Inside this issue:

<table>
<thead>
<tr>
<th>Special Focus:</th>
<th>What’s New:</th>
<th>Clinical Issues:</th>
<th>Practical Tips:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glaucoma in the setting of inflammatory eye disease: Incidence and prevalence, predispositions/underlying diseases, pathophysiology and pathomechanisms</td>
<td>Principles of medical as well as non medical management of glaucoma secondary to uveitis</td>
<td>Anterior uveitis in children: underlying diseases, differential diagnosis, screening and treatment, management of complications such as secondary glaucoma</td>
<td>Differential diagnosis and measures taken for specific entities</td>
</tr>
</tbody>
</table>

PAGE 2 | PAGE 7 | PAGE 9 | PAGE 10

LEARNING OBJECTIVES

• **Special Focus:** A detailed review of glaucoma and inflammatory eye disease covering incidence and prevalence, predispositions and underlying diseases (also glaucoma as immunogenetic inflammatory component) as well as pathophysiology and pathomechanisms.

• **What’s New:** A comprehensive summary on the principles of medical and non medical management of glaucoma secondary to uveitis.

• **Clinical Issues:** A summary reviewing the facts on anterior uveitis in children, discussing underlying diseases, differential diagnosis, screening and treatment, management of complications such as secondary glaucoma.

• **Practical Tips:** An expert discussion on differential diagnosis and measures taken for specific entities such as Posner Schlossman Syndrome and Fuchs Syndrome.

Main topic:

**Glaucoma and Inflammatory Eye Disease**

Glaucoma Now is a continuing medical education publication. Distributed worldwide, our goal is to educate and update general ophthalmologists, glaucoma specialists and ophthalmology residents.

International leaders in the field of glaucoma are invited to contribute to this journal, sharing their most recent insights.

Supported by an unrestricted educational grant, the publication is non-promotional and has a fully independent Editorial Board. For issues published from 2012, CME credits can be obtained by answering questions on our website www.glaucomanow.com

A newsletter is sent out to participants registered to the program.

**TARGET AUDIENCE**

This educational activity is aimed at general ophthalmologists, glaucoma specialists and ophthalmology residents.

**EDITORIAL BOARD**

Ivan Goldberg MBBS, FRANZCO, FRACS Sydney Eye Hospital, Sydney, NSW, Australia.

Remo Susanna MD, Professor and Head of Department of Ophthalmology, University of São Paulo, Brazil.

**Glaucoma Now** is published and administered by the editorial board and supported by an unrestricted educational grant from Allergan, Inc.

**Copyright 2010 Editorial Board.**

All rights reserved. No responsibility assumed for injury or damage to persons or property arising from the use of information or ideas contained in this publication.

**Executive officer:**

Patricia Buchholz RPh, PhD
Karlsruhe, Germany
patricia.buchholz@yahoo.de

**Production by Phosworks**

www.phosworks.com
Special Focus: Glaucoma and Inflammatory Eye Disease

Rashmi G Matthew FRCOphth, Keith Barton MD FRCP FRCS
Glaucoma Service, Moorfields Eye Hospital, London, UK

Core Concepts

- Uveitic glaucomas are complex entities whose best management might require uveitis and glaucoma specialists in tandem.
- Multiple mechanisms are involved in the pathogenesis of uveitic glaucoma.
- Gonioscopy should be performed in all patients with uveitic glaucoma to determine the mechanism of raised intraocular pressure.

Introduction

The association of glaucoma with uveitis was first described in 1813, by Joseph Beer. The condition was described as ‘arthritic iritis’, followed by glaucoma and blindness. It still remains one of the most challenging forms of glaucoma to treat, as it is commonly found in younger patients, often has a poor response to topical therapy and unpredictable surgical outcomes. Its impact is not to be underestimated, as it is the commonest cause of visual loss in uveitis patients, after cataract.

Incidence and Prevalence

Accurate incidence and prevalence data are hard to establish. Two key problems exist, firstly study populations are often enriched samples from uveitis clinics, thus creating a bias. Secondly, the diagnosis of uveitic glaucoma is inconsistent and often based on raised intraocular pressure (IOP) alone and not co-existing glaucomatous optic neuropathy.

The overall incidence quoted in the literature is between 10-20%. In a retrospective series of 1099 patients at a single Japanese centre over a 26-year period, 18% were found to have uveitic glaucoma. Their definition of glaucoma was two IOP measurements >21mmHg, requiring treatment.

In a further series of 1254 uveitics, 9.6% developed secondary glaucoma and 6.9% secondary ocular hyperten-

sion (OHT). In this series, the term glaucoma was used to describe the presence of pathological optic disc cupping and/or glaucomatous visual field defect with elevated IOP above 21mmHg. In a Scottish centre, the combined incidence of OHT and glaucoma was 11.1% after 5 years amongst 391 uveitics. Another series of 257 uveitics, found a prevalence of 41.8% for OHT and 9.6% for glaucoma. Interestingly, they found no IOP elevation in 58.2% of uveitics.

It may be that the actual incidence and prevalence of uveitic glaucoma is lower than is quoted in the literature, as patients in uveitis clinics tend to have more severe, complex disease and thus may be more prone to raised IOP.

When looking at specific uveitis subgroups, such as Fuchs heterochromic iridocyclitis, glaucoma incidence can be up to 50%.

Pathophysiology and Pathomechanisms

IOP may be reduced or elevated in episodes of uveitis. Reduction in IOP is due to diminished aqueous production and increased uveo-scleral outflow. With increasing chronicity of inflammation, a complex cacophony of mechanisms serves to elevate IOP. Uveitic glaucoma may have open or closed angle mechanism. Anterior segment examination and gonioscopy are an integral part of clinical examination, in determining the mechanism of IOP elevation.

Angle closure in uveitis

The mechanisms of angle closure are outlined in table 1.

Acute Angle Closure mechanisms:

1) Pupil block
This may be absolute pupil block, with 360 degrees of posterior synechiae and total compartmentalisation of the anterior and posterior chambers, with resultant iris bombe. The absolute pupil block is unlike the relative pupil block seen in acute angle closure (AAC), for 4 reasons.

Firstly, clinical examination often reveals a deep central anterior cham-

Table 1. mechanism of angle closure

| Relative pupil block from fibrin obstructing pupil in severe acute anterior uveitis |
| Absolute pupil block from posterior synechiae |
| Peripheral anterior synechiae (PAS) formation secondary to inflammation (inflammatory nodules in the angle, neo-vascularisation) |
| Forward movement of lens-iris diaphragm in some forms of scleritis and choroidal effusions |
| Phacomorphic |

Figure 1. Colour photograph showing relatively deep central anterior chamber and shallow periphery in uveitic pupil block. Anterior segment OCT demonstrating shallow anterior chamber and shallow periphery in acute angle closure.
ber, with temporal shallowing, unlike AAC, which tends to have a shallow central and peripheral anterior chamber (Figure 1). Secondly laser peripheral iridotomy (LPI) is often ineffective as a treatment, as the posterior chamber is often not a continuous space in those with secluded pupil, as multiple areas of adhesions can develop between the iris and lens, forming loculations. This is apparent clinically from the asymmetry in the degree of iris bombe (Figure 2a,b). Therefore LPI may resolve bombe in the immediate surrounding area of the PI, but iris bombe will persist in other areas of loculation. Also LPI has a tendency to close in the presence of ongoing inflammation. Thirdly, the iris may remain adherent to the TM and even peripheral cornea in episodes of acute inflammation due to fibrin, so relief of pupil block may not open the angle. Fourthly, absolute pupil block can occur in a pseudophakic eye, unlike PAC, where removal of the lens is the definitive treatment. In cases of secluded pupil, we recommend surgical peripheral iridectomy, viscodissection of posterior synechiae and adhesions between the iris and lens ± goniosynechiolysis as a more definitive treatment.

2) Non-Pupil block – Forward movement of the lens-iris diaphragm

In these cases, cilio-choroidal effusions cause forward movement of the lens-iris diaphragm, with resultant shallowing of the anterior chamber. On clinical examination the anterior chamber is shallower in the centre and periphery, in relation to the other eye. Ultrasound biomicroscopy or B-scan ultrasound can confirm the presence of cilio-choroidal effusions.

**Chronic Angle Closure mechanisms:**

**Peripheral anterior synechiae (PAS) formation**

This is common in uveitic glaucoma and often differs in morphology, location and speed of formation in comparison with PAS in primary angle closure (PAC). Conventionally, anatomically narrow angles are more likely to form PAS, however, in uveitics, PAS can also form in wide-open angles. The tendency is to form isolated bridging synechiae or broad PAS, which can then progress to chronic synechial closure (Figure 3).

In our experience, PAS formation occurs preferentially in the inferior angle, as inflammatory deposits gravitate inferiorly. This is in contrast to PAC, where the superior angle tends to be narrowest and therefore, most likely to incur PAS formation. Uveitic PAS formation tends to occur at a faster rate than in PAC. PAS formation is also associated with the presence of large, peripheral iris nodules, such as the Berlin nodules classically in sarcoidosis.

Gonioscopy is key, not only to determine the extent and location of PAS, but also pre-disposing factors for PAS for-
Open Angle Mechanisms:

1) Steroid induced trabecular meshwork changes

Steroid responsiveness is seen in 5% of the population and usually occurs 2-6 weeks after steroid commencement, but can occur within days when conventional outflow is compromised. Becker et al. administered betamethasone drops 4 times daily to 26 patients with normal tension glaucoma. By 6 weeks, 92% had IOP greater than 31mmHg and 16 patients had to discontinue their therapy before 6 weeks, as their IOP reached the trial exit IOP of 31mmHg. Aramo also found that dexamethasone related IOP elevation was more common in glaucoma patients.

The exact mechanism of steroid induced reduction in outflow facility is not fully understood. Some pathology studies attribute this to alteration in TM ultrastructure, with accumulation of extracellular matrix components, causing reduced outflow. There is also evidence that accumulation of trabecular debris may result from reduced TM phagocytic function.

Debate remains as to whether steroids increase aqueous production. A study looking at aqueous humour production, showed a 42% increase when oral hydrocortisone was administered in combination with intravenous epinephrine. Rice et al administered Dexamethasone 0.1% 4 times daily for a week to healthy subjects and found that although there was a significant increase in IOP, there was no effect on aqueous production.

Tissue plasminogen activator (tPA), which is responsible for the conversion of plasminogen to plasmin, has been localised in the TM. Plasmin activates matrix-metalloproteinases, which play a role in extracellular matrix degradation and maintenance of normal aqueous outflow. Recent work by Kumar et al, suggests that tPA in the TM attenuates steroid induced outflow resistance. There is also evidence that Rho / Rho-associate kinase signal transduction pathway in Schlemm’s canal endothelial cells contributes to steroid induced outflow resistance.

Clinically a steroid induced glaucoma may be elicited by the temporal relationship between commencement of topical steroids and timing of any IOP increase. Gonioscopy findings may allude to the mechanism, as steroid treated uveitides with raised IOP, may have ‘clean angles’ (ie. no pigment smudging) rendering steroid responsiveness as a likely mechanism.

The IOP may take several weeks to return to pre-treatment levels following steroid cessation.

2) Changes to the trabecular meshwork and aqueous – composition in Uveitis

This may be because of mechanical obstruction with cellular debris. Dysfunction of the trabecular lamellae and endothelium may also cause outflow resistance.

In normal eyes, the aqueous protein content is approximately 1% of serum protein. In uveitis, the aqueous protein concentration dramatically rises, giving increased aqueous viscosity and thereby resistance to outflow.

Predispositions and underlying diseases (immunogenetic inflammatory component)

Certain uveitis subgroups are at greater risk of developing raised IOP; these include Posner Schlossman syndrome, Fuchs heterochromic iridocyclitis and Herpes simplex keratouveitis. In our experience, conditions with a predisposition for hypertensive uveitis and minimal anterior chamber inflammation tend to get the highest elevations in IOP and those with marked inflammation, do not have such extreme elevation. A possible explanation may be that in severe inflammation, the trabeculitis and TM dysfunction is off-set by ciliary body shutdown. In those with minimal inflammation, there may only be trabeculitis, with little or no effect on the ciliary body.

It remains uncertain whether those with anterior uveitis are more likely to develop raised IOP or not. In the series by Merayo-Lloves two-thirds of patients with uveitic glaucoma had anterior uveitis and Takashi et al. found 73% of patients had active anterior uveitis, when the IOP was elevated. Both Neri and Herbert found no correlation between the location of uveitis and raised IOP.

The presence of chronic uveitis is more likely to be associated with raised IOP, than acute uveitis. Older age and number of years since diagnosis of uveitis have also been significantly correlated with raised IOP.

Underlying Diseases

For comments on Posner Schlossman Syndrome, Fuchs’ Heterochromic Iridocyclitis, Herpes Simplex/Zoster Varicella Virus and Juvenile Idiopathic Arthritis please see our Clinical Issues and Practical Tips sections. In addition there are:

Behcet’s Disease (BD)

BD is a chronic occlusive vasculitis affecting both arteries and veins. Ocular involvement is common. In a Turkish series of 129 BD patients, 10% developed secondary glaucoma. Interestingly, in a series of 55 patients, 70% had no active inflammation, in the presence of raised IOP. Mechanisms of raised IOP include open angle mechanisms, steroid therapy, chronic synechial closure, seclusio pupillae and angle neovascularisation.

Sarcoidosis

This is a non-caseating granulomatous condition affecting all parts of the body. Several reports have found it to be the leading cause of posterior segment uveitis, to cause glaucoma. Mechanisms include open angle, steroid therapy, chronic synechial closure, seclusio pupillae and angle neovascularisation. Approximately 20% have glaucoma. Sarcoïd NVG, is known to develop in the absence of retinal ischaemia. Regular gonioscopy is therefore important to detect new vessels.

Tuberculosis

TB is a caseating granulomatous condition affecting all parts of the eye. The mechanism resulting in raised IOP and glaucoma are similar to BD and sarcoid. In an East African series, 25% of blindness secondary to TB, was due to glaucoma.

Vogt-Koyanagi-Harada syndrome

VKH causes a bilateral chronic granulomatous panuveitis with associated neurological, auditory and integumentary manifestations. It is commoner in women, and typically affects those in their 3rd – 4th decade. In a series of 101 VKH patients, 29% developed glaucoma. Non-pupil block angle closure secondary to...
Cilio-choridal effusions is an important mechanism of raised IOP to recognise in these cases, as the treatment is immunosuppression. It can be misdiagnosed as acute angle closure, distinguishing features include; marked reduction in visual acuity, out of proportion to the corneal oedema and cataract and only moderate elevation of IOP, despite extensive angle closure.29

**Syphilis**
Syphilis currently poses a significant public health problem, with dramatic increases in incidence in UK, USA and Europe. Uveitis responds well to treatment. It rarely presents with raised IOP, but generally resolves with the treatment of ocular syphilis.

**Toxoplasmosis**
Ocular toxoplasmosis is characterised by marked inflammation and elevated IOP. The International ocular toxoplasmosis research group found that 30% of 210 patients had elevated IOP.30 This was associated with increased anterior chamber inflammation (p≤0.001) and with macular involvement (p=0.009). In a retrospective review of 61 patients, 38% had elevated IOP. Fifty percent had an IOP >30mmHg, 30% >40mmHg and 10% had IOP >50mmHg. Coincidentally, 7% had lowering of IOP at presentation. OHT resolved with steroid therapy.

**Conclusions**
Glaucoma is a significant and visually disabling consequence of uveitis. It requires regular assessment of intraocular pressure, gonioscopy and optic disc for its detection. These cases are complex; best management might involve uveitis and glaucoma specialists.
References
What’s New
Recent Advances in Uveitic Glaucoma

Jamie Lynne Metzinger MS MPH1,2, Olga Ceron MD1,2, C. Stephen Foster MD FACS FACR1,2,3

1 Massachusetts Eye Research and Surgery Institution (MERSI), Cambridge, MA, USA
2 Ocular Immunology and Uveitis Foundation (OIUF), Cambridge, MA, USA
3 Harvard Medical School, Boston, MA, USA

Core Concepts
• Owing to the underlying disease sequence and treatment with corticosteroid therapy, patients with uveitis have an increased risk of elevated intraocular pressure (IOP) and glaucoma.
• All forms of uveitis may be associated with raised IOP and glaucomatous optic neuropathy.
• Principles of management of uveitic glaucoma involve treating any identified underlying cause, controlling inflammation and managing any raised IOP by controlling its mechanisms.
• Rho-kinase inhibitors might prove to be a useful new class of antiglaucoma topical medications for the treatment of uveitic glaucoma.
• Selective laser trabeculoplasty can be a minimally-invasive, effective and safe therapeutic procedure in uveitic glaucoma.
• Glaucoma drainage devices may afford clinicians an additional surgical option with high rates of success in patients with uveitic glaucoma.

Introduction
Due to a combination of the pathogenesis of uveitis and the mainstay of therapeutic management (various forms of corticosteroids), patients with uveitis have an increased risk of glaucoma development. Uveitic glaucoma is one of the most serious sequelae of intraocular inflammation. The pathogenesis and mechanisms of glaucoma associated with uveitis are incompletely understood and multidimensional. Uveitic glaucoma has been observed in all age groups and with most uveitic entities, with some disorders posing a more significant risk. The majority of uveitic glaucoma is open angle, and presumed to be due to irreversible damage to the trabecular meshwork and/or scar formation in the anterior chamber angle from chronic inflammation.

Management of uveitic glaucoma does not align exactly with the principles of therapy of primary glaucoma; the initial aim of treatment of uveitic glaucoma is always dependent upon the presence of underlying systemic disease. The key to preservation of vision and to control the glaucoma is durable, corticosteroid-free remission of uveitis. Oftentimes, treatment of inflammation will control intraocular pressure (IOP); pressure control outcomes are better with aggressive anti-inflammatory therapy.

Medical Management
Topical first-line treatments for uveitic glaucoma include beta-blockers, carbonic-anhydrase inhibitors, and prostaglandin analogs. In the past prostaglandin analogs in uveitic glaucoma were avoided, owing to data purporting to show they increase risk for cystoid macular edema and worsening inflammation. In quiescent uveitis, no causal link and little additional risk have since been established in both prospective and retrospective trials, but long-term use has been cautioned in those patients already in need of trabeculectomy.

Research and development continues with this class of medications (particularly prostaglandin analogs of the PGE2 class which are thought to increase the release of nitric oxide), as the effect is directed and potent. Selective alpha-2 adrenergic agonists, systemic carbonic anhydrase inhibitors, and hyperosmotic agents may be considered adjuvantly if the first-line topical agents are insufficient. Maximum medical management of uveitic glaucoma may encompass a topical prostaglandin analogue, a topical beta-blocker or topical carbonic-anhydrase inhibitor or alpha agonist, and an oral carbonic anhydrase inhibitor. As with other forms of glaucoma, uveitic glaucoma also demonstrates diminished returns with the addition of more than one therapy to the initial choice.

The newest drug class in glaucoma therapy inhibits rho-associated protein kinase; pre-clinical trials show promise with regard to both safety and efficacy in primary open-angle glaucoma. Rho-kinase inhibitors treat glaucoma by relaxing trabecular meshwork facilitating increased aqueous outflow, improving blood flow to the optic nerve, protecting the health of ganglion cells and acting as an anti-fibrotic agent in glaucoma surgery. Translation of this compound to patients with uveitic glaucoma will hopefully exhibit similar positive outcomes in IOP control and optic nerve damage prevention.

Surgical Management
Approximately one quarter of uveitic glaucoma cases cannot be sufficiently managed medically and require surgery. Laser therapy is minimally invasive relative to other surgical procedures, and long-term outcomes in patients with uveitis are favorable with regards to minimizing glaucomatous damage. While Argon laser trabeculoplasty is not advised in uveitic glaucoma patients, recent data show selective laser trabeculoplasty (SLT) is not only appropriate, but can be regarded as a first-line therapy. SLT is effective, does not exacerbate inflammation, and does not damage the structural integrity of the trabecular meshwork.

Trabeculectomy, non-penetrating glaucoma surgery, and cycloablation techniques have been employed and reported in patients with uveitic glaucoma, but outcomes are either equivocal or...
Uveitis Steroid Treatment (MUST) Trial aimed to compare conventional systemic immunosuppressive therapy with a fluocinolone acetonide implant (a corticosteroid) in patients with active uveitis; patients who received the implant experienced a 4-fold greater risk of developing elevated IOP; glaucomatous damage was reported in 23%, as compared with 6% in the systemic treatment group after 48 months. Available treatments for uveitis also need improvement, and such new treatment regimens should ideally be free of corticosteroids.

Implantable devices with a radiofrequency transceiver that monitor IOP are under study in vivo models for safety and efficacy. Future application to an intraocular lens and improvement in data transmission are pending prior to commercial availability.

The future of uveitic glaucoma care is moving in several directions, and is encouraging. Much work remains in the development of highly effective, corticosteroid-sparing medical and surgical therapies that control IOP long-term without side effects.

References
Clinical Issues:
Anterior uveitis in children

Sophia L. Zagora MBBS MTMPH1,3, John R. Grigg MD FRANZCO1,2,3

1 Discipline of Ophthalmology, University of Sydney, Sydney, NSW, Australia
2 Eye and Developmental Genetics Research Group, Western Sydney Genetics Program, The Children’s Hospital at Westmead, Sydney, NSW, Australia
3 Department of Ophthalmology, The Children’s Hospital at Westmead, Sydney, NSW, Australia

Core Concepts
• Paediatric uveitis is rare
• Although many cases are idiopathic, 41–67% of uveitis in children is linked with Juvenile Idiopathic Arthritis (JIA) and 3–6% with Sarcoidosis.
• Management of the intraocular inflammation is crucial to reduce the vision threatening complications of paediatric uveitis, especially JIA associated uveitis.
• Disease-modifying antirheumatic drugs (DMARDs) are being used for systemic immunosuppression
• Complications include glaucoma, cataract, macular oedema, band keratopathy, hypotony, optic nerve oedema and epiretinal membrane

Although many cases of uveitis are of idiopathic origin, 41–67% of uveitis in children is associated with Juvenile Idiopathic Arthritis (JIA) and 3–6% with Sarcoidosis.

The screening and management of paediatric patients with uveitis is divided into two groups – JIA and Non-JIA associated uveitis. JIA is a heterogeneous group of diseases with seven subtypes including oligoarticular, polyarticular and systemic forms with onset in a child younger than age 16. JIA patients do not often complain of a red painful eye, as compared with non-JIA associated uveitis patients, masking the complications from ongoing inflammation. Screening is a crucial part of the management (Table 1). There are a number of systemic inflammatory disorders with associated ocular involvement, for example, Sarcoidosis, Kerato-uveitis from herpes simplex and Juvenile Reiter’s syndrome.

Management of the intraocular inflammation in paediatric uveitis is fundamental to reduce the vision threatening complications, as the more aggressive the control of inflammation early in the disease, the fewer or less severe the complications. Non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids (systemic or intra-articular) are only partially effective to treat the symptoms of JIA. Treatment with systemic steroid-sparing drugs like disease-modifying antirheumatic drugs (DMARDs) are increasingly being used as they seem to control the disease better. To reduce inflammation, DMARDs interfere directly with immune cells and/or their function and are classified as either biologic (e.g. Infliximab and Adalimumab) or non-biologic drugs (e.g. Methotrexate and Azathioprine).

A stepwise approach to the immunosuppression is advised. When qid (4 times a day) topical steroid eye drop regime, and local periocular steroid injections fail to control intraocular inflammation or the child is a steroid IOP (intraocular pressure)-responder then systemic immunosuppression, in consultation with a paediatrician is indicated. Oral steroids are appropriate in acute flare-ups, although a steroid sparing agent should be commenced early. A gradually increasing dose of methotrexate is usually well tolerated in children, otherwise subcutaneous methotrexate can be considered or oral mycophenolate.

If the anterior segment inflammation continues despite topical and systemic therapy then a biologic agent should be added, Infliximab or Adalimumab are the most effective currently. The long term effectiveness of the newer biologic agents depends on the continuation of a nonbiologic agent, like methotrexate, to minimise the occurrence of an immune response to the biologic agent rendering it ineffective.

Complications of paediatric uveitis include: glaucoma, cataract, macular edema, band keratopathy, hypotony, optic nerve oedema, and epiretinal membrane. Early detection and management

Table 1. American Academy of Pediatrics Guidelines for Screening Eye Examinations

<table>
<thead>
<tr>
<th>Juvenile Idiopathic Arthritis (JIA)</th>
<th>Risk of Iritis</th>
<th>Examination Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oligoarticular (arthritis affecting 1-4 joints during first 6 months of disease) or Polyarticular (arthritis affecting &gt;5 joints in the first 6 months of disease), onset &lt;7 years of age and ANA (+)</td>
<td>High risk</td>
<td>Every 3–4 months</td>
</tr>
<tr>
<td>Oligoarticular or polyarticular and ANA (-) regardless of age</td>
<td>Medium risk</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>Onset &gt;7 years of age regardless of antinuclear antibody status</td>
<td>Medium risk</td>
<td>Every 6 months</td>
</tr>
<tr>
<td>Systemic onset JIA</td>
<td>Low risk</td>
<td>Every 12 months</td>
</tr>
</tbody>
</table>

(Adapted from Ravelli and Martini)
of glaucoma is important, as the prevalence of glaucoma can be up to 20%\(^1\). Managing uveitic glaucoma in children is challenging because of the multifactorial nature of the elevated IOP. Medical treatment must be commenced even if the optic discs are normal. Glaucoma surgery is often required. The surgical options include angle surgery (gonioto-
ymy or trabeculotomy), trabeculectomy, glaucoma drainage devices and rarely ciliary body destruction. It is important to operate on a quiet eye to reduce complications. Surgical risks include: Increased inflammation, cataract, corneal decomp-
pensation, ciliary body shutdown, retinal detachment, cystoid macular edema, chori
dal effusion, flat anterior chamber, encapsulated bleb, extruded glaucoma drainage device, infection and amphy-
pia. Hypotony is a common problem in paediatric uveitic patients post glaucoma surgery even in the absence of overdrain-
age. If trabeculectomy is performed then tight scleral flap sutures are mandatory. Non-flow restricted glaucoma drainage devices (GDD) should have an intra-
luminal stent (e.g. 3/0 supramid or 3/0 nylon) in addition to an extraluminal oc-
clusive suture (e.g. 6/0 vicryl), to reduce the risk of post-operative hypotony.

Adequate immunosuppression is crucial in the management of these children. This means the early recognition of poor control with topical agents al-
lowing the institution of systemic steroid sparing agents.

The causes of unilateral elevated intraoc
ular pressure (IOP) in patients with anti-
erior uveitis are multiple. In particular,
herpetic intraocular inflammation, PSS, and FHIC are entities known to induce ocular hypertension. Each of these con-
ditions has distinctive clinical features (table 1), and must be excluded when managing hypertensive uveitis. AC paracentesis may direct specific therapy in some of these patients.\(^1\)

PSS or Glaucomatocyclitic Crisis is an entity characterized by recurrent episodes of unilateral elevated IOP. A significant rise in IOP (often to 40–60 mmHg) makes these episodes occasion-
ally acutely painful; often there is vague discomfort. During an attack there are typically few ocular signs, with the ex-
ception of a mild anterior chamber inflammatory reaction. Despite repeated episodes, the stigmata of chronic ante-
rior chamber inflammation remain ab-
sent and the angle remains open. Years may pass between episodes. When con-
sidering the possibility of PSS, exclude a herpetic etiology; carefully inspect for sectoral iris atrophy. Patients with PSS appear to develop fewer hypertensive episodes with age, and may eventually

**References**

1. Kim SJ. Diagnosis and management of non-
2. Kanski J, Shun-Shin G. Systemic uveitis syn-
3. Ravelli A, Martini A. Juvenile idiopathic arthri-
4. Kemper A, Van Mater H, Coeytaux R, Wil-
liams JJ, Sanders G. Systematic review of dis-
5. Thorne J, Woreta F, Kedhar S, Dunn J, Jabs D. Juvenile idiopathic arthritis-associated uveitis: incidence of ocular complications and visual acu-

---

**Practical Tips:**

**Diagnostic consideration in unilateral hypertensive uveitis**

*Colin Clement BSc (Hon) MBBS PhD FRANZCO*\(^{1,2}\), *Shibal Bhartiya MBBS MS* \(^{3}\)

**Sydney Eye Hospital, Sydney, Australia**

**Core concepts**

- Clinical examination permits a differ-
ential diagnosis of unilateral hyperten-
sive anterior uveitis.
- Distinguish between the various causes of unilateral hypertensive anterior uveitis, particularly Posner Schlossman Syndrome (PSS), Fuchs Heterochromic Iridocyclitis (FHIC) and Herpetic (Herpes Simplex virus, HSV and Varicella zoster virus, VZV) anterior uveitis.
- Recognize that these can co-exist with underlying chronic open angle glaucoma.
- Recognize that PSS is not always a ‘benign’ condition.
- Consider an anterior chamber (AC) paracentesis if it may alter manage-
ment of a patient, particularly in cases that are immunocompromised or with severe anterior uveitis where a target-
ed treatment is available.
- Understand which infections to ex-
clude when performing polymerase chain reaction (PCR) such as Herpes Simplex Virus (HSV) Varicella Zoster Virus (VZV), Cytomegalovirus (CMV) and Rubella. Know that not all infections are treatable.
- Treatment of infectious agents might not prevent the development of glaucomatous optic neuropathy and inflammation may return when thera-
py is ceased. The glaucoma manage-
ment in unilateral hypertensive uveitis is frequently surgical.

---

cease having episodes. Nonetheless, a subset of patients with PSS develop chronically elevated IOP, requiring long-term medical therapy or filtration surgery. Although the precise cause of this disorder is not known, CMV and HSV have been implicated as possible causative agents. If an underlying viral source is found, treatment should be aimed at its eradication.2

FHIC is a predominately unilateral condition with chronic low-grade intraocular inflammation. This disorder can be associated with glaucoma, and more commonly, cataract. There are numerous findings that may lead one to suspect FHIC as a cause of a hypertensive uveitis: keratic precipitates in this population tend to be round, small, or stellate, and to be distributed over the entire corneal endothelium (Figure 1). As with PSS, there is a notable absence of peripheral anterior synechiae. Anterior chamber reaction is moderate at most, and mild anterior vitreous inflammation may be seen. The involved eye may be hyper- or hypochromic compared with the fellow eye. Patients with this disorder tend to be asymptomatic, and do not generally require therapy for their inflammation. Glaucoma can be difficult to treat in those patients who develop IOP rise. Infectious agents have been postulated to induce FHIC, particularly Rubella, HSV and CMV.2,3

The role of AC paracentesis in management of hypertensive anterior uveitis remains contentious. It may be beneficial in patients who are immunocompromised; in severe cases of suspected HSV/ VZV anterior uveitis requiring long-term valacyclovir; or with PSS or FHIC when CMV is suspected, as it may direct treatment of these disorders (i.e. management of CMV with oral or topical gancyclovir). Topical gancyclovir has fewer side effects than oral. While some sources suggest AC paracentesis is a safe adjunct in the management of anterior uveitis, others question the routine value of this technique, suggesting it rarely changes management and carries a tangible complication risk.4,5 With a positive PCR result, therapy may be initiated, but ocular symptoms may return if therapy is stopped. Additionally, treatment of the infectious agent may not influence the progression of the glaucoma. The glaucoma in this setting frequently requires surgery. Thus, risks of long-term treatment must be weighed against disease severity.2

Table 1: Clinical findings in hypertensive anterior uveitis

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Keratic Precipitates</th>
<th>Anterior Chamber Reaction</th>
<th>Angle</th>
<th>Lens</th>
<th>Vitreous</th>
<th>Differentiating Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posner-Schlossman Syndrome</td>
<td>Usually Few</td>
<td>Mild</td>
<td>Nil, open</td>
<td>Generally normal</td>
<td>Nil</td>
<td>Few defining signs</td>
</tr>
<tr>
<td>Herpes Simplex Virus, Varicella</td>
<td>May have 'mutton fat' appearance</td>
<td>Mild-severe</td>
<td>Nil to signs of chronic uveitis</td>
<td>Generally normal</td>
<td>May have mild to severe vitritis</td>
<td>Sectoral or diffuse iris atrophy</td>
</tr>
<tr>
<td>Zoster Virus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fuchs Heterochromic Iridocyclitis</td>
<td>Stellate, diffuse</td>
<td>Mild-moderate</td>
<td>Fine vessels, open</td>
<td>Cataract (initially PSCC)</td>
<td>Mild cellular response</td>
<td>Iris heterochromia</td>
</tr>
</tbody>
</table>

References

Figure 1: Fuchs heterochromic iridocyclitis
STATEMENT OF NEED AND PROGRAM DESCRIPTION
Recent months and years have seen significant advances in our understanding of glaucoma. Much has been learned, not only about damage mechanisms and pathogenesis, but also about diagnosis and management. Treatment options – both medical and surgical – continue to expand. This program will review this new knowledge with an emphasis on incorporating recent insights into day-to-day practice.

DATE OF ORIGINAL RELEASE
Date of original release: December 2013. Approved for a period of 12 months. This issue is accredited for Continuing Medical Education (CME) by the Physicians’ Chamber of Baden-Württemberg, Germany (Local Medical Responsible: Andreas Buchholz, MD, PhD, ROph).

DISCLAIMER
Participants have an implied responsibility to use newly acquired information to enhance patient outcomes and professional development. The information presented in this activity is not meant to serve as a guideline for patient care. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patient’s conditions and possible contraindications or dangers in use, applicable manufacturer’s product information, and comparison with recommendations of other authorities.

CONTRIBUTORS
• Keith Barton MD FRCP FRCS is Consultant Ophthalmic Surgeon at the Glaucoma Service of Moorfields Eye Hospital, London, UK. He has received financial support from AMO, New World Medical, Alcon, Merck, Allergan and Refocus. He has a personal interest in AqueSys and Ophthalmic Implants Ltd., he has acted as consultant to Alcon, AqueSys, Ivantis, Refocus, Eye Tech Care, Glaukos, Alcon, Merck, Kowa, Amakem, Thea and Alimera. He has also received honoraria from Allergan and Pfizer. Rashmi G. Mathew, FRCOphth is Consultant Ophthalmologist at Moorfields Eye Hospital, London, UK. She has no commercial relationship to disclose.

• Charles Steven Foster MD FACS FACR is Clinical Professor of Ophthalmology at Harvard Medical School as well as Founder and President of the Massachusetts Eye Research and Surgery Institution (MERSI). He also works for the Ocular Immunology and Uveitis Foundation. He has no commercial relationship to disclose.

• John Grigg is Professor at Discipline of Ophthalmology, University of Sydney, Sydney, NSW, Australia. He is affiliated to Eye and Developmental Genetics Research Group, Western Sydney Genetics Program, The Children’s Hospital at Westmead, Sydney, NSW, Australia as well as the Department of Ophthalmology, The Children’s Hospital at Westmead, Sydney, NSW, Australia. He has no commercial relationship to disclose. Sophia L. Zagora MBBS MTMPH is his associate worker at Discipline of Ophthalmology, University of Sydney, Sydney, NSW, Australia. She is also affiliated to the Department of Ophthalmology, The Children’s Hospital at Westmead, Sydney, NSW, Australia. She also has no commercial relationship to disclose.

• Ridia Lim MBBS MPH FRANZCO and her co-author Steven Schendel MD FRCSC are specialists at Sydney Eye Hospital, Sydney, Australia. They have no commercial relationship to disclose.

DISCLOSURE STATEMENT
Ivan Goldberg serves on the Faculty and Advisory Boards of the following companies: Alcon, Allergan, Merck and Pfizer. Remo Susanna serves on the Faculty and Advisory Boards of the following companies: Alcon, Allergan, Merck and Pfizer.