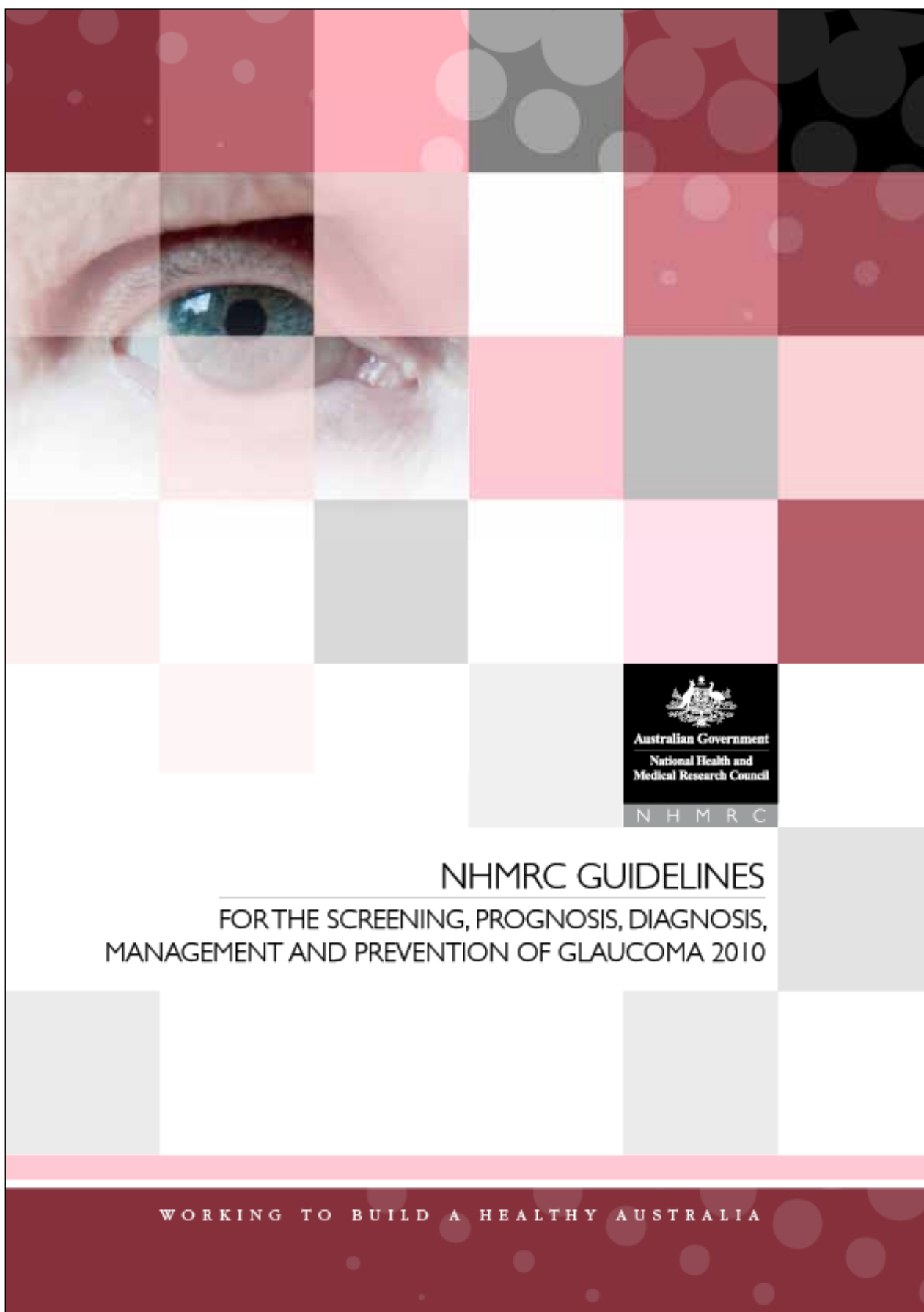




NHMRC GUIDELINES

FOR THE SCREENING, PROGNOSIS, DIAGNOSIS, MANAGEMENT AND PREVENTION OF GLAUCOMA 2010



NHMRC GUIDELINES
FOR THE SCREENING, PROGNOSIS, DIAGNOSIS,
MANAGEMENT AND PREVENTION OF GLAUCOMA 2010

WORKING TO BUILD A HEALTHY AUSTRALIA

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ISBN Print: 1864965169

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ISBN Online: 186496510x

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■ Abbreviations

AACC	Acute angle closure crisis
AAO	American Academy of Ophthalmology
AC	Angle closure
ACG	Angle closure glaucoma
ADEC	Australian Drug Evaluation Committee
AGIS	Advanced Glaucoma Intervention Study
AGREE	Appraisal of Guidelines Research and Evaluation
AOA	American Optometric Association
CAHE	Centre for Allied Health Evidence
CASP	Critical appraisal skills programme
CI	Confidence interval
CCT	Central corneal thickness
CNTGS	Collaborative Normal Tension Glaucoma Study
dB	Decibel
EGS	European Glaucoma Society
EMGTT	Early Manifest Glaucoma Treatment Trial
GLIA	Guideline Implementability Appraisal
GLT	Glaucoma Laser Trial
JGS	Japanese Glaucoma Society
IOP	Intraocular pressure
MD	Mean deviation
mmHg	Millimetres of mercury
NHMRC	National Health and Medical Research Council (Australia)
NHS	National Health Service (UK)
nm	Nanometre
NTG	Normal tension glaucoma
OAG	Open angle glaucoma
OH	Ocular hypertension
OHTS	Ocular Hypertension Treatment Study
OR	Odds ratio
PAC	Primary angle closure
PACG	Primary angle closure glaucoma
POAG	Primary open angle glaucoma
RR	Relative risk
RCO	Royal College of Ophthalmologists
SAGS	South African Glaucoma Society
SEAGIG	South East Asia Glaucoma Interest Group
SITA	Swedish interactive threshold algorithm
SMOH	Singapore Ministry of Health
UK	United Kingdom
VF	Visual field



■ Key guideline sources

American Academy of Ophthalmology [AAO] (2005a): *Primary angle closure preferred practice pattern*. San Francisco: American Academy of Ophthalmology.

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■ Glossary of terms

Afferent pupillary defect	A defect of the pupillary reflex characterised 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.
African	The literature variably refers to the increased risk of glaucoma occurring in people of African descent. This refers to people who trace their ancestry to Africa, whether this be African-Americans, African-Caribbeans, East Africans, Sub-Saharan Africans or West Africans.
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.
Argon laser trabeculoplasty	Light stimulation of the trabecular meshwork of the angle of the anterior chamber by an argon laser beam to facilitate aqueous humor outflow.
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: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	Glaucoma describes a group of eye diseases in which there is progressive damage to the optic nerve characterised by specific structural abnormalities of optic nerve head and associated patterns of visual field loss.

Glaucoma suspect	A person suspected of having glaucoma has some but not all of the criteria required for a glaucoma diagnosis. They may have one or more of the following: suspicious optic disc, optic disc margin haemorrhage, occludable drainage angle, peripheral anterior synechiae or elevated intraocular pressure.
Gonioscopy	A diagnostic procedure to examine the angle of the anterior chamber in which a specialised corneal contact lens and a biomicroscope are used.
Health care provider	Any member of the glaucoma team who provides input into the patient's glaucoma journey. Health care providers involved with glaucoma in Australia may include, but are not limited to, ophthalmologists, general medical practitioners, optometrists, ophthalmic nurses and orthoptists.
Intraocular pressure	The pressure within the eye due to the balance between the 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 primary open angle glaucoma found both extraocular and in the trabecular meshwork, optic nerve, retina, cornea, iris, ciliary body, and sclera.
Myopia	A vision condition in which close objects are seen clearly, but objects farther away appear blurred.
Nerve fibre 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 localising disturbances in the visual pathway.
Peripapillary area	Tissue surrounding the optic nerve head.
Polygenic	The traits or diseases caused by the impact of many genes, each with a small additive effect on phenotype.
Posterior chamber	The space in the eye delimited by the posterior surface of the iris, the ciliary processes, and the valleys between them, the zonule of Zinn, and the anterior surface of the crystalline lens. It includes the canal of Hanover, the canal of Petit, and the retrolental space of Berger.
Puncta	Puncta are tiny openings along the eyelid margin through which tears drain.



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	Blockage of the movement of aqueous from the anterior to the posterior chamber leading to a concave anatomical configuration of the peripheral iris.
Selective laser trabeculoplasty	Use of a q-switched Nd:YAG laser to target trabecular meshwork endothelial cells without provoking coagulative necrosis, to improve aqueous outflow.
Short-wavelength automated perimetry	A form of automated perimetry that isolates the blue cone mechanism of the visual system by utilising a two-colour 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, and which is involved in drainage of aqueous humor from the eye.
Trabeculectomy	Surgical creation of a fistula to allow aqueous outflow from the anterior chamber to the subconjunctival tissue space, bypassing the trabecular meshwork/Canal of Schlemm outflow pathway.
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 recognised.
Visual field	The area or extent of space visible to an eye in a given position.

Sources

American Optometric Association [AOA] (2002): *Optometric clinical practice guideline: Care of the patient with open angle glaucoma* (2nd edn.). St Louis: American Optometric Association.

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■ Guideline development details

Purpose

This guideline presents the current best evidence for screening, prognosis, diagnosis, management and prevention of glaucoma. Its purpose is to inform practice for Australian health care providers, particularly utilising a multi-disciplinary team approach.

Target users

This guideline is primarily targeted to Australian primary health care providers undertaking any task related to screening, prognosis, diagnosis, management and prevention of glaucoma, in any setting. Information is also provided for secondary health care providers.

Guideline development period

The systematic review underpinning these guidelines was completed in September 2008. The guideline was developed between August 2008 and June 2009. Public consultation occurred during October and November 2009.

Date of review

Given the rapid advances in knowledge regarding aspects of screening, prognosis, diagnosis, management and prevention of glaucoma, it is recommended that the literature is revisited in 2011.

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Conflict of interest

Members were required to submit any conflict of interests to NHMRC. One member identified a conflict of interest that was considered by NHMRC and deemed not to affect their membership or voting entitlement.

Funding

This guideline was commissioned by NHMRC and funded by the Department of Health and Ageing. The Expert Working Committee members received no remuneration for their involvement in the development of the guideline.

Process report

The process report for this guideline is provided in Appendix 1.

■ CHAPTER I

Recommendations and Evidence statement

The recommendations were derived from the evidence statements within each chapter.

Evidence Statement Grade Key:

For each recommendation, the Grade of Evidence is summarised and shown in an evidence table. An overall grade is represented beneath by a single capital letter, ranging from A to D. These grades are derived from the NHMRC Body of Evidence matrix (2009) and were determined in the same way that each of the five levels of evidence were determined.

"Expert/consensus opinion suggests"	Denotes evidence from expert opinion provided by the Working Committee, or from a consensus opinion statement in a published guideline. This wording used consistently for these statements.
"Evidence supports/indicates"	Denotes moderate quality published evidence. Can include evidence gradings C and D. This wording used consistently for these evidence statements.
"Evidence strongly supports/indicates"	Denotes high quality published evidence. All gradings within the matrix are A or B. This wording used consistently for these evidence statements.

Recommendation	Evidence Statements	Evidence Statement Grade
Chapter 4 – The role of population screening		
<i>Recommendation 1</i> Screen high-risk groups	Evidence strongly supports a screening approach that targets individuals at higher risk of developing glaucoma, rather than the general population.	A
Chapter 5 – Prognosis: understanding the natural history		
<i>Recommendation 2</i> Reduce intraocular pressure	Glaucoma Evidence strongly supports reducing intraocular pressure in glaucoma patients (including normal tension glaucoma), in order to preserve the visual field and reduce glaucomatous progression rates.	A
<i>Recommendation 3</i> Monitor visual field and determine rate of any field loss	Evidence strongly supports monitoring rates of visual field loss in patients with glaucoma (including normal tension glaucoma).	A
<i>Recommendation 4</i> Assess risk of conversion from ocular hypertension to glaucoma	Ocular hypertension Evidence strongly supports assessing risk of conversion of ocular hypertension to glaucoma, using factors such as intraocular pressure and central corneal thickness, in order to guide decision-making concerning which patients with ocular hypertension warrant treatment.	A

Recommendation	Evidence Statements	Evidence Statement Grade
Good Practice Points <ul style="list-style-type: none"> Patients at low risk of conversion should be considered for monitoring. Patients at high risk of conversion should be considered for treatment. Educate patients on the risks and consequences of conversion to glaucoma. 	<p>Evidence strongly supports intervention for individuals with ocular hypertension and major risk factors for the development or progression of glaucoma, in order to reduce the risk of visual loss within their expected lifespan.</p> <ul style="list-style-type: none"> Major risk factors for <i>developing glaucoma</i> include elevated intraocular pressure, increased cup:disc ratio, disc rim haemorrhage, reduced central corneal thickness, older age, strong family history and ethnicity. Major risk factors for <i>glaucoma progression</i> include elevated and/or fluctuating intraocular pressure, increased cup:disc ratio, disc rim haemorrhage and reduced central corneal thickness. 	A
	Evidence strongly supports careful monitoring, rather than active treatment of patients with ocular hypertension and low-risk status.	A
	Evidence strongly supports monitoring in order to detect conversion to glaucoma for all patients with ocular hypertension, frequency depending on other identified risk factors. Refer to Table 8.2 on p100.	A
	Early primary open angle glaucoma Evidence strongly supports implementing appropriate management plans for patients with early primary open angle glaucoma in order to reduce the risk of visual loss, and minimise glaucomatous progression within the patient's expected lifespan.	A
	Evidence strongly supports management plans that are based on an evaluation of the relative benefits and risks of treatment for each patient with glaucoma.	A
Chapter 6 – Identifying those at risk of developing glaucoma		
Recommendation 5 Identify and assess glaucoma patients and suspects (those at high risk of the disease)	Introduction Evidence strongly supports a standard approach to assessing risk factors when diagnosing patients with glaucoma, and also when identifying patients who may develop glaucoma. Standard risk assessment is also essential when making therapeutic decisions regarding who to treat, when to treat and how aggressively to treat.	A
Good Practice Points <ul style="list-style-type: none"> Identification is essential in order to make therapeutic decisions, whom to treat, and how aggressively to treat each person. All involved in their health care need to adopt a standard approach to risk factor assessment for each individual. 	Risk Factors identified from patient history – Age Evidence strongly indicates that Caucasians and Asians over the age of 50 years undertake regular ocular health checks.	A
	Evidence indicates that individuals of African descent over the age of 40 years undertake regular ocular health checks.	B

Recommendation	Evidence Statements	Evidence Statement Grade
<p>Recommendation 6 Detect glaucoma earlier</p> <p>Good Practice Points</p> <ul style="list-style-type: none"> Perform regular eye health checks for Caucasians over the age of 50, and for African-descended people over the age of 40. Perform regular eye health checks for all first-degree relatives of glaucoma patients, commencing 5-10 years earlier than the age of onset of glaucoma in their affected relative. Remind all glaucoma patients to alert first-degree relatives of the benefits of early and regular eye checks. 	<p>Risk Factors identified from patient history – Family and Genetics</p> <p>Evidence strongly supports that all first-degree relatives of individuals diagnosed with glaucoma are considered at high risk of developing glaucoma themselves. It is recommended that they undergo a full ocular examination by a qualified health care provider, and receive ongoing monitoring for the development of glaucoma.</p>	A
	<p>Evidence strongly supports the need for all patients diagnosed with glaucoma to alert first-degree relatives of the benefits of ocular examination.</p>	A
	<p>Risk Factors identified from patient history – Ethnic origin</p> <p>Evidence strongly indicates that individuals of African descent are at higher risk of open angle glaucoma than Caucasians.</p>	A
	<p>Evidence strongly indicates that individuals of Asian ethnic origin are at increased risk of angle closure, compared with other ethnic groups.</p>	A
	<p>Risk Factors identified from patient history – Myopia</p> <p>Evidence strongly indicates that individuals with myopia requiring optical correction are considered at increased risk of glaucoma.</p>	A
	<p>Risk Factors identified from patient history – Long-term steroid users</p> <p>Evidence indicates that long-term users of steroids by any route of administration are at increased risk of glaucoma, and thus require surveillance.</p>	C
	<p>Risk Factors identified from patient history – Migraine and peripheral vasospasm</p> <p>Evidence indicates that individuals with migraine and peripheral vasospasm dysfunction are at increased risk of glaucoma.</p>	C
	<p>Risk Factors identified from patient history – Eye injury</p> <p>Evidence indicates that individuals with a history of eye trauma are at increased risk of glaucoma.</p>	C
	<p>Risk Factors identified from patient history – Systematic blood pressure</p> <p>Ongoing blood pressure monitoring and management is appropriate for all patients at risk of glaucoma.</p>	A

Recommendation	Evidence Statements	Evidence Statement Grade
<ul style="list-style-type: none"> Survey for glaucoma particularly in patients greater than 50 years of age, with any myopia, with abnormal blood pressure, with a history of migraine, with diabetes, with peripheral vasospasm, with eye injury and/or with ongoing steroid use. Monitor for glaucoma particularly in patients greater than 70 years of age, with IOP >21 mmHg, large and/or asymmetric cup-to-disc ratio (compared with disc size), disc haemorrhage, and thin central corneal thickness. 	<p><i>Risk factors identified from patient history – Intraocular pressure</i></p>	A
	<p>Evidence strongly supports the assessment of intraocular pressure in all individuals with suspected glaucoma, as it is a significant risk factor for the development of all forms of glaucoma.</p>	
	<p>Evidence strongly supports using 21mmHg as the upper limit for usual intraocular pressure.</p>	A
	<p><i>Risk Factors identified from patient history – Alterations in cup:disc ratio and asymmetry</i></p>	C
	<p>Evidence supports the assessment of cup:disc ratio, and cup:disc ratio asymmetry, when assessing the risk of glaucomatous damage occurring.</p>	
	<p><i>Risk Factors identified from patient history – Optic disc haemorrhage</i></p>	B
	<p>Evidence supports past signs, or current presence, of optic disc haemorrhages as significant risk factors for the development and progression of glaucoma.</p>	
	<p>Evidence supports more aggressive treatment of patients with ocular hypertension, or glaucoma, who present with optic disc rim haemorrhages, or evidence of past optic disc rim haemorrhages.</p>	B
	<p><i>Risk Factors identified from patient history – Central corneal thickness</i></p>	B
	<p>Evidence supports the assessment of central corneal thickness in patients with ocular hypertension, or suspected cases of glaucoma.</p>	
	<p><i>Risk factors for specific glaucoma types and stages – Angle closure</i></p>	
	<p>Expert/consensus opinion suggests that hypermetropia, family history of angle closure, advancing age, female gender, Asian descent and shallow anterior chamber are risk factors for the development of angle closure, and angle closure glaucoma.</p>	
	<p><i>Risk factors for specific glaucoma types and stages – Progression of established glaucoma</i></p>	B
	<p>Evidence indicates that factors associated with greater risk of glaucoma progression include elevated/fluctuating intraocular pressure, optic disc haemorrhage, increased severity of glaucomatous disc damage and very low blood pressure. These patients require greater reduction in intraocular pressure.</p>	

Recommendation	Evidence Statements	Evidence Statement Grade
<p>Recommendation 7 Assess risk of progression of glaucomatous damage</p> <p><i>Good Practice Points</i></p> <ul style="list-style-type: none"> • Calculate the rate of visual field loss regularly (for example review every four months) for the first two years, and then less frequently (for example every six months) thereafter if stable. This will depend on the health care setting and the individual patient's risk of progression. • Reduce IOP by 20-50% in patients with glaucomatous optic neuropathy depending on the level of risk to preserve visual field and to reduce progression. • Reduce IOP more aggressively in those patients with greater risk factors for progression. • Patients diagnosed late, with more advanced glaucoma damage, suffer higher rates of progression of visual loss. More aggressive IOP reduction is required. 	<p>No Evidence Statements for Recommendation 7.²</p>	

² This recommendation was developed using expert opinion of the Working Committee

Recommendation	Evidence Statements	Evidence Statement Grade
Chapter 7 – Diagnosis of glaucoma		
<p>Recommendation 8 Assess with a comprehensive medical history, a full eye examination and investigate appropriately</p> <p><i>Good Practice Points</i></p> <ul style="list-style-type: none"> • A comprehensive medical history: identify all relevant risk factors, relevant comorbidities and concurrent topical and systemic medications, and assess the impact of visual dysfunction, social environment and support networks that may affect adherence to a treatment program. Comorbidities include hypertension, diabetes, thyroid disease, depression, asthma, liver and renal disease. • A full eye examination: anterior segment evaluation including gonioscopy, optic nerve and retinal nerve fibre layer exam stereoscopic optic disc and retinal nerve fibre assessment with a permanent record, IOP and corneal thickness measurements. 	<p>Diagnosis of glaucoma Evidence strongly supports the need for a comprehensive examination to accurately diagnose all types of glaucoma. This includes a comprehensive medical history, a full eye examination (including gonioscopy), an assessment of eye function (visual field) and measurement of intraocular pressure.</p> <p>Medical History – Risk factors Evidence strongly supports taking a comprehensive history including identification of ocular signs and symptoms, risk factors, relevant comorbid conditions and concurrent medication, to diagnose glaucoma.</p> <p>Expert/consensus opinion suggests that a comprehensive history is required to identify which management approach is most likely to be effective. A comprehensive history includes the potential impact of visual dysfunction, social environment and patient's support networks that may affect adherence to medication regimens.</p> <p>Examination of eye structure – Setting diagnostic baselines Evidence indicates that an eye structure examination that is capable of establishing a diagnostic baseline includes a stereoscopic view, and a permanent record of the optic disc and retinal nerve fibre layer.</p> <p>Expert/consensus opinion suggests that key components of a baseline optic nerve head examination include size of disc, cup:disc ratio, neuroretinal rim pattern, presence of optic disc haemorrhages and thinning of the nerve fibre layer.</p> <p>Anterior chamber assessment Expert/consensus opinion suggests that gonioscopic examination of both eyes is required when making a diagnosis of glaucoma.</p> <p>Examination of eye function – Perimetry Expert/consensus opinion suggests that visual field testing is invaluable to diagnose glaucoma.</p> <p>Expert/consensus opinion suggests that advancing age, visual acuity, patient capability, concurrent ocular conditions, oculo-facial anatomy and spectacle scotomata all impact upon the results and interpretation of visual field testing.</p> <p>Assessment pressure measurement – Timing of intraocular pressure measurements Evidence indicates that intraocular pressure can vary at different times of the day. Therefore it is important to measure intraocular pressure at different times of the day to gain a comprehensive picture of the intraocular pressure profile of a patient.</p> <p>Assessment pressure measurement – Contact tonometry Evidence strongly supports the need to maximise infection control. Minimum standards are:</p> <ul style="list-style-type: none"> – disinfecting equipment before each patient, or – using disposable covers/prisms with each patient, and between eyes for the same patient. 	<p>A</p> <p>A</p> <p>C</p> <p>C</p> <p>A</p>

Recommendation	Evidence Statements	Evidence Statement Grade
<ul style="list-style-type: none"> • Appropriate investigations: standard automated perimetry (white-on-white) including comparison with age-corrected normals on a point-wise, regional (eg. hemifield) and global basis, optic disc photography and imaging of the optic nerve and optic nerve fibre layer. • Careful and informed interpretation of results from all imaging and functional tests in order to detect disease or to detect progression. With the multi-faceted nature of glaucoma and the large variability in normal values of all tests, consider results from all tests and assessments. 	Setting target intraocular pressure at diagnosis Evidence strongly supports a minimum target intraocular pressure reduction of 20% in patients with suspected primary open angle glaucoma with high-risk status. It is advised that intraocular pressure remains under 24mmHg. Those without high-risk factors can simply be observed.	B
	Evidence strongly supports a minimum target intraocular pressure reduction of 20% in patients with early and established primary open angle glaucoma without high-risk status. It is advised that intraocular pressure remains under 16-19mmHg.	B
	Evidence strongly supports a minimum target intraocular pressure reduction of 30% in patients with established primary open angle glaucoma with high-risk status, and patients with advanced primary open angle glaucoma.	B
	Evidence strongly supports the maintenance of intraocular pressure below 18mmHg in patients with established primary open angle glaucoma, and even lower to below 15mmHg in patients with advanced primary open angle glaucoma.	B
	Professional roles in diagnosis Evidence strongly supports that all health care providers involved in glaucoma screening and diagnosis receive appropriate training and continuing support from health care providers who regularly manage glaucoma. Co-management involving an ophthalmologist is recommended.	A
	Summary of diagnostic standards Evidence strongly indicates the multifaceted nature of glaucoma and the large variability in the normal values of test findings. This evidence therefore strongly supports using findings from more than one diagnostic procedure or test before a glaucoma diagnosis can be made.	B
	Evidence strongly supports the need for health care providers only involved in the screening and diagnosis of glaucoma, to possess the skills and equipment to measure intraocular pressure (by Goldmann Applanation Tonometry or well-calibrated non-contact tonometry), test visual field, perform gonioscopy and examine the optic disc for typical glaucoma signs. They should receive appropriate training and continuing support from health care providers who manage glaucoma.	A
	Evidence supports the following assessment methods for diagnosing glaucoma, which are independent of cost and patient preference: <ul style="list-style-type: none"> – full medical history examination of eye structure with optic nerve image recording examination of eye function with two automated visual field examinations using a threshold program for determination of the baseline assessment of intraocular pressure, including diurnal variation with a calibrated tonometer checked regularly, and assessment of the angle by gonioscopy. 	B

Recommendation	Evidence Statements	Evidence Statement Grade
Chapter 8 – Monitoring: long-term care		
<p>Recommendation 9 Establish a treatment plan, with target IOP</p> <p>Good Practice Point</p> <ul style="list-style-type: none"> Target should vary depending on patient setting and risk factors. Monitor response carefully, and use it to modify goals (e.g. lower target IOP) if disease progresses. Change strategies if there are side effects. 	<p>Medical history</p> <p>Evidence strongly supports taking a comprehensive history at each review. This should include information on what has occurred in the intervening period, and the patient's ability to adhere to the prescribed medication regimen.</p>	A
	<p>Intraocular pressure</p> <p>Evidence strongly supports assessing target intraocular pressure at each ocular review, within the context of glaucomatous progression and quality of life.</p>	A
	<p>Evidence strongly supports a further 20% reduction in target intraocular pressure when glaucomatous progression is identified.</p>	A
	<p>External structure examination – External eye examination</p> <p>Evidence strongly supports using ocular examination to detect adverse reactions to eye drops, and secondary causes of glaucoma.</p>	A
	<p>Evidence supports using a preservative-free preparation when hypersensitivity to topical medication is identified during review.</p>	B
	<p>External structure examination – Anterior chamber examination</p> <p>Evidence supports undertaking gonioscopy at review, where there is an unexplained rise in intraocular pressure, suspicion of angle closure and/or after iridotomy.</p>	B
	<p>Evidence supports performing gonioscopy regularly in patients with angle closure (three to six times per year) and periodically in those with open angle glaucoma (every one to five years).</p>	B
	<p>Expert/consensus opinion suggests monitoring patients with narrow but potentially occludable angles.</p>	
	<p>External structure examination – Nerve fibre layer</p> <p>Evidence strongly supports using validated techniques (with the highest sensitivity and diagnostic odds) to detect changes in visual field or optic disc in order to diagnose early primary open angle glaucoma.</p>	A
	<p>Evidence supports the value of validated optic disc comparison techniques (simultaneous stereo photograph comparison and confocal scanning laser tomography) in order to detect longitudinal changes in the optic nerve.</p>	B
	<p>Eye function: visual field – Automated perimetry</p> <p>Evidence supports undertaking visual field testing with automated perimetry on multiple occasions at diagnosis, in order to set a reliable baseline. An assessment of likely rate of progression will require two to three field tests per year in the first two years.</p>	C

Recommendation	Evidence Statements	Evidence Statement Grade
<p>Recommendation 10 Monitor patients with primary angle-closure suspect status for progressive angle narrowing, development of synechiae, rising IOP and ischemic changes to the iris or lens</p>	<p>Monitoring recommendations in specific populations – Patients with ocular hypertension or suspected glaucoma Expert/consensus opinion suggests undertaking ocular reviews at six to twenty-four month intervals, for individuals with suspected glaucoma without high-risk factors, who are not receiving treatment.</p> <p>Monitoring recommendations in specific populations – All patients with suspected glaucoma Expert/consensus opinion suggests using automated perimetry at least annually, for patients with suspected glaucoma. Expert/consensus opinion suggests that gonioscopy should be performed at one to five year intervals depending upon degree of angle opening, and presence of prior lens extraction surgery, for patients with suspected primary angle closure glaucoma. Expert/consensus opinion suggests undertaking dilated examination of the optic nerve and optic nerve fibre layer at six to eighteen month intervals for all patients with suspected glaucoma. Undilated examination of the optic disc, looking for change, and presence of disc rim haemorrhage, should be undertaken at most visits. Expert/consensus opinion suggests examination of the optic nerve with validated comparison techniques every one to two years for all patients with suspected glaucoma. Expert/consensus opinion suggests using tonometry at every visit for all patients with suspected glaucoma, once baseline intraocular pressure has been set.</p> <p>Monitoring recommendations in specific populations – Patients with suspected glaucoma, and high-risk factors who are undergoing treatment and achieving targets Expert/consensus opinion suggests undertaking ocular reviews at three to twelve month intervals for individuals with suspected glaucoma and high-risk factors who are undergoing treatment and achieving targets.</p> <p>Monitoring recommendations in specific populations – Patients with suspected glaucoma, and high-risk factors who are undergoing treatment and failing to achieve targets Expert/consensus opinion suggests undertaking ocular reviews at less than four month intervals for individuals with suspected glaucoma, and high-risk factors, who are undergoing treatment and not achieving targets. When treatment is altered, patients should be reviewed within two months.</p> <p>Monitoring recommendations in specific populations – Established glaucoma Expert/consensus opinion suggests that in established glaucoma where intraocular pressure targets are being achieved, monitoring schedules are guided by the severity and stability of disc and visual field examinations. Expert/consensus opinion suggests that in established glaucoma where intraocular pressure targets are not being achieved, the management plan requires alteration and a review undertaken within four to six weeks.</p>	

Recommendation	Evidence Statements	Evidence Statement Grade
	<p>Expert/consensus opinion suggests that in highly unstable established glaucoma, where intraocular pressure targets are not being achieved, the management plan requires alteration and a review undertaken within one to four weeks.</p> <p>Evidence supports using tonometry on every visit, for patients with established glaucoma, once a baseline has been set.</p> <p>Expert/consensus opinion suggests that monitoring timelines for patients with angle closure glaucoma are guided by angle morphology, optic disc and/or visual field stability and intraocular pressure.</p>	
Chapter 9 – Medication		
<p>Recommendation 11</p> <p>Reduce IOP by using medications</p> <p>Good Practice Points</p> <ul style="list-style-type: none"> • Due to the potential efficacy and once-daily usage, a topical prostaglandin analogue is usually the first choice, unless contraindicated. When more than one agent is required, fixed-dose combinations should be considered to encourage improved compliance. • Topical medications may be the simplest and safest first choice for treatment, except for pregnant and lactating women. • Facilitate adherence and perseverance with a patient-centric self-management approach to a medication plan. Provide ongoing tailored information (such as from Glaucoma Australia) to reinforce a patient's understanding of glaucoma and realistic goals of treatment. 	<p>Starting medication regimens</p> <p>Evidence strongly supports using topical medications as the simplest and safest first choice for glaucoma management.</p> <p>Evidence strongly supports limiting the use of systemic medication to situations where patients cannot tolerate topical medications, are unable to safely and effectively instill topical medications, are failing to achieve intraocular pressure targets, or when laser therapy or surgery either had poor outcomes, or are contraindicated.</p> <p>Evidence strongly supports using a topical prostaglandin analogue or beta-blocker in the initial management of glaucoma unless contraindicated.</p> <p>Evidence strongly supports carbonic anhydrase inhibitors and α_2-agonists as second and third choice medication management, with dosing regimens of two to three times daily.</p> <p>Facilitating adherence</p> <p>Evidence supports a patient-centric self-management approach that facilitates optimal adherence to the medication management plan.</p> <p>Evidence supports the value of ongoing, tailored information to support patients' understanding of their disease and its management.</p> <p>Evidence strongly supports using combination preparations, rather than separate instillations of individual medications, to improve patient adherence. There is no evidence however, showing that one combination preparation is more effective than any other for reaching target intraocular pressure.</p> <p>Medication interaction</p> <p>Expert/consensus opinion suggests the need to establish the presence of other disease states when initiating, assessing or altering medication regimens for patients with glaucoma. These include, but are not limited to, diabetes, depression, hyperthyroidism, heart disease, asthma, liver and renal impairment.</p>	<p>A</p> <p>A</p> <p>A</p> <p>A</p> <p>B</p> <p>B</p> <p>A</p>

Recommendation	Evidence Statements	Evidence Statement Grade
<ul style="list-style-type: none"> Initiate, switch or add medications to one eye, using the other eye as a “control”. In these cases, reassess IOP within 2-6 weeks before treating the other eye. If there is no apparent effect check for adherence. Teach patients the “double DOT” (Don’t Open Technique and Digital Occlusion of Tear ducts) for 2-3 minutes post-instillation to minimise systemic absorption and to promote ocular penetration of eyedrops. Demonstrate instillation techniques, observe patient or carer instilling drops and repeat education till ability to instil has been proven. 	<p>Side effects</p> <p>Evidence strongly warns of the significant potential side effects from both topical and systemic medications in the management of glaucoma.</p>	A
	<p>Topical medications – Initiating treatment</p> <p>Evidence strongly supports initiating or changing medication in one eye, using the fellow eye as a control.</p>	A
	<p>Evidence strongly supports the need for reassessing responses to medication within two to six weeks before extending treatment to the fellow eye.</p>	A
	<p>Topical medications – Instillation of topical medications</p> <p>Evidence strongly supports the importance of educating patients in the effective and efficient instillation of topical medications.</p>	A
	<p>Evidence strongly supports teaching patients and carers about the punctal occlusion and eyelid closure technique when instilling eye drops, to reduce systemic absorption.</p>	A
	<p>Assessing medication efficacy – Outcome measures</p> <p>Evidence strongly supports using target intraocular pressure ranges as an early indicator of an effective glaucoma management plan.</p>	A
	<p>Evidence strongly supports monitoring disc and visual field changes as long-term indicators of a successful glaucoma management plan.</p>	A
	<p>Changing medication regimens</p> <p>Evidence strongly indicates that, where the medication regimen is well tolerated, the main indicator for changing it is failure to reach target intraocular pressures.</p>	A
	<p>Evidence strongly supports substitution rather than addition of medication when treatment is ineffective.</p>	A
	<p>Evidence strongly supports that when two or more topical medications are ineffective, consideration is given to laser therapy or surgery instead of systemic medications.</p>	A
	<p>Medication in acute angle closure crisis</p> <p>Evidence strongly supports using adjunct medications including cholinergics (miotics), hyperosmotic medications and carbonic anhydrase inhibitors to rapidly reduce intraocular pressure prior to surgery.</p>	A
	<p>Managing glaucoma successfully within specific comorbid conditions – Diabetes</p> <p>Evidence indicates caution when prescribing topical beta-blockers to patients with diabetes.</p>	C
	<p>Managing glaucoma successfully within specific comorbid conditions – Depression</p> <p>Evidence indicates caution when prescribing alpha₂-agonists or beta-blockers for patients with depression.</p> <p>Evidence supports the needs for an ophthalmic consultation for patients at risk of increased intraocular pressure, prior to commencing medications for depression, and periodically during treatment for depression.</p>	C B

Recommendation	Evidence Statements	Evidence Statement Grade
	<p><i>Managing glaucoma successfully within specific comorbid conditions – Asthma</i> Evidence indicates that using non-selective beta-blockers is generally contraindicated in patients with asthma, however cardio-selective beta-blockers may be used with caution.</p> <p><i>Managing glaucoma successfully within specific comorbid conditions – Chronic obstructive pulmonary disease</i> Evidence indicates using beta-blockers with caution in patients with chronic obstructive pulmonary disease. Preference may be given to using cardio-selective beta-blockers as they are less likely to induce bronchospasm.</p> <p><i>Managing glaucoma successfully within specific comorbid conditions – Cardiovascular disease</i> Evidence indicates using alpha₂-agonists with caution in patients with severe cardiovascular disease. A specialist cardiac opinion may be required for individual cases.</p> <p>Evidence indicates using beta-blockers with caution in patients with existing heart disease. Using these medications is contraindicated in patients with bradycardia (45–50 beats/minute), sick sinus syndrome, second or third degree atrioventricular block, severe hypotension or uncontrolled heart failure.</p> <p><i>Managing glaucoma successfully within specific comorbid conditions – Hepatic impairment</i> Evidence indicates that systemic carbonic anhydrase inhibitors are contraindicated in patients with hepatic impairment, while topical carbonic anhydrase inhibitors may be used with caution.</p> <p><i>Managing glaucoma successfully within specific comorbid conditions – Renal impairment</i> Evidence indicates that caution is required when considering systemic carbonic anhydrase inhibitors for patients with mild to moderate renal impairment, and these medications are contraindicated in patients with severe renal impairment.</p> <p><i>Medication-induced glaucoma</i> Evidence indicates caution in the administration of corticosteroids delivered by any form (i.e. oral, intranasal or ocular) for patients with glaucoma or ocular hypertension.</p> <p>Evidence supports obtaining a comprehensive medication history from all patients with ocular symptoms suggestive of acute or chronic angle closure glaucoma, to rule out potential medication-induced glaucoma.</p>	<p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p> <p>B</p>

Recommendation	Evidence Statements	Evidence Statement Grade
	<p>Managing glaucoma in specific population groups – Children</p> <p>Evidence supports using beta-blockers in infants and children where necessary.</p> <p>Evidence suggests using beta-blockers with caution in premature and small infants, as bradycardia, bronchospasm and hypoglycemia have been reported.</p> <p>Evidence indicates caution when using topical and systemic carbonic anhydrase inhibitors in children, in situations where glaucoma is resistant to other treatment and/or prior to surgery.</p> <p>Managing glaucoma in specific population groups – Breastfeeding mothers</p> <p>Evidence supports using beta-blockers in pregnancy, but with caution due to the risks of foetal bradycardia and interuterine growth restriction.</p> <p>Evidence supports laser therapy over surgical techniques in women who are pregnant or planning to conceive in the near future.</p>	<p>C</p> <p>C</p> <p>C</p> <p>C</p>
Chapter 10 – Laser therapy and surgery		
<p>Recommendation 12 Reduce IOP by using laser techniques and incisional surgery</p> <p>Good Practice Points</p> <ul style="list-style-type: none"> • Offer laser trabeculoplasty as an alternative, or additive to medications. • Offer surgical IOP reduction when medications and/or laser trabeculoplasty fail to meet targets or are unsuitable, and visual disability is threatened. There are inherent risks with invasive procedures, which must be justified by likely benefits. • Glaucoma drainage devices may control IOP long-term and may be suitable if other drainage surgery fails, or as first-line surgery in eyes with higher risks of failure (including inflammatory glaucomas and ICE syndrome). 	<p>Summary of common laser interventions: Laser options for specific glaucoma classification and stages – Open angle glaucoma</p> <p>Evidence strongly supports argon laser trabeculoplasty for older patients with glaucoma who are at risk of visual loss within their lifetime, particularly when the following factors apply:</p> <ul style="list-style-type: none"> – there is difficulty with administering eye drops – patients are unresponsive to medication alone, or – patients are poor candidates for incisional surgery. <p>Expert/consensus opinion suggests that patients undergoing laser therapy require continual comprehensive glaucoma monitoring due to the diminishing treatment benefit over time.</p> <p>Summary of common laser interventions: Laser options for specific glaucoma classification and stages – Cyclodestructive procedures in open angle glaucoma</p> <p>Evidence strongly supports using cyclodestructive surgery as a third choice treatment for patients with advanced glaucoma, who are poor candidates for incisional surgery.</p>	<p>B</p> <p>B</p>

Recommendation	Evidence Statements	Evidence Statement Grade
Recommendation 13 If indicated, perform prophylactic laser peripheral iridotomy in both eyes to prevent progressive anterior segment damage	<p><i>Summary of common laser interventions:</i> <i>Laser options for specific glaucoma classification and stages – Angle closure – patients with narrow angles/suspected angle closure but low risk status</i></p>	
	<p>Evidence supports the practice of monitoring patients with suspected angle closure, who are at low risk of immediate closure, until there is evidence of:</p> <ul style="list-style-type: none"> – elevated intraocular pressure – progressive narrowing, or – development of synechial angle closure. 	C
	<p>Evidence supports the importance of ensuring that individuals who are being monitored for angle closure (rather than being actively treated) are:</p> <ul style="list-style-type: none"> – fully informed of the risks of monitoring – aware of symptoms of closure, and – capable of accessing immediate treatment. 	C
	<p>Where these factors cannot be guaranteed, the patient should be treated as if at high risk.</p>	
	<p><i>Summary of common laser interventions:</i> <i>Laser options for specific glaucoma classification and stages – Angle closure – patients with suspected angle closure and high-risk status</i></p>	
	<p>Evidence supports using laser iridotomy for both eyes as the treatment of choice for patients with suspected angle closure, who are at high risk of closure.</p>	C
	<p><i>Summary of common laser interventions:</i> <i>Laser options for specific glaucoma classification and stages – Angle closure – patients with acute angle closure</i></p>	
	<p>Evidence supports using laser iridotomy with adjunctive pre-operative medication, as the treatment of choice for patients with acute angle closure.</p>	C
	<p>Expert/consensus opinion suggests that in patients who experience acute angle closure in one eye, the fellow eye is at high risk of future closure and therefore prophylactic iridotomy can be clinically indicated.</p>	
	<p>Evidence strongly supports using medication to rapidly reduce intraocular pressure as a short-term measure pre-operatively, in patients with acute angle closure glaucoma.</p>	A
	<p><i>Summary of common laser interventions:</i> <i>Laser options for specific glaucoma classification and stages – Angle closure – patients with chronic angle closure and chronic angle closure glaucoma</i></p>	
	<p>Evidence supports using laser peripheral iridotomy as the treatment of choice in patients with chronic angle closure.</p> <p>Expert/consensus opinion suggests that more than one patent peripheral iridotomy confers no additional benefit.</p>	C

Recommendation	Evidence Statements	Evidence Statement Grade
<p>Good Practice Point</p> <ul style="list-style-type: none"> Peripheral iridoplasty might be useful after iridotomy in individual cases. Consider cataract extraction and ongoing IOP control, including trabeculectomy as required. <p>Recommendation 14 Ensure patients are aware of risks and symptoms of angle-closure and can access care urgently as necessary</p>	<p><i>Surgical options for specific glaucoma classification and stages – Established open angle glaucoma</i></p> <p>Evidence strongly supports surgery as being at least as effective as medication for reducing intraocular pressure in established open angle glaucoma.</p> <p>Evidence strongly supports using surgery when target intraocular pressure is not being achieved with two or more medications, or adherence is problematic, and when laser has failed or is not likely to succeed.</p>	<p>B</p> <p>B</p>
	<p><i>Surgical options for specific glaucoma classification and stages – Angle closure</i></p> <p>Evidence supports surgical iridectomy as a second choice treatment for patients with acute angle closure, when primary laser iridotomy cannot be performed.</p> <p>Expert/consensus opinion suggests the value of cataract extraction or drainage surgery for patients with angle closure.</p>	<p>B</p>
	<p><i>Surgical options for specific glaucoma classification and stages – Filtering surgery</i></p> <p>Evidence supports using filtration surgery as a third choice treatment in most patients, due to the inherent risks with any invasive procedure.</p> <p>Evidence supports using filtration surgery for patients with moderate or advanced glaucoma, due to its success in lowering intraocular pressure. This is especially relevant to patients with eyes with high pressure conditions (over 30mmHg), or patients with eyes resistant to other forms of therapy.</p>	<p>B</p> <p>B</p>
	<p><i>Surgical options for specific glaucoma classification and stages – Anti-fibrotic medications</i></p> <p>Evidence supports using intra-operative and post-operative anti-fibrotics to reduce the risk of failure for patients undergoing incisional surgery.</p>	<p>B</p>
	<p><i>Surgical options for specific glaucoma classification and stages – Glaucoma drainage devices</i></p> <p>Evidence strongly supports using tube surgery for long-term intraocular pressure control. This is an appropriate first-choice surgery in patients:</p> <ul style="list-style-type: none"> – with eyes at higher risk of failure from trabeculectomy – who have failed trabeculectomy – with Iridocorneal Endothelial syndrome – with various forms of uveitic (inflammatory) glaucoma, or – with aphakic glaucoma. 	<p>B</p>
	<p><i>Surgical options for specific glaucoma classification and stages – Cataract surgery</i></p> <p>Evidence supports using cataract surgery to open the angle in most patients with primary angle closure, when laser procedures have been inadequate. This is believed to improve the safety of subsequent drainage surgery.</p>	<p>B</p>

■ CHAPTER 2

Methods

Underling research questions

A suite of review questions was answered in order to develop the Australian National Health and Medical Research Council (NHMRC) Guidelines for the Screening, Prognosis, Diagnosis, Management and Prevention of Glaucoma. These questions were applied systematically to the relevant evidence sources. This ensured a replicable and comprehensive search of the academic literature, as well as a consistent approach in summarising and reporting the findings.

The research questions comprised:

1. What is the definition of glaucoma?
2. What are the recognised types and/or classifications of glaucoma?
3. How do they differ pathophysiologically from each other?
4. What is the prevalence and incidence of glaucoma within Australia and internationally?
5. What is the natural history of glaucoma?
6. What is the best available evidence for the prognosis of patients with glaucoma, and the ability of any given intervention to alter this prognosis, from population-based studies?
7. What is the best available evidence for the prognosis of glaucoma and the ability of any given intervention to alter this prognosis from experimental studies?
8. Based on the best available evidence, what, if any, are the recognised risk factors for:
 - developing glaucoma?
 - the progression of established glaucoma?
9. Does the evidence support widespread general population screening, or targeted population screening, for glaucoma? If so, based on the best available evidence, what are the most appropriate screening methods?
10. What is the recommended methodology for the monitoring and surveillance of individuals suspected of having glaucoma, or individuals at-risk of having glaucoma?
11. What is the recommended methodology for the monitoring and surveillance of patients with established glaucoma?
12. What is the best available evidence for appropriate methods and techniques to diagnose glaucoma?
13. Does the evidence identify threshold values at which a diagnosis of glaucoma can be made?
14. What does the literature have to offer regarding the pragmatic elements and logistics of diagnosing glaucoma, with respect to the health care professionals involved, health care settings and resources required?

Literature review process

Literature inclusion

Secondary evidence was the literature of choice for the systematic review which underpins the NHMRC *Guidelines for the Screening, Prognosis, Diagnosis, Management and Prevention of Glaucoma*. This systematic review is located on the NHMRC website <https://www.nhmrc.gov.au/publications/index.htm>. This decision was based on the volume of secondary evidence available for most of the review questions. Secondary evidence comprised clinical guidelines and systematic reviews. Eligibility criteria for inclusion in the review were availability of literature in English language, in full text and published from 2000 to mid 2008.

Where there was a lack of systematic reviews for any review question, primary literature was sought. Additional primary literature was provided by the NHMRC Expert Working Committee (hereafter referred to as the Working Committee) to underpin its consensus and clinical guidance statements. In the systematic review of the literature underpinning these guidelines, the expert opinion was clearly identified as Addenda.

Literature identification

Search strategies used to identify eligible studies comprised:

- identifying medical subject index headings (MESH terms) relating directly to each of the specified clinical conditions through a preliminary search of the literature—these terms were subsequently incorporated into appropriate bibliographic search filters, in a number of electronic databases, to optimise the identification of diagnostic, prognostic and treatment publications
- recursive searching through reference lists of eligible research articles
- using clinical experts for additional references relevant to expert/consensus opinion
- using clinical experts to obtain literature not available through library channels.

Literature sources

An extensive list of electronic bibliographic databases was searched. Details regarding these databases are included in the systematic review conducted prior to constructing the clinical guidelines.

Critical appraisal

The methodological quality of the included literature was critically appraised in the manner described by the Australian National Health and Medical Research Council (NHMRC 1999, 2000a,b). Meta-analyses or systematic reviews were assessed using the Critical Appraisal Skills Program (CASP) tool developed by the Public Health Resource Unit, Oxford, UK (2007). Clinical guidelines were appraised using the Appraisal of Guidelines Research and Evaluation (AGREE) instrument (AGREE Collaboration 2003). This instrument quantitatively assesses the quality of guideline development processes across six domains: scope and purpose, stakeholder involvement, rigor of development, clarity and presentation, application, and editorial independence. Primary studies, where included, were not methodologically appraised. They were cited only in areas where no secondary evidence was available, and to support consensus/expert opinion provided by the Working Committee.

Grading the evidence

The NHMRC Body of Evidence matrix (Table 2.1) was used to determine the evidence base and consistency of evidence, the clinical impact, its applicability and generalisability.

Matrix use for the evidence statements

Using Table 2.1, each evidence statement in this guideline is underpinned with a specific matrix that refers to the evidence supporting that evidence statement (see Table 2.2). Each evidence statement matrix was provided in Chapter 1. Each evidence statement matrix was reported in its five distinct levels to guide health care providers regarding the complexity of the evidence and its clinical application.

Table 2.1: NHMRC Body of Evidence matrix (2009)

	A	B	C	D
Component	Excellent	Good	Satisfactory	Poor
Evidence base¹	One or more level I studies with a low risk of bias or several level II studies with low risk of bias	One or two level II studies with low risk of bias or a SR/multiple level III studies with low risk of bias	One or two level III studies with low risk of bias, or level I or II studies with moderate risk of bias	Level IV studies, or level I to III studies/SRS with high risk of bias
Consistency²	All studies consistent	Most studies consistent and inconsistencies may be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Population/s studied in body of evidence are the same as the target population for the guideline	Population/s studied in the body of evidence are similar to the target population for the guideline	Population/s studied in body of evidence differ to target population for guideline but it is clinically sensible to apply this evidence to target population ³	Population/s studied in body of evidence differ to target population and hard to judge whether it is sensible to generalise to target population
Applicability	Directly applicable to Australian healthcare context	Applicable to Australian healthcare context with few caveats	Probably applicable to Australian healthcare context with some caveats	Not applicable to Australian healthcare context

SR = Systematic review; several = more than two studies

¹ Level of evidence determined from the NHMRC evidence hierarchy

² If there is only one study, rank this component as 'not applicable'

³ For example, results in adults that are clinically sensible to apply to children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer



Table 2.2: Exemplar Body of Evidence matrix

Evidence base	A
Consistency	A
Clinical impact	A
Generalisability	A
Applicability	A

Guideline development

Recommendations were formed through steps outlined by the Australian National Health and Medical Research Council (NHMRC 1999, 2000a,b, 2005)¹. This approach recognises that high quality guideline development requires examination of the relevant literature using five evidence dimensions (hierarchy, methodological quality, significance, effect size, and applicability).

Throughout the glaucoma guideline development process, the drafts of guideline text and recommendations were circulated for consultation within the Working Committee. There were some instances where there was a lack of relevant research related to a clinical question. The NHMRC hierarchy does not recognise expert or clinical opinion as a formal hierarchy of evidence level; however in the absence of formal scientific evidence, it is accepted international practice that consensus recommendations be provided (Canadian Health Services Research Foundation 2005; Jones & Hunter 1995; Murphy, Black, Camping et al 1998). Therefore in this situation, the Working Committee provided evidence statements based on consensus opinion and supported by specific references as appropriate. In addition, the Working Committee and key health care providers provided clinical insights into referral processes, nomenclature and evidence interpretation. The Working Committee and key health care providers' input is clearly identified as Communications and Points of Note throughout this guideline.

The recommendations were developed by the Working Committee and were derived from the evidence statements in the relevant chapter. The 14 recommendations were considered to be the key messages for health practitioners. The Working Committee also developed good practice points which were also derived from the evidence statements.

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¹ The current NHMRC hierarchy of evidence is currently completing public consultation however it is available for guideline developers to use.



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■ CHAPTER 3

Implementation strategies

Introduction

Guideline implementation has been increasingly recognised over the past few years as a research area in its own right. Implementation strategies should reflect the purpose of the guideline, the end users, the benefit that is anticipated from application of the guideline, barriers to guideline uptake and incentives that could improve compliance with guideline recommendations (Barosi 2006). The way in which a guideline is constructed, worded and organised makes a difference to its uptake. Guidelines with visual components are more readily implemented than written guidelines (Prior, Guerin & Grimmer-Somers 2008).

Health care providers' readiness to adopt guideline recommendations reflects their capacity and willingness to reflect on, and change their behaviours. This assumes that they know what they need to know, are able to measure their performance, embrace new concepts, and reflect on changes to their practice in terms of improved patient health outcomes, and/or more cost effective practices.

Guideline implementation and evaluation of guideline effectiveness often involves iterative and interlinked qualitative and quantitative research designs. These are needed to tease out the complexities of the current best evidence versus current clinical practice, behaviour change and intention to change, barriers to change, incentives required for change and maintenance of changed behaviours. The novelty of guideline implementation research supports the lack of clear evidence for any fool-proof strategy of comprehensively putting a guideline in place.

A recent synthesis of systematic reviews identified the effectiveness of a range of published strategies used to implement guidelines (Prior et al 2008). This review highlighted that multipronged implementation strategies are required for greatest effectiveness in guideline uptake.

Effective strategies are:

- *Educational*; such as continuing medical education, educational meetings and interactive educational sessions (either face to face, using multimedia or the internet) and educational outreach (academic detailing) that typically consist of practice visits by educators, audit, feedback and peer review.
- *Long-term*; reminders, decision support systems and local opinion leaders maintain health care provider interest after a guideline has been implemented.
- *Patient centric*; patient-specific interventions designed to influence health care provider behaviour via information provided to patients, although the best way to influence patients directly is yet to be determined.

Specific interventions may be more effective for health care providers at different stages of behaviour change (Procheska, DiClemente & Narcross 1992a; Procheska, Narcross, Fowler et al 1992b) particularly when introducing guideline-based recommendations which require radical changes in practice behaviours (Michie, Johnston & Araham 2005).

Suggested implementation strategies

The guideline development team recommends a comprehensive linked set of strategies with which to disseminate the *NHMRC Guidelines for the Screening, Prognosis, Diagnosis, Management and Prevention of Glaucoma*.

Barrier analysis

Full analysis of barriers to guideline implementation, relevant to specific health care provider groups, is required in order that barriers can be proactively and effectively addressed. It is important to identify whether any recommendations run contrary to current practice, and consider the issues related to changing practice, in order to successfully adopt the new evidence-based recommendations.

Opinion leaders

Identification and engagement of national and local opinion leaders may be a useful strategy to raise and maintain health care provider interest prior to, during, and after guideline implementation.

Mass media

These guidelines will be readily available on the NHMRC website, as well as on relevant stakeholder websites and offered as a link in the Map of Medicine (www.mapofmedicine.com). The Map of Medicine is a world-wide linkage of guidelines from a variety of reputable sources, and a link between the Map of Medicine and these guidelines.

Media releases could be sent to all peak industry and health bodies in Australia, all relevant Government departments and agencies, and key industries in which glaucoma is a concern. These media releases should inform recipients of the key recommendations of the guideline, its purpose, how it will be implemented and its relevance for stakeholders. The media release should also indicate expected outcomes of guideline implementation.

Vignettes could be produced to highlight controversial recommendations, or general areas of practice which may need to change, based on the guidelines. These vignettes could be filmed with actors and made available on the NHMRC website for *e-learning*. These vignettes could also be used as case presentations for professional development programs, and for health care provider discussion groups.

Consumer guide

An easy-to-read consumer guide will be produced in printed and electronic forms. This should include as many of the recommendations as are relevant from the full guideline, and a section on Frequently Asked Questions. The consumer guide should provide clear descriptors of glaucoma, as well as statements of best evidence for its diagnosis and management.

The e-version should be made available on the NHMRC and Glaucoma Australia websites www.nhmrc.gov.au and www.glaucoma.org.au in forms that can be readily downloaded and printed. Printed versions should be provided to all health care providers for use in discussions with patients.



Continuing medical education

There are a number of different mechanisms for incorporating guidelines into continuing medical education. Consideration may be given to online learning, quick quiz formats and workshops or a more traditional face-to-face approach. Health care providers should receive professional practice credits for engaging in formal learning about these guidelines.

Education sessions could be provided widely across Australia using a ‘road show’ approach to disseminate the key guideline recommendations to health care providers as appropriate. The sessions should be formal, professionally presented, and endorsed by the relevant peak industry bodies and professional associations. These sessions should be conducted by respected peer leaders and clinical champions, and provided in a multidisciplinary forum so that guideline-uptake discussions can enhance multi-disciplinary team decision-making and treatment.

Discussions during the education sessions should provide opportunities to consider controversial recommendations relevant to clinical practice.

Incentives to adopt more radical guideline recommendations should be considered, particularly where these run contrary to common practice and/or indicate that guideline uptake will result in significant cost savings and significant health improvements for individuals with glaucoma.

Multimedia and interactive learning

Formal health care provider meetings and education sessions should incorporate interactive educational activities where possible. These should include 1:1, small groups, or multi-disciplinary team presentations using multimedia, or discussion boards/chat rooms on the internet to sustain interest after the presentation.

Didactic lectures on guideline recommendations should be avoided.

Educational outreach

Academic detailing is a strategy that assists health care providers to improve the quality and safety of their care by fitting guideline recommendations to their practice. Academic detailing is usually assisted by dedicated educators who may also be respected health care providers. Reminders and decision support systems may be useful strategies to assist in guideline implementation.

Web site

A Frequently Asked Questions section will be hosted on the NHMRC website, and/or relevant professional association websites to support ongoing interest in guideline uptake. The answers should be provided by respected peer leaders. Moderated discussion boards could also be used to stimulate debate.



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■ CHAPTER 4

The role of population screening

Recommendation 1

Screen high risk groups

Introduction

The cost-effectiveness of general population screening for glaucoma has not been clearly established.

Current literature provides no consensus regarding the timing or frequency of population screening. Population screening does not have to be limited to glaucoma detection, as it could screen for eye disease more broadly.

An optimal test, or group of tests for glaucoma screening has not been identified. A number of tests are potentially feasible for detecting glaucoma in a screening program, including optic disc assessment, visual field (VF) assessment, intraocular pressure (IOP) and angle assessment (Burr, Mowatt, Hernández et al 2007; European Guideline Society [EGS] 2008). Guidelines suggest that perimetry (frequency doubling technology) also shows promise as a population-screening tool (American Academy of Ophthalmology [AAO] 2005b).

There is consensus in the literature that targeted screening of individuals at-risk of glaucoma may be warranted. Targeted screening may be more cost-effective in specific sub-groups of the population such as older adults, African descent populations, and those with a family history of glaucoma. Further research is required to support this. This guideline details the evidence for risk factors in the development and progression of glaucoma. For specific recommendations concerning the identification of risk, refer to Chapter 6.

There is no consensus in the literature regarding which health care providers should perform population screening. There are a number of health care providers with the skills and capacity to perform the appropriate tests. However, should a screening schedule be proposed in the future, local resources, inter-professional relationships, practice guidelines and legal indemnity will help determine the most appropriate screening approach at any given location.

There is limited information regarding the use of screening in glaucoma types other than primary open angle glaucoma.



Evidence Statement

- Evidence strongly supports a screening approach that targets individuals at higher risk of developing glaucoma, rather than the general population.

POINT OF NOTE

It is beneficial to use more than one modality when screening for glaucoma.

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■ CHAPTER 5

Prognosis: Understanding the natural history

Recommendation 2

Reduce intraocular pressure

Recommendation 3

Monitor visual field and determine rate of any field loss

Recommendation 4

Assess risk of conversion from ocular hypertension to glaucoma

Good Practice Points

- Patients at low risk of conversion should be considered for monitoring
- Patients at high risk of conversion should be considered for treatment
- Educate patients on the risks for consequences of conversion to glaucoma

Introduction

The natural history of glaucoma is poorly defined and heterogeneous. There is a subgroup of people with ocular hypertension (OH) or early primary open angle glaucoma (POAG) in whom there is either no disease progression or the progression is so slow that the condition will never exert a significant effect on vision. An individual's risk of progressive and sight-threatening glaucoma cannot be predicted with precision, however there is improving evidence to specifically identify candidates for treatment. If treatment decisions wait until there are overt signs of disease, this generally results in irreversible optic damage and likely disease progression. Early treatment reduces the number of individuals who develop visual field (VF) defects. The progression of visual defects from acute or poorly controlled glaucoma may lead to rapid damage and permanent loss of vision. This can have devastating consequences. However, intervention is sometimes associated with significant side effects. Therefore, it is critical to appropriately target candidates for intervention.

Normal tension glaucoma

There is sound evidence that medical treatment is effective in preserving VF in people with normal tension glaucoma (NTG) (Sycha, Vass, Findal et al 2003). The Collaborative Normal Tension Glaucoma Study (CNTGS 1998) demonstrated that when subjects with cataracts are removed from analysis, there are progression rates of 12% for treated cases versus 35% for non-treated cases. This demonstrates the beneficial effects of treatment. However, treatments carry significant side effects (e.g. development of cataracts), and as such, the trade-off between risk and benefit should be carefully considered in each case (Sycha et al 2003).



The Collaborative Normal Tension Glaucoma Study (1998) identified a 10-fold range in deterioration rates in VF from -0.2dB/year to -2.0 dB/year, illustrating the marked variability in natural rates of deterioration in NTG. This variability prevents prediction of individual rates of VF loss. These guidelines provide recommendations for a standard process for monitoring in Chapter 8.

Evidence Statements

- Evidence strongly supports reducing intraocular pressure in patients with normal tension glaucoma, in order to preserve the visual field and reduce glaucomatous progression rates.
- Evidence strongly supports monitoring rates of visual field loss in patients with normal tension glaucoma.

Communication with patients

While lowering intraocular pressure slows or halts glaucoma progression, all interventions carry risk. Potential benefit and possible harm (the therapeutic index) need to be balanced carefully, with patient involvement where possible, in decision making.

Ocular hypertension

The majority of patients with OH will not progress to POAG in the short term (90% will not convert within five years) (Burr, Mowatt, Hernandez et al 2007). Within five years however, 9.5% of untreated patients will progress to POAG, compared to 4.4% of medically treated patients (Burr et al 2007).

Patients with an initial intraocular pressure (IOP) of 26mmHg or more are more at-risk of progressing to glaucoma. Conversion time to POAG from OH is significantly shorter for individuals not undergoing treatment (Fleming, Whitlock, Beil et al 2005).

It is reported that 37% of optic nerve fibres need to be lost before a field defect can be identified on VF testing (Kerrigan, Zack, Quigley et al 1997; Quigley, Nickells, Kerrigan et al 1995). Therefore undetected progression may be occurring in untreated individuals because current standard automated perimetry is insufficiently sensitive to detect functional loss at this stage of disease. This highlights the need for using the most sensitive methods of VF testing and structural assessments for patients with OH.

Risk factors for progression to glaucoma include elevated IOP, increased cup:disc ratio, older age, and thinner corneas (Friedman, Wilson, Liebmann et al 2004). There is also strong evidence that central corneal thickness (CCT) is a reliable indicator for the risk of conversion from OH to glaucoma.

The strongest evidence links the likelihood of conversion to poorly controlled and high IOP. In the Ocular Hypertension Treatment Study (Gordon, Beiser, Brandt et al 2002; Gordon, Torri, Miglior et al 2007; Kass, Huerer, Higginbotham et al 2002), univariate and multivariate analyses identified that every 1mmHg increase in mean IOP level was associated with a 10% increased risk of conversion from OH to glaucoma. These guidelines provide recommendations for a standard format for assessing risk (see Chapter 6) and monitoring (see Chapter 8).

Evidence Statements

- Evidence strongly supports assessing risk of conversion of ocular hypertension to glaucoma, using factors such as intraocular pressure and central corneal thickness, in order to guide decision-making concerning which patients with ocular hypertension warrant treatment.
- Evidence strongly supports intervention for individuals with ocular hypertension and major risk factors for the development or progression of glaucoma, in order to reduce the risk of visual loss within their expected lifespan.
 - Major risk factors for developing glaucoma include elevated intraocular pressure, increased cup:disc ratio, disc rim haemorrhage, reduced central corneal thickness, older age, strong family history and ethnicity.
 - Major risk factors for glaucoma progression include elevated and/or fluctuating intraocular pressure, increased cup:disc ratio, disc rim haemorrhage and reduced central corneal thickness.
- Evidence strongly supports careful monitoring, rather than active treatment of patients with ocular hypertension and low-risk status.
- Evidence strongly supports monitoring in order to detect conversion to glaucoma for all patients with ocular hypertension, frequency depending on other identified risk factors. Refer to Table 8.2 on p100.

Communication with patients

It is essential that patients understand the risks for, and consequences of, progression to glaucoma and the value of treatment.

Rates of conversion to glaucoma are initially low, however any progression and visual loss is irreversible. Timely treatment can reduce the chance of progression and/or conversion by 50%.

Early primary open angle glaucoma

The literature provides sound evidence that without treatment, individuals with OH and early POAG will convert more rapidly to advanced stages of the disease, with the inherent risks of VF loss.

A recent systematic review reports an estimate of the likely time to progress to blindness from open angle glaucoma without treatment as 23 years, and with treatment, as 35 years (Burr et al 2007). Mathematical model data presented by Burr et al (2007) concerning patients with OH and glaucoma shows a linear rate of blindness of 9% in both eyes at 20 years after diagnosis, and 26% unilateral blindness at the same follow-up point.

Hattenhauer, Johnson, Ing et al (1998) provide the following estimation of time to blindness. Follow-up of subjects with diagnosed glaucoma found that after 20 years, 22% were bilaterally blind and 54% were unilaterally blind (Hattenhauer et al 1998; Oliver, Hattenhauer, Herman et al 2002). The risk of blindness in one eye in treated classic glaucoma was 50% at 17 years in those diagnosed between 1965 and 1980 at the Mayo clinic (Burr et al 2007). Without treatment it would have been much more rapid. Recent advances in treatment and earlier diagnosis have probably improved the prognosis. Indicative timelines to blindness for glaucoma and OH are reproduced below from Hattenhauer et al (1998 p1202-1203).

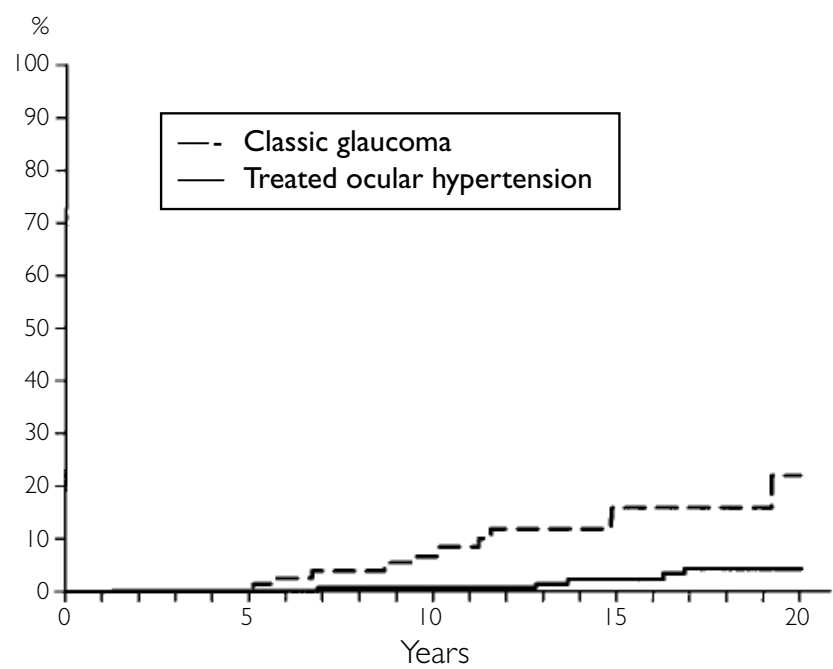


Figure 2: Kaplan-Meier cumulative probability of glaucoma-related blindness in both eyes for treated ocular hypertension and classic glaucoma

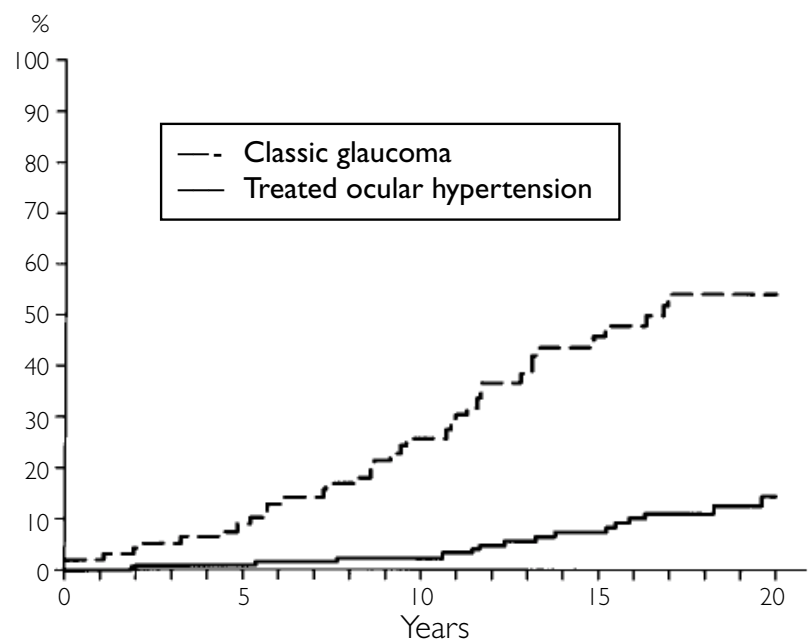


Figure 4: Kaplan-Meier cumulative probability of glaucoma-related blindness in at least one eye for treated ocular hypertension and classic glaucoma.

Evidence suggests that topical pressure-lowering treatment is effective for most individuals, as it reduces the rate of progression of OH (Maier et al 2007) or early POAG (de Moura, Paranhos & Wormald 2007). Therefore an individual's prognosis may be significantly improved by undertaking appropriate treatment. The trade-offs between treatment benefits and side effects should be considered on a case-by-case basis.

There is a substantial risk of developing cataracts with all glaucoma interventions. It is thus important to assess an individual's risk of developing cataracts and to monitor this on an ongoing basis, whilst undergoing treatment. There is a need to balance treatment benefits with side effects. The aim of treatment thus may be to minimise glaucomatous progression and congruently reduce the risk of visual loss within an individual's lifetime, rather than to prevent any level of glaucoma progression (European Guidelines Society [EGS] 2003). These guidelines provide recommendations for risk assessment (Chapter 6) and therapeutic interventions (Chapters 9 and 10).

Evidence Statements

- Evidence strongly supports implementing appropriate management plans for patients with early primary open angle glaucoma in order to reduce the risk of visual loss, and minimise glaucomatous progression within the patient's expected lifespan.
- Evidence strongly supports management plans that are based on an evaluation of the relative benefits and risks of treatment for each patient with glaucoma.

Communication with patients

With treatment 20 years ago, the average time to unilateral blindness for patients with primary open angle glaucoma was approximately 17 years. Untreated patients progress at approximately twice the speed of treated patients. In the last 20 years the rates of glaucoma blindness have dropped due to earlier diagnosis and more effective intraocular pressure-lowering treatment which significantly improves prognosis in the majority of cases. It is therefore important to comply with treatment and discuss any concerns with treatment with your health care provider.

Advanced primary open angle glaucoma

Rates of progression in subjects with high IOP (>30mmHg) are generally acknowledged to be greater than those previously described by early stage population-based studies. Patients with more severe glaucoma at diagnosis (i.e. those diagnosed later) are more likely to go blind (Oliver et al 2002).

There is scant evidence on the impact of risk factors on the progression and outcomes of patients with severe and advanced glaucoma. The results of the Advanced Glaucoma Intervention Study reported by Friedman et al (2004) suggest that older age, lower formal education, male gender and diabetes are significant risk factors for the progression of advanced glaucoma to blindness.

Reduction in maximal IOP and IOP fluctuation has some benefits for some patients, even in the advanced stage of glaucoma. However not every individual will gain the same benefits from treatment. A larger reduction in IOP is required to prevent progression in patients with more advanced glaucoma, when loss of vision is threatened. Patients with IOP below 14mmHg are reported to have the least progression (Tuulonen, Airaksinen, Erola et al 2003). Target IOPs are discussed in Chapter 7.

Communication with patients

Higher rates of progression and visual loss may occur in patients who have been diagnosed late, or who already suffer from more advanced forms of glaucoma. However, evidence continues to support the benefits of active intraocular pressure reduction, even when patients have advanced stage glaucoma.

Angle closure glaucoma

Primary angle closure glaucoma is a generic term for a group of related conditions without physical or inflammatory causes leading to narrowing, then closure of the angle, finally raised intraocular pressure produces ischemic iris changes and glaucoma-related optic nerve damage. Most patients pass through each of these phases and each of these phases has been given a name and defining features (Yip & Foster 2006).

Primary angle closure suspect (PACS) is an anatomical predisposition to closure with signs of narrowing of the angle (appositional contact between iris and trabecular meshwork) but without permanent occlusion or signs of adhesion (synechiae) between the iris and trabecular meshwork.

Primary angle closure (PAC) is a partially or totally closed angle with synechia and/or raised intraocular pressure. The optic disc and visual field are still normal but the iris shows signs of ischemic insult such as whorls or small anterior lens opacities (glaucomflecken) are present.

Primary angle closure glaucoma (PACG) includes PAC with glaucomatous changes in the optic disc (neuroretinal rim loss, cupping and excavation) along with visual field changes.

The treatment of primary angle closure-related glaucoma is two-fold; one is to manage the compromised angle and the other is to manage the glaucomatous nerve damage which is no different to the management of primary open angle glaucoma. Moreover, the prognosis regarding visual field and optic disc damage is thought to be identical, depending upon the pressure and patient susceptibility, so the previous section on primary open angle glaucoma prognosis is thought to pertain to angle closure.

The rate of developing PAC in 129 Americans classified as PACS and followed for up to five years was found to be 19.4% after 2.7 years (Wilensky et al 1993). The risk of progressing from PACS to PAC in Indians is 22% at five years (Thomas et al 2003a). Very few Indian patients with PACS progress to PAC 4 years after laser iridotomy (Pandav et al 2007).

Rate of progression from PAC to primary angle closure glaucoma. In untreated Indians is approximately 37% over several years (Thomas et al 2003b). Following laser iridotomy this rate drops to 3% at 2 years in Mongolians (Nolan et al 2000) and 9 - 11% in Indians at 4 to 5 years (Pandav et al 2007; Thomas et al 2003b).

Rate of progression of treated primary angle closure glaucoma. Laser iridotomy is commonly thought to reduce the rate of progression by maintaining an open angle and allowing greater efficacy of medications. However, approximately 48% of Mongolian subjects with primary angle closure glaucoma who have laser iridotomy will still require glaucoma drainage surgery within two years of the iridotomy (Nolan et al 2000). These reported rates are similar to those in an Indian population (Pandav et al 2007).

In summary, patients with primary angle closure require regular monitoring of their angles as well as other aspects of their glaucoma management and appear to be best served by earlier laser peripheral iridotomy. However, this does not always eliminate the need for future surgery but appears to greatly reduce the risk of their progression to primary angle closure glaucoma. There appears to be some ethnic variation in susceptibility and also rates of progression. Even after laser iridotomy is performed, a significant proportion of patients will progress and require surgery. The type of surgery best suited to their needs can often be complicated and is further discussed in the monitoring and treatment chapters.

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■ CHAPTER 6

Identifying those at risk of developing glaucoma

Recommendation 5

Identify and assess glaucoma patients and suspects (those at high risk of the disease).

Good Practice Points

- Identification is essential in order to make therapeutic decisions about whom to treat and how aggressively to treat each person.
- All involved in their health care need to adopt a standard approach to risk factor assessment for each individual.

Recommendation 6

Detect glaucoma earlier

Good Practice Points

- Perform regular eye health checks for Caucasians over the age of 50, and for African-descended people over the age of 40.
- Perform regular eye health checks for all first-degree relatives of glaucoma patients, commencing 5-10 years earlier than the age of onset of glaucoma in their affected relative. Remind all glaucoma patients to alert first-degree relatives of the benefits of early and regular eye checks.
- Survey for glaucoma particularly in patients greater than 50 years old, any myopia, abnormal blood pressure, a history of migraine, diabetes, peripheral vasospasm, eye injury and ongoing steroid use.
- Monitor for glaucoma particularly in patients greater than 70 years old, with IOP >21 mmHg, large and/or asymmetric cup-to-disc ratio (compared with disc size), disc haemorrhage, and thin central corneal thickness.

Recommendation 7

Assess risk of progression of glaucomatous damage

Good Practice Points

- Calculate the rate of visual field loss regularly (for example review every four months) for the first two years, and then less frequently (for example every six months) thereafter if stable. This will depend on the health care setting and the individual patient's risk of progression.
- Reduce IOP by 20-50% in patients with glaucomatous optic neuropathy depending on the level of risk to preserve visual field and to reduce progression.
- Reduce IOP more aggressively in those patients with greater risk factors for progression.
- Patients diagnosed late, with more advanced glaucoma damage, suffer higher rates of progression of visual loss. More aggressive IOP reduction is required.

Introduction

There is a strong body of research, developed over many years that has established the risk factors for glaucoma development and progression. However, a standard approach is still required to organise these risk factors into a hierarchy of risk, including the best ways of assessing them, and identifying how they interact with disease incidence, prevalence and progression. There are ongoing questions regarding which patients should be treated, how vigorously to treat them, and when to initiate treatment. Overall, the literature presents general agreement regarding the significant association between elevated intraocular pressure (IOP), advancing age, ethnicity and family history concerning the risks for developing most types of glaucoma.

Risk calculators have been developed to facilitate the application of research findings into clinical practice. Risk calculators work by applying risk-prediction coefficients from multivariate analysis from clinical trials and epidemiological studies into risk-modelling formulae that can be applied to individual patients. Risk calculators are based on an assumption that each patient comes from a similar population as participated in the clinical trial. Health care providers enter the patient's clinical findings into the formulae to calculate the likelihood of that patient developing glaucoma, or progressing to another stage of the disease. Risk calculators have also been useful for assisting patients and their health care providers to make decisions about treatment (Mansberger & Cioffi 2006; Gordon, Torri, Miglor et al 2007).

However, risk calculators tend not to include confidence intervals (which are often quite large) and thus can give a false impression of reliability in terms of prediction. The performance of the predictive models derived from the Ocular Hypertension Treatment Study was assessed by Meirdeiros, Zangwill, Bowd et al (2007). They concluded that the Ocular Hypertension Treatment Study-derived predictive models performed appropriately in independent patient samples. Their reduced model included age, IOP and central corneal thickness (CCT). The full model included these and visual field (VF) pattern standard deviation and vertical cup:disc ratio. Both models predicted conversion of ocular hypertension (OH) to glaucoma at five years in 70% of cases. A prediction score of 50% indicates random chance, i.e. no additional predictive value whereas 100% indicates perfect prediction. Whilst these models have some value, they are far from perfect. Future refinement of optic nerve damage indices and indicators of nerve structure should improve the accuracy of these models.

The majority of risk factors which are significantly associated with the development of glaucoma can be identified and measured using a comprehensive patient history. However other important

risk factors can only be identified through ocular examination by suitably trained health care providers. This highlights the importance of basing diagnosis and treatment decisions on multiple sources of information.


Evidence Statement

- Evidence strongly supports a standard approach to assessing risk factors when diagnosing patients with glaucoma, and also when identifying patients who may develop glaucoma.
Standard risk assessment is also essential when making therapeutic decisions regarding who to treat, when to treat and how aggressively to treat.

To date, there has been minimal organisation of risk factors into a simple usable approach for health care providers. This would be valuable, in particular for those primary health care providers who are dependent on history taking alone, and who lack the capacity to undertake an objective ocular examination.

Table 6.1 outlines risk factors that can be elicited from a patient history and may be used by primary health care providers who are without the facilities and/or expertise to undertake a full ocular examination. IOP is included as it may be mentioned by patients themselves, or the information may be contained in medical records. The risk factors in Table 6.1 are organised according to both strength of risk and strength of evidence, linking them to developing glaucoma. The data which informed the development of Table 6.1 is provided in the Appendix to this chapter.

Table 6.1: Risk factors from patient history

Strength of risk	Strength of evidence		
	A – B	C	D
EXTREMELY HIGH 12x or more	IOP >21mmHg Age over 80 years		
HIGH 3x or more	Age over 50 years Family history Specific ethnic origin		
MODERATE 1.5x or more	Diabetes Myopia Rural location		
LOW over 1x		Smoking	
Risk stated without statistics		Steroid use	Migraine Eye injury High blood pressure
<div style="text-align: center;">  </div> <div style="display: flex; justify-content: space-around; margin-top: 10px;"> <div style="border: 1px solid black; padding: 5px; text-align: center;">Refer for eye exam</div> <div style="border: 1px solid black; padding: 5px; text-align: center;">Surveillance</div> </div>			

N.B. The presence of ocular symptoms indicating possible glaucoma (as described in Chapter 7) immediately elevates the patient into the high-risk group and warrants a full ocular examination.

Surveillance activities include, but are not limited to, patient education of risk, consideration of concurrent medications and encouraging attendance for basic ocular care checks.

Risk factors identified from patient history

Age

Advancing age is a major risk factor for the development of glaucoma. The prevalence of glaucoma is four to 10 times higher in the older age groups than in individuals in their forties (American Optometric Association [AOA] 2002). In the Australian Melbourne Visual Impairment Project, this difference was substantially larger. It was 17 times more likely that participants aged 80 years and older would have glaucoma, than participants aged less than 50 years (Weih, Manjan, McCarty et al 2001). Pooled data reported by Burr, Mowatt, Hernandez et al (2007) indicate that the overall prevalence of open angle glaucoma (OAG) was 0.3% (95% CI 0.1% to 0.5%) in people aged 40 years, and increased to 3.3% (95% CI 2.5% to 4.0%) in people aged 70 years. Damage to the optic nerve from glaucoma is uncommon before the age of 50 years in Caucasians, however it appears to occur at least a decade earlier in people of African descent (AOA 2002).

Evidence Statements

- Evidence strongly indicates that Caucasians over the age of 50 years undertake regular ocular health checks.
- Evidence indicates that individuals of African descent over the age of 40 years undertake regular ocular health checks.

POINT OF NOTE

Caucasians over 50 years of age are at moderate risk, and those over 80 years of age are at high risk of developing glaucoma. A rational approach to screening for glaucoma is therefore required for Caucasians over the age of 50 years. For Caucasians without other significant risk factors for glaucoma, a glaucoma assessment could be included in the health assessment for people aged 45-49 years (inclusive) who are at risk of developing chronic disease and the health assessment for people aged 75 and older using one of four time-based Medicare Item Numbers 701 to 707 undertaken by general medical practitioners.

Family history and genetics

A family history of glaucoma puts an individual at greater risk of developing the disease (AOA 2002). In close relatives of individuals with primary open angle glaucoma (POAG), the prevalence is three to six times that of the general population. The incidence of the disease in first-degree relatives is three to five times that found in the general population. The 22% lifetime risk for glaucoma found in relatives of patients with glaucoma is almost 10 times that of controls (AOA 2002).

Burr et al (2007) conducted a meta-analysis of four studies that indicated an association between developing OAG and a positive family history, with the strongest association being observed between siblings. However, Burr et al (2007) expressed reservations about this association, noting that most of the studies relied on the verbal reporting of family history of glaucoma rather than clinical examination. Thus the results may be open to misclassification.

Mutations in transcription factor genes have been found to be responsible for developmental disorders associated with childhood glaucoma (AOA 2002). The following genetic syndromes have high associations with childhood glaucoma: Nail Patella Syndrome with the *LMX1B* gene, Axenfeld Rieger Syndrome/Anterior segment dysgenesis with the *PITX2* and *FOXC1* genes and Aniridia with the *PAX6* gene. Patients with these syndromes or mutations are usually followed closely for glaucoma (Mackey & Craig 2003). Congenital glaucoma is associated with *Cyp11B1* mutations in

17% of Australian families. Screening of children with *Cyp1B1* mutation can be used to predict the risk of subsequent offspring having congenital glaucoma (DiMasi, Hewitt, Straga et al 2007).

There is some evidence that adult-onset POAG is linked to mutations in the same genes. The situation is complex and it is likely that multiple mutations in more than one gene may be involved, given that POAG is likely to be inherited as a complex trait. Current research has identified more than 30 mutations of the myocilin gene alone, with connections to POAG in different ethnic groups. Current genetic screening for adults at-risk of glaucoma is not yet available. However, there is evolving evidence for genetic screening via a buccal swab. Readers may wish to access *The Human Genetics Society of Australasia* website www.hsga.com.au/ or the Australian and New Zealand Registry of Advanced Glaucoma website www.anzrag.com/ for further information.

Evidence Statement

- Evidence strongly supports that all first-degree relatives of individuals diagnosed with glaucoma are considered at high risk of developing glaucoma themselves. It is recommended that they undergo a full ocular examination by a qualified health care provider, and receive ongoing monitoring for the development of glaucoma.

POINT OF NOTE

A primary health care provider should advise all patients with glaucoma to inform all close relatives to undergo ocular examination as early as possible. This should occur at the age that is recommended for their ethnic group, or five to ten years earlier than the age of onset of glaucoma in their relative.

Evidence Statement

- Evidence strongly supports the need for all patients diagnosed with glaucoma to alert first-degree relatives of the benefits of ocular examination.

POINT OF NOTE

It is possible to screen children from families with *Cyp1B1* mutations, as 17% of Australian families with congenital glaucoma have a mutation in this gene. Identifying *Cyp1B1* mutations can be used to predict the risk of subsequent offspring having congenital glaucoma.

Ethnic origin

‘Black’ and ‘white’ were common terms for ethnicity reported in the systematic reviews sourced for these guidelines. There was a paucity of detail concerning the exact racial origin that was incorporated within these terms. In the majority of cases where some specification was made, ‘black’ referred to those of African origin and ‘white’ to those of Caucasian origin. There was nothing to imply that black populations included indigenous populations as relevant to the Australian context. Because of this lack of racial clarity, we report the racial groups as described in the literature.

People of African descent have been identified as having an age-adjusted prevalence for POAG, 4.3 times greater than Caucasians. Furthermore, damage to the optic nerve from glaucoma is



uncommon before the age of 50 years in Caucasians, however it is reported at least a decade earlier in people of African descent (AOA 2002).

There was limited data regarding the prevalence and incidence of glaucoma within the Indigenous population of Australia. The Australian Bureau of Statistics [ABS] (2004) 'National Aboriginal and Torres Strait Islander Health Survey 2004-05' provided data on long-term eyesight problems. Eyesight problems were the most commonly reported long-term health condition among Aboriginal and Torres Strait Islander people. However, glaucoma was not a condition specifically reported in the data. Aboriginals and Torres Strait Islanders are not considered to be at any greater risk of glaucoma than Caucasians.

Prevalence of primary angle closure glaucoma (PACG) is highest among those of Asian or Inuit descent, with rates in these populations reported to be three to 10 times greater than in other ethnic groups (Schmier, Halpern, Jones et al 2007).

POINT OF NOTE

The Working Committee note a new report 'National Indigenous Eye Health Survey: Minum Barreng Full Report' prepared by Anna-Lena Arnold, Ross A. Dunn and members of the National Indigenous Eye Health Survey Team (NIEHS) which was published 2 October 2009.

Evidence Statements

- Evidence strongly indicates that individuals of African descent are at higher risk of open angle glaucoma than Caucasians.
- Evidence strongly indicates that individuals of Asian ethnic origin are at increased risk of angle closure, compared with other ethnic groups.

POINT OF NOTE

For individuals from high-risk ethnic backgrounds, appropriate surveillance activities include, but are not limited to, patient education regarding glaucoma, individual risk, consideration of concurrent medications, and advice to attend regular standard ocular examinations.

Diabetes

The association between diabetes mellitus and POAG is controversial. The current position is summarised by Bonovas, Peponis, Filioussi et al (2004b) who conclude that people with diabetes are at a significantly increased risk of developing POAG, and should be targeted for blindness-prevention programs. Moreover, Burr et al (2007) reported that the prevalence of OAG among participants with diabetes varied from 1.2% to 5.5%, with a pooled estimate of 3.3% (95% CI 1.8% to 4.8%). There is almost twice the risk of OAG onset among individuals with diabetes as compared with those without diabetes (RR 1.93, 95% CI 1.38 to 2.69).

Myopia

Burr et al (2007) identified a number of studies which reported, after adjustment for age, a two to five times higher prevalence of POAG in patients with myopia. They highlighted that these studies are potentially subject to selection bias, due to the lack of standardised definition of myopia, the association of myopia with a number of non-glaucomatous VF defects and the difficulty of

assessing myopic discs for glaucomatous damage (Burr et al 2007). The prevalence of OAG among people with myopia ranged from 1.4% to 4.3%, with a pooled estimate of 2.7% (95% CI 1.5% to 3.9%). The pooled relative risk of OAG among participants with myopia (any definition) compared with non-myopic was estimated to be 1.88 (95% CI 1.53 to 2.31). A dose-response relationship between OAG and myopia has been postulated (the higher the myopia the more likely an individual would be to develop OAG). This relationship can be observed in the Australian Blue Mountains Eye Study (Mitchell, Smith, Attebo et al 1996), reporting an Odds Ratio of 3.3 for those with moderate to high myopia (≥ -3.0) compared with 2.3 in those with low myopia (≥ -1.0 to < -3.0). Furthermore, glaucoma and myopia have a strong familial basis and thus may share a common genetic link.

Evidence Statement

- Evidence strongly indicates that individuals with myopia requiring optical correction are considered at increased risk of glaucoma.

Environment and location

Key findings relevant to the Australian population reported by Madden, Simmons, McCarty et al (2002) were that rural populations have an increased prevalence of glaucoma. The Relative Risk for age-adjusted rural populations is 1.7 (95% CI 1.1 – 2.7) for having undiagnosed or probable glaucoma. Madden et al (2002) were unable to explain why this occurred. It is suggested that prevalence may appear higher, as rural patients are more likely to present acutely due to limited availability of health services and resources.

The majority of the information used by Madden et al (2002) was provided by the Australian Institute of Health and Welfare databases, the National Trachoma and Eye Health Program of the Royal Australian and New Zealand College of Ophthalmologists, and the Melbourne Visual Impairment Project.

Australian rural and remote populations

Primary open angle glaucoma is rare in Aboriginal and Torres Strait Islander populations. However primary open angle glaucoma has been described in Aboriginal and Torres Strait Islander patients with mixed ancestry. Practitioners are encouraged to provide patients with information about the prevalence and incidence of glaucoma and to encourage Aboriginal and Torres Strait Islander people, in particular those patients with diabetes melitus, to participate in regular eye checks.

Correctly identifying Indigenous status is an important step in determining the degree of risk. The Australian Institute of Health and Welfare has established that self reporting is the most accurate means of ascertaining an individual's Indigenous or non-Indigenous status. Accordingly, a set of standard questions has been developed to ensure accurate capture of this information (AIHW 2010).

The most common cause of glaucoma is traumatic or diabetic induced neovascular glaucoma. These are less common forms of secondary glaucoma, which are not described nor their management covered in this NHMRC glaucoma guidelines document. We summarise the knowledge to date concerning glaucoma in Aboriginal and Torres Strait Islanders.

The late Professor Fred Hollows conducted the National Trachoma and Eye Health Program amongst remote Aboriginal communities in the 1970s. Anecdotally he did not note a case of primary angle open glaucoma in the Aboriginals who were screened in these first programs.



The Australian Bureau of Statistics (ABS) (2004) “National Aboriginal and Torres Strait Island Health Survey 2004/05” provided data on long term eyesight problems. Eyesight problems were the most commonly reported long term health condition amongst Aboriginal and Torres Strait Islander peoples. However, glaucoma was not a condition specifically reported.

Several large surveys of vision loss in Aboriginal and Torres Strait Islander populations have been conducted. Long term study of vision loss in people living in from remote Western Australia, including annual surveys over 13 years up until 2007 - examined a total of 920 individuals. No cases of primary open angle glaucoma were recorded (Clark, Morgan, Kain et al 2010). This population study included a high proportion of people aged above 16 years with a mean age of 43. Cases of blindness and visual impairment were identified. The most common causes of blindness and visual impairment were cataract, diabetic retinopathy, refractive error and trauma. Whilst no cases of neovascular glaucoma or traumatic induced glaucoma were found in this survey, anecdotal reports from major teaching hospitals across Australia reveal that such cases occur.

Another large survey examining numerous groups of Aboriginal and Torres Strait Islander peoples across Australia in both metropolitan and remote communities reported its findings in 2010 (Taylor, Xie, Fox et al 2010). 1189 adults (median age 51) were examined with no cases of glaucoma found in the sample population using optic disc photos and Matrix visual field evaluation.

The comparative incidence of glaucoma in 50 year olds is less in Aboriginal and Torres Strait Islander populations generally, by 0.5%. Additionally, the proportion of blindness from glaucoma in the Aboriginal and Torres Strait Islander populations surveyed to date appears to be much less than the 14% commonly seen in non-indigenous population subsets (Yong, Morgan, Cooper et al 2006). Indigenous Australians are less likely to develop primary open angle or angle closure glaucoma, secondary forms of glaucoma, however, are occasionally seen in Aboriginal and Torres Strait Islander people who have had trauma or neovascularisation due mainly to diabetes. These forms of glaucoma are often difficult to treat and generally require referral to a major teaching hospital.

Frequency of visits to eye care providers

Increased time since last visit to an eye care provider was found to be associated with an elevated risk of undiagnosed glaucoma by the Melbourne Visual Impairment Project (Weih et al 2001).

The likelihood of being diagnosed with probable or definite glaucoma rose from no risk (OR=1) when attending an eye care provider in the last year to OR=9.8 (95% CI 3.0—31.3) when attendance had not occurred for three or more years.

Smoking

The evidence supporting the association of smoking with the pathogenesis of POAG is controversial. Although several studies have indicated that smoking is a risk factor for POAG development, other studies have refuted the notion. In a systematic review and meta-analysis by Bonovas, Filioussi, Tsantes et al (2004a), the results of six studies were analysed. This found that current smoking results in a significant increase in the risk of POAG (OR=1.37, 95% CI 1.00–1.87), while past smoking does not affect this risk (OR=1.03, 95% CI 0.77–1.38). Bonovas et al (2004a) concluded that the meta-analysis findings support an association between current smoking and POAG.

Long-term steroid users

Corticosteroids are the main cause of drug-induced glaucoma (Adis International 2004). Steroids administered by any route are associated with increases in IOP. Tripathi, Tripathi and Haggerty (2003) report that 46-92% of subjects with OAG experience an increase in IOP after topical ocular administration of corticosteroids lasting two-four weeks. Medication-induced glaucoma should be

considered a secondary glaucoma related to its external causation (South East Asian Glaucoma Interest Group [SEAGIG] 2003). Steroidal-like substances can also be found in traditional and natural medicines. Case-control and retrospective data suggest that prolonged inhaled corticosteroid use is a significant risk for developing glaucoma; however, the cumulative inhaled corticosteroid use dosage that poses a risk has not been ascertained (Leone, Fish, Szeffler et al 2003).

Evidence Statement

- Evidence indicates that long-term users of steroids by any route of administration are at increased risk of glaucoma, and thus require surveillance.

POINT OF NOTE

Surveillance activities include, but are not limited to, patient education about risk, consideration of concurrent medications, and encouraging attendance at basic ocular checks.

Migraine and peripheral vasospasm

Migraine headache and peripheral vasospasm have been identified as risk factors for progressive glaucomatous optic nerve damage by studies including the Ocular Hypertension Treatment Study (Budenz, Anderson, Feuer et al 2006) and the Blue Mountains Eye Study (Mitchell et al 1996). Peripheral vasospasm has also been proposed as one possible mechanism for, or a factor contributing to, optic nerve damage in glaucoma. This theory is supported by evidence of an association of normal tension glaucoma (NTG) with migraine headaches and Raynaud's syndrome (AOA 2002).

Evidence Statement

- Evidence indicates that individuals with migraine and peripheral vasospasm dysfunction are at increased risk of glaucoma.

Eye injury

Eye trauma is widely accepted as a risk factor for glaucoma. Traumatic glaucoma can occur immediately after a blunt trauma or penetrating injury eye, or years later (Williams 1999). Eye trauma with angle recession is a risk factor for open angle glaucoma. It is usually considered as secondary open angle glaucoma and is therefore not included in studies of POAG. It is uncommon and difficult to quantify, consequently there is little data concerning epidemiology of trauma in glaucoma.

Evidence Statement

- Evidence indicates that individuals with migraine and peripheral vasospasm dysfunction are at increased risk of glaucoma.

Systemic blood pressure

There is a paucity of evidence concerning high systemic blood pressure as a significant risk factor for glaucoma. The literature is equivocal on the association between systemic hypertension and POAG (AOA 2002). There is a complex relationship between POAG and systemic blood pressure, as both patient age and the duration of systemic hypertension impact upon the relationship between hypertension and POAG.

Low systemic blood pressure, including the nocturnal dip, also may pose a risk for NTG according to the AOA (2002). The difference between diastolic blood pressure and IOP, which largely determines perfusion pressure to the eye, appears to be a risk factor for POAG with lower blood pressure being associated with greater risk (Tielsch, Katz, Singh et al 1991).

Evidence Statement

- Ongoing blood pressure monitoring and management is appropriate for all patients at risk of glaucoma.

POINT OF NOTE

Recent publications, which were outside the scope of the literature review undertaken for these guidelines, indicate that reduced ocular perfusion pressure is strongly associated with glaucoma progression.

Risk factors identified through ocular examination

Table 6.2 outlines risk factors for developing glaucoma that can be elicited from a full ocular examination. The risk factors are organised according to strength of risk and strength of evidence. The data which informed the development of this table are provided in the Appendix to this chapter.

Table 6.2: Risk factors from ocular examination

Strength of risk	Strength of evidence		
	A – B	C	D
EXTREMELY HIGH 12x or more	IOP >24mmHg		
HIGH 3x or more	IOP 21-24mmHg		
MODERATE 2x or more		Cup:disc ratio Cup:disc ratio asymmetry Optic disc rim haemorrhage	
LOW over 1x			
Risk stated without statistics			Central corneal thickness
<div> <div>Active management</div> <div>Surveillance</div> </div>			

Intraocular pressure

The literature is clear that high IOP is a significant risk factor for glaucoma. However, the Working Committee highlights that IOP should be considered as a continuum of risk rather than as specific thresholds for concern.

The level of IOP regarded as the threshold for defining increased IOP varies in the published literature. That 95% of the normal population has an IOP between 10 and 21mmHg is the explanation for the traditional use of 21mmHg as being the upper limit of 'normal' for IOP findings (Hatt, Wormald, Burr et al 2006). For individuals with IOP from 20 to 23mmHg, the risk of developing glaucoma is reported as four times greater than for individuals with IOP below 16mmHg. This risk increases exponentially to 10 times when the IOP is ≥ 24 mmHg, and to more than 40 times the risk, when IOP is >30 mmHg (Sommer, Katz, Quigley et al 1991).

Different individuals vary in the susceptibility of their optic nerves to damage at a particular IOP. This susceptibility depends in part upon the individual nerve constitution, systemic factors such as blood pressure and the presence and severity of disease. Individuals with glaucoma who have IOP in the 'normal' range, are labelled normal tension glaucoma. High or fluctuating IOP remains a risk factor for all types and all stages of glaucoma. There is strong evidence that every 1 mmHg increase in mean IOP level is associated with a 10% increased risk of progression from OH to glaucoma, and in progressive glaucomatous damage. These guidelines recommend a standard approach to the assessment of IOP (see Chapter 7).

Evidence Statements

- Evidence strongly supports the assessment of intraocular pressure in all individuals with suspected glaucoma, as it is a significant risk factor for the development of all forms of glaucoma.
- Evidence strongly supports using 21mmHg as the upper limit for normal intraocular pressure.

Alterations in cup: disc ratio and asymmetry

High vertical cup:disc ratio, vertical cup:disc ratio asymmetry, and pattern standard deviation are good predictors of the onset of OAG, as reported in the European Glaucoma Prevention Study (European Guidelines Society [EGS] 2003). This is congruent with the Royal College of Ophthalmologists [RCO] (2004) guidelines which state the risk factors for conversion to POAG as increased cup:disc ratio, cup:disc ratio asymmetry >0.2 , previous history of disc haemorrhage, reduced CCT and retinal nerve fibre defects even in the absence of optic head pathological changes. Cup:disc ratio is a value obtained by dividing the cup diameter by the disc diameter. The closer this value is to 1, the greater the level of tissue loss and therefore damage to the disc.

Evidence Statement

- Evidence supports the assessment of cup:disc ratio, and cup:disc ratio asymmetry, when assessing the risk of glaucomatous damage occurring.



Optic disc haemorrhage

Optic disc rim haemorrhages are significant risk factors for the development of glaucoma, as indicated in the Blue Mountains Eye Study (Mitchell et al 1996). The Ocular Hypertension Treatment Study (Budenz et al 2006) reported that subjects with optic disc rim haemorrhage were twice as likely to progress to glaucoma as those without. The Early Manifest Glaucoma Treatment Trial (Leske, Heijl, Hyman et al 2004) reported that those with optic disc rim haemorrhage were more likely to progress, with a strong relationship being reported between frequency of optic disc rim haemorrhage and risk of progression. Optic disc rim haemorrhage is an effervescent finding and is clearly visible for approximately six weeks after formation. A notch or nerve fibre defect may be left after the resolution of the acute haemorrhage. This can be an indicator of development or progression of glaucoma to a health care provider examining the eye.

Evidence Statement

- Evidence supports past signs, or current presence, of optic disc haemorrhages as significant risk factors for the development and progression of glaucoma.
- Evidence supports more aggressive treatment of patients with ocular hypertension, or glaucoma, who present with optic disc rim haemorrhages, or evidence of past optic disc rim haemorrhages.

Central corneal thickness

Data from the Ocular Hypertension Treatment Study (Budenz et al 2006) suggest that individuals with thinner corneas are at increased risk of developing glaucoma. Corneal thickness is known to affect the calibration of applanation tonometry, commonly used to measure IOP. Thin corneas are associated with a greater IOP than is measured by tonometry and thus people with thin corneas may obtain less accurate IOP readings. Thus, whilst the role of central corneal thickness as a risk determinant of glaucoma still requires clarification, assessment of central corneal thickness is considered to be a useful component of assessment of risk when making a decision to treat a patient with OH (Dueker, Singh, Lin et al 2007).

These guidelines recommend a standard approach to the assessment of IOP and are detailed in Chapter 7.

Evidence Statement

- Evidence supports the assessment of cup:disc ratio, and cup:disc ratio asymmetry, when assessing the risk of glaucomatous damage occurring.

Risk factors for specific glaucoma types and stages

Angle closure

The American Academy of Ophthalmology [AAO] (2005a) states that risk factors for developing angle closure are hypermetropia, family history of angle closure, advancing age, female gender, Asian or Inuit descent and shallow anterior chamber for PACG. However, there is limited quantification of the risk. Medical interactions/effects are also a proposed risk, however even less is known about them. Schmier, Halpern and Jones (2007) state that the higher prevalence of primary angle closure (PAC) and PACG in Asian and certain indigenous ethnic groups (e.g. Inuit) suggests that ethnicity is a risk for that glaucoma type.

These guidelines report medications and conditions associated with the development of angle closure states in Chapter 9.

Evidence Statement

- Expert/consensus opinion suggests that hypermetropia, family history of angle closure, advancing age, female gender, Asian descent and shallow anterior chamber are risk factors for the development of angle closure, and angle closure glaucoma.

Secondary glaucoma

There is no evidence from the secondary literature regarding the risk factors for, or progression of secondary glaucoma.

Progression of established glaucoma

Risk factors for developing glaucoma are not necessarily the same as the risk factors for progression of diagnosed glaucoma. However, the importance of IOP in early stage glaucoma has been underlined by the results of the Ocular Hypertension Treatment Study (Budenz et al 2006), wherein univariate and multivariate analyses found that every 1 mmHg increase in mean IOP level was associated with a 10% increased risk of progression from OH to glaucoma. A meta-analysis of five relevant and adequately powered studies (Maier, Funk, Schwarzer et al 2005) also concluded that using topical pressure lowering medications for primary prevention of glaucomatous VF defects in patients with OH appears to be effective. The Ocular Hypertension Treatment Study (Budenz et al 2006) also reported that subjects with optic disc rim haemorrhage were four to six times as likely to progress to glaucoma as those without optic disc rim haemorrhage. The Early Manifest Glaucoma Treatment Trial (Leske et al 2004) concurred, reporting that patients with optic disc rim haemorrhage were more likely to progress to glaucoma, with a strong relationship established between frequency of optic disc rim haemorrhage and risk of progression.

Evidence Statement

Evidence indicates that factors associated with greater risk of glaucoma progression include elevated/fluctuating intraocular pressure, optic disc haemorrhage, increased severity of glaucomatous disc damage and very low blood pressure. These patients require greater reduction in intraocular pressure.

Progression to visual loss

To date, there is limited evidence of the impact of risk factors on the progression and outcomes of patients with severe and advanced glaucoma. The results of the Advanced Glaucoma Intervention Study (AGIS) studies reported by Friedman, Wilson, Liebmann et al (2004) provide limited evidence that older age at diagnosis, lower formal education, male sex and diabetes are significant risk factors for the progression of advanced glaucoma to blindness.

Reminder to health care providers

Health care providers should use a *patient's history* to elicit information about risk factors that are significantly associated with developing most types of glaucoma:

- elevated or fluctuating intraocular pressure
- strong family history of glaucoma
- advanced age
- African or Asian ethnicity
- current diabetes
- myopia
- rural location.

Health care providers should use a *patient examination* to elicit information about other risk factors that are significantly associated with developing most types of glaucoma:

- elevated or fluctuating intraocular pressure
- significant alterations in cup:disc ratio and cup:disc ratio asymmetry
- nerve fibre layer defects
- optic disc haemorrhage.

An assessment of these risk factors should aid in therapeutic decision-making regarding who to treat, when to treat, how to treat, and how aggressively to treat.

If appropriate, health care providers may also consider *other risk factors* which have more limited evidence of their association with developing most types of glaucoma:

- central corneal thickness
- current smoking
- current migraine and peripheral vasospasm
- long-term steroid use
- previous eye injury.

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Appendix to Chapter 6

Data which informed the development of Table 6.1 Risk factors from patient history, and Table 6.2 Risk factors from ocular examination in Chapter 6.

RISK FACTOR	Subcategory	Stated increase	Relative risk (95%CI)	Odds ratio (95%CI)	Prevalence (95%CI)	Evidence source
Ethnic origin	Black derived aged 40-49 years				1.23 (0.23-2.24)	Burr et al 2007
	Compared to whites over 40 years	Almost 4x	3.80 (2.56 -5.64)			Burr et al 2007
	Black derived aged 70-79 years				9.5 (5.83-12.48)	Burr et al 2007
	Asian/Inuit (PACG)	3-10x				Schmier et al 2007 citing AAO 2003
Age	Advanced age	4-10x				AOA 2002
	Aged 40 years				0.3 (0.1-0.5)	Burr et al 2007
	Of being diagnosed with definite glaucoma at age:40-49 years (default comparator)			1		Weih et al 2001
	50-59 years			9.5 (1.2-74.9)		Weih et al 2001
	60-69 years			21.5% (2.9-163.7)		Weih et al 2001
	Aged 70 years				3.3 (2.5-4.0)	Burr et al 2007
	70-79 years			52.7 (7.1-391.2)		Weih et al 2001
	Over 80 years	17x				Weih et al 2001
	80-89 years			104.3 (13.6-797.1)		Weih et al 2001

RISK FACTOR	Subcategory	Stated increase	Relative Risk (95%CI)	Odds Ratio (95%CI)	Prevalence (95%CI)	Evidence source
Family history	OAG among participants with a positive family history				6.7 (5.0 to 8.4)	Burr et al 2007 (pooled result)
	To general public	3-6x				AOA 2002
	Lifetime risk compared to control	10x				AOA 2002
	Close relative-age-adjusted risk of OAG	3x	3.14 (2.32 to 4.25)			Burr et al 2007
	Of being diagnosed with definite glaucoma			3.7 (2.0-6.7)		Weih et al 2001
Diabetes	OAG among participants with diabetes				3.3 (1.8 to 4.8%)	Burr et al 2007 (pooled result)
	Risk of OAG onset among people with diabetes when compared with people without diabetes	Almost twice	1.93 (1.38 to 2.69)			Burr et al 2007
Myopia	Risk of OAG in those with myopia				2.7 (1.5 to 3.9)	Burr et al 2007 (pooled result)
	Compared to those without myopia	Almost twice	1.88 (1.53 to 2.31)			Burr et al 2007
IOP	IOP>26mmHg compared to low IOP	12x	12.58 (5.07- 31.24)			Burr et al 2007
	IOP>21mmHg compared to <16mmHg	16x				AOA 2002
3+ years since visit to eye care provider	As yet undiagnosed	7-9x		7.5 (28.6-1.9)		Weih et al 2001
	In rural areas		1.7 (1.1-2.7)			Weih et al 2001

■ CHAPTER 7

Diagnosis of glaucoma

Recommendation 8

Assess with a comprehensive medical history, a full eye examination and investigate appropriately

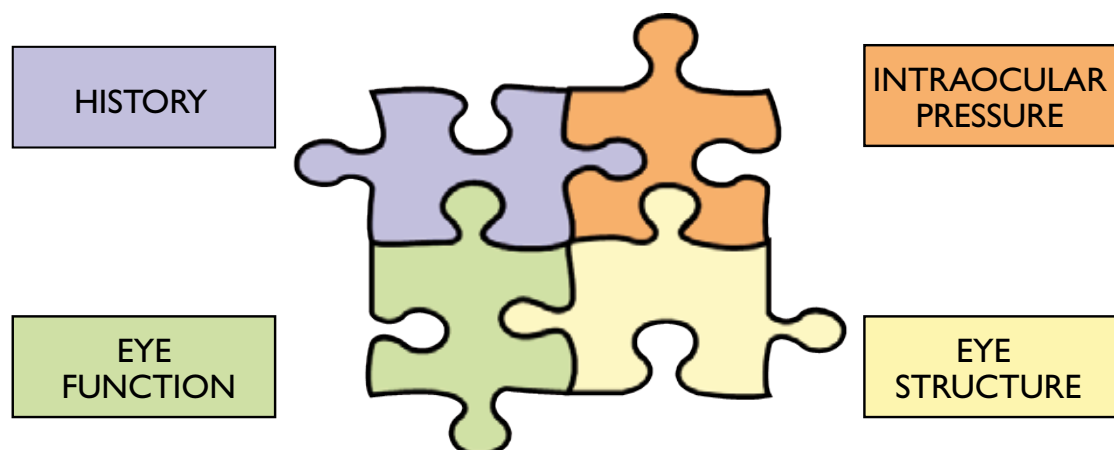
Good Practice Points

- **A comprehensive medical history:** identify all relevant risk factors, relevant comorbidities and concurrent topical and systemic medications, and assess the impact of visual dysfunction, social environment and support networks that may affect adherence to a treatment program. Comorbidities include hypertension, diabetes, thyroid disease, depression, asthma, liver and renal disease.
- **A full eye examination:** anterior segment evaluation including gonioscopy, optic nerve and retinal nerve fibre layer; stereoscopic optic disc and retinal nerve fibre assessment with a permanent record, IOP and corneal thickness measurements.
- **Appropriate investigations:** standard automated perimetry (white-on-white) including comparison with age-corrected normals on a point-wise, regional (eg. hemifield) and global basis.
- Careful and informed **interpretation of results** from all imaging and functional tests in order to detect disease or to detect progression. With the multi-faceted nature of glaucoma and the large variability in normal values of all tests, consider results from all tests and assessments.

Introduction

A diagnosis of glaucoma should be made on the basis of multiple sources of information including the presenting history, an assessment of relevant risk factors, and an ocular examination reflecting structure and function of the eye (outlined in Figure 7.1). Initial consultation should elicit a complete medical, surgical, personal and occupational history, and ascertain relevant risk factors (South African Glaucoma Society [SAGS] 2006). This consultation should be followed by a comprehensive clinical examination including slit lamp examination, tonometry, fundus and optic nerve head examination, gonioscopy, and corneal thickness. This examination may be in conjunction with special investigations to document the extent of structural damage to the optic nerve head and the retinal nerve fibre layer, using optic nerve and retinal nerve fibre layer analysis or disc photography, computer-assisted visual field (VF) analysis. Children with suspected glaucoma should be referred to a specialist health care provider in the field.

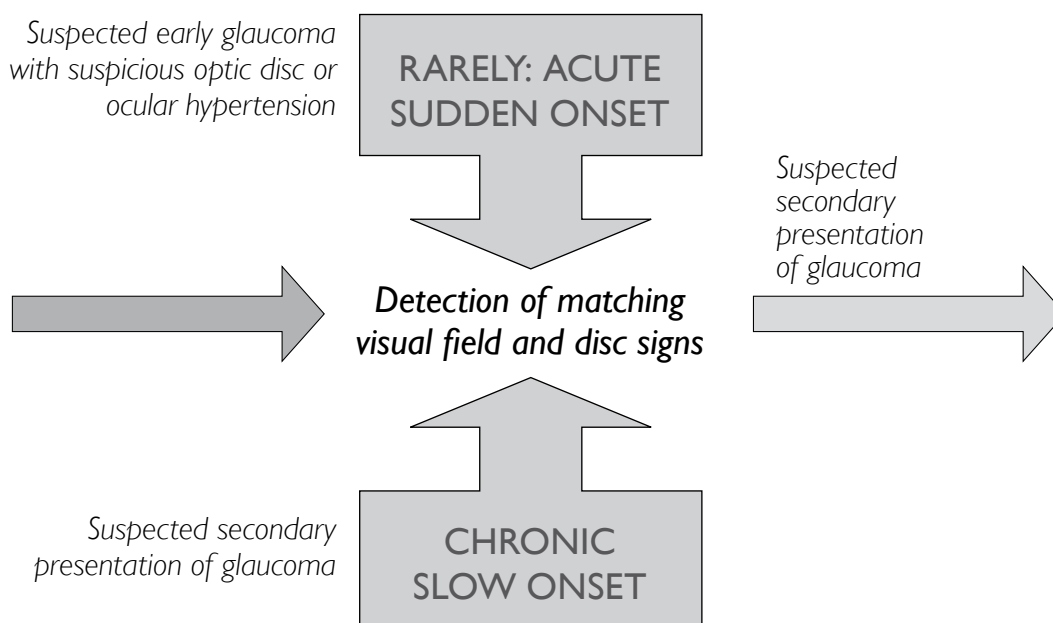
Figure 7.1: Components of the diagnostic process



Health care providers should be mindful of the different presentations of glaucoma, and the need to use a systematic approach to elicit diagnostic information. In certain cases, glaucoma can present as a medical emergency. Confirmatory diagnosis of glaucoma may require more than one consultation with a health care provider, and the involvement of an ophthalmologist. Moreover diagnosis is not made on the basis of a single test, rather a combination of test methodologies and technological tools. A diagnosis is generally made on the basis of characteristic degenerative changes in the optic disc, and matching defects in VFs.

Diagnosis may require repeated longitudinal evaluation and monitoring to document progressive changes (as outlined in Figure 7.2). Optic disc structural review is particularly important, as commonly a loss in disc neuroretinal rim and/or retinal nerve fibre loss is detected prior to VF loss. This so-called ‘pre-perimetric glaucoma’ should be considered as glaucoma, especially where accurate disc-imaging modalities have been used to detect the disc change. Up to 37% of optic nerve fibres need to be lost before a VF defect is identified with standard automated perimetry (Kerrigan, Zack, Quigley et al 1997; Quigley, Nickells, Kerrigan et al 1995). The positive and negative predictive values of the tests applied by any health care provider are important in glaucoma diagnosis.

Figure 7.2: Diagnostic continuum for patients with glaucoma



Diagnosis of glaucoma

Open angle glaucoma

Physical examination should focus on seven elements comprising:

- pupil
- anterior segment
- intraocular pressure (IOP)
- central corneal thickness (CCT)
- gonioscopy
- optic nerve head and retinal nerve fibre layer evaluation
- VF sensitivities.

Evaluation of the anterior-chamber angle using gonioscopy confirms a diagnosis of primary open angle glaucoma (POAG) by excluding other forms of glaucoma, or secondary causes of IOP elevation such as angle recession, pigment dispersion, peripheral anterior synechiae, angle neovascularisation, and trabecular precipitates.

Angle closure

The other main mechanism predisposing to glaucoma is angle closure (AC) which can present in either primary or secondary forms, in acute or chronic situations. Patients may have both, and present with acute attacks superimposed on a chronic condition. In primary angle closure (PAC), the eye is at risk of developing glaucomatous optic disc damage, particularly when associated with elevated IOP. When optic disc damage occurs, the eye is deemed to have progressed from PAC to primary angle closure glaucoma (PACG) (American Academy of Ophthalmology [AAO] 2005a). If acute angle closure (AAC) is suspected, some components of the examination (optic disc imaging, VF testing) may need to be postponed as patients may present as medical emergencies. Providing appropriate and timely treatment becomes the priority.

Evidence Statement

- Evidence strongly supports the need for a comprehensive examination to accurately diagnose all types of glaucoma. This includes a comprehensive medical history, a full eye exam (including gonioscopy), an examination of eye function (visual field) and an assessment of intraocular pressure.

Medical history

Research consistently indicates that a patient's history establishes the framework in which a diagnosis of glaucoma is made. The health care provider should review the patient's family history, and take a complete medical history. The patient's social situation should also be considered, including the capacity to attend treatment regularly, ability to pay for and adhere to treatment, and affect on the patient's life/work/family situations.

The health care provider should also consider relevant risk factors, as well as make an assessment of the impact of visual dysfunction on quality of life and activities of daily living. For further details on risk assessment see Chapter 6.



Risk factors

This section summarises the risk factors that should be assessed in a medical history.

Major

- advancing age (exponential)
- increasing IOP (exponential)
- African-derived (POAG) or Asian-derived (PACG) ethnicity
- strong family history
- diabetes

Minor

- rural lifestyle
- migraine and peripheral vasospasm (Raynaud's syndrome)
- long-term steroid use
- previous eye injury
- current cigarette smoking

Comorbid conditions

- respiratory
- cardiovascular disorders
- endocrine disorders (e.g. diabetes, thyroid eye disease, pituitary tumours)
- central nervous system (e.g. stroke/head injury, early dementia)
- psychiatric (e.g. depression)
- musculoskeletal conditions which may alter capacity to self-medicate
- renal and hepatic disorders
- ocular trauma or concurrent ocular conditions (e.g. cataract)
- pregnancy or lactation

For further details refer to Chapter 6.

Evidence Statements

- Evidence strongly supports taking a comprehensive history including identification of ocular signs and symptoms, risk factors, relevant comorbid conditions and concurrent medication, to diagnose glaucoma.
- Expert/consensus opinion suggests that a comprehensive history is required to identify which management approach is most likely to be effective. A comprehensive history includes the potential impact of visual dysfunction, social environment and patient's support networks that may affect adherence to medication regimens.

Symptoms described by the patient

Open angle glaucoma is generally symptomless in its early stages. It is not until significant neuronal damage has occurred that characteristic visual loss is observed.

Acute angle closure (AAC) is associated with significant and distressing symptoms. These may present as either an acute scenario, or as patient descriptions of past attacks.

Chronic angle closure symptoms are often absent. The symptoms that should alert health care providers to the presence of AC are detailed in Table 7.1, extracted from the European Glaucoma Society [EGS] (2003).

Table 7.1: Symptoms of angle closure

SYMPTOMS	Acute angle closure	Intermittent angle closure	Chronic angle closure
Blurred vision	✓	At time of attack presents as AAC Between attacks may be symptomless	Variable – chronic angle closure mimics primary open angle glaucoma It is asymptomatic until visual field loss interferes with quality of life
Coloured rings around lights	✓		Transient if present
Pain	✓		Not usually
Frontal headache	✓		Discomfort rather than pain
Palpitations and abdominal pain	✓		×
Nausea and vomiting	✓		×

Examination of eye structure

Glaucoma describes a group of eye diseases in which there is progressive damage to the optic nerve. This is characterised by specific structural abnormalities of optic nerve head and associated patterns of VF loss (Burr, Azuara-Blanco & Avenell 2004). Changes that occur in glaucoma include excavation of the optic nerve head (often termed cupping), loss of neuroretinal rim, and frequently, optic disc haemorrhages. It is essential to use the best possible approach to eye examination to identify these changes.

Optic disc

Ophthalmoscopy: **Direct ophthalmoscopy** is best performed with the pupils dilated and the room darkened. This provides a magnified view of the optic disc. The main disadvantage is the absence of a stereoscopic view. **Indirect ophthalmoscopy** performed with a slit lamp yields a magnified stereoscopic view of the optic disc and retinal nerve fibre layer. It is the examination method of choice.

Optic disc photography: A wide variety of digital and non-digital cameras are available to provide colour images of the optic disc. Photography has an advantage over ophthalmoscopy of a permanent recording of the optic disc. However for optimal results, it requires a dilated pupil and relatively clear media. Monoscopic photographs can be obtained with a standard fundus camera; however, the tridimensional structure of the optic disc can only be assessed by stereo photography. Stereoscopic pictures can be obtained with sequential photographs using a standard fundus camera by horizontal realignment of the camera base when photographing the same retinal image. Alternatively, simultaneous stereoscopic fundus photographs can be obtained.

Retinal nerve fibre layer

Nerve fibre photography: Assessment of the nerve fibre layer is similar to optic nerve assessment and is enhanced with red-free illumination. The appearance of the retinal nerve fibre layer may be documented using high-resolution images. The fibre bundles are seen as silver striations, most visibly radiating from the superior and inferior poles of the optic disc. The time taken for this procedure is similar to that required for optic disc photography. In the early stages of glaucoma, estimation of structural abnormalities from serial nerve fibre layer photographs may be more sensitive than assessment of the optic nerve head itself (American Optometric Association [AOA] 2002).

Scanning laser ophthalmoscopy: i.e. Heidelberg Retinal Tomography provides objective, quantitative measures of the optic disc topography and shows promise for discriminating between glaucomatous and normal eyes (Miglior, Guareschi, Albe et al 2003).

Optical coherence tomography: Optical coherence tomography is an optical imaging technique used to measure the thickness of the retinal nerve fibre layer. It is most useful to detect early glaucoma. It provides high-resolution, cross-sectional, *in vivo* imaging of the human retina in a fashion analogous to B-scan ultrasonography, using near infrared (840nm) light instead of sound (Johnson, Siddiqui, Azuara-Blanco et al 2007). Using the principles of low coherence interferometry with light echoes from the scanned structure, optical coherence tomography determines the thickness of tissues. In most commercially available optical coherence tomographies, successive longitudinal scanning in a transverse direction creates two-dimensional images. They can scan the optic nerve head, macular region as well as the peripapillary retinal nerve fibre layer. There is scant information about its diagnostic accuracy.

Scanning laser polarimetry Equipment such as GDx provide an objective, quantitative measure of the retinal nerve fibre layer thickness by using the retardation of a reflected 780nm polarized laser light source.

No single test (or group of tests) appears to be more accurate than any other for diagnosing glaucoma, regardless of the type (Burr, Mowatt, Hernandez et al 2007). Table 7.2 outlines the relative merits of eye structure examinations. The sensitivity and specificity measures are synthesised from Burr et al (2007).

Table 7.2: The relative merits of mechanisms of eye structure examination

EYE STRUCTURE	Pupil dilation	Permanent record	Stereo-scopie view	Sensitivity (Sens) (95%CI)	Specificity (Sp) (95%CI)	Diagnostic Odds Ratio (DOR) (95%CI)	Early diagnosis Sp and Sens
Direct ophthalmoscopy	YES Preferred	NO health care provider has to draw	NO	60 (34-82)	94 (76-99)	25.7 (5.79- 109.5)	NO- Sp and Sens reduced in early stage diagnosis (Wood Bosanquet 1987)
Optic disc photography	YES	YES	YES *	73 (61-83)	89 (50-99)	21.74 (3.07-148.3)	YES Sp and Sens improved in early stage diagnosis (Wollstein et al 2000)
Fundus photography	NO	YES	NO				Useful in remote situations with generic screening workers
Retinal nerve fibre layer photography	YES	YES	YES*	75 (46-92)	88 (53-98)	23.10 (4.41-123.50)	
Optical coherence tomography	Beneficial but not essential	YES	N/A	N/Av	N/Av	N/Av	YES
Scanning laser ophthalmoscopy Heidelberg Retinal Tomography	Beneficial but not essential	YES	N/A	86 (55-97)	89 (66-98)	50.93 (11.48-246.30)	YES Sp improved in early stage studies (Leong et al 2003)

* Indicates stereoscopic option available.



Setting diagnostic baselines

It is essential to establish clear baselines at the initial diagnostic examination, against which glaucomatous progression can be measured. Suggested eye structure baselines include:

- **Size of the optic disc:** The average vertical disc diameter measures between 1.6 and 2.0mm, which should be taken into account when estimating neuroretinal rim area and the significance of the size of the cup. The average optic disc diameter has the same diameter as the 5° (small) direct ophthalmoscope illumination spot. This can be used to judge whether an optic disc is small, average or large
- **Vertical cup:disc ratio:** This will tend to be greater in larger discs. A smaller cup can be significant in a small disc
- **Pattern of the neuroretinal rim:** This allows assessment of change in the usual pattern of rim width
- **Presence of disc rim haemorrhage:** This increases the likelihood of ocular hypertension converting to glaucoma by four to six times (Gordon, Beiser, Brandt et al 2002)
- **Thinning of the nerve fibre layer:** This is best viewed with red-free light at the slit lamp
- **Beta-zone peripapillary atrophy:** This is present in 20% of individuals with normal vision, however it is more common in patients with glaucoma.

Evidence Statements

- Evidence indicates that an eye structure examination that is capable of establishing a diagnostic baseline includes a stereoscopic view, and a permanent record of the optic disc and retinal nerve fibre layer.
- Expert/consensus opinion suggests that key components of a baseline optic nerve head examination include size of disc, cup:disc ratio, neuroretinal rim pattern, presence of optic disc haemorrhages and thinning of the nerve fibre layer.

POINT OF NOTE

Analysis of optic nerve and retinal nerve fibre imaging may indicate the presence of pre-perimetric glaucoma, which may be managed as established glaucoma.

Anterior chamber assessment

Biomicroscopy

Slit lamp anterior segment biomicroscopy is useful for identifying the risks of angle closure such as the depth of central and peripheral anterior chamber, contour of iris (e.g. bombe) as well as previous attacks of angle closure. These include sectoral iris atrophy, glaukomflecken, posterior synechiae and peripheral anterior synechiae. Signs of secondary glaucoma causes such as features of uveitis, pigment dispersion (iris transillumination and pigment deposits on the corneal endothelium), pseudoexfoliation (on lens capsule), iris rubeosis (neovascular causes) can also be identified. On routine follow-up, signs of corneal epithelial toxicity, conjunctival hyperaemia, and papillae can indicate adverse drug reactions.

Gonioscopy

Evaluation of the anterior-chamber angle using gonioscopy assists in confirming a diagnosis of POAG by excluding AC or secondary causes of IOP elevation such as angle recession, pigment dispersion, peripheral anterior synechiae, angle neovascularisation, and trabecular precipitates. Patients with PAC can present either acutely or chronically, or they may have both situations, and present with acute attacks superimposed on a chronic condition. Gonioscopy is the key to diagnosing AC.

Gonioscopy allows observation of the angle of the anterior chamber including the angle anatomy and appositional closure. It can also determine the extent of any peripheral anterior synechiae. Gonioscopy of both eyes should be included in any examination in order to diagnose glaucoma.

Compression (indentation) gonioscopy with a four-mirror or similar lens is particularly helpful to evaluate for appositional closure versus synechial AC and for the extent of peripheral anterior synechiae. The slit lamp beam should be reduced in size to illuminate the meshwork only, minimising light passing through the pupil that can lead to pupil constriction and artifactual angle opening.

Recent advances in technology have provided corneal topography systems which generate corneal maps and image the anterior segment of the eye. Whilst these provide the opportunity to analyse the anterior segment of the eye to a greater degree than before in a non-contact manner, they do not provide the details of signs of past AC, recession or peripheral anterior synechiae. Moreover, there is not the capacity to manoeuvre and to identify physical patency of the angle. While they may be complementary, these systems should not be used as a substitute for gonioscopy.

Evidence Statement

- Expert/consensus opinion suggests that gonioscopic examination of both eyes is required when making a diagnosis of glaucoma.

POINT OF NOTE

Anterior segment imaging technologies may be useful to augment gonioscopic examination of the anterior chamber.

Examination of eye function

Optic nerve damage in glaucoma is characterised by specific structural abnormalities of the nerve fibre layer, optic nerve head and patterns of VF loss (Burr et al 2004). Glaucoma tends to produce localised areas of VF loss in comparison to other conditions that produce diffuse VF loss. However measurement of VF can be difficult and unreliable. Repeated and consistent VF measurements are required to establish the presence of defects. Factors known to affect VF testing include:

- **Advancing age:** the retina of the normal eye becomes less sensitive with aging
- **Visual acuity:** appropriate correction is needed for close vision
- **Concurrent ocular conditions:** e.g. cataract or corneal oedema
- **Patient comprehension and cooperation:** supervision may be required for optimal performance during testing.

Despite inherent problems with reliability, the measurement of VF is invaluable for diagnosis, especially in early stages when optic disc changes may be borderline. In later stages, it becomes vital to detect and document progression of the disease as optic disc changes becomes harder to identify. It is also an invaluable way of determining a patient's disability. The time taken to perform the test is important, not only as an indicator of clinical efficiency but also to assess the difficulty for patients to maintain eye position during testing. Whichever approach is used, it is important to use a consistent examination strategy in which VF testing can be repeated.

Visual field testing

Standard automated perimetry

Standard automated perimetry has traditionally been considered to be the reference standard in VF examination of glaucomatous patients. Standard automated perimetry estimates the threshold sensitivity of several points within the VF. The target locations remain constant and the brightness is modified in a staircase approach to estimate the sensitivity. Standard automated perimetry is able to quantify the reliability, and compare the actual examination with an age-matched normal database. Examination of the visual field in glaucoma is usually limited to the central 30-degree or 24-degree area, since almost all clinically relevant defects fall within this area. The most commonly used automated perimeter in the United Kingdom (UK) in ophthalmology clinics is the Humphrey perimeter, now interpreted with Swedish Interactive Threshold Algorithm, which speeds up the testing process.

Suprathreshold automated perimetry

Suprathreshold testing with automated perimetry involves the use of stimuli that are of greater intensity than the presumed threshold at each location. This test strategy does not quantify the depth of VF defects, however is much quicker than threshold testing therefore maximising patient concentration and performance. It is only valid for screening and not for diagnosis.

Frequency doubling technology

Frequency doubling technology is a portable, relatively inexpensive instrument designed for fast and effective detection of VF loss. Frequency doubling technology offers many advantages in that it is simple to administer and interpret, well tolerated by most patients, not greatly affected by refractive error and cataract, has high test-retest reliability, offers rapid screening tests, and has different full threshold programs.

Perimetry

Perimetry with the Damato chart is a simple and inexpensive VF test. Damato campimetry consists of 20 numbers located on a flat, white card within the central 30 degrees of VF. The subject is required to refixate from number to number, sequentially reporting whether the central 1.5-mm black spot remains visible. There is a 40-cm hinged piece that serves to maintain the appropriate test distance and occludes the non-tested eye. Any point missed, other than the physiological blind spot area, is confirmed once, before considering it a true missed point.

The relative merits of each form of eye function examination are outlined in Table 7.3. Unless otherwise stated, this information was distilled from Burr et al (2007).

Table 7.3: The relative merits of each form of eye function examination

EYE FUNCTION		Time	Port- able	Sensi- tivity (95%CI)	Speci- ficity (95%CI)	DOR (95%CI)	Early diagnosis specificity and sensitivity
Frequency doubling technology	FDT C-20-I	<45 sec normals 2 min advanced	YES	92 (65-99)	94 (73-99)	181.2 (25.49-2139)	Abnormal test result defined as more than one depressed test point in the total deviation probability plot (Heeg et al 2005) For TD > 1, sens all participants (90), early glaucoma excluded (100) Spec all participants (100), early glaucoma excluded (81)
	FDT C-20-5	<45 sec normals 2 min advanced		78 (19-99)*	75 (57-87)	10.14 (0.72-249)	NR
	FDT C-20 full threshold test	3-4 minutes per eye		86 (29-100)	90 (79-96)	57.54 (4.42 – 1585)	NR
	FDT C-20 (Humphrey Matrix 24-2)	1 minute per eye in supra- threshold mode		100	27	N/a	NR
Perimetry		3-4 minutes per eye	YES	86 (29-100)	90 (79-96)	57.54 (4.42-1585)	Spec higher in early/ moderate glaucoma (94%) (Harper, Hill, Reeves 1994; leong, Murdoch, Cousens, Healey, Theodossades 2003)
Standard automated perimetry	Threshold testing	5-18 minutes for both eyes	NO	88 (65-97)	80 (55-93)	29.87 (5.59-159.3)	Sp and Sens higher in early /moderate glaucoma (Katz et al 1991) (Enger, Sommer 1987)
	Supra- threshold testing			71 (51-86)	85 (73-93)	14.42 (CI 6.39-33.73)	Sp higher in early/ moderate glaucoma 95 (82-99) (leone et al 2003)

NR = not reported; N/a = not applicable

Testing a 24-degree field (24-2 strategy) often represents the best compromise between speed, comfort and amount of reliable information gained. There are some exceptions where a smaller field (10-degrees) should be tested in severe glaucoma. It is noted that 30-2 may be more sensitive at detecting some early cases of glaucoma. Therefore should a 24-2 visual field remain normal despite the index of suspicion remaining high, it may be useful to conduct a 30-2 test as well.

Evidence Statement

- Expert/consensus opinion suggests that visual field testing is invaluable to diagnose glaucoma.

POINT OF NOTE

A consistent approach to testing visual function at diagnosis, monitoring and follow-up may facilitate assessment of progression across professional settings. Health care providers are advised to utilise equipment that allows comparisons with normal visual fields, and has demonstrated reproducibility to facilitate comparisons with measures taken over time. Health care providers need to interpret product claims with caution when choosing their equipment.

Evidence Statement

- Expert/consensus opinion suggests that advancing age, visual acuity, patient capability, concurrent ocular conditions, oculo-facial anatomy and spectacle scotomata all impact upon the results and interpretation of visual field testing.

Using visual fields to grade glaucoma

Burr et al (2007) describes a continuum of glaucoma severity as:

- **No glaucomatous impairment:** Under observation as a glaucoma suspect, however not on medication, and no glaucoma visual field defect in either eye.
- **Mild glaucoma:** On treatment, no binocular visual field loss, unilateral glaucoma visual field defect.
- **Moderate glaucoma:** Up to five missed points (<10 dB mean deviation, or average loss) in binocular central 20° of visual field.
- **Severe glaucoma:** Binocular visual field loss below UK driving standard (adapted from Crabb et al 2004, 2005). Six or more adjoining missed points (<10 dB), and any additional separate missed point(s) or a cluster of four or more adjoining missed points (<10dB), either of which is either wholly or partly within the central 20-degree superior or inferior hemispheric field.
Note: For use in Australia, Australian driving standards should be substituted.
- **Visual impairment:** Includes as per criteria for severe, except binocular visual field loss includes both the upper partial sight, blind, and lower fields of vision.

The use of a universal grading system promotes clear communication between health care providers, enables application of evidence-based results and highlights when patients require advice and intervention regarding activities of daily living such as driving. The stability of the glaucoma state and the likelihood of progression to a more severe grade are equally important when grading a patient's glaucoma severity.

POINT OF NOTE

A standard classification of glaucoma severity that incorporates current visual field loss and risk of progression would enhance information-sharing between health care providers.

Intraocular pressure measurement

A diagnosis of open angle glaucoma (OAG) must be based on multiple sources of information. This condition can occur in eyes with normal or raised IOP. The concept that POAG only occurs with pressures over 21mmHg is outdated. However, whilst increasing emphasis is now placed upon the morphological changes occurring at the optic nerve head and retinal nerve fibre layer, IOP measurement remains core to any diagnosis and management of glaucoma. A target IOP should be nominated at diagnosis, depending upon the glaucoma severity, presenting IOP, and other risk factors. This then enables monitoring to assess the efficacy of intervention.

There are a number of instruments that measure IOP, having either contact or no contact with the cornea. Applanation tonometry (such as Goldmann Applanation Tonometry) infers the IOP from the force required to flatten a constant area of the cornea. This requires contact with the cornea. Non-contact tonometry uses rapid air pulses (air puffs) to flatten the cornea. IOP is estimated by detecting the force of the air jet at the instance of flattening. There is no contact with the cornea. The issues surrounding each approach are discussed in the following sections.

Central corneal thickness

Measurement of CCT assists in both the interpretation of IOP measurements and the assessment of patient risk. Using the Goldmann Applanation Tonometry method assumes an average CCT of 520µm. A meta-analysis of values reported in the literature (Burr et al 2007) indicates that 'normal' individuals have a significant variation in CCT (535 +/- 31µm). This influences the accuracy of this measurement. Cannulation studies indicate that a 10% change in CCT alters mean IOP (measured by Goldmann Applanation Tonometry) by 1 - 3.5mmHg. Standard tonometry is calibrated for average corneal thickness of approximately 535µm. In thinner corneas tonometers read falsely low, in thicker corneas they read falsely high. There is no acceptable correction formula applicable to all populations across the spectrum of measured IOP, and any correction is unlikely to be linear. Measuring CCT remains an important component of management and should guide decision-making in glaucoma (Dueker, Singh, Lin et al 2007).

Applanation tonometry is influenced by CCT and perhaps by biomechanical properties of the cornea. The applanation principle is used in the Goldmann Applanation Tonometry as well as in non-contact tonometry. Goldmann Applanation Tonometry remains the current 'gold standard'. However recent publications suggest that the accuracy of this 'gold standard' has to be corrected by the pachymetric evaluation of the cornea. Several new forms of tonometry (e.g. Dynamic Contour Tonometry, Ocular Response Analyser) have been designed to provide IOP measurements which are less influenced by the biomechanical properties of the cornea, including CCT, however these are yet to be widely used in practice.

Timing of intraocular pressure measurements

The literature recommends that IOP should be measured at different times during the day, as IOP can vary diurnally. *'The assessment may also benefit from determining diurnal IOP fluctuations on different days, which may be indicated when disc damage exceeds the amount expected based on a single IOP measurement'* (AAO 2005b pp 10).

Evidence Statement

- Evidence indicates that intraocular pressure can vary at different times of the day. Therefore it is important to measure intraocular pressure at different times of the day to gain a comprehensive picture of the intraocular pressure profile of a patient.

Contact tonometry

In contact tonometry, there is direct physical contact between the measuring instrument and the surface of the eye, which highlights the need for infection control (EGS 2003; Whitacre, Stein & Hassanein et al 1993). Concerns regarding transmissible disease arise due to contact with the cornea and the tear film in Goldmann Applanation Tonometry. All equipment should undergo chemical disinfection after use to reduce the risk of cross-infection (Whitacre et al 1993). Salvi, Sivakumar and Sidiki (2005) recommend using disposable prisms for Goldmann and Perkins tonometry, or disposable covers for the Tono-Pen tip. Salvi et al (2005) also report that disposable prism tonometry is potentially a reliable alternative to Goldmann Applanation Tonometry.

Evidence Statement

- Evidence strongly supports the need to maximise infection control. Minimum standards are:
 - disinfecting equipment before each patient, or
 - using disposable covers/prisms with each patient, and between eyes for the same patient.

Applanation tonometry

In applanation tonometry, a specially calibrated disinfected probe attached to a slit lamp biomicroscope is used to flatten the central cornea by a fixed amount. Because the probe makes contact with the cornea, a topical anaesthetic, such as oxybuprocaine, tetracaine, proxymetacaine or proparacaine is introduced onto the surface of the eye in the form of eye drops. A yellow fluorescein dye is used in conjunction with a cobalt blue filter to aid the health care provider to determine IOP.

The preferred method of applanation tonometry has traditionally been the Goldmann Applanation Tonometry. There are a significant number of factors that impact upon applanation tonometry measurements (South East Asia Glaucoma Interest Group [SEAGIG] 2003). These include:

- diurnal variation (commonly with a peak IOP in the morning, trough in the evening, usual diurnal variation 3-6mmHg)
- central corneal thickness (a correction is required of 1-3mmHg per 40µm deviation from 525µm)
- advancing age (increase for each decade over 40 years)
- exercise, which can increase (head down positions) or decrease (dehydration) IOP by 2-6mmHg
- lifestyle (alcohol and marijuana decreases IOP, rapid fluid intake increases IOP)
- posture (horizontal or head down position increases IOP)
- artificially reading low (insufficient fluorescein in tear film)
- artificially reading high (excessive fluorescein in tear film, eyelid pressure on globe from blepharospasm, digital pressure on globe to hold lids apart, obesity, patient straining to reach head/chin rest, patient breath-holding, patient wearing constricting clothing, hair lying across cornea, lens-corneal apposition)
- technical difficulties (corneal abnormalities, marked corneal astigmatism, small palpebral aperture, nystagmus, tremor (patient or health care provider))
- elevated systolic blood pressure.

POINT OF NOTE

Peaks and troughs in intraocular pressure occur at different times in different people. The true correction for central corneal thickness is not known, and any value is at best an approximation.

Non-contact tonometry

Pneumatometry: Air-puff tonometry uses a rapid air pulse to applanate the cornea. Corneal applanation is detected via an electro-optical system. IOP is estimated by detecting the force of the air jet at the instance of applanation. Non-contact tonometry is especially useful for very young children, patients unable to reach a slit lamp due to disability, patients who are uncooperative during applanation tonometry, or patients with corneal disease in whom contact tonometer cannot be accurately performed. In addition, it should be considered for patients who simply cannot tolerate physical contact on the cornea.

Alternative forms of tonometry

Electronic indentation tonometry

Tono-Pen (Reichert, Inc) is a form of electronic indentation tonometry. It is a portable electronic, digital pen-like instrument that determines IOP by making contact with the cornea, after topical anaesthetic eye drops have been applied.

Perkins tonometry

This is a specific type of portable applanation tonometer to measure IOP in children, patients unable to cooperate for slit lamp exam, and supine anesthetised patients.

The relative merits of each form of tonometry are outlined in Table 7.4. This information was extracted from Burr et al (2007).

Table 7.4: The relative merits of each form of tonometry

IOP measurement	Glaucoma stage	Sensitivity (95%CI)	Specificity (95%CI)	DOR (95%CI)
Goldmann Applanation Tonometry	Pooled all stages	46 (22-71)	95 (89-97)	4.95 (4.48-48.95)
Non-contact (air-puff) tonometry	Pooled all stages	92 (62-100)	92 (90-94)	134.88 (17.15-1061.1)

The use of non-applanation tonometry (i.e. dynamic contour forms) has recently been reported in the literature. There is insufficient evidence to date of the true place of dynamic contour tonometry or other tonometric methods compared to Goldmann Applanation Tonometry. Future updates of this guideline will address this issue should research become available.

POINT OF NOTE

To accommodate patient preference and to ensure secondary confirmation of findings, a variety of methods for measuring intraocular pressure are required.

Setting target intraocular pressure at diagnosis

A target IOP should be nominated at diagnosis, depending upon the glaucoma severity, presenting IOP, familial and other risk factors. Usual recommendations suggest a 25% reduction from baseline at diagnosis (Leske, Heijl, Hyman et al 2004; Heigl, Leske, Bengtsson et al 2002) with further 20% reductions if further progression occurs (Canadian Glaucoma Study Group 2006). A lower IOP is required when glaucoma is more severe (The Advanced Glaucoma Intervention Study [AGIS] Investigators 2000, 2002). Target IOPs are outlined in Table 7.5 with reference sources.

Table 7.5: Target pressures for diagnostic decision-making

Glaucoma classification		Individual risk status	Percentage lower than compared to pre-treatment		Specified level	Source
Glaucoma type	Stage		Min	Max	mmHg	
POAG	Suspect	Low	n/s	NR	No treatment unless IOP rising 20%	SEAGIG(2003)
		Moderate or not specified	20	NR		AAO (2005c) SEAGIG(2003)
		High	20	NR	≤24mmHg	EGS(2003) SEAGIG(2003)
	Early	n/s	NR	NR	≤19mmHg	JGA(2004)
	Established	Moderate	20	NR	NR	AAO (2005b) RCO(2004) SEAGIG(2003)
			NR	NR	≤16mmHg	JGS(2004)
		High	30	NR	Or close to episcleral venous pressure	SEAGIG(2003)
	Advanced	NR	30	50	NR	AOA(2002)
		NR	NR	NR	All ≤18mmHg	AAO (2005b) EGS(2003)
					Majority ≤15mmHg	RCO(2004)
					≤14mmHg	JGS(2004)
NTG	NR	NR	30	NR	Or close to episcleral venous pressure	SEAGIG(2003) JGS(2004)

NR = not reported

Evidence Statements

- Evidence strongly supports a minimum target intraocular pressure reduction of 20% in patients with *suspected primary open angle glaucoma with high-risk status*. It is advised that intraocular pressure remains under 24mmHg. Those without high-risk factors can simply be observed.
- Evidence strongly supports a minimum target intraocular pressure reduction of 20% in patients with *early and established primary open angle glaucoma without high-risk status*. It is advised that intraocular pressure remains under 16-19mmHg.
- Evidence strongly supports a minimum target intraocular pressure reduction of 30% in patients with established primary open angle glaucoma with high-risk status, and patients with advanced primary open angle glaucoma.
- Evidence strongly supports the maintenance of intraocular pressure below 18mmHg in patients with established primary open angle glaucoma, and even lower to below 15mmHg in patients with advanced primary open angle glaucoma.

POINT OF NOTE

Target pressures should always be appropriate to the individual situation/condition.

Diagnosing specific glaucoma types

Angle closure

A definitive diagnosis of AC and ACG requires multiple sources of information. Diagnostic recommendations are based on the stage of disease. Specific examination components should include:

- ***Assessment of refractive status:*** this is important to assess as hypermetropic eyes, especially in older patients, have narrower anterior-chamber angles and are at increased risk of angle closure.
- ***The size and reactivity of the pupil should be examined:*** this includes pupil size, regularity and reactivity.
- ***External examination:*** this includes examining the conjunctival hyperaemia and corneal status
- ***Slit-lamp biomicroscopy:*** this assesses central and peripheral anterior-chamber depth, anterior chamber inflammation, corneal oedema, iris atrophy (especially sectoral; posterior synechiae; or mid-dilated pupil suggestive of a recent or current attack), signs of previous angle closure attacks (e.g. peripheral anterior synechia, segmental iris atrophy, glaukomflecken, posterior synechiae, pupillary dysfunction).
- ***A dilated examination:*** this may not be advisable in patients with anatomic narrow angles or angle closure.
- ***Evaluation of the fundus and optic nerve:*** this should use the direct ophthalmoscope or biomicroscope.
- ***For patients with PAC or PACG:*** pupil dilation might be contraindicated until an iridotomy has been performed.
- ***Gonioscopy of both eyes on all patients:*** this is undertaken to evaluate angle anatomy, and to detect appositional closure and/or the presence of peripheral anterior synechia.

The frequency and severity of findings will vary between acute, intermittent and chronic forms of closure. Table 7.6 provides a summary extracted from EGS (2003).

Table 7.6: Signs of angle closure: acute intermittent and chronic

SIGN	Acute angle closure	Intermittent angle closure	Chronic angle closure
IOP raised	✓	Not necessarily	✓
Reduced visual acuity	✓	May be normal	May be normal
Corneal oedema	✓	Not necessarily	NR
Pupil mid dilated and unreactive	✓	Often round and reactive between attacks	NR
Shallow/flat anterior chamber	✓	✓	✓
Iris pushed forward	✓	Patchy iris atrophy and torsion	Peripheral anterior synechia
Gonioscopic closure 360	✓	✓	✓
Venous congestion	✓	NR	NR
Fundus changes (disc oedema and splinter haemorrhage)	✓	Optic disc rim atrophy	Substantial glaucomatous damage
Bradycardia/arrhythmia	✓	NR	NR

NR = not reported

Pigmentary glaucoma

Health care providers should use the same comprehensive evaluation for this type of glaucoma as for POAG, however additional key signs include:

- pigment on the anterior surface of the iris often as concentric rings within the iris furrows
- spoke-like transillumination defects in the midperiphery of the iris
- pigment in the anterior and posterior chambers, and possibly Krukenberg's spindles on the corneal endothelium
- a dense, homogeneously pigmented trabecular meshwork, especially posteriorly
- an open, deep anterior chamber angle with possible posterior bowing (concavity) of the iris
- rise of the IOP to rather high levels, with dramatic fluctuation
- pigment release resulting from pupillary dilation or strenuous exercise which requires assessment of the IOP after dilation.

Pseudoexfoliation glaucoma

Health care providers should use the same clinical approach for this glaucoma type as the initial and follow-up evaluations of a glaucoma suspect for POAG, with special attention to biomicroscopy and gonioscopy.

The evolution from first pigmentary and lens changes to full-scale pseudoexfoliation syndrome may take up to five to ten years. Additional key signs include:

- 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

- transillumination defects in the iris near the pupil, and patchy pigmentation of the trabecular meshwork located in the superior angle and anterior to Schwalbe's line. Pigment granules may form a whorled pattern over the sphincter muscle on the surface of the iris
- depigmentation of pupillary ruff
- poor pupillary response to topical mydriatic medications
- accelerated cataract formation
- trabecular pigmentation which may precede the appearance of pseudoexfoliative material on the surface of the lens, even though this material is present in the conjunctiva.

The ability to diagnose pseudoexfoliation syndrome can be improved by up to 20% when biomicroscopy is performed through a dilated pupil. However pupillary dilation can cause pigment dispersion, resulting in a spike in IOP that necessitates post-dilation tonometry. Biopsy of the conjunctiva, although rarely used clinically, may enable diagnosis prior to any clinical evidence of pseudoexfoliation syndrome in the anterior or posterior chambers. IOP can be extremely high in pseudoexfoliation glaucoma, which has a more serious clinical course than POAG and greater propensity for VF loss at the time of diagnosis. Among newly diagnosed cases of pseudoexfoliation glaucoma, 69% are unilateral, compared with 46% of those with POAG (AOA 2002).

Professional roles in diagnosis

These guidelines encourage the establishment and nurturing of networks between primary health care providers, and between primary health care providers and ophthalmologists, to ensure best quality comprehensive care is provided to patients suspected of having, or diagnosed with glaucoma.

Given the limited evidence base and ongoing changes in professional boundaries in Australia, the Working Committee notes that there are three essential issues that direct the most appropriate management pathway for a patient. These issues are:

1. ***Degree of diagnostic suspicion:*** In the primary health care setting, if the degree of diagnostic suspicion of glaucoma is low, unnecessary referral of a patient to an ophthalmologist may lead to system overload. Low-risk patients may well be monitored by the most appropriate primary health care provider within the patient's location, using the established network for advice. If the degree of diagnostic suspicion of glaucoma is high however, the network should still be used for advice, and the appropriate decision may be a direct referral to a health care provider able to initiate treatment.
2. ***Degree of urgency and severity:*** If suspicion is very high with marked signs of nerve damage, and/or the IOP is very high (e.g. cupped disc with IOP >35) then patients need urgent referral, with or without IOP-lowering treatment in the meantime, depending upon the waiting period for referral. Acute angle closure presents as a medical emergency and requires immediate referral to a specialist.
3. ***Referral/cooperative management:*** The Working Committee recommends that the professional roles, responsibilities and referral pathways are best determined in individual cases based on location, resources, skill-base of local health care providers and patient choice. Classically, referral occurs to an ophthalmologist when significant suspicion of glaucoma is raised. In some parts of the country optometrists and or general practitioners can initiate treatment.



Irrespective of the location and manner in which patients with glaucoma are managed, the literature suggests that health care providers involved in the diagnosis of glaucoma should have the skills and equipment to measure:

- IOP either by Goldmann Applanation Tonometry or well calibrated non-contact tonometer
- visual field
- optic disc
- anterior chamber
- gonioscopy.

Health care providers involved in only the screening and/or diagnosis of glaucoma, should receive appropriate training and continuing support from health care providers who manage glaucoma (Azuara-Blanco, Burr, Thomas et al 2007; Burr et al 2007). Students in each health care discipline should be alerted to the importance of cooperation between disciplines in the screening, diagnosis and management of glaucoma.

POINT OF NOTE

The Working Committee recommends that the professional roles, responsibilities and referral pathways are best determined in individual cases based on location, resources, skill-base of local health care providers and patient choice.

Evidence Statement

- Evidence strongly supports that all health care providers involved in glaucoma screening and diagnosis receive appropriate training and continuing support from health care providers who regularly manage glaucoma. Co-management involving an ophthalmologist is recommended.

Summary of diagnostic standards

Tuulonen, Airaksinen, Erola et al (2003 pp5) in the Finnish Guidelines for OAG provide a hierarchical table regarding use of reference examination tests (reproduced in Table 7.7). This has been modified to take account of evidence concerning the validation of optic nerve imaging technologies and their ability to detect subsequent change and hence identify progression (Burgoyne 2004). The hierarchy of examinations required for reliable diagnosis is outlined in this table, and the modifications are in *italics*.

Whilst it is commonly accepted that health care providers involved in the screening and diagnosis of glaucoma should have the skills and equipment to examine the optic disc for typical glaucoma signs and optic disc rim haemorrhages. There are situations, particularly in rural/remote communities, where this may not be available. Fundus photography should be considered in such situations as it provides a permanent record of the disc and nerve fibres that can be relayed to other health care providers to facilitate a diagnosis.

Table 7.7: Hierarchy of glaucoma examination required for reliable diagnosis, extracted from Tuulonen et al (2003) and modified by information from Burgoyne (2004)

Very good level*	IOP** and Gonioscopy and Visual Field *** and Optic disc images and RNFL images
Good	IOP** and Gonioscopy and Visual Field *** and Optic disc images or RNFL images
Satisfactory	IOP** and Gonioscopy and Visual Field *** and <i>Clinical optic disc examination</i>
Insufficient	IOP

* Examination with blue-on-yellow perimetry, the central 10 degree VF and quantitative optic nerve head analysis (e.g. Heidelberg Retinal Tomography) may provide useful additional information

** Diurnal IOP when needed. Regular calibration of the tonometer is required.

*** Preferably two automated VF examinations with a threshold program for determination of the baseline

POINT OF NOTE

In rural/remote settings, fundus photography is valuable if the results are to be relayed to a diagnosing health care provider.

For a summary of examination components refer to the end of this chapter for sections on:

- *What should I examine to identify open angle glaucoma?*
- *What should I examine to identify angle closure?*

Evidence Statements

- Evidence strongly indicates the multifaceted nature of glaucoma and the large variability in the normal values of test findings. This evidence therefore strongly supports using findings from more than one diagnostic procedure or test before a glaucoma diagnosis can be made.
- Evidence strongly supports the need for health care providers only involved in the screening and diagnosis of glaucoma, to possess the skills and equipment to measure intraocular pressure (by Goldman Applanation Tonometry or well-calibrated non-contact tonometry), test visual field, perform gonioscopy and examine the optic disc for typical glaucoma signs. They should receive appropriate training and continuing support from health care providers who manage glaucoma.
- Evidence supports the following assessment methods for diagnosing glaucoma, which are independent of cost and patient preference:
 - full medical history
 - examination of eye structure with optic nerve image recording
 - examination of eye function with two automated visual field examinations using a threshold program for determination of the base line
 - assessment of intraocular pressure, including diurnal variation with a calibrated tonometer checked regularly
 - assessment of the angle by gonioscopy.

Questions to ask patients with suspected glaucoma

What are your symptoms?
Do you have any first-degree relatives with eye disorders (e.g. parents or siblings)?
What is your age?
Do you have existing eye conditions? (e.g. myopia and hypermetropia, eye trauma)
Do you other medical conditions? (e.g. diabetes)
Are you of African or Asian descent?
Are you taking any prescription or over-the-counter medicines, if so what?
Are you pregnant or breastfeeding?
When did you last have an eye examination?
Have you heard of glaucoma?
What do you know about glaucoma?

Questions to ask patients with established glaucoma

How are you? How are your eyes and vision?
Are you managing to take your medication as advised? If no, what are the problems and difficulties you face?
Is there anything about your condition or treatment plan you would like explained?
Are you experiencing any side effects from the medication?
Do you have other medical conditions? If yes, have they been exacerbated recently?
Are you taking any prescription or over-the-counter medicines, if so what?
Do you have plans to conceive/are you already pregnant? If yes, do you plan to breastfeed?
When did you last attend an eye exam or have your condition monitored?
At what age were you diagnosed and how long ago was that?

What should I examine to identify open angle glaucoma?

Assess anterior chamber and angle with gonioscopy and biomicroscopy

Key signs

- abnormal trabecular meshwork
- abnormal ciliary base (angle or cyclodialysis cleft)
- blood reflux in Schlemm's canal



Assess and record eye structure with the best available instrument

- ocular examination including
 - refractive status
 - pupil size and reactivity
 - external appearance eye
 - optic nerve head
 - visual field

Key signs

- typically superotemporal or inferotemporal optic disc neuroretinal rim loss with excavation
- disc haemorrhage
- cup:disc ratio and cup:disc ratio asymmetry
- nerve fibre layer atrophy
- peripapillary atrophy

Assess and record eye function with best available instrument

Key signs

- defects that are
 - asymmetrical and cross midline
 - located in mid periphery (5-25 from midline)
 - clustered in neighbouring points
 - correlate to defects on optic disc

Assess IOP using best available instrument and taking patient preference into consideration

Key levels

- less than 21mmHg – consider normal tension glaucoma
- over 26mmHg consider ocular hypertension
- consider diurnal variation

What should I examine to identify angle closure?

Assess anterior chamber and angle with gonioscopy and biomicroscopy

Key signs of closure

- peripheral anterior synechiae
- trabecular meshwork pigment patches
- iris insertion above scleral spur
- angle structures (trabecular meshwork) not being visible

Assess and record eye structure with the best available instrument

- refractive status
- pupil size and reactivity
- external appearance eye

Assess and record eye function with best available instrument

Assess IOP using best available instrument and taking patient preference into consideration.

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■ CHAPTER 8

Monitoring: long-term care

Recommendation 9

Establish a treatment plan, with target IOP.

Good Practice Points

- Target should vary depending on patient setting and risk factors. Monitor response carefully, and use it to modify goals (e.g. lower target IOP) if disease progresses. Change strategies if side effects.

Recommendation 10

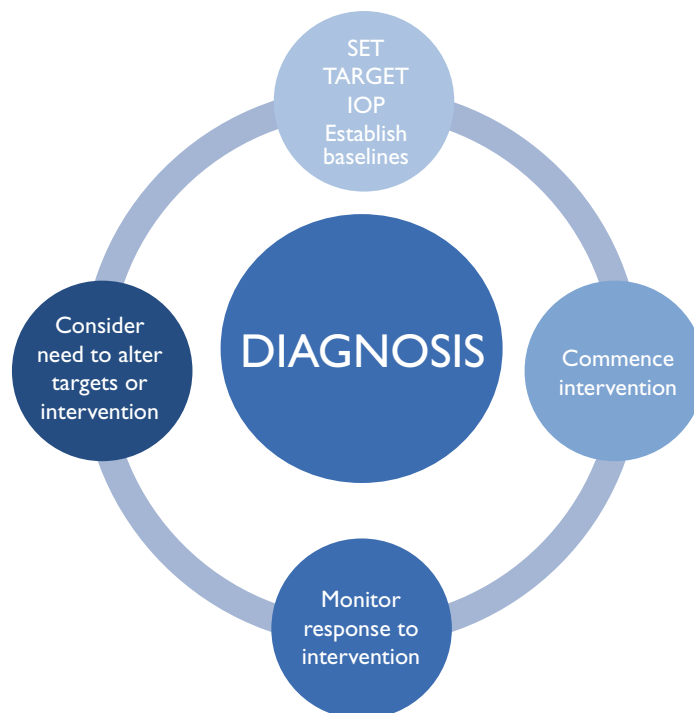
- Monitor patients with primary angle-closure suspect status for progressive angle narrowing, development of synechiae, rising IOP and ischemic changes to the iris or lens.

Introduction

The aims of monitoring patients diagnosed with glaucoma are to detect progression, evaluate the effects of treatment, re-assess risk factors for progression and note changes in health that may influence glaucoma management plans. Appropriate monitoring plans will ensure that patients who are at risk of glaucoma, and patients with established glaucoma, do not worsen through inadequate, or inappropriate medical care. It is not always possible to stop disease progression. However, it can usually be slowed significantly with appropriate treatment. The aim of treatment is to halt disease progression, or at least retard it, so that any resultant visual loss has the least impact on the patient's quality of life. Similar to diagnosis, monitoring is not based on a single test; rather it is based on a combination of test methodologies and technological tools. Lowering intraocular pressure (IOP) is the strategy with the greatest evidence of effectiveness to achieve these goals. Therefore IOP measurement is vital in follow-up, with changes in visual field (VF) and fundus being the criteria for the alteration of target IOP. Once glaucoma has been diagnosed and patients placed on a treatment regimen, monitoring the patient's capacity for adherence to the regimen and engaging the patient with treatment maintenance (including attendance at future appointments) is essential to best practice. The monitoring cycle is outlined in Figure 8.1.

Monitoring occurs at review appointments. The patient's risk profile, disease state and capacity to self-manage dictate the frequency of review.

Figure 8.1: The monitoring cycle



Medical history

The collection of information from patients being monitored for glaucoma progression should include an adequate history of the patient's health since last visit, as well as questions regarding ocular history, new systemic medications, and any side effects from ocular medications since last assessment. Frequency and time of the last IOP-lowering medication administration and review of use of systemic medications should also be included (American Optometric Association [AOA] 2002).

Assessing a patient's capacity to adhere to a medication regimen is essential, otherwise medication management may need to be escalated, on an assumption of medically unresponsive glaucoma. Health care providers should thus develop a patient-by-patient understanding of the factors associated with individual adherence to glaucoma management strategies. Health care providers should then develop strategies in partnership with the patient to assist in addressing barriers to ongoing adherence with management programs. Understanding the patient's social and behavioural responses to a diagnosis of a chronic eye condition such as glaucoma is essential. This enables health care providers to assist the patient to manage their condition in the best possible manner for them. This optimises the patient's quality of life, and reduces complications and the likelihood of deterioration of their condition. Accurate and timely information on the patient's use of prescription and over-the-counter medications for other health conditions is essential, as is an understanding of the patient's capacity to self-administer and to pay for glaucoma medications.

This guideline provides ideas regarding Questions to Ask Your Patient at the end of this chapter.

Evidence Statement

- Evidence strongly supports taking a comprehensive history at each review. This should include information on what has occurred in the intervening period, and the patient's ability to adhere to the prescribed medication regimen.

Intraocular pressure

A specific target IOP should be established for each patient at diagnosis. A primary purpose of any review is to assess whether this target has been achieved, and whether there is evidence of glaucoma progression. This provides a basis for continuing or changing the glaucoma management plan.

IOP is generally measured in the sitting position, although occasionally a supine measure is useful. IOP can vary during the day and night and therefore diurnal curves for IOP are valuable. Recording the time of IOP measurement at each contact with a health care provider allows practical clinical assessment of daytime diurnal variation. Useful information regarding glaucoma progression at apparently low IOP levels may be gained from one to two hourly IOP measurements over a 12 to 24 hour period. Attention needs to be given to glaucoma treatments that are effective over 24 hours (AOA 2002).

Recent independent evidence shows better field preservation with smaller diurnal fluctuations in IOP (European Glaucoma Society [EGS] 2003, citing the Advanced Glaucoma Intervention Study [AGIS] Investigators).

In clinical practice, a patient's target pressure is that which is judged by the health care provider to have the best probability of limiting disease progression. The goal is to achieve it, or to approach it with minimal treatment-induced adverse effects on quality of life. Thus exact margins for failure to achieve target IOP cannot be precisely defined, and the IOP measurement error is approximately 1–2 mmHg. The target IOP is often recorded as an acceptable range of IOPs rather than a single IOP value. Target IOP serves as a guide, which may be changed according to clinical need.

When target IOP is achieved, but there has been progression in damage to optic nerve or retinal nerve fibre layer structure and function, a further 20% reduction in IOP should be planned (Canadian Glaucoma Study Group 2006), provided non-adherence to treatment regimens between visits has been excluded as a cause. Further factors that should be considered when reviewing the target IOP include the patient's quality of life within the current management regimen, new systemic or ocular conditions and the risk:benefit ratio of the medication management required to achieve the target IOP.

Evidence Statements

- Evidence strongly supports assessing target intraocular pressure at each ocular review, within the context of glaucomatous progression and quality of life.
- Evidence strongly supports a further 20% reduction in target intraocular pressure when glaucomatous progression is identified.

POINT OF NOTE

Evidence supports the use of information on diurnal intraocular pressure curves. These are valuable in identifying fluctuations in intraocular pressure, and could contribute to a clearer picture of risk for patients with normal tension glaucoma.

Eye structure examination

External eye examination

Biomicroscopy should be undertaken to examine the lids, conjunctiva, cornea, and anterior chamber of the eye. This will detect adverse reactions to eye drops or signs of the development of secondary glaucoma (AOA 2002). Topical therapies often contain preservatives which can cause inflammation to the surface of the eye, and certain families of medication have a greater chance of doing so (primarily α_2 -agonists, carbonic anhydrase inhibitors, prostaglandin analogues). When a patient exhibits sensitivity that is adversely affecting adherence, it is worth considering preservative-free preparations.

Evidence Statements

- Evidence strongly supports using ocular examination to detect adverse reactions to eye drops, and secondary causes of glaucoma.
- Evidence supports using a preservative-free preparation when hypersensitivity to topical medication is identified during review.

Anterior chamber examination

Gonioscopy should be employed to rule out the development of an angle closure component. This should be repeated periodically for all patients with suspected or established glaucoma. Anterior imaging techniques may augment, but not substitute for gonioscopic examination. Gonioscopy is indicated in routine assessment for all patients. Specific indications for gonioscopy include:

- suspicion of an angle closure component, anterior chamber shallowing or anterior chamber angle abnormalities
- an unexplained change in IOP, and/or
- post-laser iridotomy that identifies residual angle closure (American Academy of Ophthalmology [AAO] 2005; EGS 2003).

Gonioscopy should also be undertaken when review indicates commencement of drugs known to induce angle closure (EGS 2003).

In the absence of specific indications, it has been recommended that gonioscopy is performed regularly in patients with angle closure (South East Asia Glaucoma Interest Group [SEAGIG] 2003) and periodically in those with open angle glaucoma (OAG) i.e. 1-5 years (AAO 2005a,b,c,).

Evidence Statements

- Evidence supports undertaking gonioscopy at review, where there is an unexplained rise in intraocular pressure, suspicion of angle closure and/or after iridotomy.
- Evidence supports performing gonioscopy regularly in patients with angle closure (three to six times per year) and periodically in those with open angle glaucoma (every one to five years).
- Expert/consensus opinion suggests monitoring patients with narrow but potentially occludable angles.

POINT OF NOTE

Angle closure can develop with ageing and lens change in any individual. Experts indicate that gonioscopy be performed more frequently than recommended by current guidelines, at intervals of one to two years for most individuals labelled as having open angle glaucoma. Less frequent observation may be justified in some individuals following cataract extraction.

Optic nerves

Visible damage to the optic nerve occurs early in the disease process, usually before visual field (VF) loss is detectable. Once VF defects have been established and optic nerve damage is severe, there may be little optic nerve neural tissue remaining to change. Therefore whilst optic nerve changes are a sensitive indicator of early and moderate glaucomatous damage, sequential perimetry may be a more sensitive indicator for progressive advanced glaucomatous damage.

The review process should aim to identify subtle changes in the optic nerve head including:

- further focal or generalised thinning of the neuroretinal rim
- increase in nerve fibre layer defect
- new disc rim haemorrhages which confer increased risk of progression (Heijl, Leske, Bengtsson et al 2002; Leske, Heijl, Hyman et al 2004).

Suitable techniques for examining the optic nerve are discussed in Chapter 7. Sequential photography or imaging enhancement technology can be particularly valuable to detect subtle changes in the optic nerve or nerve fibre layer. The Working Committee acknowledges that access to these technologies may not be widely available.

Fundus photography can provide a clinically useful and resource-appropriate level of information on longitudinal change in optic nerve structure. Photography through a dilated pupil can facilitate detection of change. Digital imaging analysis of such photos may be a valuable adjunct. Current clinical and trial standards use flicker analysis of photographs (Heijl et al 2002; Leske et al 2004) or rapid side-by-side comparison of photos (Gordon, Beiser, Brandt et al 2002), with the greatest sensitivity coming from flicker analysis of simultaneous stereo photographs (Barry, Eikelboom, Kanagasingam et al 2000).

There is less than perfect concordance between VF loss and disc damage (Artes & Chauhan 2005). Disc damage is more noticeable earlier in the disease. Of the available objective techniques to detect change, only confocal scanning laser tomography has been rigorously evaluated (Burgoyne 2004). Although retinal nerve fibre layer defects are also seen in other neurological disorders as well as in normal individuals, examination of the retinal nerve fibre layer is useful to detect early glaucomatous damage.

Nerve fibre layer

Assessment of the nerve fibre layer is similar to an optic nerve assessment, however it uses red-free illumination. In the early stages of glaucoma, estimation of structural abnormalities from serial nerve fibre layer photographs may be more sensitive than assessment of the optic nerve (AOA 2002). Visible structural alterations of the optic nerve head or retinal nerve fibre layer, and development of peripapillary choroidal atrophy frequently occur before VF defects can be detected. 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.



Colour stereo photography or computer-based image analysis of the optic nerve head and retinal nerve fibre layer are the best currently available methods to document optic disc morphology. Imaging techniques to assess the nerve fibre layer include scanning laser polarimetry and optical coherence tomography. For full details, refer to Chapter 7. Whilst any assessment of glaucoma should always integrate a range of sources of information, imaging is likely to play a more central role in the monitoring of glaucoma in the future, as the cost and availability of, and access to, equipment improves.

Evidence Statements

- Evidence strongly supports using validated techniques (with the highest sensitivity and diagnostic odds) to detect changes in visual field or optic disc in order to diagnose early primary open angle glaucoma.
- Evidence supports the value of validated optic disc comparison techniques (simultaneous stereo photograph comparison and confocal scanning laser tomography) in order to detect longitudinal changes in the optic nerve.

POINT OF NOTE

It is important to detect progression of damage to the optic nerve and retinal nerve fibre layer early in the disease process.

Automated perimetry

Due to inherent variability in the VF and the psychometric nature of the test (making VF testing a learning curve for many patients in order to perform well), threshold perimetry needs to be performed often in the first two years after glaucoma diagnosis.

Two VF tests (occasionally three) should be performed in the first year in order to account for patient learning and performance improvement. A validated device with proven ability should be used to compare the test with age-matched normals and good reproducibility characteristics to allow for comparison over time. The best of these early VF tests should be used as a baseline to facilitate future comparison. Depending upon the patient's clinical risk factors for progression (IOP, severity of disease, optic nerve haemorrhage, prior progression), the frequency of VF testing should be adjusted to once or twice per year. Occasionally more frequent tests are required if a significant change is suspected.

Visual comparisons of repeated threshold results, and/or statistical methods, are needed to detect the most subtle VF changes due to glaucoma. Subtle VF changes in localised areas of VF loss are identified using one of two main strategies: event analysis or trend analysis.

Event analysis is where the health care provider makes a judgement that a change from baseline has, or has not, occurred. A change is called an 'event'. A minimum of two stable field tests is required to form a baseline, as the first field test often provides a learning experience for the patient. Thereafter repeated losses from baseline are considered on a point-wise basis to establish an 'event'. Common definitions of VF progression generally use 24 degree radius fields with nasal extension to 30 degrees, containing 52 test points using a static white-on-white background stimulus. Generally, three or four adjacent points with significant reduction in sensitivity from

baseline, tested and confirmed on three occasions, is required to identify an 'event'. The definition of significant sensitivity reduction varies, for instance:

- using Glaucoma Change Probability Maps with average variability measures from age-matched patients, using either the age-corrected threshold values; or pattern deviation values, where global effects on VF from corneal or cataract changes have been minimised (Heijl et al 2002; Leske et al 2004). These forms of software analysis are available commercially with some VF equipment
- using set threshold reductions, which is a cruder, although still useful technique. For example, three points with ≥ 10 dB loss, or with three times the short term fluctuation is proposed (Spry & Johnson 2002). A cluster of three points each 15dB removed from baseline provides another definition of event (Optometrists Registration Board of Victoria 2008).

Trend analysis is regression analysis which quantifies the rate of loss in a VF index and/or the rate of loss in individual sectors or points of VF. It requires additional computer software and analysis of the regression. Linear regression is used, and slopes of change calculated as those slopes which are significantly different from zero (Spry & Johnson 2002). This allows easier prediction of time to severe visual loss (to reach approximately -20dB mean deviation for example) or blindness (-30dB). The accuracy of the trend, similar to event analysis, depends partly upon the variability of the VF tests. Regressions are notoriously subject to outlier effects and particularly to the final datum. Methods for managing these problems have been described, such as using only three tests per year, and a 3-omitting logic (Gardiner & Crab 2002).

A number of guidelines have made recommendations for the frequency of VF monitoring. However it has been noted by the AOA (2002) that for any recommended interval, factors that determine frequency of evaluations should include the severity of damage (mild, moderate, severe), proximity of damage to fixation (more frequent evaluations for more severe disease), the rate of progression, the extent to which the IOP exceeds the target pressure, and the number and significance of other risk factors for damage to the optic nerve. Currently no single recommendation appears to take all these factors into account. Therefore the available recommendations have been combined to provide the most comprehensive level of recommendation currently available. These recommendations are based on guidelines and expert opinion, and are outline in Table 8.1.

It is important that health care providers employ sound clinical reasoning, for in certain cases, follow-up VF testing may be required more, or less, frequently than the recommended intervals. For instance, a second test may be required to establish a baseline for future comparisons, to clarify a suspicious test result, or to overcome an apparent testing artefact (AAO 2005c).

Table 8.1: Time period (years) required to detect various rates of mean deviation (MD) change with 80% power in visual fields with low, moderate and high degrees of variability with 1(a), 2(b) and 3(c) examinations per year (Chauhan, Garway-Heath, Goñi et al 2008)

One examination/year			
Variability			
Progression rate (dB/yr)	Low	Moderate	High
0.25	13	19	30
0.5	9	13	19
1.0	6	9	13
2.0	5	6	9
Two examinations/year			
0.25	6.5	9.5	15
0.5	4.5	6.5	9.5
1.0	3	4.5	6.5
2.0	2.5	3	4.5
Three examinations/year			
0.25	4.3	6.3	10
0.5	3	4.3	6.3
1.0	2	3	4.3
2.0	1.7	2	3

Evidence Statement

- Evidence supports undertaking visual field testing with automated perimetry on multiple occasions at diagnosis, in order to set a reliable baseline. An assessment of likely rate of progression will require two to three field tests per year in the first two years.

Indications to change regimen

The indications for adjusting a glaucoma management plan are:

- target IOP is not achieved
- the patient has progressive optic nerve or VF damage despite achieving the target IOP. The validity of the diagnosis and target pressure should be reassessed. Additional evaluation may identify conditions that are contributing to the progression of damage, and serve as a justification to escalate treatment. These evaluations include obtaining diurnal IOP measurements, repeating the central corneal thickness (CCT) measurement to verify a thin cornea or a change in corneal thickness after refractive surgery, or seeking evidence of unrecognised low ocular perfusion pressure. A neurologic evaluation also may be considered

- the patient is intolerant of the prescribed medical regimen
- the patient does not adhere to the prescribed medical regimen
- contraindications to individual medicines develop, and/or
- stable optic nerve status and low IOP occurs for a prolonged period in a patient on pressure-lowering medications. Under these circumstances, a carefully monitored attempt to reduce the medical regimen may be appropriate (AOA 2002).

Downward adjustment of target pressure should be made in the event of progressive optic disc or VF change. Upward adjustment of target pressure should be considered if the patient has been stable, and/or if the patient either requires less medication because of side effects, or personal choice. Whenever regimen changes are implemented, a follow-up visit is indicated within two to eight weeks to assess the response, as well as side effects from washout of the old medication, and onset of maximum effect of the new medication (AAO 2005c).

Monitoring recommendations in specific populations

Patients with ocular hypertension or suspected glaucoma

A number of systematic reviews have discussed the importance in the reduction of IOP in patients with OH to slow the progression to glaucoma (Collaborative Normal-Tension Glaucoma Study [CNTGS] 1998; Kass, Huerer, Higginbotham et al 2002). The purpose of the follow-up examination is to periodically evaluate the status of the patient's IOP, VF, appearance of optic disc and retinal nerve fibre layer, and to determine if there is evidence of development of glaucomatous damage (AOA 2005a). These guidelines report consensus of the Working Committee in the absence of conclusive scientific evidence. The interaction between person and disease is unique for every patient, and thus management should be individualised. The importance of assessing risk factors has been previously identified, therefore the recommendations are provided according to risk, current intervention (if any) and success of achieving target IOP under active management. Table 8.2 summarises monitoring recommendations for patients with suspected glaucoma.

Any patient who shows evidence of optic nerve deterioration based on optic nerve head appearance, increased optic disc cupping with rim loss, retinal nerve fibre layer loss, or VF changes consistent with glaucomatous damage, should be diagnosed as having developed OAG, and treated and monitored as described for established OAG.

POINT OF NOTE

Clinical judgement on a case-by-case basis is essential.

For newly diagnosed patients with glaucoma, and those who have undergone significant changes in treatment, assess the visual field two to three times per year, in the first two years, and then one to two times per year thereafter depending upon other risks, signs and symptoms.

Image the optic nerve every one to two years in glaucoma suspects and annually in glaucoma patients. A significant exception is for patients with substantial glaucomatous optic disc damage, with little remaining nerve tissue, and vertical cup:disc ratios (0.9 – 1.0). In these cases optic nerve imaging has little chance of detecting change in the remaining few fibres; there may not be a need to image at all.

Many field abnormalities on initial testing may not reproduce on subsequent tests.

There are a number of techniques which can be used to assess the visual field.

Table 8.2: Summary of recommendations for monitoring of glaucoma suspects (AAO 2005a,b,c; AOA 2002; South African Glaucoma Society [SAGS] 2006)

TREATMENT	STATUS	SUCCESS	FREQUENCY					
On medication	High Risk	Achieving target	Review	Tonometry	Gonioscopy	Optic nerve and nerve fibre layer	Stereoscopic, digitally assisted imaging on /nfl	Automated threshold perimetry
NO	NO	N/A	6–12/24 months	Multiple/ every visit	Sufficient to set baseline – then annually	6–24 months or every other visit	Sufficient to set baseline – then every two years	Sufficient to set baseline – then annually
	YES	N/A	3–12 months			6–18 monthly		
YES	YES	YES	3–12 months			6–18 monthly		
		NO	<4 months			3–12 monthly		

Evidence Statement

- Expert/consensus opinion suggests undertaking ocular reviews at six to twenty-four month intervals, for individuals with suspected glaucoma without high-risk factors, who are not receiving treatment.

All patients with suspected glaucoma

Evidence Statements

- Expert/consensus opinion suggests using automated perimetry at least annually, for patients with suspected glaucoma.
- Expert/consensus opinion suggests that gonioscopy should be performed at one to five year intervals depending upon degree of angle opening, and presence of prior lens extraction surgery, for patients with suspected primary angle closure glaucoma.
- Expert/consensus opinion suggests undertaking dilated examination of the optic nerve and optic nerve fibre layer at six to eighteen month intervals for all patients with suspected glaucoma. Undilated examination of the optic disc, looking for change, and presence of disc rim haemorrhage, should be undertaken at most visits.
- Expert/consensus opinion suggests examination of the optic nerve with validated comparison techniques every one to two years for all patients with suspected glaucoma.
- Expert/consensus opinion suggests using tonometry at every visit for all patients with suspected glaucoma, once baseline intraocular pressure has been set.



Patients with suspected glaucoma, and high-risk factors who are undergoing treatment and achieving targets

Evidence Statement

- Expert/consensus opinion suggests undertaking ocular reviews at three to twelve month intervals for individuals with suspected glaucoma and high-risk factors who are undergoing treatment and achieving targets.

Patients with suspected glaucoma, and high-risk factors who are undergoing treatment and failing to achieve targets

Whenever medication regimen changes are implemented, a follow-up visit is indicated within two to eight weeks to assess the response, as well as side effects from wash-out of the old medication, and onset of maximum effect of the new medication (AAO 2005c).

Evidence Statement

- Expert/consensus opinion suggests undertaking ocular reviews at less than four month intervals for individuals with suspected glaucoma, and high-risk factors, who are undergoing treatment and not achieving targets.

When treatment is altered, patients should be reviewed within two months.

Conversion from suspected to diagnosed open angle glaucoma

A patient who shows evidence of glaucomatous optic nerve deterioration (from optic nerve head appearance, optic disc cupping, retinal nerve fibre layer loss, or characteristic VF change) should be diagnosed as having developed primary open angle glaucoma (POAG). Therefore recommended treatment and review processes should occur as indicated in the previous summary table.

Newly diagnosed glaucoma

It has been identified that two field tests (occasionally three) should be performed in the first year in order account for patient learning and performance improvement. As noted by Chauchan (2008 p.9) '*clinical decisions on patient management require more than an formulaic approach based on visual field progression because risk factors such as baseline damage, age, and IOP may have different relative weights in driving these decisions*'. Therefore the recommendations in this guideline are not a protocol, rather a practical guide and template, to be used within a wider framework of clinical judgement.

Established glaucoma

Patients with POAG should receive regular follow-up evaluations and care to monitor and treat their disease. The recommendations in this guideline have been produced by a process of combining current recommendations with input from experts in the field.

Based on understanding of the effect of CCT on IOP measurements, pachymetry should be repeated after any event (e.g. refractive surgery) that may alter CCT. When monitoring IOP, the frequency of review is dependent upon the achievement of target pressures which were set at baseline. The evidence suggests the following monitoring approach.



1. Target achieved

Follow-up reviews are dictated by the stability of the VF and the disc findings.

2. Target not achieved

Health care providers should fully review patients' capability to adhere to the medication regimen. When reviewing patients who have previously undergone surgery, it is important to review drainage blebs.

The therapeutic regimen should then be altered, as appropriate. This guideline provides evidence-based hierarchies of choice regarding therapeutic intervention (see the Chapters on medication (9), laser therapy and surgery (10)). Options include increased support for adherence, change of medication, laser or surgery. Frequent review (every four to six weeks) may be required whilst altering treatment and re-establishing baseline IOP.

3. Target not achieved and concurrent fluctuation of intraocular pressure

When there is very unstable IOP, more frequent review (every one to four weeks) may be required, whilst altering treatment and re-establishing baseline IOP.

Evidence Statements

- Expert/consensus opinion suggests that in established glaucoma where intraocular pressure targets are being achieved, monitoring schedules are guided by the severity and stability of disc and visual field examinations.
- Expert/consensus opinion suggests that in established glaucoma where intraocular pressure targets are not being achieved, the management plan requires alteration and a review undertaken within four to six weeks.
- Expert/consensus opinion suggests that in highly unstable established glaucoma, where intraocular pressure targets are not being achieved, the management plan requires alteration and a review undertaken within one to four weeks.
- Evidence supports using tonometry on every visit, for patients with established glaucoma, once a baseline has been set.
- Expert/consensus opinion suggests that monitoring timelines for patients with angle closure glaucoma are guided by angle morphology, optic disc and/or visual field stability and intraocular pressure.

After surgery for primary open angle glaucoma

This section outlines the evidence for monitoring patients after surgery. This evidence has been distilled from guidelines included in this review.

Post-laser treatment for glaucoma

The laser treatments for glaucoma tend to require very similar post-operative care. The only exception here is cyclodiode laser. The commonest lasers performed for glaucoma are YAG laser iridotomy, Argon laser trabeculoplasty, laser iridoplasty and selective laser trabeculoplasty. All these four laser types can cause an elevation in intraocular pressure which may last from hours to days or weeks. The most likely situation in which this will occur is in elderly patients, those with narrowed angles and, in particular, those with an inflammatory component to their glaucoma. All of these laser procedures should be treated with an alpha-2 agonist (Brimonidine or Iopidine) prior to or just after the laser is performed (using one drop in the treated eye).

YAG laser peripheral iridotomy creates a small hole in the iris using laser energy to disrupt tissue. This disruption sends fragments of tissue into the aqueous humour which then flows to the trabecular meshwork and can transiently cause blockage and pressure elevation. Normally this is not significant but in patients who are elderly, those with numerous peripheral anterior synechia (hence with little remaining functional trabecular meshwork) or those with an inflammatory component, the risk of pressure elevation may be higher. These patients at higher risk should have their intraocular pressure checked within hours after the laser is performed. Any other patients who may be at risk should also have their pressure checked within hours of the laser being performed. Other patients should have their pressure checked within a week of laser surgery being performed. It is usual for patients to receive a weak topical steroid drop to use several times a day for four or five days following laser iridotomy.

Argon laser trabeculoplasty causes burns to the trabecular meshwork which can be inflammatory in nature. It is not uncommon for a pressure rise to occur and this pressure rise appears to be more common in patients with damaged angles from either angle closure; trauma or inflammatory eye conditions. Indeed Argon laser trabeculoplasty in patients with these conditions is frequently considered to be relatively contra-indicated. If Argon laser trabeculoplasty is performed on these patients their pressure should be checked within hours of the laser. Other patients should be checked within a week. These patients will normally be given a weak steroid drop to use several times a day for the first four or five days. Argon laser trabeculoplasty and selective laser trabeculoplasty generally take six weeks to have maximal pressure-lowering effect.

Laser iridoplasty generally causes little pressure rise although can cause inflammation. In addition to an alpha-2 agonist, patients should be given a topical steroid 4 times a day for 4 days and be reviewed within a week.

Selective laser trabeculoplasty does not cause as much inflammation and a topical steroid is not normally required post-laser, although some clinicians will give patients a single use sample (minims) to use twice a day for one to two days after the laser is performed. Patients with an inflammatory component or with damaged or partly closed angles are at risk of developing a post-laser pressure rise and should be treated as high risk subjects and have their pressure checked within hours of the laser being performed. All patients should have their pressure checked within a week of the laser being performed.

Cyclodiode laser uses high powered laser to actually burn the ciliary processes within the eye enough to destroy their function. The power required to do this always causes significant inflammation and usually a lot of pain post-laser. Patients having cyclodiode laser should be given a strong topical steroid (Maxidex or Prednefrin Forte) at least four times a day for several days post-laser. Pain relieving medications such as Panadeine Forte will often be required for several days. IOP spikes in first 24 hours are quite common, so we recommend a pressure check in first 24 hours and prophylactic treatment with medications to minimize any pressure rise. The pressure usually falls within a few days of cyclodiode laser and takes some weeks to stabilise. It is not uncommon for two to three treatments to be performed before a more stable and lower pressure is reached.

Post-argon laser trabeculoplasty

Monitoring should occur one hour post-operatively.

- Measure IOP and check for corneal abrasions.
- If normal, re-evaluate patient one to two weeks later. If IOP is elevated or corneal abrasion is present, provide treatment. Monitoring should then occur four to eight weeks post-laser intervention, and then revert to standard monitoring.



Post-filtering surgery

- Follow-up evaluation should be undertaken by the surgeon on the first post-operative day (12 to 36 hours after surgery).
- Evaluation should then occur at least once, from the second to the tenth post-operative day, to evaluate visual acuity, IOP, and status of the anterior segment.
- In the absence of complications, additional regular post-operative visits should be undertaken over the next six weeks to evaluate visual acuity, IOP, and status of the anterior segment.
- More frequent follow-up visits should occur, as necessary, for patients with post-operative complications such as a flat or shallow anterior chamber, or evidence of early bleb failure, increased inflammation, or Tenon's cyst formation.

After laser therapy or surgical treatment, a proportion of patients will be able to reduce or cease their medication. This may raise issues for monitoring. Health care providers should be sure that patients understand the chronic nature of their disease and the continued need for monitoring. A member of the health care team should take responsibility for monitoring these patients despite their independence from medication management.

After surgery for angle closure

Following iridotomy, patients should have their angles reassessed to ensure opening of the angle. If the angle has not opened, further intervention (such as peripheral iridoplasty) should be considered. Patients may have an open anterior chamber angle or an anterior chamber angle, with a combination of open sectors, with areas occluded by peripheral anterior synechia. When associated with glaucomatous optic neuropathy, the latter condition is sometimes designated as combined mechanism glaucoma.

Immediate post-operative regimens should include:

- Evaluation of the patency of iridotomy
- IOP measurement immediately (one to three hours post-operatively), and again at one week. Earlier review may be necessary if the angle is not well opened or the trabecular meshwork is altered. Prophylactic medication should be provided to prevent spikes
- Gonioscopy should be repeated as clinically indicated
- Fundus examination should be undertaken as clinically indicated (AOA 2005b,c; EGS 2003).

After iridotomy, patients may be classified as residual open angle, or a mix of open angle and peripheral anterior synechia. Patients in whom glaucomatous damage has occurred should be monitored as recommended for POAG. Patients who do not have glaucomatous optic neuropathy should be monitored in a manner similar to a POAG suspect (AAO 2005c).

Professional roles within the team

Monitoring

Disc-imaging and photography can be performed by registered optometrists and ophthalmologists, and may be delegated to other appropriately trained and supervised health care providers. Most diagnostic and therapeutic procedures can be performed safely on an outpatient basis.

Most glaucoma management is performed in the out-patient setting. Hospitalisation may be required to ensure adequate application of treatments, such as for poorly responsive acute angle closure attack. This is so patients can be monitored closely after surgical procedures associated with a high risk of

serious short-term post-operative complications. Hospitalisation may also be indicated for patients in whom surgical complications have occurred or for patients who have special medical or social needs. Children with suspected glaucoma should be immediately referred to a specialist ophthalmologist and may need to be anaesthetised for assessment. Patients should be informed about which health care provider is responsible for particular aspects of their glaucoma care.

Referral

Using established networks, primary health care providers are encouraged to engage with an ophthalmologist when a glaucoma diagnosis is suspected or confirmed. Various formal and ad-hoc relationships between general practitioners, nurses, ophthalmologists, optometrists and orthoptists exist around the country to maximise the use of diagnostic resources which should be encouraged.

Close cooperation between optometrists and ophthalmologists should provide an optimal environment for the management of glaucoma. This may vary according to the patient's location and the cooperation may involve optometric and general practice treatment initiation with ophthalmologist follow up especially where ready access to an ophthalmologist is not available. Cooperation between all three professional groups is recommended for all patients diagnosed with glaucoma. Patients with significant visual impairment or blindness should be referred to, and encouraged to use, appropriate vision rehabilitation and social services to enhance their quality of life and independence.

Questions to ask your patient with glaucoma at review

How are you? How are your eyes and vision?

Are you managing to take your medication as discussed? If no, what are the problems and difficulties you face?

Is there anything about your condition or your treatment plan that you would like explained?

Are you experiencing any side effects from the medication?

Do you have other medical conditions? If yes, have they been exacerbated recently?

Are you taking any prescription or over-the-counter medicines, if so what?

Do you have plans to conceive/are you already pregnant? If yes, do you plan to breastfeed?

When did you last attend an eye examination or have your condition monitored?

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■ CHAPTER 9

Medication

Recommendation 11

Reduce IOP by using medication

Good Practice Points

- Due to potential efficacy and once-daily usage, a topical prostaglandin analogue is usually the first choice, unless contraindicated. When more than one agent is required, fixed-dose combinations should be considered to encourage improved compliance.
- Topical medications may be the simplest and safest first choice for treatment, except for pregnant and lactating women.
- Facilitate adherence and perseverance with a patient-centric self-management approach to a medication plan. Provide ongoing tailored information (such as from Glaucoma Australia) to reinforce a patient's understanding of glaucoma and realistic goals of treatment.
- Initiate, switch or add medications to one eye, using the other eye as a "control". In these cases, reassess IOP within 2-6 weeks before treating the other eye. If there is no apparent effect check for adherence.
- Teach patients the "double DOT" (Don't Open Technique and Digital Occlusion of Tear ducts) for 2-3 minutes post-instillation to minimise systemic absorption and to promote ocular penetration of eyedrops.
- Demonstrate instillation techniques, observe patient or carer instilling drops and repeat education till ability to instill has been proven.

Introduction

Medication is generally the first management choice² by health care providers for most patients with glaucoma. Medication is used to reduce intraocular pressure (IOP) by enhancing aqueous outflow and/or reducing aqueous production. There are five main families of glaucoma medications, each with recognised actions, side effects and contraindications.

When prescribing glaucoma medication, many factors should be considered including IOP-lowering potency, additive effects, interaction with concomitant medications and disease states, side effects and ease of administration. Persistence with and adherence to medication regimens is vital in the management of chronic disease. Glaucoma medication must be suited to an individual patient's capacity to effectively self-administer.

Conventional medication management of glaucoma usually begins with topical eye drops. However, in situations where patients are unable to instill eye drops safely or effectively, or where reduction in IOP is less than desired, oral acetazolamide may be used. This form of delivery however, is

² NB: First choice refers to medications that a treating health care provider prefers to use as the initial intervention. First line refers to a medication that has been approved by an official controlling body for initial intervention (European Guideline Society [EGS] 2003). This guideline refers to first choice as it provides guidance to health care provider



associated with a greatly increased risk of developing side effects and, up to 50% of patients treated with acetazolamide do not tolerate it. Systemic use of beta-blockers is not as effective in reducing IOP as topical medications and the concurrent use of topical and systemic beta-blockers should be avoided.

POINT OF NOTE

This text is only a general guide to medications. It does not claim to contain all the medications, side effects and contraindications related to the treatment of glaucoma, and only the most common and relevant are discussed. Medication discovery and design is constantly evolving, therefore the information in this guideline has been updated since the publication of the associated systematic review. Before a health care provider commences a patient on a course of medication, it is advised that the product information sheet is carefully read and, if required, an expert opinion sought.

Medication families

Medications used for the long-term management of glaucoma fall into five classes: beta-blockers, prostaglandin analogues, α_2 -agonists, carbonic anhydrase inhibitors and cholinergic agonists. Hyperosmotic medications such as mannitol are given to lower IOP in emergency situations, however as they are not used for long-term management, they are not completely described in this chapter. Glaucoma medications reduce IOP by increasing aqueous outflow and/or decreasing aqueous production. Each medication family has a different method of action, and can have significant side effects.

The time taken to achieve maximal reduction in IOP is dependent on both the individual and the type of medication used. Initial reduction in IOP typically occurs within minutes to hours after administration, while maximal reduction in IOP can take weeks to months. For example, the known maximum IOP-lowering effect of prostaglandin analogues occurs after three to five weeks (EGS 2003). Therefore, response to newly initiated medications should be assessed after two to four weeks.

When medications are ceased, it is important to note that they may have some continued effect on reducing IOP. The approximate time it takes for IOP to return to baseline levels after ceasing medications, also known as the wash-out period, is listed in Table 9.1. Table 9.1 also provides information on medications available in Australia, their mechanism of action, daily dosage requirements, efficacy, order of treatment choices and wash-out periods.

Hierarchies of intervention

There is general consensus that medications should be the first choice of management for almost all patients with glaucoma. Even when patients present in emergency situations with acute angle closure, medication is used to reduce IOP, to clear corneal oedema and to reduce pain, in preparation for laser therapy or surgery. There is increasing interest in using laser techniques earlier in the glaucoma management hierarchy. Evidence supports the use of laser therapy as first choice intervention in angle closure and for specific patient groups with open angle glaucoma (OAG) who are at-risk of visual loss within their lifetime. Further details are provided in Chapter 10.

The most appropriate point-in-time medication should be prescribed for individuals relevant to their specific disease state. As disease states change, and/or as patients become less (or more) able to manage the administration of a particular medication type, other treatment choices can be made. A wide range of anti-glaucoma medications are available. The literature highlights that the type

and actions of medications available for glaucoma management are also continually changing, as a result of ongoing research. For instance, current evidence supports the use of medication to lower IOP as having the most beneficial effect on prognosis. However Costa, Harris, Stefansson et al (2003), in a systematic review of studies investigating ocular blood flow improved by medications, indicated that reducing the IOP may not be the only way to treat glaucoma. This review suggested that in the future, glaucoma may also be treated by employing strategies that are additive, or synergistic, to IOP control.

Table 9.1: Medications available in Australia that are used in the management of glaucoma

Preparations by class	Mechanism of action	Efficacy	Daily dosage	Wash-out period	Order of treatment choices
Prostaglandin analogues Latanoprost 0.005% Travoprost 0.004% Bimatoprost 0.03%	Increase aqueous outflow	25-30%	1x	4-6 weeks	FIRST
Beta-blockers <i>Non-selective agents</i> Timolol 0.25%, 0.5%, 0.1% Levobunolol 0.25% <i>Selective agents</i> Betaxolol 0.25%, 0.5%	Decrease aqueous production	20-25%	1x to 2x	2-5 weeks	FIRST
Proprietary-fixed combinations Combigan (brimonidine 0.2%/timolol 0.5%) Cosopt (dorzolamide 2%/timolol 0.5%) DuoTrav (travoprost 0.004%/timolol 0.5%) Xalacom (latanoprost 0.005%/timolol 0.5%)	As for individual components	25-30%	2x 2x 1x 1x	As for individual components	SECOND
Alpha2-agonists Brimonidine 0.2% Apraclonidine 0.5%	Increase aqueous outflow and decrease aqueous production	20-25%	2x to 3x	1-3 weeks	SECOND
Carbonic anhydrase inhibitors <i>Topical</i> Dorzolamide 2% Brinzolamide 1% <i>Systemic</i> Acetazolamide 250mg	Decrease aqueous production	15-20% 25-30%	2x to 3x 2x to 4x	1 week 3 days	SECOND THIRD
Cholinergics (Miotics) Pilcarpine 1%, 2% Carbachol 1.5%, 3%	Increase aqueous outflow	20-25%	3x to 4x	3 days	THIRD

POINT OF NOTE

In the majority of cases, medication is the first choice of management for patients with glaucoma. There is an ever-increasing range of medication options and regimens that can be tailored to individual needs. The selection will depend upon glaucoma subtype, stage of disease and personal situation.

Starting medication regimens

Health care providers and patients should choose medications based on the greatest chance of achieving target IOP, the best safety profiles, the most convenient delivery method and most affordable (South-East Asia Glaucoma Interest Group [SEAGIG] 2003). To facilitate adherence to medication regimens, health care providers should start with the simplest, most appropriate medication. Particularly for OAG, treatment should be initiated at the lowest effective concentration of medication, preferably administered once daily (Royal College of Ophthalmologists [RCO] 2004).

There is general consensus that topical preparations are the first choice management for most glaucoma patients. When patients cannot tolerate prostaglandin analogues or topical beta-blockers, they should be offered one of the other topical medications first, prior to being offered a systemic medication. This is due to their improved efficacy, ease of instillation (once daily dosing), lower incidence of side effects, relatively limited contraindications or precautions to use and lack of significant interactions with other medications. Hierarchies of use are outlined in Table 9.1.

Combination eye drops are becoming a more popular medication management choice. Anti-glaucoma eye drops can be combined with each other, as well as offered in conjunction with laser therapy and surgical management. Combination eye drops are preferred to two separate instillations of individual medications for improving patient adherence and reducing inconvenience.

Currently all available fixed combination eye drops contain timolol with a prostaglandin analogue, carbonic anhydrase inhibitor or alpha2-agonist. It is essential that the components of combination products are carefully considered before prescribing to ensure all precautions and contraindications to use are taken into account. Also, as medications from the same class should not be used in conjunction with each other, it is important that the choice of a combination product does not duplicate existing medication management (i.e. timolol or betaxolol should not be used along with any of the current fixed dose combinations, all of which already contain timolol). The effect of combined topical medications should be measured in terms of IOP reduction, as for single medication preparations. Currently no specific combination of medications has been identified as preferable, in terms of visual field (VF) preservation or ocular nerve head (optic nerve head) health.

Systemic administration of acetazolamide may be indicated when patients cannot tolerate topical medications, are unable to safely and effectively instill the medications topically, or are failing to achieve IOP targets and glaucomatous stability. This form of delivery however, is associated with a significantly increased risk of developing side effects. For instance up to 50% of patients treated with acetazolamide do not tolerate it. Therefore laser therapy or surgery is often considered as an alternative at this stage.

Evidence Statements

- Evidence strongly supports using topical medications as the simplest and safest first choice for glaucoma management.
- Evidence strongly supports limiting the use of systemic medication to situations where patients cannot tolerate topical medications, are unable to safely and effectively instill topical medications, are failing to achieve intraocular pressure targets, or when laser therapy or surgery either had poor outcomes, or are contraindicated.
- Evidence strongly supports using a topical prostaglandin analogue or beta-blocker in the initial management of glaucoma unless contraindicated.
- Evidence strongly supports carbonic anhydrase inhibitors and alpha2-agonists as second and third choice medication management, with dosing regimens of two to three times daily.

Facilitating adherence

Optimum medication management of glaucoma requires a high level of adherence to medication administration. The largely asymptomatic, chronic and incurable nature of glaucoma is also responsible for significant non-adherence with treatment, as the adverse effects of not following a treatment plan are not severe (or are without immediate consequences in the short term) (EGS 2003). Despite the availability of effective medications, non-adherence in patients with glaucoma has been reported to vary from 24% to 59% (Tsai 2006 citing Rotchford 1998; American Academy of Ophthalmology [AAO] 2005a; South African Glaucoma Society [SAGS] 2006). Adherence is influenced by the frequency of topical medication (drop) instillation, side effects, cost and lack of understanding of the disease process (SAGS 2006).

Patient education and informed participation in treatment decisions improves adherence as well as the overall effectiveness of medication management (Osterberg & Blaschke 2005). Patient involvement is recommended as best practice for the management of other chronic diseases (Holman & Lorig 2000; Lorig, Sobel, Stewart et al 1999; Lorig, Holman, Sobel et al 2000). The literature reviewed for these guidelines consistently endorsed that health care providers should develop patient-by-patient understanding of the factors that may constrain their adherence with glaucoma management strategies. Health care providers should then develop strategies to address patient-specific barriers to optimise patient adherence to management programs. Understanding patients' social and behavioural responses to the diagnosis of a chronic eye condition such as glaucoma is essential for health care providers to assist them to manage their condition in the best possible manner. Management strategies should aim to optimise quality of life, and reduce complications whilst decreasing deterioration of the condition. Self-management strategies that engage patients in their own care are successful compared with health-professional-directed 'paternalistic' care (Nys 2008). Potentially simple, patient-centred approaches are the most effective long-term strategies for effective glaucoma management.

To maximise patient adherence with medication, health care providers are advised to simplify the medication regimen wherever possible. The lowest dose of the most effective medication should be used for each patient in order to reach the target IOP and prevent progression of structural damage and VF defects. A once-daily medication dose appears to increase patient satisfaction and adherence can be improved through the use of combination eye drops (Tsai 2006 citing Stewart 2004). Many pharmacies have the capacity to provide a medicines profile, listing the prescription, OTC and complementary medicines being taken by a particular patient. The profiles are used to support patients in managing their medicines and can also be used as an effective communication tool when seeing other health professionals.

Evidence Statements

- Evidence supports a patient-centric self-management approach that facilitates optimal adherence to the medication management plan.
- Evidence supports the value of ongoing, tailored information to support patients' understanding of their disease and its management.
- Evidence strongly supports using combination preparations, rather than separate instillations of individual medications, to improve patient adherence. There is no evidence however, showing that one combination preparation is more effective than any other for reaching target intraocular pressure.

Practical actions to promote adherence were modified from Stamper, Lieberman and Drake (1999) (cited by American Optometric Association [AOA] 2002). These include:

- continually stress to patients the need for adherence and persistence with medication management strategies
- continually educate patients about the risks and prognosis of their disease
- make treatment decisions in cooperation with the patient
- write down in large font the medication regimen for patients, including time of day, number of drops and a clear method of identifying the medications (i.e. colour of bottle cap or number system)
- take a team approach to patient management by involving all relevant health care providers in glaucoma care decisions
- communicate regularly in writing, as appropriate, with relevant health care providers about glaucoma care decisions
- ensure that all medications have clear labels and information about their use
- give patients information to improve their understanding, such as literature from Glaucoma Australia
- put patients in touch with consumer groups for ongoing support and information.

Communication to health care providers

Glaucoma Australia provides a range of educational resources for patients and their families, to assist them to understand and manage their disease. Contact details for Glaucoma Australia, and other useful resources, are found in Chapter 12.

POINT OF NOTE

Educational resources about glaucoma should be widely available from every member of the glaucoma health care team. At diagnosis, patients should be provided with written information to support their understanding.

Medication interaction

Each medication family for the management of glaucoma has the potential to interact with any other, as well as with medications taken for other conditions. The additive effect of glaucoma medications is outlined in Table 9.2, derived from the EGS Guidelines (2003) and modified by expert opinion. The significance and severity of these interactions can vary greatly, so it is essential that accurate and timely information on a patient's use of all prescription and over-the-counter medications is obtained.

Medications for glaucoma may also interact with patients' medical conditions, regardless of whether medications are being taken for other medical conditions or not. Therefore, for patients with other medical conditions, health care providers should be aware of any precautions or contraindications regarding the use of medications for the management of glaucoma. A summary of these interactions is provided in Table 9.3.

Table 9.2: Additive effects of medications used in the treatment of glaucoma (modified from EGS 2003)

Class of medication	Alpha₂-agonists	Beta-blockers	Topical carbonic anhydrase inhibitor	Cholinergic	Prosta-glandin analogues	Sympatho-mimetics
Alpha ₂ -agonists		+	+	+	+	-
Beta-blockers	+		+	+	+	+
Topical carbonic anhydrase inhibitor	+	+		+	+	+
Cholinergic	+	+	+		+/-	+
Prostaglandin analogues	+	+	+	+/-		

+ good additive IOP-lowering effect

- additional IOP-lowering effect is relatively poor

* available in combined preparation

Evidence Statement

- Expert/consensus opinion suggests the need to establish the presence of other disease states when initiating, assessing or altering medication regimens for patients with glaucoma. These include, but are not limited to, diabetes, depression, hyperthyroidism, heart disease, asthma, liver and renal impairment.

POINT OF NOTE

Communication between health care providers is important to ensure safe and effective medication management.

Table 9.3: Summary of medications and their respective contraindications, precautions and interactions

Class	Contraindications	Precautions to use	Interactions
Prostaglandin Analogues Latanoprost Travoprost Bimatoprost		Intraocular inflammation (iritis, uveitis)—relatively contraindicated if active; monitor carefully if history of disease. Aphakia, pseudophakia, torn posterior lens or capsule, known risk factors for macular oedema—increased risk of developing macular oedema	NSAIDs (eye drops)—reduce efficacy of prostaglandin analogues
Beta-blockers <i>Non-selective agents</i> Timolol Levobunolol <i>Selective agents</i> Betaxolol	Reversible airways disease, e.g. asthma—use is generally contraindicated, however cardio-selective agents, i.e. betaxolol, may be used with care. Brady arrhythmia Heart block	Diabetes Hyperthyroidism Cardiac Failure COPD—betaxolol preferred Depression—may aggravate Elderly—Systemic adverse effects are more common, e.g. hypotension (may cause falls) Children—May cause bradycardia, bronchospasm and hypoglycaemia	Systemic beta-blockers—potential additive effects Catecholamine-depleting medications Medications that reduce BP, cardiac contractility and conduction—potential additive effects Verapamil—only use under specialist supervision
Alpha₂-agonists Brimonidine Apraclonidine	Monoamine oxidase inhibitors therapy Children younger than two years—use with caution in children younger than seven years	Severe cardiovascular disease—may worsen; use with caution. Depression—may aggravate	CNS depressant: Alcohol Barbiturates Opiates Sedatives Anaesthetics Tricyclic anti-depressants Hypotensive agents—potential additive effect
Carbonic Anhydrase Inhibitors <i>Topical</i> Dorzolamide Brinzolamide	Corneal grafts, endothelial dystrophy—may cause corneal oedema and precipitate corneal decompensation. Allergy to sulfonamides—may increase risk of allergy to carbonic anhydrase inhibitors	Severe hepatic/renal impairment	None reported, but potential exists for similar interactions as for systemic carbonic anhydrase inhibitors

Class	Contraindications	Precautions to use	Interactions
<i>Systemic</i> Acetazolamide	Sulfonamide allergy Renal stones/failure Respiratory/metabolic acidosis Hypokalaemia Hyponatraemia Severe renal impairment	Hepatic failure Mild to moderate renal impairment Gout Diabetes	Aspirin (high dose) Lithium Cyclosporine Diuretics Digoxin
Cholinergics (Miotics) Pilcarpine Carbachol	Uveitis - exacerbates blood-ocular barrier breakdown Secondary glaucomas associated with extensive outflow obstruction—ineffective, may worsen	Asthma Urinary-tract obstruction High myopia, aphakia, peripheral retinal degeneration, previous retinal detachment—increased risk of retinal detachment	
Proprietary fixed combinations Combigan (brimonidine/timolol) Cosopt (dorzolamide/timolol) DuoTrav (travoprost/timolol) Xalacom (latanoprost/timolol)	As for individual components	As for individual components	As for individual components

Side effects

Health care providers should not underestimate the potentially significant side effects associated with either topical or systemic use of medications for glaucoma. Side effects can be life-threatening and particular caution should be exercised when prescribing medications for infants and the elderly who may be more susceptible to various side effects (RCO 2004). Some side effects occur immediately, but most occur over time. Thus optimum management of patients with glaucoma should include regular monitoring and review of medication regimens. Details of side effects related to glaucoma medications are reported in Tables 9.4 and 9.5. Data were taken from the EGS (2003) and the Australian Medicines Handbook [AMH] (2009).

Evidence Statement

- Evidence strongly warns of the significant potential side effects from both topical and systemic medications in the management of glaucoma.

Table 9.4: Summary of ocular side effects

Preparations by class	Topical ophthalmic side effects	Systemic side effects
Alpha₂-agonists Brimonidine 0.2% Apraclonidine 0.5%	Ocular allergic reaction Burning Stinging Blurring Foreign-body sensation Itching Hyperaemia Lid retraction Conjunctival blanching Photophobia Mydriasis (Apraclonidine)	Central nervous system depression Oral dryness Headache Fatigue Drowsiness Bradycardia Systemic hypotension Hypothermia Apnoea Taste disturbance Syncope
Beta-blockers <i>Non-selective agents</i> Timolol 0.25%, 0.5%, 0.1% Levobunolol 0.25% <i>Selective agents</i> Betaxolol 0.25%, 0.5%	Burning Stinging Photophobia Itching Tearing Decreased corneal sensitivity Hyperaemia Punctate keratitis Diplopia	Bronchospasm Hypotension Bradycardia Heart block Mask hypoglycaemia Adversely affects lipid profile Impotence Fatigue Depression Reduced exercise tolerance Syncope Confusion Alopecia
Carbonic Anhydrase Inhibitors <i>Topical</i> Dorzolamide 2% Brinzolamide 1%	Burning Stinging Itching Punctate epithelial keratopathy Blepharoconjunctivitis Corneal endothelial cell-decompensation	Bitter taste Headache Nausea Fatigue Dry mouth Dizziness Anaphylaxis
<i>Oral</i> Acetazolamide 250mg	Transient myopia	(Up to 50% of patients do not tolerate acetazolamide) Fatigue/lethargy Anorexia/weight loss Gastro intestinal upset Paraesthesia Depression Loss of libido Taste disturbance Stevens-Johnson syndrome Blood dyscrasias Renal stones/failure Metabolic acidosis Hypokalaemia Agranulocytosis Aplastic anaemia Neutropenia Thrombocytopenia Anaphylaxis

Preparations by class	Topical ophthalmic side effects	Systemic side effects
Cholinergics Pilcarpine 1%, 2% Carbachol 1.5%, 3%	Eye pain Decrease in night vision Blurred vision Miosis Myopic shift Retinal detachment Aggravation of papillary block Lacrimation	Headache Salivation Urinary frequency Diarrhoea Abdominal cramps Tremor Bronchospasm Hypotension Bradycardia Nausea Vomiting
Prostaglandin Analogues Latanoprost 0.005% Travoprost 0.004% Bimatoprost 0.03%	Blurred vision Burning Stinging Conjunctival hyperaemia Foreign-body sensation Itching Increased pigmentation of the iris/periorbital skin Longer-darker, and thicker lashes Reversible macular oedema Reactivation of herpetic infection Iritis/uveitis	Unlikely, but possible. Consult product information.
Hyperosmotic agents Mannitol 10%, 20% Glycerol	NA	Headache Chills Dizziness Hypotension Tachycardia Dry mouth Thirst Pulmonary oedema
Proprietary fixed combinations Combigan (brimonidine 0.2%/timolol 0.5%) Cosopt (dorzolamide 2%/timolol 0.5%) DuoTrav (travoprost 0.004%/timolol 0.5%) Xalacom (latanoprost 0.005%/timolol 0.5%)	As for individual components	As for individual components

Table 9.5: A summary of side effects

Class	Prostaglandin Analogues	Beta-blockers	Alpha ₂ -agonists	Carbonic Anhydrase Inhibitors		Cholinergics (Miotics)
				Systemic	Topical	
Brady arrhythmias hypotension		✓				
Tachycardia hypertension						✓
Depression		✓	✓	✓		
Masks hypoglycaemia		✓				
Bronchospasm	rare	✓				
Elevated serum lipids		✓				
Falls in elderly		✓				
Anaphylaxis				✓		
Altered taste	✓			✓		
Dizziness	✓					
Parasthesia	✓			✓		
Impotence		✓				
Other minor systemic	✓*			✓**		
Apnoea in infants	✓		✓			
Drowsiness/fatigue		✓	✓			✓
Dry mouth		✓	✓	✓	✓	✓
Ocular symptoms minor	✓	✓	✓	✓	✓	
Ocular symptoms major	✓					

* headaches, pruritus, urticaria

** hearing dysfunction, GI disturbance, reduced libido

NB While the same cautions apply to non-selective and relatively selective beta-blockers, there is a wider margin of safety for the latter (betaxolol)

Topical medications

Initiating treatment

There is general consensus that for most patients with glaucoma, initial medication management should commence in one eye only, using the other eye as a control to check for therapeutic response. Treatment should be initiated with topical medication, the least invasive approach. If possible, treatment should commence in the worst eye, and the response to lowering the IOP should be checked within two to six weeks, as should adherence to the medication regimen and instillation method. Side effects should be regularly assessed. For example, the known maximum IOP-lowering effect of prostaglandin analogues occurs after three to five weeks (EGS 2003). Therefore, response to newly initiated medications should be assessed after two to four weeks. This is generally considered to be a suitable time frame for the medication to reach full effect before extending treatment to the fellow eye.

Evidence Statements

- Evidence strongly supports initiating or changing medication in one eye, using the fellow eye as a control.
- Evidence strongly supports the need for reassessing responses to medication within two to six weeks before extending treatment to the fellow eye.

Instillation of topical medications

Topical medications often contain preservatives which can cause ocular surface inflammation. Irrespective of the type of topical preparation, patients should be instructed carefully on how best to administer the medication to the eye to ensure accurate, effective and appropriate instillation. Patients need to understand how to instill topical medications effectively and efficiently. The technique of instillation should be demonstrated to the patient as many times as necessary. The patient needs to be observed instilling the eye drops to ensure that they are able to instill safely, effectively and appropriately. When the patient has a carer who may instill the medication, the carer needs to be trained and observed. The preferred method for eye drop self-instillation includes holding the head horizontal with punctal occlusion and eyelid closure for three minutes (DOUBLE DOT: Digital Occlusion of Tear Duct and Don't Open Technique) as systemic absorption can be reduced (by up to 70%) with this technique. If two or more drops are being instilled, there should be an interval of at least five minutes between drops.

Patient adherence and capacity to instill eye drops safely and effectively is of paramount importance when determining the most appropriate medication instillation. If more than two topical medications are required to lower the IOP, then other more invasive treatment options should be considered (EGS 2003).

Glaucoma Australia has produced a DVD on 'How to instill eye drops' with funding from the Department of Health and Ageing. Health care providers are encouraged to become familiar with this resource, and to recommend it to their patients. There are several instillation devices available that may assist patients to instill their medication successfully.

Evidence Statements

- Evidence strongly supports the importance of educating patients in the effective and efficient instillation of topical medications.
- Evidence strongly supports teaching patients and carers about the punctal occlusion and eyelid closure technique when instilling eye drops, to reduce systemic absorption.

POINT OF NOTE

Effective education on the instillation of eye drops includes:

- demonstrating the technique to the patient and carers
- observing patient and carers instilling the drops correctly
- repeating education, demonstration and observation until the health care provider is satisfied that patient and carers are fully capable of instilling the drops correctly.

Assessing medication efficacy

Outcome measures

Currently, evidence only supports IOP-lowering management as having a beneficial effect on patients' prognosis. Therefore using a target IOP is the best way to measure the short-term efficacy of a treatment regimen, and medication is thus prescribed to achieve a stable target IOP. Target IOP is a theoretical value that will minimise progression of optic nerve and VF loss, and typically ranges from a 30-50% reduction in pre-treatment (baseline) IOP. Therapeutic efficacy should be judged against the capacity of the intervention to achieve the target value. Target IOPs are not static and may need to be refined given patients' response to treatment.

Glaucoma progression may still occur in individuals with apparently stable IOP, therefore longitudinal evaluation of the disc and VF are more important than IOP, for determining the longer term success of any given management plan.

Evidence Statements

- Evidence strongly supports using target intraocular pressure ranges as an early indicator of an effective glaucoma management plan.
- Evidence strongly supports monitoring disc and visual field changes as long-term indicators of a successful glaucoma management plan.

Changing medication regimens

Change in well-tolerated medication regimens and the use of additional medications are only supported in situations where target IOP has not been reached despite the patient's adherence to the regimen. If the initial choice of medication management was ineffective in achieving target IOP, and the IOP response to the medication was poor, switching to a different class of medication is justified. A wash-out period is required followed by a repeated one-eye trial. Exceeding the recommended dosage will not lower IOP further, and might increase the likelihood of side effects. In the presence of an adequate but non-target IOP response, an additional medication may be required to achieve the target. If more than two topical medications are required to lower the IOP, then other treatment options should be considered. Significant side effects are frequently encountered with systemic medication (EGS 2003). In this instance laser therapy or surgery are considered as second choice management options.

Evidence Statements

- Evidence strongly indicates that, where the medication regimen is well tolerated, the main indicator for changing it is failure to reach target intraocular pressures.
- Evidence strongly supports substitution rather than addition of medication when treatment is ineffective.
- Evidence strongly supports that when two or more topical medications are ineffective, consideration is given to laser therapy or surgery instead of systemic medications.

Medication in acute angle closure crisis

For acute angle closure, medical management is usually initiated to lower IOP, to reduce pain and to clear corneal oedema in preparation for laser therapy. Medications that suppress aqueous humor formation (beta-adrenergic antagonists, carbonic anhydrase inhibitors) may be ineffective because they will have decreased capacity to reduce aqueous formation if the ciliary body is ischemic (AAO 2005).

Pre-operative cholinergics (miotics) may improve the effectiveness of laser iridotomy or iridoplasty. For emergency cases, the use of systemic medications such as oral/parenteral hyperosmotic medications and oral/parenteral carbonic anhydrase inhibitors should be considered in order to rapidly reduce IOP and avoid permanent damage to both the posterior and anterior segments of the eye. Topical timolol and brimonidine/apraclonidine may be considered (Singapore Ministry of Health [SMOH] 2005) along with topical carbonic anhydrase inhibitors. Post-operatively, topical anti-inflammatory medications are usually also indicated. Saw, Gazzard and Friedman (2003) suggest introducing latanoprost additive medication before glaucoma surgery. Latanoprost appears particularly promising if the IOP is less than 25mmHg, and/or when there have been fewer than three previous failed incisional glaucoma operations.

Evidence Statement

- Evidence strongly supports using adjunct medications including cholinergics (miotics), hyperosmotic medications and carbonic anhydrase inhibitors to rapidly reduce intraocular pressure prior to surgery.

Addressing the impact of comorbidities

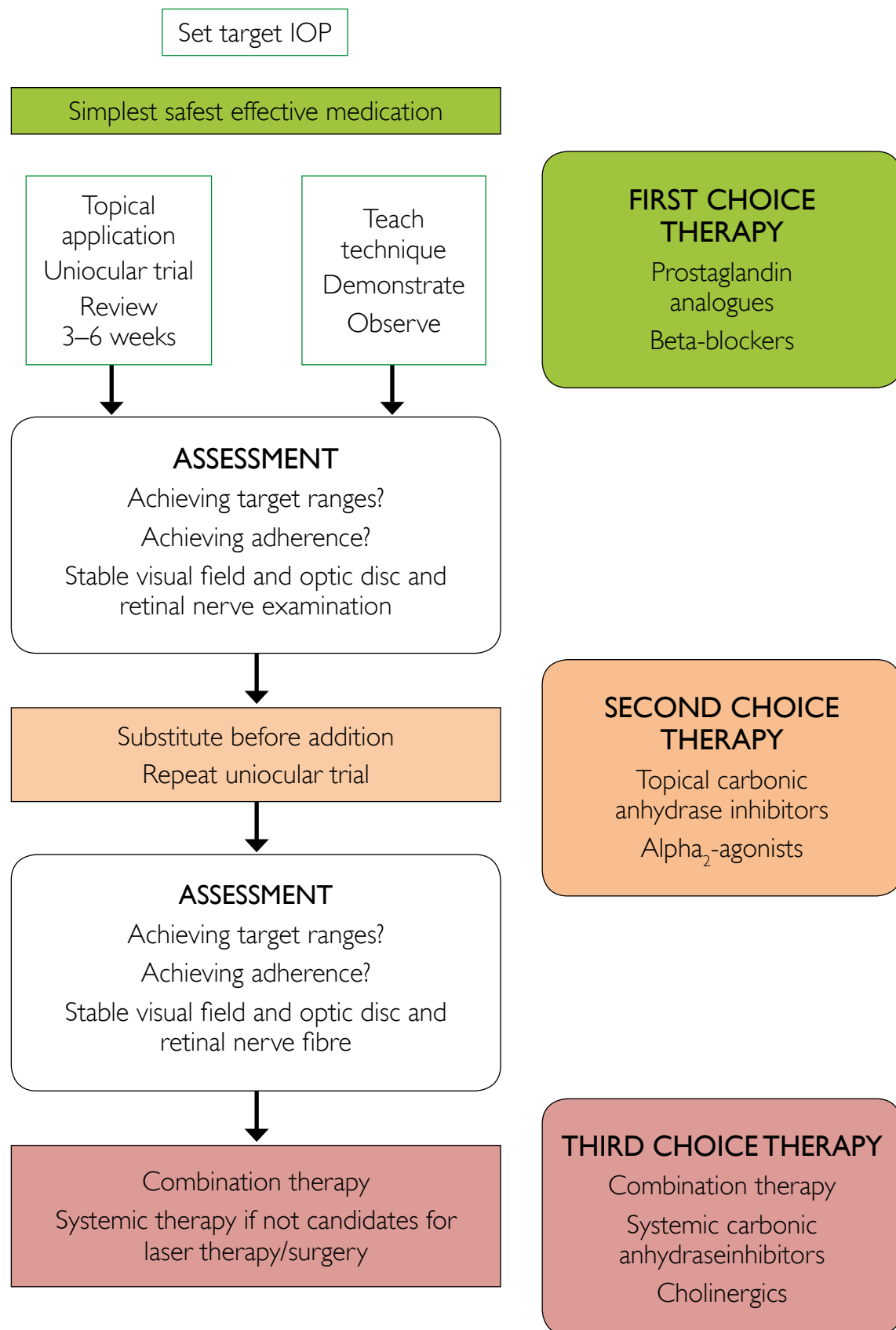
Older age is a risk factor for OAG, as well as for a range of other systemic diseases (such as diabetes). There is a high probability that elderly patients with glaucoma will also be receiving active treatment for other health conditions. These concurrent conditions limit patients' capacity to self-treat (for instance cognitive impairment, poor hearing and arthritis). Thus health conditions associated with older age may mitigate against adherence to glaucoma treatment, unless patient-specific management strategies are put in place (SEAGIG 2003).

There is thus the potential for age-related comorbidities to impact on the outcome of glaucoma interventions via:

- patient adherence to, and persistence with glaucoma medication regimens
- interaction of medications for other health conditions which are taken concurrently with glaucoma medications
- medication-induced glaucoma resulting from medications taken for other health conditions
- side effects from glaucoma medications interacting with comorbid conditions and/or their treatment.

There is consistent evidence from the chronic disease self-management literature that patients with multiple chronic diseases can be as well managed, and have successful health outcomes, as patients with one chronic disease. In fact, where another comorbid condition is present that requires regular contact with health care providers, patients might actually be better monitored. Therefore regular treatment for comorbid conditions might improve the potential for good health outcomes for patients suspected of having, or diagnosed with, glaucoma. Figure 9.1 provides an overview of medication decision-making in glaucoma management.

Figure 9.1: Medication in glaucoma management care decisions





Managing glaucoma successfully within specific comorbid conditions

Diabetes

Individuals with diabetes have almost twice the risk of OAG compared with individuals without diabetes (RR 1.93, 95%CI 1.38 to 2.69) (Burr, Mowatt, Hernandez et al 2007). However, the association between systemic disorders, diabetes and the vascular factors implicated in glaucoma is not well understood.

As beta1-selective beta-blockers have been shown to be safe and effective in patients with type 2 diabetes, the use of the beta1-selective beta-blocker betaxolol may be considered in patients with glaucoma and diabetes. While the risks associated with topical use of beta-blockers in patients with diabetes are unknown, systemic absorption does occur, and thus they should be used with caution. Patients should be made aware of the potential for glaucoma medications to mask signs and symptoms of hypoglycaemia (e.g. tachycardia, tremor).

Evidence Statement

- Evidence indicates caution when prescribing topical beta-blockers to patients with diabetes.

Depression

There are a number of potential interactions between glaucoma medications, depressive states and anti-depressant medications (EGS 2003).

Tricyclic anti-depressants have been reported to blunt the hypotensive effect of systemic clonidine (selective α_2 -agonist). It is not known whether the concurrent use of tricyclic anti-depressants with topical α_2 -agonists (brimonidine and apraclonidine) can lead to interference in IOP-lowering effect, although this is unlikely³.

Depression is a reported side effect associated with the use of topical α_2 -agonists and beta-blockers. Therefore, as the potential exists for aggravating existing depressive symptoms, caution should be exercised when these medications are used in patients with depression. Tricyclic anti-depressants and selective serotonin re-uptake inhibitors can cause acute angle closure glaucoma in susceptible patients (Li, Tripathi & Tripathi 2008).

Evidence Statements

- Evidence indicates caution when prescribing α_2 -agonists or beta-blockers for patients with depression.
- Evidence supports the needs for an ophthalmic consultation for patients at risk of increased intraocular pressure, prior to commencing medications for depression, and periodically during treatment for depression.

³ Source: Product Information from brimonidine (Alphagan®) checked with Stockley's Drug Interactions



Hyperthyroidism

Caution is advised when prescribing beta-blockers to patients with hyperthyroidism because these medications may mask clinical signs (e.g. tachycardia) (AMH 2009).

Asthma

Exacerbation of asthmatic conditions has been commonly reported with the use of beta-blockers, although rarely with the use of prostaglandin analogues (e.g. latanoprost) and cholinergics (e.g. pilocarpine).

Because they may exacerbate bronchospasm, non-selective beta-blockers are contraindicated in patients with reversible airways disease (i.e. asthma) (EGS 2003).

Selective beta-blockers (e.g. betaxolol) may be used, but with caution, as the tendency to exacerbate bronchospasm remains, although it is greatly reduced (EGS 2003; Japanese Glaucoma Society [JGS] 2004). The severity of an individual's asthma should be taken into account, and patients with severe asthma may require treatment with medications other than a beta-blocker. A recent Cochrane review suggests that systemic cardio-selective beta-blockers are safe, but should be used with caution, in patients with asthma (Salpeter, Ormiston, Salpeter et al 2002).

Evidence Statement

- Evidence indicates that using non-selective beta-blockers is generally contraindicated in patients with asthma, however cardio-selective beta-blockers may be used with caution.

Chronic obstructive pulmonary disease

Patients with chronic obstructive pulmonary disease usually have a minimal reversible airways component, and so are unlikely to experience adverse events from the introduction of a beta-blocker. However the possibility remains for beta-blockers to exacerbate bronchospasm and therefore these medications should be employed with caution. A recent Cochrane review demonstrated the safety of systemic cardio-selective beta-blockers in patients with chronic obstructive pulmonary disease, stating that chronic obstructive pulmonary disease is not a contraindication to their use (Salpeter, Ormiston, Salpeter 2005).

Evidence Statement

- Evidence indicates using beta-blockers with caution in patients with chronic obstructive pulmonary disease. Preference may be given to using cardio-selective beta-blockers as they are less likely to induce bronchospasm.

Cardiovascular disease

Beta-blockers have a number of potentially significant interactions with medications used in the treatment of cardiovascular disease. As beta-blockers produce a hypotensive effect, concurrent use with other hypotensive medications can result in an additive effect and possible excessive reduction in blood pressure. This interaction may be more significant in elderly patients as hypotension can increase the risk of falls. As beta-blockers also cause bradycardia, concurrent use with other medications that reduce heart rate can result in potentially fatal heart block. For this reason,



beta-blockers should not be used together with verapamil, diltiazem or digoxin (unless under specialist cardiac supervision). If a calcium channel blocker must be used, beta-blockers can be used safely with dihydropyridines (i.e. amlodipine, nifedipine, nimodipine) as they have little to no effect on cardiac conduction. However, the potentially additive hypotensive effect remains.

It is important to note that the use of beta-blockers is contraindicated in patients with bradycardia (45–50 beats/minute), sick sinus syndrome, second or third degree atrioventricular block, severe hypotension or uncontrolled heart failure (AMH 2009). Beta-blockers may also impair peripheral circulation and exacerbate symptoms of severe peripheral vascular disease and Raynaud's syndrome.

Alpha₂-agonists should be used with caution in patients with severe cardiovascular disease as these medications may worsen symptoms (AMH 2009). Other medications used in the management of glaucoma are safe in patients with cardiovascular disease.

Evidence Statements

- Evidence indicates using alpha₂-agonists with caution in patients with severe cardiovascular disease. A specialist cardiac opinion may be required for individual cases.
- Evidence indicates using beta-blockers with caution in patients with existing heart disease. Using these medications is contraindicated in patients with bradycardia (45–50 beats/minute), sick sinus syndrome, second or third degree atrioventricular block, severe hypotension or uncontrolled heart failure.

Hepatic impairment

Systemic use of acetazolamide (carbonic anhydrase inhibitor) is contraindicated in patients with hepatic impairment or cirrhosis, due to the risk of hepatic encephalopathy (AMH 2009). The manufacturers of topical carbonic anhydrase inhibitors (dorzolamide and brinzolamide) advise using them with caution in patients with hepatic impairment, as these medications have not been adequately studied in this patient group.

Evidence Statement

- Evidence indicates that systemic carbonic anhydrase inhibitors are contraindicated in patients with hepatic impairment, while topical carbonic anhydrase inhibitors may be used with caution.

Renal impairment

Systemic use of acetazolamide, a carbonic anhydrase inhibitor, is contraindicated in patients with severe renal impairment (i.e. when CrCl < 10 mL/minute) as there is an increased risk of profound acidosis. In patients with moderate renal impairment it is recommended that the dose be reduced (i.e. when CrCl between 10–30 mL/min) (AMH 2009). It is also important to note that acetazolamide increases the risk of urolithiasis (kidney stones).

There is much less information available about the use of topical carbonic anhydrase inhibitors in patients with renal impairment. The manufacturers of topical carbonic anhydrase inhibitors (dorzolamide and brinzolamide) recommend against using them in patients with severe renal impairment, as they have not been adequately studied in this patient group. Therefore, as systemic absorption does occur, the same precautions should be followed as for the systemic use of acetazolamide.

Evidence Statement

- Evidence indicates that caution is required when considering systemic carbonic anhydrase inhibitors for patients with mild to moderate renal impairment, and these medications are contraindicated in patients with severe renal impairment.

POINT OF NOTE

There is limited information about the use of topical carbonic anhydrase inhibitors in patients with renal impairment. As some systemic absorption will occur, it is wise to use these medications with caution, and/or seek advice from a renal specialist.

Medication-induced glaucoma

Open angle glaucoma

There is moderate evidence linking a range of medications to medication-induced glaucoma. Steroids, irrespective of the route of administration is utilised, are associated with ocular hypertension (OH) or OAG. Steroidal-like substances can also be found in traditional and natural medicines, and thus patient history taking should include use of prescription and over-the-counter medications. Corticosteroids are the main culprits in medication-induced glaucoma (Adis International 2004). Medication-induced glaucoma should be considered as secondary glaucoma related to its external causation (SEAGIG 2003). Corticosteroids raise the IOP when administered in any form. Tripathi, Tripathi and Haggerty (2003) report that 46-92% of subjects with OAG experience an increase in IOP after topical ocular administration of corticosteroids for two to four weeks.

Topiramate (an anti-migraine systemic medication) can cause supraciliary effusion, ciliary block and acute angle closure.

Evidence Statement

- Evidence indicates caution in the administration of corticosteroids delivered by any form (i.e. oral, intranasal or ocular) for patients with glaucoma or ocular hypertension.

POINT OF NOTE

Any patient taking steroids on a long-term basis is advised to undergo regular ocular checks to monitor intraocular pressure.

Angle closure and angle closure glaucoma

Several medications can precipitate angle closure glaucoma. This occurs by narrowing the angle of the anterior chamber, by pupillary dilation and/or forward movement of the iris/lens diaphragm (pupillary block glaucoma), and by swelling of the ciliary body epithelium, lens or vitreous body (Li et al 2008).

Patients who are being treated for other conditions could be opportunistically identified as at risk for primary angle closure (PAC), if they are identified as having shallow anterior-chamber angles with normal or raised IOP. There is strong evidence that patients with PAC, or who have developed primary angle closure glaucoma (PACG), should avoid or use with caution, any prescription or



over-the-counter medications that have the potential to increase IOP. A list of prescription and over-the-counter medications that can induce angle closure glaucoma and increase IOP is provided in Table 9.6.

Acute angle closure crisis (AACC) from pupillary block can be induced by adrenergic medications, either locally (phenylephrine drops, nasal ephedrine, or nebulised salbutamol), or systemically (epinephrine for anaphylactic shock, medications with anticholinergic effects including tropicamide and atropine drops, tri and tetracyclic anti-depressants, and even cholinergic medications such as pilocarpine).

Sulpha-based medications (acetazolamide, hydrochlorothiazide, cotrimoxazole, and topiramate) can cause AACC by ciliary body oedema and anterior rotation.

Evidence Statement

- Evidence supports obtaining a comprehensive medication history from all patients with ocular symptoms suggestive of acute or chronic angle closure glaucoma, to rule out potential medication-induced glaucoma.

POINT OF NOTE

A large number of over-the-counter and prescription medications have been linked with acute angle closure crisis and/or raised intraocular pressure. Counselling could be offered for individuals who are identified as being at risk of angle closure glaucoma, regarding medication use.

Table 9.6: Medications that may induce angle closure glaucoma (SEAGIG 2007; Li et al 2008).

Medication by class	Possible mechanism
Sulpha-based medications	
Anticonvulsants <ul style="list-style-type: none"> • Topiramate Carbonic anhydrase inhibitors <ul style="list-style-type: none"> • Acetazolamide Thiazide diuretics <ul style="list-style-type: none"> • Hydrochlorothiazide Sulphonamides <ul style="list-style-type: none"> • Cotrimoxazole 	Ciliary body oedema with anterior rotation of the lens-iris diaphragm.
Medications producing pharmacological mydriasis	
Adrenergic agents <ul style="list-style-type: none"> • Topical agents (phenylephrine) • Nasal sprays (ephedrine) • Inhaled nebulised solutions (salbutamol, terbutaline) Anticholinergic agents <ul style="list-style-type: none"> • Tropicamide • Atropine • Cyclopentolate • Ipratropium bromide • Anti-depressants/anti-anxiety agents (Tricyclic anti-depressants and selective serotonin reuptake inhibitors) Histamine receptor antagonists (ranitidine)	Induced pupillary mydriasis. Relative pupillary block.
Medications associated with ciliary block glaucoma	
Cholinergic agents <ul style="list-style-type: none"> • Pilocarpine • Anticholinesterases (donepezil) • Carbachol 	Ciliary block.

Managing glaucoma in specific population groups

When prescribing or monitoring glaucoma medications, health care providers should consider the special needs of children, pregnant women, breastfeeding mothers and other vulnerable groups of patients at risk of, or with glaucoma.

Children

There is a lack of evidence regarding the efficacy of management strategies for children with glaucoma. The mainstay of management for congenital glaucoma is surgery (goniotomy, trabeculotomy, trabeculectomy, tube drainage devices and cyclodestructive procedures). However many children require medication management as either long-term treatment or as a temporising measure (Moore & Nischal 2007).



Care must be taken in instilling topical ophthalmic medications to children. This is due to higher absorption, greater circulating concentrations (due to reduced blood volumes), and immature metabolic pathways increasing the half-life for elimination. Moreover medications are generally only available in adult dosages. To limit potential adverse effects, it is important to adhere to dosage times, use nasolacrimal system occlusion (if at all possible in small children) and use the minimum dose or limit the number of medications required.

Treatment of children with glaucoma requires specialist consultation. While medications used in the treatment of glaucoma may not be licensed for use in children, many of them can be used safely. Topical medication is generally well tolerated however there are some notable exceptions. Table 9.7 provides an overview of the different medication options and special notes for their use in children. In particular, the central nervous system depressant effects of alpha2-agonists should not be underestimated.

It is essential that all contraindications, precautions and interactions are taken into consideration when prescribing anti-glaucoma medications for children, just as for adults. When choosing a medication, the lowest possible concentration should be used in conjunction with techniques to reduce systemic absorption to minimise the potential for side effects (see Table 9.8).

Evidence supports the use of topical beta-blockers, carbonic anhydrase inhibitors and prostaglandin analogues for the treatment of children with glaucoma, but with caution. Alpha2-agonists should be limited to children older than seven years of age. The alpha2-agonists have more and potentially serious adverse effects for children and are contraindicated for children younger than two years of age. Systemic use of carbonic anhydrase inhibitors is usually the last choice of management in situations where glaucoma is not satisfactorily controlled with other topical medications. They may also be considered when attempting to avoid/delay surgical intervention and prevent further glaucomatous optic neuropathy.

Table 9.7: Treatment of glaucoma in children

Medication class	Information on use in children
Beta-blockers	Beta-blockers are often used as first choice treatment for glaucoma in children (Moore & Nischal 2007). Beta-blockers should be avoided in premature and small infants as these agents can cause bradycardia, bronchospasm and hypoglycaemia. In general, beta-blockers should be used at the lowest concentration and dose possible.
Carbonic anhydrase inhibitors	Dorzolamide is reported to be a better choice for children than brinzolamide because its topical use causes less burning, stinging, and itching (Coppens, Stalmans, Zeven et al 2009). The use of topical and systemic carbonic anhydrase inhibitors has been associated with causing metabolic acidosis in infants, which can present as failure to thrive. Therefore infants on these medications should be observed to ensure they are feeding well and gaining weight. Despite this potential side effect, topical carbonic anhydrase inhibitors are often used as first or second choice treatment in young children (Moore & Nischal 2007). Systemic treatment with acetazolamide is usually last choice, and is used in situations when glaucoma remains unsatisfactorily controlled with other topical medications or in an attempt to avoid/delay surgical intervention and prevent further glaucomatous optic neuropathy. This is based on the increased risk of side effects associated with systemic carbonic anhydrase inhibitor therapy (Coppens et al 2009).
Prostaglandin analogues	While prostaglandin analogues substantially reduce IOP in adults, there is some evidence to suggest that they may not be as effective in reducing IOP in many paediatric glaucomas. Prostaglandin analogues are usually used as second choice therapy in children but administration as first choice therapy is acceptable as these agents are often effective in these settings and are well tolerated with the added convenience of once daily administration (Moore & Nischal 2007).
Alpha ₂ -agonists	Alpha ₂ -agonists are contraindicated in children less than two years of age and should only be used with caution in children younger than seven years of age as children are particularly sensitive to the central nervous system depressant effects of these medications. Several case reports of somnolence, respiratory depression and hypotony have been reported after use in children (Coppens et al 2009). Apraclonidine and brimonidine are usually used as second or third choice agents in the management of glaucoma in children and are useful as short-term adjunct therapy pre- and post-surgery (Moore & Nischal 2007). The use of apraclonidine is usually limited to short-term therapy, while brimonidine may be used long-term (AMH 2009).

Evidence Statements

- Evidence supports using beta-blockers in infants and children where necessary.
- Evidence suggests using beta-blockers with caution in premature and small infants, as bradycardia, bronchospasm and hypoglycemia have been reported.
- Evidence indicates caution when using topical and systemic carbonic anhydrase inhibitors in children, in situations where glaucoma is resistant to other treatment and/or prior to surgery.

Women wishing to conceive

Women with childbearing potential, who have glaucoma, should be encouraged to discuss their reproductive plans with a health care provider prior to becoming pregnant. This allows treatment choices to be planned appropriately, optimising benefits for the mother and minimising risks for the foetus by managing and potentially reducing medication exposure during critical early stages of foetal development. An appropriate treatment plan will depend on the degree of the patient's glaucomatous damage, the level of her IOP and personal preferences. It may be appropriate to offer primary surgical intervention to women with glaucoma who wish to conceive.

Pregnant women

Appropriate management of the pregnant woman at risk of, or with diagnosed glaucoma requires a balance between the treatment's risk to the foetus and the risk to the mother if treatment is reduced or suspended.

Pregnancy often alters IOP, which tends to be lower in mid to late term, possibly from hormonal changes or decreased episcleral venous pressure. This may allow certain patients to be monitored on reduced medications or without treatment during pregnancy (SEAGIG 2003). Some health care providers and patients opt for wide margins of safety, avoiding the use of medication for early or mild disease when the risk of significant glaucomatous progression during the course of the pregnancy is small.

As many pregnancies are unplanned, exposure to medication typically occurs before women know they are pregnant. While no glaucoma medications are known to be human teratogens, none have been proven to be completely risk-free either. Therefore, when prescribing medications for pregnant women or women planning a pregnancy, careful consideration of the risks and benefits of treatment is important. Table 9.8 provides a summary of medication use for the treatment of glaucoma during pregnancy. A summary of the Australian Drug Evaluation Committee (ADEC) Pregnancy Categories is also provided to assist decision-making. There are case reports of the safe and effective use of all anti-glaucoma medications during pregnancy. However the data are often limited and as such, general caution over the use of all anti-glaucoma medications is recommended. Health care providers may consider contacting a specialist pregnancy drug information centre to discuss the optimal glaucoma management of pregnant patients.

In some situations, glaucoma during pregnancy may be best managed through surgery, however, this management path is not without its risks. The additional risks associated with glaucoma surgery in pregnant patients include the use of local anaesthetics, post-operative medications, gastro-oesophageal reflux and its associated complications and an increased risk of aortic and vena cava compression by the uterus in the 2nd and 3rd trimesters due to supine positioning. For these reasons laser therapy may be considered first as it offers significant advantages over surgical management of glaucoma during pregnancy. These include the use of only topical anaesthesia, upright positioning during procedure, faster rehabilitation, and reduced need for post-operative medications both in dosage and duration (Chung, Kwok & Chung 2004).

The Australian categorisation of risk of drug use during pregnancy comprises the following categories:

Category A: Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus.

Category C: Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible.

Category B1: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an observed increase in the frequency of malformation or other direct or indirect harmful effects in the human foetus. Studies in animals have not shown evidence of an increased occurrence of foetal damage.

Category B2: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an observed increase in the frequency of malformation or other direct or indirect harmful effects in the human foetus. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased risk of foetal damage.



Category B3: Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects in the human foetus having been observed. Studies in animals have shown evidence of an increased occurrence of foetal damage the significance of which is considered uncertain in humans.

Category D: Drugs which have caused, are expected to have caused or may be expected to cause, an increased risk of human foetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects.

Category X: Drugs which have such a high risk of causing permanent damage to the foetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

Note: For drugs in the B1, B2, and B3 categories, human data are lacking or inadequate, and sub-categorisation is therefore based on available animal data. **The allocation of a B category does not imply greater safety than the C category.** Drugs in category D are not absolutely contraindicated in pregnancy (e.g. anticonvulsants). Moreover, in some cases the 'D' category has been assigned on a basis of 'suspicion' (<http://www.tga.gov.au/docs/html/mip/medicine.htm#cata>).

Glaucoma medications and pregnancy category

Category C, B1 and B2 medications would be the preferred medications during pregnancy. Category B3 medications would only be used after consideration of the risks and benefits of treatment. There are case reports of the safe and effective use of all of these medications during pregnancy and no indication for teratogenic effects. However, the current evidence base is not strong, and therefore caution is advised. If topical medications are used, systemic absorption should be minimised with the use of punctal occlusion.

Health care providers should contact a specialist pregnancy drug information centre to discuss the risks of glaucoma medication (AMH 2009). Examples of medications in each of the Australian categorisation of risk of drug use during pregnancy are:

- Category C: timolol, betaxolol, levobunolol
- Category B1: brimonidine
- Category B2: pilocarpine
- Category B3: apraclonidine, latanoprost, bimatoprost, travoprost, brinzolamide, dorzolamide and acetazolamide.

The current evidence base underpinning the medication management of glaucoma during pregnancy is detailed in Table 9.8.

Note: The medications in Table 9.8 have been sorted in approximate order of use in pregnancy, i.e. beta-blockers first and the prostaglandins as last choice. Most evidence based review articles, regard beta-blockers and alpha2-agonists as equal choice as first choice medication management, leaving it up to the health care provider to make the risk:benefit assessment.

Table 9.8: Summary of medication management for glaucoma during pregnancy

Medication class	Information on use during pregnancy
Beta-blockers Timolol Betaxolol Levobunolol All ADEC Category C	Suitable if necessary, may cause foetal bradycardia (AMH 2009) The systemic use near delivery of some beta-blockers has resulted in persistent beta-blockade in the newborn. Thus, newborns exposed <i>in utero</i> to timolol should be closely observed during the first 24-48 hours after birth for bradycardia and other symptoms. Use of systemic beta-blockers during the 2 nd and 3 rd trimester has been associated with intrauterine growth restriction, however, there is limited data for topical beta-blockers used for glaucoma (Briggs & Freeman 2005).
Alpha₂-agonists Brimonidine – ADEC Category B1 Apraclonidine – ADEC Category B3	Apraclonidine, avoid use (AMH 2009). Brimonidine, suitable if necessary (AMH 2009).
Cholinergics Pilocarpine – ADEC Category B1	Limited data available (AMH 2009). No adverse reports from human pregnancies. Probably suitable to use if necessary (Briggs & Freeman 2005).
Carbonic anhydrase inhibitors Dorzolamide Brinzolamide Acetazolamide All ADEC Category B3	Avoid use; no human data available (AMH 2009). Where the use of carbonic anhydrase inhibitors is deemed absolutely necessary, preference should be made for the use of topical therapies as there are case reports of adverse effects in infants born to mothers treated with acetazolamide during pregnancy (Maris, Mandal & Netland 2005).
Prostaglandin analogues Latanoprost Bimatoprost Travoprost All ADEC Category B3	Avoid use; no data available (AMH 2009). Since prostaglandins increase uterine tone and can cause reduced perfusion to the foetus, general caution is advised. However, if there are compelling treatment indications in a case of severe glaucoma, they should not be withheld. The dosage should be kept as low as therapeutically possible and punctal occlusion used to limit systemic absorption (Schaefer, Peters & Miller 2007).

Breastfeeding mothers

In the majority of cases, medications used for glaucoma can be used safely in women who are breastfeeding. Particular caution should be exercised however, if a breastfeeding mother is taking beta-blockers or alpha₂-agonists. The infant should be monitored closely for evidence of systemic toxicity, although this is unlikely. Both timolol and acetazolamide are listed by the American Academy of Pediatrics (2001) as compatible with breastfeeding. When managing glaucoma in women wishing to breastfeed, consider using the minimum number of medications or concentration sufficient to achieve target IOP. The use of punctal occlusion should also be emphasised to reduce the potential for systemic absorption and therefore reduce potential transfer into breast milk (American Academy of Pediatrics 2001) (Table 9.9).

Table 9.9: Safety of glaucoma medications during lactation (AMH 2009)

Medication class	
Beta-blockers	Unlikely to cause adverse effects at usual doses. Timolol listed as compatible with breastfeeding by the American Academy of Pediatrics.
Alpha ₂ -agonists	No data available, unlikely to be of concern. Monitor infant for adverse effects.
Carbonic anhydrase inhibitors	No human data regarding topical carbonic anhydrase inhibitors. Acetazolamide listed as compatible with breastfeeding by the American Academy of Pediatrics.
Prostaglandin analogues	No data available, but unlikely to be of concern. Latanoprost is safe to use.
Cholinergics	Safe to use.

Evidence Statements

- Evidence supports using beta-blockers in pregnancy, but with caution due to the risks of foetal bradycardia and interuterine growth restriction.
- Evidence supports laser therapy over surgical techniques in women who are pregnant or planning to conceive in the near future.

POINT OF NOTE

The Working Committee notes that treating pregnant women with glaucoma is always difficult and health care providers may have their own preference regarding treatment. The information presented in this guideline should allow health care providers to make an informed decision based on the current best evidence.

Other vulnerable patients

Glaucoma is a chronic disease that requires long-term management. However, unlike other chronic diseases, patients may be initially symptom-free. Furthermore, patients must be highly dexterous to master the instillation techniques required in common topical medication management strategies. This means that certain groups of patients may have to rely on others for assistance. All these aspects make it likely that some people suffering from glaucoma may experience challenges with maintaining their medication regimens, which may impact on the successful management of their disease.

There is a paucity of information regarding the management of glaucoma in elderly patients such as those in nursing homes and aged care facilities. For example, beta-blockers have been shown to increase the risk of falls in the elderly (SEAGIG 2003). More research may be available to inform subsequent revisions of this guideline.

POINT OF NOTE

Vulnerable patients may have particular difficulty in adhering to the sustained medication regimens required for glaucoma management. An individual's capacity to adhere to a medication regimen should inform clinical decisions regarding appropriate management strategies, and the need to organise patient support services.

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■ CHAPTER 10

Laser therapy and surgery

Recommendation 12

Reduce IOP by using laser techniques and incisional surgery.

Good Practice Points

- Offer laser trabeculoplasty as an alternative, or additive to medications.
- Offer surgical IOP reduction when medications and/or laser trabeculoplasty fail to meet targets or are unsuitable, and visual disability is threatened. There are inherent risks with invasive procedures, which must be justified by likely benefits.
- Glaucoma drainage devices may control IOP long-term and may be suitable if other drainage surgery fails, or as first-line surgery in eyes with higher risks of failure (including inflammatory glaucomas and ICE syndrome).

Recommendation 13

If indicated, perform prophylactic laser peripheral iridotomy in both eyes to prevent progressive anterior segment damage.

Good Practice Point

- Peripheral iridoplasty might be useful after iridotomy in individual cases. Consider cataract extraction and ongoing IOP control, including trabeculectomy as required.

Recommendation 14

Ensure patients are aware of risks and symptoms of angle-closure and can access care urgently as necessary.

Introduction

All clinical guidelines highlight the importance of choosing the most appropriate management approach on a case-by-case basis. Traditionally, glaucoma treatment has begun with medications, proceeding to laser therapy and surgery when necessary. This approach was designed to maximise the benefit of treatment while minimising risk to the patient. When making the choice of a specific form of treatment or the decision to alter or provide additional treatment, the overriding consideration must be to minimise the risks and maximise the benefit to the patient. All forms of treatment for glaucoma have potential side effects or complications, and the possible impact of the treatment, must be evaluated from a social, psychological, financial, and convenience standpoint.

The available non-medication interventions are broadly grouped into laser techniques, incisional and implant surgery. The primary purpose of laser therapy and surgery is to make a selective lesion in one or more structures of the eye to reduce the intraocular pressure (IOP). The outcomes of these interventions focus on the ability to achieve and maintain a lowered IOP, retention of an open angle with functional trabecular meshwork, reduction of anti-glaucoma medication usage, improvement of visual acuity and minimisation of visual field (VF) loss. Other outcomes include the reduced need for additional surgery and minimisation of adverse/harmful effects. Figure 10.1 illustrates the anatomy of the glaucomatous eye as a guide to the terminology reported for the interventions described in this chapter. Figure 10.2 illustrates the two main types of glaucoma (open angle and angle closure).

Figure 10.1: The anatomy of the eye (Source: Members of the NHMRC Working Committee)

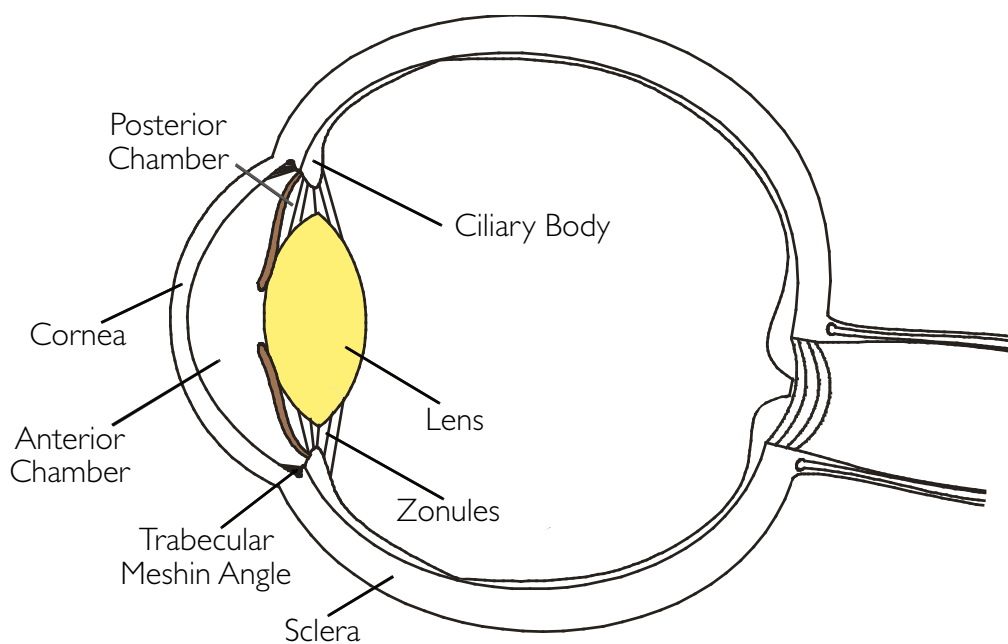
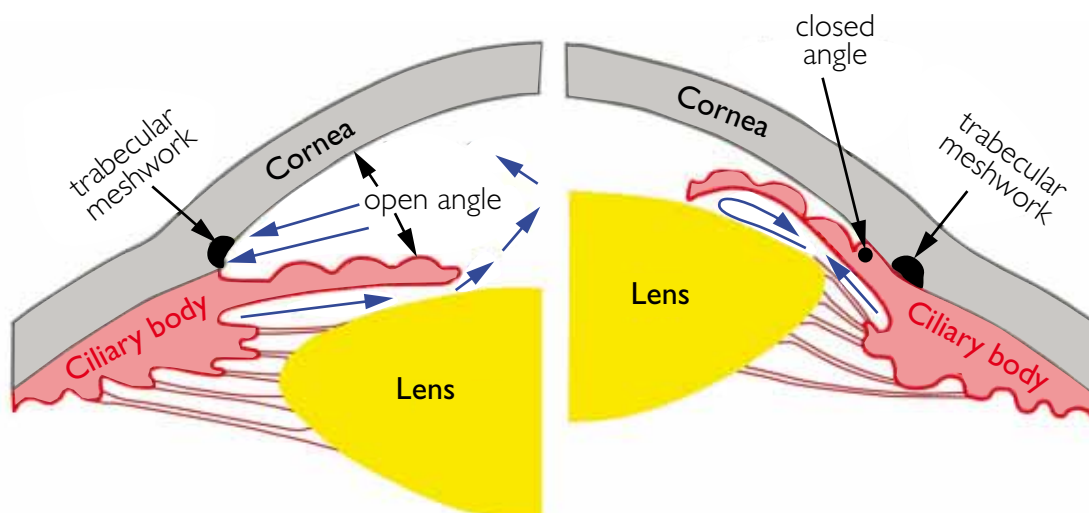


Figure 10.2 : An illustration of open angle and angle closure glaucoma with trabecular meshwork (Source: www.angleclosureglaucoma.cn)





Summary of common laser interventions

Laser iridotomy

Laser iridotomy is used to treat angle closure. This technique creates a hole in the iris in order to break the pupil block, which is the most common cause of angle closure. It is most frequently undertaken by Nd:YAG laser iridotomy, however when this form is not available, an argon laser may be utilised (European Glaucoma Society [EGS] 2003).

Laser iridoplasty

Laser iridoplasty is used in angle closure following iridotomy when the angle remains appositionally closed or occludable. Contraction burns are applied to the peripheral iris to pull it away from the trabecular meshwork.

Laser trabeculoplasty

Laser trabeculoplasty is used in open angle glaucoma. Applications to the trabecular meshwork alter the drainage tissue, generally increasing aqueous outflow.

Combination laser surgery

Iridotomy is often combined with iridoplasty, where laser is applied to shrink the peripheral iris away from the trabecular meshwork to improve the aqueous flow.

Cyclodestructive procedures

Transcleral cyclophotocoagulation is a form of laser therapy which treats glaucoma by damaging the ciliary body. The laser is aimed through the sclera at the ciliary body, which secretes aqueous humor. This form of laser treatment lowers IOP by decreasing aqueous humor production. Currently, cyclodestructive procedures are commonly performed using a transscleral laser delivery system, however they can also be performed endoscopically (Pastor et al 2001, cited in American Academy of Ophthalmology [AAO] 2005b).

Laser options for specific glaucoma classification and stages

Open angle glaucoma

Literature reviews of controlled trials of argon laser trabeculoplasty report an average reduction in IOP of 30% in most eyes with primary open angle glaucoma (POAG) (Royal College of Ophthalmologists [RCO] (2004). However in clinical practice the effectiveness of laser therapy is influenced by patient risk factors including age (tends to be less successful in young patients), and type of glaucoma (tends to be more successful in pseudoexfoliation and pigment dispersion glaucoma).

There appears to be a progressive diminution of the effect of laser therapy over time in some patients, and glaucoma control can be lost quickly. Therefore patients who have had laser treatment should be monitored frequently.



The literature indicates that one year after laser therapy, for open angle glaucoma (OAG) the condition is successfully controlled in approximately 80% of patients (American Optometric Association [AOA] 2002). After the first year, this rate declines by about 5–15% per year. In general, glaucoma is successfully controlled in approximately 50% of patients five years after laser therapy and 10–30% of patients 10 years after laser therapy (AOA 2002). When laser trabeculoplasty is given as primary treatment, approximately 50% of patients do not require medication for one to two years after treatment (Tuulonen, Airaksinen, Erola et al 2003). The IOP-lowering effect of laser trabeculoplasty diminishes by approximately eight percent per year and follow-up of up to seven years suggests that only 20% of patients manage without medication (Tuulonen et al 2003).

Repeated laser therapy has a lower success rate and a higher risk of poor outcomes than one administration of laser therapy only (AOA 2002).

Selective laser trabeculoplasty appears to be equivalent to argon laser trabeculoplasty in lowering IOP. Patients who previously failed to improve with argon laser trabeculoplasty may have a greater reduction in IOP when treated with selective laser trabeculoplasty (AOA 2002). Usually, medications should continue following laser therapy, and in only 25% of cases can it be reduced from pre-laser levels. The risk of failure to control the progression of glaucoma with laser therapy is higher in younger patients, when pre-treatment IOP is very high, and when glaucoma is more severe (AOA 2002).

Evidence Statements

- Evidence strongly supports argon laser trabeculoplasty for older patients with glaucoma who are at risk of visual loss within their lifetime, particularly when the following factors apply:
 - there is difficulty with administering eye drops
 - patients are unresponsive to medication alone, or
 - patients are poor candidates for incisional surgery.
- Expert/consensus opinion suggests that patients undergoing laser therapy require continual comprehensive glaucoma monitoring due to the diminishing treatment benefit over time.

Communication with patients

Irrespective of the way in which glaucoma is managed, health care providers should continue to educate patients about the need for monitoring. They should ensure that patients understand that even if successful, laser therapy does not equate to a cure.

POINT OF NOTE

Expert opinion indicates that the high success rates of argon laser trabeculoplasty obtained in clinical trials may not be easily achieved in clinical practice.

POINT OF NOTE

After a patient undergoes laser therapy, the health care provider responsible for long-term monitoring should be clearly identified, particularly when medication is no longer required.

POINT OF NOTE

Expert opinion highlights that although the literature is heavily weighted towards argon laser trabeculoplasty, there is also considerable, recent literature about the equivalence of argon laser trabeculoplasty with selective laser trabeculoplasty. Health care providers therefore need to be aware of emerging literature on different techniques and their outcomes.

Cyclodestructive procedures in open angle glaucoma

Cyclodestructive procedures have been associated with subsequent decrease of visual acuity and, rarely, as sympathetic ophthalmitis. These procedures are less often used as primary treatment, and more often reserved for eyes with reduced visual acuity, and for patients who are poor candidates for incisional surgery (AAO 2005b, Bloom 1997, Egbert 2001, both cited in Burr, Azuara-Blanco & Avenell 2004). According to reviews of short-term follow-up studies, trans-scleral Krypton laser cyclophotocoagulation is often an effective and well-tolerated means of lowering IOP in refractory glaucoma. However, these procedures often need to be repeated (Tuulonen et al 2003). Prior to cyclophotocoagulation, patients should be given additional IOP-lowering medication in order to avoid post-laser pressure spikes (Tuulonen et al 2003).

Evidence Statement

- Evidence strongly supports using cyclodestructive surgery as a third choice treatment for patients with advanced glaucoma, who are poor candidates for incisional surgery.

Angle closure

The management aims for any patient with actual or suspected angle closure are to:

- re-open or prevent angle closure
- control IOP elevation
- minimise damage to the optic nerve.

Patients with narrow angles/suspected angle closure but low risk status

Patients with narrow but open angles, not identified as at immediate risk of closure, and with normal IOP, should be monitored for IOP elevation, progressive narrowing, or development of synechial angle closure (AAO 2005a). While modern laser treatments for glaucoma are relatively safe, all laser interventions incur some risk. Complications from laser iridotomy include increased IOP, corneal, lens, or retinal burns, posterior synechiae, and possible 'ghost imaging' in vision.

Evidence Statement

- Evidence supports the practice of monitoring patients with suspected angle closure, who are at low risk of immediate closure, until there is evidence of:
 - elevated intraocular pressure
 - progressive narrowing, or
 - development of synechial angle closure.

Evidence Statement

- Evidence supports the importance of ensuring that individuals who are being monitored for angle closure (rather than being actively treated) are:
 - fully informed of the risks of monitoring
 - aware of symptoms of closure
 - capable of accessing immediate treatment.
- Where these factors cannot be guaranteed, the patient should be treated as if at high risk.

Patients with suspected angle closure and high-risk status

With improvements in laser techniques, and the consequent changes in risk:benefit ratio, laser iridotomy is indicated for patients with suspected angle closure, who are at high-risk of closure (Saw, Gazzard & Friedman 2003).

Circumstances under which this should be considered are (AAO 2005a):

- for patients with narrow angles who require repeated pupil dilation for treatment of other eye disorders (e.g. age-related macular degeneration, diabetic retinopathy)
- when there is progressive narrowing of the angle
- when medication is required which may provoke pupillary block
- when symptoms are present that suggest prior angle closure
- when the patient's occupation/avocation makes it difficult to access immediate ophthalmic care (e.g. the patient travels frequently to developing countries, works on merchant vessels), and/or
- for the fellow eye in patients who have had an attack of acute primary angle closure (PAC).

Evidence Statement

- Evidence supports using laser iridotomy for both eyes as the treatment of choice for patients with suspected angle closure, who are at high risk of closure.

Patients with acute angle closure

For patients with acute angle closure (AAC), the preferred treatment is laser peripheral iridotomy with adjunctive pre-operative medication management to lower IOP, gain corneal clarity, reduce pain and preserve the available VF). If this is impossible due to corneal oedema, the next choice is an incisional iridectomy (Saw et al 2003). There are also other choices including peripheral iridoplasty to break the attack, central corneal indentation and lens extraction. Studies indicate that 'chronic miotic therapy' is not an appropriate alternative either for prophylaxis of the fellow eye, or for treatment of established angle closure, nor is it a substitute for iridotomy (AAO 2005a).

There is consistent evidence that in the event of an acute angle closure crisis (AACC) which is a medical emergency, additional systemic medication, such as osmotic diuretics and oral/parenteral carbonic anhydrase inhibitors, may need to be employed to rapidly reduce the IOP to avoid permanent nerve damage and vision loss.

The fellow eye of a patient with an attack of AAC should be evaluated since it is at high risk for a similar event. Salmon (1998, cited in AAO 2005a), reports that 39% of fellow eyes treated with miotics will suffer an acute attack within five years, and many eyes with angle closure suffer progressive formation of synechial angle closure with miotic use.

Evidence Statements

- Evidence supports using laser iridotomy with adjunctive pre-operative medication, as the treatment of choice for patients with acute angle closure.
- Expert/consensus opinion suggests that in patients who experience acute angle closure in one eye, the fellow eye is at high risk of future closure and therefore prophylactic iridotomy can be clinically indicated.
- Evidence strongly supports using medication to rapidly reduce intraocular pressure as a short-term measure pre-operatively, in patients with acute angle closure glaucoma.

Patients with chronic angle closure and chronic angle closure glaucoma

For patients with chronic angle closure, peripheral iridotomy is usually performed to relieve the pupillary block component and this usually halts the progression of synechial closure and progressive IOP elevation. However between three and nine percent of primary angle closure cases will progress to glaucoma within two years despite iridotomy (Nolan, Foster, Devereux et al 2000). Iridotomy is described as the intervention of choice (AAO 2005a) as miotics may aggravate pupillary block due to anterior rotation of the ciliary body. There is evidence that for some patients, laser interventions need to be repeated over time, and that they become less effective on repeated administrations. When laser therapy does not successfully lower IOP, or if IOP begins to rise again, the next course of action may be a filtering procedure.

Generally, only one laser iridotomy is required, as more than one iris hole has no greater effect on pupil block. Usually a single hole will remain open indefinitely. However, in patients with uveitis, the iris hole can close and may require re-opening.

POINT OF NOTE

After an iridotomy, between three and nine percent of primary angle closure cases will still progress to glaucoma within two years. A greater number of patients will progress to glaucoma in a slower manner, and retain occludable angles, or angles that re-narrow. Therefore post-iridotomy patients need to be kept under regular review.

Laser iridoplasty: Following laser iridotomy, the angle may remain narrow with appositional contact between the iris and trabecular meshwork, or open a little then re-narrow. The mechanisms include large lens, ciliary block, and plateau iris amongst others. It will not work in synechial closure or most other forms of secondary angle closure. Contraction laser burns applied to large areas of peripheral iris will straighten peripherally curved iris and pull it away from the trabecular meshwork in some cases. A recent publication, which was outside the scope of this literature review, highlighted the paucity of literature concerning this therapy (Ng, Ang & Azzurro Blanco 2009).

Failure of laser therapy: Surgery should be considered when the angle closes further, in spite of laser and medication treatment, and when the eye continues to demonstrate significant pressure elevation or risk of acute angle closure. Patients with enlarged lens or ciliary block component should have lens extraction performed prior to drainage surgery.

POINT OF NOTE

Expert opinion indicates that laser iridoplasty improves angle configuration in approximately half the patients with chronic angle closure. The effect of laser frequently reduces over one to two years. The treating health care provider must avoid over-treatment, as there is a risk of inducing iris atrophy and permanent mydriasis.

Evidence Statements

- Evidence supports using laser peripheral iridotomy as the treatment of choice in patients with chronic angle closure.
- Expert/consensus opinion suggests that more than one patent peripheral iridotomy confers no additional benefit.

The evidence to support any specific laser intervention for patients with open angle glaucoma is variable. The purpose of laser and surgical treatment for open angle glaucoma is to prevent glaucoma-induced visual disability.

Laser or incisional surgery is also an option for patients who cannot administer topical medications successfully. There is debate regarding the choice between laser therapy or surgery, and oral administrations of anti-glaucoma medications. The adverse effects and contraindications of oral medications, versus the potential for permanent damage and infection associated with more invasive techniques, must be taken into consideration. The timing of surgical intervention depends largely upon the stage of disease and risk of blindness.

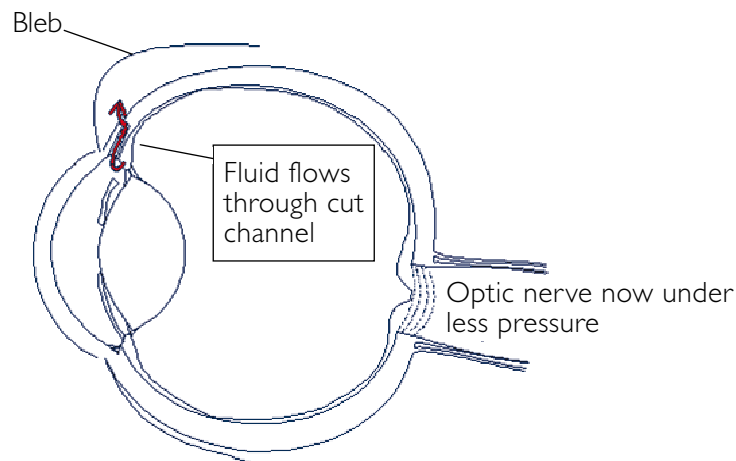
Summary of common surgical interventions

Trabeculectomy

Incisional filtering microsurgery involves surgically creating a drainage channel between the anterior chamber and subconjunctival space (see Figure 10.3). This is not a true fistula because the subconjunctival space is only loose connective tissue with a large capacity for fibrosis. The surgical dissection and subsequent aqueous flow are believed to stimulate this fibrosis which reduces the outflow of aqueous over time. Standard trabeculectomy five-year survival is reported to be 80% (AGIS 2002).

Trabeculectomy may be undertaken as a primary procedure, or when laser therapy does not successfully lower IOP, or if the IOP begins to rise. Serious intra-operative complications include suprachoroidal haemorrhage and choroidal effusion. Early and late post-operative complications include flat anterior chamber, cataract formation, bleb leaks, persistent hypotony and bleb infections/endophthalmitis.

Several of these complications can occur years after the original surgery. Since excessive scarring in the operative area will lead to failure of filtering surgery, anti-fibrotic medications such as 5-fluorouracil and Mitomycin C are frequently applied locally to retard healing. A serious drawback with anti-metabolites is that some of the complications associated with filtering blebs are increased, such as a higher rate of bleb leaks and infections (Advanced Glaucoma Intervention Study [AGIS] 2000; AGIS 2002).

Figure 10.3: Purpose of incisional filtering microsurgery (Source: Members of the Working Committee)

Iridectomy

An iridectomy is the surgical removal of part of the iris. This procedure is most frequently performed in the treatment of angle closure glaucoma and iris melanoma. However, this procedure has been largely superseded by Nd:YAG laser iridotomy, because the laser procedure is much safer. Iridectomy is most commonly used in trabeculectomy to prevent iris occlusion of the channel. It can also be performed when corneal clarity or lack of equipment prevents performing a laser iridotomy.

Incisional non-penetrating surgery

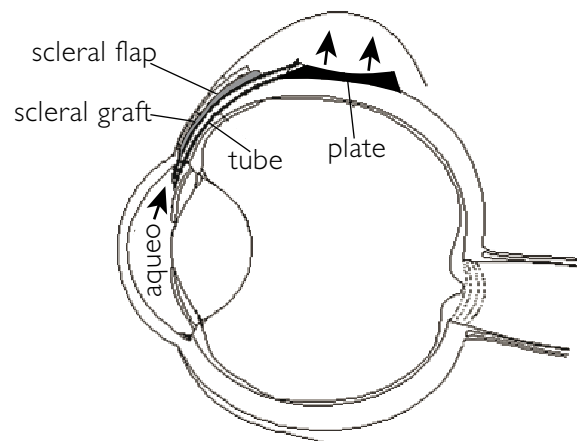
Non-penetrating trabecular surgery is filtering surgery without opening the internal trabecular structures. It includes techniques such as deep sclerectomy and viscocanalostomy. Advocates suggest that they can reduce potential complications associated with ocular entry, such as hypotony, multiple small bleb formation and subsequent cataract (Papadopoulos 2001) however there is a paucity of rigorous literature comparing these procedures with trabeculectomy.

Glaucoma drainage devices (implants and shunts)

Glaucoma drainage devices are employed to control IOP. They are generally employed in secondary glaucomas or where trabeculectomy has failed, (Minckler, Vedula, Li et al 2006). They are the first procedure of choice in some forms of glaucoma such as Iridocorneal Endothelial syndrome, some chronic uveitic forms and for some severe traumatic forms of glaucoma. The term *aqueous shunt* is preferred by the American National Standards Institute as most appropriate for the group of devices referred to in current peer-reviewed literature as glaucoma drainage devices, tube-implants, and tube-shunts. Glaucoma drainage devices are also inappropriately referred to as setons, a term that should be reserved for non-lumen devices (Minckler et al 2006).

Tube shunts work by allowing aqueous to flow along a plastic tube to a plate surface, which creates a conduit and reservoir that cannot be obliterated by local fibrosis (see Figure 10.4). The five-year IOP control success rate is between 50–100% (Molteno, Bevin, Herbison et al 2001) depending upon the study although a meta-analysis suggests approximately 10% failure rate per year for the first three years (Mills, Reynold & Grand 1996 cited in Hong, Arosemena & Zurakowski 2004). Newer devices are under development and use, however there is currently a lack of evidence regarding their long-term efficacy and safety.

Figure 10.4: Tube shunts (Source: Members of the Working Committee)



Surgical options for specific glaucoma classification and stages

Ocular hypertension and suspected open angle glaucoma

There is consensus that surgery is not the intervention of choice for patients with suspected OAG (AAO 2005c; Saw et al 2003; EGS 2003). Health care providers should use a step-ladder approach, with medication as the first step. If medication is unsuccessful (or unsuitable), the next least invasive and effective treatment option should be considered.

Established open angle glaucoma

For patients with OAG, the evidence to support any specific intervention over another is less consistent. The purpose of surgical treatment for OAG is to prevent glaucoma-induced visual disability. Incisional surgery is often considered a third choice approach after medication and laser therapy.

Incisional surgery is also an option for patients who cannot administer topical medications successfully. Similarly to angle closure and angle closure glaucoma, there is debate regarding the choice between laser therapy or surgery, and systemic administrations of anti-glaucoma medications. The adverse effects and contraindications of systemic medications, versus the potential for permanent damage and infection associated with more invasive techniques must be taken into consideration.

A Cochrane review by Sycha, Vass, Findl et al (2003) investigated the use of a number of medications and surgical interventions for normal tension glaucoma (NTG). It concluded that surgical intervention had a greater IOP-lowering effect on NTG than medications. However surgery was also associated with a greater incidence of cataracts. A surgical intervention is merited in a conventional setting where prior treatment has failed. It may not be a suitable choice as first choice treatment in this subgroup of POAG, when the risk and benefits are fully explored (Sycha et al 2003).

There is some evidence that surgery is more effective than medication in the management of glaucoma for patients with established OAG, however this evidence needs to be interpreted with caution. Burr et al (2004) compared medication with Scheie's procedure and initial trabeculectomy.

Many of the included primary studies looked only at IOP control as their measure of success, where it is clear that surgery has an advantage. However the evidence from the Collaborative Normal Tension Glaucoma Study (Lichter et al 2001 cited in EGS 2003) is less clear concerning differences in VF protection.

Evidence Statements

- Evidence strongly supports surgery as being at least as effective as medication for reducing intraocular pressure in established open angle glaucoma.
- Evidence strongly supports using surgery when target intraocular pressure is not being achieved with two or more medications, or adherence is problematic, and when laser has failed or is not likely to succeed.

Angle closure

The management aims for angle closure are to:

- reverse or prevent the angle closure process
- control IOP elevation and/or
- minimise damage to the optic nerve.

The extent of surgical intervention depends largely upon the stage of disease and the risk of future angle closure. Laser iridotomy is usually the treatment of choice, however other manoeuvres such as incisional iridectomy may be necessary to open the angle prior to drainage surgery (Saw et al 2003). Standard care may include trabeculectomy and/or cataract surgery. The treatment decision is dependent upon the residual degree of angle closure and its cause.

Evidence Statements

- Evidence supports surgical iridectomy as a second choice treatment for patients with acute angle closure, when primary laser iridotomy cannot be performed.
- Expert/consensus opinion suggests the value of cataract extraction or drainage surgery for patients with angle closure.

POINT OF NOTE

The most appropriate management for an individual, given the person-specific balance of risks and benefits at any one time, may not fit within the current accepted hierarchy of treatment.

Filtering surgery

Surgery is recommended for many patients with moderate or advanced glaucoma to lower the IOP into the target range, especially in NTG or eyes resistant to other forms of treatment (AOA 2002). Surgical treatment reduces IOP more than medication or laser treatment (EGS 2003). Moreover, the diurnal variation of IOP is better controlled with surgical treatment than with medication or laser treatment. In spite of lower levels of IOP, surgical treatment does not always reduce or halt progression of VF defects. After trabeculectomy, VF defects may progress despite the decrease in IOP (AAO 2005b, Tuulonen et al 2003). Early surgical treatment has been reported to slow the progression of VF damage more than laser or medications, only if the initial IOP is high (>30 mmHg) (Tuulonen et al 2003). At present, there is insufficient evidence to conclude that



clinical outcomes of trabeculectomy differ substantially from those of aqueous shunts in similar patients with complicated glaucomas (Minckler et al 2006). Filtration procedures appear less successful in patients of African descent, in patients with neovascular or uveitic glaucoma, in children, in patients following cataract surgery, and in patients whose eyes have undergone previous filtration surgery (AGIS 2000, 2004).

Various filtration surgery techniques to control glaucomatous damage have been shown to have success rates of 75–95% in previously unoperated eyes (AOA 2002). Post-operative medications are needed in 15–50% of these patients (AOA 2002). Second and subsequent filtration procedures have a lower success rate without anti-fibrotics. With anti-fibrotics, a second trabeculectomy has an equivalent 10 year success rate of 70% compared to initial trabeculectomy (AGIS 2002). The use of intra-operative and post-operative anti-fibrotics, such as 5-fluorouracil or Mitomycin C, has improved the success rates for both initial and repeat filtration surgery. Different surgical techniques appear to be similarly effective for altering the prognosis of the disease, as well as within different subtypes. It is not possible to draw an overall conclusion on the efficacy of each surgical technique for each subtype and stage of disease, as many different techniques are reported.

Meta-analysis of two trials comparing shunts to trabeculectomy reinforces the commonly held impression among glaucoma surgeons that trabeculectomy, especially with anti-fibrotic enhancement intra-operatively, is likely to lower IOP (Minckler et al 2006). Similarly, trials comparing medication to trabeculectomy have favoured the surgical intervention, particularly regarding reducing IOP-lowering. However these results may need to be interpreted with caution as the evidence concerning differences in VF protection is less clear (refer to Chapter 10 Appendix).

Evidence Statements

- Evidence supports using filtration surgery as a third choice treatment in most patients, due to the inherent risks with any invasive procedure.
- Evidence supports using filtration surgery for patients with moderate or advanced glaucoma, due to its success in lowering intraocular pressure. This is especially relevant to patients with eyes with high pressure conditions (over 30mmHg), or patients with eyes resistant to other forms of therapy.

Anti-fibrotic medications

Anti-fibrotic medications used to reduce fibroblastic proliferation and other scarring activities, are an important adjunct in ocular and periorbital surgeries. Anti-fibrotic medications such as the Mitomycin C and 5-Fluorouracil have been used successfully to decrease the fibrous reaction following trabeculectomy operation. However, the advantages of Mitomycin C at the time of the glaucoma drainage device implantation remain unclear.

There is evidence that 5-Fluorouracil is beneficial if the risk for failure of trabeculectomy is high (Wilkins, Indar & Wormald 2002; Wormald, Wilkins & Bunce 2000). There is however less evidence for its routine use in Caucasian populations (Tuulonen et al 2003). The use of intra-operative Mitomycin C is more effective than placebo, and reduces the risk of surgical failure in patients whose eyes have not undergone previous surgery, or patients whose eyes are at high risk of failure from surgery (Wilkins et al 2005). These patients frequently have difficult-to-manage glaucoma (such as glaucoma secondary to intraocular inflammation, congenital glaucoma and neovascular glaucoma). They may also have had previous glaucoma drainage or cataract surgery.

Evidence Statement

Evidence supports using intra-operative and post-operative anti-fibrotics to reduce the risk of failure for patients undergoing incisional surgery.

Glaucoma drainage devices

There is no evidence to support the clinical superiority of one aqueous shunt over another regarding safety or efficacy in reducing IOP. Ophthalmologists should thus base their choice of device on their own experience, and continue to utilise the shunt with which they are most comfortable. Tube surgery produces significant long-term IOP control with results suggesting that IOP control lasts longer than with trabeculectomy (Molteno comparison). Tube surgery tends to be limited to eyes at higher risk of failure with trabeculectomy or those in which trabeculectomy has failed. Tube surgery should be considered for the primary procedure in cases of Iridocorneal Endothelial syndrome, various forms of uveitic (inflammatory) glaucoma, aphakic glaucoma and in patients whom trabeculectomy is likely to fail (Doe, Budenz, Gedde et al 2001). Such situations include some severely traumatised eyes and secondary paediatric glaucomas (Molteno et al 2001). To date there have been no randomised studies which directly compare tube surgery and trabeculectomy.

Evidence Statements

- Evidence strongly supports using tube surgery for long-term intraocular pressure control. This is an appropriate first-choice surgery in patients:
 - with eyes at higher risk of failure from trabeculectomy
 - who have failed trabeculectomy
 - with Iridocorneal Endothelial syndrome
 - with various forms of uveitic (inflammatory) glaucoma, or
- with aphakic glaucoma.

Cataract surgery

Results for cataract surgery in glaucoma have been variable and largely dependent on the outcome measure used. Friedman, Jampel, Lubornski et al (2002) report good evidence that long-term IOP control is greater with combined procedures than with cataract extraction alone. They report fair to moderate evidence that trabeculectomy alone lowers long-term IOP more than combined extra-capsular cataract extraction and trabeculectomy. Friedman and Vedula (2006) indicated that there was no evidence of benefit with lens extraction in terms of progression of VF loss, visual acuity or medication use. It was noted that the studies had significant limitations that affected the ability to draw conclusions, for instance small sample sizes and unit analysis error (where both eyes were used in some patients). In eyes previously damaged by creeping angle closure, goniosynechiolysis and trabeculotomy are combined with cataract extraction (plus intraocular lenses implantation). This works well to reduce IOP and prevent synechiae reformation (Japanese Glaucoma Society [JGS] 2004). Trabeculectomy accelerates the development of cataracts (AGIS 2000) and promotes tendencies for angle closure due to ciliary block or lens/anterior segment disproportion. The latter occurs when the increase in lens size from ageing or cataract leads to crowding and displacement of the ciliary processes and iris, exacerbating plateau iris, iris to angle proximity and ciliary block, even in the presence of iridotomy. In subjects with persistent angle narrowing after iridotomy and/or iridoplasty, careful consideration is required regarding the



above angle narrowing factors. It is often safer to remove the lens first and in these situations the angle usually opens further, with a concomitant reduction in IOP. Should the IOP not be reduced sufficiently, then trabeculectomy can be safely performed.

In subjects with open angle glaucoma and coexistent cataract requiring trabeculectomy, the consensus is that the cataract should be removed first, when the optic nerve is not severely damaged. In patients with POAG and without prior surgery, approximately 50% will gain a useful reduction in IOP from cataract surgery alone, although this reduction tends to be short-lived (in the order of six months). Should trabeculectomy be required, it can be performed more safely several months later, without risk of inducing cataract. The difficult cases are those with severe glaucoma and cataract, where it is often necessary to perform combined cataract and trabeculectomy surgery to reduce the risk of a pressure spike.

Evidence Statement

Evidence supports using cataract surgery to open the angle in most patients with primary angle closure, when laser procedures have been inadequate. This is believed to improve the safety of subsequent drainage surgery.

POINT OF NOTE

Cataract surgery in patients with advanced glaucoma can lead to loss of remaining vision and/or bleb failure in eyes which have undergone prior trabeculectomy.

Therapeutic indications for laser therapy and or surgery

Laser therapy is considered in patients who fail to maintain IOP within the specified target range, and who are resistant to other forms of treatment (AOA 2002). Emerging evidence suggests that laser therapy is a strategy for IOP reduction that needs to be considered at different stages of the management spectrum for individual patients, considering its benefits and drawbacks on a one-by-one basis (see Table 10.1). This guideline provides recommendations regarding first, second and third choice treatments. For the role of medication and the indications to change treatment, refer to Chapter 9.

Table 10.1: Summary of indicators for surgical/laser treatments

Surgery	Source	Contraindication	Indications for use	Benefits	Drawbacks
Argon laser trabeculoplasty	AOA (2002) RCO (2004)	Uveitic glaucoma Young patients, especially children Narrow or closed angles		Reduces IOP in MOST eyes by an average of 30%	Effect diminishes over time. May increase the chance of future surgical failure.
Nd:YAG laser iridotomy	RCO(2004)	Caution required – watch for post-laser IOP rise in those with marked synechial angle closure	In the absence of symptoms of intermittent angle closure		Only effective with narrow but open drainage angles and some iris-trabecular contact
Cyclodiode laser	AOA (2002)	Some uveitis	Where other modalities have failed		
Incisional filtration Surgery	AOA(2002)	Contraindicated in eyes that are already blind or patients with severe systemic illness	In NTG or POAG resistant to other forms of therapy	Dramatic and stable reduction in POAG	Many patients must remain on medication and may require additional filtration or other surgery
Anti-fibrotic use	AOA (2002)	The elderly or those with frail conjunctiva	Eye at risk of later failure due to scarring of the drainage bleb		Caution required especially for those with high potency

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Appendix to Chapter 10

Key experimental studies which have informed current evidence in the guidelines cited in this chapter *Sourced in part from the AAO (2005b).*

Trial name	Patient type	Intervention	Outcome
Scottish Glaucoma Trial (Jay & Allan 1989)	Newly diagnosed POAG	Medication vs trabeculectomy	Trabeculectomy lowered IOP more than medication; the medication group had more deterioration in VF than trabeculectomy group.
Moorfields Primary Treatment Trial (Migdal et al 1994)	Newly diagnosed POAG	Medication vs. laser trabeculoplasty vs. trabeculectomy	Trabeculectomy lowered IOP the most; laser trabeculoplasty and medication groups had more deterioration in VF than trabeculectomy group.
Glaucoma Laser Trial (1990) (GLT)	Newly diagnosed POAG	Medication vs laser trabeculoplasty	Initial laser trabeculoplasty was at least as effective as initial treatment with topical timolol maleate to lower IOP and preserve VF and optic disc status.
Glaucoma Laser Trial Follow-up Study (GLT) (1995)	Follow-up of GLT patients	Medication vs laser trabeculoplasty	Longer follow-up reinforced the earlier findings that initial laser trabeculoplasty was at least as effective as initial treatment with topical timolol maleate to lower IOP and preserve VF and optic disc status.
Ocular Hypertension Treatment Study (Gordon et al 1999, Kass et al 2002)	Patients with OH	Medication vs. no treatment	Lowering IOP with medication reduced by half the rate of conversion to OAG.
Collaborative Normal Tension Glaucoma Study (Collaborative Normal-Tension Study Group 1998)	POAG in eyes with normal IOP		Lowering IOP retarded the progression rate of VF loss compared with untreated eyes.
Early Manifest Glaucoma Trial (Heijl et al 2002, Leske et al 2003)	Newly diagnosed POAG	Medication and laser trabeculoplasty vs. no treatment	Lowering IOP with medication and trabeculoplasty inhibited progression of optic disc and VF damage.
Collaborative Initial Glaucoma Treatment Study (Lichter et al 2001)	Newly diagnosed POAG	Medication vs. trabeculectomy	Lowering IOP with initial filtering as surgery was as effective as medication to inhibit progression of VF damage, though the amount of reduction was slightly greater after surgery.

Trial name	Patient type	Intervention	Outcome
Advanced Glaucoma Intervention Study (AGIS) (The AGIS Investigators 2000, 2004)	POAG after medication failure with no previous surgery	POAG after medication failure with no previous surgery: laser trabeculoplasty vs. trabeculectomy	Surgical outcome varied by race; patients with African ancestry did better with trabeculoplasty as first surgery, while in the longer term (4+ years) Caucasian American patients did better with trabeculectomy as first surgery. Lower IOP during follow-up after surgical interventions protected against further VF deterioration in patients with advanced glaucoma.
European Glaucoma Prevention Study (Miglior 2002, 2005)	Patients with OH	Medication (dorzolamide) vs. placebo (the vehicle of dorzolamide)	Medication lowered IOP by 15% to 22%; placebo lowered IOP by 9% to 19%. No significant difference was found between medication and placebo in reducing the incidence of POAG. The study protocol did not require any target IOP reduction to be achieved during the trial.



■ CHAPTER 11

Patient journeys

Introduction

Glaucoma is a chronic and complex disorder. A patient's journey often begins before a formal diagnosis has been made, as a diagnosis of glaucoma rarely occurs after a single visit to any health care provider. It may require multiple visits to health care providers and sustained longitudinal monitoring by a range of different health care providers in order to arrive at a definitive diagnosis. As glaucoma is also defined as '*a group of eye diseases in which there is progressive damage to the optic nerve characterised by specific structural abnormalities of optic nerve head and associated patterns of visual field loss*' (Burr, Azuara-Blanco & Avenell 2004 p2), the patient's journey from detection to diagnosis and intervention will depend to a great extent on the type of glaucoma with which the patient has been diagnosed.

These guidelines discuss the recommendations for the detection, diagnosis, and management of glaucoma in separate sections for ease of use by the health care provider who may participate in any of these events. It is also important for the multidisciplinary glaucoma health care team, and the patient, to view the full journey that may lie ahead for their specific form of glaucoma. To assist this, separate pathways have been drafted for open angle and angle closure glaucoma.

These pathways draw together the evidence for managing each stage of the disease. They provide both a composite base for discussion between health care providers and patients, and a reference for patients. Internationally, patient pathways for other conditions have been made available electronically. Health care providers can use these to discuss disease progression with their patients, what they can expect to happen next, and available management options.

Care pathways

Care pathways are usually developed for the entire patient journey for particular conditions and include the process of decision-making, care options, and patient progress.

They integrate the activities of different health care providers, or health care organisations, and they promote multidisciplinary care instead of individual 'usual' practice. 'Usual' practice mostly comprises independent decision-making and relatively isolated clinical activities (Bryan, Holmes, Prostlehwaite et al 2002). Pathways attempt to translate broad guideline recommendations or best evidence from research into an integrated action plan for health care providers and patients.

Pathways detail available best evidence diagnoses, treatments or procedures which could be adopted, their timing and sequencing, and the health care provider best placed to undertake each task (Bragato & Jacobs 2003; Bryan et al 2002; Walldal, Anund & Furak 2002).

The use of integrated care pathways has been promoted worldwide in an attempt to increase local uptake of agreed national guidelines. Many more guidelines are written than are implemented (Delamothe 1994). Less than adequate attention and support is given to translating and implementing established guidelines into local management protocols (Campbell, Hotchkiss, Bradshaw et al 1998).



Jones (2000, *p.216*) suggests that clinical pathways take one of two forms: either '*reflecting the care and treatment of a particular diagnosis*' or '*the process of care from one agency or care boundary to another*.' The latter is concerned with the timing and sequencing of the care process. This is to improve coordination and communication between health care providers, thus making care processes more effective, integrated and efficient.

Patient pathways for glaucoma should encompass all the aspects noted by Jones (2000), so they have the potential to impact favourably upon multiple outcomes of care.

Are care pathways appropriate in glaucoma?

The aims of care pathways are appropriate to glaucoma diagnosis and management (Campbell et al 1998). Care pathways aim to:

- facilitate introduction of guidelines, and systematic and continuing audit into clinical practice
- improve multidisciplinary communication and care planning, within and between sectors (e.g. primary and secondary)
- reach or exceed existing quality standards
- decrease unexplained practice variation
- improve health care providers and patient communication and satisfaction
- identify research and development questions.

Care pathways were first developed for relatively common conditions with predictable outcomes, and for surgical interventions with stable and established routines post-surgery. Glaucoma is a complex condition with a range of treatment options. The evidence-base to support decision-making is often limited and expert opinion is used as the guide. Thus it is not surprising that care pathways are in their infancy for this condition.

Glaucoma management has evolved rapidly in recent years. The demography of glaucoma is changing, and patients are presenting earlier for screening and diagnosis. There are more options available for treatment, and there is a concerted drive to maintain a lower IOP across the continuum of glaucoma patients. This trend may lead to an increased workload for health care providers. This may relate to increased monitoring and surveillance activities, due to greater medication use and higher likelihood of false positive diagnoses related to earlier presentations. A care pathway developed for glaucoma, approved by relevant professional bodies and underpinned by current clinical evidence, has the potential to ensure a more efficient and accessible system of care for patients. It may also facilitate a shared-care environment that supports health care providers with clearly stated responsibilities. Pathway development may take different approaches, and a brief explanation of different development methods is outlined in the next section.

Pathways embedded in guidelines

The majority of international guidelines sourced for the systematic literature review on which these NHMRC Guidelines for the Screening, Prognosis, Diagnosis, Management and Prevention of Glaucoma are based, contain detailed preferred practice patterns for each aspect of glaucoma diagnosis and management. These patterns are often written for individual professional groups (for instance American Academy of Ophthalmology 2005a,b,c; American Optometric Association 2002). Others state accepted standards of practice without reference to the health care providers who are responsible (for instance European Glaucoma Society 2003; South East Asia Glaucoma



Interest Group [SEAGIG] 2003). Current models of glaucoma care emphasise co-management between professional groups and between primary and secondary care sectors. Thus it may be appropriate to provide profession-specific pathways within companion documents to this guideline, in conjunction with a multidisciplinary pathway that informs shared-care arrangements.

Creating integrated care pathways

Integrated care pathways differ from simple documented pathways or patient journeys, in that they combine an explicit evidence-based course of action with a written record of care. Thus how care is documented, and by whom, is an important element of the pathway. It serves as a visible record of health care providers' involvement, with all the related legal implications (Hunter & Segrott 2008). Integrated care pathways for glaucoma involve a number of steps, which are focused on specific local contexts. These are essential to maximise the translation of national guidelines into local clinical practice (Campbell et al 1998).

Steps to create integrated care pathways include:

- map out the entire care process as it currently exists in the local context
- identify best practice through examining research evidence and guidelines
- critically review and revise current practice in the light of the evidence
- create pathways that provide avenues for recording variance
- implement the guideline as an active stage of the pathway's development, in which health care providers may reshape the document.

The National Health Service in the UK has moved towards outlining integrated care pathways for glaucoma, in order to align them with national data management. The Glaucoma Clinical Care Pathway and Dataset represent the clinical information required to manage a patient with glaucoma along each step of the care pathway, from detection, referral, diagnosis, care planning and management. The aims are to use the pathway in primary and secondary care and by relevant health care providers at each step. Its purpose is to document clinical management, and facilitate transfer of relevant information within, and between, clinical teams to enable consistent and high quality patient care.

POINT OF NOTE

Care pathways are not a substitute for clinical judgement. They should be recognised as a way of encouraging the translation of national guidelines into local protocols, and the subsequent application of local protocols into individual clinical practice.

There are a number of methods by which to achieve the integration of best practice protocols into clinical practice, of which developing integrated care pathways is one option.

Each proposed patient journey/clinical pathway in these guidelines requires in-depth delineation of roles and responsibilities of health care providers. These should be sufficiently flexible to incorporate variations between planned care as agreed by health care providers and professional bodies, and actual care based on local service arrangements/protocols and service limitations. It is beyond the scope of this document to provide this refinement.

It should also be noted that other important adjuncts to the ophthalmic care of the patient with glaucoma may be incorporated in future versions, by including team members such as social workers and vocational rehabilitation coordinators.

Patient pathways in open angle glaucoma

Figure 11.1 presents the current best evidence for the most appropriate care of the ‘average’ patient with open angle glaucoma. There are many factors which impact on the decision-making of the different health care providers who are responsible for the management of individual patients. Glaucoma is a complex group of diseases, which often occurs in older individuals with comorbid conditions. These may impact upon the choice and effectiveness of available treatment options. It is beyond the scope of the proposed patient pathway to incorporate wider aspects of a patient journey with glaucoma, for instance social, emotional and economic elements. In all stages, it is important that appropriate support is provided by health care providers to the patient with glaucoma and their carer(s). This may be provided by ensuring links to important consumer groups such as Glaucoma Australia (refer to Chapter 12) and by clear written and verbal communication. In advanced stages, low vision rehabilitation is a valuable adjunct to the glaucoma management plan.

Patient pathways in angle closure glaucoma

Figure 11.2 represents the current best evidence for the most appropriate care of the ‘average’ patient with intermittent or chronic angle closure. Angle closure may present as an acute crisis, requiring emergency management. These guidelines provide clear information regarding the signs and symptoms of an angle closure crisis.

Figure 11.1: Open angle glaucoma pathway (see Table 8.2 for more information p100)

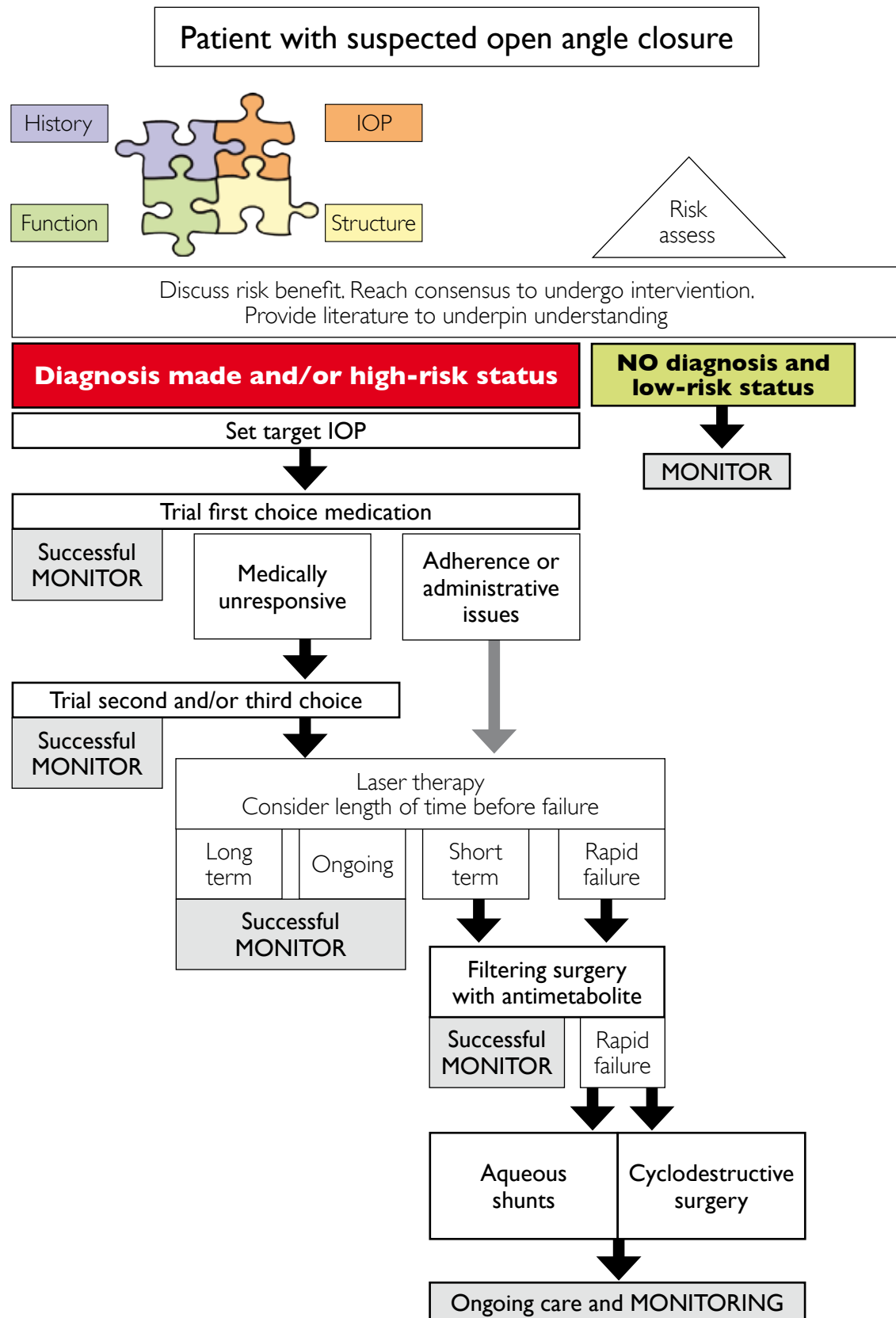
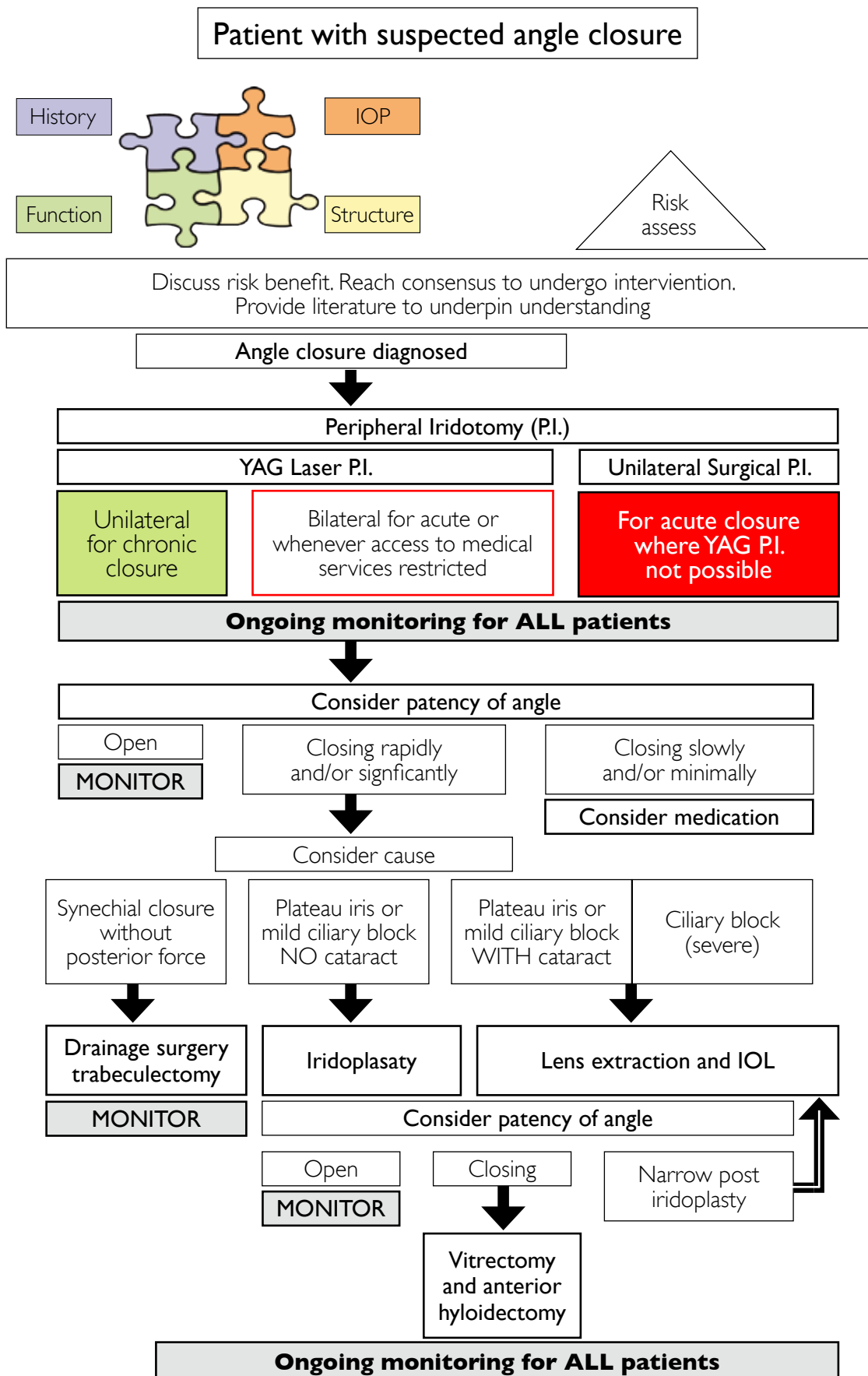


Figure 11.2: Intermittent or chronic angle closure pathway





Reference

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■ CHAPTER 12

Resources

Consumer-oriented organisations

Glaucoma Australia

<http://www.glaucoma.org.au/>

Glaucoma Australia's (formerly The Glaucoma Foundation of Australia Inc.) mission is to minimise visual disability from glaucoma. Their sole purpose is:

- increasing community awareness and understanding of glaucoma and the need for regular eye checks
- supporting glaucoma patients and their families, especially with information and telephone support
- funding glaucoma research.

Vision Australia

<http://www.visionaustralia.org/>

Vision Australia is a living partnership between people who are blind, sighted or have low vision. They are united by their passion that in the future people who are blind or have low vision will have access to and fully participate in every part of life they choose.

Royal Society for the Blind

<http://www.rsb.org.au/>

The Royal Society for the Blind (RSB) is the primary provider of services for South Australians who have severe vision impairment. These services are delivered by a professional, committed and highly qualified team supported by volunteers, drawn from all age groups and walks of life. Blindness or vision impairment can have a severe impact on a person's lifestyle. The RSB is here to assist people to overcome their vision impairment and participate independently in the community.

Guide Dogs Australia

<http://www.guidedogsaustralia.com/>

Guide Dogs Australia is a brand that represents all of Australia's state based Guide Dog organisations. Together, as the nation's leading providers of orientation and mobility services, including Guide Dogs, they assist people who are blind or have a vision impairment gain the freedom and independence to move safely and confidently around the community and to fulfil their potential.

Association for the Blind of WA

<http://www.abwa.asn.au/>

Their mission is to maximise the quality of life of people who are blind or vision impaired by building confidence, promoting wellness, and creating connection.

Health Insite

<http://www.healthinsite.gov.au/topics/Glaucoma>

Through this site you will find a wide range of up-to-date and quality assessed information on important health topics such as glaucoma, diabetes, cancer, mental health and asthma.

Profession-specific organisations

Orthoptic Association of Australia

<http://orthoptics.org.au>

The Orthoptic Association of Australia Inc (OAA) is the national peak body for Orthoptists in Australia. The role of the OAA is to:

- promote and develop the profession of orthoptics
- represent and support its members
- contribute to excellence in eye health care in the community.

Optometrists Association Australia

<http://www.optometrists.asn.au/>

Optometrists Association Australia is the professional association for Australian optometrists. The website includes a 'find an optometrist' function, enabling consumers to find an optometrist by location.

The Royal Australian and New Zealand College of Ophthalmologists (RANZCO)

<http://www.ranzco.edu/>

The College's mission is the improvement of the already high standard of eye care in Australia and New Zealand. In pursuit of this mission, the College provides a variety of services centered on its core roles as a higher educational institution and learned society.

The Pharmacy Guild of Australia

<http://www.guild.org.au>

The Pharmacy Guild of Australia is the professional body representing community pharmacies in Australia. The website includes a 'Find a Pharmacy' function, enabling consumers and health professionals to find a pharmacy by location.

Australian Ophthalmic Nurses Association

<http://www.aonavic.com.au/>

The Australian Ophthalmic Nurses Association is the professional association for Ophthalmic Nursing in Australia, with branches located NSW, QLD and VIC. The association aims to provide and communicate current information from a variety of clinical aspects, including nursing, medical and allied health professionals.



Pregnancy-specific information

New South Wales

Mother Safe

Phone (02) 9382 6539, Toll free (NSW) 1800 647 848

Queensland

Queensland Drug Information Centre

Phone (07) 3636 7098

Information for health professionals only

South Australia

Women's and Children's Hospital

Phone (08) 8161 7222

Victoria

Royal Women's Hospital

Phone (03) 9344 2277

Western Australia

Women's & Children's Health Services

Phone (08) 9340 2723



■ APPENDIX I

Process report

A Systematic Literature Review on the Detection, Diagnosis, Management and Prevention of Glaucoma

GUIDELINE DEVELOPMENT TEAM

Centre for Allied Health Evidence (CAHE) University of South Australia technical team

Professor Karen Grimmer-Somers

Ms Judith Lowe

Ms Anthea Worley

Ms Janine Dizon

Ms Lucylynn Lizarondo

Tasks

The CAHE technical team undertook all the technical tasks related to writing these guidelines:

- the systematic review of the literature which underpins these guidelines (see NHMRC website)
- drafting the guideline text and recommendations for each question
- collating the strength of the body of evidence related to each recommendation, and designing the star grading system
- designing the layout of the guidelines
- managing the rounds of consultation with the NHMRC Expert Working Committee to modify wording and content of the draft guidelines
- finalising the guideline wording and editing the document
- addressing comments as appropriate from the public consultation phase.

Contact details

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NHMRC Expert Working Committee

(referred to as the Working Committee throughout the guidelines)

Professor William Morgan (Ophthalmologist)

Lions Eye Institute (CHAIR)

Associate Professor Ivan Goldberg (Ophthalmologist)

Eye Associates Glaucoma Services Sydney Eye Hospital

Professor Jonathon Crowston (Ophthalmologist)

Centre for Eye Research Australia

Associate Professor David Mackey (Epidemiologist/Ophthalmologist)

Royal Victorian Eye and Ear Hospital

Professor Algis Vingrys (Optometrist)

Department of Optometry and Visual Sciences University of Melbourne

Dr Philip Anderton (Optometrist rural)

Associate Professor Amanda McBride (Head of General Practice School of Medicine, Sydney)

The University of Notre Dame Australia and General Practitioner in Woollahra, Sydney

Dr Genevieve Napper (Optometrist, low vision service provider)

Victorian College of Optometry

Mr Grant Martin (Director, Professional Services)

Pharmaceutical Society of Australia

Ms Jill Grasso (Ophthalmic Nurse)

Representing the Ophthalmic Nurses Association

Ms Beverly Lindsell (Glaucoma Australia Representative)

Glaucoma Australia

Ms Tania Straga (Orthoptist)

Representing the Orthoptic Association of Australia

Ms Helen Robbins

Representing the Optometrists Association Australia (Observer)

Tasks

The Working Committee represented comprehensive and unfunded stakeholder group perspectives on guideline intent, content and wording. Members provided content knowledge, professional perspectives and clinical expertise, and assisted the technical writers to understand the nuances of the literature relevant to Australian patients and settings. The Working Committee also provided clinical insights into referral processes, nomenclature and evidence interpretation in clinical settings. Members of the team assisted with editing the final guideline document.

Internal Reference Group

Mr Luke Grzeskowiak, Pharmacist

University of South Australia

Tasks

Provide expert pharmaceutical advice as required.



NHMRC Project Staff

Ms Vesna Cvjeticanin (Director, Evidence Translation)
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Ms Marion Hewitt (Project Officer, Evidence Translation Section)
National Health and Medical Research Council (2010)

Ms Kay Currie (Director, National Institute for Clinical Studies (NICS)
National Health and Medical Research Council

Tasks

NHMRC staff coordinated the guideline development process, facilitated the dissemination of information between the Technical Team and the Working Committee, and assisted as required with resolution of debate on wording and guideline intent.

Contact details

glaucoma@nhmrc.gov.au

Guideline purpose

This guideline presents the current best evidence for screening, prognosis, diagnosis, management and prevention of glaucoma. Its purpose is to inform practice for Australian health care providers, particularly utilising a multi-disciplinary team approach.

Target users

This guideline is primarily targeted to Australian primary health care providers undertaking any task related to screening, prognosis, diagnosis, management and prevention of glaucoma, in any setting. Information is also provided for secondary health care providers.

Review questions

Specific review questions were formulated by the CAHE Technical Team and the Working Committee. The review questions were addressed in the underpinning NHMRC Systematic Review of the literature, which provided a comprehensive synthesis of the current literature for the screening, prognosis, diagnosis, management and prevention of glaucoma. The research questions comprised:

1. What is the definition of glaucoma?
2. What are the recognised types and/or classifications of glaucoma?
3. How do they differ pathophysiologically from each other?
4. What is the prevalence and incidence of glaucoma within Australia and internationally?
5. What is the natural history of glaucoma?
6. What is the best available evidence for the prognosis of patients with glaucoma, and the ability of any given intervention to alter this prognosis, from population-based studies?
7. What is the best available evidence for the prognosis of glaucoma and the ability of any given intervention to alter this prognosis from experimental studies?
8. Based on the best available evidence, what, if any, are the recognised risk factors for:
 - developing glaucoma?
 - the progression of established glaucoma?
9. Does the evidence support widespread general population screening, or targeted population screening, for glaucoma? If so, based on the best available evidence, what are the most appropriate screening methods?
10. What is the recommended methodology for the monitoring and surveillance of individuals suspected of having glaucoma or individuals at-risk of having glaucoma?
11. What is the recommended methodology for the monitoring and surveillance of patients with established glaucoma?
12. What is the best available evidence for appropriate methods and techniques to diagnose glaucoma?
13. Does the evidence identify threshold values at which a diagnosis of glaucoma can be made?
14. What does the literature have to offer regarding the pragmatic elements and logistics of diagnosing glaucoma, with respect to the health care professionals involved, health care settings and resources required?

Systematic review methods

Each question was interpreted using a PECOT format, which assisted in defining the scope, search terms/ key words and inclusion/ exclusion criteria. These search terms were systematically applied to a range of library databases to ensure a replicable and comprehensive search of the academic literature. The literature for each question was examined using five evidence dimensions (hierarchy, methodological quality, significance, effect size, and applicability). A consistent approach was taken to critically appraise the literature for each question, and to summarise and report the findings.

The methodology of the systematic review which underpins these guidelines is reported in full in Systematic Literature Review on the Detection, Diagnosis, Management and Prevention of Glaucoma, prepared for NHMRC and the Department of Health and Ageing, by the Centre for Allied Health Evidence, University of South Australia, Division of Health Sciences (Sept 2008). This report is available on www.nhmrc.gov.au.



The Systematic Review provided Addenda throughout, which reported additional input from the Working Committee to enhance the literature findings. These Addenda variously described operationalisation of literature findings in local contexts, expert opinion where there was scant evidence from the literature, and/ or provided new references (or seminal references which fell outside the timeframe of the search). The Addenda also flagged emergent research areas which should be considered in more detail in the review of the Systematic Review (proposed for 2011).

Guideline recommendations

Recommendations were formed using steps outlined by the Australian National Health and Medical Research Council (NHMRC 1999, 2000a,b, 2005).

Throughout the guideline development process, drafts of guideline text and recommendations were circulated between members of the Guideline Development Team. Some recommendations were underpinned by strong research evidence and they required little debate in terms of their wording, intent or operationalisation. However other recommendations were not so strongly supported by research evidence, thus the expertise of the Working Committee was required to ensure that these recommendations reflected the intent of current evidence operationalised for local contexts.

There were some instances where there was a lack of relevant research related to a clinical question. The NHMRC hierarchy does not recognise expert or clinical opinion as a formal evidence level; however in the absence of formal scientific evidence, it is accepted international practice that consensus recommendations be provided (Canadian Health Services Research Foundation 2005; Jones & Hunter 1995; Murphy, Black, Camping et al 1998). When this situation arose, the Working Committee constructed recommendations based on expert opinion. The Working Committee provided specific references or examples as appropriate, to support these recommendations.

Where guidance was required to operationalise recommendations, Communications to Health Care Providers, Communications to Patients, and Points of Note were used.

Each recommendation was underpinned with the NHMRC matrix which summarises the underpinning strength of the body of evidence (See Chapter 2 of the Guideline, Table 2.1). Each matrix was reported in its five elements to provide guidance to health care providers on the subtleties and complexity of the evidence, and its clinical applicability and relevance.

For each recommendation, the overall grade is represented beneath by a single capital letter, ranging from A to D. These grades are derived from the NHMRC Body of Evidence matrix (2009) and were determined in the same way that each of the five levels of evidence were determined.

Consultation

Public consultation occurred during October-November 2009. Key professional associations and consumer groups were targeted for comment, as well as general comments sought from the public. Stakeholder comments were collated by NHMRC and were addressed, as indicated, by the CAHE Technical Team. A document detailing the public consultation process and the Guideline Development Team's response to feedback is provided on the NHMRC website.

Consumer involvement

Consumers' interests were represented on the Working Committee by Ms Beverly Lindsell (Glaucoma Australia).

Revision of the guideline

The volume of research evidence for glaucoma screening, diagnosis, monitoring and management is growing rapidly. Emerging technologies were noted in the Systematic Review, and by the Working Committee. With further research these technologies may change the way in which glaucoma is detected and managed. Given the speed of change and the likelihood of new research being published, the CAHE Technical Team recommends that the literature for the review questions is revisited in 2011.

Implementation

The Guideline Development Team discussed issues of guideline implementation in detail throughout the guideline development period. The Guideline Development Team was in agreement that an agreed and well articulated implementation plan was essential to ensure cost-efficient and effective roll-out of the guidelines, and appropriate auditing of guideline uptake at a later date. This discussion also assisted the team to clarify guideline users and purpose, as well as wording of recommendations which would assist in evidence uptake. The wording could also be used to inform audit processes undertaken at a later date. Guideline Chapter 3 outlines the implementation considerations of the Guideline Development Team.

References

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