The ABCs of ACG
COPE Course ID: 61470-GL

Sarah MacIver, OD, FAAO
Derek MacDonald, OD, FAAO

WOVS CE 2019
June 14 2019

UW School of Optometry and Vision Science
Financial Disclosures

Honoraria:  
Alcon (DM)  
Allergan (DM)  
Carl Zeiss Meditec (DM)  
Eye Recommend (DM)

The content and format of this course is presented without commercial bias and does not claim superiority of any commercial product or service
Epidemiology

Glaucoma is the second leading cause of blindness worldwide
  • estimated to affect 80 million people by 2020\(^1\)

Primary angle-closure glaucoma (PACG):
  • represents ~25% of all cases of glaucoma\(^2\)
    • nearly 20 million will be affected by 2020
  • is responsible for a disproportionate amount of severe vision loss
    • nearly 50% of the cases of glaucoma-related blindness\(^3\)
    • risk of blindness is 4x greater in ACG than in OAG\(^4\)

## Risk factors

### Advancing age
- nearly 50x more common for ages ≥70 versus <50\(^1\)
  - lens thickens, chamber depth decreases, angle narrows
  - PACG at an age <40 tend to be plateau iris\(^2\)

### Female sex
- 3 to 5x more common in women than men\(^3\)
  - smaller eyes, narrower angles, longer lifespans

### Asian ethnicity
- nearly 50% of people with PACG are found in China\(^4\)
- ~90% of glaucoma-related blindness in Asia is due to PACG
  - PACG prevalence is highest in the Inuit population\(^5\)
  - up to 50x more common in Inuit than in Europeans

---

## Risk factors

### Family history
- up to 7x more common in siblings of Asians with PACG\(^1\)

### Ocular biometry
- hyperopia: short axial length, shallow anterior chamber depth, small cornea, thicker and more anterior lens\(^2\)

### Crystalline lens size, shape, and position
- all ages: thicker and/or more anteriorly positioned\(^3\)
- advancing age: thickening exacerbates angle crowding\(^4\)

### Exfoliation
- lax zonules: anterior lens shift and angle crowding\(^5\)

---

Diagnosis

“The current gold standard for the detection of [primary angle closure] is still gonioscopy, and the importance of routine gonioscopy in a clinical situation cannot be overstated.”

Gonioscopy:
• differentiates open angle from angle closure glaucoma
• differentiates primary from secondary glaucoma

In angle closure glaucoma, gonioscopy:
• detects iridotrabecular contact (ITC, the hallmark of PACG)
  • compression/indentation gonioscopy:
    • differentiates appositional from synechial closure
    • helps detect plateau iris

For an excellent reference, visit www.gonioscopy.org

## Misdiagnosis

Despite being essential, gonioscopy is very underutilized by both optometrists and ophthalmologists

<table>
<thead>
<tr>
<th>Gonioscopy is performed less than half the time in the 5 years preceding glaucoma surgery¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>As many as one in eight patients referred for CE (by both ODs and OMDs) have undocumented narrow angles²</td>
</tr>
<tr>
<td>75% of referrals by OMDs for tertiary glaucoma care did not include angle status ...</td>
</tr>
<tr>
<td>... and one in ten patients referred for POAG had PACG³</td>
</tr>
</tbody>
</table>

### Although POAG is ~3x more common than PACG, it is diagnosed 32x more often than PACG in North America⁴

---

For 50 years, Van Herick angle assessment (VHA) has been used to compare peripheral anterior chamber depth to peripheral corneal thickness in the screening of non-glaucomatous patients\(^1\)

- an angle is felt to be “open” when peripheral chamber depth is >1/4 peripheral corneal thickness

However:

- VHA cannot detect synechiae or secondary mechanisms
- inter-examiner sensitivity and specificity vary widely
- VHA fails to detect as many as 40% of angles judged to be narrow by gonioscopy\(^2\)

“... clinical assessment of anterior chamber angle configuration is best accomplished with gonioscopy ...”

---

Performing indirect gonioscopy with a 4-mirror corneal lens

1. Instil anesthetic in both eyes
2. Place the lens on the cornea
   • the patient may initially look up, then straight ahead
3. Use low ambient lighting and a short narrow beam
   • avoid pupil constriction, which can deepen the angle
4. Begin with the superior mirror and proceed clockwise
   • inferior angle tends to be deepest and most pigmented, making angle structures easier to identify
5. Use mid- to high magnification to identify angle details
6. Tilt the lens toward the angle to “look over” a steep iris
   • tilt toward any bubbles to eliminate them
7. Indent to differentiate appositional from synechial closure
Angle structures: posterior to anterior

Iris: note contour (concave, flat, convex) and angle of approach

---

Angle structures: posterior to anterior

Ciliary body (CB): pink/brown/grey band at iris root

Angle structures: posterior to anterior

Scleral spur (SS; insertion of ciliary muscle): white band between CB and TM (obscured by benign iris processes or pathologic PAS)

Angle structures: posterior to anterior

Posterior (pigmented) trabecular meshwork (PTM): functional two-thirds of TM; visibility suggests angle open in that quadrant
Angle structures: posterior to anterior

Anterior trabecular meshwork (ATM): non- or lightly pigmented (and non-functional) anterior one-third of TM

Angle structures: posterior to anterior

Schwalbe line (SL; termination of Descemet membrane): fine line; variable pigmentation (Sampaolesi line); suggests narrow angle
Open anterior chamber angle

- Ciliary body
- Iris processes
- Scleral spur
- Pigmented TM
- Schwalbe line

https://www.researchgate.net/figure/221919422_fig1_Fig-1-Gonioscopy-of-open-angle-seen-by-three-mirrored-Goldmann-lens-Normal-iris
Open anterior chamber angle

https://www.researchgate.net/figure/221919422_fig1_Fig-1-Gonioscopy-of-open-angle-seen-by-three-mirrored-Goldmann-lens-Normal-iris
Open anterior chamber angle

Ciliary body  Scleral spur  Iris processes  Pigmented TM  Schwalbe/Sampaolesi line

https://www.researchgate.net/figure/221919422_fi1_Fig-1-Gonioscopy-of-open-angle-seen-by-three-mirrored-Goldmann-lens-Normal-iris
Diagnosis

Indentation gonioscopy

If the posterior TM is not visible, the angle is narrow or closed
  • ITC may be appositional or synechial\(^1\)
    • indentation will not open an angle closed by PAS
    • appositional closure (±/- iris processes) will open

A pigmented appositionally-closed angle opens with indentation

Interpretation of gonioscopy

- Scleral spur
  - Visible 360
    - Open angle
  - Visible < 180
    - Indentation gonioscopy
      - Synechiae present
        - PAC (synechiae)
      - No synechiae
        - Check IOP
          - Raised IOP
            - PAC (appositional)
          - Normal IOP
            - PACS

Posterior TM (more conservative)
Angle grading

Standardized angle grading systems
• include those of Shaffer, Spaeth, and Scheie\textsuperscript{1-3}

The Shaffer system is based on the angle between iris and cornea:
closure is unlikely at >20°, possible at <20°, and likely at <10°

Angle grading

Standardized angle grading systems
  • include those of Shaffer, Spaeth, and Scheie


The Spaeth system is a complex extension of the Shaffer system: also describes iris contour (top right) and insertion (bottom)
Angle grading

Standardized angle grading systems

• include those of Shaffer, Spaeth, and Scheie\textsuperscript{1-3}

The Scheie system grades the angle based on visible structures: from ciliary body (wide open) to no structures (grade IV; closed)

Angle grading

Standardized angle grading systems

- include those of Shaffer, Spaeth, and Scheie\textsuperscript{1-3}

The Scheie system grades the angle based on visible structures: from ciliary body (wide open) to no structures (grade IV; closed)

Angle grading

Standardized angle grading systems
- include those of Shaffer, Spaeth, and Scheie

The Scheie system grades the angle based on visible structures: from ciliary body (wide open) to no structures (grade IV; closed)

Angle grading

Standardized angle grading systems
• include those of Shaffer, Spaeth, and Scheie¹⁻³

The Scheie system grades the angle based on visible structures: from ciliary body (wide open) to no structures (grade IV; closed)

Angle grading

Standardized angle grading systems
- include those of Shaffer, Spaeth, and Scheie\textsuperscript{1-3}
- a modified Scheie system may be most clinically useful:
  - in each quadrant, specify the most posterior visible angle structure, and a qualitative description of iris approach and any abnormalities (PAS, pigment, etc.)

\begin{itemize}
  \item ATM flat
  \item trace TM pig
  \item PTM flat
  \item mod TM pig
  \item CB flat
  \item sig TM pig
  \item iris processes
  \item no SL flat
  \item SL flat
  \item SL flat
  \item ATM flat
  \item single PAS
\end{itemize}

Ancillary diagnostic procedures

Anterior segment optical coherence tomography

- most common technique in current clinical practice\(^1\)
- helpful as an adjunct if gonioscopy is difficult/inconclusive\(^2\)
- helpful in the detection of plateau iris
  - poor visualization of structures posterior to iris
- quantification of AC width, area, volume (all less in ACG)
- quantification of lens vault (predisposes to pupillary block)\(^3\)

Prevention

Given that the pathophysiology of PACG is solely IOP elevation secondary to mechanical obstruction of the TM, PACG is a preventable disease if the angle closure can be halted in the early stages.\(^1\)

Identifying those patients at risk is of paramount importance given the risk of significant vision loss.

---

Classification

Primary angle closure suspect (PACS):

- at least 180° of iridotrabecular contact (ITC) on gonioscopy
- posterior (pigmented) TM not visible ≥180°
- normal IOP and no glaucomatous optic neuropathy (GON)

Progression of PACS is variable:

- 5 to 25% progress to PAC (develop IOP elevation and/or peripheral anterior synechiae) within 5 to 6 years
- exacerbated by (topical/systemic) pupil dilation

Routine monitoring of both angle and IOP is indicated

- routine prophylactic laser peripheral iridotomy (LPI) is not indicated, but may be considered in patients at higher-risk (ITC ≥270°) or requiring routine pupil dilation

Angle closure

convex iris plane: pupillary block

No visible angle structures: if <180° PTM visible, the angle is at risk of closure (indent to differentiate apposition from synechiae)

Classification

Primary angle closure (PAC):
- an “intermediate stage” with at least 180° of ITC, elevated IOP (≥21mmHg) and/or PAS, but no GON\(^1\)
  - asymptomatic, but evidence of TM dysfunction\(^2\)
  - not secondary to any other cause or concurrent disease

PAC can progress:
- ~30% of PAC progressed to PACG over 5 years\(^3\)

**Prophylactic laser peripheral iridotomy (LPI)** is recommended
- may require adjunctive medical (similar to OAG) and/or surgical treatment to adequately control IOP\(^4\)
  - a visually significant cataract should be removed

---

Peripheral anterior synechiae

Following prolonged appositional closure, peripheral anterior synechiae (PAS; broad adhesions between the iris and angle structures, often anterior to TM) can form.

https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/Peripheral-anterior-synechiae.htm
Iris processes versus PAS

Normal iris processes: fine strands of peripheral iris that do not cross the TM

Pathologic PAS: broad areas of adhesion of iris to/anterior to TM, often superiorly

https://www.slideshare.net/suneelnarahari/gonioscopynew
Classification

Primary angle closure glaucoma (PACG):
• PAC becomes PACG with evidence of GON\textsuperscript{1}
  • angle closure is more commonly chronic (slow insidious closure) or intermittent, rather than acute
    • chronic PACG is usually asymptomatic (much like OAG\textsuperscript{2})
      • in the absence of gonioscopy, misdiagnosed as OAG

Because of its relatively slow and insidious clinical course, the optic neuropathy of PACG can also be similar to that of POAG:
• NRR loss violating ISNT Rule; vessel baring; βPPA
  • however, PACG may have more severe central visual field loss and more inter-eye asymmetry\textsuperscript{3}

Classification

**Prompt treatment** of PACG recommended:

- **therapeutic LPI**
  - augmented by medical treatment similar to OAG\(^1\)
  - pilocarpine (and to a lesser extent, brimonidine) cause pupillary miosis, reopening the angle

- **cataract or clear lens extraction**
  - with uncontrolled IOP or PAS >180°, CE may be accompanied or followed by trabeculectomy\(^2,3\)

---

Classification

**Acute angle closure crisis (AACC):**

- leads to a sudden and dramatic elevation in IOP
  - often ≥70mmHg
  - signs/symptoms: pain, headache, corneal edema, blur, haloes, redness, nausea/vomiting, mid-dilated pupil
- significant and permanent vision loss can occur rapidly

Following an AACC attack, patients may be left with:

- pigmented anterior chamber precipitates
- irregular iris atrophy
- glaukomflecken (anterior lens opacities)

Some patients present with mild (incomplete) angle closure attacks, characterized by similar but less serious symptoms: these may be considered “warning signs” of impending AACC

---

Acute angle closure crisis

Classic signs of AACC, including:

• vascular congestion, mid-dilated pupil, and corneal edema with symptoms of pain, nausea/vomiting, and blur/haloes

Acute angle closure crisis

AACC: vascular congestion, mid-dilated and irregular pupil, and corneal edema (blurred reflex)

Post-AACC: glaukomflecken (small ASC opacities due to necrosis) and iris atrophy

http://eyerounds.org/atlas/pages/glaukomflecken/index.htm
Classification

**Prompt treatment** of AACC essential:
- immediate topical and/or oral medications to lower IOP\(^1\)
- therapeutic LPI as soon as possible
- cataract or clear lens extraction
  - with uncontrolled IOP or PAS >180°, CE may be accompanied or followed by trabeculectomy

The optic neuropathy following acute angle closure may resemble that of anterior ischemic optic neuropathy more than POAG:
- pale disc with relatively shallow cupping\(^2\)

PACG, whether chronic or acute, is a bilateral disease:
- treatment of the fellow eye (prophylactic LPI) is critical
  - untreated, 50% will develop AACC within 25 years\(^3\)

---

Emergency treatment of AACC

1. Immediate IOP lowering with medications
   i. begin with topical beta blocker (no more than 2gtt)
   ii. add topical CAI or alpha agonist (2gtt 30 min apart)
   iii. add systemic CAI (acetazolamide 2 x 250mg PO)
      hyperosmotics

2. Topical q15min to treat inflammation

3. Once IOP <40mmHg and iris perfusion has improved
   • indentation gonioscopy may help break pupillary block

4. Once corneal edema has decreased, therapeutic LPI
   • prophylactic LPI is necessary for the fellow eye
   • CE may be an alternative to, or addition to LPI

5. Recheck IOP after 30 to 60 minutes if still in-office

In-office AACC toolkit:

1. topical beta-blocker
2. topical CAI or alpha agonist (ideally fast-acting lopidine) not sustained release
3. oral CAI (2 x 250mg acetazolamide)
4. topical pilocarpine

Mechanism

Appositional closure

1. Pupillary block
   - the primary mechanism for angle closure\textsuperscript{1}
   - irido-lenticular contact at pupil inhibits aqueous flow\textsuperscript{2}
   - increasing IOP in posterior chamber causes anterior iris bowing and appositional angle closure
   - more common with:
     - shallow anterior chamber
     - thicker (more pigmented) iris
     - thicker and/or more anterior lens
     - advancing age, cataract, exfoliation

Mechanism

Appositional closure

2. a. Plateau iris configuration (PIC; pre-surgical diagnosis):
   • angle crowding due to iris compression between a large anteriorly positioned CB and the TM\(^1\)
   • more common in younger hyperopic women\(^2\)
   • flat central iris (deep central chamber) turns sharply posteriorly before inserting into CB (narrow angle)
   • “double-hump” sign on compression gonioscopy
   • iris curves over peripheral CB and central lens
   • may lead to widespread PAS and increased IOP
   • in PIC, there is still an element of pupillary block

2. b. Plateau iris syndrome (PIS; post-surgical diagnosis):
   • persistent ITC despite a patent LPI\(^3\)

Plateau iris

Indentation gonioscopy causing a “double hump” in plateau iris: the peripheral hump is over the CB, the central is over the anterior lens (inset: as seen by AS-OCT)

http://webeye.ophth.uiowa.edu/eyeforum/cases/143-plateau-iris.htm
Mechanism

UBM image of pupillary block: irido-lenticular contact causing anterior bowing of the peripheral iris and appositional angle closure

UBM image of plateau iris: anterior rotation of the ciliary body creating appositional angle closure (note flat central iris and deep central chamber)

Mechanism

Appositional closure

3. Angle crowding
   • anterior segment imaging has suggested that a bulkier or thicker peripheral iris may narrow the angle
   • may occur in the absence of, or in combination with pupillary block or plateau iris
     • may be more common in, and help explain the higher prevalence of ACG in Asian eyes
   • iris thickness is greatest in AACC and least in PACS

Most cases of PACG are due to more than one mechanism, although an element pupillary block is essentially universal
Mechanism

Synechial closure

• with prolonged appositional closure (more common in chronic ACG), broad PAS form\(^1\)
  • IOP increase can be significant, and difficult to control
  • permanent trabecular damage is possible\(^2\)
• PAS usually require more treatment than LPI alone:
  • argon laser peripheral iridoplasty
  • lens extraction
• more extensive PAS (≥180°) may necessitate:
  • goniosynechialysis (+/- CE)
  • trabeculectomy\(^3\)

---

Peripheral anterior synechiae

Following prolonged appositional closure, peripheral anterior synechiae (PAS; broad adhesions between the iris and angle structures, often anterior to TM) can form

https://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/Peripheral-anterior-synechiae.htm
# Medical treatment of chronic PACG

## Aqueous suppressants:
- beta-blockers, alpha agonists, and carbonic anhydrase inhibitors can be effective in initial IOP control\(^1\)
  - brimonidine may also cause helpful pupillary miosis\(^2\)

## Prostaglandin analogs (PGA):
- effective in PACG even in the presence of extensive PAS\(^3\)

## Parasympathomimetics (miotics):
- first used in the late 1800s
- ciliary muscle contraction mechanically opens the TM
- pupil constriction pulls the iris away from the TM
  - particularly helpful in preventing AACC in plateau iris\(^4\)

---

Laser treatment

Laser peripheral iridotomy (LPI):
• has been first-line treatment for ACG for nearly 50 years\textsuperscript{1}
• reduces pupillary block by reducing IOP differential between anterior and posterior chambers\textsuperscript{2}
  • iris flattens and CB moves posteriorly, opening angle
• can reduce the progression from PACS to PAC to PACG
  • more effective in early disease\textsuperscript{3}
  • less effective in the presence of extensive PAS
• relatively good safety profile\textsuperscript{4}
  • with a thick and darkly pigmented iris, LPI can induce significant inflammation and pigment release, leading to a post-treatment pressure spike\textsuperscript{5}

\begin{itemize}
  \item Robin AL, Pollack IP. Argon laser peripheral iridotomies in the treatment of primary angle closure glaucoma. \textit{Arch Ophthalmol} 1982;100:919-23.
  \item Sun X, et al. Primary angle closure glaucoma: what we know and what we don’t know. \textit{Prog Ret Eye Res} 2017;58:26-45.
\end{itemize}
Laser treatment

Although most angles widen post-LPI:

• up to 25% will show persistent angle closure
• angle width significantly narrows 6 to 18 months post-LPI
• angle closure can recur following initially successful LPI
  • nearly 60% of PAC eyes with ≥180° persistent appositional closure go on to develop PACG

Annual gonioscopy is still required in patients post-LPI

Laser treatment

Argon laser peripheral iridoplasty (ALPI):

- superficial thermal burns pull peripheral iris away from TM, widening angle
  - more effective in combination with LPI
  - effective in plateau iris to reduce ITC post-LPI
  - can be used post-pilocarpine administration in AACC
    - immediate effect
  - may help prevent subsequent PAS formation
    - possible adverse effect: Urrets-Zavalia syndrome (prolonged pupil dilation following ALPI)

## Surgical treatment

There is little consensus, and some controversy, on the best approach to surgically manage angle closure disease\(^1\)

### Anterior chamber paracentesis
- leads to a rapid short-term decrease in IOP in AACC\(^2\)
  - can be technically difficult in a crowded inflamed eye

### Goniosynechialysis (GSL):
- strips PAS and allows aqueous to access the TM\(^3\)
  - effective early: prolonged PAS irreversibly damage TM
  - usually used in combination with LPI, ALPI, and/or CE\(^4\)

---

Surgical treatment

Goniosynechialysis (GSL):
- viscoelastic is injected to deepen the peripheral chamber
- PAS are broken by posterior pressure on the peripheral iris
  - success is visualization of the scleral spur

Surgical treatment

Trabeculectomy:
- with permanent TM dysfunction, the surgical treatment of PACG becomes similar to that of POAG
- adequate IOP control in nearly 70% of cases\(^1\)
  - however, technically challenging in a narrow angle
  - risk of complications is greater in PACG than POAG\(^2\)
  - most commonly, shallow or flat anterior chamber\(^3\)
  - high IOP: malignant (ciliary block) glaucoma
    - post-operative inflammatory CB swelling\(^4\)
    - increased pressure in the vitreous causing anterior movement of CB, iris, and lens\(^5\)
  - hypotony: choroidal effusion

Surgical treatment

Cataract or clear lens extraction (CE)
• many studies have suggested that CE is effective in PACG\(^1\)
  • all anterior segment parameters improve significantly following CE (more so than following LPI\(^2-4\))
    • effectively eliminates pupillary block
    • increased chamber depth and angle width
      • no residual angle closure (vs. ~25% post-LPI)
    • lower IOP and fewer post-treatment medications
    • improved BCVA post-CE
  • can be used in combination with GSL and trabeculectomy

CE can be technically difficult in ACG: shallow chamber, thick lens
• plateau iris configuration may persist post-CE\(^5\)

Surgical treatment

EAGLE Study

- Effectiveness in Angle-closure Glaucoma of Lens Extraction
  - 419 patients ≥50 years old with PAC (IOP ≥30mmHg) or PACG randomized to LPI or CE

At 36 months, initial CE rather than LPI resulted in:

- significantly better quality of life scores
- significantly lower IOP
- significantly fewer post-treatment medications
  - further surgical treatment (CE and trabeculectomy) was 3x more common post-LPI

Surgical treatment

EAGLE Study:
“... initial treatment [with CE] was superior to [LPI] plus topical medical treatment for participants with [PAC and PACG] ...”¹

“The potential importance of this definitive procedure to correct persistent pupillary-block and angle crowding after LPI in both the treatment and prevention of acute and chronic angle closure glaucoma cannot be overstated.”²

Primary angle closure is very under-diagnosed, and responsible for a disproportionate amount of severe vision loss. As such, the identification of patients at risk of progressing to primary angle closure glaucoma is of paramount importance. While imaging techniques are useful adjuncts, gonioscopy remains the gold standard of angle assessment.

When primary angle closure or primary angle closure glaucoma is identified, surgical intervention is indicated to reduce the risk of ongoing appositional or synechial angle closure and permanent trabecular damage:

- laser peripheral iridotomy, often in conjunction with (and perhaps soon to be replaced by) cataract surgery
Are there any questions about my presentation?

Yes.

Did you brush your teeth too aggressively and accidentally stab yourself in the brain?

Can you be more specific?

Frontal lobes?