁸ The risk may be greater in siblings than in parents or children.^{117,118} A family history of glaucoma puts a person with OH at greater risk of developing the disease.^{119,120} Ocular characteristics associated with glaucoma, including IOP^{113,121} and the cup-to-disc ratio,¹²² have been associated with moderate familial risk.

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Mutations in transcription factor genes have been found responsible for developmental disorders associated with glaucoma.¹²³ 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.¹²⁴ Many forms of POAG probably result from a combination of mutations in more than one gene.^{124,125} Among at least six major genes for glaucoma that have been localized,¹²⁴ certain mutations have a higher incidence in specific types of OAG, such as normal tension glaucoma.¹²⁶

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.¹²⁷ A myocilin gene mutation may be present in 3–5 percent of patients with OAG.^{128,129} 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.¹²⁷ Screening for the myocilin gene includes taking a buccal swab and examining its genetic material. 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.¹⁰⁸

There is no conclusive evidence that gender is a risk factor for glaucoma.^{7,130}

b. Ocular

Intraocular pressure has a strong, direct relationship with the prevalence and long-term risk for glaucoma.^{6,7,116,131} 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.^{2,11} 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.⁹⁹ Even in NTG, the higher the pressure, the greater the risk.^{132,133} Asymmetric levels of IOP in individual pairs of eyes correlate

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with asymmetric damage to the ON.^{132,133} Lowering the IOP reduces the risk for ON damage.¹³⁴

Long-term studies have consistently shown that a large percentage of persons with statistically elevated IOP (>21 mm Hg) do not develop glaucoma,^{2,9,10,72,73,76,99,135,136} while many persons with glaucoma have IOP well within the statistically normal range.^{2,10,11,77} Population-based studies have demonstrated that one-tenth or fewer of those with elevated IOP suffer VF loss when monitored over several years.^{2,9,10,72} The incidence of glaucoma among persons with OH is at most 1 percent per year.^{76,135,136} One-third to one-half of persons with glaucoma have IOP at or below 20 mm Hg at initial diagnosis.^{2,9,10,72,99}

Various 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,^{131,137-139} and the symmetry of the optic cups.¹⁴⁰ Though potentially subject to selection bias, several studies have demonstrated, after adjustment for age, a 2- to 5-fold higher prevalence of POAG in patients with myopia.^{119,141,142}

c. Nonocular

The association of diabetes mellitus with both elevated IOP and POAG has been controversial.¹³⁰ Several studies lend support to a higher prevalence of OH¹⁴³ and POAG¹⁴⁴⁻¹⁵⁰ in persons with diabetes, for whom the relative risk of POAG ranges from 1.6 to 4.7.^{119,151,152} Others have found no relationship between the presence of diabetes and the development of OH or POAG.^{99,116,120,131,143,151,153-155}

Vasospasm has been proposed as one possible mechanism for, or as a factor contributing to, ON damage in glaucoma.^{156,157} This theory is supported by evidence of an association of NTG with migraine headaches and Raynaud's syndrome.¹⁵⁸ The literature is equivocal on whether there is an association between systemic hypertension and POAG.^{7,116,131,143,151,152,154,159} The Baltimore Eye Survey suggested the complexity of the relationship between POAG and systemic blood

pressure.¹⁶⁰ Patient age and the duration of systemic hypertension modify its effect on POAG. Lower perfusion pressure (BP-IOP) was significantly associated with an increased prevalence of POAG. Low systemic blood pressure,^{161,162} including the nocturnal dip,^{161,163,164} also may pose a risk for NTG.

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.^{2,11,72,73} Age-controlled data analysis has shown a higher prevalence of OH in African Americans than in Caucasians.¹⁰⁰

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

Table 1
Risk Factors for Primary Open Angle Glaucoma

General	Ocular	Nonocular
Age	Elevated or asymmetric levels of IOP	Diabetes mellitus
Race	Diffuse or focal enlargement of cup	Vasospasms
Family history	portion of optic nerve	Systemic
	Diffuse or focal narrowing of neuroretinal rim	hypertension
	Asymmetry of cup-to-disc ratios >0.2	
	Myopia	

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.¹⁶⁵⁻¹⁶⁷ There are two theories concerning how this specific damage occurs. One stresses the reduction in blood flow to the axons;¹⁶⁸ the other is based more on mechanical damage as the axons pass through the lamina cribrosa scleralis.^{166,169} The premise for both hypotheses involves abnormality—abnormal IOP or 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.^{170,171} Once glaucomatous damage has occurred in one eye, the risk for damage in the other eye increases.¹⁷² 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.¹⁷¹

There is great variability in the susceptibility of the ON to glaucomatous damage. Some persons with relatively low IOP (normal tension glaucoma) incur ON damage, while others with rather high IOP (OH) never show such damage. Even with the most sensitive clinical test currently 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.¹⁷³ A recent study showed a 25 percent loss of retinal ganglion cells in patients for whom threshold automated perimetry revealed a 5-dB loss of retinal sensitivity. The authors concluded that at least a 25–35 percent loss of ganglion cells is associated with typical clinical criteria used for detecting abnormalities.¹⁷⁴



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, inconveniences, and costs 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.⁶ The presence of certain ocular, systemic, and general risk factors increases the probability that a person will develop glaucoma. Among these risk factors, only blood pressure and IOP can be altered.⁶

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.^{134,175,176} 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.^{130,175-178}

Even screening protocols using multivariate predictive models do not adequately distinguish between persons affected and unaffected by glaucoma.¹⁷⁶ Glaucoma screening procedures may include, but are not limited to:

- **Tonometry.** Measurement of IOP is not a reliable screening procedure for detecting glaucoma.^{176,179,180} No level of IOP provides the necessary balance between sensitivity and specificity.¹⁷⁶ Moreover, as many as one-half of persons with glaucoma may have IOPs below 22 mm Hg at screening,^{2,10,64,99} and most with elevated IOPs do not have, and may never develop, glaucoma.^{2,76,135,136}
- **Optic nerve assessment.** Despite the large ON cups in eyes that eventually develop glaucoma, the clinical finding of a 0.6 cup-to-

disc ratio has only about a 60 percent (41%–77%) sensitivity for predicting which cases of OH will convert to the disease.¹⁸¹⁻¹⁸³ There is no cutoff value for cup-to-disc ratio that changes this conclusion.¹⁷⁶ Determining the cup-to-disc ratio by direct ophthalmoscopy is even less precise, due to intraobserver and interobserver variability.^{2,181,184} The evidence suggests even greater variability in assessment of the notching or width of the neuroretinal rim.¹⁸¹ Topography of the ON and configuration of the neuroretinal rim may be more sensitive and specific than the cup-to-disc ratio in the detection of glaucoma.¹⁸⁵

- **Photography.** Stereoscopic fundus photography is useful for evaluating the ON because it reduces observer variability in assessment of the cup-to-disc ratio.¹⁸¹ However, stereoscopic fundus photography assessment of neither the horizontal or vertical cup-to-disc ratio nor the narrowest neuroretinal rim width achieves a sensitivity-specificity balance adequate for screening.¹⁷⁶ Photography may be of value in assessing the NFL,¹⁸⁶ except that media changes common in the age groups screened for glaucoma diminish the quality of the photographs.¹⁷⁵ The sensitivity and specificity of NFL assessment are highest when the photographs are of high quality.^{187,188}
- **Perimetry.** The use of automated perimeters for mass screenings has not been practical because of the size and cost of most modern instruments.¹⁷⁵ In the past, perimetry results in mass screenings were quite variable.¹⁸⁹ 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.⁶⁶

More recently, 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 a 95 percent specificity, compared with standard automated perimetry, and an 85 percent sensitivity for moderate to advanced VF loss.

Statement of the Problem 17

The sensitivity and specificity of FDT varies, depending on the mode of testing (screening vs. thresholding)^{190,191} and the severity of the disease in the population being tested. For moderate and advanced glaucoma, FDT has sensitivity¹⁹² and specificity values above 90 percent for detecting glaucomatous VF loss.^{190,191,193-196} FDT sensitivity in the detection of early glaucomatous damage has been lower and more variable between studies.^{190,191,193,196}

FDT perimetry has demonstrated better patient reliability,¹⁹⁷ less intratest and intertest variability,¹⁹⁸ and results that are comparable to or better than standard automated perimetry for the detection of glaucoma.^{193,197} It appears that FDT can facilitate the diagnosis and grading of the extent of glaucoma.¹⁹⁹

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.



II. CARE PROCESS

This Guideline describes the optometric care provided 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.^{134,138,200} The difficulty of distinguishing between eyes without glaucoma and eyes with early or subtle glaucoma is widely acknowledged.²⁰¹ Furthermore, there is no unanimous opinion on what constitutes the first signs of damage in glaucoma.²⁰²

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).²⁰³ Baseline data are established for important clinical parameters that must be evaluated longitudinally in the proper management of glaucoma.²⁰⁴

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.

b. Ocular Examination

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

- **Visual acuity.** Corrected and uncorrected distance or near vision acuity, or both, should be measured as one indicator of the integrity of the central vision system.
- **Pupils.** Careful evaluation of the pupils should be performed to reveal the presence of a relative afferent defect.²⁰⁵
- **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 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.²⁰⁶ Attention should be directed toward differences between the IOPs of the two eyes¹³³ and changes in pressure over time.²⁰⁷

IOP measurement by Goldmann tonometry assumes an average central corneal thickness (CCT) of 520 nm.²⁰⁸ Meta-analysis of values reported in the literature indicates that "normal" individuals have a significant variation in CCT (0.535 +/- 0.031 nm),²⁰⁹ which could influence the accuracy of this measurement. In fact, cannulation studies have indicated that a 10 percent change in CCT can result in a mean change in IOP (measured by Goldmann tonometry) of 1–3.5 mm Hg.^{210,211} A thick cornea may influence the measurement of IOP more with non-contact tonometry than with Goldmann tonometry.²¹²

Even large-scale studies have failed to provide unequivocal outcomes concerning the significance of measuring CCT for the diagnosis and treatment of glaucoma. Many studies have demonstrated above-average



CCTs in some individuals classified as having OH²¹³⁻²²² and below-average CCTs in some patients diagnosed with NTG.^{214,215,218-220,223} 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.^{215,219} Another study has recommended that CCT be measured so that OHs with thick corneas are not over diagnosed and those with thin corneas are not under diagnosed. African Americans may have thinner central corneas than Caucasians, potentially resulting in underestimation of their actual IOPs.²²⁴ Similarly, a decrease in CCT following in situ keratomileusis could result in underestimation of actual IOP.^{225,226}

The general consensus seems to be that measuring CCT by pachometry is only necessary in rare circumstances.^{209,221,227} The effect of CCT variation on applanation tonometry readings does not appear sufficient to influence treatment decisions.^{220,227}

- **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 many secondary glaucomas. It may be valuable to evaluate the angle both before and after dilation of the pupil.⁹⁷
- **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 60 D lens, a 66 D lens, or a contact fundus lens will enable the best stereopsis. Evaluation of the ON includes ruling out other potential causes of optic 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.

Computerized topographic imaging of the ON is receiving increased attention in the diagnosis and treatment of glaucoma. Users of confocal scanning laser tomography (CSLT) have concentrated on the early detection 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.²²⁸ Because of significant physiological variation of the ONH within the normal population, even with an ideal imaging system it is very difficult to identify early glaucoma accurately in a single session.²²⁸

The advantages of CSLT include the ability to obtain images without pupil dilation,²²⁹ 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. Newer inflection-point analysis may help to alleviate this problem.²³⁰

Although with CSLT there is a tendency to overestimate the neuroretinal rim and to underestimate the cup-to-disc ratio,²³¹ several recent studies have shown that the parameters generated by this technology are adequate for discrimination between normal ONHs and those of patients with OH²³² and early glaucoma.^{232,233} CSLT has a sensitivity of 89 percent and a specificity of 84 percent for differentiating between subjects with early glaucomatous VF defects and normal eyes.²³⁴

Longitudinal studies are just beginning to report the results of using CSLT. Several of these studies 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.^{235,236}

- **Nerve fiber layer assessment.** The procedure for evaluating the integrity of the NFL is similar to that described for the ON. The NFL is best visualized using stereo photographic techniques with red-free illumination and high-resolution black and white film.^{187,188,237} Serial NFL examination is more sensitive than color ON evaluation in detecting the conversion of eyes 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.¹⁸⁰ 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.²³⁸

Significant advances have occurred in techniques for assessing the NFL in the detection and progression of glaucoma. Studies have investigated the capabilities of scanning laser polarimetry,²³⁹⁻²⁴¹ optical coherence tomography,²⁴²⁻²⁴⁶ and scanning laser ophthalmoscopy^{247,248} in distinguishing normal and OH eyes from those with POAG,^{240,241,243-248} as well as the reproducibility of results obtained with these instruments.^{239,242} Although the study results are encouraging with respect to accurate measurement of NFL thickness, whether these instruments have the sensitivity and specificity to detect the onset and the progression of glaucomatous damage remains to be determined.²⁴⁶ The correlations between VF indices and peripapillary NFL thickness have been weak,^{245,247,248} 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.^{240,241}

- **Peripapillary area (PPA) assessment.** Peripapillary atrophy occurs more frequently in eyes with glaucoma than in those with OH or in normal eyes.²⁴⁹⁻²⁵⁷ IOP may not significantly affect the extent of peripapillary atrophy,^{250,255,258,259} but both zone alpha and zone beta are significantly more extensive in eyes with glaucoma.^{253,256} Zone beta occurs significantly more often in glaucoma than in normal individuals,^{251-253,255,256} yet the measurement of zone beta may be of limited usefulness in the detection or followup of glaucoma.^{249,251,260}

There is a correlation between the loci of peripapillary atrophy and ON and VF damage.^{250-252,256,261,262} In the normal eye, peripapillary atrophy is more extensive and more frequently located in the temporal horizontal sector.^{251,253}

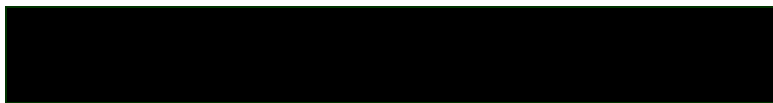
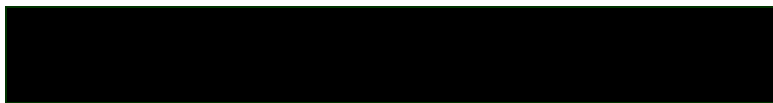
The value of following the changes in peripapillary atrophy in glaucoma suspects or individuals with glaucoma has not been well established.^{260,263} Some studies have found a correlation between the progression of peripapillary atrophy and the progression of both

POAG^{256,263,264} and NTG.^{255,265} Others have found no significant difference between the prevalence of peripapillary atrophy in eyes with progressive glaucoma and those with non-progressive OH.^{182,249,260}

- **Fundus photography.** Clinical evaluation of the ON, NFL and the surrounding PPA is useful, but fundus photography may improve accurate diagnosis and followup.²⁶⁶ Stereoscopic photography through a dilated pupil is preferable. Qualitative evaluation of the ON, NFL, and surrounding PPA by direct observation and the assessment of photographs may offer more diagnostic precision than quantitative evaluation (e.g., digital imaging analysis and planimetry) for correctly determining the presence of structural glaucomatous damage at the stage of early VF loss.¹⁸⁵ Measurement of both structure (features of the ON, NFL, and PPA) and function (VF parameters) helps identify early glaucomatous damage.^{185,267} Photographic documentation every 2 years may be appropriate for establishing the baseline appearance of the ON, NFL, and the PPA layer to aid detection of tissue changes in glaucoma suspects over time.²⁶⁶ Stereoscopic photography may be indicated each time the ON or NFL changes.
- **Visual fields.** Measurement of threshold levels in areas of the VF likely to be affected by glaucomatous damage of the ON should be made by perimetry through a pupil of adequate size.²⁶⁸ 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.²⁶⁹ The clinician should consider factors that can influence interpretation of the findings, including the patient's learning curve.²⁷⁰

c. Supplemental Testing

Other procedures may be used to detect the earliest loss of vision function from glaucoma. Although measurement of color vision,²⁷¹⁻²⁷³ 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.²⁷⁴ Tonography²⁷⁵ and provocative testing²⁷⁶ are



of little value in the diagnosis of OAG, due to their poor sensitivity and specificity.⁶

Short-wavelength automated perimetry (SWAP) is useful in evaluating early or subtle diseases of the ON and retina.²⁷⁷ 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.²⁷⁸⁻²⁸¹ SWAP facilitates prediction of future defects that can eventually be found with white-on-white perimetry.^{277,278,280,282} The VF defects found with SWAP are larger and progress more rapidly than those localized with white-on-white automated perimetry.^{278,280}

SWAP results, which may be predictive of which eyes with early glaucomatous VF loss are most likely to progress,²⁷⁸ can be correlated with structural changes in the ON^{283,284} and NFL.²⁸¹ Moreover, an association between the prevalence of localized SWAP defects and other risk factors is predictive of the development of glaucoma in patients with OH.^{279,282} Of clinical concern are the longer duration of testing and the fluctuation of patient responses that may occur with SWAP.

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.¹⁸⁵ Continual changes in any one of these parameters may provide the first clinical recognition of the earliest stages of glaucoma.²⁸⁵

Individuals with one or more risk factors, who have higher probabilities of developing POAG, need 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 to assess 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 and may include, but is not limited to the following assessments:^{203,286}

- **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.²⁸⁶
- **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 glaucomas.
- **Tonometry.** Diurnal IOP curves and IOP measurements with the patient in the supine position²⁸⁷ may be needed in certain glaucoma patients, especially those with NTG.^{288,289}
- **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 followup of patients on miotic therapy.
- **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.²⁶⁷ Sequential stereoscopic photography or imaging enhancement technology can be valuable in detecting

subtle changes in the ON or NFL.¹⁸⁵ Visible damage to the ON can occur early in the disease process, before detectable VF loss.^{137,290} Once VF defects have been established, sequential perimetry may be a more sensitive indicator of progressive glaucomatous damage.²⁹⁰

- **Nerve fiber layer assessment.** Assessment of the NFL is similar to ON assessment but uses red-free illumination. In the early stages of glaucoma, estimation of structural abnormalities from serial NFL photographs may be more sensitive than assessment of the ON.¹⁸²
- **Fundus photography.** When the patient's condition is unstable, stereophotography through a dilated pupil can be useful. Digital imaging analysis may become a valuable alternative.
- **Automated perimetry.** Threshold perimetry should be performed at least once per year; more frequent testing may be needed for cases of advanced glaucoma. Comparison of repeated threshold perimetry results and statistical analyses are required to detect the most subtle VF changes due to glaucoma.²⁹¹ Three to five perimetric tests may be needed to show the progression of VF loss in glaucoma.²⁹²
- **Supplemental testing.** Other tests that may be performed to detect the progression of vision loss include color vision, short-wavelength automated perimetry, FDT perimetry, and contrast sensitivity.

B. Diagnosis of Secondary Open Angle Glaucoma

1. Pigmentary Glaucoma

Differential diagnosis of PG involves the same clinical approach as the comprehensive initial and follow-up evaluations of a glaucoma 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.^{79,293}

The clinical presentation of PDS with associated PG includes:

- Spoke-like transillumination defects in the midperiphery of the iris⁴²
- Pigment on the anterior surface of the iris often as concentric rings within the iris furrows⁸¹
- Pigment in the anterior and posterior chambers, and possibly Krukenberg's spindles on the corneal endothelium²⁹⁴
- A dense, homogeneously pigmented trabecular meshwork, especially posteriorly^{81,82,295}
- An open, deep anterior chamber angle with possible posterior bowing (concavity) of the iris^{33,83}
- Rise of the IOP to rather high levels, with dramatic fluctuation^{295,296}
- Pigment release resulting from pupillary dilation²⁹⁷ or strenuous exercise,²⁹⁸ 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 a glaucoma suspect for POAG, and special attention to biomicroscopy and gonioscopy. The evolution from first pigmentary and lens changes to full-scale PES may require 5 to 10 years.²⁹⁹ The clinical presentation of pseudoexfoliation syndrome 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^{43,44}
- Transillumination defects in the iris near the pupil, and pigmentation of the trabecular meshwork.^{43,44} Pigment granules may form a whorled pattern over the sphincter muscle on the surface of the iris³⁰⁰
- Depigmentation of pupillary ruff
- Poor pupillary response to topical mydriatic agents
- Accelerated cataract formation

The ability to diagnose PES can be increased by 10–20 percent when biomicroscopy is performed through a dilated pupil.³⁰¹ 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.³⁰²

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.^{57,97} Pupillary dilation can cause pigment dispersion,^{58,59} resulting in a spike in IOP⁵⁸ that necessitates post-dilation tonometry.³⁰³ 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.⁶⁰ Biopsy of the conjunctiva, although rarely used clinically, may enable diagnosis prior to any clinical evidence of PES in the anterior or posterior chambers.⁶⁰

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.³⁰⁴ Among newly diagnosed cases of PEG, 69 percent are unilateral, compared with 46 percent of those with POAG.³⁰⁵

C. Management of Open Angle Glaucoma

The authority for an optometrist to provide treatment for OAG is determined by state law. If care of the patient with OAG requires services or procedures outside an individual optometrist's scope of practice, referral to another eye care provider experienced in the treatment of glaucoma would be required. The optometrist may participate in the comanagement of the patient, including preoperative and postoperative care when appropriate (see Appendix Figure 2).

1. Basis for Treatment

The fundamental rationale for treating glaucoma is that abnormal IOP plays a major role in glaucomatous optic neuropathy. Although high IOP is certainly not the only factor contributing to ON damage, it is one of the few risk factors that can be clinically modified.³⁰⁶ Medically lowering IOP in patients with OH may reduce the incidence of glaucoma.¹³⁴ In at least two-thirds of patients with high-tension glaucoma, marked lowering of the IOP stops progression of the disease.³⁰⁶⁻³¹⁰ Even in NTG patients, the level of the IOP is a risk factor related to the degree of glaucomatous damage.^{132,133,311,312}

More compelling evidence from randomized, controlled clinical trials is needed to document the efficacy of the various forms of treatment for glaucoma and the value of treating OH. The National Eye Institute (NEI) of the National Institutes of Health is sponsoring several long-term, controlled, randomized clinical trials that will provide valuable information regarding the basis for the treatment of glaucoma. The Ocular Hypertension Treatment Study has determined that topical ocular hypotensive medication is effective in delaying or preventing the onset of OAG in patients with elevated IOP. The Early Manifest Glaucoma Trial is comparing the effect of immediate therapy to lower IOP versus late treatment or no treatment on the progression of newly detected OAG.³¹³

Studies on the management of OH are almost equally divided between those that have found early medical treatment effective in preventing or slowing the progression to glaucoma,^{134,200,314,315} and those that have found no clear benefit from treatment.³¹⁶⁻³²¹

Research on the effects of lowering the IOP in early to moderate glaucoma has been inconclusive. Some have shown that a significant reduction in IOP by medical^{310,322-325} or surgical³²⁶⁻³²⁸ means slows the progression of the disease. Others have found that lowering IOP may not have a uniform effect on differentiating glaucoma patients with progressive loss of VFs from those that are stable.^{31,304,329-335}

The Advanced Glaucoma Intervention Study (AGIS)³³⁶ demonstrated that sustaining IOP below 18 mm Hg and averaging 12.3 mm Hg resulted in little change in the 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,^{307-309,337-341} a significant reduction in IOP may not necessarily protect the eye of a patient with advanced glaucoma from future VF loss.^{306,334,337,342-344} It does appear that glaucoma patients with higher peak IOP,^{31,322-324,329,332,342,345} and with wide variability (fluctuation) in IOP^{31,306,321,322,324,329,331,332,335,336,338,342} 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 vision function.^{6,31,182} 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).

Table 2

Suggestions for the Medical Management of Primary Open Angle Glaucoma*

-
1. Determine an appropriate target pressure and readjust when necessary.
 2. Use the fewest medications in the lowest concentration needed to achieve the target pressure.
 3. When the treatment is ineffective, initially substitute, rather than add, medication.
 4. Initiate or change therapy with a unioocular trial.
 5. Stop treatment periodically to assess its continuing efficacy.
 6. Continually stress the need for treatment compliance with the patient.
 7. Make the treatment regimen as convenient for the patient as possible.
 8. Teach the patient the correct method for 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 the risks and prognosis of the disease and the 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.



To achieve the goal of treatment, a "target pressure" must be established for each patient. 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 level;³⁴⁶ it cannot simply be "normal" pressure, because some patients with glaucomatous damage have baseline IOPs that are similar to those of normal eyes.³⁴⁷ This target pressure may need further reduction over time; therefore, it requires routine re-evaluation.

In estimating the initial target pressure, the clinician can use knowledge about the existing damage to the ON, the degree of VF loss, the patient's age and highest IOP, along with clinical experience (see Table 3).³⁴⁸ 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.

Table 3
Clinical Stages of Primary Open Angle Glaucoma

Mild		
ON		Mild concentric narrowing or partial localized narrowing of the neuroretinal rim, disc hemorrhage, 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, nasal depression or step, diffuse depression
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*
VF		Complete arcuate scotoma in at least one hemifield
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 ¹⁷³
VF		Complete arcuate scotoma in both hemifields, 5°– 10° central island of vision

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

2. Available Treatment Options

Traditionally, glaucoma treatment has begun with pharmacological intervention, proceeding to laser therapy and surgery when necessary.³⁴⁹ This approach was designed to maximize the benefit of treatment while minimizing risk to the patient. Recently, this method has been challenged as less effective than other sequences of therapy.³²⁶⁻³²⁸ Many glaucoma patients may require all three treatment options, and all should be made available to each patient, because glaucoma is a chronic, progressive disease with no known cure.

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.³⁵⁰⁻³⁵² The possible impact of the treatment, from a social, psychological, financial, and convenience standpoint, must be evaluated.

a. Medical (Pharmaceutical)^{†*}

The treatment of OAG includes the use of orally administered or topical agents that enhance aqueous outflow or reduce aqueous production or both (see Table 4).^{350,351,353}

* Every effort has been made to ensure that the drug dosage recommendations are accurate at the time of publication of the Guideline. 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 Management of Primary Open Angle Glaucoma**

Cholinergic Agonists—Miotics
Pilocarpine – solution, gel or membrane-bound wafer Carbachol
Adrenergic Agonists
Nonselective Epinephrine Dipivefrin
Selective Apraclonidine Brimonidine
Beta-Adrenergic Blocking Agents
Nonselective Carteolol Levobunolol Metipranolol Timolol
Selective Betaxolol
Carbonic Anhydrase Inhibitors
Systemic—Oral Acetazolamide—Injection or sustained release Dichlorphenamide Methazolamide
Topical Dorzolamide Brinzolamide
Prostaglandin Analogs
Bimatoprost Latanoprost Travoprost Unoprostone isopropyl

- **Miotic agents.** Pilocarpine is the miotic drug most commonly used in treating POAG. It is instilled topically, generally 2-4 times per day in doses ranging from 0.5% to 4%. Higher dosages may be considered for use in darkly pigmented individuals.³⁵⁴ The

duration of action is at least 6 hours. Pilocarpine also is available in a 4% gel preparation, as well as in membrane-bound wafers that are placed into the conjunctival sac (Ocuser[®]). The purpose of these alternative delivery systems is to reduce ocular side effects and increase patient compliance.^{355,356} Adverse reactions and contraindications for pilocarpine^{350,353,357} are listed in Table 5.

- **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,³⁵⁸ the lower concentration of dipivefrin is equivalent in effectiveness to a 1%–2% concentration of epinephrine.³⁵⁹ In general, epinephrine compounds are not as effective as other categories of drugs in lowering IOP in glaucoma patients.

Because of its efficacy and reduced potential for ocular and systemic side effects,³⁵³ dipivefrin is the drug of choice among epinephrine drops in the treatment of glaucoma.³⁶⁰ Adverse reactions and contraindications for epinephrine compounds^{350,353,361,362} are listed in Table 5. The frequency of using epinephrine compounds to treat glaucoma is decreasing.

- **Other direct-acting adrenergic drugs.** As a single topical agent, the α 2-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.³⁶³ By lowering IOP about 25 percent, apraclonidine is also effective in minimizing precipitous IOP increases after cycloplegia in patients with POAG.³⁶⁴ Apraclonidine also can decrease significant IOP elevations in glaucomatous eyes undergoing trabeculectomy combined with extracapsular cataract surgery.³⁶⁵

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 Hg³⁶⁶ for up to 90 days. Some eyes may not benefit from this additional treatment, however.

Used 3 times per day, apraclonidine (0.5%) lowers IOP to the same degree as timolol (0.5%) used twice per day.³⁶⁷ It also has an additive effect (in 17%–22% of patients) with topical timolol maleate in lowering IOP,³⁶⁸ and 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),³⁶⁹ tachyphylaxis,³⁶⁶ and marked reduction in conjunctival oxygen tension, probably as a result of vasoconstriction.³⁶⁹ Adverse reactions to apraclonidine^{366,367,369,370} are listed in Table 5.

Brimonidine is an α 2-adrenergic agonist with 23–32 times more selectivity than apraclonidine for alpha-2 receptors.³⁷¹ In a 0.2% solution, brimonidine reduces IOP about 23–27 percent,^{372,373} with no apparent tachyphylaxis.³⁷⁴ Brimonidine used twice a day is more effective than betaxolol³⁷⁵ and similar in effect to timolol maleate, although not at the trough measurement.^{374,376,377-379} When used as monotherapy, it is not as effective as latanoprost.³⁸⁰ Brimonidine is additive with timolol^{381,382} and latanoprost,³⁸⁰ and it can be used as combination or replacement therapy.³⁷² Like apraclonidine, it can be used to prevent IOP spikes after ALT.³⁸³

In animal models, brimonidine has a neuroprotective effect through mechanisms that are not clearly understood.³⁸⁴⁻³⁸⁶ One possible mechanism is the inhibition of extracellular glutamate accumulation in the retina in response to ischemic stress.³⁸⁷ Brimonidine has no effect on retrobulbar³⁸⁸ or retinal³⁸⁹ blood flow, blood lipids,³⁷⁴ heart rate,^{374,376,378,379} or pulmonary function.^{375,376,378} Adverse reactions and contraindications for brimonidine^{373,374,376,379-391} are listed in Table 5. Brimonidine appears to elicit a lower incidence of ocular allergic reactions than apraclonidine.^{373,374,379}

- **Beta-blocking drugs.** Topical beta-blockers, the drugs often used for the initial medical management of POAG, are either nonselective (i.e., blocking both beta-1 and beta-2 receptors) or selective (blocking beta-1 receptors).^{350,353} Timolol (maleate, hemihydrate, preservative-free, or gum-based) and betaxolol (suspension) are beta-blockers in unique 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.³⁹²

The selective beta-blocker betaxolol may cause fewer pulmonary and cardiovascular side effects,³⁹³ but it is less effective in lowering IOP than the nonselective beta-blockers, timolol, carteolol, levobunolol, and metipranolol.³⁹⁴ Betaxolol may have a neuroprotective effect, by altering ion channels in retinal ganglion cells, resulting in a decreased influx of calcium.^{395,396} Betaxolol does not increase retinal or retrobulbar blood flow.³⁹⁷ Adverse reactions and contraindications for beta-adrenergic blocking agents^{350,353,398} are listed in Table 5.

- **Carbonic anhydrase inhibitors (CAIs).** CAIs are administered orally 1–4 times per day in doses ranging from 25 mg to 1 g daily, depending on the drug used and the severity of the glaucoma. One CAI, acetazolamide, is available for injection and in sustained-release capsules (Sequels).

CAIs usually lower IOP by about 20 percent.³⁹⁹ The most effective doses are 500 mg of acetazolamide Sequels^{®400} 1–2 times per day and 50 mg of methazolamide 2–3 times per day.⁴⁰¹ The best-tolerated CAIs are acetazolamide Sequels[®] and methazolamide tablets,⁴⁰² which produce fewer kidney stones.⁴⁰³ There is no evidence that routine blood testing will help predict or prevent possible blood dyscrasias, which can result from CAI treatment.^{404,405} Although they are effective in significantly lowering IOP, CAIs are poorly tolerated. Table 5 presents a list of adverse reactions and contraindications for CAIs.^{353,400,402-405}

Several thienothiopyran-2-sulfonamides have been approved as topical CAIs for use in the treatment of glaucoma. Dorzolamide

hydrochloride ophthalmic solution has been approved for topical use in patients with OH and OAG. Studies have shown that using a 2% concentration of dorzolamide 3 times per day lowers IOP 3–5 mm Hg for 1 year. When used as adjunctive therapy, dorzolamide is approximately equivalent to 2% pilocarpine in further lowering IOP.⁴⁰⁶

Brinzolamide 1% solution is a topical CAI that is equal to dorzolamide 2% (t.i.d.) in lowering IOP,⁴⁰⁷⁻⁴⁰⁹ but not quite equal to timolol maleate 0.5%.^{409,410} The IOP-lowering effect of brinzolamide appears to be the same, whether used 2 or 3 times per day.^{410,411} Brinzolamide⁴¹²⁻⁴¹⁴ and dorzolamide^{381,382,406,414} twice daily are additive to timolol.

Brinzolamide increases ONH blood flow in animals without affecting systemic blood pressure or heart rate.⁴¹⁵ In humans, dorzolamide accelerates blood velocity in the superficial vessels of the retina and ONH, but it does not affect retrobulbar hemodynamics.⁴¹⁶ Dorzolamide also has a positive effect on perimacular circulation,⁴¹⁷ and on ocular pulse amplitude (an estimate of choroidal perfusion).⁴¹⁸

Adverse reactions^{411,413,419} and contraindications for topical CAIs are presented in Table 5. Patients have found brinzolamide more comfortable to use than dorzolamide.^{407-409,419-421}

- **Prostaglandins.** Latanoprost 0.005% is a synthetic prodrug of prostaglandin F_{2α} that lowers IOP by 27–35 percent when given once a day.⁴²²⁻⁴²⁵ Its 24-hour efficacy⁴²⁶ makes latanoprost equal to⁴²⁵ or more effective^{423,427,428} than timolol maleate 0.5% in lowering IOP. Latanoprost seems to be more effective when administered in the evening,^{422,426,429} and there appears to be no tachyphylaxis.⁴²³ Latanoprost has been approved for use in individuals with OAG or OH who are intolerant of other antiglaucoma medications or whose level of IOP is inadequately controlled. Latanoprost enhances pulsatile ocular perfusion^{430,431} and is effective in lowering IOP⁴³² and increasing ocular perfusion

pressure⁴³³ in NTG. It is additive with dipivifren,⁴³⁴ acetazolamide,⁴³⁵ dorzolamide,⁴³⁶ and timolol.^{382,422,426}

Bimatoprost 0.03% is a synthetic prostamide similar in mode of action and effectiveness to latanoprost. It reduces IOP up to 33 percent.⁴³⁷

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. Phase II and III Food and Drug Administration (FDA) studies indicate that travoprost has a potentially higher effectiveness than other active agents in lowering IOP in African Americans.⁴³⁸

The adverse reactions^{423,425,427,428,439-443} and contraindications^{441,444-446} for bimatoprost, latanoprost and travoprost are listed in Table 5. Eyelash changes include an increase in number, length, thickness, curvature, and pigmentation.⁴³⁹ Those who use latanoprost immediately following cataract surgery may benefit from concurrent use of a topical non-steroidal anti-inflammatory eye drop to prevent anterior uveitis and minimize the development of cystoid macular edema.⁴⁴¹

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.^{424,447,448} In some studies the efficacy of unoprostone 0.12% was statistically equal to timolol 0.5% in controlling diurnal IOP levels⁴⁴⁹ for 1 month to 1 year.^{448,450-452} Unoprostone is also additive to timolol.⁴⁵³ In NTG, unoprostone reduced IOP by 11 percent,⁴⁵⁴ however, it is not as effective an ocular hypotensive agent as latanoprost.^{424,455}

The results of studies of the effect of unoprostone isopropyl on ocular blood flow have been equivocal. Three to five hours after

instillation of unoprostone, blood flow had increased in the choroid and retina but not in the ONH.⁴⁵⁶ On the other hand, increased blood flow was found in the ONH and choroid-retina after 3 weeks of treatment with the same drug.⁴⁵⁷ Unoprostone had no effect on pulsatile ocular blood flow in normal volunteers.⁴⁵⁸

The adverse reactions^{447,449,451,459} and contraindications for unoprostone isopropyl are listed in Table 5. Changes in iris pigmentation were reported in one case.⁴⁶⁰

- **Combination Medications.** The rationale for combining separate topical glaucoma medications into a single formulation is to decrease the number of applications per day, thereby increasing compliance. Cosopt[®], consisting of 2% dorzolamide and 0.5% timolol maleate, was found, after 3 months of use, to be more effective in decreasing IOP (28%–33%) than monotherapy with either dorzolamide (15%–20%) or timolol (22%).⁴⁶¹ The combination drug is equally as effective when both component drugs are given concomitantly, except in the early morning and afternoon, for up to 12 months.⁴⁶² The net effect of Cosopt[®] is about a 3–4 mm Hg reduction in IOP below the baseline for timolol 0.5%.⁴⁶³ The adverse effects and contraindications for Cosopt[®] are similar to those listed in Table 5 for the component drugs.

Latanoprost once daily lowered IOP (23.2%) more than the dual therapy of timolol and dorzolamide given twice a day (17.9%) for up to 3 months.⁴⁶⁴ Other combination drugs are being developed.

Table 5
Major Adverse Reactions and Contraindications of Pharmaceuticals Used in the Treatment of Glaucoma

Pharmaceutical Agents	Adverse Reactions		Contraindications	
	Ocular	Systemic	Ocular	Systemic
Pilocarpine	Stinging, irritation Ciliary spasms (myopia) Miosis (vision) Pupillary block Retinal detachment	Headache, pain Sweating Vomiting/diarrhea Salivation Bradycardia Arrhythmia Dyspnea	History of retinal detachment Severe myopia Cataracts Inflammation/infection Aphakia/pseudophakia	Asthma Ulcers Bladder dysfunction Parkinson's disease
Epinephrine**	Stinging, burning Mydriasis Allergic sensitivity Pigment deposits Cystoid macular edema Increased IOP	Increased blood pressure Increased heart rate Severe headaches Anxiety	Aphakia/pseudophakia Narrow angles	Systemic hypertension Heart disease Hyperthyroidism Diabetes mellitus Certain medications
Alpha-2 agonists	Allergic sensitivity† ³ Minimal mydriasis† Lid retraction† Conjunctival vasoconstriction† Stinging, burning Foreign body sensation Hyperemia Conjunctival follicles	Gastrointestinal discomfort Taste abnormalities Headache Fatigue/drowsiness Oral dryness	None	None
Topical beta-blockers	Stinging, burning Superficial punctate keratitis Allergic sensitivity Decreased corneal sensitivity Uveitis§	Dyspnea‡ Bronchiole constriction‡ Decreased heart rate‡ Arrhythmias‡ Decreased blood pressure Depression, confusion Gastrointestinal discomfort Impotence Sleep disturbance Serum lipoprotein alterations Masking symptoms of diabetes mellitus and hyperthyroidism	Narrow angles	Chronic obstructive Pulmonary disease Systemic hypotension Bradycardia Diabetes mellitus Myasthenia gravis Certain medications

* Adverse ocular reactions and contraindications are less with dipivefrin than with epinephrine

† Adverse ocular reactions are less common with brimonidine

Table 5 Continued . . .

Pharmaceutical Agents	Adverse Reactions		Contraindications	
	Ocular	Systemic	Ocular	Systemic
Oral carbonic anhydrase inhibitors	None	Malaise Depression, confusion Metallic taste Anorexia Diarrhea Paresthesias Kidney stones Metabolic acidosis Blood dyscrasias	None	History of kidney stones Liver disease Sulfonamide allergy Cardiac disease Addison's disease Renal disease Severe chronic obstructive pulmonary disease
Topical Carbonic anhydrase inhibitors	Stinging/burning Allergic sensitivity Blurred vision Superficial punctate keratitis Corneal edema	Altered taste	Corneal endothelium compromise	Sulfonamide allergy
Prostaglandin analogs	Blurred vision Stinging, burning Hyperemia Foreign body sensation Itching Increased iris pigmentation¶ Eyelash changes Punctate epithelial keratitis Cystoid macular edema Iritis Herpes simplex keratitis	Headaches Upper respiratory tract symptoms	History of uveitis, CME, herpes simplex keratitis, complicated cataract surgery	None

§ Metipranolol.

‡ May be less severe with betaxolol.

¶ Only one reported change in iris coloration with unoprostone isopropyl.

b. Laser

The second level of treatment for POAG involves the use of systemic medication or laser procedures. As an alternative to drug therapy,^{465,466} argon laser trabeculoplasty (ALT) is a common treatment after topical medication for POAG. Aside from avoiding the use of oral CAI, the long-term benefits of ALT for the treatment of glaucoma remain controversial,⁴⁶⁷ because its effectiveness diminishes over time.^{465,467-470}

ALT involves placing from 50 to 100 laser burns (50-micron size, 0.1 seconds in duration, at a power of 500–1,000 MW) around 180° or 360° of the anterior one-third of the trabecular meshwork, a procedure adequate to produce a visible tissue response.^{352,471} Laser trabeculoplasty has also been successful when performed with krypton, Nd:YAG, and diode lasers.^{472,473} Selective laser trabeculoplasty involves the use of a q-switched Nd:YAG laser for selectively targeting pigmented trabecular meshwork cells without causing coagulative damage to the meshwork structure or nonpigmented cells.⁴⁷⁴

Although its mechanism of action is not well understood, several theories have been proposed to explain how ALT increases the rate of aqueous outflow.³⁵² One theory relates 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.⁴⁷⁵ Other possibilities include changing the physiology of the trabecular endothelial cells to effect an increase in either their phagocytic activity or their number.^{476,477}

Possible complications of ALT include an increase in IOP within hours of the procedure⁴⁷⁸⁻⁴⁸⁰ and inflammation, which may lead to the formation of peripheral anterior synechiae.⁴⁸⁰⁻⁴⁸² A rise in IOP immediately after ALT can be reduced by antiglaucoma medications such as apraclonidine.⁴⁸³ Long-term scarring of the anterior chamber angle by ALT may result in a delayed rise in IOP.^{484,485} Table 6 provides recommendations for the postoperative management of patients following ALT.

The use of ALT is contraindicated in patients with corneal edema or opacities that prevent a clear view of the anterior chamber angle,³⁵² in those who have post-traumatic or uveitic secondary glaucomas, and in situations requiring a large decrease in IOP.⁴⁷⁰



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

One Hour Postoperative

- Measure IOP and check for corneal abrasions.
If normal, re-evaluate patient 1-2 weeks later.
If IOP is elevated or corneal abrasion is present, provide treatment.

One to Two 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.

Four to Eight 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.

c. Surgery

Surgical intervention, the third level of treatment for POAG, is required in many moderate or advanced glaucoma patients, to lower the IOP into the target range,⁴⁸⁶ especially in NTG or eyes resistant to other forms of therapy.^{487,488} Filtration surgery usually results in a dramatic and stable

48. Open Angle Glaucoma

reduction in IOP.^{310,339,342} 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 various filtering procedures used to lower IOP are thermal sclerostomy, posterior or anterior lip sclerectomy, trephination, and trabeculectomy.³⁵² Cyclodestructive procedures, which damage the ciliary body and thereby decrease aqueous production, are less commonly used, being reserved for the most advanced stages of the disease.³⁵²

New surgical techniques for OAG involve two types of non-penetrating deep sclerectomies (NPDS): the Aquaflo[®] collagen wick (CW) and viscocanalostomy (VC).⁴⁸⁹⁻⁴⁹¹ 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.⁴⁸⁹⁻⁴⁹¹

The advantages of NPDS include no penetration into the anterior chamber, less use of antimetabolites, less postoperative hypotony, rapid recovery of visual acuity, fewer filtration blebs (VC), less bleb fibrosis (CW),^{489,492,493} and, in general, fewer complications than with trabeculectomy.^{485,494} The disadvantages of NPDS are the procedure's difficulty and length,⁴⁹² a lower success rate than trabeculectomy,^{492,495,496} and the need for ancillary procedures to maintain control of IOP postoperatively.

Short-term complications from filtration surgery include the development of shallow anterior chambers, hypotony, choroidal detachment, uveitis, blebitis, hyphema, suprachoroidal hemorrhages,^{349,352,497} and loss of a remaining small island of central vision.⁴⁹⁸ Long-term complications include corneal edema, infection, leaking or failure from fibrosis of the subconjunctival bleb, cataract formation, and endophthalmitis.^{352,498-502} Filtration surgery is contraindicated in eyes that are already blind and in patients with severe systemic medical problems.³⁵²



Postoperative subconjunctival injection of the human monoclonal antibody CAT-152 is being investigated 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.⁵⁰³

Complications from NPDS include perforation of Descemet's membrane,⁵⁰⁴ iris plugging, hyphema, and encapsulated blebs^{495,505} Although filtration blebs are not suppose to develop with VC, subconjunctival microcysts or blebs have been found in one-third⁴⁹⁵ to one-half of reported cases.^{491,505}

d. Alternative Strategies

Several clinical trials have evaluated ALT^{327,480,506,507} and filtration surgery³²⁶⁻³²⁸ as initial (primary) treatments for POAG. The multicenter, randomized Glaucoma Laser Trial (GLT) and the Glaucoma Laser Trial Follow-up Study evaluated the efficacy and safety of ALT as an alternative to topical medication for the initial treatment of POAG.⁴⁸⁰ Eyes treated initially with ALT had lower IOP (1.2 mm Hg), better VFs (0.6 dB), better ON status, and fewer days of medication than their fellow eyes, which were treated initially with topical medication through 9 years of followup.⁴⁸⁰ Other investigators, who have questioned the GLT research design, including assessment of the crossover effect of timolol, have interpreted the initial results more cautiously.⁵⁰⁸

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 accounted for nearly twice as many medication step changes in the laser-treated eyes as the non-laser-treated eyes.^{466,480}

A 2-year prospective, randomized study compared ALT with pilocarpine as the initial treatment in patients with OAG. Especially with PEG, ALT was more effective than pilocarpine in decreasing IOP and preserving the ONH and VF in high tension glaucoma.⁵⁰⁹⁻⁵¹¹

When filtration surgery was compared to medical therapy for the initial treatment of glaucoma, the surgical group (success rate, 98%) consistently showed better IOP control and less VF deterioration than the medically treated group (success rate, 80%) after a minimum of 4 years' followup.³²⁷ 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 using laser therapy (success rate, 60%) as the initial treatment. Primary trabeculectomy has a higher success rate (98%) than surgery following medical treatment (79%).⁵¹²

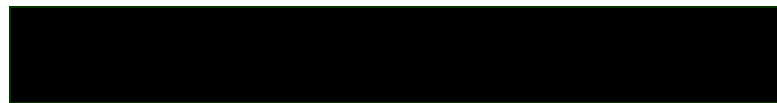
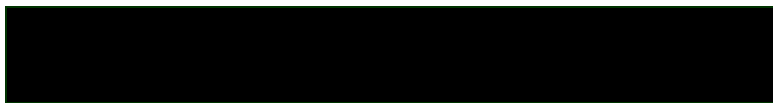
The NEI is now conducting the Collaborative Initial Glaucoma Treatment Study, a randomized, controlled clinical trial to determine whether patients with newly diagnosed OAG are best managed by the conventional approach of topical medications or by immediate filtration surgery.

e. Treatment of Pigmentary Glaucoma

The goals and approaches to the treatment and management of PG are similar to those for POAG.^{295,296} Its medical management involves the use of the same drug regimens. Miotic drugs not only provide improved aqueous outflow but may also benefit the eye by decreasing the area of contact between the posterior surface of the iris and the lens zonules.^{295,296} However, miotic agents are not well tolerated by young people,³⁶⁰ and these drugs may increase the risk for retinal detachment in patients with PDS or PG.^{79,80,513} A thorough examination of the peripheral retina is needed before instituting miotic therapy. Although the initial results of ALT in PG are often good, the failure rate may be greater and occur more quickly than in POAG.⁵¹⁴ With PG, younger patients seem to respond better to ALT than do older people.⁵¹⁵ Argon laser iridoplasty⁵¹⁶ and laser peripheral iridotomy⁵¹⁷ are also being evaluated for the treatment of PG.

f. Treatment of Pseudoexfoliation Glaucoma

The goals and approach to the treatment and management of PEG are similar to those for POAG. Miotic agents have multiple beneficial actions in eyes with PES. Patients with PES may respond less favorably



to timolol and other ocular hypotensive agents.⁵¹⁸ The IOP levels in PEG are often higher and seem more difficult to manage than in POAG.^{304,519-524} ON and VF damage tends to be greater in patients with PEG than in those with POAG.^{324,525} ALT is particularly effective early in the course of PEG;⁵²⁶ however, the failure rate may be greater, and occur more quickly, than in POAG.^{527,528} The results of filtration surgery are similar to those for patients with POAG, but complications may occur more often.⁵²⁹ ALT and filtration surgery are used earlier and more often in PEG than in POAG.^{519,525} Developed for PEG, trabecular aspiration is a procedure in which trabecular debris is aspirated under direct visualization.⁵³⁰

3. Patient Education

The proper management of glaucoma requires full compliance by the patient.^{286,531,532} 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.^{286,531} Inasmuch as the disease is basically asymptomatic, patients often choose not to comply with the prescribed therapy.^{533,534}

One-fourth to one-half of glaucoma patients do not take their medications properly.^{535,536} 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.³³⁸ Patient education regarding the benefits and risks of the treatment and proper use of medications is critical to ensure maximum compliance.^{286,531,532,537} 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.⁵³⁸

When initiating treatment for glaucoma or modifying the therapy, it is appropriate for the clinician to conduct a uniocular trial, except with beta-blocking agents, due to their crossover effect^{286,531,532} (which can be reduced by the use of nasolacrimal occlusion or punctal plugs). This uniocular trial can help determine the treatment effectiveness and

indicate potential side effects or adverse reactions. The patient should be well educated regarding all possible side effects of the medications. 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.^{286,531,532,537}

4. Prognosis and Followup

Once treatment for glaucoma has been initiated, follow-up examinations are required to monitor: stability of the IOP, ON, VF, and PPA; patient compliance with the therapy; the presence of side effects associated with the treatment; and the effectiveness of patient education. Followup also provides an opportunity to reconfirm the diagnosis.²⁸⁶ 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.⁵³⁹

a. Frequency of Followup

The frequency of follow-up evaluation of a glaucoma patient under active treatment depends on the level of IOP^{306,307,309,323,345} and the stability and severity of the disease^{306,309,486} (see Appendix Figure 3). “Stability” relates to the status of IOP, ON, and VF. The higher the IOP or the more severe the glaucoma, the more frequently the patient needs evaluation.⁵⁴⁰ Every patient diagnosed with glaucoma should be seen at least every 6 months. A dilated fundus examination and perimetry, preferably threshold testing, should be performed at least once per year. The recommended frequency for followup of patients with glaucoma:

- Stable mild-stage disease. Every 4–6 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 glaucoma and the IOP.
- Unstable disease. Cases in which IOP, ON, or VF is unstable require adjustment of therapy, which could involve weekly or biweekly followup 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.³⁵²

b. Therapy Modification

Unstable glaucoma requires re-evaluation of the treatment regimen, including reassessment of the patient's target pressure.^{286,531} The need to modify the therapy can arise from too high an IOP or target pressure, lack of full compliance, side effects developing from the treatment, contraindications to the treatment, or simply progressive damage, despite maintenance of the target IOP.

Adjustments in therapy must be weighed against the benefit or risk to the patient. The use of unioocular trials at the time of modification of medical therapy is appropriate.²⁸⁶ Following therapy modification, the clinician needs to see the patient more frequently until stability in the progression of the disease is re-established.

c. Effectiveness of Treatment

Interpretation of the effectiveness of treatment for glaucoma is hindered by the lack of consensus on a clear definition of progression of the disease.^{6,329} The rate of VF loss in POAG is usually slow.⁵⁴¹ Patients who are diagnosed with early glaucoma and receive appropriate treatment may not reach end-stage disease status for 33–38 years.^{171,542}

A prospective study showed that one-third of eyes with POAG or NTG deteriorated during an average followup of 9 years. The rate of vision loss was 3 percent per year for patients in both groups. The 3 percent per year rate of vision loss was similar for patients in both groups.⁵⁴² Although the rate of deterioration in that study was a mean deviation of less than 0.7 dB per year,⁵⁴² others have found higher rates of deterioration (mean deviation, approximately 1–5 dB per year).^{31,543,544} Worsening of VFs in patients with POAG has been shown by various studies to range from 25 to 80 percent (average, about 50%) over 5 years.^{31,304,306,309,310,323,326,342,343,524,544-549}

A few clinical studies have addressed the effectiveness of medical therapy for glaucoma.^{6,134,307} At least 40 percent of glaucoma patients respond immediately and consistently to low doses of medication.⁵⁵⁰ The GLT demonstrated, however, that after 2 years only 30 percent of medically treated glaucoma was controlled by a single beta-blocker.⁴⁸⁰ Approximately three quarters of eyes under medical therapy showed progression of the disease when followed for up to 10 years.^{304,546,547}

The rate at which patients experience VF deterioration is variable⁵⁴ and often is associated with age.^{541,543} 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.^{486,487} 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.³²³ Thus, most treated glaucoma patients whose IOP is in the "normal" range do show progression of the disease.^{202,304}

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.⁴⁷⁰ 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.^{481,482,551}



After 1 year, the rate of success in controlling OAG with ALT has been reported to be about 80 percent.⁴⁶⁷⁻⁴⁷⁰ After the first year, this rate declines about 5–15 percent per year.^{465-468,552,553} In general, glaucoma is successfully controlled in about one-half of patients 5 years after ALT;^{465,468,554} and one-tenth^{467,554} to one-third⁴⁶⁸ 10 years after ALT. Repeated ALT has a lower success rate and a higher risk.⁵⁵⁵ Selective laser trabeculoplasty appears to be equivalent to ALT in lowering IOP.⁵⁵⁶⁻⁵⁵⁸ Patients who previously failed to improve with ALT may have a greater reduction in IOP when treated with selective laser trabeculoplasty.^{506,508}

Successful control of glaucoma was achieved with ALT in 77 percent of eyes in a predominately African American population after a mean follow-up time of 2 years.⁵⁵⁹ After 5 years' extended followup, the same population showed an overall success rate of 46 percent. ALT was more successful in Caucasians than in African Americans (65% and 32%, respectively).⁴⁶⁹ Other studies have found no racial differences in success rates for ALT.

Usually, drug therapy must continue following ALT^{467,469}; only infrequently (25% of cases) can it be reduced from pre-laser levels.^{551,560} The risk of failure to control the progression of glaucoma with ALT is higher in younger patients,^{483,561} when pretreatment IOP is very high, and when glaucoma is more severe.^{465,469}

Various types of filtration surgery to control glaucomatous damage have been shown to have success rates of about 75–95 percent in previously unoperated eyes.^{349,562} Postoperative medical therapy is needed in 15–50 percent of these patients.⁵⁶³⁻⁵⁶⁶ The risk of permanent vision loss due to surgery is about 5 percent.³⁴⁷ Second filtration procedures have a much lower success rate (36%).^{567,568} The use of intraoperative⁵⁶⁹ and postoperative⁵⁷⁰ antimetabolites, such as 5-fluorouracil (5-FU) or 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.^{307,309,548} 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,³⁰⁸ and a mean IOP of 13.1 with a 17 percent rate of progression after 10 years.³⁴⁰ Although 15 mm Hg may be considered a target pressure following filtration surgery,³⁰⁷ long-term followup has demonstrated progressive VF loss following filtration surgery in 18–40 percent of patients with POAG, despite having IOPs in the normal range.^{306,307,309,329,331,343-345,500,562,565,567,571}

Filtration procedures are less successful in African Americans, in patients with neovascular or uveitic glaucoma, in children, following cataract surgery, and in eyes that have undergone previous filtration surgery.³⁵² In research focusing on the sequence of treatment modalities, the AGIS found racial differences in the progression of advanced glaucoma. The trabeculectomy-ALT-trabeculectomy (TAT) sequence resulted in a greater reduction of IOP than the ALT-trabeculectomy-trabeculectomy (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 followup, but thereafter, the TAT sequence resulted in less progression of VF loss.⁵⁷²

With outcomes slightly less favorable than those for trabeculectomy, collagen wick non-penetrating deep sclerectomy surgery (NPDS) has helped to reduce IOPs to the lower to middle teens.^{491,492} The success rate of NPDS may or may not be higher with CW.⁴⁹² Early results from a Food and Drug Administration trial of CW shows 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.⁴⁸⁹ Other studies have shown a decline in success rate with CW over time, and a greater success with the addition of post-operative antiglaucoma medications.^{492,496} Postoperative outcomes are also positively influenced (15%–41%) by injections of 5-FU (25%) or goniopuncture with a Nd:YAG laser.^{493,496}

Viscocanalostomy was dramatically successful in reducing IOP below 22 mm Hg in a study of black Africans whose IOP was previously uncontrolled;⁵⁷³ however, the 85 percent success rate reported for this procedure has not been achieved by others.^{495,505} VC does not result in as low a postoperative IOP as trabeculectomy,⁴⁴⁵ and VC success rates are higher when topical antiglaucoma medications are used

postoperatively.^{495,505} A prospective study comparing VC with trabeculectomy in Caucasians who had no history of surgery found 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.⁵⁷⁴

The high rates of progression of glaucoma in patients under treatment, especially those only using topical medications (50%–75%), indicates 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.^{307,309,323,334,335,338,339,480,548,575,576} A 30 percent reduction in pretreatment IOP is usually an effective goal.^{309,311,312,326,340,577} In the AGIS, an IOP of 18 mm Hg or less at every follow-up visit and averaging 12.3 mm Hg for 6–8 years resulted in little change in the VF.³³⁶ 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.⁵⁷⁵ Target pressures need to be adjusted 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.^{487,488,576} It appears that lowering the IOP to 10–12 mm Hg can slow the progression of VF loss in NTG.^{485,486,577-580} The Collaborative Normal-Tension Glaucoma Study clearly demonstrated that reducing the IOP by at least 30 percent, by whatever means, results in a slower rate of VF loss,^{311,312} a finding that was reconfirmed after followup periods of 5⁵⁸¹ and 10⁵⁸² years. Almost 60 percent of patients with NTG can maintain a 30 percent reduction in IOP with topical medication or ALT treatment or both.³⁴⁶ Nevertheless, even after lowering IOP by 30 percent, the disease continued to progress in 12% of eyes with NTG.³¹¹ The study of normal tension glaucoma also found that NTG is either slow or nonprogressive in nature: About 65 percent of untreated eyes showed no progression of the disease over 4 years,⁵⁸³ and about one-half showed no change over 5–7 years.³¹¹ In those eyes that did have progressive disease, the changes occurred

slowly, and there was a great variation in the rate of deterioration.^{311,312,584}

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.³⁸ About one-half of persons with PG eventually require laser or surgical treatment.⁷⁹ 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.⁵¹⁵ 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.⁴⁷¹ A higher percentage of patients with PG than with POAG, especially men,^{79,80} 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.^{32,293,585} 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.⁷⁹

- **Pseudoexfoliation glaucoma.** Eyes with PEG often manifest with higher IOP,⁹⁷ more rapid VF loss,⁵²⁰ and poorer response to medical therapy than those with POAG.⁵²¹⁻⁵²³ Though often successful initially, medical treatment of PEG is not very satisfactory over the long term.⁵¹⁹ One study³⁰⁴ found similar rates of VF deterioration (70%–80%) in POAG and PEG patients after mean followup of 10.2 and 9.1 years, respectively. Treatment consisting of ALT^{515,551} and filtration surgery^{519,586-589} and supplemental medical therapy is equally or more effective for PEG as for POAG. Because eyes with PEG may fail at a faster rate than those with POAG after both initial and consecutive ALT treatments, close postoperative surveillance is mandated.⁵⁸⁹

Trabeculectomy ab externo as a primary procedure had a success rate of 79 percent at 3 years and 64 percent at 5 years in patients receiving medication for PEG.⁵⁸⁸

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,*⁴ 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
- 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 ocular morbidity and enhance the quality of life. In addition to optical intervention, the evaluation should include the need for non-optical devices, special

*Refer to the AOA's Optometric Clinical Practice Guideline on Care of the Patient with Low Vision.

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, 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 (NTG), 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. Repeated 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 ALT and then filtration surgery. However, the traditional sequence in the treatment of glaucoma is being challenged by positive results from several studies that have used ALT or filtration surgery as the initial modality of treatment for OAG.

Coordination of the patient's care, which is essential to increasing the probability of success, involves communication with the patient's family doctor, periodic consultation with a glaucoma specialist, patient education regarding the disease, proper patient instruction, and diligence to ensure maximum patient compliance with the therapeutic regimen. The 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 if the IOP is maintained at about 16–17 mm Hg. 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. Progression of VF loss following filtration surgery can be minimized when the IOP is maintained at about 15 mm Hg. 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, Vitale S. Models of open-angle glaucoma prevalence and incidence in the United States. *Invest Ophthalmol Vis Sci* 1997; 38:83-91.
2. Leibowitz HM, Krueger DE, Maunder 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.
3. 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.
4. 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.
5. Hiller R, Kahn HA. Blindness from glaucoma. *Am J Ophthalmol* 1975; 80:62-9.
6. Leske MC, Rosenthal J. The epidemiologic aspects of open-angle glaucoma. *Am J Epidemiol* 1979; 109:250-72.
7. Tielsch JM. The epidemiology of primary open angle glaucoma. *Ophthalmol Clin North Am* 1991; 4:649-57.
8. Lewis TL. Definition and classification of glaucomas. In: Fingeret M, Lewis TL, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw-Hill, 2001:3-5.
9. Bengtsson B. The prevalence of glaucoma. *Br J Ophthalmol* 1981; 65:46-9.

10. Hollows FC, Graham PA. Intraocular pressure, glaucoma, and glaucoma suspects in a defined population. *Br J Ophthalmol* 1966; 50:570-86.
11. 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.
12. Alvarado J, Murphy C, Juster R. Trabecular meshwork cellularity in primary open-angle glaucoma and nonglaucomatous normals. *Ophthalmology* 1984; 91:564-79.
13. 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.
14. Grierson I. What is open angle glaucoma? *Eye* 1987; 1:15-28.
15. 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.
16. 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.
17. Kerrigan LA, Zack DJ, Quigley HA, et al. TUNEL-positive ganglion cells in human primary open-angle glaucoma. *Arch Ophthalmol* 1997; 115:1031-5.
18. Nickells RW. Retinal ganglion cell death in glaucoma: the how, the why, and the may be. *J Glaucoma* 1996; 5:345-56.

References 65

19. 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.
20. Olney JW. Glutamate-induced retinal degeneration in neonatal mice: electron microscopy of the acutely evolving lesion. *J Neuropath Exp Neurol* 1969; 28:455-74.
21. Pow DV, Barnett NL, Penfold P. Are neuronal transporters relevant in retinal glutamate homeostasis? *Neurochem Int* 2000; 37:191-8.
22. Sucher NJ, Lipton SA, Dreyer EB. Molecular basis of glutamate toxicity in retinal ganglion cells. *Vision Res* 1997; 37:3483-93.
23. 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.
24. 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.
25. Dawson VL, Dawson TM, Bartley DA, et al. Mechanisms of nitric oxide-mediated neurotoxicity in primary brain cultures. *J Neurosci* 1993; 13:2651-61.
26. Dawson TM, Dawson VL. Nitric oxide: actions and pathological roles. *Neuroscientist* 1994; 1:9-20.
27. 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.

66 Open Angle Glaucoma

28. 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.
29. Neufeld AA, Hernandez MR, Gonzalez M. Nitric oxide synthase in the human glaucomatous optic nerve head. *Arch Ophthalmol* 1997; 115:497-503.
30. Cockburn DM. Does reduction of intraocular pressure (IOP) prevent visual field loss in glaucoma? *Am J Optom Physiol Opt* 1983; 60:703-11.
31. 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.
32. Levovitch-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.
33. Campbell DG. Pigmentary dispersion and glaucoma. A new theory. *Arch Ophthalmol* 1979; 97:1667-72.
34. Campbell DG, Schertzer RM. Pathophysiology of pigment dispersion syndrome and pigmentary glaucoma. *Curr Opin Ophthalmol* 1995; 6:96-101.
35. Karickhoff JR. Reverse pupillary block in pigmentary glaucoma: followup and new developments. *Ophthalmic Surg* 1993; 24:562-3.
36. Campbell DG. Iridotomy, blinking and pigmentary glaucoma. *J Glaucoma* 1993; 2:44-9.
37. Pavlin CJ, Macken P, Trope GE, et al. Accommodation and iridotomy in the pigment dispersion syndrome. *Ophthalmic Surg Lasers* 1996; 27:113-20.

References 67

38. 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.
39. Richardson TM, Hutchinson BT, Grant WM. The outflow tract in pigmentary glaucoma: a light and electron microscopic study. *Arch Ophthalmol* 1977; 95:1015-25.
40. Epstein DL. Pigment dispersion and pigmentary glaucoma. In: Chandler PA, Grant WM, eds. *Glaucoma*. Philadelphia: Lea & Febiger 1979:122-9.
41. Jerndal T. Goniodysgenesis and pigmentary glaucoma. *Acta Ophthalmol* 1969; 47:424-9.
42. Donaldson DD. Transillumination of the iris. *Trans Am Ophthalmol Soc* 1974; 62:89-106.
43. Sugar HS. Pigmentary glaucoma and the glaucoma associated with exfoliation-pseudoexfoliation syndrome: update. Robert N Shaffer lecture. *Ophthalmology* 1984; 91:307-10.
44. Sugar HS. The pseudoexfoliation syndrome. *Metab Pediatr Syst Ophthalmol* 1982; 6:227-35.
45. 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.
46. Speakman JS, Ghosh M. The conjunctiva in senile lens exfoliation. *Arch Ophthalmol* 1976; 94:1757-9.
47. Konstas AG, Marshall GE, Camerson SA, Lee W. Morphology of iris vasculopathy in exfoliation glaucoma. *Acta Ophthalmol (Copenh)* 1993; 71:751-9.
48. Morrison JC, Green WR. Light microscopy of the exfoliation syndrome. *Acta Ophthalmol (Copenh)* 1988; 184(Suppl):5-27.

68. Open Angle Glaucoma

49. Schlötzer-Schrehardt U, Naumann GO. A histopathologic study of zonular instability in pseudoexfoliation syndrome. *Am J Ophthalmol* 1994; 118:730-43.
50. Asano N, Schlötzer-Schrehardt U, Naumann GOH. A histopathologic study of iris changes in pseudoexfoliation syndrome. *Ophthalmology* 1995; 102:1279-90.
51. Ringvold A, Husby G. Pseudo-exfoliation material--an amyloid-like substance. *Exp Eye Res* 1973; 17:289-99.
52. 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.
53. Eagle RC Jr, Font RL, Fine BS. The basement membrane exfoliation syndrome. *Arch Ophthalmol* 1979; 97:510-5.
54. Davanger M. The pseudo-exfoliation syndrome: a scanning electron microscopy study. I. The anterior lens surface. *Acta Ophthalmol* 1975; 53:809-20.
55. Streeten BW, Dark AJ, Barnes CW. Pseudoexfoliative material and oxytalan fibers. *Exp Eye Res* 1984; 38:523-31.
56. Aasved H. Intraocular pressure in eyes with and without fibrilloglucan epitheliocapsularis. *Acta Ophthalmol* 1971; 49:601-10.
57. Roth M, Epstein DL. Exfoliation syndrome. *Am J Ophthalmol* 1980; 89:477-81.
58. Krause U, Helve J, Forsius H. Pseudoexfoliation of the lens capsule and liberation of pigment. *Acta Ophthalmol* 1973; 51:39-46.
59. Mapstone R. Pigment release. *Br J Ophthalmol* 1981; 65:258-63.

References 69

60. Prince AM, Streeten BW, Ritch R, et al. Preclinical diagnosis of pseudoexfoliation syndrome. *Arch Ophthalmol* 1987; 105:1076-82.
61. Vesti E, Kivelä T. Exfoliation syndrome and exfoliation glaucoma. *Prog Ret Eye Res* 2000; 19:345-68.
62. Benedikt O, Roll P. The trabecular meshwork of a non-glaucomatous eye with the exfoliation syndrome. *Virchows Archiv A* 1979; 384:347-55.
63. Prevent Blindness America. Vision problems in the U.S. Schaumburg, IL: PBA, 1994.
64. 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.
65. 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.
66. Klein BE, Klein R, Sponsel WE, et al. Prevalence of glaucoma. The Beaver Dam Eye Study. *Ophthalmology* 1992; 99:1499-504.
67. Leske MC. The epidemiology of open-angle glaucoma: a review. *Am J Epidemiol* 1983; 118:166-91.
68. 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.
69. Wensor MD, McCarty CA, Stanislavsky YL, et al. The prevalence of glaucoma in the Melbourne Visual Impairment Project. *Ophthalmology* 1998; 105:733-9.

70. Open Angle Glaucoma

70. 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.
71. 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.
72. Banks JL, Perkins ES, Tsolakis S, Wright JE. Bedford glaucoma survey. *Br Med J* 1968; 1:791-6.
73. Armaly MF. On the distribution of appplanation pressure and arcuate scotoma. In: Paterson G, Miller SJH, Paterson GD, eds. *Drug mechanisms in glaucoma*. Boston: Little, Brown, & Co, 1966:167-89.
74. 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.
75. 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.
76. Kitazawa Y, Horie T, Aoki S, et al. Untreated ocular hypertension. A long-term prospective study. *Arch Ophthalmol* 1977; 95:1180-4.
77. Sommer A. Intraocular pressure and glaucoma. *Am J Ophthalmol* 1989; 107:186-8.
78. Ritch R, Steinberger D, Leibmann JM. Prevalence of pigment dispersion syndrome in a population undergoing glaucoma screening. *Am J Ophthalmol* 1993; 115:707-10.
79. 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.

References 71

80. Scheie HG, Cameron JD. Pigment dispersion syndrome: a clinical study. *Br J Ophthalmol* 1981; 65:264-9.
81. Sugar HS. Pigmentary glaucoma. A 25-year review. *Am J Ophthalmol* 1966; 62:499-507.
82. Sugar HS, Barbour FA. Pigmentary glaucoma: a rare clinical entity. *Am J Ophthalmol* 1949; 32:90-2.
83. Davidson JA, Brubaker RF, Ilstrup DM. Dimensions of the anterior chamber in pigment dispersion syndrome. *Arch Ophthalmol* 1983; 101:81-3.
84. Mandelkorn RM, Hoffman ME, Olander KW, et al. Inheritance and the pigmentary dispersion syndrome. *Ophthalmic Paediatr Genet* 1985; 6:85-91.
85. McDermott JA, Ritch R, Berger A, Wang RF. Familial occurrence of pigmentary dispersion syndrome (abstract). *Invest Ophthalmol Vis Sci* 1987; 28(suppl):136.
86. 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.
87. Dell WM. The epidemiology of the pseudo-exfoliation syndrome. *J Am Optom Assoc* 1985; 56:113-9.
88. Cashwell LF Jr, Shields MB. Exfoliation syndrome. Prevalence in a southeastern United States population. *Arch Ophthalmol* 1988; 106:335-6.
89. Hiller R, Sperduto RD, Krueger DE. Pseudoexfoliation, intraocular pressure, and senile lens changes in a population based survey. *Arch Ophthalmol* 1982; 100:1080-2.

72 Open Angle Glaucoma

90. Kozart DM, Yanoff M. Intraocular pressure status in 100 consecutive patients with exfoliation syndrome. *Ophthalmology* 1982; 89:214-8.
91. 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.
92. Ball SF. Exfoliation prevalence in the glaucoma population of South Louisiana. *Acta Ophthalmol* 1988; 66(suppl 184):93-8.
93. 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:S512 (abstr).
94. Mizuno K, Muroi S. Cycloscopy of pseudoexfoliation. *Am J Ophthalmol* 1979; 87:513-8.
95. Layden WE, Shaffer RN. Exfoliation syndrome. *Am J Ophthalmol* 1974; 78:835-41.
96. Kivelä T, Hietanen J, Uusitalo M. Autopsy analysis of clinically unilateral exfoliation syndrome. *Invest Ophthalmol Vis Sci* 1997; 38:2008-15.
97. 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.
98. Horven I. Exfoliation syndrome: incidence and prognosis of glaucoma capsulare in Massachusetts. *Arch Ophthalmol* 1966; 76:505-11.
99. 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.

References 73

100. Coulehan JL, Helzlsouer KJ, Rogers KD, Brown SI. Racial differences in intraocular tension and glaucoma surgery. *Am J Epidemiol* 1980; 111:759-68.
101. Martin MJ, Sommer A, Gold EB, Diamond EL. Race and primary open-angle glaucoma. *Am J Ophthalmol* 1985; 99:383-7.
102. Wilensky JT, Gandhi N, Pan T. Racial influences in open-angle glaucoma. *Ann Ophthalmol* 1978; 10:1398-402.
103. Wilson R, Richardson TM, Hertzmark E, Grant WM. Race as a risk factor for progressive glaucomatous damage. *Ann Ophthalmol* 1985; 17:653-9.
104. 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.
105. 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.
106. 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.
107. Foster PJ, Wong JS, Wong E, et al. Accuracy of clinical estimates of intraocular pressure in Chinese eyes. *Ophthalmology* 2000; 107:1816-21.
108. Netland PA, Wiggs JL, Dreyer EB. Inheritance of glaucoma and genetic counseling of glaucoma patients. *Int Ophthalmol Clin* 1993; 33:101-20.

74 Open Angle Glaucoma

109. Teikari JM. Genetic factors in open-angle (simple and capsular) glaucoma: a population-based twin study. *Acta Ophthalmol* 1987; 65:715-20.
110. Miller SJ. Genetics of glaucoma and family studies. *Trans Ophthalmol Soc UK* 1978; 98:290-2.
111. Rosenthal AR, Perkins ES. Family studies in glaucoma. *Br J Ophthalmol* 1985; 69:664-7.
112. Perkins ES. Family studies in glaucoma. *Br J Ophthalmol* 1974; 58:529-35.
113. Armaly MF, Monstavičius BF, Sayegh RE. Ocular pressure and aqueous outflow in siblings. *Arch Ophthalmol* 1968; 80:354-60.
114. Becker B, Kolker AE, Roth FD. Glaucoma family study. *Am J Ophthalmol* 1969; 50:557-67.
115. Kellerman L, Posner A. The value of heredity in detection and study of glaucoma. *Am J Ophthalmol* 1955; 40:681-5.
116. Leske MC, Connell AM, Wu SY, et al. Risk factors for open-angle glaucoma. The Barbados Eye Study. *Arch Ophthalmol* 1995; 113:918-24.
117. 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.
118. 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.
119. 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.

References 75

120. Seddon JM, Schwartz B, Flowerdew G. Case-control study of ocular hypertension. *Arch Ophthalmol* 1983; 101:891-4.
121. Levene RZ, Workman PL, Broder SW, Hirschhorn K. Heritability of ocular pressure in normal and suspect ranges. *Arch Ophthalmol* 1970; 84:730-4.
122. Armaly MF. Genetic determination of cup/disc ratio of the optic nerve. *Arch Ophthalmol* 1967; 78:35-43.
123. Craig JE, Mackey DA. Glaucoma genetics: Where are we? Where will we go? *Curr Opin Ophthalmol* 1999; 10:126-34.
124. 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.
125. 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.
126. 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.
127. Budde WM. Heredity in primary open-angle glaucoma. *Curr Opin Ophthalmol* 2000; 11:101-6.
128. Stone EM, Fingert JH, Alwand WL, et al. Identification of a gene that causes primary open angle glaucoma. *Science* 1997; 275:668-70.
129. 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.

76 Open Angle Glaucoma

130. Tielsch JM. The epidemiology and control of open angle glaucoma: a population-based perspective. *Annu Rev Public Health* 1996; 17:121-36.
131. 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.
132. 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.
133. 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.
134. 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.
135. Armaly MF. Ocular pressure and visual fields. A ten-year follow-up study. *Arch Ophthalmol* 1969; 81:25-40.
136. Perkins ES. The Bedford Glaucoma Survey. I. Long-term follow-up of borderline cases. *Br J Ophthalmol* 1973; 57:179-85.
137. Pederson JE, Anderson DR. The mode of progressive disc cupping in ocular hypertension and glaucoma. *Arch Ophthalmol* 1980; 98:490-5.
138. 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.

References 77

139. 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.
140. 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.
141. Perkins ES, Phelps CD. Open angle glaucoma, ocular hypertension, low-tension glaucoma, and refraction. *Arch Ophthalmol* 1982; 100:1464-7.
142. Mitchell P, Hourihan F, Sanbach J, Wang JJ. The relationship between glaucoma and myopia: the Blue Mountains Eye Study. *Ophthalmology* 1999; 106:2010-15.
143. 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.
144. Becker B. Diabetes mellitus and primary open-angle glaucoma: The XXVII Edward Jackson Memorial Lecture. *Am J Ophthalmol* 1971; 71:1-16.
145. Clark CV, Mapstone R. The prevalence of diabetes mellitus in the family history of patients with primary glaucoma. *Doc Ophthalmol* 1986; 62:161-3.
146. 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.
147. Klein BE, Klein R, Moss SE. Intraocular pressure in diabetic persons. *Ophthalmology* 1984; 91:1356-60.

78. Open Angle Glaucoma

148. Klein BE, Klein R, Jensen SC. Open-angle glaucoma and older-onset diabetes. The Beaver Dam Eye Study. *Ophthalmology* 1994; 101:1173-7.
149. Mitchell P, Smith W, Chey T, Healey PR. Open-angle glaucoma and diabetes: the Blue Mountains Eye Study, Australia. *Ophthalmology* 1997; 104:712-8.
150. Reynolds DC. Relative risk factors in chronic open angle glaucoma: an epidemiological study. *Am J Optom Physiol Optics* 1997; 54:116-20.
151. Katz J, Sommer A. Risk factors for primary open angle glaucoma. *Am J Prev Med* 1988; 4:110-4.
152. Morgan RW, Drance SM. Chronic open-angle glaucoma and ocular hypertension. An epidemiological study. *Br J Ophthalmol* 1975; 59:211-5.
153. Armaly MF, Baloglou PJ. Diabetes mellitus and the eye. II. Intraocular pressure and aqueous outflow facility. *Arch Ophthalmol* 1967; 77:493-502.
154. Christiansson J. Intraocular pressure in diabetes mellitus. *Acta Ophthalmol (Copenh)* 1961; 39:155-67.
155. 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.
156. 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.
157. Gasser P. Ocular vasospasm: a risk factor in the pathogenesis of low-tension glaucoma. *Int Ophthalmol* 1989; 13:281-90.

References 79

158. Phelps CD, Corbett JJ. Migraine and low-tension glaucoma. A case-control study. *Invest Ophthalmol Vis Sci* 1985; 26:1105-8.
159. Leske MC, Podgor MJ. Intraocular pressure, cardiovascular risk variables, and visual field defects. *Am J Epidemiol* 1983; 118:280-7.
160. 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.
161. Ishida K, Yamamoto T, Kitazawa Y. Clinical factors associated with progression of normal-tension glaucoma. *J Glaucoma* 1998; 7:372-7.
162. 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.
163. Meyer JH, Brandi-Dohrn J, Funk J. Twenty-four hour blood pressure monitoring in normal tension glaucoma. *Br J Ophthalmol* 1996; 80:864-7.
164. Graham SL, Drance SM, Wijsman K, et al. Ambulatory blood pressure monitoring in glaucoma. The nocturnal dip. *Ophthalmology* 1995; 102:61-9.
165. Quigley HA. Reappraisal of the mechanism of glaucomatous optic nerve damage. *Eye* 1987; 1:318-22.
166. 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.
167. 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.

80 Open Angle Glaucoma

168. 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.
169. Zeimer RC, Ogura Y. The relationship between glaucomatous damage and optic nerve head mechanical compliance. *Arch Ophthalmol* 1989; 107:1232-4.
170. Palmberg P. The rationale and effectiveness of glaucoma therapy. Distributed at the Ann Meeting Am Glaucoma Soc, Miami, FL, December 1988.
171. Jay JL, Murdoch JR. The rate of visual field loss in untreated primary open angle glaucoma. *Br J Ophthalmol* 1993; 77:176-8.
172. Kass MA, Kolker AE, Becker B. Prognostic factors in glaucomatous visual field loss. *Arch Ophthalmol* 1976; 94:1274-6.
173. 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.
174. 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.
175. Tielsch JM. Screening for glaucoma continuing dilemma. *Proc New Orleans Acad Ophthalmol* 1991; 40:1-11.
176. 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.
177. Levi L, Schwartz B. Glaucoma screening in the health care setting. *Surv Ophthalmol* 1983; 28:164-74.

References 81

178. Gottlieb LK, Schwartz B, Pauker SG. Glaucoma screening. A cost-effectiveness analysis. *Surv Ophthalmol* 1983; 28:206-26.
179. Eddy DM, Sanders LE, Eddy JF. The value of screening for glaucoma with tonometry. *Surv Ophthalmol* 1983; 28:194-205.
180. 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.
181. Tielsch JM, Katz J, Quigley HA, et al. Intraobserver and interobserver agreement in measurement of optic disc characteristics. *Ophthalmology* 1988; 95:350-6.
182. 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.
183. Motolko M, Drance SM. Features of the optic disc in preglaucomatous eyes. *Arch Ophthalmol* 1981; 99:1992-4.
184. Lichter PR. Variability of expert observers in evaluating the optic disc. *Trans Am Ophthalmol Soc* 1976; 74:532-72.
185. O'Connor DJ, Zeyen T, Caprioli J. Comparisons of methods to detect glaucomatous optic nerve damage. *Ophthalmology* 1993; 100:1498-503.
186. Komulainen R, Tuulonen A, Airaksinen PJ. The follow-up of patients screened for glaucoma with non-mydratic fundus photography. *Int Ophthalmol* 1992; 16:165-9.
187. Airaksinen PJ, Drance SM, Douglas GR, et al. Diffuse and localized nerve fiber loss in glaucoma. *Am J Ophthalmol* 1984; 98:566-71.

82 Open Angle Glaucoma

188. Sommer A, Quigley HA, Robin AL, et al. Evaluation of nerve fiber layer assessment. *Arch Ophthalmol* 1984; 102:1766-71.
189. Keltner JL, Johnson CA. Mass visual field screening in a driving population. *Ophthalmology* 1980; 87:785-92.
190. Burnstein Y, Elish 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.
191. Quigley HA. Identification of glaucoma-related visual field abnormality with the screening protocol of frequency doubling technology. *Am J Ophthalmol* 1998; 125:819-29.
192. 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.
193. 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.
194. Johnson CA, Cioffi GA, Van Buskirk EM. Evaluation of two screening tests for frequency doubling technology perimetry. The Hague, the Netherlands: Kugler: 1999.
195. Johnson CA, Samuels SJ. Screening for glaucomatous visual field loss with frequency-doubling perimetry. *Invest Ophthalmol Vis Sci* 1997; 38:413-25.
196. Tribble JR, Schultz RO, Robinson JC, Rothe TL. Accuracy of glaucoma detection with frequency-doubling perimetry. *Am J Ophthalmol* 2000; 129:740-5.
197. Cioffi GA (by invitation), Mansberger S, Spry P, et al. Frequency doubling perimetry and the detection of eye disease in the community. *Tr Am Ophth Soc* 2000; 98:195-202.

References 83

198. 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.
199. 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.
200. 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.
201. Douglas GR. Diagnostic concepts in open-angle glaucoma. *Curr Opin Ophthalmol* 1992; 3:162-9.
202. Greve EL. The effect of treatment on progression of glaucoma (summary). *Surv Ophthalmol* 1989; 33(suppl):431-3.
203. 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.
204. 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.
205. Kohn AN, Moss AP, Podos SM. Relative afferent pupillary defect in glaucoma without characteristic field loss. *Arch Ophthalmol* 1979; 97:294-6.
206. 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.

84 Open Angle Glaucoma

207. Schwartz B, Talusan AG. Spontaneous trends in ocular pressure in untreated ocular hypertension. *Arch Ophthalmol* 1980; 98:105-11.
208. Goldmann H. Applanation tonometry. In: Newell FW, ed. *Glaucoma Transactions of the Second Conference*. New York: Josiah Macy Jr. Foundation. 1957:167-220.
209. 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.
210. Ehlers N, Bramsen T, Sperling S. Applanation tonometry and central corneal thickness. *Acta Ophthalmol (Copenh)* 1974; 53:34-43.
211. Whitacre MM, Stein RA, Hassanein K. The effect of corneal thickness on applanation tonometry. *Am J Ophthalmol* 1993; 115:592-6.
212. 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. *Jap J Ophthalmol* 2000; 44:691.
213. Argus WA. Ocular hypertension and central corneal thickness. *Ophthalmology* 1995; 102:1810-2.
214. 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.
215. Copt RP, Thomas R, Mermound A. Corneal thickness in ocular hypertension, primary open-angle glaucoma, normal tension glaucoma. *Arch Ophthalmol* 1999; 117:14-6.

References 85

216. Herman DC, Hodge DO, Bourne WM. Increased corneal thickness in patients with ocular hypertension. *Arch Ophthalmol* 2001; 119:334-6.
217. Herndon LW, Choudhri SA, Cox T, et al. Central corneal thickness in normal, glaucomatous, and ocular hypertensive eyes. *Arch Ophthalmol* 1997; 115:1137-41.
218. Monrad Y, Sharon E, Hefetz L, Nemet P. Corneal thickness and curvature in normal-tension glaucoma. *Am J Ophthalmol* 1998; 125:164-8.
219. 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.
220. 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.
221. 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.
222. 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.
223. Emara BY, Tingey DP, Probst LE, Motolko MA. Central corneal thickness in low-tension glaucoma. *Can J Ophthalmol* 1999; 34:319-24.
224. 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.

86 Open Angle Glaucoma

225. Abbasoglu OE, Bowman WR, Cavanagh DH, McCulley JP. Reliability of intraocular pressure measurements after myopic excimer photorefractive keratectomy. *Ophthalmology* 1998; 105:2193-6.
226. 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.
227. Brubaker RF. Tonometry and corneal thickness. *Arch Ophthalmol* 1999; 117:366-70.
228. Flanagan JG. Imaging of the optic nerve and nerve fiber layer in glaucoma. In: Fingeret M, Lewis TL, eds. *Primary care of glaucomas*, 2nd ed. New York, NY: McGraw-Hill, 2001:187-200.
229. 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.
230. 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.
231. 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.
232. 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; 37:2393-2401.
233. Wollstein G, Garway-Heath DF, Hitchings RA. Identification of early glaucoma cases with the scanning laser ophthalmoscope. *Ophthalmology* 1998; 105:1157-63.

References 87

234. 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.
235. 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.
236. Farra T, Flanagan JG, Trope GE. The detection of glaucomatous progression using scanning laser tomography. *Invest Ophthalmol Vis Sci* 1999; 39(suppl):389.
237. Litwak AB. Evaluation of the retinal nerve fiber layer in glaucoma. *J Am Optom Assoc* 1990; 61:390-7.
238. 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.
239. Colen TP, Tjon-Fo-Sang MJ, Mulder PG, Lemij HG. Reproducibility of measurements with the nerve fiber layer analyzer (NfA/GDx). *J Glaucoma* 2000; 9:363-70.
240. 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.
241. Weinreb RN, Zangwill L, Berry CC, et al. Detection of glaucoma with scanning laser polarimetry. *Arch Ophthalmol* 1998; 116:1583-9.
242. 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.

88 Open Angle Glaucoma

243. 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.
244. 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.
245. 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.
246. 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.
247. 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.
248. 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.
249. 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.
250. 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).

References 89

251. Jonas JB, Fernandez MC, Naumann GO. Glaucomatous parapapillary atrophy. Occurrence and correlations. *Arch Ophthalmol* 1992; 110:214-22.
252. Jonas JB, Naumann GO. Parapapillary chorioretinal atrophy in normal and glaucoma eyes. II. Correlations. *Invest Ophthalmol Vis Sci* 1989; 30:919-26.
253. 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.
254. Primose J. Early signs of the glaucomatous disc. *Br J Ophthalmol* 1971; 55:820-5.
255. 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.
256. Uhm KB, Lee DY, Kim JT, Hong C. Peripapillary atrophy in normal and primary open-angle glaucoma. *Korean J Ophthalmol* 1998; 12:37-50.
257. Wilensky JT, Kolker AE. Peripapillary changes in glaucoma. *Am J Ophthalmol* 1976; 81:341-5.
258. Buus DR, Anderson DR. Peripapillary crescents and halos in normal-tension glaucoma and ocular hypertension. *Ophthalmology* 1989; 96:16-9.
259. Jonas JB, Xu L. Parapapillary chorioretinal atrophy in normal-pressure glaucoma. *Am J Ophthalmol* 1993; 115:501-5.
260. Tuulonen A, Jonas JB, Välimäki S, et al. Interobserver variation in the measurements of peripapillary atrophy in glaucoma. *Ophthalmology* 1996; 103:535-41.

90 Open Angle Glaucoma

261. Heijl A, Samander C. Peripapillary atrophy and glaucomatous visual field defects. *Doc Ophthalmol* 1985; 42:403.
262. 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.
263. Uchida H, Ugurlu S, Caprioli J. Increasing peripapillary atrophy is associated with progressive glaucoma. *Ophthalmology* 1998; 105:1541-5.
264. Rockwood EJ, Anderson DR. Acquired peripapillary changes and progression in glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1988; 226:510-5.
265. 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.
266. Tuulonen A, Lehtola P, Airaksinen PJ. Nerve fiber layer defects with normal visual fields. Do normal optic disc and normal visual field indicate absence of glaucomatous abnormality? *Ophthalmology* 1993; 100:587-97.
267. Caprioli J. Discrimination between normal and glaucomatous eyes. *Invest Ophthalmol Vis Sci* 1992; 33:153-9.
268. Heijl A, Drance SM, Douglas GR. Automated perimetry (COMPETER). Ability to detect early glaucomatous field defects. *Arch Ophthalmol* 1980; 98:1560-3.
269. Heijl A, Lindgren G, Olsson J. A package for the statistical analysis of visual fields. *Doc Ophthalmol Proc Ser* 1987; 49:153-68.
270. Heijl A, Lindgren G, Olsson J. The effect of perimetric experience in normal subjects. *Arch Ophthalmol* 1989; 107:81-6.

References 91

271. 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.
272. Lakowski R, Drance SM. Acquired dyschromatopsias: the earliest functional losses in glaucoma. *Doc Ophthalmol Proc Ser* 1979; 19:159-65.
273. 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.
274. 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.
275. Fisher RF. Value of tonometry and tonography in the diagnosis of glaucoma. *Br J Ophthalmol* 1972; 56:200-4.
276. Rasmussen KE, Jorgenson HA. Diagnostic value of the water-drinking test in the early detection of simple glaucoma. *Acta Ophthalmol* 1976; 54:160-6.
277. 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.
278. 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.
279. 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.
280. Sample PA, Weinreb RN. Progressive color visual field loss in glaucoma. *Invest Ophthalmol Vis Sci* 1992; 33:2068-71.

92 Open Angle Glaucoma

281. 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.
282. 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.
283. 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.
284. 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.
285. 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.
286. Fingeret M. Medical management of glaucoma. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*. New York, NY: McGraw Hill, 2001:333-63.
287. 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.
288. Hatsuda TA. Low-tension glaucoma. *Folia Ophthalmol Jpn* 1977; 28:244-9.
289. 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.
290. Zeyen TG, Caprioli J. Progression of disc and field damage in early glaucoma. *Arch Ophthalmol* 1993; 111:62-5.

References 93

291. 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.
292. Hoskins HD. Does computerized perimetry offer practical advances in choice of therapy in the glaucoma patient? *Eye* 1992; 6:43-6.
293. Speakman JS. Pigmentary dispersion. *Br J Ophthalmol* 1981; 65:249-51.
294. Becker B, Podos SM. Krukenberg's spindles and primary open-angle glaucoma. *Arch Ophthalmol* 1966; 76:635-9.
295. Farrar SM, Shields MB. Current concepts in pigmentary glaucoma. *Surv Ophthalmol* 1993; 37:233-52.
296. Fingeret M, Thimons JJ. Common secondary glaucomas. In: Lewis TL, Fingeret M, eds. Primary care of the glaucomas. New York, NY: McGraw Hill, 2001:461-75.
297. 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.
298. 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.
299. Jerndal T. Open angle glaucoma and the pseudo-exfoliation syndrome. In: Glaucoma, Vol II Cairns JE, ed. London:Grune & Stratton, 1986; 661-7.
300. Prince AM, Ritch R. Clinical signs of pseudoexfoliation syndrome. *Ophthalmology* 1986; 93:803-7.

94 Open Angle Glaucoma

301. Aasved H. Mass screening for fibrillopathia epitheliocapsularis, so-called senile exfoliation or pseudoexfoliation of the anterior lens capsule. *Acta Ophthalmol* 1971; 49:334-43.
302. Aasved H. Incidence of defects in the pigmented pupillary ruff in eyes with and without fibrillopathia epitheliocapsularis. *Acta Ophthalmol* 1973; 51:710-5.
303. Cavallerano AA, Alexander LJ. The secondary glaucomas. In: Classe' JG, ed. Optometry clinics, vol 1. Norwalk,CT: Appleton & Lange, 1991:127-64.
304. Pohjanpelto P. Long-term prognosis of visual field in glaucoma simplex and glaucoma capsulare. *Acta Ophthalmol* 1985; 63:418-23.
305. Tarkkanen A. Pseudoexfoliation of the lens capsule. *Acta Ophthalmol Copenh* 1962; 40:(Suppl 71):1-98.
306. Kidd MN, O'Connor M. Progression of field loss after trabeculectomy: a five-year follow-up. *Br J Ophthalmol* 1985; 69:827-31.
307. Odberg T. Visual field prognosis in advanced glaucoma. *Acta Ophthalmol* 1987; 65(Suppl 182):27-9.
308. 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.
309. 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.

References 95

310. 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.
311. 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.
312. 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.
313. Kass MA, Heuer DK, Higginbotham EJ, et al, and the Ocular Hypertension Treatment Study Group. 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.
314. Kitazawa Y. Prophylactic therapy of ocular hypertension: a prospective study. *Trans Ophthalmol Soc NZ* 1981; 33:30-2.
315. Shin DH, Kolker AE, Kass MA, et al. Long-term epinephrine therapy of ocular hypertension. *Arch Ophthalmol* 1976; 94:2059-60.
316. Chauhan BC, Drance SM, Douglas GR. The effect of long-term intraocular pressure reduction on the differential light sensitivity in glaucoma suspects. *Invest Ophthalmol Vis Sci* 1988; 29:1478-85.
317. Chisholm IA, Stead S, Tan L, Melenchuk JW. Prognostic indicators in ocular hypertension. *Can J Ophthalmol* 1980; 15:4-8.

96 Open Angle Glaucoma

318. David R, Livingston DG, Luntz MH. Ocular hypertension -- a long-term follow-up of treated and untreated patients. *Br J Ophthalmol* 1977; 61:668-74.
319. Graham PA. The definition of pre-glaucoma. A prospective study. *Trans Ophthalmol Soc UK* 1969; 88:153-65.
320. Schulzer M, Drance SM, Douglas GR. A comparison of treated and untreated glaucoma suspects. *Ophthalmology* 1991; 98:301-7.
321. Odberg T. Visual field prognosis in early glaucoma. A long-term clinical follow-up. *Acta Ophthalmol* 1993; 71:721-6.
322. 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.
323. 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.
324. Bergeå B, Bodin L, Svedbergh B. Impact of intraocular pressure regulation on visual fields in open-angle glaucoma. *Ophthalmology* 1999; 106:997-1005.
325. Tsai CS, Shin DH, Wan JY, Zeiter JH. Visual field global indices in patients with reversal of glaucomatous cupping after intraocular pressure reduction. *Ophthalmology* 1991; 98:1412-9.
326. 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.
327. Migdal CS, Hitchings RA. Control of chronic simple glaucoma with primary medical, surgical and laser treatment. *Trans Ophthalmol Soc UK* 1986; 105:653-6.

References 97

328. Smith RJ. The enigma of primary open-angle glaucoma. The Lang lecture 1986. *Trans Ophthalmol Soc UK* 1986; 105:618-33.
329. Chauhan BC, Drance SM. The relationship between intraocular pressure and visual field progression in glaucoma. *Graefes Arch Clin Exp Ophthalmol* 1992; 230:521-6.
330. Holmin C, Krakau CE. Regression analysis of the central visual field in chronic glaucoma cases. A follow-up study using automatic perimetry. *Acta Ophthalmol (Copenh)* 1982; 60:267-74.
331. Weber J, Koll W, Kriegelstein GK. Intraocular pressure and visual field decay in chronic glaucoma. *Ger J Ophthalmol* 1993; 2:165-9.
332. 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.
333. Schultz JS, Werner EB, Krupin T, et al. Intraocular pressure and visual field defects with argon laser trabeculoplasty in chronic open-angle glaucoma. *Ophthalmology* 1987; 94:553-7.
334. 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.
335. 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.
336. 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.

98 Open Angle Glaucoma

337. 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.
338. 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.
339. Quigley HA, Maumenee AE. Long-term follow-up of treated open-angle glaucoma. *Am J Ophthalmol* 1979; 87:519-25.
340. 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.
341. 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.
342. Werner EB, Drance SM, Schulzer M. Trabeculectomy and the progression of glaucomatous visual field loss. *Arch Ophthalmol* 1977; 95:1374-7.
343. Popovic V, Sjostrand J. Long-term outcome following trabeculectomy. II. Visual field survival. *Acta Ophthalmol (Copenh)* 1991; 69:305-9.
344. 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.
345. Zeimer RC, Wilensky JT, Gieser DK, Viana MAG. Association between intraocular pressure peaks and progression of visual field loss. *Ophthalmology* 1991; 98:64-9.

References 99

346. Schulzer M. Intraocular pressure reduction in normal-tension glaucoma patients. *Ophthalmology* 1992; 99:1468-70.
347. Quigley HA. Open-angle glaucoma. *N Engl J Med* 1993; 328:1097-106.
348. Jampel HD. Target pressure in glaucoma therapy. *J Glaucoma* 1997; 6(2):133-8.
349. Quigley HA. A reevaluation of glaucoma management. *Int Ophthalmol Clin (Fall)* 1984; 24:1-11.
350. Bartlett JD, Jaanus SD. Ocular hypotensive drugs. In: Bartlett JD, Jaanus SD, eds. *Clinical ocular pharmacology*, 4th ed. Boston: Butterworth-Heinemann, 2001:167-204.
351. 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, a Wolters Kluwer Co, 2003:1061-75.
352. Werner EB. Tertiary glaucoma surgical procedures. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*. New York, NY: McGraw Hill, 2001:411-7.
353. Erickson K, Schroeder A. Pharmacology of antiglaucoma medications. In: Lewis TL, Fingeret M, eds. *Primary care of the glaucomas*. New York, NY: McGraw Hill, 2001:313-32.
354. 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.
355. Brown HS, Meltzer G, Merrill RC, et al. Visual effects of pilocarpine in glaucoma, comparative study of administration by eyedrops or by ocular therapeutic systems. *Arch Ophthalmol* 1976:1716-9.

100 Open Angle Glaucoma

356. Krause K, Kuchle HJ, Baumgart M. Comparative studies of pilocarpine gel and pilocarpine eye drops. *Klin Monatsbl Augenheilkd* 1985; 187:178-83.
357. Zimmerman TJ. Pilocarpine. *Ophthalmology* 1981; 88:85-8.
358. Mandell AI, Stentz F, Kitabchi AE. Dipivalyl epinephrine: a new pro-drug in the treatment of glaucoma. *Ophthalmology* 1978; 85:268-75.
359. Kaback MB, Podos SM, Harbin TS Jr, et al. The effects of dipivalyl epinephrine on the eye. *Am J Ophthalmol* 1976; 81:768-72.
360. Anderson JA. Systemic absorption of topical ocularly applied epinephrine and dipivefrin. *Arch Ophthalmol* 1980; 98:350-3.
361. Kolker AE, Becker B. Epinephrine maculopathy. *Arch Ophthalmol* 1968; 79:552-62.
362. Podos SM, Ritch R. Epinephrine as the initial therapy in selected cases of ocular hypertension. *Surv Ophthalmol* 1980; 25:188-94.
363. 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.
364. Hill RA, Minckler DS, Lee M, et al. Apraclonidine prophylaxis for postcycloplegic intraocular pressure spikes. *Ophthalmology* 1991; 98:1083-6.
365. 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.

References 101

366. 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.
367. 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.
368. Morrison JC, Robin AL. Adjunctive glaucoma therapy. A comparison of apraclonidine to dipivefrin when added to timolol maleate. *Ophthalmology* 1989; 96:3-7.
369. Serdahl C, Galustian J, Lewis RA. The effects of apraclonidine on conjunctival oxygen tension. *Arch Ophthalmol* 1989; 107:1777-9.
370. Robin AL. Short-term effects of unilateral 1 percent apraclonidine therapy. *Arch Ophthalmol* 1988; 106:912-5.
371. Burke J, Schwartz M. Preclinical evaluation of brimonidine. *Surv Ophthalmol* 1996; 41(Suppl 1):S9-18.
372. 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.
373. 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.

102 Open Angle Glaucoma

374. 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.
375. 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.
376. 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.
377. 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.
378. 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.
379. 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.
380. 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.

381. 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:S481.
382. 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.
383. 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.
384. 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:S114.
385. 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.
386. 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.
387. 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.
388. Lachkar Y, Migdal C, Dhanjil S. Effect of brimonidine tartrate on ocular hemodynamic measurements. *Arch Ophthalmol* 1998; 116:1591-4.

389. 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.
390. Byles DB, Frith P, Salmon JF. Anterior uveitis as a side effect of topical brimonidine. *Am J Ophthalmol* 2000; 130:287-91.
391. Williams GC, Orengo-Nania S, Gross RL. Incidence of brimonidine allergy in patients previously allergic to apraclonidine. *J Glaucoma* 2000; 9:235-8.
392. Yalon M, Urinowsky E, Rothkoff L, et al. Frequency of timolol administration. *Am J Ophthalmol* 1981; 92:526-9.
393. van Buskirk EM, Weinreb RN, Berry DP, et al. Betaxolol in patients with glaucoma and asthma. *Am J Ophthalmol* 1986; 101:531-4.
394. 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.
395. Osborne NN, Cazeveille 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.
396. 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.
397. 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.

References 105

398. Wilson RP, Spaeth GL, Poryzees E. The place of timolol in the practice of ophthalmology. *Ophthalmology* 1980; 87:451-4.
399. 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.
400. Epstein DL, Grant WM. Carbonic anhydrase inhibitor side effects: serum chemical analysis. *Arch Ophthalmol* 1977; 95:1378-82.
401. Stone RA, Zimmerman TJ, Shin DH, et al. Low-dose methazolamide and intraocular pressure. *Am J Ophthalmol* 1977; 83:674-9.
402. Lichter PR, Newman LP, Wheeler NC, Beall OV. Patient tolerance to carbonic anhydrase inhibitors. *Am J Ophthalmol* 1978; 85:495-502.
403. 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.
404. 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.
405. Mogk LG, Cyrilin MN. Blood dyscrasias and carbonic anhydrase inhibitors. *Ophthalmology* 1988; 95:768-71.
406. 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.
407. 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.

106 Open Angle Glaucoma

408. 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.
409. 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.
410. 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.
411. 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-S153.
412. Nardin G. Activity of the topical CAI MK-507 bid when added to timolol bid. *Invest Ophthalmol Vis Sci* 1991; 32(Suppl): 989-95.
413. 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.
414. 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.

References 107

415. 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.
416. 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.
417. 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):S269.
418. 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.
419. 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.
420. Donohue EK, Wilensky JT. Trusopt, a topical carbonic anhydrase inhibitor. *J Glaucoma* 1996; 5:68-74.
421. 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):S559.
422. 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.

108 Open Angle Glaucoma

423. Camras CB and the United States Lantanoprost 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.
424. 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.
425. 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.
426. Rác 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.
427. 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.
428. 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.
429. 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.
430. 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.

431. 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.
432. 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.
433. 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.
434. 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.
435. 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.
436. Vanlandingham BD, Brubaker RF. Combined effect of dorzolamide and latanoprost on the rate of aqueous humor flow. *Am J Ophthalmol* 1998; 126:191-6.
437. 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.
438. 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.

439. 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.
440. Fechtner RD, Khouri AS, Zimmerman TJ, et al. Anterior uveitis associated with latanoprost. *Am J Ophthalmol* 1998; 126:37-41.
441. 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.
442. Rowe JA, Hattenhauer MG, Herman DC. Adverse side effects with latanoprost. *Am J Ophthalmol* 1997; 124:683-5.
443. 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.
444. Dios Castro E, Maquet Dusart JA. Latanoprost-associated recurrent herpes simplex keratitis. *Arch Soc Esp Oftalmol* 2000; 75:775-8.
445. 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.
446. Wand M, Gilbert CM, Liesegang TJ. Latanoprost and herpes simplex keratitis. *Am J Ophthalmol* 1999; 127:602-4.
447. 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.

References 111

448. 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.
449. 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.
450. 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.
451. Yamamoto T, Kitazawa Y, Azuma I, Masuda K. Clinical evaluation of UF-201 (Rescula®; isopropyl unoprostone). *Surv Ophthalmol* 1997; 41(Suppl 2):S99-103.
452. 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.
453. Nakamatsu T, Okinami S, Oono S. The ocular hypotensive effect of concomitantly applied isopropyl unoprostone and timolol. *J Eye* 1996; 13:439-41.
454. 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.
455. 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.

112 Open Angle Glaucoma

456. Kojima S, Sugiyama T, Azuma I, et al. Effect of topically applied isopropyl unoprostone on microcirculation in the human ocular fundus evaluated with a laser speckle microcirculation analyser. *Nippon Ganka Gakkai Zasshi* 1997; 101:605-10.
457. Makimoto Y, Sugiyama T, Kojima S, Azuma I. Long-term effect of topically applied isopropyl unoprostone on microcirculation in the choroid-retina. *Nippon Ganka Gakkai Zasshi* 2000; 104:39-43.
458. Kitaya N, Yoshida A, Ishiko S, et al. Effect of timolol and UF-021 (a prostaglandin-related compound) on pulsatile ocular blood flow in normal volunteers. *Ophthalmic Res* 1997; 29:139-44.
459. 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.
460. Yamamoto T, Kitazawa Y. Iris-color change developed after topical isopropyl unoprostone treatment. *J Glaucoma* 1997; 6:430-2.
461. 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.
462. 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.

463. 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.
464. Polo V, Larrosa M, Gomez ML, et al. Lantanoprost versus combined therapy with timolol plus dorzolamide: IOP-lowering effect in open-angle glaucoma. *Acta Ophthalmol Scand* 2001; 79:6-9.
465. 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.
466. Lichter PR. Practice implications of the glaucoma laser trial. *Ophthalmology* 1990; 97:1401-2.
467. 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.
468. Shingleton BJ, Richter CU, Dharma SK. Long-term efficacy of argon laser trabeculoplasty. A 10-year follow-up study. *Ophthalmology* 1993; 100:1324-9.
469. 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.
470. Wise JB. Ten year results of laser trabeculoplasty. Does the laser avoid glaucoma surgery or merely defer it? *Eye* 1987; 1:45-50.
471. Reiss GR, Wilensky JT, Higginbotham EJ. Laser trabeculoplasty. *Surv Ophthalmol* 1991; 35:407-28.

472. 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.
473. 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.
474. 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.
475. Wise JB. Glaucoma treatment by trabecular tightening with the argon laser. *Int Ophthalmol Clin* 1981; 21:69-78.
476. van Buskirk EM, Pond V, Rosenquist RC, Acott TS. Argon laser trabeculoplasty. Studies of mechanism of action. *Ophthalmology* 1984; 91:1005-10.
477. Bylsma SS, Samples JR, Acott TS, Van Burskirk EM. Trabecular cell division after argon laser trabeculoplasty. *Arch Ophthalmol* 1988; 106:544-7.
478. 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.
479. 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.
480. 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.

References 115

481. Schwartz AL, Whitten ME, Bleiman B, Martin D. Argon laser trabeculoplasty in uncontrolled phakic open-angle glaucoma. *Ophthalmology* 1981; 88:203-12.
482. Wilensky JT, Jampol LM. Laser therapy for open angle glaucoma. *Ophthalmology* 1981; 88:213-7.
483. Robin AL. Argon laser trabeculoplasty medical therapy to prevent the intraocular pressure rise associated with argon laser trabeculoplasty. *Ophthalmic Surg* 1991; 22:31-7.
484. Wilensky JT, Weinreb RN. Early and late failures of argon laser trabeculoplasty. *Arch Ophthalmol* 1983; 101:895-7.
485. Hoskins HD Jr, Hetherington J Jr, Minckler DS, et al. Complications of laser trabeculoplasty. *Ophthalmology* 1983; 90:796-9.
486. Chandler PA. Long-term results in glaucoma therapy. *Am J Ophthalmol* 1960; 49:221-46.
487. 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.
488. de Jong N, Greve EL, Hoyng PF, et al. Results of a filtering procedure in low-tension glaucoma. *Int Ophthalmol* 1989; 13:131-8.
489. Bylsma S. Nonpenetrating deep sclerectomy: collagen implant and viscocanalostomy procedures. *Int Ophthalmol Clin* 1999; 39:103-19.
490. Crandall AS. Nonpenetrating filtering procedures: viscocanalostomy and collagen wick. *Semin Ophthalmol* 1999; 14:189-95.

116 Open Angle Glaucoma

491. Mermoud A. Sinusotomy and deep sclerectomy. *Eye* 2000; 14:531-5.
492. 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.
493. Sanchez E, Schnyder CC, Sickenberg M, et al. Deep sclerotomy: results with and without collagen implant. *Int Ophthalmol* 1996-1997; 20:157-62.
494. 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.
495. Carassa RG, Bettin P, Fiori M, et al. Viscocanalostomy versus trabeculectomy: a 12 month randomized prospective trial. *Invest Ophthalmol Vis Sci* 2000; 41:S744.
496. Karlen M, Sanchez E, Schnyder CC, et al. Deep sclerectomy with collagen implant: medium term results. *Br J Ophthalmol* 1999; 83:6-11.
497. Sharir M, Zimmerman TJ. Initial treatment of glaucoma: medical therapy. *Surv Ophthalmol* 1993; 37:299-304.
498. Lichter PR, Ravin JG. Risk of sudden visual loss after glaucoma surgery. *Am J Ophthalmol* 1974; 78:1009-13.
499. Mills KB. Trabeculectomy: a retrospective long-term follow-up of 444 cases. *Br J Ophthalmol* 1981; 65:790-5.
500. D'Ermo F, Bonomi L, Doro D. A critical analysis of the long-term results of trabeculectomy. *Am J Ophthalmol* 1979; 88:829-35.

References 117

501. 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.
502. Hitchings RA, Grierson I. Clinico-pathological correlation in eyes with failed fistulizing surgery. *Trans Ophthalmol Soc UK* 1983; 103:84-8.
503. 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:S744.
504. Unlu K, Aksunger A. Descemet membrane detachment after viscocanalostomy. *Am J Ophthalmol* 2000; 130:833-4.
505. 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.
506. Tuulonen A. Laser trabeculoplasty as primary therapy in chronic open angle glaucoma. *Acta Ophthalmol (Copenh)* 1984; 62:150-5.
507. 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.
508. van Buskirk EM. The laser step in early glaucoma therapy. *Am J Ophthalmol* 1991; 112:87-90.
509. 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.

118. Open Angle Glaucoma

510. 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.
511. 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.
512. Lavin MJ, Wormald RP, Migdal CS, Hitchings RA. The influence of prior therapy on the success of trabeculectomy. *Arch Ophthalmol* 1990; 108:1543-8.
513. Migliazzo CV, Shaffer RN, Nykin R, Magee S. Long-term analysis of pigmentary dispersion syndrome and pigmentary glaucoma. *Ophthalmology* 1986; 93:1528-36.
514. Liebmann JM, Ritch R. Pigment dispersion syndrome and pigmentary glaucoma. In: Fingeret M, Lewis TL, eds. *Primary care of the glaucomas*, 2nd ed. New York, NY: McGraw-Hill, 2001:429-41.
515. Ritch R, Liebermann J, Robin A, et al. Argon laser trabeculoplasty in pigmentary glaucoma. *Ophthalmology* 1993; 100:909-13.
516. Walker JD. A suggested role for argon laser iridoplasty in management of pigmentary glaucoma. *Ophthalmic Surg* 1986; 17:762-3.
517. 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.
518. Aasved H, Seland JH, Slagsvold JE. Timolol maleate in the treatment of open-angle glaucoma. *Acta Ophthalmol (Copenh)* 1979; 57:700-8.

References 119

519. Brooks AM, Gillies WE. The presentation and prognosis of glaucoma in pseudoexfoliation of the lens capsule. *Ophthalmology* 1988; 95:271-6.
520. 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.
521. Tarkkanen A. Treatment of chronic open angle glaucoma associated with pseudoexfoliation. *Acta Ophthalmol (Copenh)* 1965; 43:514-23.
522. 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.
523. 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.
524. Olivius E, Thornburn W. Prognosis of glaucoma simplex and glaucoma capsulare: a comparative study. *Acta Ophthalmol (Copenh)* 1978; 56:921-34.
525. 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.
526. 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.
527. 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.

120 Open Angle Glaucoma

528. 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.
529. Ritch R, Liebmann JM. Exfoliation syndrome and exfoliation glaucoma. In: Fingeret M, Lewis TL, eds. *Primary care of the glaucomas*. 2nd ed. New York, NY: McGraw-Hill, 2001:443-59.
530. Jacobi PC, Kriegelstein GK. Trabecular aspiration. A new mode to treat pseudoexfoliation glaucoma. *Invest Ophthalmol Vis Sci* 1995; 36:2270-6.
531. 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.
532. 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.
533. Bloch S, Rosenthal AR, Friedman L, Caldarolla P. Patient compliance in glaucoma. *Br J Ophthalmol* 1977; 61:531-4.
534. Vincent P. Patient viewpoints of glaucoma therapy. *Sight Saving Rev (Winter)* 1973:213-21.
535. Kass MA, Gordon M, Morley RE Jr, et al. Compliance with topical timolol treatment. *Am J Ophthalmol* 1987; 103:188-93.
536. Kass MA, Meltzer DW, Gordon M, et al. Compliance with topical pilocarpine treatment. *Am J Ophthalmol* 1986; 101:515-23.
537. MacKean JM, Elkington AR. Compliance with treatment of patients with chronic open-angle glaucoma. *Br J Ophthalmol* 1983; 67:46-9.

References 121

538. Spaeth GL. Visual loss in a glaucoma clinic. I. Sociologic considerations. *Invest Ophthalmol* 1970; 9:73-82.
539. Heijl A, Lindgren G, Olsson J. Normal variability of static perimetric threshold values across the central visual field. *Arch Ophthalmol* 1987; 105:1544-9.
540. Richardson KT. Medical control of glaucomas. *Br J Ophthalmol* 1972; 56:272-7.
541. 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.
542. Rasker MT, van den Enden A, Bakker D, Hoyng PF. Rate of visual field loss in progressive glaucoma. *Arch Ophthalmol* 2000; 118:481-8.
543. Katz J, Gilbert D, Quigley HA, Sommer A. Estimating progression of visual field loss in glaucoma. *Ophthalmology* 1997; 104:1017-25.
544. Smith SD, Katz J, Quigley HA. Analysis of progressive change in automated visual fields in glaucoma. *Invest Ophthalmol Vis Sci* 1996; 37:1419-28.
545. 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.
546. Hart WM Jr, Becker B. The onset and evolution of glaucomatous visual field defects. *Ophthalmology* 1982; 89:268-79.
547. Mikelberg FS, Schulzer M, Drance SM, Lau W. The rate of progression of scotomas in glaucoma. *Am J Ophthalmol* 1986; 101:1-6.

122 Open Angle Glaucoma

546. Chumbley LC, Brubaker RF. Low-tension glaucoma. *Am J Ophthalmol* 1976; 81:761-7.
549. 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.
550. Watson PG, Grierson I. The place of trabeculectomy in the treatment of glaucoma. *Ophthalmology* 1981; 88:175-96.
551. Thomas JV, Simmons RJ, Belcher CD 3rd. Argon laser trabeculoplasty in the presurgical glaucoma patient. *Ophthalmology* 1982; 89:187-97.
552. Wickham MG, Worthen DM. Argon laser trabeculoplasty: long-term followup. *Ophthalmology* 1979; 86:495-503.
553. 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.
554. Moulin F, Haut J. Argon laser trabeculoplasty. Results over 10 years. *J Fr Ophtalmol* 1994; 17:93-8.
555. Richter CU, Shingleton BJ, Bellows AR, et al. Retreatment with argon laser trabeculoplasty. *Ophthalmology* 1987; 94:1085-9.
556. 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.
557. Kajiya S, HayaKawa K, Sawaguchi S. Clinical results of selective laser trabeculoplasty. *Jpn J Ophthalmol* 2000; 44:574-5.

References 123

558. Latina MA, Sibayan SA, Shin DH, et al. Q-switched 532NM Nd:YAG laser trabeculoplasty (selective laser trabeculoplasty): a multicenter, pilot, clinical study. *Ophthalmology* 1998; 105:2082-8.
559. Schwartz AL, Kopelman J. Four-year experience with argon laser trabecular surgery in uncontrolled open-angle glaucoma. *Ophthalmology* 1983; 90:771-80.
560. 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.
561. Safran MJ, Robin AL, Pollack IP. Argon laser trabeculoplasty in younger patients with primary open-angle glaucoma. *Am J Ophthalmol* 1984; 97:292-5.
562. Nouri-Mahdavi K, Brigatti L, Weitzman M, Caprioli J. Outcomes of trabeculectomy for primary open-angle glaucoma. *Ophthalmology* 1995; 102:1760-9.
563. Watson PG, Grierson I. Early trabeculectomy in the treatment of chronic open-angle glaucoma in relationship to histological changes. *Int Ophthalmol Clin (Fall)* 1984; 24:13-32.
564. Tornqvist G, Drolsum LK. Trabeculectomies: a long-term study. *Acta Ophthalmol (Copenh)* 1991; 69:450-4.
565. Jerndal T, Lundstrom M. 330 trabeculectomies: a long time study (3 - 5 1/2 years). *Acta Ophthalmol (Copenh)* 1980; 58:947-56.
566. Robinson DI, Lertsumitkul S, Billson FA, Robinson LP. Long-term intraocular pressure control by trabeculectomy: a ten-year life table. *Aust N Z J Ophthalmol* 1993; 21:79-85.

124 Open Angle Glaucoma

567. Inaba Z. Long-term results of trabeculectomy in Japanese: an analysis by life-table method. *Jpn J Ophthalmol* 1982; 26:361-73.
568. 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.
569. Palmer SS. Mitomycin as adjunct chemotherapy with trabeculectomy. *Ophthalmology* 1991; 98:317-21.
570. The Fluorouracil Filtering Surgery Study Group. Fluorouracil filtering surgery study one year follow-up. *Am J Ophthalmol* 1989; 108:625-35.
571. Vesti E, Raitta C. A review of the outcome of trabeculectomy in open-angle glaucoma. *Ophthalmic Surg Lasers* 1997; 28:128-32.
572. AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 4. Comparison of treatment outcomes in race. *Ophthalmology* 1998; 105:1146-64.
573. Stegmann R, Pienaar A, Miller D. Visco canalostomy for open-angle glaucoma in black African patients. *J Cataract Refract Surg* 1999; 25:316-22.
574. Jonescu-Cuyppers C, Jacobi P, Konen W, Krieglstein G. Primary visco canalostomy versus trabeculectomy in white patients with open-angle glaucoma. A randomized clinical trial. *Ophthalmology* 2001; 108:254-8.
575. Stewart WC, Sine CS, LoPresto C. Surgical versus medical management of chronic open-angle glaucoma. *Am J Ophthalmol* 1996; 122:767-74.
576. Gillies WE, Dallison IW, Brooks AM. Long-term results with argon laser trabeculoplasty. *Aust N Z J Ophthalmol* 1994; 22:39-43.

References 125

577. 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.
578. Daugeliene L, Yamamoto T, Kitazawa Y. Effect of trabeculectomy of visual field in progressive normal-tension glaucoma. *Jpn J Ophthalmol* 1998; 42:286-92.
579. 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.
580. 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.
581. Hitchings RA, Wu J, Poinosawmy D, McNaught A. Surgery for normal tension glaucoma. *Br J Ophthalmol* 1995; 79:402-6.
582. Pecori Giralardi J, De Benedetti G, Santarelli S, et al. Normal tension glaucoma: a ten-year follow-up. *Acta Ophthalmol Scand Suppl* 1997; 224:17-8.
583. 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.
584. Anderson DR, Drance SM, Schulzer M. Collaborative Normal-Tension Glaucoma Study Group. Natural history of normal-tension glaucoma. *Ophthalmology* 2001; 108:247-53.
585. Ritch R. Pigmentary glaucoma: a self-limited entity? *Ann Ophthalmol* 1983; 15:115-6.

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586. Jerndal T, Kriisa U. Results of trabeculectomy for pseudoexfoliative glaucoma. A study of 52 cases. *Br J Ophthalmol* 1974; 58:927-30.
587. Raitta C. Filtering surgery in capsular glaucoma. *Acta Ophthalmol suppl* 1988; 184:148-9.
588. Tanihara H, Negi A, Akimoto M, et al. Surgical effects of trabeculectomy ab externo on adult eyes with primary open angle glaucoma and pseudoexfoliation syndrome. *Arch Ophthalmol* 1993; 111:1653-61.
589. 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**

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- 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. Gonioscopy**
Open or closed angle
Primary or secondary glaucoma
 - 7. Assessment of Optic Nerve**
Stereoscopic evaluation through a dilated pupil
Tomography
 - 8. 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
 - 9. Assessment of Peripapillary Area**
 - 10. Fundus Stereo Photography**
Photodocumentation of optic nerve and nerve fiber layer
 - 11. 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**

Patient history and examination

Assessment and diagnosis

Initial treatment/stepwise medical therapy
Categories of drugs

- Adrenergic antagonists: beta-blockers
- Prostaglandin analogs
- Alpha-2 adrenergic agonist
- Topical carbonic anhydrase inhibitor
- Adrenergic agonists—epinephrine compounds
- Miotics
- Oral carbonic anhydrase inhibitors

Long-term management*

Schedule for periodic re-evaluation,
per Guideline

Laser therapy

Surgical therapy

- Filtering procedures
- Cyclodestructive procedures

* The 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 3
Suggested Frequency and Composition of Evaluation and Management Visits for Open Angle Glaucoma

Composition of Follow-up Evaluations

Type of Patient	Frequency of Examination	Tonometry	Gonioscopy
New glaucoma patient or new glaucoma suspect	Weekly or biweekly to achieve target pressure	Multiple readings may be necessary to establish baseline	Standard classification and drawing at initial visit
Glaucoma suspect	6-12 months, depending on level of risk	Multiple readings may be necessary to establish baseline	Annual
Stable – mild stage	4-6 months	Every visit	Annual
Stable – moderate stage	2-4 months	Every visit	Annual
Stable – severe stage	1-3 months	Every visit	6 months
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 a reassessment
Recently established stability	1-3 months	Every visit; re-establish baseline	Depends on severity of the glaucoma

Figure 3 Continued . . .

ON/NFL Assessment	Stereoscopic ON, NFL, and PPA Documentation CSLI*	Perimetry**	Management Plan
Dilate; optic nerve drawing at initial visit	As part of initial glaucoma evaluation	Repeat to establish baseline	Prepare problem list with treatment plan
Dilate every other visit	Every 2 years; CSLI Annual*	Annual	Review
Dilate every other visit	Annual	Annual	Review
Dilate every other visit	Annual	6-12 months, depending on prior data	Review
Dilate every other visit	Annual; CSLI ?*	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 interim visit	Annual or each time ON or NFL changes	Depends on severity of the disease	Review

* Confocal scanning laser imaging (CSLI) is recommended once annually in glaucoma suspect patients and those with mild to moderate disease who can respond to standard testing. CSLI may be performed up to 2 times per year for patients in whom visual fields or tonometry cannot be assessed or in patients with unstable borderline control and other glaucoma risk factors. CSLI may not be useful for monitoring stable-severe or end-stage disease.

**Threshold automated perimetry is recommended.



Figure 4

ICD-9-CM Classification of Open Angle Glaucoma

Glaucoma	365
<i>Excludes: blind hypertensive eye [absolute glaucoma] (360.42) congenital glaucoma (743.20-743.22)</i>	
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) iritidocyclitis (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
ATT	- ALT-trabeculectomy-trabeculectomy
CAI	- Carbonic anhydrase inhibitor
CCT	- Central corneal thickness
COPD	- Chronic obstructive pulmonary disease
CSLT	- Confocal scanning laser tomography
CW	- Collagen wick
dB	- Decibel
FDA	- Food and Drug Administration
FDT	- Frequency doubling technology
GLT	- Glaucoma Laser Trial
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
OH	- Ocular hypertension
ON	- Optic nerve
ONH	- Optic nerve head
PDS	- Pigmentary dispersion syndrome
PEG	- Pseudoexfoliation glaucoma
PES	- Pseudoexfoliation syndrome
PG	- Pigmentary glaucoma
POAG	- Primary open angle glaucoma
PPA	- Peripapillary area
SWAP	- Short-wavelength automated perimetry
TAT	- Trabeculectomy-ALT-trabeculectomy
TIGR	- Trabecular meshwork-induced glucocorticoid response protein
VC	- Visco canalostomy
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, that is 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.

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 extraocular 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, 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.

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

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 retroental 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 that is located between the canal of Schlemm and the anterior chamber which is 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.

