Glaucoma

Glaucoma is a group of eye diseases traditionally characterized by increased intraocular pressure (IOP). However, glaucoma is more accurately defined as an optic neuropathy and may not always be associated with increased IOP.

- Classification:

  1. **open-angle glaucoma:** an optic neuropathy characterized by progressive peripheral visual field loss followed by central field loss in a typical pattern. It is usually but not always in the presence of elevated intraocular pressure (IOP).

  2. **Angle-closure glaucoma:** characterized by narrowing or closure of the anterior chamber angle which is lead to inadequate drainage of the aqueous humor leads to increased IOP and damage to the optic nerve.

- Risk factors:

<table>
<thead>
<tr>
<th>Risk Factors for Glaucoma</th>
<th>POAG</th>
<th>PACG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated IOP</td>
<td>Elevated IOP</td>
<td>Advancing age</td>
</tr>
<tr>
<td>African or Hispanic descent</td>
<td>African or Hispanic descent</td>
<td>Asian or Eskimo ethnicity</td>
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<tr>
<td>Family history of glaucoma</td>
<td>Family history of glaucoma</td>
<td>Female sex</td>
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<tr>
<td>Older age</td>
<td>Older age</td>
<td>Hyperopia</td>
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<tr>
<td>Thinner CCT</td>
<td>Thinner CCT</td>
<td>Shallow anterior chamber</td>
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<tr>
<td>Type 2 diabetes</td>
<td>Type 2 diabetes</td>
<td>Family history of angle-closure glaucoma</td>
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<tr>
<td>Low ocular perfusion pressures</td>
<td>Low ocular perfusion pressures</td>
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<tr>
<td>Myopia</td>
<td>Myopia</td>
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</table>

  CCT, central corneal thickness; IOP, intraocular pressure; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma.
open-angle glaucoma

Clinical presentation:

- Open-angle glaucoma rarely experience symptoms, is generally detected incidentally during comprehensive ophthalmic examination.
- High elevations of intraocular pressure (IOP), up to 40. Increased aqueous production and/or decreased outflow are possible mechanisms for elevated intraocular pressure.

Diagnosis: fundus examination and visual field testing

- Evidence of optic nerve damage from either or both of the following:
  - Optic disc or retinal nerve fiber layer structural abnormalities (eg, thinning, cupping)
  - Reliable and reproducible visual field abnormalities

- Lowering intraocular pressure (IOP) is the primary goal of therapy, which has been shown to reduce the progression of visual field loss.
- There is no clear consensus regarding a threshold IOP for the initiation of treatment:
  - Most clinicians would initiate treatment for a patient with two instances of IOP >25 mmHg, while some would do so for IOP >22 mmHg.
  - A patient with an IOP of 18 who has cupping and field loss should be treated for glaucoma.
  - Patients at high risk for visual field deterioration should also be treated.

- Open-angle glaucoma tends to be bilateral but can be quite asymmetric. The decision to treat is made for each eye rather than for each patient. Monocular treatment may be indicated, at least initially.

Treatment:

- Intraocular pressure (IOP) can be lowered by pharmacologic therapy, laser therapy, and/or surgery.
- Therapy must be individualized, taking into account the patient’s disease state, target pressure, and medical comorbidities.
Pharmacologic therapy:

Topical medications work either by increasing aqueous outflow (prostaglandins, alpha adrenergic agonists, cholinergic agonists) or by decreasing aqueous production (alpha adrenergic agonists, beta blockers, carbonic anhydrase inhibitors).

1. Prostaglandins:
   The topical prostaglandins are increasingly chosen over topical beta blockers and other medications as initial therapy in open-angle glaucoma.

   - Latanoprost, Bimatoprost, Travoprost, Tafluprost

   **Usual dose:** one drop every night.

   ✓ effective and well tolerated, with few systemic side effects.

   ✓ may decrease IOP more than beta-blockers [Latanoprost and Bimatoprost were found to have greater reductions in IOP compared with timolol.]

   ✓ have the advantage of once--daily dosing.

2. Beta blockers:
   Have traditionally been considered first-line therapy, but more recent publications promote prostaglandins for initial therapy.

   - Nonselective (intrinsic sympathomimetic activity): Timolol, Metipranolol, Carteolol, Levobunolol.
   - Selective (beta 1): Betaxolol.

   **Usual dose:** one drop twice a day.
3. Alpha adrenergic agonists:
   ✓ appear to be similarly effective to beta blockers in lowering IOP.
   ✓ but are associated with a number of ocular side effects including allergic conjunctivitis, hyperemia, and ocular pruritus.

   - Apraclonidine, Brimonidine
   - Usual dose: one drop two to three times a day.

4. Cholinergic agonists:
   ✓ have fewer systemic adverse effects than beta blockers, but ocular side effects such as fixed, small pupils, myopia, and increased subjective visual disturbance.

   - Pilocarpine
   - Usual dose: one drop two to three times a day.

5. Carbonic anhydrase inhibitors:
   Topical carbonic anhydrase inhibitors do not appear to be as effective in treating open-angle glaucoma compared with other pharmacologic therapy.

   - Topical: Brinzolamide, Dorzolamide.
     Usual dose: two to three times a day.
   - Systemic:
     - Acetazolamide (125-250 mg two to four times a day.)
     - Methazolamide (25-50 mg two to three times a day).
**Combination products:**
From different classes (ie, beta blocker plus prostaglandin, or beta blocker plus carbonic anhydrase inhibitor).

- Can cause a greater reduction in the IOP than monotherapy
- Adding a second medication is reasonable if initial monotherapy is not effective.
- Several drugs are available as fixed combination products: timolol-dorzolamide, timolol-brimonidine, brinzolamide-brimonidine, timolol-latanoprost, timolol-Bimatoprost.

<table>
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<tr>
<th>Agents that reduce intraocular pressure</th>
<th>Class</th>
<th>Examples</th>
<th>Side effects</th>
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</thead>
<tbody>
<tr>
<td><strong>Agents that suppress aqueous inflow</strong></td>
<td>Beta adrenergic blockers</td>
<td>Betaxolol, carteolol, levobunolol, metipranol, timolol</td>
<td>Ocular irritation and dry eyes. Contraindicated in patients with bradycardia, heart block, heart failure, asthma, or obstructive airway disease.</td>
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<tr>
<td></td>
<td>Alpha-2 adrenergic agonists</td>
<td>Apraclonidine, brimonidine</td>
<td>Red eye and ocular irritation. CNS effects and respiratory arrest in young children (brimonidine). Caution in patients with cerebral or coronary insufficiency, Raynaud phenomenon, postural hypotension, hepatic or renal impairment.</td>
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<tr>
<td></td>
<td>Carbonic anhydrase inhibitors</td>
<td>Dorzolamide and brinzolamide (topical), acetazolamide and methazolamide (oral)</td>
<td>Oral form can cause transient myopia, nausea, diarrhea, loss of appetite and taste, paraesthesias, lassitude, renal stones, and hematological problems. Topical forms much less likely to cause systemic side effects but can cause local irritation and redness.</td>
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<tr>
<td><strong>Agents that increase aqueous outflow</strong></td>
<td>Prostaglandin analogues, (prostamides)</td>
<td>Bimatoprost, latanoprost, tafluprost, travoprost, unoprostone</td>
<td>Brown discoloration of iris, lengthening and darkening of eyelashes, ocular irritation and redness, macular edema or iritis in susceptible individuals.</td>
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<td>Apraclonidine, brimonidine</td>
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<td>Cholinergic agonists</td>
<td>Pilocarpine, carbachol</td>
<td>Ciliary spasm leading to headaches especially in younger patients, myopia, dim vision (small pupil). Cataracts and iris-lens adhesions in long term.</td>
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</tbody>
</table>
**Laser therapy:**

Laser therapy (trabeculoplasty) increases aqueous outflow.

- The cost-effectiveness of laser therapy compared with prostaglandin medications for newly diagnosed, mild open-angle glaucoma is about equivalent in one modelling study; laser therapy may be slightly more cost-effective if, as expected, medical adherence in community settings is lower than reported in clinical trials, while medication provides somewhat greater value assuming optimal adherence.

**Surgery:**

Surgical therapy involves the creation of a filtration bleb to allow egress of aqueous humor from the eye.

- Surgery sometimes fails because of excessive scar tissue formation. There are reports of the use of adjuncts before, during, or after surgery, such as beta irradiation and antimetabolites (5-fluorouracil and mitomycin C), to increase the rate of surgical success.
- Surgical therapy is associated with a number of attendant risks and complications, including cataract and permanent loss of vision.

**TARGET INTRAOCULAR PRESSURE:**

- There are no standard guidelines for IOP, Ophthalmologists must determine appropriate target pressures for individual patients and individual eyes.
- The target pressure must be lowered if nerve damage occurs despite achieving the target.
- Data from EMGT and the Collaborative Initial Glaucoma Treatment Study (CIGTS) have suggested a target IOP of ≥25 to 30 percent below initial IOP

**Monitoring:**

- lifetime monitoring of intraocular pressure (IOP), the optic disc, and visual fields at least twice yearly.
- Patients with progressive disease may require assessment every one to three months.
# Angle-Closure Glaucoma

- Ocular pressure: Generally between 40 to 70 mmHg (normal is approximately 8 to 21 mmHg).
- Usually one eye is affected at a time, but both eyes must be carefully examined.

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<th>Symptoms:</th>
<th>Diagnosis:</th>
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| Rate of onset and degree of IOP increase determine symptoms, patients may experience some or all of the following symptoms:  
- Decreased vision, Headache  
- Halos around lights, Severe eye pain  
- Nausea and vomiting  
- If the rise in IOP is slower and does not reach very high levels, the patient may be symptom-free. |  
- Gonioscopy—anterior-chamber angles will be closed. Peripheral anterior synechiae may be present.  
- Applanation tonometry—when symptoms are present, IOP may be \( > 30 \) mm Hg \( 4.0 \) kPa  
- Slit lamp grading of anterior chamber depth. |

## Treatment:

### Management of acute angle-closure glaucoma:

- Management of acute attacks involves **medical control of elevated intraocular pressure (IOP)** followed by **reversal of angle-closure by laser peripheral iridotomy**:

1. Control intraocular pressure:
The eye pressure should be checked 30 to 60 minutes after giving pressure-lowering drops.

- If the is still significantly elevated, the same drops could be given again, but the patient should also be examined immediately by an ophthalmologist.
- In refractory cases, the ophthalmologist may consider performing an anterior chamber paracentesis to remove some aqueous humor and immediately lower the eye pressure temporarily, which may help to break the attack.

2. Laser iridotomy:
   - This procedure use laser energy to create a tiny hole in the peripheral iris through which aqueous humor can flow and reach the angle.
   - The IOP is rechecked 30 to 120 minutes after the iridotomy is performed.
   - Repeat gonioscopy is then performed to determine if the angle is wider.
   - The fellow eye should be examined, if a narrow angle is found, prophylactic laser peripheral iridotomy should be performed to prevent future attacks.
3. **Surgical peripheral iridectomy:**
   - If laser peripheral iridotomy fails to remain patent, or the cornea is too cloudy to visualize the iris.
   - In this procedure, the ophthalmologist makes an incision into the anterior chamber and surgically excises a small amount of iris tissue to create a passage for aqueous humor to reach the angle.
   - Topical corticosteroid may be employed to decrease inflammation postoperatively.

**Management of chronic angle-closure glaucoma:**

- Laser peripheral iridotomy is the first step to relieve any pupillary block component.
- If scarring has already damaged the drainage angle, the remaining glaucoma is treated medically and surgically much as in open-angle glaucoma.
References:


Done by Pharm D students: Marwa Bani Melhem, Amal Al-dhoon.

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