

**GLAUCOMA ALGORITHM
AND
GUIDELINES FOR GLAUCOMA**

SOUTH AFRICAN GLAUCOMA SOCIETY 2016

GLAUCOMA ALGORITHM AND GUIDELINE FOR GLAUCOMA

The South African Glaucoma Society (SAGS), which is affiliated to the Ophthalmological Society of South Africa, would like to present the updated treatment algorithm and guidelines for glaucoma to the Council for Medical Schemes and other Regulatory Bodies to improve the mutual understanding of glaucoma, in addition to providing a rational approach to the diagnosis and management of glaucoma based on evidence from prospective Randomized Clinical Trials (RCT's).

The document has been endorsed by the Ophthalmological Society of South Africa.

Glaucoma is the only eye disease classified as a chronic disease, amongst the legislated 25 chronic disease conditions. It is important, since it is one of the leading causes of blindness in South Africa and as such deserves adequate, up to date management. The prevalence of glaucoma is around 5 to 7% in the black population and 3% to 5% in the white population of South Africa. It thus has a major impact on the visual health of our nation. With proper treatment the quality of vision and of life can be maintained, but inadequate treatment can lead to blindness and the resultant socio-economic burden to the State.

These guidelines for glaucoma present the view of the South African Glaucoma Society and are in line with other International Glaucoma Societies Guidelines (EGS 2014). They include the classification and definition of glaucoma, an algorithm, initial patient examination tests, patient follow up examination tests, terminology, and references based on reviews of publications.

Clinical care must be individualised for the patient, the treating Ophthalmologist and the socioeconomic milieu. The availability of Randomized Controlled Trials (RCT's) makes it possible to apply scientific evidence to clinical recommendations. Economical factors must be considered by physicians, in order to provide sustainable healthcare.

The South African Glaucoma Society disclaims responsibility for any adverse medical or legal effects resulting directly or indirectly from the use of any definitions, diagnostic techniques or treatments described in the Guidelines. The SAGS does not endorse any product, procedure, company or organisation.

MISSION STATEMENT

The goal of glaucoma treatment is to maintain the patient's visual function and related quality of life, at a sustainable cost. The cost of treatment in terms of inconvenience and side effects as well as financial implications for the individual and society requires careful evaluation. Quality of life is closely linked with visual function. Patients with early to moderate glaucoma damage have good visual function and a modest reduction in quality of life, while quality of life is considered reduced if both eyes have advanced visual function loss.

COST EFFECTIVENESS OF GLAUCOMA CARE

Treatment of Glaucoma and Ocular Hypertension (OHT) in Preventing Visual Disability

There is high- level evidence that treatment (including medical, laser and surgical treatment) decreases intraocular pressure and reduces the risk of development (in patients with OHT) and deterioration (in patients with established glaucoma) of optic nerve damage and visual field loss compared to no treatment. However, the direct effects of treatments on visual impairment and the comparative efficacy of different treatments are not clear. Which treatments improve patient- reported outcomes is also unclear. Based on the economic simulation models in US, UK, Holland and China, treating glaucoma appears to be cost effective compared to “no treatment”. There is uncertainty whether to treat none, some, or all patients with ocular hypertension.

When treated, the cost effectiveness models of different therapeutic interventions give variable results.

Follow –Up Protocols and Models of Care

There is no solid evidence of the optimum monitoring schemes (e.g., frequency and timing of visits, technologies used for detecting progression) for patients with manifest glaucoma and ocular hypertension. Some modelling and retrospective studies suggest that more treatment may allow less frequent monitoring visits in ocular hypertension and stable glaucoma. One RCT suggests that shared care may save costs.

I. CLASSIFICATION AND TERMINOLOGY

- 1) Primary congenital forms/ childhood glaucoma
- 2) Primary open-angle glaucoma
- 3) Secondary glaucoma
- 4) Primary Angle- Closure
- 5) Secondary Angle- Closure

PRIMARY CONGENITAL FORMS / CHILDHOOD GLAUCOMAS

Primary congenital glaucoma is a rare disease but has a major impact on the child's development and quality of life over his/ her whole life span. Early diagnosis and appropriate therapy can make a huge difference in the visual outcome and can prevent lifelong disability. Surgical treatment is always necessary.

The treatment of paediatric glaucoma cases is particularly challenging due to the nature of the disease and to the intrinsic difficulties in operating on and in examining patients of this age. Treatment is to be adapted to the primary anomaly and the mechanism of IOP evaluation. Whenever possible, these cases should be referred to Tertiary centres.

PRIMARY OPEN- ANGLE GLAUCOMAS (POAG)

The open- angle glaucomas are chronic, progressive optic neuropathies that have in common characteristic morphological changes at the nerve head and retinal fibre layer in the absence of other ocular disease or congenital anomalies. Progressive retinal ganglion cell death and visual field loss are associated with these changes.

Epidemiology

Glaucoma is the second leading cause of blindness worldwide. It is the most frequent cause of irreversible blindness. POAG is unusual under the age of 50 years. Its prevalence increases with age. However, the reported percentage largely depends on definition.

RISK FACTORS FOR THE DEVELOPMENT OF OAG

a) Age

Cross- sectional population- based studies have consistently reported that the prevalence of OAG increases dramatically with age. Longitudinal population- based studies have confirmed that older age is an important risk factor for OAG. Two studies reported a 6% and 4% increase risk per year of age at baseline – developing OAG.

b) Intraocular pressure (IOP)

Higher IOP have been consistently associated with the prevalence and incidence of OAG. According to longitudinal data, OAG increases by 11% - 12% in Caucasians, 10% of people of African origin and 18%

Latinos, for each mm Hg increase in IOP is the only modifiable risk factor for OAG.

c) Race/ ethnicity

The prevalence of glaucoma is several time higher in Americans than in Caucasians.

d) Family history of glaucoma

Individuals with a family history of glaucoma have between 6 and 9 times the likelihood of developing glaucoma.

e) Central corneal thickness

In two populations based studies, there was a 41% and 30% increased risk of development of OAG per 40 micro thinner CCT.

f) Myopia

Several cross- sectional based studies identified moderate to high myopia (greater than -3 Diopters) as a factor associated with increased OAG prevalence.

g) Ocular perfusion pressure

The association of low ocular perfusion with increased OAG prevalence has been a consistent finding in population based studies. Recent evidence suggests that this association may depend on whether subjects are treated for systemic hypertension or not. A phenotype characterized by vascular dysregulation has been described. The Barbados Eye Study confirmed that low perfusion pressure increases the risk for the development of OAG. Because of our limited understanding of this complex variable and of its interaction with potential risk factors for glaucoma, the exact place of ocular perfusion pressure management remains unclear.

PRIMARY OPEN-ANGLE GLAUCOMA SUSPECT

Features

The visual field and/ or optic disc and/ or fibre layer are normal or suspicious with at least one being suspicious. The IOP can be normal or increased.

Treatment

Risks and benefits of treatment need to be weighed against the risk of the development of glaucomatous disc damage. The risk of developing glaucoma increases with the number and strength of risk factors.

Ocular Hypertension (OH)

Features

The IOP is > 21 mm HG without treatment and visual field normal. Optic disc and retinal nerve fibre layer normal. Gonioscopy: open anterior angle (exclude intermittent angle closure). No history or signs of other eye disease or steroid use.

Treatment:

Although in the past it has been used as a diagnosis, Ocular Hypertension should be used to indicate that the IOP is consistently outside 2 or 3 standard deviations above the mean. A modest increase in IOP is not sufficient reason for treatment, but consider it in patients with repeated IOPs in the high twenties, even without risk factors.

If left untreated, 9.5% develop glaucoma over five years of follow-up. The risk increases with increasing IOP. Each patient should be assessed individually when deciding whether or not to treat.

SECONDARY GLAUCOMAS

Secondary glaucomas are a heterogeneous group of conditions in which elevated IOP is the leading pathological factor causing glaucomatous optic neuropathy. Most forms of secondary glaucoma like uveitic or traumatic glaucoma have complex pathomechanisms including both open or closed angle.

Secondary Open- Angle Glaucoma can be caused by Ocular disease like Exfoliative (Pseudoexfoliative) glaucoma, Pigmentary Glaucoma, Lens- induced Glaucoma, Glaucoma associated with intraocular haemorrhage, uveitic glaucoma, neovascular glaucoma, glaucoma due to ocular trauma, glaucoma due to steroid treatment.

Treatment

- a) Treatment of the underlying disease
- b) Topical and systemic IOP lowering medication
- c) Glaucoma surgery

PRIMARY ANGLE-CLOSURE GLAUCOMA

Scientific publications on angle- closure have suffered from the lack of uniform definition and specific diagnostic criteria. Only in recent years has there been recognition of the need to standardize the definitions of various types.

Angle-closure is defined by the presence of irido-trabecular contact (ITC). This can be either appositional or synechial. Either can be due to any one of a number of possible mechanisms. Angle closure may result in raised IOP and cause structural changes in the eye. Primary angle-closure (PAC) is defined as an occludable drainage angle and features indicating that trabecular obstruction by the peripheral iris has occurred. The term glaucoma is added if glaucomatous optic neuropathy is present: Primary angle-closure glaucoma (PACG). The main reason to distinguish Primary angle-closure glaucoma from Primary open-angle glaucoma is the therapeutic approach (i.e iridectomy) and the possible late complications (synechial closure of the chamber angle) or the complications resulting when this type of glaucoma undergoes filtering surgery (uveal effusion, cilio- lenticular block leading to malignant glaucoma).

SECONDARY ANGLE CLOSURE

There are many different causes of secondary angle-closure and the clinical signs vary according to the underlying condition. For example, in secondary acute angle- closure, the chamber angle is closed by iridotrabecular contact that can be reversed, whereas in chronic secondary angle-closure, the angle-closure is irreversible due to peripheral anterior synechiae. Secondary Angle- closure can occur e.g., with pupillary block, uveitic glaucoma, neovascular glaucoma, iridocorneal endothelial syndrome or aqueous misdirection.

II. TREATMENT PRINCIPLES AND OPTIONS

The goal of glaucoma treatment is to maintain the patient's visual function and related quality of life, at a sustainable cost. The cost of treatment in terms of inconvenience and side effects as well as financial implications for the individual and society requires careful evaluation. Quality of life is closely linked with visual function and, overall, patients with early to moderate glaucoma damage have good visual function and modest reduction in quality of life. Quality of life is considerably reduced if both eyes have advanced visual function loss.

Individualised glaucoma treatment aims at providing glaucoma management tailored to the individual needs of the patient; patients with severe functional loss or younger patients with manifest disease should have more aggressive treatment and closer follow-up than patients with little or no risk of visual loss, e.g., patients with ocular hypertension or elderly patients with mild field loss and low IOP levels.

Primary Open Angle Glaucoma is treated by reducing intraocular pressure using medication, laser or incisional surgery. So far, there is no evidence for other suggested treatment modalities, e.g., neuroprotection or modifying blood flow.

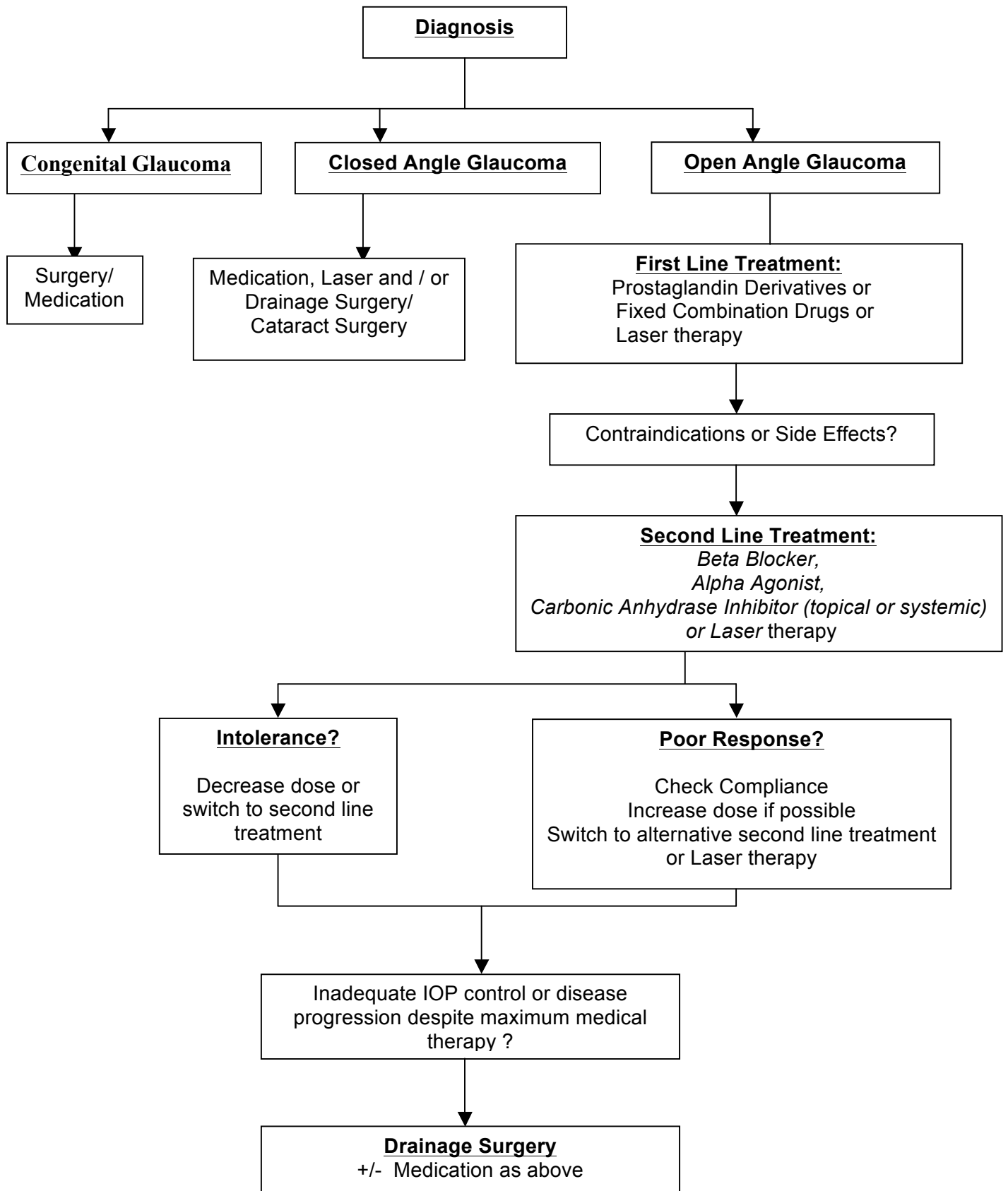
In most western countries, approximately half of the patients with manifest glaucoma are undiagnosed.

TARGET IOP AND QUALITY OF LIFE

Therapy in glaucoma management aims to lower IOP to slow the rate of visual field deterioration. Target IOP is the upper limit of the IOP estimated to be compatible with slowing the rate of progression sufficiently slow to maintain vision-related quality of life in the expected lifetime of the patient. It should be evaluated regularly and, additionally, when progression of disease is identified or when ocular or systemic co-morbidities develop.

There is no single Target IOP level that is appropriate for every patient, so the Target IOP needs to be estimated separately for each eye of every patient.

III GLAUCOMA ALGORITHM



GLAUCOMA DIAGNOSIS AND MANAGEMENT

INITIAL DIAGNOSIS: First Visit, New Patients, Baseline Tests in adequately equipped Ophthalmology practice setting

- Lengthy initial consultation to elicit complete medical and surgical history and ascertain relevant risk factors
- Comprehensive clinical examination including slitlamp examination, tonometry, fundus and optic nerve head examination, gonioscopy, corneal thickness
- Special investigations to document the extent of structural damage to the optic nerve head and the retinal nerve fibre layer: optic nerve and retinal nerve fibre layer analysis or disc photography, computer assisted visual field analysis (OCT, GDx, HRT)
- Comprehensive discussion and information session to inform patient type of glaucoma, disease prognosis and implications, treatment options, importance of treatment compliance, and to answer patient questions from patients.

CONTROLLED PATIENTS: Follow Up and Management

- Patients should be seen 3 times per year. The first follow up visit within two months after diagnosis to ascertain IOP control / target pressure
- At each visit the following should be performed:
 1. History of possible side effects, drug efficacy, compliance, additional medical history
 2. Comprehensive clinical examination including slitlamp examination, tonometry, optic nerve head examination and gonioscopy.
- Special examinations must be repeated annually:
 1. Structural assessment of the optic disc and/or RNFL by disc photography, HRT, GDx or OCT alone or in combination
 2. If any interim corneal surgery is done repeat the central corneal thickness measurement.

UNCONTROLLED PATIENTS: Follow up and Management

- Patients may need to be seen up to 6 times per year
- At each visit the following should be performed:
 1. History of possible side effects, drug efficacy, compliance, additional medical history
 2. Comprehensive clinical examination including slitlamp examination, tonometry, optic nerve head examination and gonioscopy.
- Special examinations must be repeated annually:
 1. Structural assessment of the optic disc and/ or RNFL by disc photography, HRT ,GDx or OCT alone, or in combination.
 2. In any interim corneal surgery is done repeat the central corneal thickness measurement.

GLAUCOMA DIAGNOSIS AND MANAGEMENT

COMPLICATED PATIENTS: Follow up and Management

- Patients must be seen up to 6 times per year
- At each visit the following should be performed:
 1. History of possible side effects, drug efficacy, compliance, additional medical history
 2. Comprehensive clinical examination including slitlamp examination, tonometry, optic nerve head examination and gonioscopy
- Special examinations must be repeated annually:
 1. Structural assessment of the optic disc and/ or RNFL by disc photography, HRT, GDx or OCT alone, or in combination.
 2. If any interim corneal surgery repeat central corneal thickness measurement

CONGENITAL GLAUCOMA PATIENTS: Follow up and Management

- As above, but includes regular examinations under anaesthesia, 2 to 6 times per year until adequate intraocular pressure control is achieved.

GLAUCOMA TERMINOLOGY

1. COMPLIANCE:

Since glaucoma is a long-standing, progressive disease, requiring regular topical medication and regular follow-up appointments, a patient's continuous co-operation is essential for successful management. Compliance is influenced by the frequency of drop instillation, drug side effects, cost of medication and the lack of understanding of the disease.

2. FIRST LINE DRUGS :

First line drugs such as prostaglandin derivatives or fixed combination drugs are drugs approved by the South African Glaucoma Society according to evidence-based data for efficient initial intraocular pressure lowering therapy.

3. FIXED COMBINATION DRUGS:

Fixed combination anti-glaucoma drugs contain two different drugs with better compliance, fewer bottles and drops need to be used, less toxicity by preservatives, no washout effect on an adjunctive drug, and, reduced administration time.

4. INTRAOCULAR PRESSURE (IOP) :

The 'normal' IOP is a statistical description of the range of IOP in the population with a peak at 15 mm Hg. The IOP follows a circadian cycle often with a maximum between 8am and 11am and a minimum between midnight and 2 am. The diurnal variation can be between 3mm and 5 mm Hg and is wider in untreated glaucoma. It is important to establish the diurnal variation to adjust treatment accordingly and to prevent wide diurnal IOP fluctuation on glaucoma treatment because this leads to glaucoma progression.

The most frequently used instrument to measure IOP is the Goldmann Applanation Tonometer. The central corneal thickness influences the above measurement and has to be measured once with every new glaucoma patient and repeated after any form of corneal surgery.

5. SECOND LINE TREATMENT

Drugs such as beta-blockers, alpha-agonists, carbonic-anhydrase inhibitors and miotics, are used in addition to or instead of, first line drugs when the target pressure has not been achieved.

6. TARGET PRESSURE (TP)

A target pressure is an estimate of the mean IOP obtained, which is expected to prevent further glaucomatous damage. The goal is to achieve the therapeutic response with the least amount of medication and side effects.

7. QUALITY OF LIFE (QoL)

The quality of life of glaucoma patients is affected by functional visual loss, inconvenience and side effects of medication, cost of treatment and the fear of blindness from the disease.

GLAUCOMA CODES

Initial Diagnosis:

- 0190 Consultation
- 3009 Basic Capital Equipment
- 3014 Tonometry
- 3003 Fundus Examination with Diagnostic Lens
- 3002 Gonioscopy
- 3026 Disc and Nerve Fibre Layer Analysis or
- 3027 Disc Photography
- 3028 Optical Coherence Tomography (OCT)
- 3017 or 3016 Computer Assisted Visual Field Analysis
- 3020 Central Corneal Thickness Measurement

Follow Up and Maintenance Tests

- 0190 Consultation x 3 per year
- 3009 Basic Capital Equipment x 3 per year
- 3014 Tonometry x 3 per year
- 3003 Fundus Examination with Diagnostic Lens x 3 per year
- 3002 Gonioscopy x 3 per year
- 3026 Disc and Nerve Fibre Layer Analysis x 1 per year or
- 3027 Disc Photography x 1 per year
- 3028 Optical Coherence Tomography (OCT)
- 3017 or 3016 Computer Assisted Visual Field Analysis x 2 per year
- 3018 Retinal Threshold Trend Evaluation x 1 per year
- 3020 After any corneal surgical intervention: repeat Central Corneal Thickness Measurement

Management of Uncontrolled and Complicated Patients

- 0190 Consultation x 6 per year
- 3009 Basic Capital Equipment x 6 per year
- 3014 Tonometry x 6 per year
- 3003 Fundus Examination with Diagnostic Lens x 6 per year
- 3002 Gonioscopy x 6 per year
- 3026 Disc and Nerve Fibre Layer Analysis x 2 per year or
- 3027 Disc Photography x 2 per year
- 3028 Optical Coherence Tomography (OCT) yearly
- 3017 or 3016 Computer Assisted Visual Field Analysis x 3 per year
- 3020 After any corneal surgical intervention: repeat Central Corneal Thickness Measurement

*If more than 6 examinations per year are asked for, the Ophthalmologist needs authorization from a Glaucoma Expert.

GLAUCOMA CODES

Management of Post Operative Glaucoma Patients

3021 Retinal function including refraction after ocular surgery x 2

Management of Congenital Glaucoma Patients

3080 Examination under anaesthesia 4 x per year

Glaucoma Surgery Codes

3061 Drainage Procedure
 3062 Implantation of Aqueous Shunt Device
 3063 Cyclocryotherapy or Cyclolaser
 3064 Laser Trabeculoplasty + 3201 Laser Hire Fee
 3065 Removal of Blood from Anterior Chamber
 3067 Goniotomy
 3149 Iridotomy or Iridectomy Surgical
 3153 Laser Iridectomy or Iridotomy +3201 Laser Hire Fee
 3157 Division Anterior Synechiae
 3158 Repair of Iris Dialysis and Anterior Chamber Reconstruction
 3199 Repair of Conjunctiva by Grafting
 3196 Use of Own Diamond Knife

Material Used With Glaucoma Surgery

Mitomycin C
 5 Fluoro-Uracil
 Visco Elastics
 Various Drainage Devices (see SAGS Glaucoma Drainage Device Document)

ICD10 Codes

Glaucoma	H40
Glaucoma suspect	H40.0
Primary open-angle glaucoma	H40.1
Primary angle-closure glaucoma	H40.2
Glaucoma secondary to eye trauma	H40.3
Glaucoma secondary to eye inflammation	H40.4
Glaucoma secondary to other eye disorders	H40.5
Glaucoma secondary to drugs	H40.6
Other glaucoma	H40.7
Glaucoma, unspecified	H40.8
Congenital glaucoma	Q15.0

References

- 1) American Academy of Ophthalmology. Preferred Practice Patterns for Glaucoma. www.aaopt.org.
- 2) European Glaucoma Society (EGS). Terminology and Guidelines for Glaucoma. www.eugso.org
- 3) Japan Glaucoma Society. Guidelines for Glaucoma. www.ryokunaisho.jp
- 4) The Ocular Hypertension Treatment Study. A randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of POAG. Arch Ophthalmol 2002;120:701-703.
- 5) Feuer WJ Parrish RK, Shiffman JC et al. The Ocular Hypertension Treatment Study: Reproducibility of cup/disc ratio measurements over time at an optic disc reading centre. Am J Ophthalmol 2002;133:19-28.
- 6) Gordon MO, Beiser JA, Brandt JD, Heuer DK, Higginbotham E, Johnson C, Keltner J, Miller PJ, Parrish RK, Wilson RM, Kass MA, for the Ocular Hypertension Treatment Study. The Ocular Hypertension Treatment Study. Baseline factors that predict the onset of primary open angle glaucoma. Arch Ophthalmol 2002;120:714-720.
- 7) Brand JD, Beiser JA, Kass MA, Gordon MO, for the Ocular Hypertension Treatment Study (OHTS) Group. Central corneal thickness in the Ocular Hypertension Treatment Study (OHTS). Ophthalmology 2001;108:1779-1788.
- 8) Lichter PR, Musch DC, Gillespie BW, Guire KE, Janz NK, Wren PA, Mills RP and the CIGTS Study Group Interim Clinical Outcomes in the Collaborative Initial Glaucoma Treatment Study comparing initial treatment randomized to medication or surgery. Ophthalmology 2001;108:1943-1953.
- 9) Schultzer M. Errors in the diagnosis of visual field progression in normal tension glaucoma. Ophthalmology 1994;101: 1589-1594.
- 10) Comparison of glaucomatous progression between untreated patients with normal-tension glaucoma and patients with therapeutically reduced intraocular pressures. Collaborative Normal Tension Glaucoma Study Group. Am J Ophthalmology 1998; 126: 487 - 497.
- 11) The effectiveness of intraocular pressure reduction in the treatment of normal tension glaucoma. Collaborative Normal Tension Glaucoma Study Group. Am J Ophthalmol 1998;126: 498-505.
- 12) The AGIS Investigators: The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. Am J Ophthalmol. 2000;130:429-440.
- 13) The AGIS Investigators. The Advanced Glaucoma Intervention Study (AGIS): 4. Comparison of treatment outcomes within race. Ophthalmology 1998;105:1146-1164.

References

- 14) The AGIS Investigators: The Advanced Glaucoma Intervention Study, 6: Effect of cataract on visual field and visual acuity. *Arch Ophthalmol.* 2000;118:1639-1652
- 15) The AGIS Investigators: The Advanced Glaucoma Intervention Study, 8: Risk of cataract formation after trabeculectomy. *Arch Ophthalmol* 2001;119:1774-1780.
- 16) The AGIS Investigators: The Advanced Glaucoma Intervention Study (AGIS): 9. Comparison of glaucoma outcomes in black and white patients within the treatment groups. *Am J Ophthalmol* 2001;132:311-320.
- 17) Leske MC, Heijl A, Hyman L, Bengtsson B. Early Manifest Glaucoma Trial: design and baseline data. *Ophthalmology* 1999; 106:2144-2153.
- 18) Heijl A, Leske MC, Bengtsson B, Hyman L, Hussein M. Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression. Results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2002;120:1268-1279.
- 19) Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Konaroff E., for the Early Manifest Glaucoma Trial Group. Factors for glaucoma progression and the effect of treatment. The Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2003;121:48-56.
- 17) Pillunat LE, Stodtmeister R, Marquardt R, Mattern A. Ocular perfusion pressures in different types of glaucoma. *Int Ophthalmol* 1989;13:37-42.
- 18) Nicolea MT, Walman BE, Buckley AR, Drance SM. Ocular hypertension and primary open angle glaucoma: a comparative study of their retrobulbar blood flow velocity. *J. Glaucoma* 1996;5:308-310.
- 19) Drance SM. Some factors in the production of low tension glaucoma. *Br J Ophthalmol* 1972 56(3):229-242.
- 20) Fechtner R, Weinreb R. Mechanisms of optic nerve damage in primary open angle glaucoma. *Surv Ophthalmol* 1994;39:23-42.
- 21) Flammer J, Orgul S, Costa VP, Orzalesi N, Kriegelstein GK, Serra LM, Renard JP, Steffansson E. The impact of ocular blood flow in glaucoma. *Prog. Retin Eye Res* 2002;21:359-393.
- 22) Sampaolesi R. Corneal diameter and axial length in congenital glaucoma. *Can J Ophthalmol* 1988;2:42-44.

References

- 23) Lowe RF, Ritch R. Angle closure glaucoma. Mechanisms and epidemiology. In: Ritch R, Shields MB, Krupin T. The Glaucomas. St. Louis, Mosby, 1996;37:801-820.
- 24) Traverso CE. Angle closure glaucoma. In: Duker JS and Yanoff M (eds). Ophthalmology. St. Louis, Mosby 2002:ch. 12.13.
- 25) Oliver JE, Hattenhauer MG, Herman D et al. Blindness and Glaucoma: A comparison of patients progressing to blindness from glaucoma with patients maintaining vision. Am J Ophthalmology. June 2002;133(6):764-772.
- 26) O'Connor DJ, et al. Additive intraocular pressure lowering effects of various medications with latanoprost. Am J Ophthalmology 2002;133:836-837.
- 27) Dubiner H. Travatan administration results ineffective diurnal reduction in intraocular pressure over 36 hours and lower pressures up to 3.5 days without further dosing. Presented at the 2002 ARVO Meeting, May 2002; Fort Lauderdale, Florida.

References Recommending Prostaglandins as First Line Therapy

1. Laibovitz RA, Van Denburgh AM, Felix C, David R, Batoosingh A, Rosenthal A, Cheetham J. Comparison of the ocular hypotensive lipid AGN 192024 with timolol. Arch Ophthalmol 01;119(7):994-1000.
2. DuBiner H, Cooke D, Dirks M, Stewart WC, Van Denburgh AM, Felix C. Efficacy and safety of bimatoprost in patients with elevated intraocular pressure: A 30-day comparison with latanoprost. Surv Ophthalmol 2001;45(Suppl 4):S353-S360.
3. Gandolfi S, Simmons ST, Sturm R, Chen K, Van Denburgh AM. Three-month comparison of bimatoprost and latanoprost in patients with glaucoma and ocular hypertension. Adv Ther 2001;18(3):110-121. A randomized clinical trial comparing the intraocular pressure-lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. Am J Ophthalmol 2003;135(1):55-63.
- 4) Noecker RS, Dierks MS, Choplin NT, Bernstein P, Batoosingh AL, Whitcup SM. A six month randomized clinical trial comparing the intraocular pressure-lowering efficacy of bimatoprost and latanoprost in patients with ocular hypertension or glaucoma. Am J Ophthalmol 2003;135 (1) 55-63

References

5. Parrish RK, Palmberg P, Sheu W-P. A comparison of latanoprost, bimatoprost, and travoprost in patients with elevated intraocular pressure: A 12-week randomized, masked, masked-evaluator multicentre study. *Am J Ophthalmol* 2003;135(5):688-703.
6. Sharif NA, Crider JY, Husain S, Kaddour-Djebbar I, Ansari HR, Abdel-Latif AA. Human ciliary muscle cell responses to FP-class prostaglandin analogs: phosphoinositide hydrolysis, intracellular Ca²⁺ mobilization and MAP kinase activation. *J Ocul Pharmacol Ther* 2003;19(5):437-455.
7. Sharif NA, Kelly CR, Crider JY. Human trabecular meshwork cell responses induced by bimatoprost, travoprost, unoprostone, and other FP prostaglandin receptor agonist analogues. *Invest Ophthalmol Vis Sci* 2003;44(2):715-721.
8. Sharif NA, Kelly CR, Crider JY, Williams GW, Xu SX. Ocular hypotensive FP prostaglandin (PG) analogs: PG receptor subtype binding affinities and selectivities, and agonist potencies at FP and other PG receptors in cultured cells. *J Ocul Pharmacol Ther* 2003;19(6):501-515
9. Woodward DF, Phelps RL, Krauss AH-P, Weber A, Short B, Chen J, Liang Y, Wheeler LA. Bimatoprost: a novel antiglaucoma agent. *Cardiovasc Drug Rev* 2004;22(2):103-120.
10. Richter M, Krauss AH-P, Woodward DF, Lütjen-Drecoll E. Morphological changes in the anterior eye segment after long-term treatment with different receptor selective prostaglandin agonists and a prostamide. *Invest Ophthalmol Vis Sci* 2003;44(10):4419-4426.
11. Christiansen GA, Nau CB, McLaren JW, Johnson DH. Mechanism of ocular hypotensive action of bimatoprost (Lumigan) in patients with ocular hypertension or glaucoma. *Ophthalmology* 2004;111(9):1658-1662.
12. Matias I & Chen J, De Petrocellis L, Bisogno T, Ligresti A, Fezza F, Krauss AH-P, Shi L, Protzman CE, Li C, Liang Y, Nieves AL, Kedzie KM, Burk RM, Di Marzo V, Woodward DF. Prostaglandin ethanalamides (prostamides): in vitro pharmacology and metabolism. *J Pharmacol Exp Ther* 2004;309(2):745-757.
13. Chen J, Senior J, Marshall K, Abbas F, Dinh H, Dinh T, Wheeler LA, Woodward DF. Studies using isolated uterine and other preparations show bimatoprost and prostanoid FP agonists have different activity profiles. *Br J Pharmacol*. In press.

References continued

14. Spada CS, Krauss AH-P, Woodward DF, Chen J, Protzman CE, Nieves AL, Wheeler LA, Scott DF, Sachs G. Bimatoprost and prostaglandin F2a selectively stimulate intracellular calcium signaling in different cat iris sphincter cells. *Exp Eye Res* 2005;80:135-145.
15. Williams RD. Efficacy of bimatoprost in glaucoma and ocular hypertension unresponsive to latanoprost. *Adv Ther* 2002;19(6):275-281.
16. Gandolfi SA, Cimino L. Effect of bimatoprost on patients with primary open-angle glaucoma or ocular hypertension who are non responders to latanoprost. *Ophthalmology* 2003;110(3):609-614.

References Relevant to Fixed Combination Glaucoma Drugs

1. Honrubia FM, Larsson LI, Spiegel D. (2002). A comparison of the effects on intraocular pressure of latanoprost 0.005% and the fixed combination of dorzolamide 2% and timolol 0.5% in patients with open-angle glaucoma. *Acta Ophthalmologica Scandinavica* 80(6):635-641.
2. Dong Shin et al. The Efficacy and Safety of Fixed Combinations Latanoprost/Timolol versus Dorzoamide/Timolol in patients with elevated intraocular pressure. *Ophthalmology* Vol. 111 No 2 February 2002.
3. A Konstas et al. The 24 hr Diurnal Curve Comparison of Commercially available Latanoprost 0.05% versus Dorzolamide and Timolol Fixed Combination. *Ophthalmology* 2003; Vol.110:1357-1360.

