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GLAUCOMA

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I. Definition, incidence, and risk factors.

Glaucoma is a condition in which the pressure inside the eye is sufficiently elevated to result ultimately in optic nerve damage and potential visual field loss via capillary microinfarction causing optic nerve ischemia. This combines with mechanical damage to the nerve by slippage of the lamina cribrosa. Glaucoma is the third leading cause of blindness worldwide behind cataract and trachoma, and in the United States, it is the third leading cause of blindness behind cataract and macular degeneration. Approximately 1.25 million Americans have the diagnosed condition, but another 1 million Americans have glaucoma and are unaware of it. Nearly 120,000 are bilaterally blind, and 1.6 million have visual field defects. It is the single most frequent irreversible cause of blindness among African-Americans and it affects more than 2% of all whites. Detection of glaucoma patients is, therefore, an important public health problem. There are more than 40 different types of glaucoma. Glaucoma can also affect younger people, and measurement of eye pressure is an important part of a routine eye examination. **Risk factors** for glaucoma include high intraocular pressure (IOP), old age, African-American race, family history of glaucoma, myopia, diabetes, and high blood pressure. The disease in primary form is hereditary by a yet-undefined polygenic mechanism.

II. Physiologic mechanisms of various glaucomas.

Aqueous humor is produced by the ciliary body and flows into the posterior chamber, then between the posterior iris surface and lens, around the pupil edge, into the anterior chamber. It exits from the anterior chamber via ***trabecular*** and ***nontrabecular*** routes. The trabecular route is at the angle of the anterior chamber, formed by the iris base and peripheral cornea, flowing through the **trabecular meshwork (TM)** of the sclera, into Schlemm's canal (Fig. 10.1F). Via the collector channels in the sclera, the aqueous is carried to the episcleral vessels, where aqueous mixes with blood. On slitlamp examination, clear limbal aqueous veins can often be observed carrying aqueous into blood-filled episcleral veins. The latter can be identified by a laminated appearance of the blood–aqueous mixture. The level of IOP at any time represents a balance between the rate of formation of aqueous humor and the amount of resistance to its flow out of the anterior chamber. In almost every case of glaucoma, increased IOP is due to an abnormality in outflow from the anterior chamber, rather than to above-normal rates of aqueous humor formation. The nontrabecular aqueous route occurs through ***uveoscleral outflow*** via the supraciliary and suprachoroidal spaces and out along nerves and vessels coursing through the sclera. This route may be as important as the TM exit.

Fig. 10.1. Anterior chamber angle depth and anatomic structures of the angle. **A:** Grade O: Slit or closed angle. **B:** Grade 1: extremely narrow angle; closure probable. I-C (iris–corneal angle) = 10 degrees. **C:** Grade 2: moderately narrow angle; closure possible. I-C = 20 degrees. **D:** Grade 3: moderately open angle; no closure possible. I-C = 20 to 35 degrees. **E:** Angle wide open; no closure possible. I-C = 35 to 45 degrees. **F:** Anatomic landmarks of wide open angle as seen by gonioscopy. (Adapted from Anterior Chamber Angle Estimation Card, Allergan Pharmaceutical Co., Irvine, California.)

A. In open-angle glaucoma

the aqueous humor has unimpeded access to the TM in the angle of the anterior chamber, but there is abnormally high resistance to the fluid flow through the TM (uveal, corneoscleral, and juxtacanalicular—the last being the site of primary outflow resistance), into Schlemm's canal, and then into the scleral venous plexus. The peripheral iris does not interfere with the access of aqueous humor to the draining angle structures.

1. **Primary open-angle glaucoma (POAG)** is the most common form of glaucoma. The underlying abnormality in the trabecular angle tissue causing abnormal resistance to fluid flow is not known. The disease is not secondary to another eye disease or condition. POAG is a silent, surreptitious process. Usually there are no symptoms. Gradual loss of peripheral vision occurs. Loss of central vision is usually the last to occur. Only actual measurement of the IOP and inspection of the

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optic nerve head with an ophthalmoscope can detect POAG in its early stages.

2. **Secondary open-angle glaucoma** occurs as a result of or in association with another eye disease or condition such as uveitis or trauma, resulting in secondary blockage or damage to the canals and collector channels.

B. In angle-closure glaucoma

the peripheral iris tissue covers the TM, preventing access of the aqueous humor to the TM. This type of glaucoma

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is often intermittent, with acute symptoms that are reversible when the peripheral iris is moved away from draining angle structures. In pure angle-closure glaucoma, the TM and Schlemm's canal angle tissue have inherently normal resistance to fluid flow. The IOP is elevated only when the peripheral iris covers the TM, preventing egress of the aqueous.

1. In **primary angle-closure glaucoma,** relative **pupillary block** is the mechanism of angle closure. This means that there is relative resistance to fluid flow of aqueous humor between the posterior iris surface and lens due to an abnormally close approximation at the pupil. This tends to occur in eyes with small anterior segments or short axial length. Relative pupillary block increases the pressure of aqueous in

the posterior chamber, forcing the peripheral iris forward over the TM (Fig. 10.1). The state of relative pupillary block depends greatly on pupillary size and rigidity of the peripheral iris. For example, relative pupillary block may be increased and angle-closure glaucoma produced by putting a patient in a dark room or by using dilating medications that move the pupil into a middilated state. Drug-induced miosis may produce a very small pupil, blocking posterior chamber aqueous passage and thus pushing the iris forward to close the angle. Most eyes subject to possible angle-closure glaucoma can be recognized by the shallowness of their axial anterior chamber depth.

2. **Secondary angle-closure glaucoma** occurs as a result of or in association with another eye disease or condition, such as a swollen cataract or diabetic neovascularization pushing or pulling the iris over the TM.

III. Methods of examination

A. Flashlight.

After examining pupillary light reactions, the physician should direct the flashlight to the temporal side of each eye, perpendicular to the corneal limbus, and note the shadow produced by the nasal peripheral iris against the cornea. In eyes with shallow anterior chambers that might be subject to angle-closure glaucoma, the relatively forward position of the iris will cause the nasal side to be in shadow. This flashlight examination should be performed in all patients before routine pupillary dilation. In eyes with shallow anterior chambers, the pupil should not be dilated until IOP is checked and gonioscopy is performed.

B. Slitlamp examination

1. The **axial and peripheral anterior chamber depth** may be measured and expressed in terms of corneal thickness. Direct a narrow slit beam onto the cornea at 60° just anterior to the limbus (Van Herick method). If the distance between the posterior corneal surface and the anterior iris surface is less than one-fourth the corneal thickness, the chamber is shallow. Anterior chamber depths less than three corneal thicknesses axially are also suspect and gonioscopy should be performed to assess angle narrowing.

2. **Other diagnostic signs** during slitlamp examination may be noted: for example, the presence of inflammatory cell deposits (keratic precipitates [KPs]) on the corneal epithelium, anterior chamber cells and flare, Krukenberg pigmented spindle on corneal endothelium, dandruff-like dusting on the lens capsule, iris heterochromia and transillumination (by placing the vertically narrowed beam coaxially in the pupil to create a red reflex back through the pupil), and abnormal iris vessels.

C. Measurement of IOP

Measurement of IOP may be taken by Goldmann slitlamp or handheld applanation tonometry, other electronic or pneumotonometry, finger tension (estimate), Schiötz tonometry, applanation, or air-puff noncontact tonometry (see Chapter 1, sec. II.F.). Mean normal IOP is 16± mm Hg, although some eyes may sustain damage with IOP in the teens and other have none with IOP in the 30s. **An IOP greater than 22 mm Hg should be considered suspicious,** if not frankly abnormal, and the patient

should be followed. Schiötz readings are falsely low in high myopes and in thyroidopathy due to low scleral rigidity. Considerable diurnal variation of IOP occurs normally (2 to 6 mm Hg), but IOP is greater in glaucoma patients (even down to normal levels); therefore, inspection of the optic disk and neural rim is just as important as the actual measurement of the IOP.

D. Ophthalmoscopy of the optic nerve cup.

Atrophy of connective tissue associated with the hyaloid artery during embryogenesis results in a depression of the internal (vitreous) surface of the optic disk termed the *cup.*

1. **The normal physiologic disk cup** varies considerably. Large physiologic cups are usually round in shape, unlike the vertical elongation that occurs in glaucoma. The amount and the contour of disk tissue present in the rim of the optic disk between the end of the cup and the edge of the disk proper are important (Fig. 10.2). Not until the cup extends toward the edge of the disk does frank glaucomatous field loss occur. It is important to recognize that many glaucomatous and normal patients have a circular halo around the optic disk in which the retinal pigment epithelium and choroidal pigment is deficient, so that the physician is actually viewing the sclera underneath. The end of this peripapillary halo should not be misinterpreted as the edge of the disk in assessing the disk rim tissue. Statistically, ***patients with large, round physiologic cups with a cup-to-disk ratio exceeding 0.6 are more at risk of developing glaucoma,*** and they should be followed. Round cups with intact disk rim tissue, however, are not necessarily abnormal in the absence of other changes.

Fig. 10.2. Progressive glaucomatous atrophic cupping of the optic nerve head with commonly associated visual field defects. **A:** Early enlargement of physiologic cup. Field normal. **B:** Inferotemporal notching of the cup. Field shows enlarged blind spot and superonasal Bjerrum scotoma. **C:** Increased notching, thinning of rim of cup, and visible lamina cribrosa. Field shows constriction of superonasal field and advancing superior Bjerrum scotoma. **D:** Advanced generalized thinning of rim of cup with nasalization of vessels. Field shows further superior constriction and new inferior field defect resulting from damage to superior retinal nerve fibers. **E:** Total atrophy of the rim; pale, deep cup. Vessels disappear under rim. Field shows small central and temporal island of vision remaining. (Adapted from Paton D, Craig J. *Glaucomas: diagnosis and management.* Clinical Symposia. Summit, NJ: Ciba Pharmaceutical Co., 1976.)

2. **The glaucomatous disk (nerve head)** may be recognized by certain changes in contour of the optic nerve cup. **Cupping** appears to be the result of faulty autoregulation of blood flow to the optic disk in the face of IOP. ***Early signs of glaucomatous optic neuropathy include generalized or focal enlargement of the cup (vertical elongation or rim notching), asymmetry of cupping between the two eyes, superficial splinter hemorrhages, loss of nerve fiber layer (NFL), neuroretinal rim translucency, and nasalization of vessels.***

    a. **Parallax** should be used in monocular (direct ophthalmoscope) examination of the optic disk to assess the contour of the disk tissue. **Stereo viewing** through a dilated pupil with a fundus contact lens, a +78 or +90 diopter (D) handheld lens, or Hruby lens at the slitlamp is critical. With glaucomatous damage to the nerve, actual loss of nerve tissue and its vascular and glial supporting tissue occurs. Such atrophy results in both contour (cupping) and color (pallor) changes in disk appearance. The **optic disk rim** is made up of ganglion cell nerve fibers and is best evaluated by viewing the fundus with a **green light (red-free).** The **nerve fiber** bundles appear as radiating striations toward the disk and may be best documented with high-contrast black and white photos. Their loss may be diffuse or focal. Decreased visibility or white-out areas of the NFL at the rim and entering the retina are detectable in 90% of glaucomatous nerves before or during early visual field loss. In elderly people, however, nuclear sclerotic changes (early cataracts) often impart a rosy color to the disk and may be confusing. In primary optic atrophy, not due to glaucoma, change in pallor of the disk occurs with no change in contour.

    b. **In glaucoma, the cup usually enlarges vertically.** The increased cupping commonly progresses first toward the inferior pole of the disk and then enlarges superiorly, but there is considerable variation. Very rarely, the optic cup may extend straight temporally first rather than vertically. In such cases, **macular fibers may be affected early** in the course of the disease, with resulting ***loss of***

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central vision. Cupping close to or at the inferior pole of the disk will, of course, result in superior field loss; cupping close to the superior pole of the disk will result in inferior field loss. Occasionally, glaucomatous damage to the optic disk produces a shallower background bowing of disk tissue rather than excavation. The latter is called ***saucerization. Temporal pallor*** is rarely seen in glaucoma and, if noted, should raise the suspicion of an ***intracranial compressive lesion, arteritic ischemia,*** or old ***trauma.***

    c. **Asymmetry** in the appearance of the right and left optic disk cups may be an early sign of glaucoma, even though each is within normal limits.

    d. **Enlargement** in the size of the cup occurs before visual field loss results. Inspection of the appearance of the optic disk cup is an important part of glaucoma screening procedures. During long-term follow-up, the size and shape of the cup are noted in addition to the IOP and visual field. If

enlargement of the cup occurs during follow-up, then, regardless of the absolute level of IOP, that pressure level is too high and additional glaucoma therapy is initiated. It is useful to record the appearance of the cup size and shape on a diagram (Fig. 10.2).

E. Visual fields

1. **Techniques** include confrontation (usually bedside examination) and various forms of automated static and kinetic perimetry (see Chapter 1, sec. II.I. and Chapter 13, sec. I.A., sec. I.B., sec. I.C., sec. I.D., sec. I.E. and sec. I.F.). Glaucoma patients are followed with visual field examinations every 6–12 months as a routine; the latter time period is reasonable if the optic nerves are healthy, if no known field defect is present, and if the pressure is well controlled.

2. If **visual field loss progression** occurs while the patient is being followed, then, regardless of the level of IOP, that pressure is too high and glaucoma therapy should be adjusted. Similar considerations apply to progression of optic disk cupping. Except in myopes or in glaucoma patients with episodes of extremely high pressure elevation, visual field changes should correspond with optic disk cupping. For example, superior field loss does not occur unless the disk shows increased cupping to the inferior pole.

3. **Follow-up field examination** should be done with the pupil at the same size as in baseline examinations, so that a similar condition of retinal test object illumination exists for the follow-up fields added. Miotic glaucoma therapy may need to be reversed by dilation for field examinations with 2.5% phenylephrine or 1.0% tropicamide. Should the patient develop lens opacities, continued examination with the smaller test objects may produce artifactual field defects. The **size of the test object** should be graded to the visual acuity.

4. **Glaucoma field defects** characteristically respect the horizontal meridian (unlike chiasmal lesions, which respect the vertical) (Fig 10.2). This is because glaucoma characteristically produces a nerve fiber bundle defect—an arcuate defect or Bjerrum scotoma, or a variant of these, such as a nasal step. The temporal nerve fibers in the retina sweep either superiorly or inferiorly around the macula and do not cross the horizontal raphe. Because it would be purely chance that exactly symmetric nerve fibers in the superior and inferior fields would be similarly affected, glaucoma defects characteristically show some discontinuity at the horizontal meridian, such as a nasal step. The papillomacular fibers are usually relatively resistant to chronic pressure effects until late in the disease, and visual acuity changes do not occur early. After central vision is lost from glaucoma, typically all that is left is a temporal island of vision. Automated perimetry or Goldmann fields may be the first to detect early defects. **Patterns of**

glaucomatous field loss include:

a. **Paracentral scotoma**—an island of relative or absolute loss within 10° of fixation.

b. **Arcuate scotoma**—arc-shaped loss 10 to 20° above or below fixation (nerve fiber bundle damage).

c. **Nasal step**—relative depression of one horizontal hemifield compared to the other (damage to superior or inferior nerve fibers outside paracentral area).

d. **Temporal wedge or step**—a wedge-shaped defect from blind spot toward the periphery (damage to nerve fibers serving retina above or below optic nerve head blind spot).

e. **Loss of all but small central and temporal islands of vision.**

F. Gonioscopy.

The angle is viewed by indirect slitlamp gonioscopy with a Goldmann two- to three-mirror lens using a viscous contact gel, or a Zeiss four-mirror lens with an Unger handle and no gel. Direct gonioscopy is done with the patient recumbent with use of a Koeppe-type dome lens and handheld microscope (see Chapter 1, sec. II.Q.). The angle is assessed for shallowness and possible susceptibility to angle-closure glaucoma, as well as for other abnormalities such as pigment, synechiae, exfoliation, new blood vessels, inflammatory deposits, and evidence of old injury such as angle recession. Generally, if the scleral spur can be seen through the entire circumference and the iris is not excessively convex, the eye is not likely to be susceptible to angle closure and the pupil can be safely dilated. One commonly used **angle rating system** adapted from *Schaeffer* is depicted in Fig. 10.1. The *Spaeth* system expands this to include description of the peripheral iris contour, insertion of the iris root, and the effects of indentation gonioscopy on the angle configuration. It should be noted that narrow-angle eyes can look distinctly different at different examinations, perhaps reflecting different rates of aqueous production and differing relative pupillary block. Repeat examination in such narrow-angle eyes is usually indicated. The Zeiss gonioscopic lens is useful for rapidly viewing the angle, although it readily causes indentation of the eye and artificial deepening of the anterior chamber. The latter is deliberately utilized to ***differentiate appositional from synechial angle closure*** in the Spaeth system.

G. Optic nerve head and nerve fiber layer (NFL) imaging.

The most common method of imaging the optic nerve is by conventional photography. This is a useful means by which to document optic nerve head appearance and to perform longitudinal comparison to look for onset or progression of optic nerve cupping. Newer methods for imaging the nerve head and NFL include ***optical coherence tomography (OCT, NFL), scanning laser polarimetry (NFL), and confocal laser scanning ophthalmoscopy*** (three-dimensional imaging of optic nerve head and NFL using tomography) (see Chapter 1, sec. II.I. and sec. II.J.). NFL imaging takes advantage of the fact that the loss of retinal ganglion cells, and hence their axons, will result in a thinning of the NFL in the peripapillary region. Because the density of nerve fibers is less in the

peripapillary region than at the optic nerve head itself, NFL imaging is likely to pick up earlier changes in thickness. The Nerve Fiber Analyzer (I and II) and the Gdx (Laser Diagnostic Technologies) combine polarimetry with scanning laser ophthalmoscopy to quantitate the thickness of the NFL. It is hoped that the use and development of NFL imaging will allow earlier detection of damage and progression before functional changes have occurred. These methods should be considered as adjunctive to visual field testing, however, and will likely not replace the visual field as a method for evaluating and diagnosing glaucoma. In the end, the visual field is the only means by which the physician can truly determine what the patient sees.

IV. Principles of therapy

In all cases of glaucoma it is essential to establish whether the glaucoma is open or closed angle. This is

accomplished by placing a gonioscopic contact lens on the eye and actually viewing the angle structures.

A. In the therapy of **open-angle glaucoma** the physician usually first treats the condition medically to lower the IOP. This pressure may be lowered by increasing the facility of aqueous outflow from the anterior chamber through the angle tissues, or by decreasing the rate of aqueous humor formation by the ciliary body, or both. Laser trabeculoplasty (LTP) is usually used alone or in conjunction with medical therapy to control IOP, nerve cupping, or progressive visual loss. Studies have shown that LTP is effective as primary medical therapy or to minimize use of medical treatment. Surgery is used when all other methods have failed.

B. **Angle-closure glaucoma** may initially be treated medically, but it is primarily a surgical (laser) disease, requiring peripheral iridotomy (placing a hole through the peripheral iris) to relieve pupillary block permanently. Posterior chamber aqueous pressure is thus relieved by aqueous flowing through this extra opening, and the peripheral iris falls away from the meshwork.

V. Medical treatments and side effects.

Studies indicate that most ocular hypotensive drugs may achieve maximal effect with less frequent administration and lower concentrations if **nasolacrimal occlusion** is applied (finger pressure) for 3 minutes during and after drug instillation. This may also result in fewer side effects. (See Appendix A for listings of drugs, dosages, and commercial names.)

A. Beta-adrenergic blockers

(timolol, betaxolol, carteolol, levobunolol, metipranolol)

1. **Mechanism of action.** Timolol, levobunolol, carteolol, and metipranolol are **nonselective** $beta_1$- (cardiac) and $beta_2$- (smooth muscle, pulmonary) receptor

blocking agents. Betaxolol has 100 times more affinity for $beta_1$- than $beta_2$-receptors.

2. **Physiologic effects.** The nonselective drugs decrease IOP by blockade of $beta_2$-receptors in the ciliary processes, resulting in decreased aqueous production. The mechanism for betaxolol is unknown because there are so few $beta_1$-receptors in the eye, but there may be “spill over” to bind $beta_2$-receptors as well. There is no effect on facility of outflow. The drug molecule timolol (and probably betaxolol and levobunolol) releases from the beta-receptor site as early as 3 hours after topical administration, yet clinical effect may last up to 2 weeks. This prolonged effect may result from rerelease of beta-blocker from depots in the iris pigment epithelial melanin. Carteolol, unlike the other beta-blockers, has intrinsic sympathomimetic activity, possibly resulting in fewer side effects. It also **lacks** timolol's tendency to **increase** serum **cholesterol** and **decrease high-density lipoproteins,** a factor to consider in cardiovascular patients.

3. **Indications** are primary and secondary open-angle glaucomas including inflammatory glaucomas, acute and chronic primary and secondary angle-closure glaucomas, ocular hypertension, and childhood glaucomas.

4. **Precautions and contraindications** include known drug allergy. These drugs should be used with caution or not at all, depending on severity of disease, in patients with asthma, emphysema, chronic obstructive pulmonary disease, bronchitis, heart block, congestive heart failure, cardiovascular disease, or cardiomyopathy. Although betaxolol is the blocker of choice in patients at risk for pulmonary reaction because of its greater $beta_1$ (cardiac) selectivity, the drug may induce bronchospasm in some patients.

5. **Available preparations.** Timolol, 0.25% to 0.50%; betaxolol and levobunolol, 0.25%; metipranolol, 0.3%; carteolol, 1% eye drops. Timolol XE 0.25% or 0.50% gel qd is equivalent in effect to bid drops.

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6. **Recommended dosage** is qd or q12h topically. All beta-blockers may be used with significant additive effect in **combination** with miotic agents, $alpha_2$-agonists, prostaglandin analogs, or carbonic anhydrase inhibitors (CAIs).

7. **Side effects**

    a. Bradycardia, cardiac arrest, acute asthma, and pulmonary edema have all been reported in susceptible individuals and result from systemic absorption of topical drug. **Lacrimal canalicular compression** should be practiced by patients at any risk, and the drug used with caution or not at all in those patients with moderate to severe cardiac or pulmonary disease.

    b. Full adult dosage should be **avoided** in **children** because **apnea** may result; 0.25% qd to bid with canalicular compression is the lower advisable dosage.

    c. **Nursing mothers** will excrete the drugs in breast milk; beta-blocker treatment of the mother should be considered carefully if she is breast-feeding.

d. **Other side effects are lethargy, depression, impotence, hallucinations, and gastrointestinal symptoms.**

e. **Ocular effects** include allergy, punctate keratitis, and diplopia. Corneal anesthesia may result from the membrane-stabilizing effects of timolol, but is less with the other beta-blockers.

B. Alpha$_2$-adrenergic agonists

(apraclonidine and brimonidine).

1. The **mechanism of action** and **physiologic effects** are unclear but appear to be alpha$_2$-receptor stimulation that results in decreased aqueous humor formation.

2. **Indications** are to control increases in IOP after anterior segment laser surgery (U.S. Food and Drug Administration [FDA] approved), acute short-term pressure spikes, and in chronic primary or secondary glaucomas.

3. **Contraindications** include known allergy to the drug and cardiac disease with untreated arteriovenous block or bradycardia.

4. **Available preparations.** Apraclonidine is available as a 0.5% and 1% solution and brimonidine is available as a 0.2% solution.

5. **Usual dosage.** One drop 1 hour before laser surgery and one drop immediately after the procedure or just one drop immediately postlaser appears equally effective and superior to any other glaucoma drug. This dose decreases the incidence of postlaser pressure spikes of 10 mm Hg or more to less than 2% and lasts 12 hours. **Chronic glaucoma treatment** is one drop of 0.5% apraclonidine or one drop of 0.2% brimonidine bid. There is a 30% allergic response to the 0.50% apraclonidine and approximately 10% to 15% allergy rate for brimonidine. A new preparation of brimonidine, utilizing a different preservative, promises to have a lower allergy rate. Beta-adrenergic blockers are the usual concomitant drugs, but prostaglandin analogs, miotics, epinephrine, and CAIs may be added as well for additive effect.

6. **Side effects** include possible transient upper lid retraction, conjunctival blanching, mydriasis, burning or itching sensation, and subconjunctival hemorrhage. Systemically, there may be gastrointestinal reaction and cardiovascular effect such as bradycardia, vasovagal attack, palpitations, or orthostatic hypotension. Central nervous system disturbances include somnolence, insomnia, irritability, and decreased libido, all of which are transient.

C. Prostaglandin analogs

(latanoprost, bimatoprost, travoprost, and unoprostone)

1. **Mechanism of action.** Lowering of IOP by increasing uveoscleral outflow through a

prostaglandin F_2 α-mediated mechanism.

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2. **Indications.** Additive therapy for lowering of high IOP.
3. **Preparation and dosage.** Latanoprost (Xalatan) 0.005%, bimatoprost (Lumigan) 0.03%, and travoprost (Travatan) 0.004% are each given once daily, usually at bedtime. Unoprostone (Rescula) 0.15% is given twice daily. Latanoprost is temperature sensitive and needs to be refrigerated prior to and after opening.
4. **Side effects** include increased iris pigmentation, darkening of the eyelid skin, increased thickness and number of eyelashes, ocular irritation (redness, itching, etc.), uveitis, cystoid macular edema, and probable reactivation of *herpes simplex* virus.

D. Carbonic anhydrase inhibitors (CAIs).

Acetazolamide, methazolamide and dichlorphenamide are oral agents. Acetazolamide is an intravenous (i.v.) agent as well, and dorzolamide and brinzolamide are topical agents.

1. **Mechanism of action.** CAIs inhibit the enzyme carbonic anhydrase.
2. **Physiologic effects.** The ciliary body enzyme, carbonic anhydrase, is related to the process of aqueous humor formation, most likely via active secretion of bicarbonate. CAIs decrease the rate of aqueous humor formation.
3. **Indications.** CAIs are additive therapy in the management of various acute glaucomas, but also in the chronic management of primary and secondary open-angle and angle-closure glaucomas not adequately controlled by topical medication.
4. **Contraindications.** Because of the metabolic and possible respiratory acidosis effects, patients with significant respiratory disease should be given oral CAIs cautiously and in lower dosages. Patients with a history of calcium phosphate kidney stone formation should be given the oral medication cautiously and only after consultation with their primary care provider. Known allergy is a contraindication. Patients with allergies to other sulfonamides should be given these agents with caution.
5. **Available preparations** include acetazolamide (Diamox, generic) 125 and 250 mg tablets, 500 mg capsules, 500 mg per 5 mL i.v.; methazolamide tablets (Neptazane, Glauctabs, MZM, generic) 25 mg and 50 mg tablets; dichlorphenamide (Daranide) 50 mg tablets bid to qid; dorzolamide (Trusopt) 2% drops; and brinzolamide (Azopt) 1% drops (see Appendix A).
6. **Recommended dosage.** Established dosages for near-maximum effect are acetazolamide tablets 250 mg q6h; methazolamide tablets 50 to 100 mg bid to tid; acetazolamide sustained-release capsules 500 mg q12h; and dichlorphenamide tablets 50 mg bid to qid. Because acetazolamide is excreted unchanged by the kidneys, patients with renal disease such as diabetic nephropathy should be started

on lower than standard dosages. Methazolamide or dichlorphenamide may be used more safely in this situation. Dorzolamide 2% drops and brinzolamide 1% tid decrease IOP by » 20%.

7. Side effects. Unfortunately, 40% to 50% of glaucoma patients are unable to tolerate systemic CAIs long term because of various disabling side effects. A symptom complex of **malaise, fatigue, depression, anorexia,** and **weight loss** is the most frequent side effect. **Loss of libido,** especially in young males, may also occur. These symptoms show some correlation with the degree of systemic metabolic acidosis on therapy. They may have a gradual, insidious onset over several months. Often neither the patient nor the physician relates these symptoms to the systemic CAI therapy. **Frequently, patients erroneously undergo extensive medical evaluations searching for occult malignancies.**

    a. **Simultaneous CAI and chlorothiazide** systemic hypertensive therapy may produce frank **hypokalemia,** and the patient

    should have potassium supplementation. In the absence of this concomitant chlorothiazide therapy, changes in serum potassium tend to be small and there is no symptomatic benefit from potassium supplementation.

    b. **Gastrointestinal** side effects occurring with oral CAI therapy tend to behave as local irritative phenomena, sometimes responding to administering the CAI with food, switching to a sustained-release preparation, or simultaneous mild alkali therapy.

    c. **Malaise** symptoms occur in some patients. Decreasing the dosage will sometimes improve tolerance. In particular, using one 500-mg acetazolamide capsule a day (which has an effect for more than 18 hours) is very useful. In many of these patients this dosage will result in an undertreatment of their glaucoma, but in others, near-maximum effects will be maintained.

    d. **Kidney stones** developing during oral CAI therapy are believed to be a result of calcium precipitation secondary to a decrease of citrate or magnesium excretion or both in the urine. The former is believed to be a direct consequence of the drugs making normally acid urine alkaline, which, with reduced citrate, induces calcium carbonate stone formation. There is a far ***lower incidence of kidney stone formation with methazolamide*** than with acetazolamide. Methazolamide has minimal action on citrate concentration or on the kidney. Management of kidney stone patients involves use of methazolamide in as low a dosage as the severity of the glaucoma permits, restriction of dietary calcium, and possibly concomitant use of chlorothiazide diuretics to alter the calcium–magnesium ratio in the urine. Electrolyte imbalance should be watched for in patients taking diuretics. Nephrologic consultation and measurement of urinary pH, calcium, and citrate should be obtained if stone formation is suspected.

    e. **Blood dyscrasias** are rare. Thrombocytopenia, agranulocytosis, and aplastic anemia may occur as idiosyncratic reactions. Periodic blood tests would not be

expected to anticipate these reactions and are not routinely performed. A history of a mouth or body sore that does not heal may be a clue to the occurrence of a blood dyscrasia.

f. **Myopia** occurs rarely as an idiosyncratic acute reversible phenomenon. It is believed to be due either to a change in hydration of the lens or shallow choroidal effusions, and it may be associated with a shallowing of the anterior chamber.

E. Miotics

1. **Pilocarpine**

   a. **Mechanism of action.** Pilocarpine is a direct-acting parasympathomimetic (muscarinic) **cholinergic** drug.

   b. **Physiologic effects.** The drug is used in chronic open-angle glaucoma to increase the facility of aqueous outflow. The mechanism of action is probably exclusively mechanical, via ciliary muscle contraction and pull on the scleral spur and TM. It is used in acute angle-closure glaucoma to move the iris away from the angle. Miosis is a side effect and is of no therapeutic benefit.

   c. **Indications** are chronic open-angle glaucoma, acute angle-closure glaucoma, chronic synechial angle-closure glaucoma (following peripheral iridectomy), and following cyclodialysis surgery.

   d. **Contraindications** are inflammatory glaucoma, malignant glaucoma, or known allergy.

   e. **Available preparations** are 0.25% to 10.0% eye drops, Ocusert P-20 diffusion membranes, and 4% gel (see Appendix A).

   f. **Recommended dosage**

      1. **Eye drops.** Except in very darkly pigmented irides, maximum effect is probably obtained with a 4% solution. In milder

      open-angle glaucoma, therapy is usually initiated with a 1% concentration. Duration of effect is 4 to 6 hours. It is usually prescribed for use every 6 hours.

      2. **Ocuserts** are changed once weekly. P-20s are generally used in patients controlled with 2% drops or less.

      3. **The gel** can be used alone at bedtime or as an adjunct to daytime medication.

2. **Combination.** Pilocarpine can be used in conjunction with other glaucoma medications and, in most instances, confers additional pressure-lowering effects.

3. **Side effects**

    1. **Ocular**

        a. **Contact allergy** is fairly rare.

        b. Contraction of the ciliary muscle results in accommodation and ensuing **fluctuating myopia.** In younger patients this is usually a disabling visual side effect that prevents use of pilocarpine. Continuous low-level, **constant-delivery ocular insert devices,** such as the Ocusert, are very effective in young patients with glaucoma who require pilocarpine therapy. These low levels of continuous delivery result in small amounts of myopia that tend to be steady and correctable, if necessary, with spectacles. Most patients above the age of 50 years do not develop such pilocarpine-induced myopia, presumably because of an inelasticity of their lens that is also responsible for their presbyopia.

        c. Pupillary **miosis** is a definite side effect of pilocarpine, which again exerts its antiglaucoma effect via ciliary muscle traction on the angle structures. This miosis results in **diminished night vision** and often some **contraction in peripheral visual field.** If the patient has early axial lens opacities, this miosis may result in **diminished visual acuity.** On the other hand, the miosis may result in a pinhole effect and an actual improvement in visual acuity.

        d. **Shallowing of the anterior chamber** may occur with higher doses of pilocarpine by forward movement of the lens–iris diaphragm subsequent to ciliary muscle contraction and relaxation of zonular tension. This shallowing may result in an increase in relative pupillary block, and it may convert an open-angle glaucoma with narrow angles into **partial angle-closure glaucoma.** This is true for all the standard miotic glaucoma therapies (carbachol, echothiophate iodide, demecarium bromide). In susceptible individuals, it seems to be dose related. There may be varying amounts of anterior chamber shallowing on miotic therapy. Similarly, in angle-closure glaucoma, lower concentrations of pilocarpine are used initially to minimize this axial shallowing and possible increase in relative pupillary block.

    2. **Systemic side effects.** Occasional patients are particularly sensitive and may develop sweating and gastrointestinal overactivity with usual dosages. **Sweating, salivation, nausea, tremor, headache, brow pain, bradycardia,** and **hypotension** have sometimes been observed as results of too vigorous treatment of angle-closure glaucoma with pilocarpine.

4. **Carbachol**

    a. **Mechanism of action.** A **cholinergic** similar to pilocarpine.

    b. **Physiologic effects.** Similar to pilocarpine.

    c. **Indications.** Carbachol eye drops are longer acting that pilocarpine, thus

having a greater stabilizing effect on diurnal pressure

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and myopia fluctuation. It may also be used in patients allergic to pilocarpine; otherwise, the indications are similar to pilocarpine. An intracameral preparation for intraoperative use induces miosis and inhibits postoperative pressure increase.

d. **Contraindications.** Similar to pilocarpine.

e. **Available preparations** are 0.75%, 1.5%, and 3.0% eye drops and 0.01% for intraocular use.

f. **Recommended dosage.** Carbachol 3% is approximately equivalent to pilocarpine 4%, and 1.5% carbachol is roughly equivalent to 2% pilocarpine. The effect is reported to last up to 8 hours. Dosage tid (compared to qid with pilocarpine) may be a distinct advantage in certain patients.

g. **Side effects.** Similar to pilocarpine.

5. **Anticholinesterase agents** (echothiophate iodide, demecarium bromide, physostigmine, isofluorphate 0.025%). Echothiophate is currently out of production but may become available again soon.

a. **Mechanism of action.** Indirect-acting parasympathomimetic activity by virtue of binding to the enzyme, acetylcholinesterase, allows endogenous acetylcholine to accumulate.

b. **Physiologic effects.** Ciliary muscle and iris sphincter muscle contraction occur similar to and possibly more marked than that occurring with other miotics, e.g., pilocarpine and carbachol. Miosis is a side effect of no therapeutic benefit.

c. **Indications** are chronic open-angle glaucoma (especially with aphakia), chronic synechial angle-closure glaucoma (following peripheral iridectomy), and following cyclodialysis surgery. These agents are more potent than pilocarpine or carbachol and should be used only when pilocarpine 4% is no longer effective.

d. **Contraindications.** Anticholinesterase agents should never be used in narrow-angle glaucoma without an iridototomy because of the extreme miosis they produce, as well as possible forward lens movement, which may actually increase pupillary block. Similarly, open-angle glaucoma with open but narrow angles may worsen because of partial-angle closure as a result of this therapy. Repeat gonioscopy on therapy is indicated. Other contraindications are inflammatory glaucoma or known allergy. These agents should be used cautiously in patients who are predisposed to **retinal detachment,** e.g., patients with lattice degeneration or family history of nontraumatic detachments.

e. **Preparations** include echothiophate iodide 0.03% to 0.25%, demecarium bromide 0.25% and 0.50%, isofluorphate 0.025%, and physostigmine 0.25% to

0.5%. Physostigmine ointment 0.25% is available for bedtime use.

f. **Usual dosage.** Anticholinesterase agents are administered twice a day. Because side effects are dose related, the lower concentration should be tried initially for pressure control.

g. **Side effects**

1. **Ocular**

a. Possible side effects include **accommodative spasm** and **shallowing of the anterior chamber** as well as **diminished night vision** and **peripheral field,** similar to and possibly more marked than that occurring with other miotics, e.g., pilocarpine and carbachol. These **cataractous** changes are related to drug concentration, frequency of dosage, age of the patient, and patient susceptibility. These agents should be used only when pilocarpine 4% is no longer effective, and the lower concentrations should be tried initially for pressure control. The lens changes have been

classically described as mossy anterior subcapsular opacities, but posterior subcapsular opacities and progression of nuclear sclerosis have also been described.

b. **Pupillary cysts** may occur with anticholinesterase therapy and may lessen with concomitant daily phenylephrine 2.5% eye drop therapy. These agents may induce a breakdown of the blood–aqueous barrier and **increase anterior chamber flare.** They should not be used in the presence of active uveitis. There seems to be some small risk of **retinal detachment** with this therapy, possibly resulting from traction and forward movement of the ora serrata as a result of intense ciliary muscle contraction. If feasible, glaucoma patients should have dilated indirect ophthalmoscopy with scleral depression before initiation of strong miotic therapy. **Lacrimal punctal stenosis, conjunctival goblet cell,** and **tear abnormalities** have been reported.

2. **Systemic**

a. Anticholinesterase agents may cause **diarrhea, nausea,** and **abdominal cramps** if excessively absorbed. These toxic symptoms are cumulative and therefore appear only after many months of therapy. Patients should be instructed in lacrimal occlusion with digital pressure when taking drops to minimize systemic absorption and pharyngeal–alimentary passage of these agents. **Internists should be especially suspicious of gastrointestinal or systemic malaise complaints in glaucoma patients under chronic therapy with anticholinesterase or CAI**

agents (see sec. V.D.7**, above). Because both of these agents frequently produce undesired systemic effects only after months of therapy, the correct diagnosis is too frequently missed.**

b. **Serum pseudocholinesterase,** which hydrolyzes succinylcholine and procaine, is often **decreased** in patients taking chronic topical anticholinesterase therapy, and therefore prolonged apnea may occur following use of succinylcholine in surgical procedures. It takes 4 to 6 weeks after cessation of topical anticholinesterase therapy for serum enzyme levels to return to normal, so **succinylcholine anesthesia should be avoided, if possible, in patients recently taking these agents.**

F. Epinephrine and dipivefrin hydrochloride (epinephrine [DPE])

DPE is an epinephrine prodrug in which the two pivalic acids are cleaved from an epinephrine molecule in the eye. It was synthesized for use on epinephrine-allergic as well as nonsensitized glaucoma patients.

1. The **mechanism of action** is unclear, but appears to be a function of both alpha- and beta-receptor stimulation.
2. **Physiologic effects.** Epinephrine both increases aqueous outflow (alpha- and beta-receptor stimulation) and decreases aqueous humor formation (alpha-receptor stimulation in the ciliary body). It is additive to the cholinergics, anticholinesterases, and CAIs in pressure-lowering effects.
3. **Indications.** It is primarily used in open-angle glaucoma or in conjunction with miotics with mildly shallowed chambers. Certain patients show a greater pressure lowering following several weeks of epinephrine therapy than following a single, acute dosage.
4. **Contraindications** include narrow-angle glaucoma or known allergy.
5. **Available preparations.** Epinephrine is available in strengths 0.5% to 2.0% to treat open-angle glaucoma as a borate, bitartrate, or

hydrochloride eye drop. There is no significant difference in the clinical efficacy of the preparations. The bitartrate has only 50% drug available as free base, however. DPE is available as a 0.1% solution.

6. **Usual dosage** is epinephrine 1% bid to tid. There is some evidence that, at least in patients with dark irides, epinephrine 2% may be more potent than 1%. DPE 0.1% is used once every 12 to 24 hours and is roughly equivalent to the effect of 2% epinephrine. DPE should probably not be used with anticholinesterases such as echothiophate iodide because the latter may inhibit the esterases necessary for

cleavage of the pivalic acid groups. DPE should probably not be used until at least 4 hours after instillation of beta-blockers, as noted under epinephrine.

7. **Side effects**

    a. Occasionally, paradoxic **pressure increase** may occur with epinephrine (with open angles); certain patients, for unknown reasons, have minimum pressure lowering on epinephrine therapy.

    b. Approximately 10% to 15% of patients are unable to tolerate long-term epinephrine therapy because of the development of **topical allergy.** Switching brands of epinephrine is rarely effective, and usually epinephrine must be discontinued.

    c. Epinephrine causes **cystoid macular edema (CME)** in 20% to 30% of aphakic patients after 1 week to months of therapy. This is almost always reversible on cessation of therapy.

    d. Oxidation products of epinephrine can result in **dark pigmented conjunctival deposits** as well as a **canalicular (tear duct) obstruction.**

    e. Occasional complaints of **palpitation, tachycardia, headache,** and **faintness** have been recorded in patients after topical usage. Although theoretically a concern (one drop of epinephrine 2% = 0.1 mg), epinephrine can almost always be given safely to patients with cardiovascular disease, especially if patients are taught how to **perform nasolacrimal compression** following topical administration to decrease systemic absorption by pressing over the medial lid area for 5 minutes.

    f. With DPE the incidence of adrenochrome deposits or CME, especially if the posterior capsule is intact, is unclear, but appears to be notably lower than that with epinephrine.

G. Hyperosmotic agents

(mannitol, glycerin, isosorbide).

1. **Mechanism of action.** Reduction of IOP by increasing plasma tonicity sufficiently to draw water out of the eye.

2. **Indications.** Additive therapy for rapid reduction of high IOP. Onset of action is 30 minutes and lasts 4 to 6 hours.

3. **Preparation and dosage**

    a. **Glycerin** (Osmoglyn) dosage is 1.0 to 1.5 g of glycerin per kg body weight given orally (p.o.). Osmoglyn is a 50%, lime-flavored solution with dosage 2 to 3 mL per kg (4 to 6 oz per patient). It is better tolerated served on cracked ice and may be given qd to tid. Topical glycerin (Ophthalgan) is a viscous solution

used to clear corneal edema for a better view of the intraocular structures.

b. **Isosorbide** is a 45%, mint-flavored solution with dosage of 1 to 2 g per kg (1.5 to 3.0 mL per lb body weight) given p.o. over ice qd to qid.

c. **Mannitol** is a 5% to 20% hyperosmotic given warm (38 to 39°C to dissolve crystals) i.v., in dosage of 0.5 to 2 g per kg body weight. Most common is 25 to 50 mL of 25% solution given by slow i.v. push.

4. **Side effects** may include severe systemic hypertension aggravation, nausea, vomiting, confusion, congestive heart failure, pulmonary edema, or diabetic hyperglycemia (mannitol). The drugs are contraindicated in oliguria or anuria.

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H. Calcium channel blockers

such as diltiazem, nifedipine, and verapamil inhibit calcium influx in vascular smooth muscle, decrease vascular tone, and increase blood flow. Studies have not proven that these oral drugs are effective in **low-tension glaucoma** by increasing optic nerve blood flow.

VI. Argon and neodymium:yttrium, aluminum, and garnet (Nd:YAG) laser therapy

(see also Chapter 8, sec. XI.).

A. General considerations.

The **argon laser** uses the heating, coagulative (less bleeding), and disrupting effect of the laser energy to create tissue burns or openings. The **Nd:YAG laser** produces a sudden focal expansion with tearing and disruption of tissue by delivering high-powered near-infrared irradiances in small, focused spots. In open-angle glaucomas, **argon laser trabeculoplasty (ALT)** application of nonpenetrating laser burns to the TM often results in improvement in the outflow of aqueous humor by an undetermined mechanism. Both mechanical and biologic effects have been postulated. In angle-closure glaucoma, the argon laser, YAG laser, or both have been used to create a small opening in the peripheral iris, thus alleviating pupillary block, which is the mechanism for angle-closure glaucoma.

B. Argon laser trabeculoplasty (ALT)

1. **Indications.** ALT should be attempted in almost all forms of open-angle glaucoma not adequately controlled with maximum tolerated medical therapy and prior to considering filtration surgery: phakic, aphakic, pseudophakic, pseudoexfoliative, pigmentary, and in noncompliant patients. Eyes with poor prognosis for beneficial laser effects (0% to 15% success) have steroid, neovascular, juvenile, or inflammatory glaucomas. In the chronic treatment of open-angle glaucoma, evaluating the benefit–risk ratio, ALT should probably be employed prior to the use

of cholinesterase inhibitors or even p.o. CAIs because of their side effects. Because ALT seems to be more effective in phakic eyes, it should be performed prior to cataract surgery in patients with borderline control. **ALT as a primary procedure** is also a good approach. After 2 years, eyes treated with ALT first, and medications added later as needed, had lower mean IOPs and fewer medicines needed than medicine-only treated eyes. At 5 and 10 years post-ALT, 50% and 66% of the eyes, respectively, required further laser treatment or surgery for adequate control.

2. **Contraindications** to ALT are total angle closure and hazy media obscuring angle structures. Relative contraindications are: secondary open-angle glaucomas (such as inflammatory or neovascular) because there is negligible effect but risk of pressure spike, a serious complication, such as high-pressure spike after ALT in the first eye, uncooperative patients, and the need for urgent IOP control where filtration surgery would have a more rapid effect.

3. **Technique.** Continue all glaucoma drugs before ALT. Instill 1% apraclonidine or 0.2% brimonidine 1 hour before ALT and immediately postlaser. For narrowed angles, use 1% pilocarpine. If apraclonidine is contraindicated, CAIs and hyperosmotic agents are alternatives. Use topical 0.5% proparacaine anesthesia (retrobulbar block for nystagmus or poor cooperation). An antireflective Goldmann mirrored gonioscopic lens is applied with goniogel and using the 25× oculars on the slitlamp. The beam is focused on the **anterior** region of the TM to minimize post-ALT IOP increase and synechiae. The desired reaction of focal blanching on the TM is achieved with a 0.1-second duration, 50 μm spot size, and power between 700 and 1,200 mW. Bubble formation or pigment scatter means the power is too high. Forty to 50 burns over 180 degrees or 80 to 100 burns over 360 degrees are placed.

4. **Follow-up.** Acute pressure elevations (>10 mm Hg) occur in 10% to 15% of patients within 1 to 2 hours of ALT. IOP increase should be

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prevented or lessened by a second 1% apraclonidine drop immediately post-ALT (see sec. V.F., above) and CAIs. Current antiglaucomatous therapy is maintained and topical steroids tid to qid added and tapered over 1 to 2 weeks. The first post-ALT visit should be at 24 to 48 hours, 5 to 7 days after treatment, and at 4 to 6 weeks, at which time the IOP lowering effect is assessed. IOP and anterior segment inflammatory signs should be assessed. If inflamed, the patient should be examined with a gonioscope (for which the Zeiss lens is convenient) to look for inflammatory deposits in the angle or beginning peripheral anterior synechiae, and the steroid dosage thereby adjusted.

5. **Complications**

    a. **Peripheral anterior synechiae**

        1. Usually low and not functional, but if “high” can cause worsening of glaucoma (convert open-angle to combined chronic angle-closure glaucoma).

        2. If observed, decrease number and power of applications for any second

treatment, and increase steroid dosage.

b. **Corneal burns** (usually transient).

c. **Hyphema**

1. Caused by blood in Schlemm's canal or wandering vessel (rule out undiagnosed neovascular glaucoma or increased episcleral venous pressure).

2. If encountered at time of ALT, increase pressure in eye by indenting with goniolens or decrease limbal compression in involved segment by tilting goniolens.

d. **Iritis,** especially in patients under 40 years of age, should be treated with topical steroids.

e. **Worsening of open-angle glaucoma,** about 3% incidence.

f. **Closure of the peripheral iridotomy (PI)** is more frequent (up to 40%) with argon than Nd-YAG PI.

6. **Repeat ALT** is generally not effective for long-term IOP control, is more a temporizing measure for 1 to 2 years, and has the usual risks of ALT. Retreatment using 50 µm spot, 700 to 900 mW power, 0.1-second duration, 40 to 50 burns over 180 degrees or 80 to 100 burns over 360 degrees to the treated area has resulted in a second hypotensive response for at least a year in about 21% of patients.

C. Selective laser trabeculoplasty (SLT)

1. **Indications.** SLT is a newly approved method of performing laser trabeculoplasty with a Q-switched, frequency-doubled Nd:YAG laser. Indications are similar to conventional ALT. It may be considered in patients who have a history of failed ALT, patients who have had their full complement of ALT, patients with poor compliance, and most types of open-angle glaucoma (POAG, pigmentary, pseudoexfoliation, juvenile, and angle recession). This technique specifically targets the pigmented TM cells in the absence of thermal or structural damage to nonpigmented TM cells and surrounding tissue.

2. **Contraindications.** SLT is contraindicated in inflammatory glaucomas, congenital glaucoma, narrow-angle disease, or inability to adequately view the TM (corneal opacification, lack of cooperation).

3. **Technique** is similar to ALT, with 180 degrees of the angle being treated at each session.

4. **Complications.** IOP spikes and inflammation.

5. **Repeat SLT.** Repeat treatment with SLT may be performed without increasing the

failure rate of the surgery.

D. Laser iridotomy (LI)

1. **Indications.** Argon, YAG LI, or both should always be attempted before considering surgical peripheral iridectomy. Except in chronic inflammation or rubeosis, in which a large surgical PI is less likely to close, indications for LI are a narrow “occludable” angle, postoperative

pupillary (iridovitreal) block, imperforate surgical iridectomy, malignant “ciliary” block glaucoma, nanophthalmos, and combined-mechanism (open and narrow) glaucoma.

2. **Technique of argon LI.** It is often helpful to treat the patient with pilocarpine 1% to 2% before LI to stretch and thin the iris and to maintain miosis. Instill topical anesthetic and 1% apraclonidine or 0.2% brimonidine 1 hour prelaser and immediately postlaser, to prevent a spike in pressure. A contact lens with a +66-D button such as the Abraham Wise lens dramatically improves the ease of the procedure. On the slitlamp, 25× ocular power should be used. Many methods involve pretreatment of the iris with **gonioplasty,** a peripheral arc of 100- to 300-mW, 0.2-second, 250-mm spots about 1.5 to 2.5 mm from the iris root deepen the chamber by stretching or thinning the iris. The LI is then done around 11 or 1 o'clock sites by the “chipping away technique,” in which applications are superimposed with 50-mm, 0.2-second, 700- to 1500-mW settings for light irides and 0.02- to 0.05-second, 1,000- to 1,500-mW for dark irides until the iris is penetrated with 1 to 100 applications, more for darker eyes (a puff or pigment debris heralds this). The aiming beam must be crisply focused on the iris. If corneal endothelial clouding occurs, succeeding applications will have less effect, and laser applications must be immediately stopped in this area. When “pigment clouds” are dispersed into the anterior chamber, the treating surgeon should pause to allow their clearance before continuing with more laser applications. The lens capsule must be visualized to ensure that a full-thickness opening in the iris has been achieved. Transillumination can be misleading. In enlarging the opening, the circumference of the opening should be treated rather than strands bridging across the opening. Less laser energy will thus be absorbed by the crystalline lens. The procedure is performed ideally without causing any lens “whitening.”

   If the cornea is hazy from elevated IOP, medical therapy should be used to decrease IOP and topical glycerin should be used to clear the cornea. With the “chipping away” method, one is usually able to penetrate the iris, although these “acute” LIs may close more commonly than those done in quiet eyes. If penetration of the iris is not achieved with attempted LI in an acute angle-closure eye, pupillary distortion induced by one or two 500 μm midiris laser spots often relieves pupillary block acutely with subsequent placement of the LI.

3. **Technique of YAG LI.** Premedication and lens use are the same as for argon LI. Power settings are 4 to 6 mJ and bursts of one to four pulses per shot should create

the iridotomy. More pulses may increase the chances of lens damage. The beam is aimed on the iris in an area that will be covered by the upper lid and fired at a site about two-thirds of the distance between the pupil margin and the visible periphery. Blue irides perforate more readily than brown. Additional pulses should be delivered to the edge of the opening if enlargement is needed not directly over the lens capsule. Failure to penetrate the iris is usually the result of poor focus (e.g., corneal edema), iris edema, or use of insufficient laser energy. Another area may be tried. **Combined argon and Nd:YAG** is performed (argon 0.02 to 0.05 second, 1,000 mW, 50 µm, 5 to 25 applications followed by Nd:YAG 4 to 5 mJ and one burst of two to four pulses) or the procedure is terminated and retreatment is performed later after additional therapy, as indicated, has been given.

4. **Follow-up.** An acute increase in IOP within 1 to 2 hours of LI may occur and should be managed as discussed under ALT (see sec. VI.B., above). LI can close anytime during a 6-week period (less often with YAG than argon). Therefore, it is best not to treat patients with

dilating drops at home, but rather to dilate the pupil in the physician's office at follow-up visits if necessary. Topical steroids should be used approximately tid to qid for 1 to 2 weeks and then tapered. At follow-up visits, the patency of the iridectomy should be documented by visualizing the lens capsule, and gonioscopy should be performed to document relief of pupillary block by observing deepening of the angle access. If the iridotomy closes, retreatment is necessary. At the 6-week office visit, the pupil should always be dilated to conclude that the iridectomy is patent and to rule out plateau iris.

5. **Complications**

    a. **Lens injury.** No long-term adverse effect on the lens has been documented, even in eyes with areas of lens whitening post-LI.

    b. **Elevated IOP.** This elevation is usually controlled with mild antiglaucomatous therapy. Occasionally, IOP can be elevated to very high levels, sometimes shortly after the procedure. This should be monitored and appropriately treated. Often, increased steroid dosage is beneficial.

    c. **Iritis,** spontaneous angle closure from iridectomy closing, corneal burns (especially endothelial), and corectopia may occur and require therapy as indicated.

    d. **Bleeding** is more common with Nd:YAG than argon, because it is noncoagulative. Patients should not be taking anticoagulants, if possible, and iris vessels should be avoided at time of therapy.

VII. Surgical approaches.

When medical or laser therapy fails, surgery is performed that results in a bypass of the conventional outflow pathways and allows drainage of aqueous humor from inside the eye.

Antimetabolites are often used because they improve IOP lowering efficacy. These operations are called filtration procedures and are done before the other operations discussed below. Surgical outcomes vary by race, with African-Americans faring better with laser trabeculoplasty and whites doing better with trabeculectomy.

A. Filtering operations

Filtering operations were, in the past, full-thickness procedures (corneoscleral trephine, posterior lip, and thermal sclerectomies). Because of notably fewer complications (prolonged hypotony, flat anterior chamber, choroidal effusion), however, the development of guarded filtration has made **trabeculectomy** the most common of these procedures today, with full-thickness filtration used primarily in patients with advanced or low-tension glaucoma, requiring especially low IOP (6 to 10 mm). In trabeculectomy, a partial-thickness portion of the corneoscleral limbus is excised under a partial-thickness scleral flap. Five-year follow-up has shown a mean **IOP** of 15 mm Hg. Filtration surgery is generally associated with about 50% probability of preserving vision from progression to blindness. Those with poorest prognosis have more advanced field loss at the time of surgery.

1. **Blebitis therapy.** Infection of a filtering bleb is an emergency. It is characterized by bleb purulence with or without anterior segment inflammation. If there is no clinical endophthalmitis, cultures are taken and topical ofloxacin or levofloxacin q1h round the clock is started. A systemic quinolone similar to the drops is therapeutically advisable. If there is vitritis or notable anterior chamber reaction, the approach should be the same as discussed in Chapter 9, VII, Endophthalmitis.

   Nonpenetrating filtration surgeries (**viscocanulostomy** and **deep sclerectomy** with collagen implant) have gained popularity over the past few years as alternatives to the trabeculectomy. In these procedures a partial thickness scleral flap is fashioned as in a trabeculectomy, and an additional scleral flap is dissected in the bed of the initial flap down to the level of Descemet's membrane and then excised. In

   viscocanulostomy, Schlemm's canal is entered and viscoelastic material is injected on both sides of the excised flap with the goal of clearing any resistance to outflow that exists in Schlemm canal. In deep sclerectomy with collagen implant, a collagen wick is placed in the bed of the scleral flap (with or without prior 5-fluorouracil [5-FU]) and dissolves over several months, leaving an area of filtration. Nonpenetrating filtration surgery has fewer immediate postoperative complications (hypotony, flat chamber, hyphema, or choroidal effusion), but the IOP control is not as good as with standard trabeculectomy. Up to one-third of the patients with nonpenetrating filtration surgery will require subsequent laser opening of Descemet's membrane for pressure control, converting the procedure to a conventional trabeculectomy.

B. Antimetabolites.

Use of adjunctive mitomycin C or 5-FU (fluorouracil), both cidal to fibroblasts, usually

yields IOPs lower than trabeculectomy alone and comparable to full-thickness procedures.

1. **5-FU** is increasingly used as a single intraoperative application. A cellulose sponge soaked with 50 mg per mL 5-FU is held for up to 5~minutes in the bed and then rinsed off carefully before entering the eye. The drug may also be used at the first signs of filtering bleb failure or starting 1 day postoperatively with five 5-mg subconjunctival 5-FU injections administered 90 to 180 degrees away from the bleb over a 2-week period. It should **not** be given if a corneal graft was also done.
2. **Mitomycin C** has replaced 5-FU as the antimetabolite used by a number of glaucoma surgeons, especially in darkly pigmented patients. It may be used when a corneal graft is also done, and is applied only once and at surgery. A cellulose sponge moistened with a 0.2 to 0.4 mg per mL (0.02% to 0.04%) mitomycin C is applied to the bed of the trabeculectomy flap for 1 to 5 minutes before the eye is opened, followed by profuse saline irrigation.
3. **Adverse side effects** can occur with both drugs and are less at frequent at lower doses, e.g., leaks, epithelial defects, hypotony corneal haze, conjunctival congestion, and discomfort. A therapeutic soft contact lens will decrease 5-FU-induced discomfort, but the more serious side effects indicate treatment be stopped.

C. Procedures when standard filtration fails

1. **Setons** include nonvalved devices such as the Baerveldt and Molteno, and valved devices such as Krupin and Ahmed implants. Each is a subconjunctival implant connected to a tube that enters the anterior chamber. Aqueous is shunted to the implant and diffuses away. These devices are used in refractory glaucoma or as a primary procedure in neovascular glaucoma with active iris neovascularization or keratoprosthesis, in which routine filtering surgery will likely fail.
2. **Ciliodestructive procedures** to reduce aqueous production are often last-resort treatments for intractable glaucoma, including aphakic, pseudophakic, and neovascular disease and in patients unsuitable for standard filtration surgery (poor health, mental retardation, etc.).
    a. **Cyclocryothermy,** the transscleral freezing destruction of 180 degrees of ciliary body, has been used for decades with success, but can be associated with significant patient discomfort and ocular inflammation.
    b. **Transscleral** laser cyclophotocoagulation includes use of the solid-state ruby laser, and the Nd:YAG:glass laser for destruction of the ciliary body. Laser therapy is usually superior to cyclocryotherapy in visual and IOP outcome, postoperative pain, and need for retreatment. Complications are infrequent but include hypotony or phthisis. Retreatment is required in approximately half of the patients to control IOP.

D. Goniotomy in congenital glaucoma

Goniotomy in congenital glaucoma refers to an incision with a knife into the TM (see Chapter 11, sec. XVII.).

E. peripheral iridectomy

A surgical **peripheral iridectomy** is the removal of a peripheral portion of iris, alleviating pupillary block in angle-closure glaucoma by giving an extra opening for aqueous flow between chambers (see sec. VI.D., above).

VIII. Primary open angle glaucoma (POAG)

A. General considerations.

POAG is the most common form of glaucoma, affecting 1% to 2% of the world population; POAG is four to five times more common in African-Americans. In most cases, the disease develops in middle life or later and can be familial. The onset is usually gradual and asymptomatic, and tends to become progressively worse. The angle remains open at all times. Despite a normal appearance on gonioscopy, the TM outflow channels are functionally abnormal, and the facility of aqueous outflow from the anterior chamber is constantly subnormal in most cases (see sec. II.A., above). The diurnal IOP may vary from normal to significantly elevated levels. This most likely represents variation in the rate of aqueous secretion, while the outflow facility remains subnormal. The facility of aqueous outflow usually becomes worse with time. Sometimes with age there is also a decline in the rate of aqueous production, and therefore this progressive impairment of outflow facility does not invariably result in further elevation of IOP. Nevertheless, in most cases, stronger medical therapy is required to control the IOP.

B. Glaucoma detection

1. A **spectrum** exists from normality to borderline abnormality to early glaucoma to frank glaucoma. The test of time is most useful in identifying patients with early glaucoma. Patients with an IOP of 22 mm Hg or greater, or those with optic disks with suspicious or asymmetric cupping regardless of the IOP (see sec. XIV., below), should be followed as **glaucoma suspects** or **ocular hypertensives.** POAG differs from ocular hypertension in that the latter is a primary condition manifested by elevated IOP in the presence of open angles, but with no evidence of optic nerve damage or field loss. Approximately 2% of the population has ocular hypertension. About 5% of ocular hypertensives with IOP of 25 to 30 mm Hg will go on to develop nerve damage and field defects within 10 years. The diagnosis is then changed to POAG and appropriate therapy started. Therapy may also be started in the absence of damage if the IOP is sufficiently high, i.e., high 20s to low 30s, because it is likely that damage is inevitable should treatment be withheld.

2. **Glaucoma suspects** should be followed two to four times a year with IOP measurements and with careful inspection and drawing of the optic nerve cupping. Stereo disk photographs are useful. Visual fields should be performed once a year and optic nerve head and NFL analyses may also be performed on a periodic basis.

3. **Monocular glaucoma.** POAG always affects both eyes, although the disease may be more advanced in one eye. If glaucoma is truly monocular, other causes of secondary glaucoma must be investigated. Gonioscopy is often useful in diagnosis.

C. Symptoms.

POAG is almost always a silent disease process with slowly progressive elevation of IOP. Occasionally, in younger patients, rapid increases in IOP may occur that result in corneal epithelial edema and symptoms of haloes, blurred vision, and pain, much as in pigmentary glaucoma (see sec. XV., below).

D. Indications for treatment

1. **Early stage POAG.** The optic nerves of different patients differ in their susceptibility to the same level of IOP. For example, certain patients with NTG will show progression of disk cupping at ostensibly normal IOP (<22 mm Hg). It is generally believed that optic disks with thicker neuroretinal veins tolerate a given level of IOP better than those with thinner veins and glaucomatous damage. Patients off therapy generally require close follow-up. It is useful to check the IOP

at different times of day at different visits to detect significant diurnal peaks.

Often in early glaucoma, it is a borderline decision whether the patient should be treated. It is often useful to explain the situation and to let the patient have input into the decision. Often a trial of medical therapy to one eye is of value; if side effects occur, the patient may be followed off therapy a while longer. If therapy is efficacious and well tolerated, the patient often will prefer to have continued treatment, at least in one eye, often in both. In addition, by treating one eye initially, the efficacy of the therapy can be better evaluated.

2. **Change in disk cup appearance** indicates that medical therapy should be initiated. Different ophthalmologists have different cutoffs of IOP above which medical antiglaucoma therapy will be initiated regardless of disk appearance. With tensions chronically in the low 30s, glaucoma therapy should be routinely begun, provided there are not significant side effects. Certainly all patients with tensions in the upper 30s to 40s should be treated. Patients with wide cupping (even though it may be physiologic) with pressures in the upper 20s should also be treated. Patients with some glaucomatous damage to the nerve are treated to lower their IOP into the normal range (at least initially below 22 mm Hg).

3. **Progressive disk cupping or field changes in follow-up,** regardless of measured IOP, indicate that pressure is too high for the optic nerve and that further therapy

should be added. Similarly, patients who present with extreme glaucomatous damage and IOP in the low 20s require vigorous therapy to achieve as low a pressure as possible (10 to 12 mm Hg). Even if the IOP is subnormal with medical and laser therapy, should future progression occur (as often may happen in patients with totally cupped disks and extensive field loss), then glaucoma filtering surgery is indicated to achieve as low an IOP as possible.

4. **Medical therapy** is usually begun with a beta-blocker, a topical CAI, an alpha-agonist, or a prostaglandin analog. ***Miotics*** are usually ***avoided in younger patients*** because of the accommodation and miosis. Allergies may occur with topical CAIs and alpha-agonists. Most but not all older patients tolerate pilocarpine well. With increased medical therapy, combinations of topical agents are often effective oral CAIs. Laser trabeculoplasty is usually reserved for patients not well controlled on maximum topical therapy, although it may reasonably be the initial treatment. It can be used at any point with medical treatment should IOP be inadequately controlled or if the patient cannot tolerate medical treatment.

5. **If maximum medical therapy** (i.e., that treatment the patient is able to tolerate locally and systemically) **fails** to control the IOP, glaucoma filtering surgery is indicated.

IX. Primary acute angle-closure glaucoma

A. Clinical findings

1. **Symptoms.** In acute angle-closure glaucoma, the relative pressure in the posterior chamber is increased as a result of pupillary block, and the peripheral iris is forced forward over the TM. The IOP increases rapidly because of the sudden blockage of aqueous outflow, resulting in the acute onset of severe pain, blurred vision, and perception of colored haloes about lights. The last two symptoms are from corneal epithelial edema that results from the rapidity of the IOP increase. The pain is usually quite severe. Often, it is not localized to the eye but involves the whole head and may be accompanied by nausea and vomiting. **The correct diagnosis may be missed by physicians who are not ophthalmologists, because they may misinterpret the headache and abdominal symptoms.**

2. **Signs.** Corneal epithelial edema can be detected on flashlight examination as a fine, rough haziness in the light reflex. The pupil is usually middilated (4 to 5 mm) and nonreactive to light, and the eye is red. Slitlamp examination reveals a shallowness of the axial and peripheral anterior chamber. There may be significant flare and a few cells as well in the anterior chamber. If the IOP has been elevated for a prolonged period during a previous attack, gray atrophy of the iris stroma and glaukomflecken (small white opacities in or under the anterior lens capsule) may be observed. Gonioscopy should be performed after clearing the corneal epithelial edema with topical glycerin (after a drop of topical anesthetic) and should confirm

the angle closure (the peripheral iris covering over the TM).

B. Differential diagnosis

1. The physician should look carefully for the presence of new blood vessels or inflammatory cells on the iris and in the angle that would indicate a diagnosis of **neovascular or uveitis angle-closure glaucoma** rather than primary angle-closure glaucoma. The differential diagnosis also includes **acute open-angle glaucomas,** such as glaucomatocyclitis crisis or other uveitides, and pigmentary glaucoma. The physician should always examine the fellow eye with a gonioscope to confirm that it also is narrow and potentially closeable, with prominent iris convexity and the scleral spur not visible. If the fellow eye is not narrow, the physician should be careful that the correct diagnosis has in fact been made in the first eye and should then consider the differential diagnosis of true **monocular angle-closure glaucoma.** This includes acute central retinal vein occlusion, dislocated lens, phacomorphic glaucoma choroidal detachment or effusion, peripheral anterior synechiae secondary to uveitis, essential iris atrophy, and significant anisometropia (extreme difference in refractive error). In the emergency room, the diagnosis most commonly involves distinguishing primary angle-closure glaucoma from neovascular glaucoma.
2. **Inflamed red eyes** should always be suspicious for possible angle-closure glaucoma. In acute **conjunctivitis** there is usually a discharge with cells in the tear film, the cornea is clear, the vision is near normal, pupillary size and reaction are normal, and there is no true pain, unlike acute glaucoma. If the physician is suspicious of glaucoma in a red eye, it is important to measure the IOP. The Schiötz tonometer with a tonofilm cover is very valuable in these cases. In acute **anterior uveitis,** the pupil is usually small (unlike the middilation in acute glaucoma), the redness is more prominent in the area about the limbus, and the anterior chamber usually contains significantly more cells and flare than in acute angle-closure glaucoma. The cornea in uveitis is usually clear except for the presence of keratic precipitates. The vision is usually blurred and there may be considerable pain. All patients with uveitis should have their IOP measured, both to rule out angle-closure glaucoma and to detect the secondary open-angle glaucoma that may accompany uveitis, especially in the later stages.

C. Therapeutic implications of pupillary block.

A coincidence of various physiologic and anatomic factors is responsible for an increase in pupillary block of posterior chamber aqueous flow to the anterior chamber, so that iris is pushed forward to cause angle closure. Pupillary size, rate of aqueous formation, rigidity of the iris, and axial position of the lens all influence the magnitude of pupillary block.

1. **Pupillary middilation** produces an increase in relative pupillary block. This middilated position may occur spontaneously because of illumination, e.g., an attack

may occur when a patient visits a movie theater, or it may result from either topical or systemic administration of a pupillary dilating agent such as cyclopentolate, phenylephrine, or

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atropine. Patients with narrow angles are asymptomatic before and after acute angle-closure attacks. The dilating agents must be used with care in patients found to have shallow anterior chambers on routine flashlight or slitlamp examination (see sec. III.A. and sec. III.B., above). The importance of assessing anterior chamber depth in ostensibly normal patients before use of these agents needs to be emphasized. In suspicious cases gonioscopy should be performed. Although topical agents are more frequently involved, cases of angle-closure glaucoma have been precipitated by **systemic** use of **atropine-like drugs** and inhalation of **bronchodilators.**

2. **Treatment of acute angle-closure glaucoma with miotics** moves the pupil from the middilated state to a smaller size, where there is less relative pupillary block. With excessive miosis, however, as may occur with use of **anticholinesterase agents,** an increase in relative pupillary block may actually occur, and thus these agents are **contraindicated in angle-closure glaucoma.** In addition, use of higher strengths of pilocarpine (4% to 6%) and other stronger miotics may move the lens forward because of zonular relaxation subsequent to ciliary muscle contraction, and this may actually increase relative pupillary block. For this reason, lower concentrations of pilocarpine (1% to 2%) are used initially to treat angle-closure glaucoma. Thus, in treatment of angle-closure glaucoma, ciliary muscle contraction may be an undesired side effect of pilocarpine therapy.

3. **Maximum pupillary dilation** pulls the iris sphincter away from the lens, and this relieves pupillary block. Attacks of angle closure may actually be broken by maximum pupillary dilation, although for surgical and laser considerations this is less desirable than miosis. After use of a topical mydriatic, the pupil may rapidly pass through the stage of middilation without angle closure, only to have a full-blown attack occur as the pupil returns from the widely dilated state toward a more normal size.

4. By **decreasing aqueous production, beta-blockers, alpha-agonists, and CAIs** may decrease the relative pressure force in the posterior chamber and lessen relative pupillary block. It is important to perform gonioscopy in the fellow eye before administration of CAIs or osmotic agents, which dehydrate the vitreous, because these agents may effect a temporary deepening of the anterior chamber.

5. **Small attacks of angle-closure glaucoma** may be spontaneously arrested by spontaneous movement of the pupil and by decrease in the rate of aqueous formation. The latter may occur temporarily as a result of the sudden elevation of IOP. Following an attack the eye may become hypotonous, and with the presence of some cells and flare, a mistaken diagnosis of uveitis may be made. Clues to the presence of previous attacks are areas of gray iris stromal atrophy, glaukomflecken, and shallow anterior chamber depth (also in the fellow eye). A history of episodes of colored haloes, pain, and blurred vision should be sought. Provocative tests, such as

the dark room prone test, should be performed (see sec. X.C., below).

D. Treatment of acute angle-closure glaucoma

1. Topical aqueous suppressants, miotics, and CAIs (either orally or i.v.).
2. **Systemic hyperosmotics** (glycerol or isosorbide p.o., or mannitol i.v. [see sec. **V.I.,** above, for dosage]) and i.v. acetazolamide (250 to 500 mg) should be given initially to lower the IOP below 50 to 60 mm Hg. Topical medications should be updated to lower the pressure further. At higher pressures the iris sphincter is ischemic and unresponsive to pilocarpine. Because miotics may allow forward lens movement by relaxation of zonular tension, a reduction in vitreous volume via the use of osmotics is probably useful in most cases. **Pilocarpine 1%** should be administered initially q15min. If the attack fails to respond to this

therapy, higher strengths of pilocarpine, up to 2% ***(not higher, or pupillary block may increase),*** may be substituted.

Once the IOP is lowered, it is important to examine the patient with a gonioscope to ensure the angle has opened. Use of osmotics, beta-blockers, and CAIs may result in a temporarily lowered IOP despite persistent angle closure.

3. **Once the attack is broken,** LI should be performed (see sec. VI.C., above). If this procedure is delayed, the patient is usually maintained on pilocarpine 1% q4 to 6h until LI. The fellow asymptomatic eye may also be treated prophylactically. It is often useful to treat the patient with topical PF in addition to glaucoma medications for 1 to 2 hours before PI to allow the cornea to clear and to quiet the eye.
4. If medical therapy fails to break the attack, then LI should be performed as an emergency procedure. The use of osmotics almost always results in a temporarily sufficient IOP lowering and in less need for emergency surgery. The IOP, however, should not be allowed to remain above 60 mm Hg for more than a few hours, because permanent loss of vision from optic atrophy may result. If LI cannot be performed and if high pressure persists, surgical peripheral iridectomy should be performed.
5. **Prolonged attack** may result in permanent adhesions of the peripheral iris to the meshwork; i.e., **peripheral anterior synechiae** may form. In such cases, peripheral iridectomy will relieve pupillary block but will not restore normal IOP because of the residual chronic angle closure. LI with follow-up gonioscopy will help assess angle closure. If laser is unsuccessful, however, at the time of surgery a **chamber deepening technique** should be performed. The apparent angle closure viewed preoperatively may be due to a potentially reversible apposition of iris to TM or to true synechiae. In the chamber deepening technique, fluid is injected into the anterior chamber via a limbal paracentesis slit opening and gonioscopy performed to assess the extent of the peripheral anterior synechiae formation. If extensive peripheral anterior synechiae have formed (more than 90% of the angle), a filtering

procedure rather than a peripheral iridectomy should be performed. (New techniques are being developed in which laser applications to the peripheral iris, termed *iridogonioplasty,* may break recently formed peripheral anterior synechiae with functional improvement in outflow) (see sec. VI.C.2., above.)

6. **Prophylactic laser peripheral iridotomy** should be performed on the fellow asymptomatic eye within a few days after surgery on the first eye, unless there are circumstances of true monocular angle closure.

X. Subacute and chronic primary angle-closure glaucoma

A. Subacute and chronic angle-closure glaucoma

Subacute and chronic angle-closure glaucoma result if the iris does not cover the TM in the full circumference of the angle. This may cause intermittent moderate elevation of IOP that is roughly proportional to the extent of closure. These subacute episodes may occur with mild symptoms of colored haloes, blurred vision, and red eye. A condition of continuous chronic partial-angle closure may occur and mimic open-angle glaucoma in its lack of symptoms and maintained elevation of IOP.

B. Differentiation

Differentiation of chronic angle-closure glaucoma from open-angle glaucoma with narrow but open angles in which full width of TM can be seen is important. In cases of suspected partial chronic angle-closure glaucoma, the relative effects of bright light, thymoxamine (alpha-blocker) drops, or weak (0.5% to 1.0%) pilocarpine on gonioscopic angle appearance and IOP may establish the correct diagnosis. **Thymoxamine** causes miosis but has no effect on facility of outflow.

C. The dark room prone test

The dark room prone test may be done on patients with suspiciously narrow angles who are not seen during an acute attack and who do not have glaukomflecken or gray iris stromal atrophy. This test may be

utilized to identify dangerously narrow (but open at the time of examination) angles. In this test, IOP is measured and the patient is seated for 30 to 60 minutes in a darkened room with his or her head down on a cushioned table. The IOP is again measured in the darkened room. An increase of 6 to 8 mm Hg or greater or a significant asymmetric rise in pressure between the two eyes that is accompanied by gonioscopic confirmation of further angle closure is a positive test, and a prophylactic LI is indicated. It is important to perform all phases of this test in a darkened room. Miosis from external light or from the focal illuminator during gonioscopy may quickly reverse the angle closure. Placing the patient in a brightly lit room for 5 minutes after this test and observing a significant reduction of IOP will further confirm a positive test.

D. A pharmacologic mydriatic test

A pharmacologic mydriatic test (2.5% phenylephrine) is sometimes used as a provocative test. Such a test is distinctly nonphysiologic and has significant false negatives. Most important, the angle may not close during the pupillary dilation, but rather may close many hours later as the pupil contracts. If such a test is performed, the patient should be kept under observation for several hours until the pupil returns to normal size.

XI. Plateau iris.

Very rarely, a mechanism of primary angle closure may be the direct expansion of the peripheral iris against the TM as the peripheral iris thickens during pupillary dilation. This mechanism is independent of, but may coexist with, pupillary block and is called a *plateau iris*.

A. Slitlamp examination

Slitlamp examination reveals a discrepancy between the central anterior chamber which is deep and the peripheral anterior chamber which is narrow. On gonioscopy the iris plane is somewhat flat, and the peripheral iris is very close to the TM, with a characteristic small roll and trough just before the iris insertion on the ciliary body band.

B. Therapy

Therapy of patients with angle-closure glaucoma who have a plateau iris configuration includes an LI and, during convalescence, a provocative test with a weak mydriatic. A patient with true plateau iris will demonstrate a pressure elevation and gonioscopic angle closure. Such patients are managed successfully with long-term weak miotic therapy that prevents pupillary dilation and iris crowding of the angle. In those patients with a negative provocative test with pupillary dilation postiridectomy, it is believed that pupillary block was the mechanism of the preoperative angle closure despite the suspicious plateau configuration. The majority of plateau configuration patients fall into this latter category, which is why peripheral iridectomy should always be performed first in these patients.

XII. Differential diagnosis of pressure elevation following surgical peripheral iridectomy for angle closure

A. Plateau iris.

Treat with weak miotics.

B. Imperforate peripheral iridectomy.

Treat with a laser or repeat iridectomy.

C. Malignant glaucoma

Malignant glaucoma is a condition in which there is maintained increase in total vitreous

volume (or perhaps classically a pocket of aqueous trapped in or behind the vitreous) that results in flattening of the anterior chamber and closure of the angle. It occurs postoperatively after glaucoma or cataract surgery. Key to the diagnosis is a marked shallowing of the axial anterior chamber depth that results from the vitreous expansion. B-scan ultrasound will rule out choroidal detachment or suprachoroidal hemorrhage. A patent PI rules out pupillary block. **Treatment** consists of administration of daily 1% atropine drops used indefinitely, beta-blockers, CAIs, and short term systemic osmotics. If this is not successful, vitreous aspiration with puncture of the hyaloid is required. Aphakic eyes almost never respond to medical treatment.

D. Topical cycloplegic and steroid postoperative medications

Topical cycloplegic and steroid postoperative medications may be responsible for elevated IOP through an ill-defined open-angle glaucoma mechanism. Such therapy may result in elevation of IOP in patients

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with POAG more characteristically. Axially, the anterior chamber is not flattened, and the glaucoma responds to cessation of the drops.

E. Extensive peripheral anterior synechiae

Extensive peripheral anterior synechiae may progress if iridotomy fails to break the attack because synechiae already exist. Filtering surgery should be performed following the chamber deepening procedure.

XIII.Combined open-angle and angle-closure glaucoma

A. Angle-closure glaucoma

Angle-closure glaucoma can occur occasionally in patients who have or subsequently develop **open-angle glaucoma.** Whether the latter is POAG or a result somehow of the episodes of high pressure elevation while the angle was closed is disputed. It has definitely been noted that some patients develop open-angle glaucoma several years after successfully treated angle-closure glaucoma.

B. Gradual, progressive partial angle-closure glaucoma

Gradual, progressive partial angle-closure glaucoma may occur in some patients with well-documented, long-standing POAG. With aging, most individuals, both those with and without glaucoma, will show some tendency toward shallowing of the angle, most likely the result of an increase in size of the lens. The effect of miotic therapy on lens position may also be a factor. This partial angle closure will result in further chronic pressure elevation. Patients whose POAG worsens with therapy or age should always be **reexamined with a gonioscope** to rule out coexisting additive partial angle closure (or other unusual glaucoma, such as occult KPs in the meshwork). When 120 degrees or more of the angle is judged to be closed and the recent IOP course is consistent, LI is usually indicated.

C. Subacute or chronic angle-closure glaucoma suspects

Subacute or chronic angle-closure glaucoma suspects may, with the application of bright light, thymoxamine, or weak pilocarpine, have a dramatic lowering of IOP and total opening of the angle, although the IOP is still definitely above normal. Such patients should be suspected of having combined open-angle and angle-closure glaucoma and residual glaucoma after an LI.

XIV. Normal-tension (low-tension) glaucoma (NTG).

The optic nerves of different patients have differing susceptibilities to similar levels of IOP. In the extreme, there are certain patients who demonstrate progressive disk cupping and field loss with normal or mildly elevated IOP. Such patients are generally referred to as having NTG and are usually elderly. About 10% to 50% of all POAGs fall into the low-tension glaucoma category. Factors predisposing to progressive nerve damage include preexisting wide physiologic cupping and factors affecting nerve perfusion such as faulty vascular autoregulation, arteriosclerotic vascular disease, systemic hypotension, carotid artery disease, arrhythmias, and diabetes mellitus. A cardinal sign of **optic nerve ischemia** is **flame-shaped hemorrhaging on the disk** in up to 40% of patients (rarer in POAG), making treatment all the more urgent. **Medical therapy** is aimed at rapidly reducing the IOP to the lowest level possible, not just at treating on the basis of current extent of cupping and field loss. A full medical evaluation should be carried out and systemic therapy, medical or surgical (e.g., carotid), to control problems relating to vascular perfusion initiated. Neuroimaging should be considered in patients with optic nerve pallor out of proportion to cupping or in patients with a significant color vision deficit. **Calcium channel blockers** are vasodilators and may have some favorable but unproven therapeutic effect on NTG (see sec. **V.J.,** above). **Laser trabeculoplasty** has only equivocal effects. Because of the low level of IOP that causes nerve damage, **filtration surgery** is frequently the only means of obtaining a low enough IOP.

XV. Pigmentary dispersion syndrome and glaucoma

Pigmentary dispersion syndrome and glaucoma are the result of primary loss of pigment from the posterior surface (neuroepithelium) from the midperipheral iris. This pigment is disseminated intraocularly and deposited on various intraocular structures such as the corneal endothelium, where it may form a **Krukenberg spindle,** and in the TM, where it forms a dense continuous band of pigment throughout the circumference. The latter may

occur with inconspicuous corneal endothelial pigmentation—a reason the condition may often be missed.

A. Time of onset

Time of onset is at a younger age than most other open-angle glaucomas; it appears in the 20- to 40-year-old group. The occurrence of this glaucoma in young myopic males is another good reason to perform routine applanation tonometry in all cooperative patients regardless of age.

B. Wide fluctuations in IOP

Wide fluctuations in IOP may result in crises of high pressure elevation with corneal epithelial edema. Gonioscopy always shows the angle to be open and to contain the characteristic pigment band. Liberation of large amounts of circulating pigment into the anterior chamber is sometimes associated with these pressure elevations, and may be misinterpreted as cells of uveitis. In a few patients, exercise may induce such anterior chamber pigment liberation. During routine visits small numbers of circulating pigment particles can occasionally be seen in the anterior chamber in pigmentary dispersion syndrome patients. Because of the wide pressure fluctuations in this condition, a single normal IOP does not rule out the presence of pigmentary glaucoma. Approximately half of the patients with pigment dispersion syndrome will eventually develop glaucoma.

C. Examination

Examination by viewing the iris stroma directly will not reveal the loss of posterior iris pigment (although occasionally pigment can be deposited on the anterior iris surface). **Transillumination** using a fiberoptic light source applied to the lower lid or sclera, or pupillary transillumination on the slitlamp will demonstrate typical linear slit-like defects in the midperiphery of the iris, which is the key to the diagnosis. Gonioscopy often reveals significant backbowing of the peripheral iris, in addition to a dense pigment band covering the TM. In the presence of an elevated IOP, if sufficient backbowing of the iris is present, some authorities advocate laser iridotomy to relieve the “reverse” pupillary block that is postulated to exist in pigment dispersion.

D. Treatment

Treatment is similar to that for POAG. Because of the patient's younger age and accommodation, however, there is poor tolerance to miotics, except perhaps the pilocarpine Ocusert.

XVI. Pseudoexfoliation syndrome (PXF)

A. Clinical findings

Clinical findings in PXF include an amorphous gray **dandruff-like** material present on the pupillary border, anterior lens surface, posterior surface of the iris, zonules, and ciliary processes. This may represent basement membrane material from multiple ocular sites. The central area of the anterior lens capsule often has a dull, lusterless appearance through the undilated pupil; when the pupil is dilated the gray membrane is seen to end in the midperiphery in a scalloped border, often with curled edges. **Transillumination** of the iris frequently reveals loss of pigment from the posterior iris surface adjacent to the pupil, in contradistinction to pigmentary dispersion syndrome, in which defects occur in the midperiphery. This loss of pigment from the iris may result in an abnormal accumulation of pigment in the TM.

B. Glaucoma may or may not occur in PXF.

Dandruff may be observed as an incidental finding during a routine examination in a patient with normal IOP. Such patients should be followed for possible future development of glaucoma, because exfoliation syndrome is often associated with a chronic open-angle glaucoma that may be initially monocular. Exfoliation glaucoma behaves similarly to and is **treated** like POAG. It may become more resistant to medical treatment with time than POAG, but fortunately is the type of glaucoma that usually responds best to laser trabeculoplasty.

XVII. Glaucoma from contusion of the eye

A. Early onset

1. **Acute glaucoma** may follow blunt trauma to the eye. This condition may be secondary to direct contusion injury to the trabecular angle

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tissue, or it may be because of the deposition of inflammatory or blood elements from traumatic hyphema in the outflow pathways. The obstruction of aqueous outflow may be masked by coexisting hyposecretion of aqueous humor that may occur for a variable period following the injury.

2. **Treatment** of acute traumatic glaucoma consists of use of aqueous suppressants and oral CAIs. Topical **miotics** should be **avoided** because they possibly promote posterior synechiae and increase the inflammation in the eye. Should the IOP fail to be controlled with persistent pressures above the upper 40s, paracentesis and irrigation of the blood elements should be performed.

3. **Chronic erythroclastic (ghost cell) glaucoma** may be seen with prolonged hyphemas, but more commonly with vitreous hemorrhages in which the blood elements may remain in the vitreous for several days before passing into the anterior chamber. Red blood cells may degenerate into red cell ghosts with rigid cell membranes and **Heinz bodies** that are much more obstructive to aqueous outflow than the more pliable, fresh red cells, and a severe glaucoma may result. These red cell ghosts are khaki or off-white in color and must be distinguished from the white blood cells in inflammation. **Treatment** of chronic ghost cell glaucoma consists of use of topical aqueous suppressants and oral CAIs and, these failing, paracentesis and anterior chamber irrigation. If significant increased IOP persists, vitrectomy to remove hemorrhagic debris may be necessary.

4. **Uveitis** often accompanies the acute contusion injury and should be treated with topical cycloplegics and steroids. If there is a severe acute uveitis, the IOP is usually low due to hyposecretion. Occasionally, the glaucoma following within days of contusion injury may respond somewhat to topical steroids, and they should be attempted in this time period. In persistent glaucoma the physician should be careful to identify correctly the presence of ghost cell glaucoma, which does not respond to

topical steroids.

B. Late onset

1. **Angle-recession glaucoma** may occur months to many years after blunt injury to the eye. It results from contusion to the trabecular angle tissue with associated tears in the uveal meshwork and ciliary muscle causing a more posterior, i.e., recessed, insertion of the iris onto the ciliary body band. This recession is not the cause of the glaucoma per se, but is associated with the glaucoma-producing trabecular injury. It is subtle, and **simultaneous gonioscopy in both eyes** is best to identify it correctly. Although acute tears may be observed in the TM, these heal with time. In chronic angle-recession glaucoma, the TM itself may not appear abnormal.
2. **Evaluation of patients with significant blunt trauma** to the eye that results in hyphema should include gonioscopy several weeks after the injury to identify possible angle recessions. Patients so identified, usually with greater than 180 degrees of recession, are at some risk of developing glaucoma in the future and should be so informed and followed. Fortunately, the majority of such patients will not develop glaucoma. Tonography may be of value in determining the frequency of follow-up.
3. **Differential diagnosis** of subtle angle recession must include other causes of true monocular glaucoma. Simultaneous gonioscopy must be performed to rule them out.
4. **Treatment** of angle-recession glaucoma is the same as that for POAG. It may become refractory in the later stages. It may also be associated with the histological development of a cuticular membrane in the angle.

XVIII. Glaucoma due to intraocular inflammation

A. Anterior uveitis

1. In **acute anterior uveitis** there is probably some obstruction to outflow that is masked at least initially by the more predominant hyposecretion of aqueous that results in hypotony. Later in the course, when with topical steroid treatment, aqueous production increases, this obstruction may become manifest with an elevation of IOP.
2. **Steroid-induced open-angle glaucoma** may also be involved in certain patients. When faced with open-angle glaucoma in uveitis, it is usually unclear whether more or less topical steroid should be given. A trial of the former is usually useful to treat possible inflammation in the meshwork.
3. **Angle-closure glaucoma** may also result from uveitis from posterior iris–lens synechiae formation causing **pupillary block with iris bombé.** Peripheral anterior

synechiae may also form from primary inflammatory adhesions in the angle without pupillary block.

4. **Treatment** consists of using topical aqueous suppressants and oral CAIs and increasing or decreasing the steroid dosage. Miotics are contraindicated. In treating inflammatory pupillary block, medications, usually intensive mydriatic–cycloplegic therapy, should be utilized to move the iris away from the lens into a dilated stage. If this fails, laser peripheral iridotomy will relieve the pupillary block.

B. Glaucomatocyclitic crisis (Posner-Schlossman syndrome)

1. **Crises of intermittent unilateral acute open-angle glaucoma** that are associated with very minimum but definite signs of anterior chamber inflammation characterize this disease of unknown etiology. Usually only a few cells and one or two areas of smudginess on the corneal endothelium are observed. Corneal epithelial edema may be present due to the sudden IOP increase. The eye is only mildly hyperemic and the patient has only slight discomfort. Repeated attacks may occur over the years and be benign. On the other hand, a patient may go on to develop chronic uveitis and open-angle glaucoma in later years. There is usually a great discrepancy between the acute glaucoma and the amount of anterior segment inflammation. Recent studies have shown **herpes simplex** antigen in the aqueous and therapeutic response to p.o. acyclovir.

2. **Gonioscopy** always reveals the angle to be open, although occasionally KPs are seen. The disease must be distinguished by gonioscopy from acute angle-closure glaucoma.

3. **Treatment** consists of beta-blockers, epinephrine, DPE, CAIs, or topical steroids, or any combination, and possibly a 10-day course of acyclovir. An attack may spontaneously abate without treatment within a few days to weeks.

C. Herpes simplex and zoster.

Open- or closed-angle glaucoma may occur in these diseases associated with uveitis. Either may have an early or late **trabeculitis** in a white and quiet eye, but with notable increase in IOP. Treatment is primarily high-dose topical steroids with taper and antiglaucoma drops as needed. If the pressure increase is not from trabeculitis but from steroids therapy, aqueous suppressants (not miotics) should be utilized to treat the IOP in addition to adjustments in steroid dosage discussed above (see sec. XVIII.A.4., above; Chapter 5, sec. IV.D. and sec. IV.E.; and Chapter 9, sec. VIII.A.2, sec. VIII.A.3.). Prostaglandin analogs should be used with care in patients with herpetic eye disease because they may cause uveitis. Patients with known ocular herpes simplex should be considered for prophylactic acyclovir 400 mg p.o. bid if taking prostaglandin analogs. Prostaglandin analogs should be used with some caution because they may exacerbate the

underlying inflammation.

D. Fuchs heterochromic iridocyclitis

Fuchs heterochromic iridocyclitis is characterized by chronic anterior uveitis in a white and quiet eye with no synechiae formation, but with

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iris heterochromia (usually the lighter iris) and cataract formation. Filamentary precipitates on the corneal endothelium are also typical. This form of iridocyclitis is probably degenerative rather than inflammatory.

1. **Glaucoma** develops probably in a minority of such patients. It usually occurs late and develops gradually, although it often proves **refractory to topical medical therapy.** This may be due to a hyaline membrane histology.
2. **Treatment** is standard anti-open-angle glaucoma therapy and then LTP. If this fails, patients do well with filtration surgery. Cataract surgery is also uncomplicated, but does not influence the course of the glaucoma. Topical steroids do not influence the glaucoma.

E. Keratic precipitate (KP) glaucoma

Keratic precipitate (KP) glaucoma in the angle may occur occultly in a white and quiet eye with no apparent intraocular inflammation, but with elevated IOP that may mimic POAG. This condition is another reason to examine all glaucoma patients with a gonioscope. The precipitates may be very subtle and are best seen by retroillumination. With time they may organize and result in irregular peripheral anterior synechiae and an uneven insertion of the iris in the angle. This occult disease responds well to **topical steroid therapy,** but not to conventional topical antiglaucoma therapy, except perhaps timolol. Patients with presumed POAG who are placed on treatment and return with no apparent effect or even higher IOP should always be reexamined with a gonioscope to rule out this (and other) causes.

XIX. Neovascular glaucoma

A. Clinical characteristics.

In certain patients with long-standing hypoxic retinopathy such as **diabetes, central retinal artery or vein occlusion, or carotid artery insufficiency,** a fibrovascular membrane will grow over the TM and ultimately result in total angle closure. Glaucoma may be present at a time when the membrane has not yet contracted and caused synechiae formation and the angle is still “open.” Patients present with acute glaucoma that must be distinguished from primary angle-closure glaucoma by the presence of new blood vessels in the angle and almost always on the surface of the iris as well. Topical glycerin should be used to clear the corneal edema. A history of severe visual loss several months before the glaucoma may be helpful in identifying patients with central retinal vein occlusion. Other retinopathies and

malignant melanoma may be associated with the development of neovascular glaucoma in rare cases.

B. Treatment.

In eyes with total angle closure, treatment consists of use of aqueous suppressants and oral CAIs (methazolamide if renal function is impaired) to lower the IOP and topical steroids and cycloplegics for comfort. If the visual potential is good, filtration surgery or tube shunt placement often succeeds. Ciliodestructive procedures are now improved and often successful, although they are the last resort (see sec. **VII.C.3.,** above). In eyes with early neovascular glaucoma, panretinal photocoagulation will often lead to a regression or delay in the disease process.

XX. Abnormal episcleral venous pressure

A. Intracranial vascular malformations

Intracranial vascular malformations, such as those seen in patients with carotid–cavernous sinus fistulas and dural shunts in patients with Sturge-Weber disease, may produce an elevation of venous pressure that is transmitted back to the eye and results in a secondary open-angle glaucoma. This **elevated episcleral venous pressure** may also occur idiopathically in certain glaucoma patients. Usually a key to the diagnosis is the presence of prominent or abnormal episcleral vessels on slitlamp examination. These prominent episcleral vessels may be misinterpreted as indicating episcleritis or other inflammatory disease.

B. Treatment

Treatment is standard open-angle glaucoma therapy, although the IOP cannot be lowered below true episcleral venous pressure, because the vessels constitute the draining bed for aqueous humor after it has passed

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through the angle tissue. Glaucoma filtering surgery may be successful, although these patients are at risk of developing **intraoperative choroidal effusions** due to the elevation of venous pressure. This should be anticipated and treated intraoperatively by a preliminary posterior sclerotomy.

XXI. Corticosteroid glaucoma

A. Clinical characteristics.

Steroid glaucoma is anatomically indistinguishable from POAG: the pressure is elevated, angles are open and appear normal, outflow facility is decreased, and, with time, the nerves are progressively cupped and visual fields are compromised. Increased IOP may develop within 2 weeks of initiating steroid use or after many months or even years of use. The more potent agents such as dexamethasone and prednisolone are more likely to induce pressure increases sooner and higher than softer agents such as loteprednol, rimexolone,

or fluorometholone. Patients who were formerly but no longer taking steroids and who had steroid glaucoma may be misdiagnosed as having low-tension glaucoma because of the presence of glaucomatous cupping, visual field defects, and normal pressures. Successfully controlled glaucoma patients may go out of control if steroid therapy is added to their drug regimen, and infants treated with steroid may develop a picture similar to that of primary congenital open-angle glaucoma. Close relatives of patients with POAG stand a significantly greater chance of developing steroid glaucoma (20%) than the rest of the population (4%). **The history of patient steroid drug therapy is essential to making the correct diagnosis.**

B. Medical therapy

Medical therapy is first and foremost to stop or at least reduce the steroids or switch to loteprednol, rimexolone, or fluorometholone if possible. Reducing or discontinuing the drug will almost invariably result in spontaneous resolution of increased IOP within 2 to 6 weeks. If IOP does not return to normal but is reduced simply by discontinuing the steroid, it is likely that an underlying undiagnosed POAG was simply unmasked or aggravated by steroid usage. There is no definitive proof that these drugs cause permanent alterations in the ocular outflow channels. If steroids cannot be stopped or if the IOP is unacceptably high while waiting for spontaneous resolution, therapy as for POAG may be initiated to prevent progression of ocular damage. Alpha-agonists, CAIs, beta-blockers (except in asthmatics taking steroids), miotics (except in inflamed eyes), and sympathomimetics all may have a beneficial effect in this form of glaucoma.

C. Surgical therapy

Surgical therapy is rarely used for this condition and only in those cases where IOP does not return to acceptable levels despite stopping steroids and initiating antiglaucoma medical treatment. Subconjunctival depot injections may have to be resected, although they have usually washed out by 2 weeks. Laser trabeculoplasty is ineffective.

XXII. Crystalline lens-induced glaucoma

(see also Chapter 7, sec. V.H.3.).

A. Clinical characteristics.

An acute secondary open-angle glaucoma **(phacolytic glaucoma)** may result from a leaking hypermature or mature (rarely immature) cataract. There is usually rapid onset of ocular pain and redness with often very high pressures and corneal epithelial edema. Light projection may be faulty. Gonioscopy reveals the angle to be open, which distinguishes this disease from acute angle-closure glaucoma. Cellular reaction in the anterior chamber is usually minimal to moderate, although there is usually a heavy flare. Circulating white particles, which are larger than white cells and probably represent small portions of lens material, aggregated lens protein, or swollen macrophages can be seen frequently in the aqueous. The cataract often has patchy white deposits, which are probably macrophages, on the anterior lens capsule.

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B. Mechanism.

Phacolytic glaucoma is most likely the result of direct mechanical obstruction of the outflow pathways by the liberated lens proteins that leak from the cataract. Macrophages that act to clear lens material from the eye may also be involved in the obstruction to outflow. The **diagnosis** of phacolytic glaucoma is made by paracentesis and aspiration of aqueous humor, microscopic examination of which usually reveals the presence of engorged macrophages. Biochemical analysis for lens proteins may also be useful (see Chapter 1, sec. III.L.).

C. Dislocated lenses.

In cases of cataractous lenses that are dislocated into the vitreous, the findings in phacolytic glaucoma may be quite subtle. The **differential diagnosis** includes angle-recession glaucoma, POAG, and an idiopathic type of chronic open-angle glaucoma apparently not related to lens reaction or obvious signs of angle recession.

D. Retained lens cortex.

Glaucoma may result from the obstructive properties of liberated lens particles on the outflow pathways following extracapsular cataract surgery or lens injury. An inflammatory component may be additive.

E. Differential diagnosis.

Phacolytic glaucoma must be distinguished from inflammatory glaucoma. Some KPs may be present on the cornea in phacolytic glaucoma. Consideration of the above factors will usually lead to the correct diagnosis but, especially in the rare cases of phacolytic glaucoma with immature cataracts, a trial of topical steroids may be useful. In phacolytic glaucoma, such steroid therapy will not result in a lasting improvement of IOP, and cataract surgery should then be contemplated. Again, diagnostic paracentesis will usually establish the correct diagnosis.

F. Treatment

Treatment is cataract extraction. In general, the eyes show short-lived response to topical antiglaucoma or antiinflammatory therapy. There is usually significant reduction of IOP with use of a beta-blocker, alpha-agonists, CAIs, and osmotic agents, but the pressure frequently continues to increase again to high levels (40 to 80 mm Hg). All patients with presumed phacolytic glaucoma should have urgent cataract extraction, especially if the pressure continues to increase to these high levels. In the case of retained lens cortex, medical therapy with a beta-blocker, epinephrine, DPE, CAIs, cycloplegics, and possibly topical steroids should be tried, but if the glaucoma remains severe, the remaining lens material must be surgically removed.

XXIII. Intraocular lens (IOL)-associated glaucoma

Intraocular lens (IOL)-associated glaucoma may stem from any of the previously mentioned causes such as exacerbation of preexistent POAG, pupillary block, malignant glaucoma following pupillary block, viscoelastic substance (see sec. XXIV., below) or vitreous herniation into the anterior chamber blocking the TM, or chronic peripheral anterior synechiae. In addition, IOLs uniquely predispose to three other causes of glaucoma: smoldering chronic iridocyclitis, anterior chamber (and TM) mechanical distortion, and pseudophakic pigmentary dispersion. **Therapy** of all but the last three has already been discussed. For these three a decision must be made as to whether the IOL should be removed or medical therapy will suffice. IOL iritis is often associated with mechanical distortion of the anterior chamber due to improper lens sizing or placement. Steroid and, if needed, antiglaucoma therapy may control the process. If progressive adhesions or cystoid macular edema develop, however, the lens should probably be removed in the absence of other contraindications. In pigment dispersion (seen with iris plane and posterior chamber IOLs), the pupil and iris may be immobilized with longer-acting miotics to minimize mechanical rubbing against the lens. The IOL usually does not have to be removed.

XXIV. Viscoelastic substance-induced glaucoma

Viscoelastic substance-induced glaucoma is a secondary open-angle glaucoma seen postoperatively after use of these vitreous-stimulating materials. The newer such gels are much less prone to inducing IOP increase.

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Clinical characteristics. Viscoelastic gels, although a great boon to anterior and posterior segment surgery, may have the undesirable side effect of transiently blocking the aqueous outflow system occasionally, with resulting severe increase in IOP.

Pressure increase may begin within an hour or two of closing the eye in the case of residual anterior chamber material, and at 72 hours in situations in which viscoelastic substance has been left in the posterior segment and has then moved forward. Symptoms may be absent or similar to acute IOP increase with ocul