

Glaucoma

Anterior-segment outflow disorders and optic-nerve injury

Mechanisms • Morphology • Clinicopathologic reasoning

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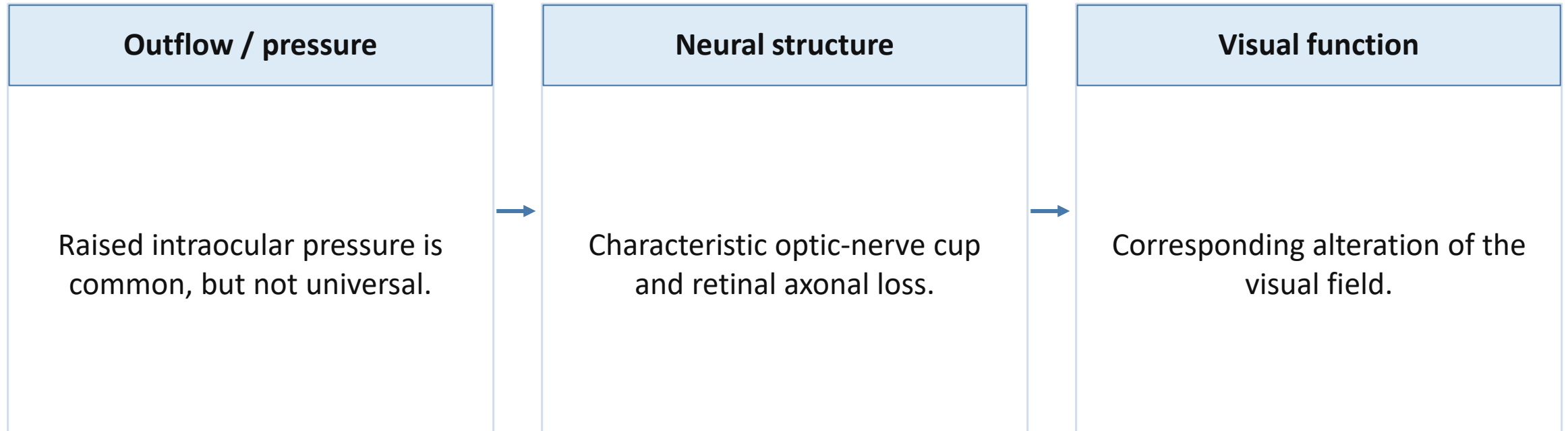
Learning objectives

- Trace aqueous humor from production to trabecular outflow.
- Distinguish open-angle from angle-closure mechanisms and primary from secondary causes.
- Explain selected secondary glaucomas through outflow resistance, venous pressure, or physical angle obstruction.
- Relate chronic pressure-associated injury to the retina, optic nerve, and visual field.

Glaucoma: A structural–functional disease

- The name encompasses disease processes with characteristic optic-nerve cupping and visual-field changes.
- Elevated intraocular pressure is usually associated, but is not indispensable.
- The clinically important endpoint is optic-neural injury, not pressure elevation alone.

Two linked expressions of glaucomatous injury



Intraocular pressure and glaucoma are not identical

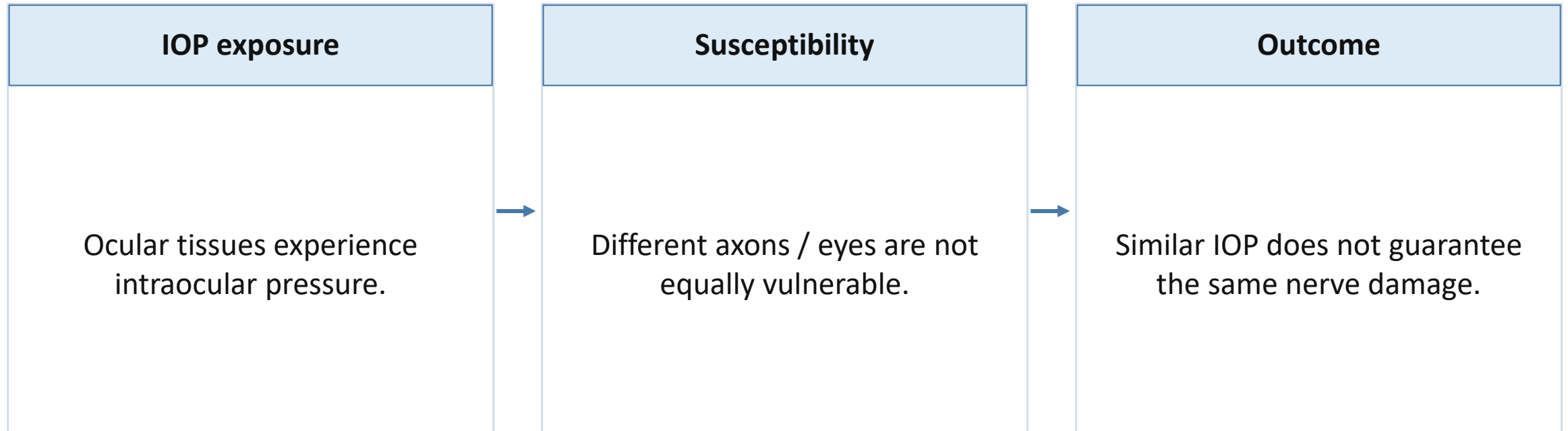
Normal-tension glaucoma

- Characteristic cupping and visual-field change
- IOP may remain within a normal range
- Neural susceptibility cannot be inferred from IOP alone

Pressure elevation without glaucoma

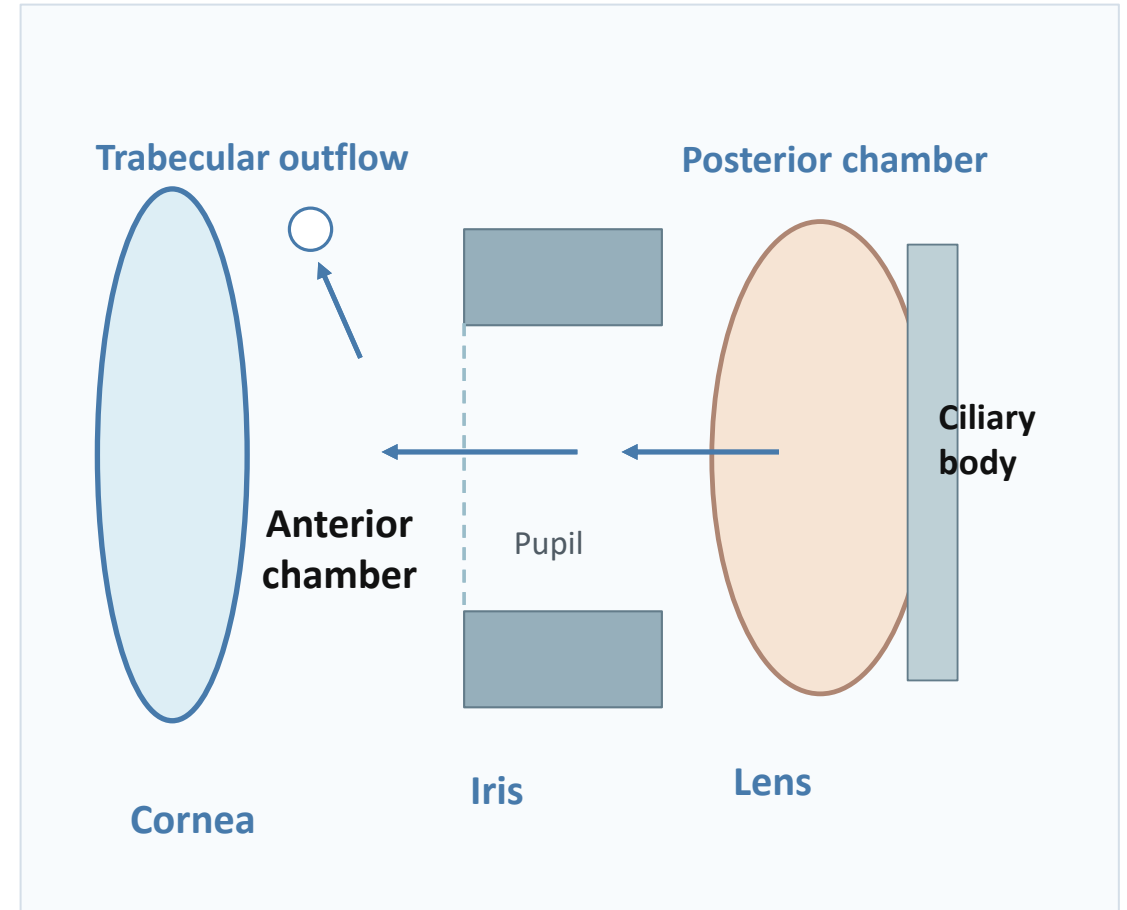
- Some eyes remain without characteristic cupping
- Visual fields may be preserved on long follow-up
- Elevated IOP is a risk context, not a complete definition

Neuronal susceptibility is heterogeneous



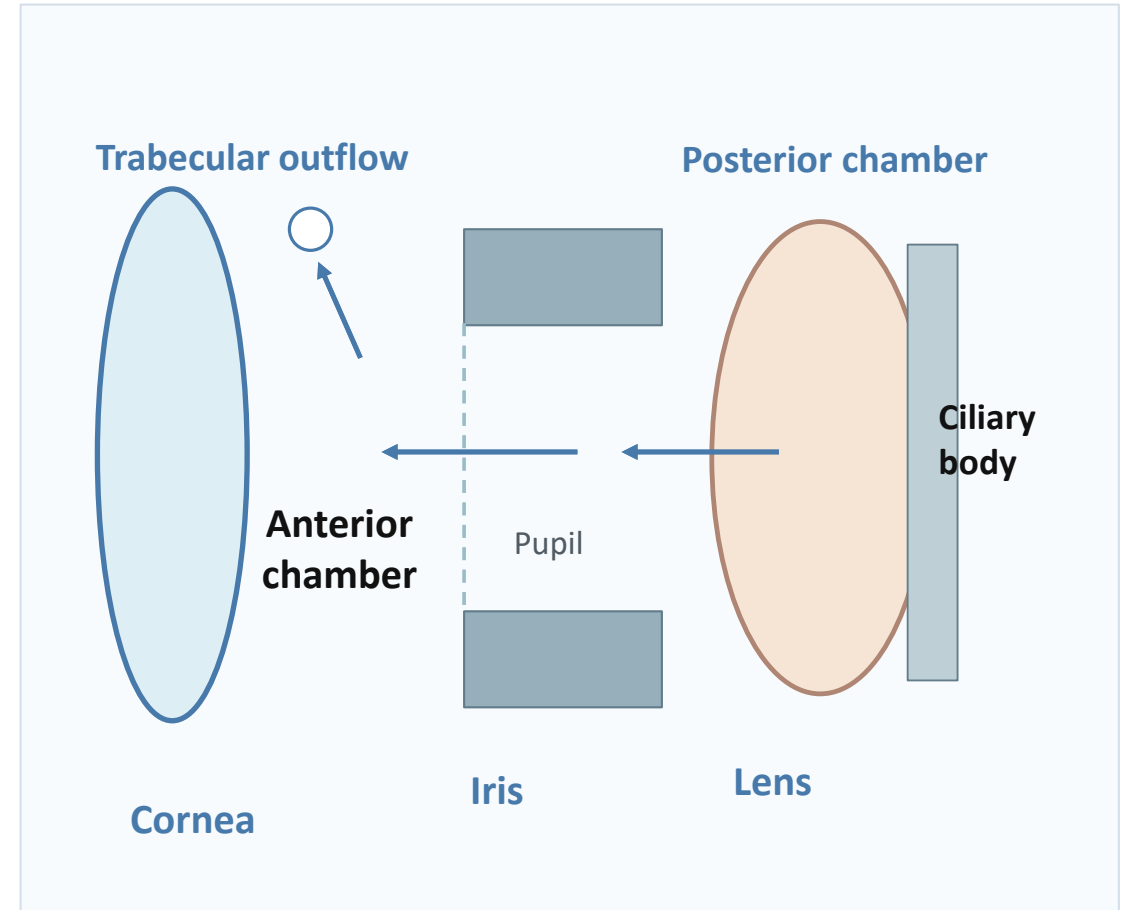
Anterior-segment compartments

- The anterior chamber lies between cornea and iris.
- The posterior chamber lies behind the iris, in front of the lens.
- These chambers communicate through the pupil.

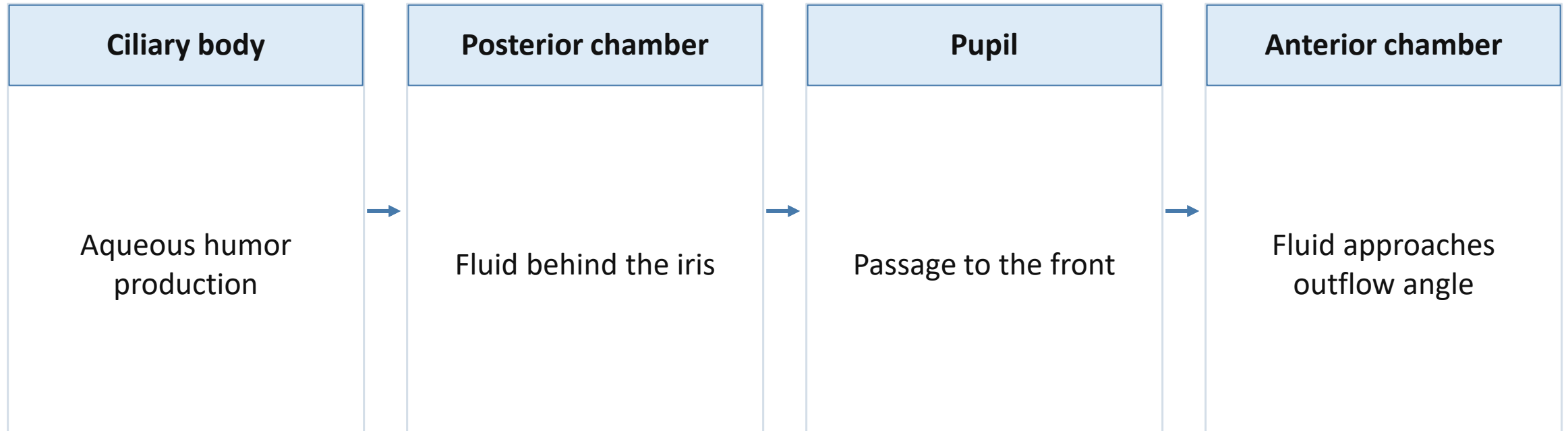


Ciliary body: Origin of aqueous humor

- Aqueous humor forms at the ciliary body, specifically its pars plicata.
- Newly produced fluid enters the posterior chamber.
- Ongoing production matters when the pupil or angle becomes obstructed.

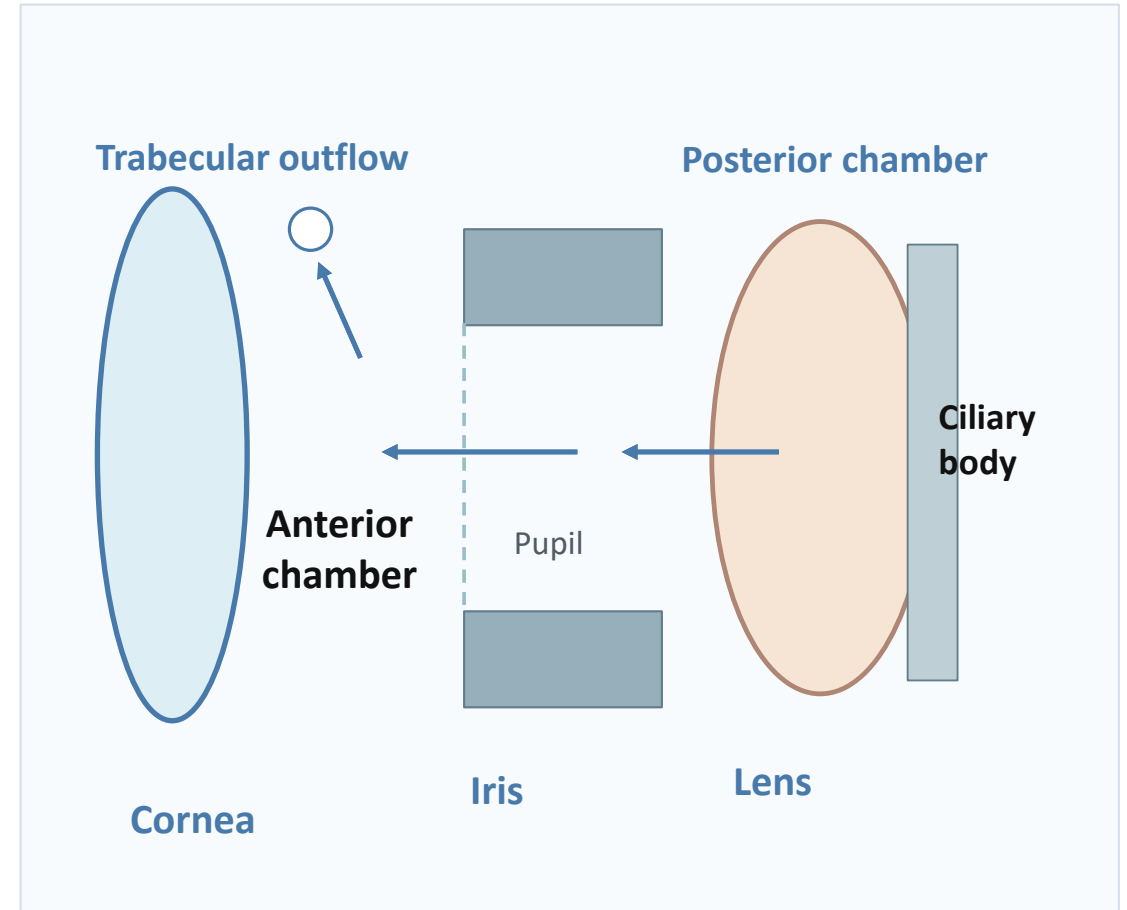


Normal aqueous-humor circulation

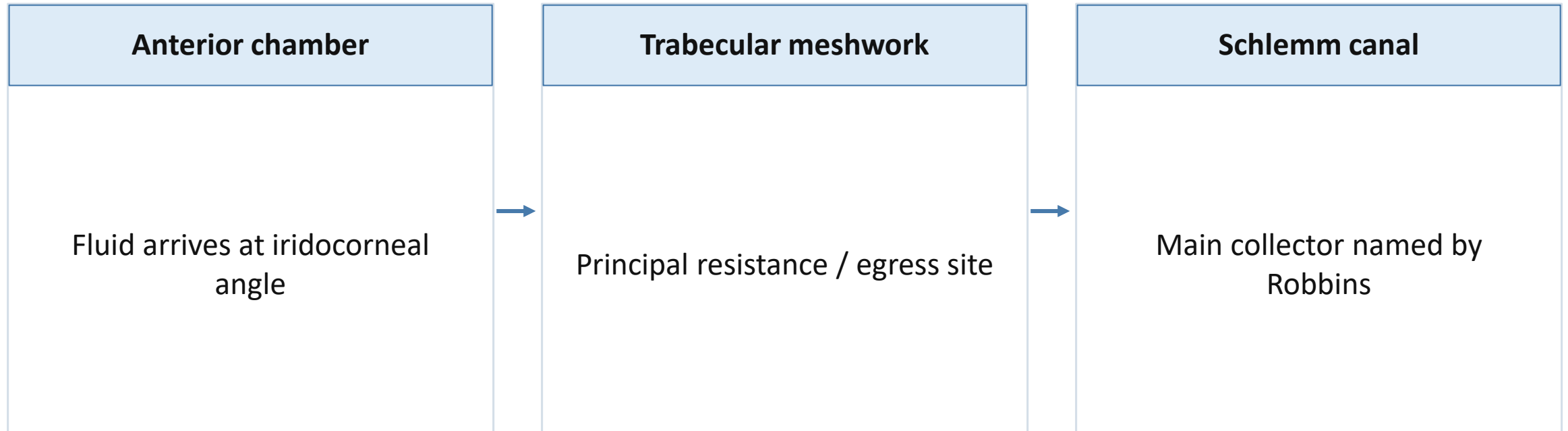


The drainage angle is peripheral

- The major drainage site is at the corneal periphery.
- The anterior surface of the iris meets the corneal periphery at the angle.
- Access to the trabecular meshwork determines whether the angle is functionally open.



Trabecular outflow route



Major and minor routes of outflow

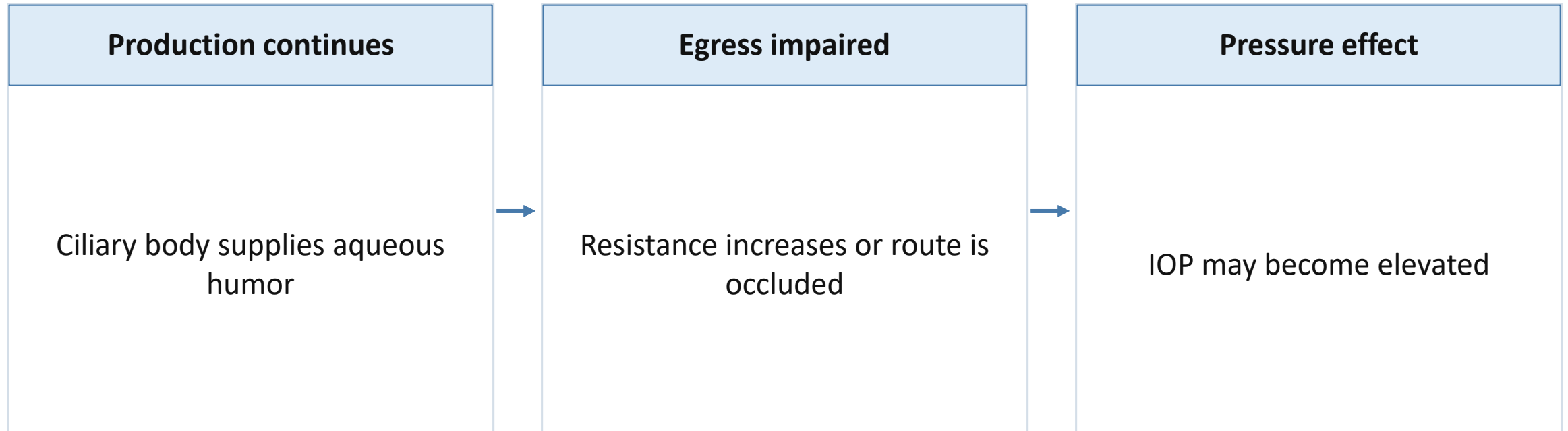
Trabecular pathway

- Accounts for most aqueous-humor drainage
- At the anterior chamber angle
- Leads into Schlemm canal

Alternative pathways

- Uveoscleral outflow also occurs
- A minor route involving the iris
- Not the central mechanism of its glaucoma classification

Why outflow impairment can raise pressure



Two classification axes in glaucoma

Angle configuration	Primary process	Secondary process
Open angle	Primary open-angle glaucoma	Pseudoexfoliation; debris; raised venous pressure
Closed / obstructed angle	Primary angle-closure glaucoma	Neovascular membrane; mass effect; synechiae

Open angle and angle closure: Decisive distinction

Open-angle mechanism

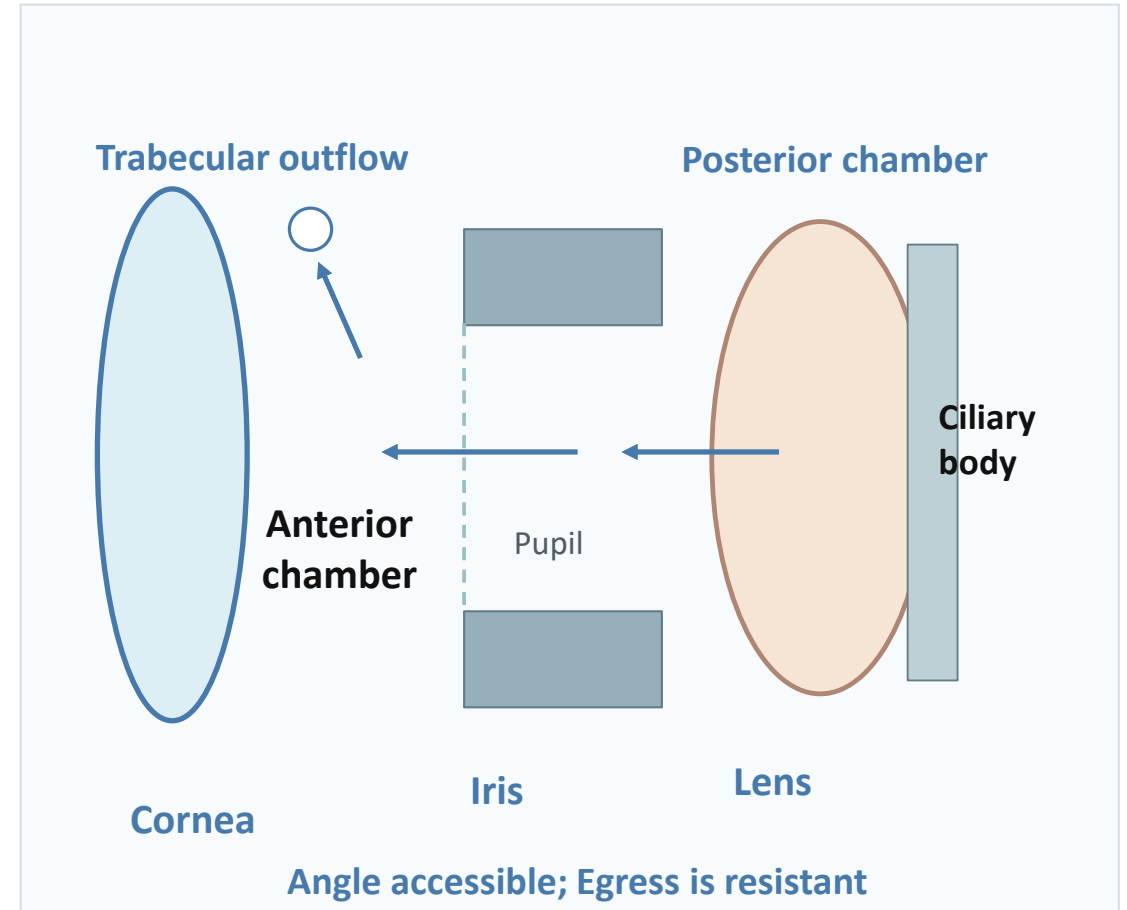
- Trabecular meshwork physically accessible
- Increased resistance to outflow
- Angle may appear structurally unobstructed

Angle-closure mechanism

- Peripheral iris impedes angle outflow
- Apposition or adhesions can obstruct meshwork
- Anatomical interference dominates

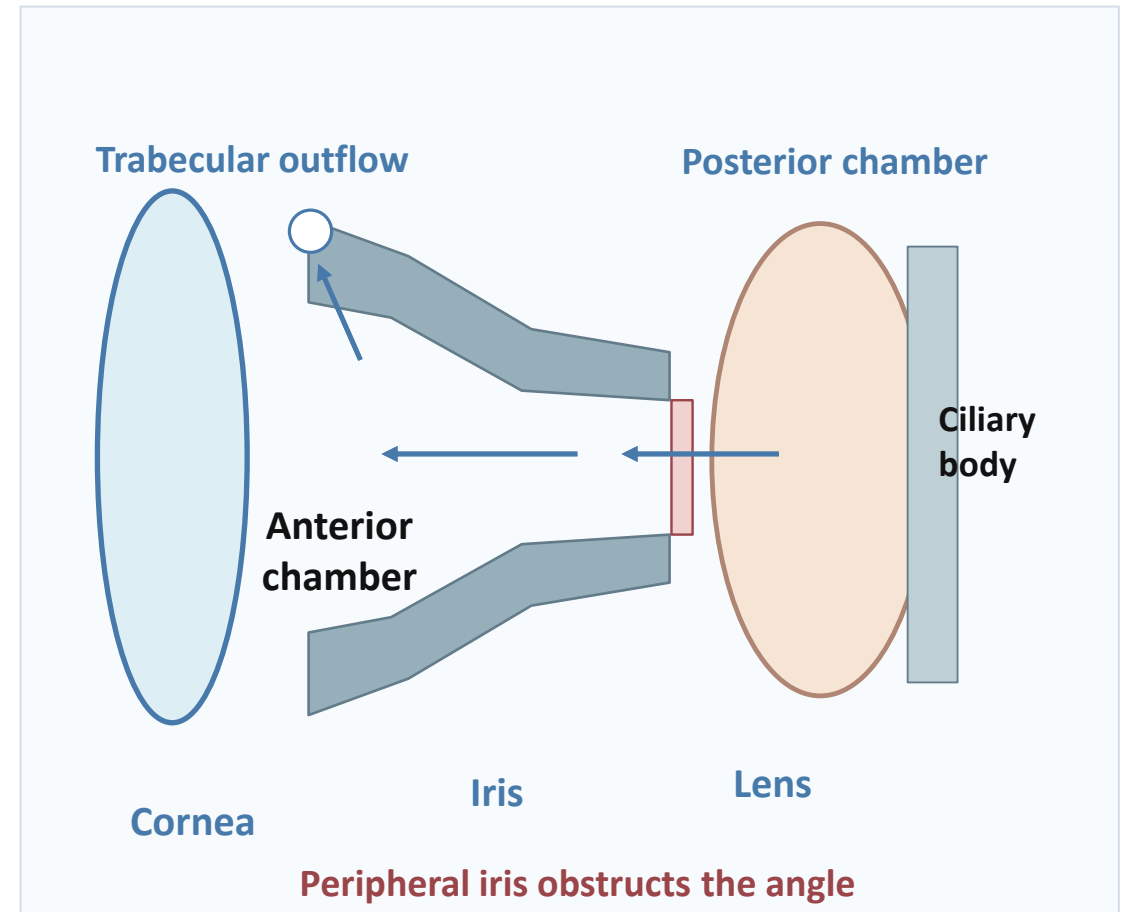
Open angle: Access is preserved

- An open-angle eye retains physical access to trabecular meshwork.
- Outflow may nevertheless meet elevated resistance.
- “Open” does not imply normal pressure regulation.



Angle closure: The iris blocks access

- Peripheral iris position or adhesion can obstruct trabecular outflow.
- Anatomical obstruction may cause a marked elevation in intraocular pressure.
- Pupillary block and contracting membranes are distinct routes to closure.



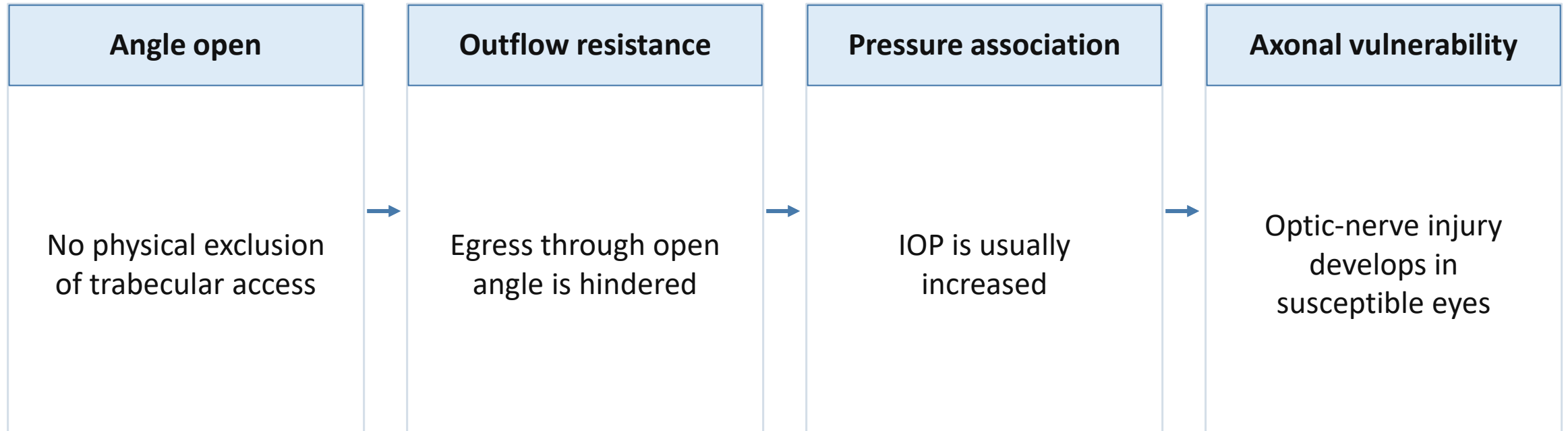
Primary versus secondary is a separate question

Type	Source-based organizing concept	Example
Primary	Disease form without a separately identified precipitating ocular disorder	Primary open-angle glaucoma
Secondary	A recognizable process alters outflow or venous drainage	Pseudoexfoliation glaucoma
Secondary	External mechanical obstruction of the angle	Neovascular glaucoma

Primary open-angle glaucoma

- This as the most common form of glaucoma.
- The drainage angle remains anatomically open.
- Relatively few obvious structural changes are apparent in the angle.
- Impaired outflow is attributed to increased resistance.

Primary open-angle glaucoma: Mechanistic inference



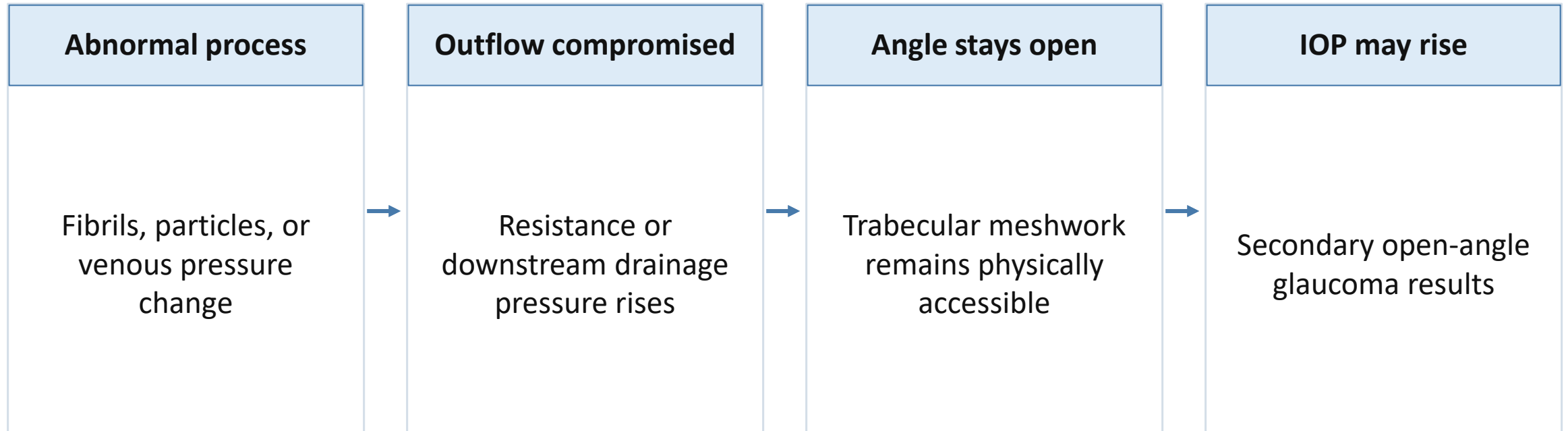
Primary open-angle glaucoma: Etiologic uncertainty

- The proximate cause of increased resistance remains uncertain in the Robbins account.
- Genetic factors are suspected contributors.
- An anatomically patent angle must not be misinterpreted as normal outflow function.

Genetic association is not a complete mechanism

- Genome-wide association studies implicating 40 genes in open-angle glaucoma.
- Association does not identify a single causal lesion that accounts for all cases.
- Avoid converting the gene-association count into a deterministic diagnostic test.

Secondary open-angle glaucoma: Shared endpoint



Pseudoexfoliation: Fibrillar accumulation

- Robbins calls pseudoexfoliation the most common secondary open-angle glaucoma.
- Fibrillar material of varying composition is deposited through the anterior segment.
- The deposit-associated outflow abnormality occurs despite an open angle.

Pseudoexfoliation extends beyond the ocular angle

In the eye

- Fibrillar deposits throughout anterior segment
- Deposits associated with secondary open-angle glaucoma
- Local accumulation interferes with aqueous drainage

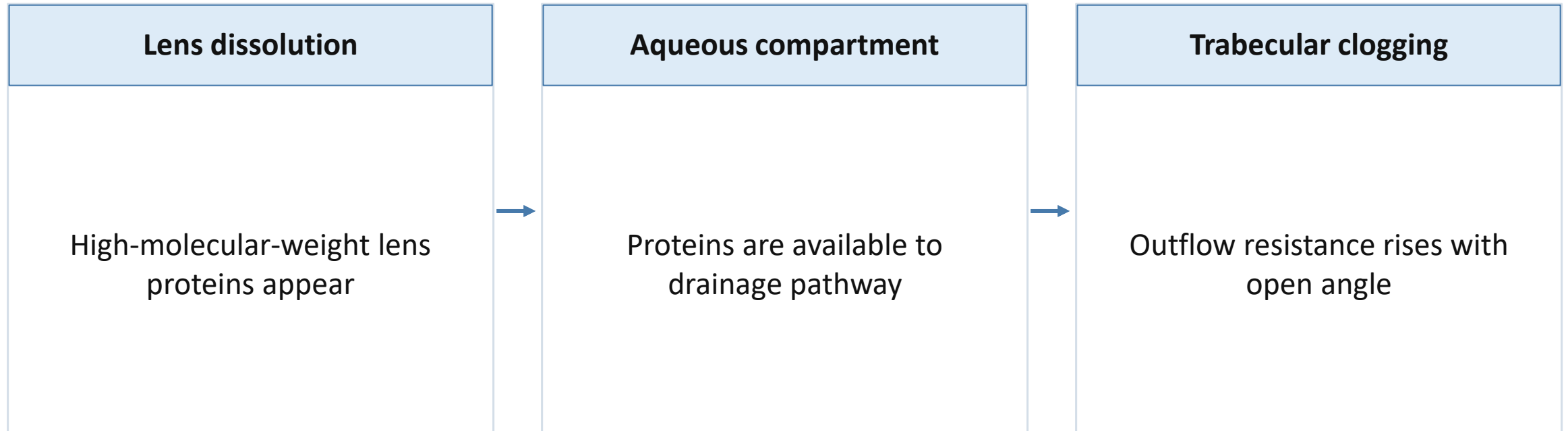
Extraocular distribution

- Connective tissue around blood vessels
- Other visceral organs may contain deposits
- Liver, kidney, and gallbladder

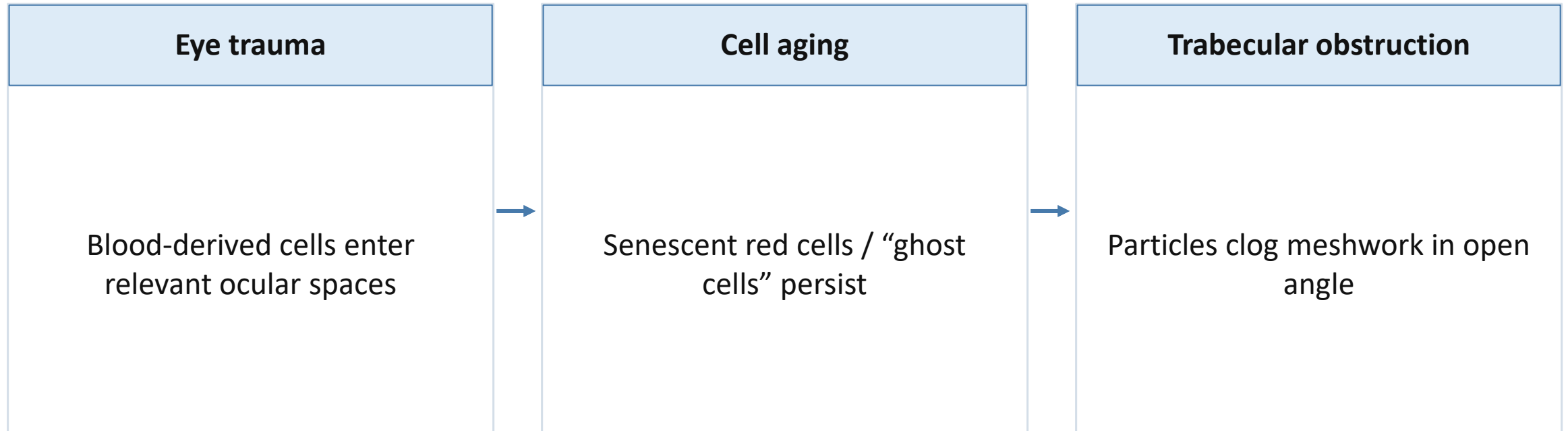
Debris can obstruct an anatomically open meshwork

- Physical openness of the angle does not prevent particles reaching the meshwork.
- Obstructing material may derive from lens, blood, iris epithelium, or tumor.
- The identity of the debris defines clinically meaningful secondary subtypes.

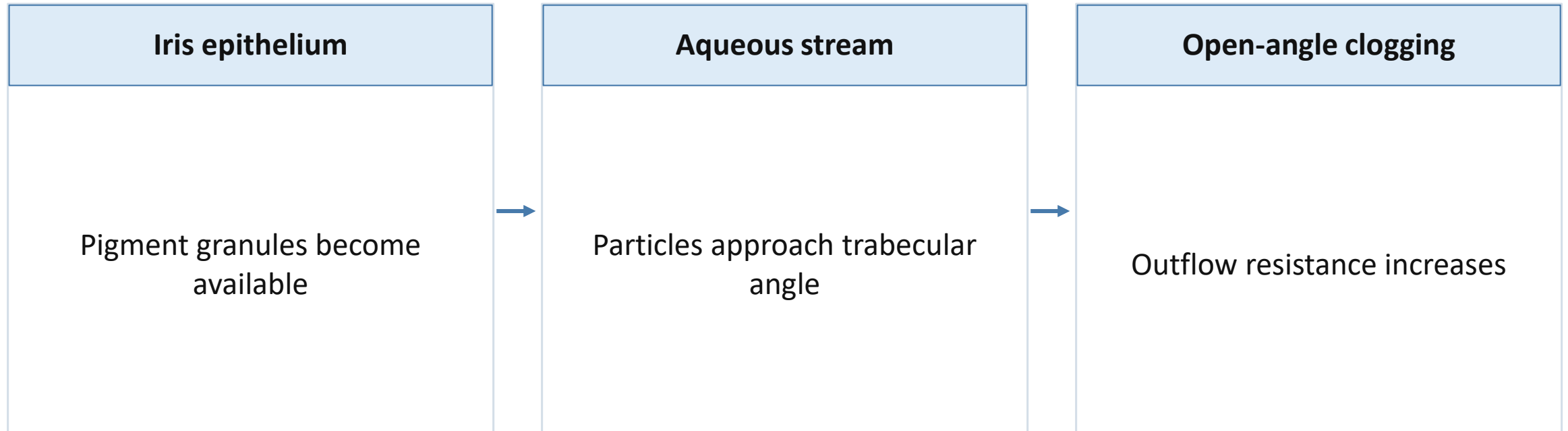
Phacolytic glaucoma: Proteinaceous obstruction



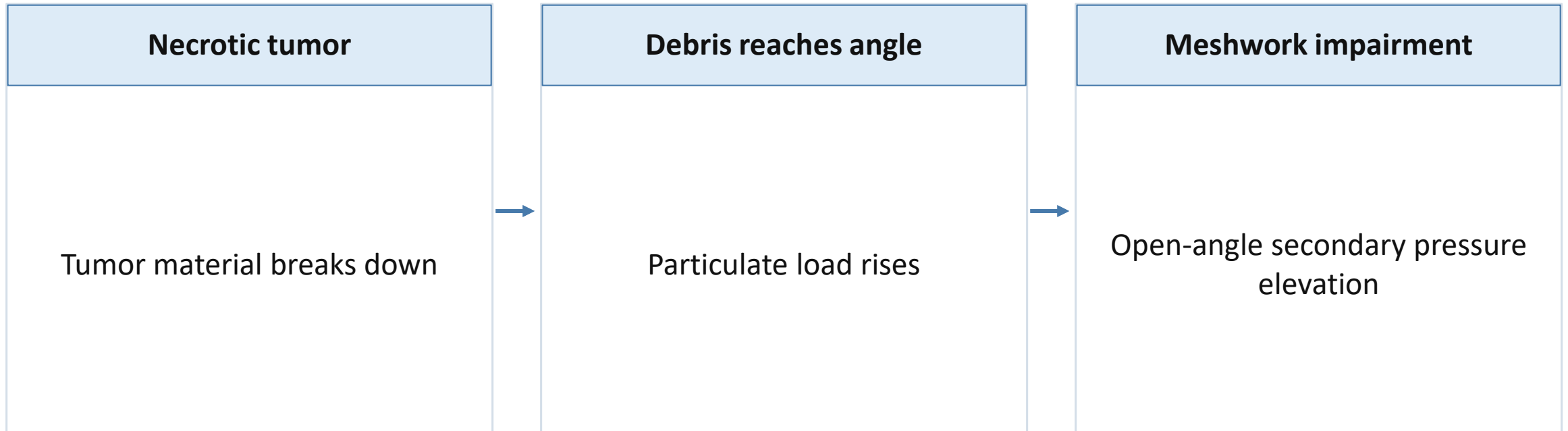
Ghost-cell glaucoma: Post-traumatic cellular debris



Pigmentary glaucoma: Iris epithelial granules



Melanomalytic glaucoma: Tumor-derived material



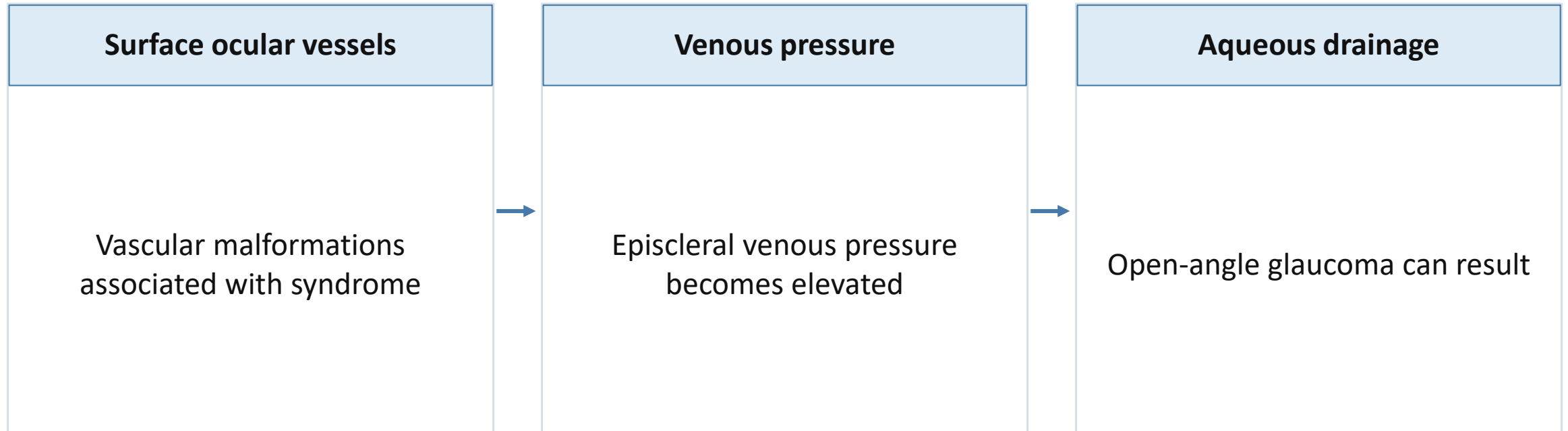
Particle-associated open-angle subtypes

Named form	Obstructing material	Source context
Phacolytic	High-molecular-weight lens proteins	Dissolving lens
Ghost-cell	Senescent red blood cells	After trauma
Pigmentary	Iris epithelial pigment granules	Pigment dissemination
Melanomalytic	Necrotic tumor material	Tumor breakdown

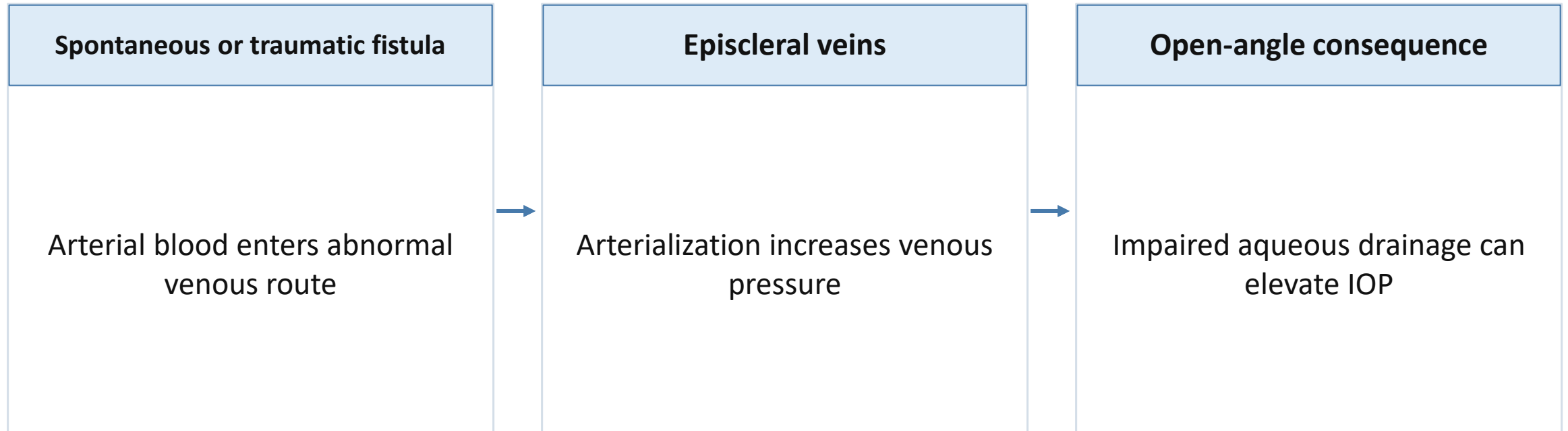
High episcleral venous pressure: A different route

- The trabecular angle may remain anatomically open.
- Higher pressure in venous drainage at the eye surface impedes effective aqueous egress.
- This secondary route differs from plugging the trabecular meshwork with particles.

Sturge–Weber syndrome: Vascular link



Carotid–cavernous fistula: Arterialized veins



Open-angle secondary mechanisms compared

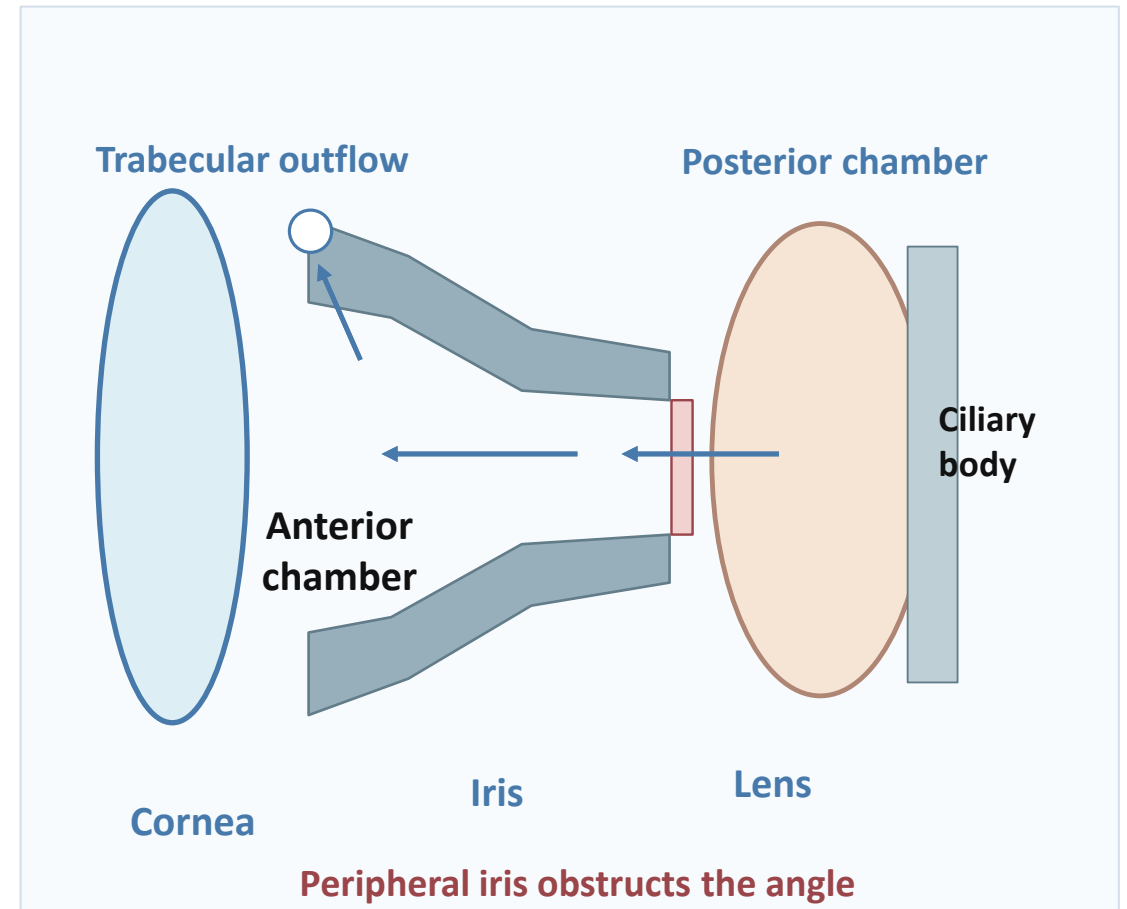
Mechanism	Representative cause	Impaired step
Fibrillar deposits	Pseudoexfoliation	Trabecular outflow
Particle obstruction	Lens / red cells / pigment / tumor	Trabecular meshwork
Venous back-pressure	Sturge–Weber; carotid–cavernous fistula	Downstream venous drainage

Primary angle closure: Anatomical predisposition

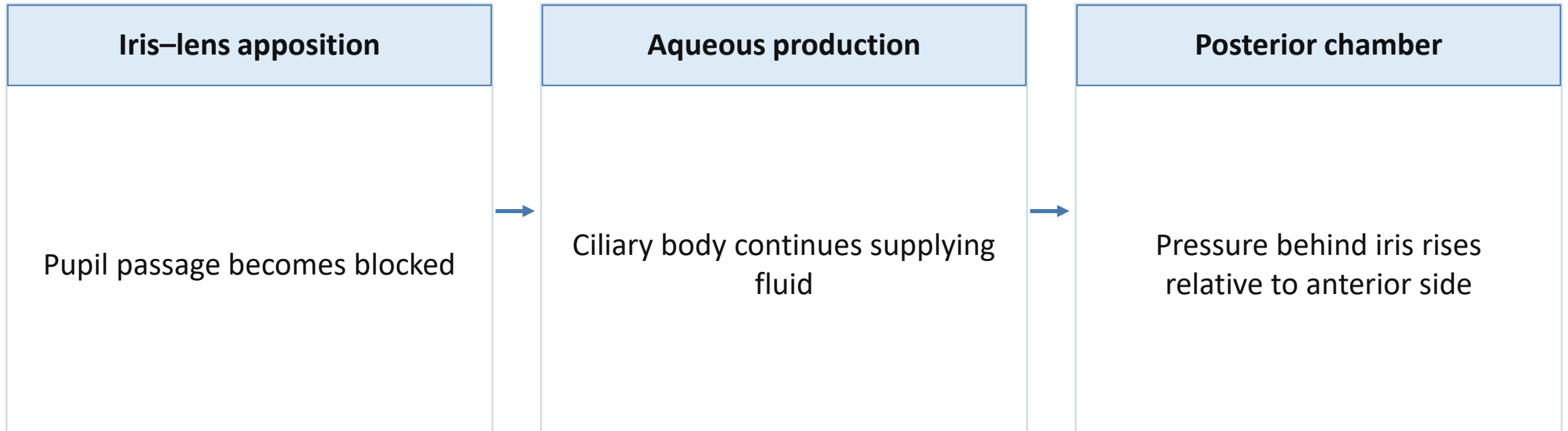
- A shallow anterior chamber favors primary angle closure.
- Frequent association with hyperopia.
- The peripheral iris can obstruct the outflow angle when pressure and spatial relations change.

Pupillary block begins at iris–lens apposition

- The pupillary iris margin comes transiently against the anterior lens surface.
- Aqueous flow through the pupil is impeded.
- Production behind the iris does not stop when the pupil blocks.

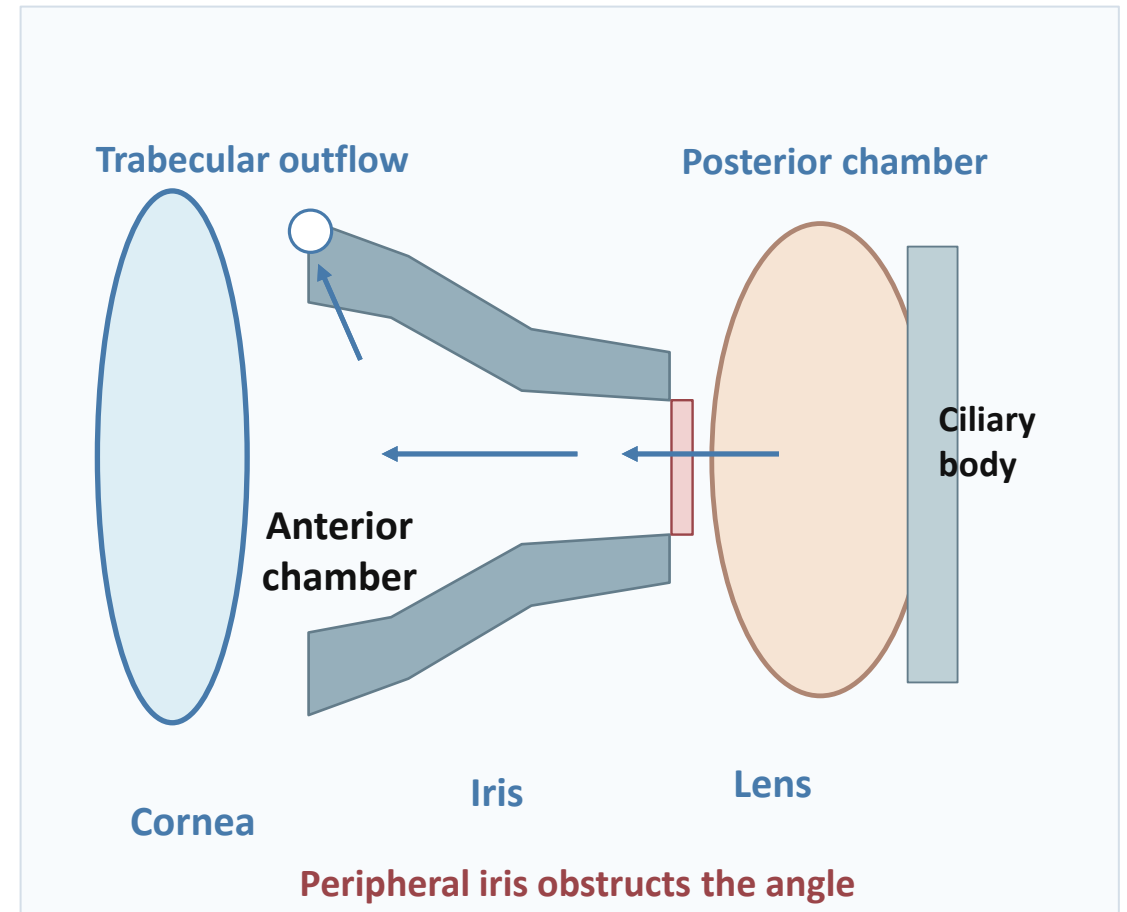


Pupillary block creates a posterior pressure gradient

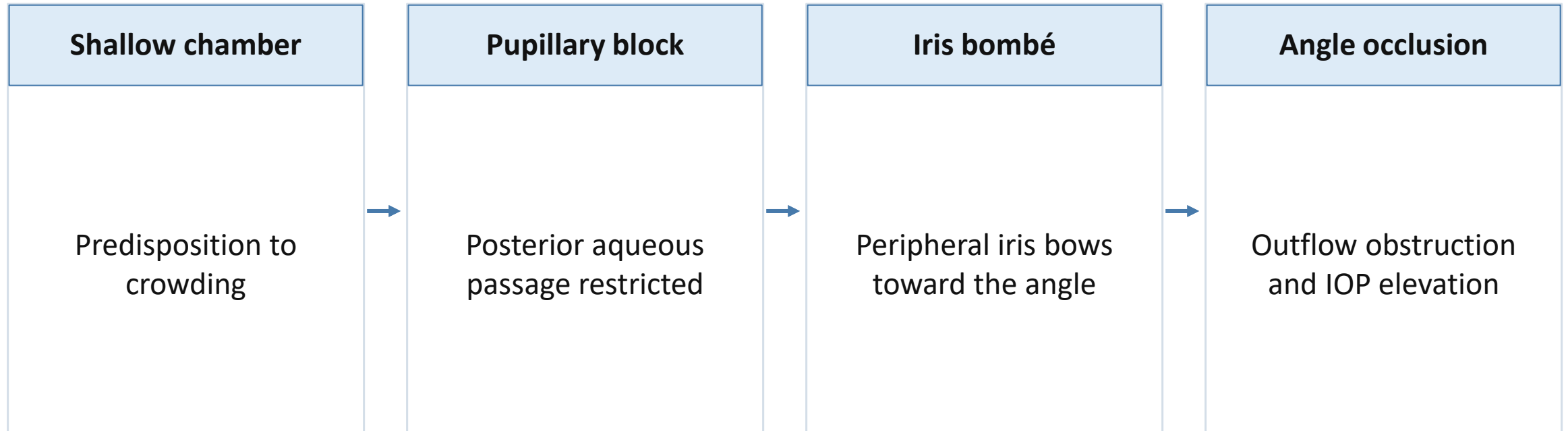


Iris bombé: Pressure bows the iris forward

- Accumulated posterior-chamber pressure pushes the peripheral iris anteriorly.
- Forward bowing is termed iris bombé.
- This change brings the iris into contact with trabecular outflow structures.



Primary angle closure: Full causal sequence



Two different obstructions in primary angle closure

At the pupil

- Iris margin contacts anterior lens
- Posterior-to-anterior flow is blocked
- Posterior chamber pressure accumulates

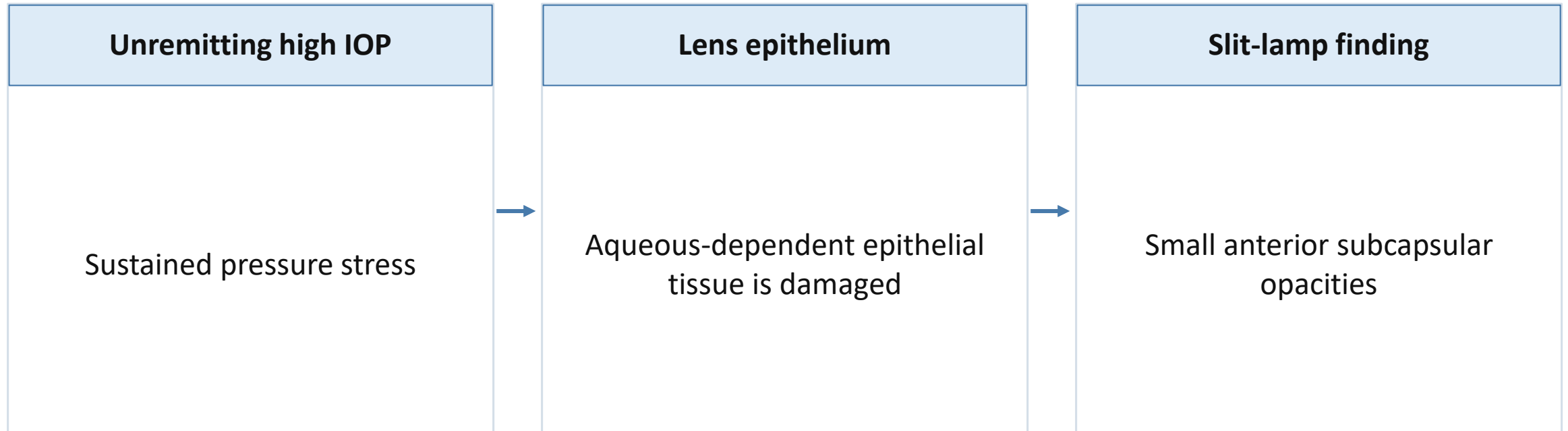
At the angle

- Bowed iris meets peripheral trabecular region
- Aqueous egress is directly obstructed
- Intraocular pressure can rise markedly

Why elevated pressure can injure the lens

- The crystalline lens is avascular.
- Lens epithelium depends on aqueous humor for nutrition.
- Unremitting elevation of pressure can damage the epithelium and produce minute anterior subcapsular opacities.

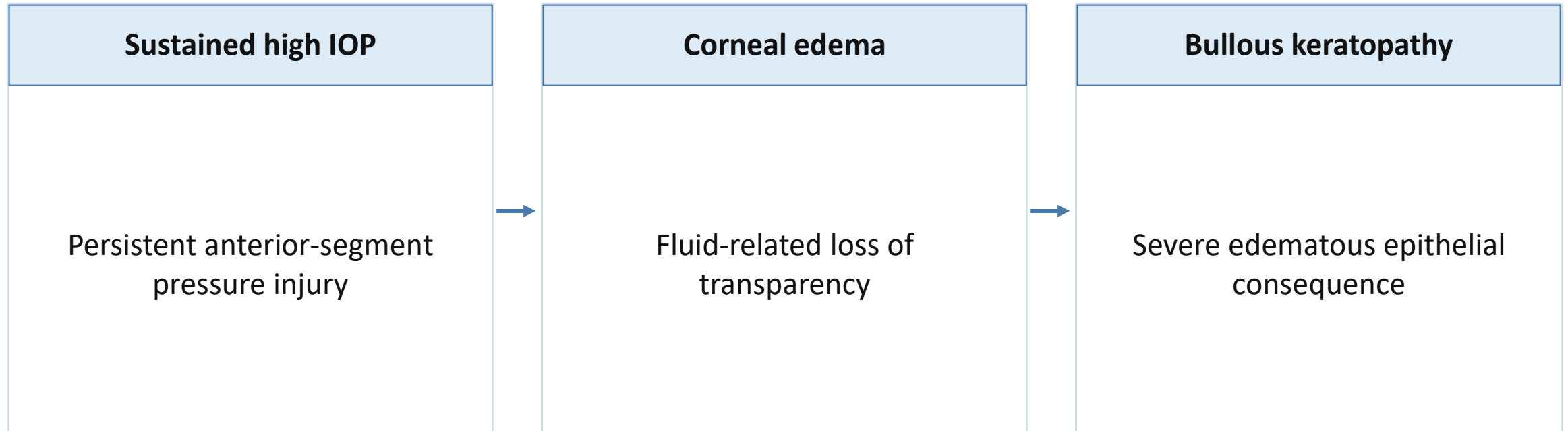
Anterior subcapsular lens changes after angle closure



Corneal edema despite normal endothelial cell number

- Persistently elevated IOP can produce corneal edema.
- This may occur despite an otherwise healthy complement of endothelial cells.
- Corneal edema in this setting need not indicate primary endothelial dystrophy.

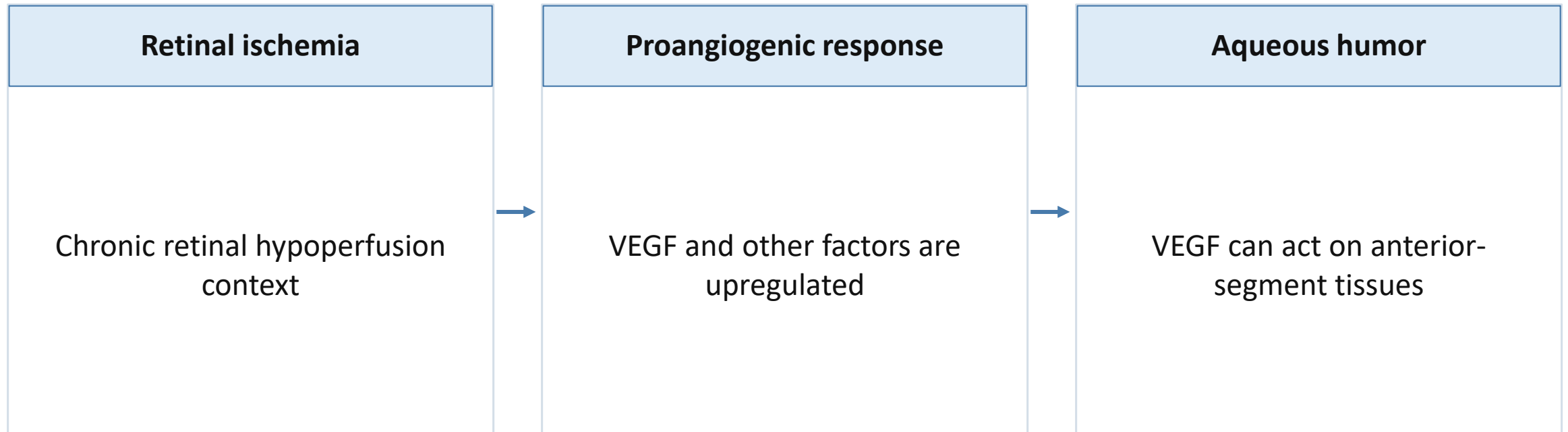
From pressure elevation to bullous keratopathy



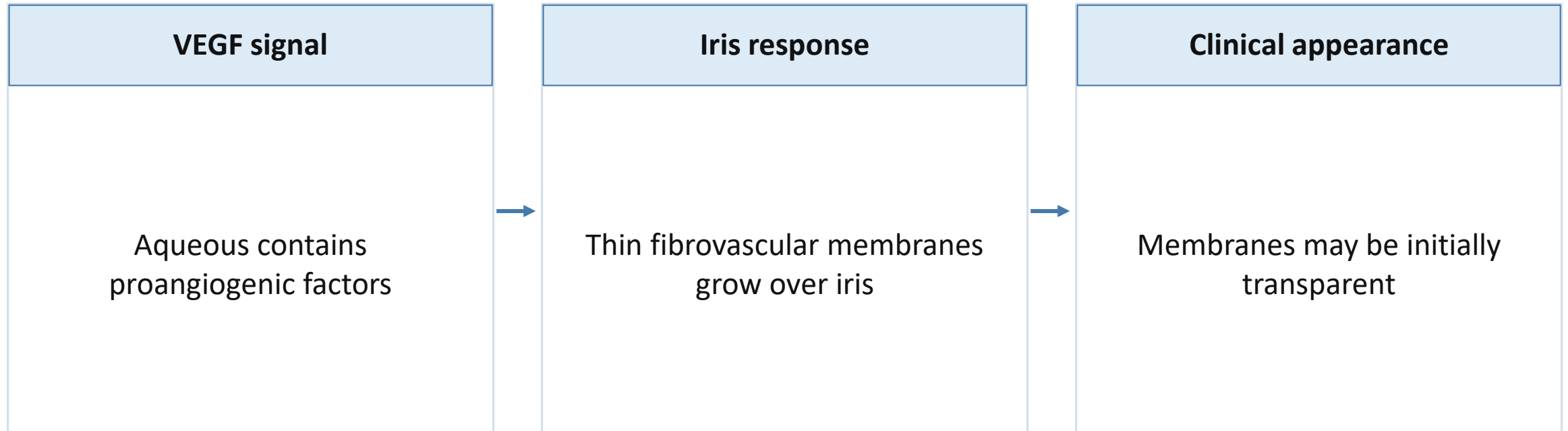
Secondary angle closure: A membrane can move the iris

- Abnormal membranes may form on the iris surface.
- Contractile components pull peripheral iris over the meshwork.
- The angle becomes physically obstructed even without the primary pupillary-block mechanism.

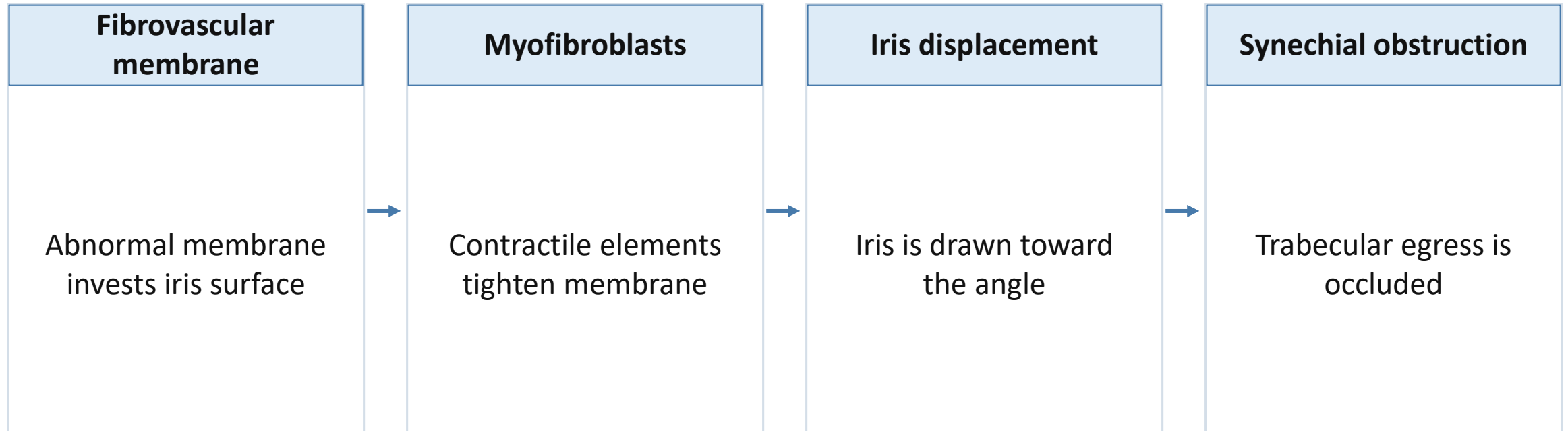
Chronic retinal ischemia creates a proangiogenic signal



Neovascular glaucoma: Membrane formation

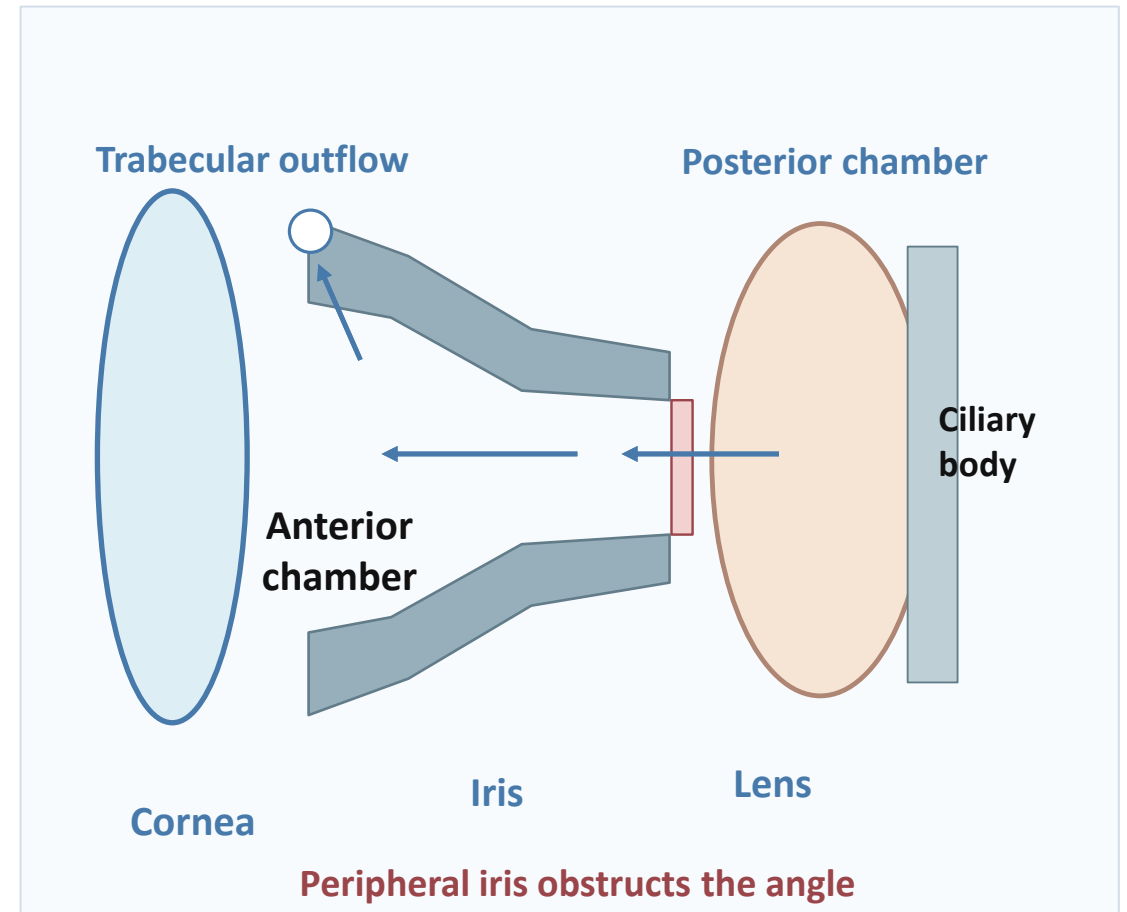


Myofibroblasts turn neovascularization into closure

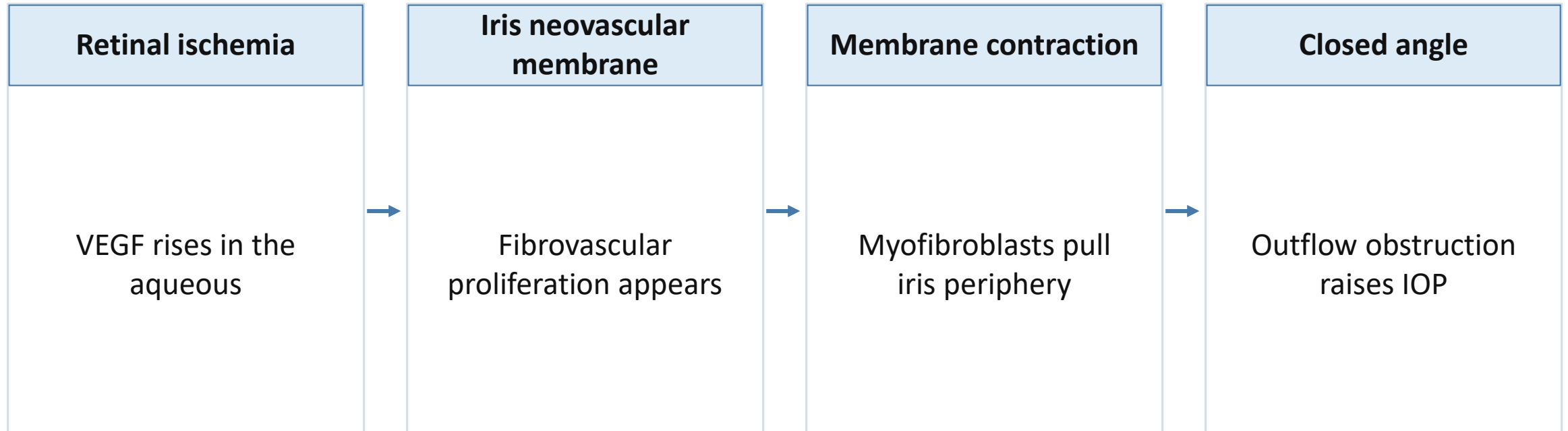


Neovascular glaucoma: Traction closes the angle

- Membranes change iris surface architecture and may smooth normal crypts.
- Myofibroblast contraction favors peripheral anterior synechiae.
- Synechial closure blocks aqueous outflow.



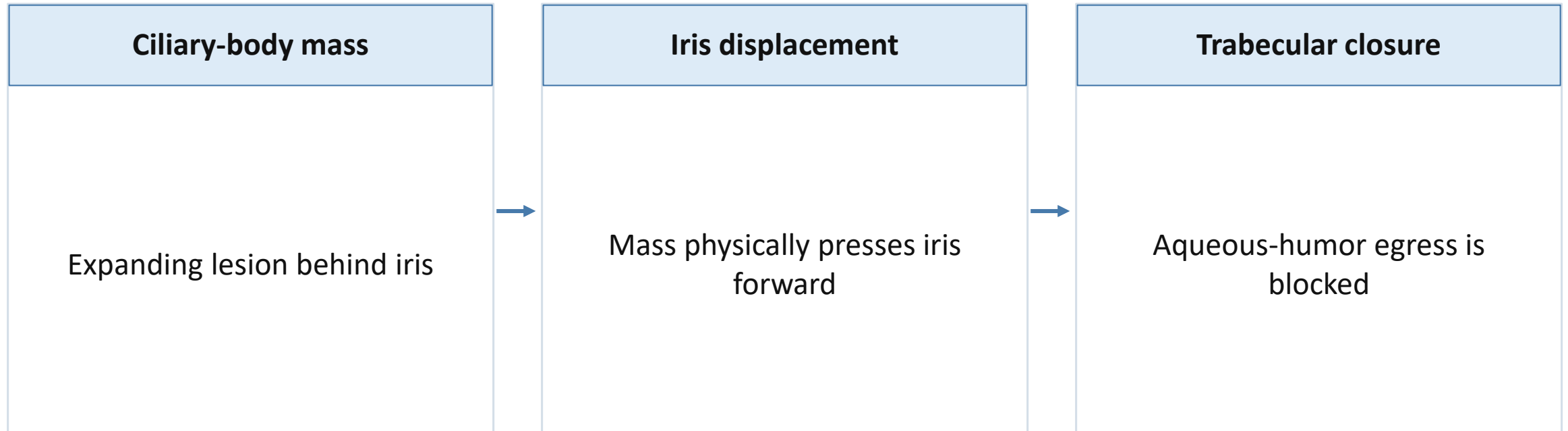
Neovascular glaucoma: Integrated mechanism



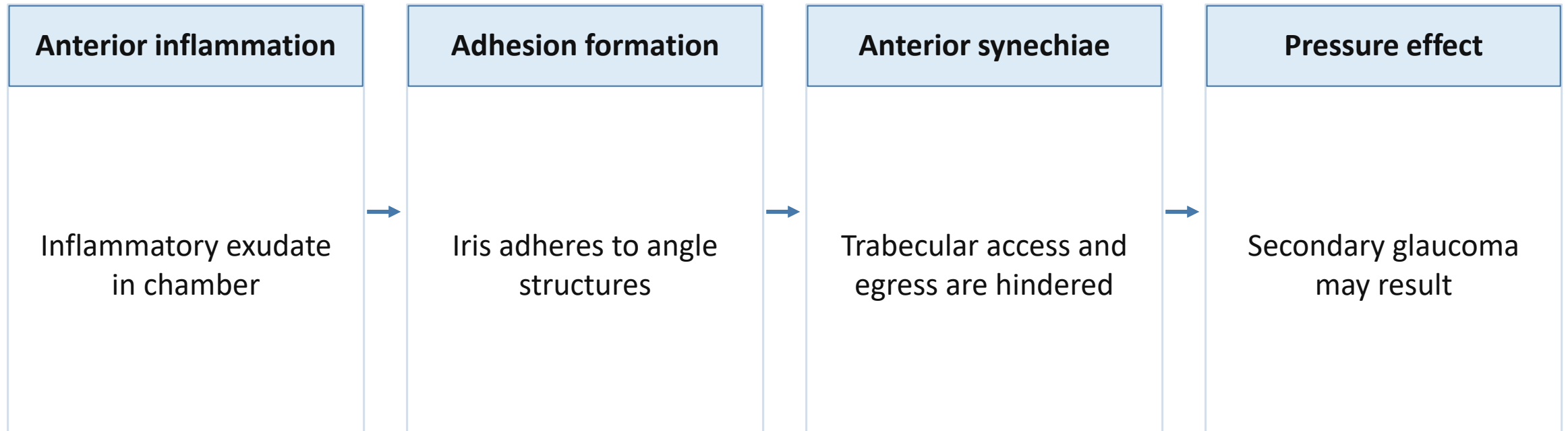
Necrotic retinoblastoma can drive iris neovascularization

- Necrotic tumors, particularly retinoblastoma, as causes of iris neovascularization.
- The resulting membrane can participate in secondary angle closure.
- Tumor-driven neovascular closure is distinct from tumor debris clogging an open angle.

Ciliary-body tumor: Direct mechanical angle closure



Inflammatory synechiae can also obstruct outflow



Secondary angle closure: Compare causal pathways

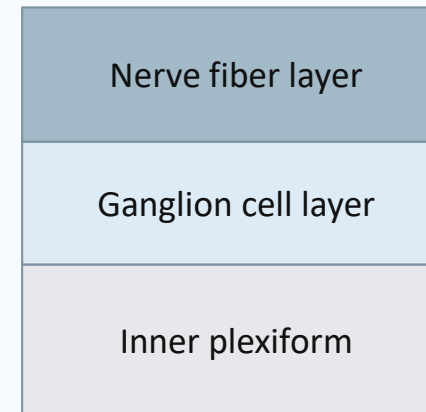
Pathway	Initiating abnormality	Mechanism of closure
Neovascular	Retinal ischemia / tumor-driven neovessels	Contracting iris fibrovascular membrane
Mass effect	Ciliary-body tumor	Iris mechanically pressed against meshwork
Inflammatory	Anterior-segment exudate	Anterior synechiae block angle

Retinal ganglion cell depletion in glaucoma

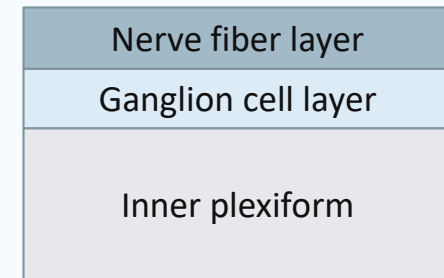
- Long-standing disease features loss of retinal ganglion cells.
- The retinal nerve fiber layer becomes thinner as ganglion-cell axons are lost.
- These structural changes link anterior-segment mechanisms to optic neuropathy.

Schematic — not a histologic image

Normal



Long-standing glaucoma



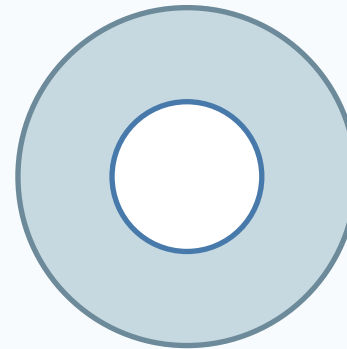
Loss of ganglion cells accompanies thinning of their nerve fibers.

Optic-nerve cupping is a structural hallmark

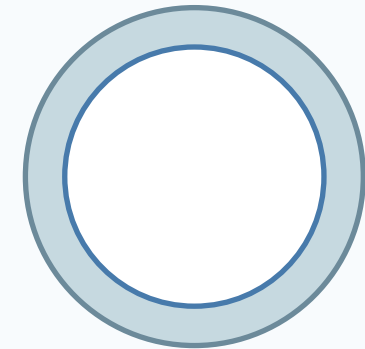
- Advanced glaucomatous disease shows an enlarged optic-nerve cup.
- The optic nerve is also atrophic.
- The conjunction of cupping and atrophy as characteristic.

Schematic — not a histologic image

Usual configuration

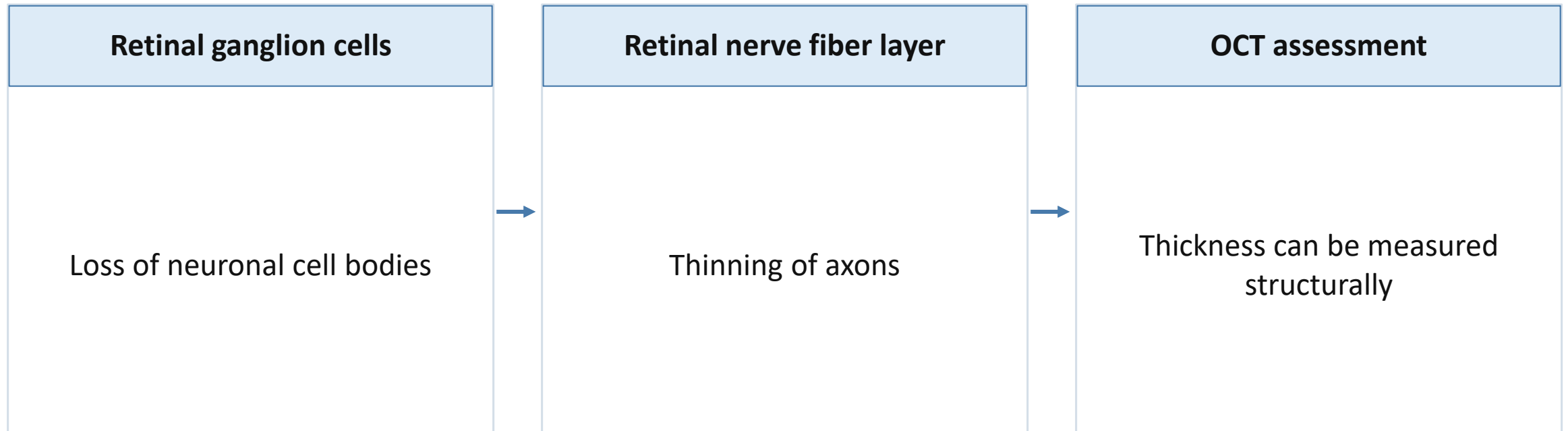


Advanced glaucoma



Glaucomatous cupping coexists with optic-nerve atrophy.

Optical coherence tomography and disease morphology



Elevated IOP has age-dependent ocular consequences

Infants and children

- Globe may enlarge: Buphthalmos
- Corneal enlargement: Megalocornea
- Immature tissues respond to elevated IOP with enlargement

Adult-sized eye

- Prolonged elevation may thin sclera locally
- Ectatic sclera can be lined by uveal tissue
- Result may be termed staphyloma

Case: Open angle with lens-derived material

CLINICOPATHOLOGIC VIGNETTE

An eye retains an open iridocorneal angle, but dissolving lens material releases abundant high-molecular-weight proteins into aqueous humor.

Which named secondary mechanism is most consistent with this description?

Interpretation: Phacolytic glaucoma — lens proteins can clog an otherwise accessible trabecular meshwork.

Case: Shallow chamber with iris bombé

CLINICOPATHOLOGIC VIGNETTE

An eye with a shallow anterior chamber develops transient iris–lens apposition. Continued aqueous production bows the iris forward against the angle.

What sequence explains the pressure increase?

Interpretation: Pupillary block → posterior-chamber pressure increase → iris bombé → trabecular angle closure.

Case: Retinal ischemia followed by angle obstruction

CLINICOPATHOLOGIC VIGNETTE

Chronic retinal ischemia is followed by fine fibrovascular membranes over the iris surface. The membranes contract and draw the iris peripherally.

Which category and mechanism best explain the obstruction?

Interpretation: Secondary angle-closure glaucoma caused by neovascular membrane contraction and peripheral anterior synechiae.

Case: High pressure without glaucomatous cupping

CLINICOPATHOLOGIC VIGNETTE

An eye has had elevated intraocular pressure on repeated evaluations, but characteristic optic-nerve cupping and visual-field loss have not appeared during prolonged follow-up.

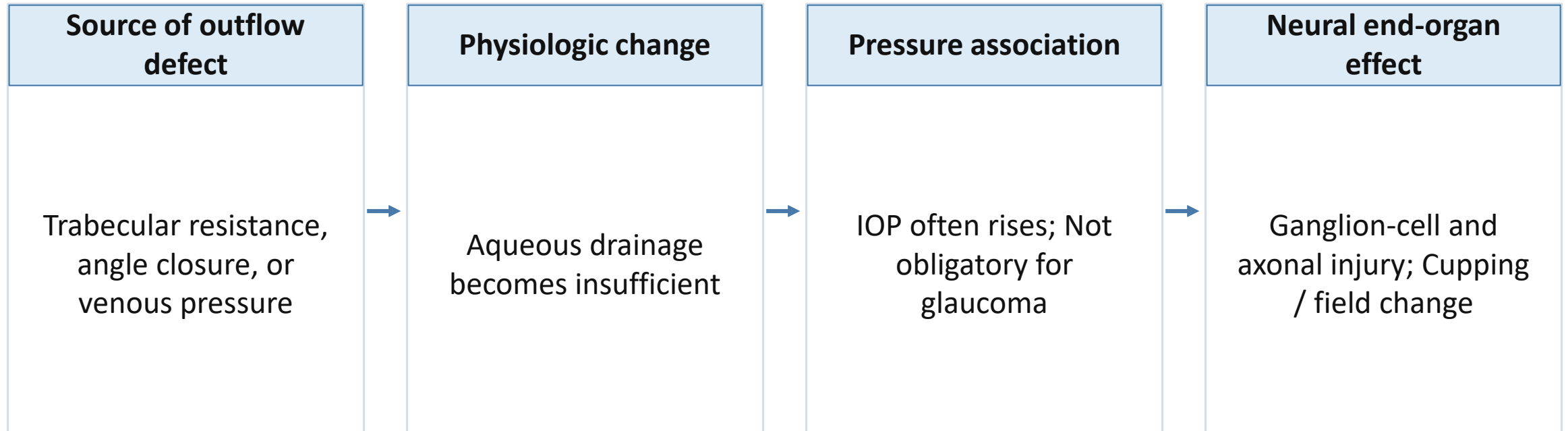
Why should the terms pressure elevation and glaucoma not be conflated?

Interpretation: There is variable neural susceptibility; A high IOP does not by itself demonstrate glaucomatous optic neuropathy.

Mechanistic classification: High-yield synthesis

Finding	Most directly supported interpretation	Common trap
Angle open, resistant outflow	Open-angle glaucoma	Assuming “open” means normal flow
Shallow chamber; iris bombé	Primary angle-closure mechanism	Confusing pupil block with meshwork obstruction
Fibrovascular iris membrane	Secondary neovascular angle closure	Assuming all angle closures require pupil block
Cupping and nerve-fiber loss	Glaucomatous neural injury	Using IOP alone as the disease definition

The complete clinicopathologic chain



Core distinctions to retain

- Glaucoma is defined by characteristic optic-neural and visual-field change; Pressure is strongly related but not synonymous.
- Open-angle disease reflects resistance despite access; Angle closure reflects physical iris obstruction.
- Secondary open-angle mechanisms include fibrils, cells / proteins / pigment / tumor debris, and high episcleral venous pressure.
- Angle closure may follow pupillary block, fibrovascular traction, tumor mass effect, or inflammation.

Selected primary reading and scope

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026).
- Primary teaching basis: the glaucoma section on aqueous dynamics, mechanisms, and major disease categories.
- Adjacent section context: anterior-segment inflammation and glaucomatous optic-nerve damage.
- Original diagrams in this deck are explanatory schematics, not reproductions of textbook figures.