

Childhood glaucoma

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When a child is given a diagnosis of glaucoma, the impact upon that child and their family is enormous; equivalent to the diagnosis of a cancer [14]. This article outlines the knowledge, techniques and approaches that offer solutions to the significant challenges faced in this rewarding area of ophthalmology. Topics have been chosen according to their importance and usefulness within the article's constraints.

Epidemiology

The incidence of congenital glaucoma in the UK is a minimum of one in 18,500 live births / year. Primary congenital glaucoma (PCG) is nine times commoner in the UK amongst children of Pakistani origin compared to Caucasians [1].

Populations with higher rates of consanguinity have more PCG; PCG is usually autosomal recessive. Rates of disease amongst Romany families and children in Saudi Arabia are about 10 times those of a 'native' European population, though penetrance differs [2,3].

Local variations in genetics cause influence the phenotype and hence the response to surgery [4], in particular angle surgery. Presentations in the Middle East are characterised by early (true congenital) onset, severe buphthalmia and secondary corneal effects, with a poor response to angle surgery. Severe cases are associated with specific mutations in CYP1B1 (p.Gly61Glu and p.Arg469T) [5].

The internationally recognised diagnostic categories for childhood glaucomas are shown by the diagnostic pathway in Figure 1 [6].

In the UK, primary congenital glaucoma (PCG) is the commonest cause of glaucoma (45%), followed by glaucoma following cataract surgery (GFCS) (16%) and Sturge-Weber related glaucoma (10%) [1].

Assessment

In order to make a diagnosis of glaucoma and describe the sub-type, the clinician needs to be able to describe the distinguishing variables given in Figure 1. The diagnosis of glaucoma can mostly be made without general anaesthesia (GA), though sub-typing often needs closer examination. Corneal diameter and thickness, axial length, Haab striae, angle morphology and discs are best described under general anaesthesia in toddler-aged children. This also allows ultrasound biomicroscopy (UBM) and optimised

handheld optical coherence tomography (HHOCT).

Rebound tonometry (RBT) has transformed practice. Following its introduction at our unit, we avoided 211 examinations under anaesthesia in a year [7]. Intraocular pressure (IOP) measurement is now usually possible without GA. Pitfalls from RBT include:

- a) A probe rebounding from areas of increased focal corneal rigidity (e.g. band keratopathy, or fibrosis) leads to over-estimated IOP.
- b) Corneal oedema causes under-estimation. A normal rebound intraocular pressure is often found in the context of corneal oedema even when the IOP is pathologically raised.
- c) Minor over-estimation of IOP (vs. Goldmann) occurs at physiological levels. Greater over-estimation occurs measuring raised IOPs [8,9].
- d) Over-estimation occurs with increased corneal thickness [10].

Whilst a child is under GA there are many variables which commonly become non-physiological. These impact upon IOP via different mechanisms with different lag-times.

- a) Mean arterial pressure (MAP) acts almost immediately upon IOP, with the relationship being proportional; 1mmHg IOP for 10mmHg MAP [11]. MAP is increased by endotracheal intubation more than a laryngeal mask airway, yet many anaesthetic agents lower blood pressure, hence lower IOP.
- b) Choroidal vasodilation correlates with venous tone. It acts quickly on IOP and is influenced by pCO₂. Higher pCO₂ correlates with higher IOP.
- c) Extraocular muscle tone impacts IOP immediately. Depolarising muscle blockers (e.g. suxamethonium) increase muscle tone and hence IOP, however muscle relaxants (e.g. succinylcholine) can have an ameliorating effect.

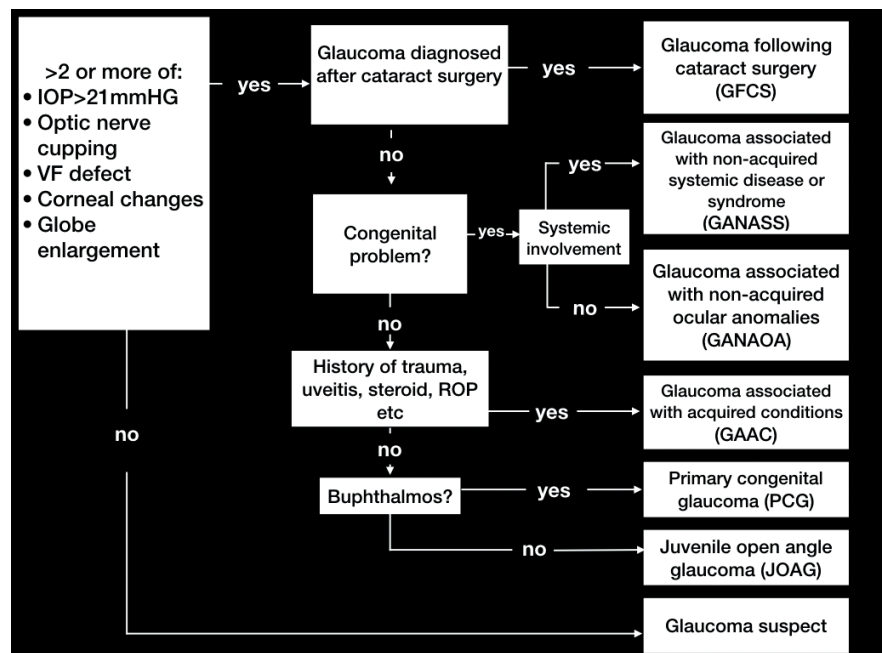


Figure 1: World Glaucoma Association diagnostic pathway.

d) Pharmacological impacts from GA on aqueous secretion and outflow are complex and take longer (minutes) to impact IOP. They mostly lower IOP, with the notable rare exception of mydriatics, causing angle closure in susceptible patients.

The best estimates of IOP under GA are after a-priori discussion with an experienced paediatric anaesthetist. Good options are ketamine anaesthesia with a benzodiazepine pre-medication to blunt the sympathomimetic IOP spike. An alternative is immediate tonometry upon sevoflurane induction, though every minute lost after induction equates to an approximate 2mmHg drop in IOP [12]. By the time the child arrives in theatre, the drop can be 10mmHg or more [13].

Management

Childhood glaucomas have a devastating impact upon quality of life, equivalent to a diagnosis of leukaemia or organ transplantation [14]. Early fostering of a collaborative family-centred approach is very important. There is often a long journey ahead. Patient-held records or health passports can help inform families, address communication gaps and optimise patient / family ownership of the condition [15]. A trusting relationship between the surgeon and the child and their family, is a key factor. The developmental glaucomas in children may be associated with systemic problems, especially in the context of an infant who is not thriving, has systemic dysmorphism or co-existing cataracts. It is critical to have a multi-disciplinary

holistic approach. Examples of systemic syndromes that may co-exist with glaucoma include: Lowe syndrome, Sturge-Weber syndrome, Axenfeld-Rieger syndrome, Neurofibromatosis Type 1, Marfan syndrome (especially the neonatal form), Rubinstein-Taybi and Muscle-Eye-Brain disease. Systemic syndromes associated with glaucoma may not always be diagnosed at the initial point of contact and one should have a low threshold for repeated paediatric assessment. Anirida, especially the sporadic form, is associated with Wilms' tumour and requires specialist-lead, abdominal imaging unless genetic tests exclude the WT-1 mutation.

Relatives of children with inheritable forms of glaucoma require screening.

Conditions that mimic glaucoma in infancy include tyrosinaemia type 2, early onset blepharokeratitis and various corneal pathologies, including posterior polymorphous corneal dystrophy.

Childhood glaucomas mostly require surgery. During the year following diagnosis, 94% of PCG cases and 64% of secondary glaucomas require surgery [1].

Children have a greater tendency for wound (or sclerostomy) leakage and brisker inflammation, fibrosis and healing. There are particular challenges for postoperative assessment and modulatory procedures, such as bleb manipulation. The relative rarity of childhood glaucomas presents an obstacle to generating high-level evidence, which can guide adult glaucoma practice.

“There is new evidence that the success of angle surgery can be predicted from the UBM appearance of the dysmorphic drainage angle in PCG.”



Surgery

The choice of intervention is specific to the individual. The following factors inform the decision:

- 1) The mechanism or type of glaucoma, in particular angle morphology.
- 2) Ocular comorbidity (especially widespread anterior segment dysgenesis, lens-status, choroidal haemangiomas, corneal clarity, hypotony risk).
- 3) Adherence, social deprivation, access issues.
- 4) Visual prognosis (especially amblyopia in asymmetrical disease).

There are few absolute rules regarding choice of procedure and there is variability between experts. These are some general principles:

- a) GFCS (aphakic / pseudophakic glaucoma) or glaucoma co-existing with a cataract requiring imminent surgery, carries a higher chance of bleb-failure because of inflammatory mediators in the aqueous; hence trabeculectomy is not a good option.

Table 1: Relative incidence of childhood glaucomas in the UK. (Primary congenital glaucoma, PCG; juvenile open angle glaucoma, JOAG, glaucoma following cataract surgery, GFCS; glaucoma associated with acquired condition, GAAC; glaucoma associated with non-acquired systemic disease or syndrome, GANASS; glaucoma associated with non-acquired ocular anomaly, GANAOA.)

WGA definition			%
PCG			45
JOAG			2
GFCS		Aphakia	11
		Pseudophakia	5
GAAC	Uveitis (10%)	JIA	3
		Idiopathic	6
		Intermediate	1
GANASS	Phacomatosis (12%)	Sturge-Weber	10
		Neurofibromatosis	1
		Kippel-Trenaunay-Weber	1
GANAOA	Anterior segment dysgenesis (6%)	Axenfeld anomaly	1
		Reiger anomaly	1
		Peter anomaly	3
		Aniridia	1

- b) PCG (isolated goniodysgenesis) is the major clinical indication for angle surgery.
- c) Hypotony is particularly hazardous in the context of naevus flammeus-related glaucoma (GANASS) because of the increased risk of suprachoroidal haemorrhage and possibly sympathetic ophthalmia. Surgeons should modify their technique and choice of surgery accordingly.
- d) After failed angle surgery, aqueous shunt surgery carries a better chance of lasting pressure control than trabeculectomy in younger children, especially those 24 months of age or younger [18].

Cycloablation

Trans-scleral cyclo-photo coagulation (TSCP) [19] should be carefully targeted, that is, the anterior border of the ciliary body should be repeatedly confirmed by transillumination to guide placement of the 810nm diode laser via the fibre-optic G-probe. Significant inflammation is the commonest adverse outcome and depot subconjunctival steroid is recommended in addition to topical steroids.

Micro-pulse delivery may allow reduced inflammation and a closer relationship between treatment dose and the IOP lowering effect.

Endoscopic delivery is an option in pseudophakic and aphakic children, though there is no clear evidence of significantly improved efficacy to justify a dedicated intraocular procedure.

Angle surgery

The aim of angle surgery is to overcome resistance to aqueous passage between the anterior chamber and Schlemm's canal (SC). There are an increasing number of ways of achieving this, though goniotomy [20] remains the original standard against which newer techniques are compared. Factors predicting failure from angle surgery include severe disease, characterised by early onset and enlarged ocular dimensions (axial length >24mm) [16].

Goniotomy

Goniotomy is characterised by transcorneal visualisation of the angle with a direct gonio lens and opening SC with a blade across the anterior chamber (Figure 2). Hoskin-Barkan lenses are useful for very small palpebral fissures, but an improved field of view and better globe stabilisation is achieved with a Khaw lens [Ocularinc, code OKSG]. Surgical access in neonates and pre-term infants is enhanced by a lateral canthotomy. Intraoperative excyclo- and incyclo- rotation around the y-axis of Fick allows the incision

length to extend to about 180 degrees and is well facilitated by an assistant using locking toothed forceps gripping the vertical recti insertions transconjunctivally. Success depends upon correctly identifying intraoperative landmarks and intact drainage via collector channels from SC. The procedure can be repeated to the untreated angle by a corneal incision directly opposite the first, during the same procedure or subsequently. Success rates vary depending on the study population, being 30-38% in Tanzania [17] to 88% in the UK [1].

Trabeculotomy ab-externo

Traditional teaching dictates that when the view through the cornea is too poor to allow a goniotomy, an alternative procedure, to cannulate SC ab-externo and in-fracture the internal wall, provides another way to achieve the same end. This technique was described 60 years ago using a suture [21] and refined by the development of a dedicated rigid instrument for cannulation: the trabeculotome [22]. In recent years there has been a return to suture material cannulation [18], which has the advantage of reaching further into SC and allowing in-fracture of the entire 360 degrees, rather than being limited to the reach of the trabeculotome, which can only treat about 160 degrees. A further development is the use of an illuminated fibre optic, allowing direct visualisation of the tip as it passes around SC which avoids the unintentional sub-retinal passage, a known complication of a suture trabeculotomy. There is early evidence that surgery with a fibre-optic is more effective at lowering pressure than with a trabeculotome [23], though the risk of hyphaema and possibly Descemet's detachment is greater.

Each of these approaches involves a conjunctival incision (cf. goniotomy) and a partial thickness scleral flap, both of which are secured in place upon completion of the in-fracture.

Trabeculotomy ab-interno

Angle surgery by gonioscopy-assisted transluminal trabeculotomy (GATT) [24] is increasingly popular for treatment of open angle glaucoma in juveniles and adults. During GATT, the operator inserts a modified suture [25] or fibre-optic into SC via the AC under direct gonio lens visualisation, then pulls to achieve in-fracture of the trabecular meshwork. Instrumentation can be minimised by the use of a purpose-built device; a trab-360 TM (Sight Sciences), which holds real promise for paediatric cases when the corneal view allows.

Trabeculectomy

The Moorfields Safer Surgery technique popularised by Khaw et al. has improved the safety and outcomes from trabeculectomy. Posterior drainage is the key to avoid thin-walled, anterior blebs with the associated problems of endophthalmitis (a particular problem in children), dysaesthesia and failure. Key modifications of the technique are those which optimise *posterior drainage, control and comfort* respectively: modifications for posterior drainage are fornix-based conjunctival incisions (to reduce scar-related, fibrosis-obstruction of posterior drainage), rectangular flaps with reduced side incision to the limbus, mitomycin-inhibition of posterior fibroblasts, meticulous conjunctival wound closure by overlapping limbal suture closure and protection of the anterior conjunctiva with a dedicated clamp (Duckworth-and-Kent.com, conjunctival T clamp No 2-686). *Control* is achieved by releasable and adjustable sutures (adjusted with dedicated forceps; DuckworthandKent.com, No 2-502) on the scleral flap, subsequent anti-metabolite top-up with 5-fluorouracil injections and rigorous postoperative care with scheduled examinations under anaesthesia at weeks one, three and five postoperatively. A smaller sclerostomy and tighter scleral flap (cf adults) limit early



Figure 2: Goniotomy with a direct gonio lens.

aqueous egress; crucial to avoid over-drainage in the phase before conjunctival resistance develops. Comfort is important to minimise distress, inflammation and rubbing, all of which affect outcome, and is achieved by generous long-acting sub-Tenon anaesthesia and limbal and releasable sutures buried in the cornea. A quiet and comfortable eye gives the best chance of a meaningful postoperative examination in a child.

Complications from trabeculectomy are commoner in children than adults, including failure and over-drainage, especially in buphthalmic eyes. These are amongst the reasons that tube surgery is a favoured option in younger children for many specialists in Europe and the Americas.

Aqueous shunts

Aqueous shunts can be an excellent option for children with glaucoma if angle surgery has failed.

These devices drain aqueous via a silicone tube from the anterior chamber, plumbed to a plate of varying sizes and materials; some with a luminal valve (Ahmed), some without (Baerveldt and Molteno).

A common paediatric operation in the UK comprises a Baerveldt 350mm² implant with or without MMC, depending upon target pressure and the likelihood and consequence of hypotony. Intraoperative control with an anterior chamber maintainer is mandatory. A 6-0 occlusive Vicryl tie over the proximal tube prevents immediate postoperative drainage. An intraluminal 3-0 non-absorbable polyfilament suture (Supramid®) is used to control the flow after the Vicryl tie has given way six to seven weeks postoperatively. This can be adjusted to titrate intraocular pressure, with a longer intraluminal length giving greater resistance and higher pressure. There are a number of methods of facilitating drainage before the Vicryl tie gives way, including fenestration of the tube distal to the tie. The tube is usually covered with a donor scleral graft before closing the conjunctiva, though there are other techniques.

Final intraocular pressures are lower with larger plates. By employing the precautions of an intraluminal suture and Vicryl tie, larger 350mm² plates can be used in most cases, except 'brittle' hyposecretory cases, uveitic eyes and microphthalmic eyes.

A common issue is anterior migration of the tube towards the cornea threatening endothelial health. Repositioning is needed in up to a third of children under two years of age [18]. An alternative can be to trim the tube using a bimanual intracameral technique.

An excessively short tube may retract out

of the AC altogether; probably commoner in children during ocular growth. A good solution is the tube-in-tube extension technique [26,27].

Hypotony requires an escalating response of intracameral viscoelastics, re-stenting, partial ligature occlusion, total ligature occlusion, or finally, complete tube-shunt removal from the anterior chamber.

Medications

Seventy-one percent of children still require medications 12 months after diagnosis, showing the importance of pharmacological adjuncts to surgery [1].

A comprehensive guide cannot be provided within the constraints of this paper. Other reviews have addressed the topic [28]. Beta-blockers need to be cautioned in the context of respiratory symptoms, including cough and not just wheeze. Alpha-agonists, in particular brimonidine, can cause CNS depression in children; brimonidine is contra-indicated in children under eight years old.

Future developments

There are many developments in evolution including home IOP monitoring and also medical therapies, including neuro-protective agents. New surgical techniques, including minimally invasive technologies are in an exciting phase of investment and diversification.

As our understanding of genetic aetiology improves, we can better characterise a particular patient's phenotype, itself understood better, by improved imaging of the angle and drainage structures. This allows a customised approach to pharmacological and procedural interventions for the individual child.

We have strategies which are sometimes wonderfully effective, releasing a child and their family from a 'glaucoma life'. Angle surgery can 'cure' a child for many decades. However not uncommonly, children need multiple surgeries and lifelong medications and assessments. The rarity of childhood glaucoma has stimulated increased international cooperation and data sharing in an effort to improve the evidence-based management. There remains much work to be done to improve the experience and outcomes for children with glaucoma and their families.

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TAKE HOME MESSAGE

- Goniotomy or trabeculotomy historically have been the primary procedures of choice for PCG. These procedures are low risk and can facilitate good control for many years.
- Aqueous shunts are a preferred option to trabeculectomy, especially in younger children. Trabeculectomy still has a role, particularly in older children with JOAG.
- New methods of angle surgery include intubation of Schlemm's canal and in-fracture ab-interno (GATT), or ab-externo with an illuminated fibre optic.
- The success of angle surgery can be predicted with high quality anterior segment imaging.

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