

Uveitis

Clinicopathologic mechanisms, morphology and interpretation

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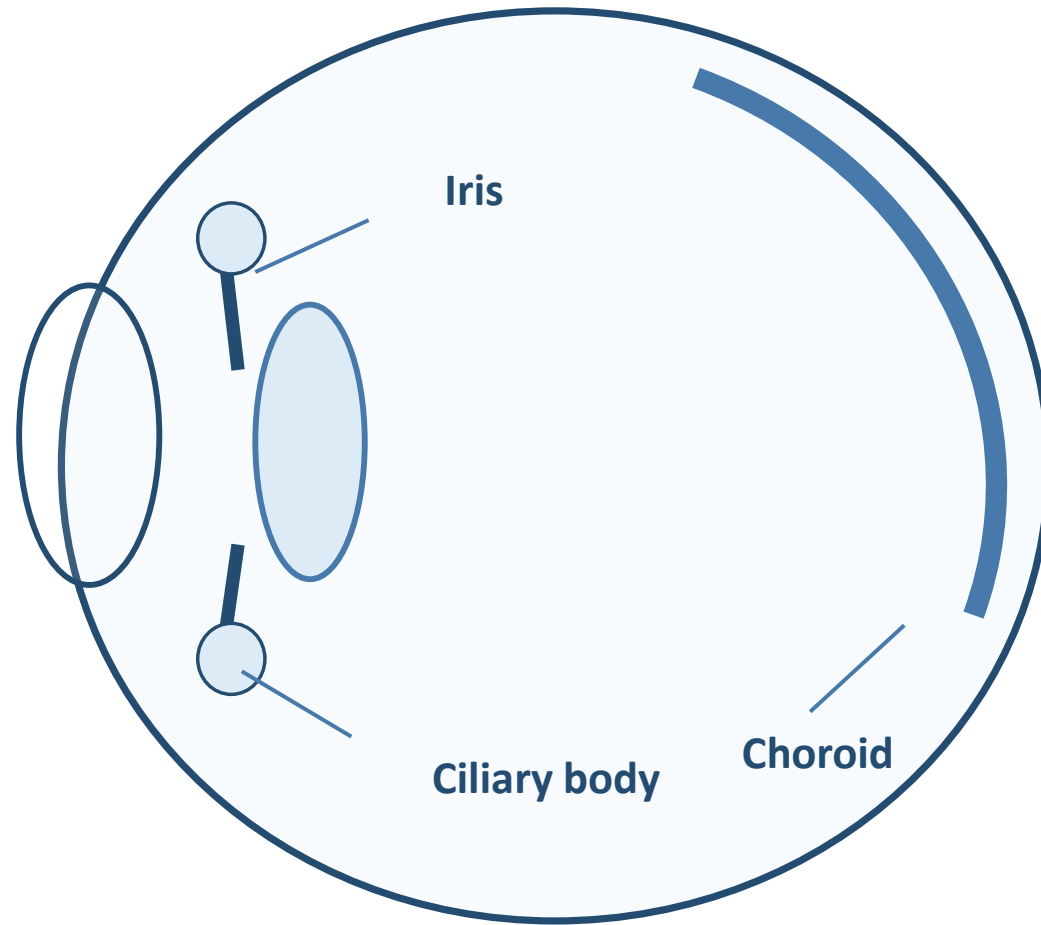
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Learning objectives

- Localize inflammation within the iris, ciliary body, choroid and adjacent retina.
- Explain anterior-segment inflammatory signs and their structural consequences.
- Distinguish sarcoid, infectious and sympathetic forms of uveitis.
- Connect morphology to diagnosis while recognizing limits of individual signs.

The uvea comprises three structures

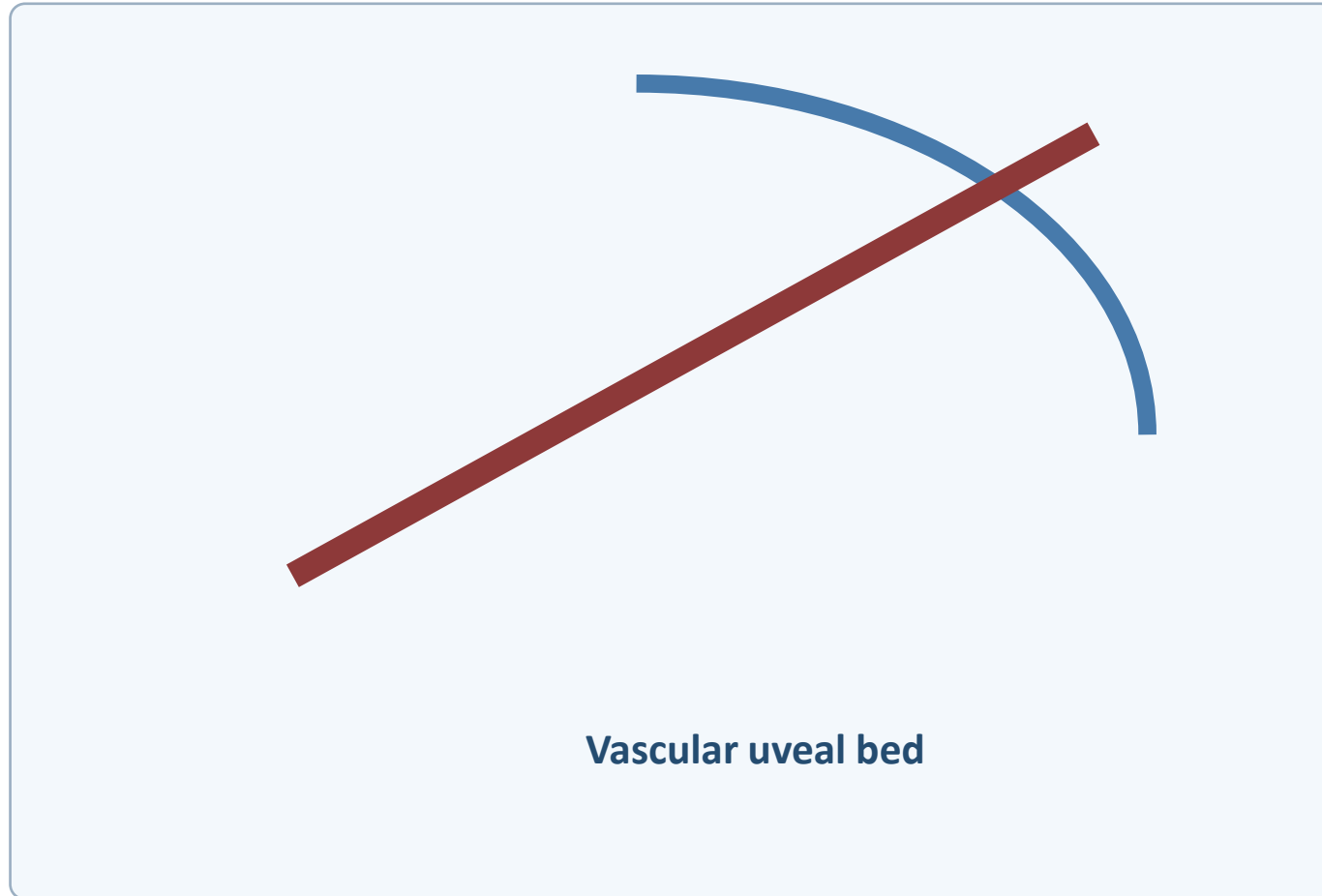
Schematic



- Iris: Regulates the pupillary aperture.
- Ciliary body: Forms aqueous humor and belongs to the anterior uvea.
- Choroid: Richly vascular tissue between sclera and retina.

The choroid is exceptionally vascular

Schematic



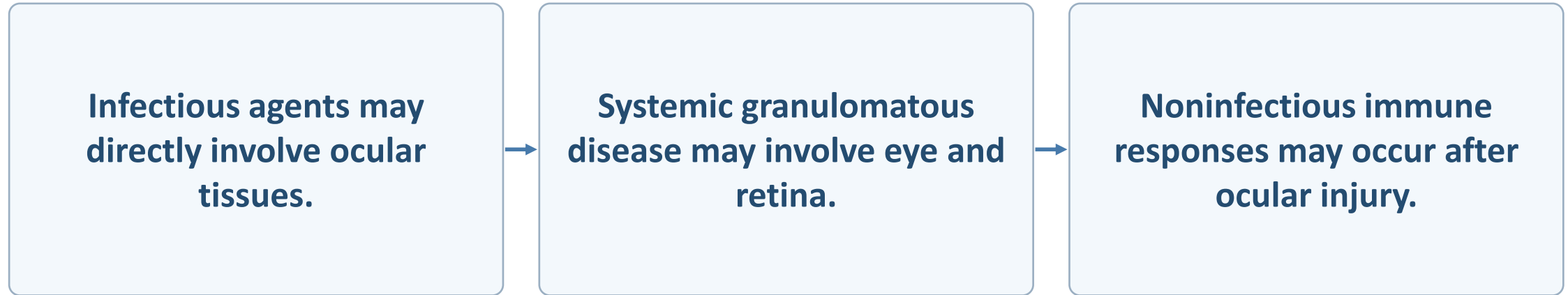
- The choroid as one of the most richly vascularized tissues.
- Inflammation in the choroid can be associated with clinically important retinal abnormalities.
- Posterior uveitis therefore requires assessment beyond the visible anterior chamber.

Uveitis is an anatomic and clinical term

- Broadly: Inflammation of one or more uveal tissues.
- In routine clinical usage: A heterogeneous group of ocular or systemic inflammatory diseases.
- Traumatic iritis and corneal-ulcer–associated iritis meet the broad definition but are not the whole clinical category.

Multiple mechanisms produce uveal inflammation

Schematic



The mechanism cannot be inferred from anatomy alone.

Anatomic classification guides examination

Iris / anterior chamber

Vitreous / middle segment

Choroid and retina

Anterior: Inflammation centered in the anterior chamber.

Intermediate: Inflammation centered in the vitreous.

Posterior: Retina or choroid is the principal site.

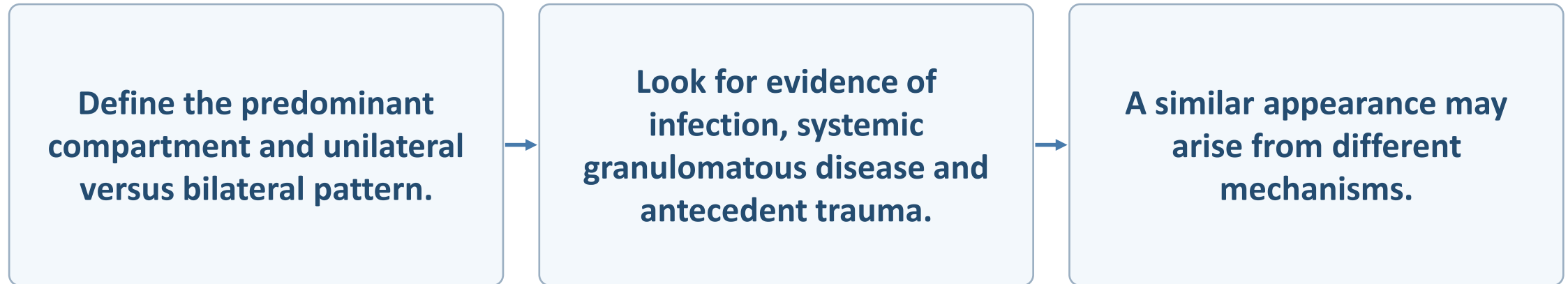
Panuveitis: Inflammation involving all major ocular compartments without one predominant site.

Chronic inflammation is clinically consequential

- Chronic uveitis as a heterogeneous group of disorders.
- Inflammatory exudates can damage structures even after the initiating trigger is absent.
- Persistent inflammation may generate synechiae, cataract or glaucoma.

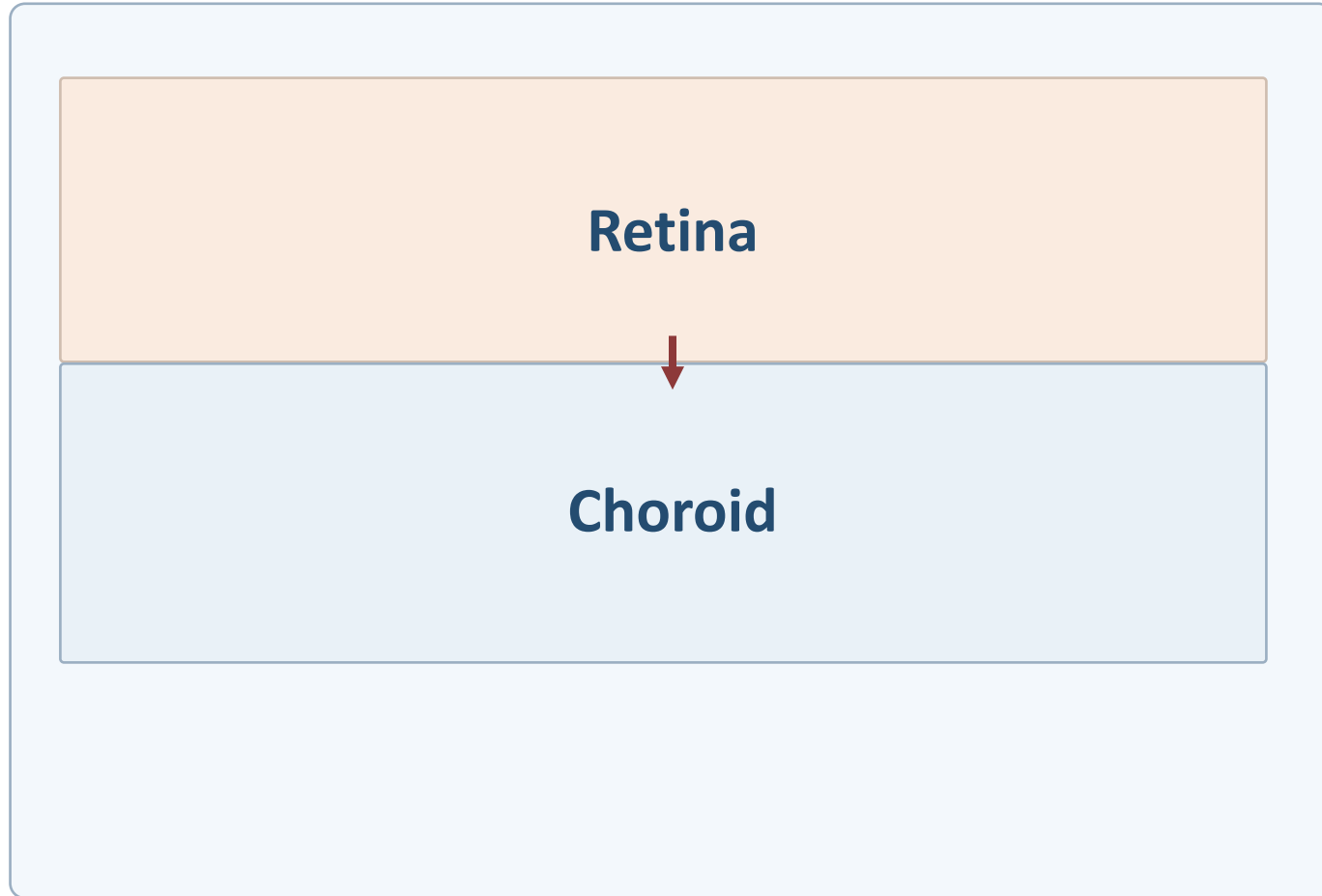
A useful etiologic approach is not a single diagnosis

Schematic



Retinal abnormalities often accompany uveitis

Schematic



- Retina and choroid are adjacent but anatomically distinct.
- Inflammation in one frequently coexists with inflammation in the other.
- Posterior-segment findings may drive visual loss even when anterior signs are modest.

Site and tissue response must be kept separate

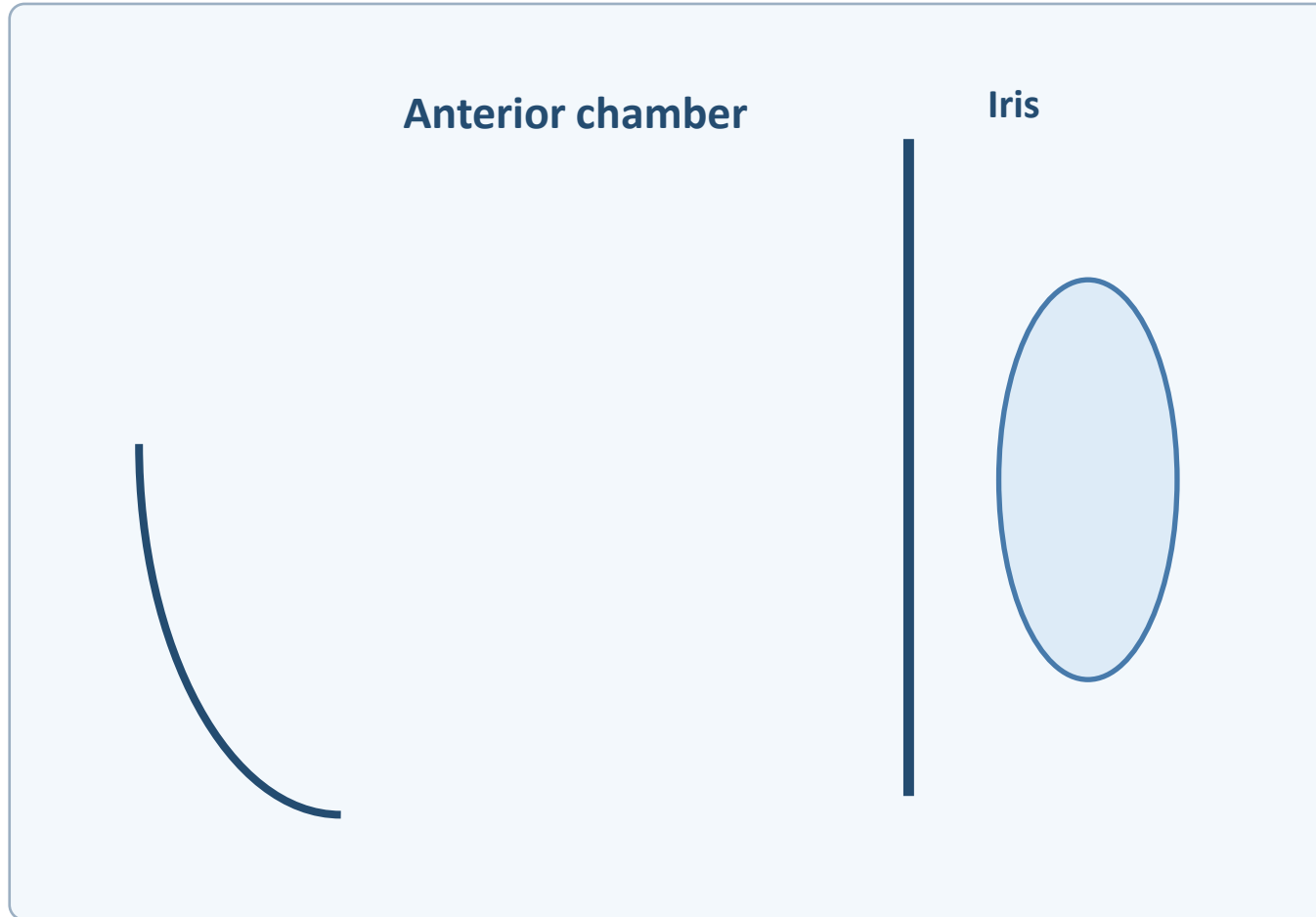
Anatomic location: Anterior, intermediate, posterior or panuveitis.

Histologic reaction: Granulomatous or non-granulomatous pattern.

Etiologic category: Infectious, systemic inflammatory or ocular-specific immune response.

The anterior chamber sits behind the cornea

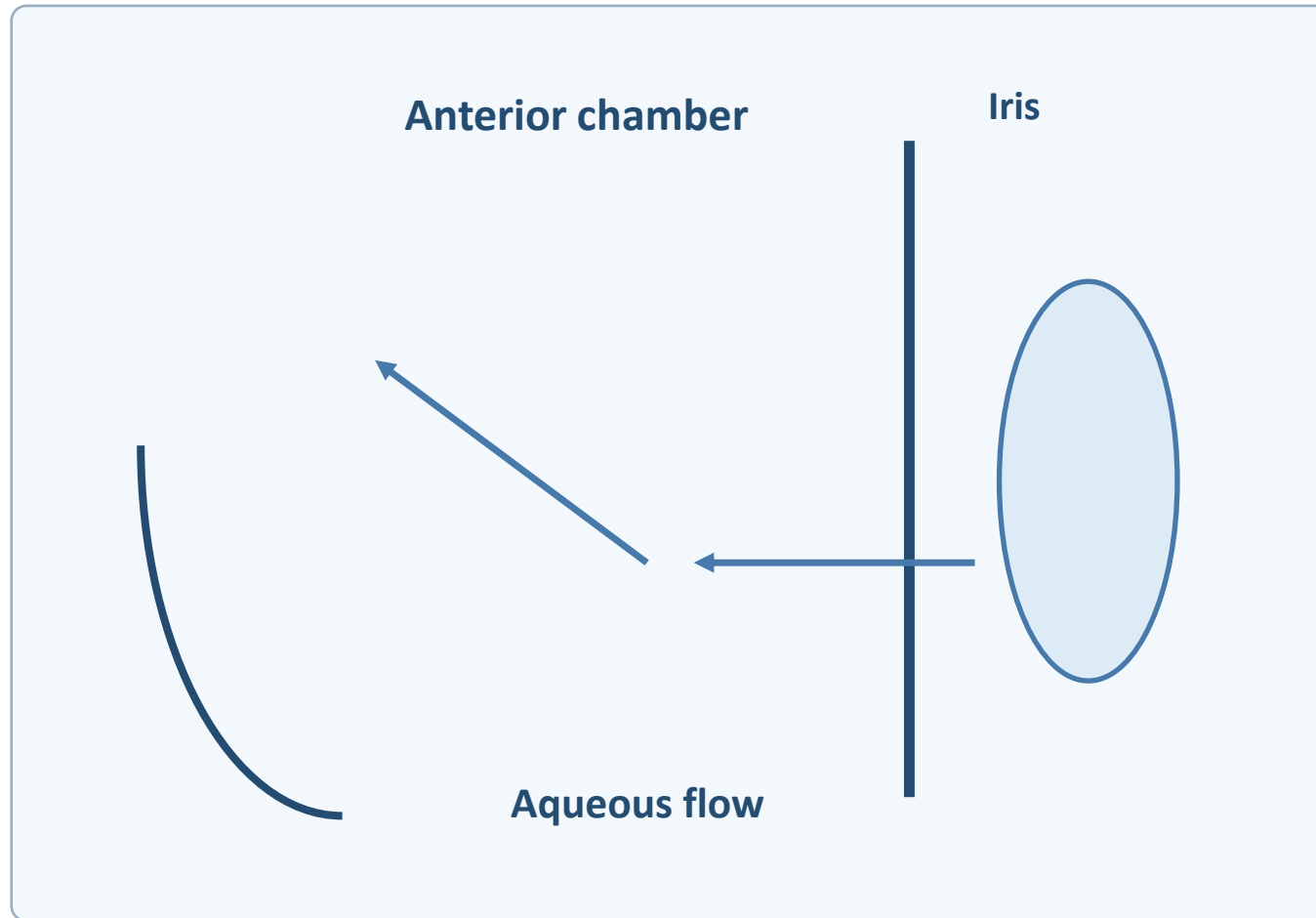
Schematic



- Anterior boundary: Corneal endothelium.
- Posterior boundary: Iris; Peripheral boundary: Angle and trabecular meshwork.
- Inflammatory exudates accumulate in the chamber and may form adhesions.

Aqueous humor traverses the pupil

Schematic



- Ciliary processes produce aqueous humor into the posterior chamber.
- Fluid flows through the pupil to reach the anterior chamber.
- Aqueous outflow depends on patency of the anterior chamber angle.

Inflammatory exudate arises from ocular vessels

Schematic

**Acute corneal inflammation
can provoke an exudative
response from iris and
ciliary-body vessels.**



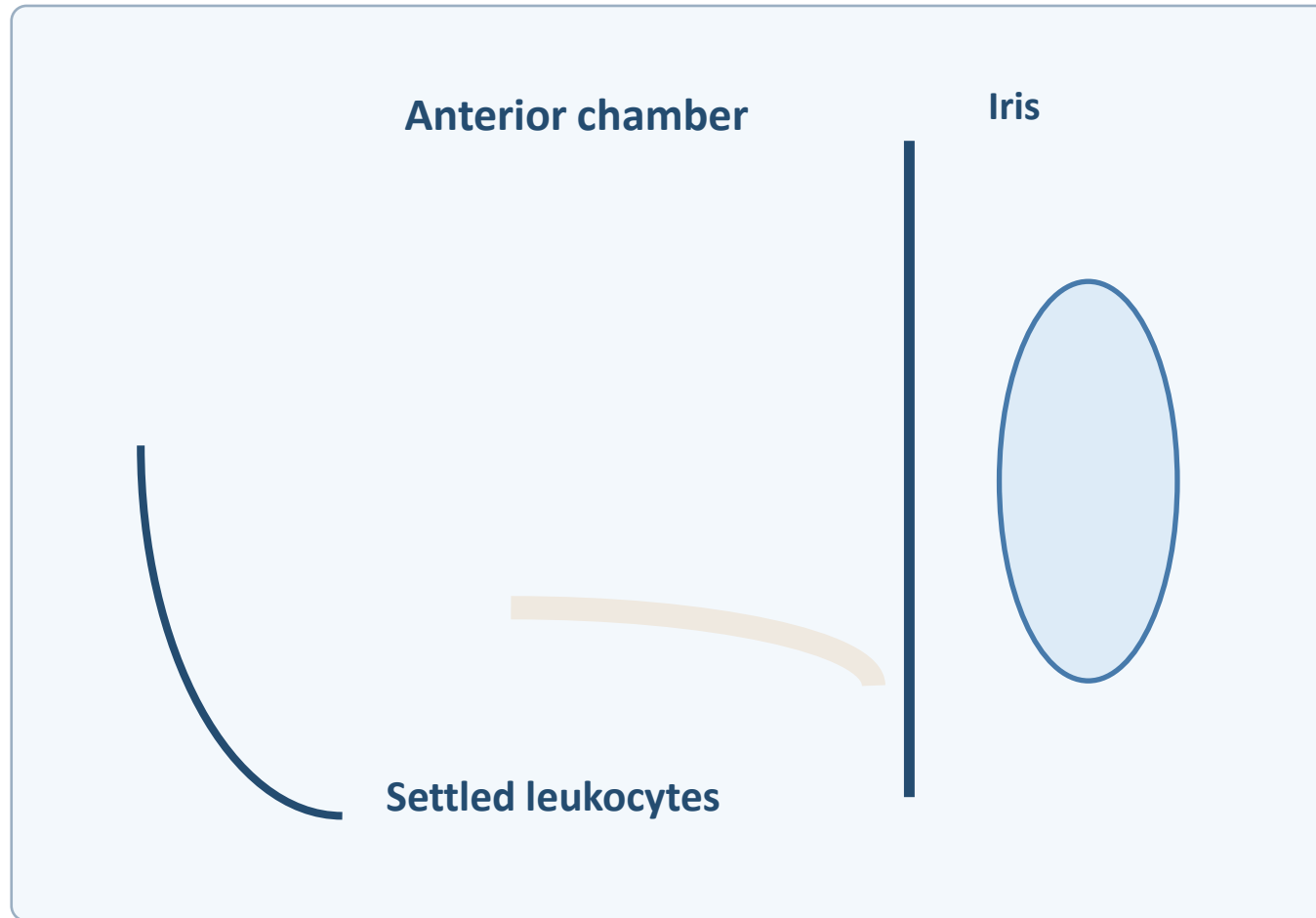
**The exudate contains
inflammatory cells and
proteins.**



**A normally optically clear
chamber becomes turbid.**

Hypopyon reflects gravitational sedimentation

Schematic



- Leukocytes may settle in the inferior anterior chamber.
- The resulting white layer is visible clinically as a hypopyon.
- Hypopyon reports inflammation but does not independently establish the responsible organism.

A hypopyon is not equivalent to endophthalmitis

Anterior-chamber hypopyon	Endophthalmitis
White leukocytic layer	Vitreous involvement
May be sterile	Inflammation extends into vitreous
Does not define etiology	Defines anatomic involvement

Hypopyon associated with an infected cornea seldom contains organisms.

Slit-lamp “cells” indicate leukocytes

- Discrete inflammatory cells scatter reflected light against a dark background.
- The normal aqueous chamber should be optically clear.
- Cells are evidence of an active inflammatory cellular response.

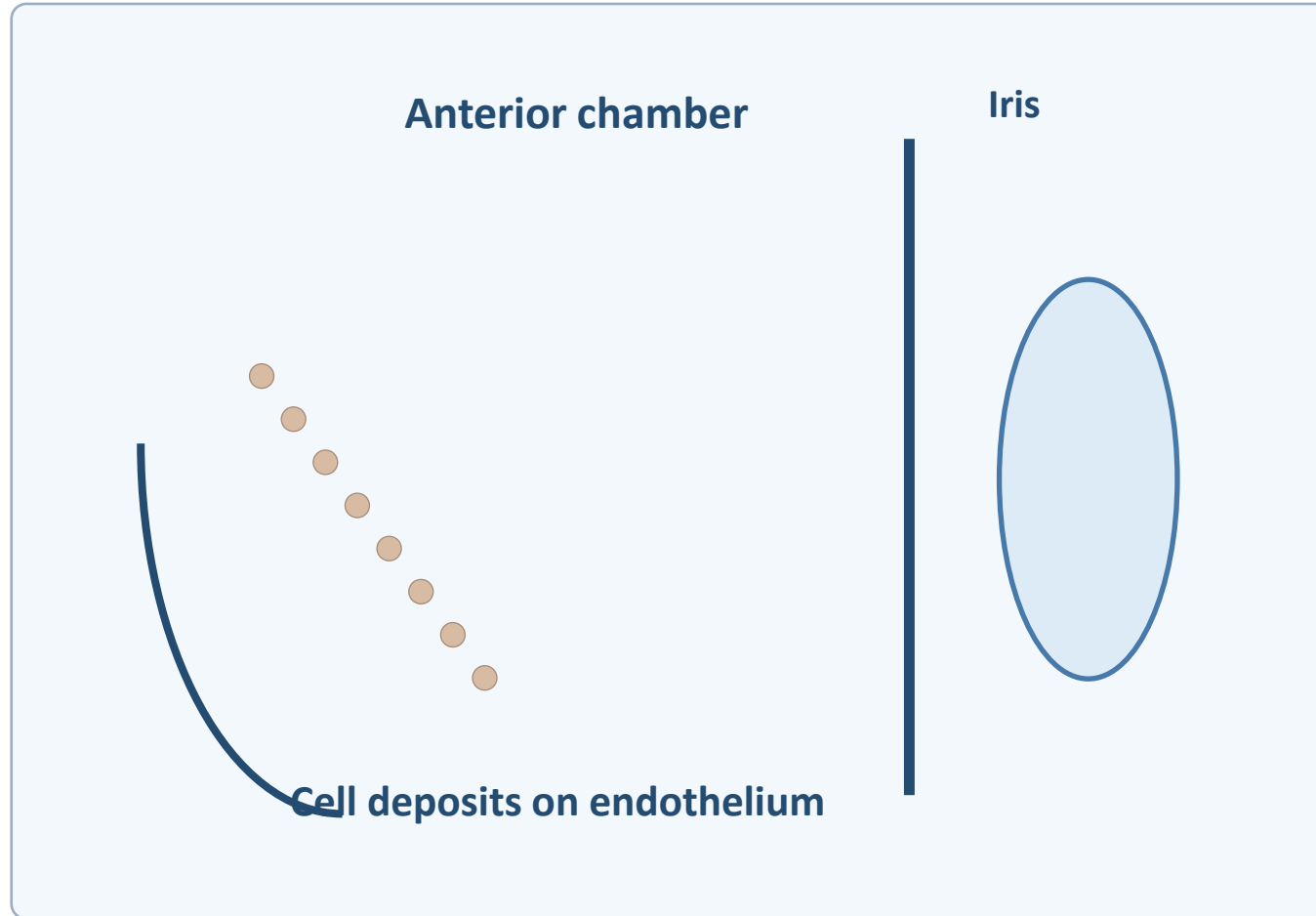
Slit-lamp “flare” indicates proteinaceous exudate

Cells	Flare
Particulate inflammatory cells	Protein-rich aqueous haze
Discrete dots in slit beam	Diffuse light-scattering beam
Cellular recruitment	Increased vascular permeability

Breakdown of the normal aqueous barrier increases visible protein in chamber fluid.

Keratic precipitates form on endothelium

Schematic



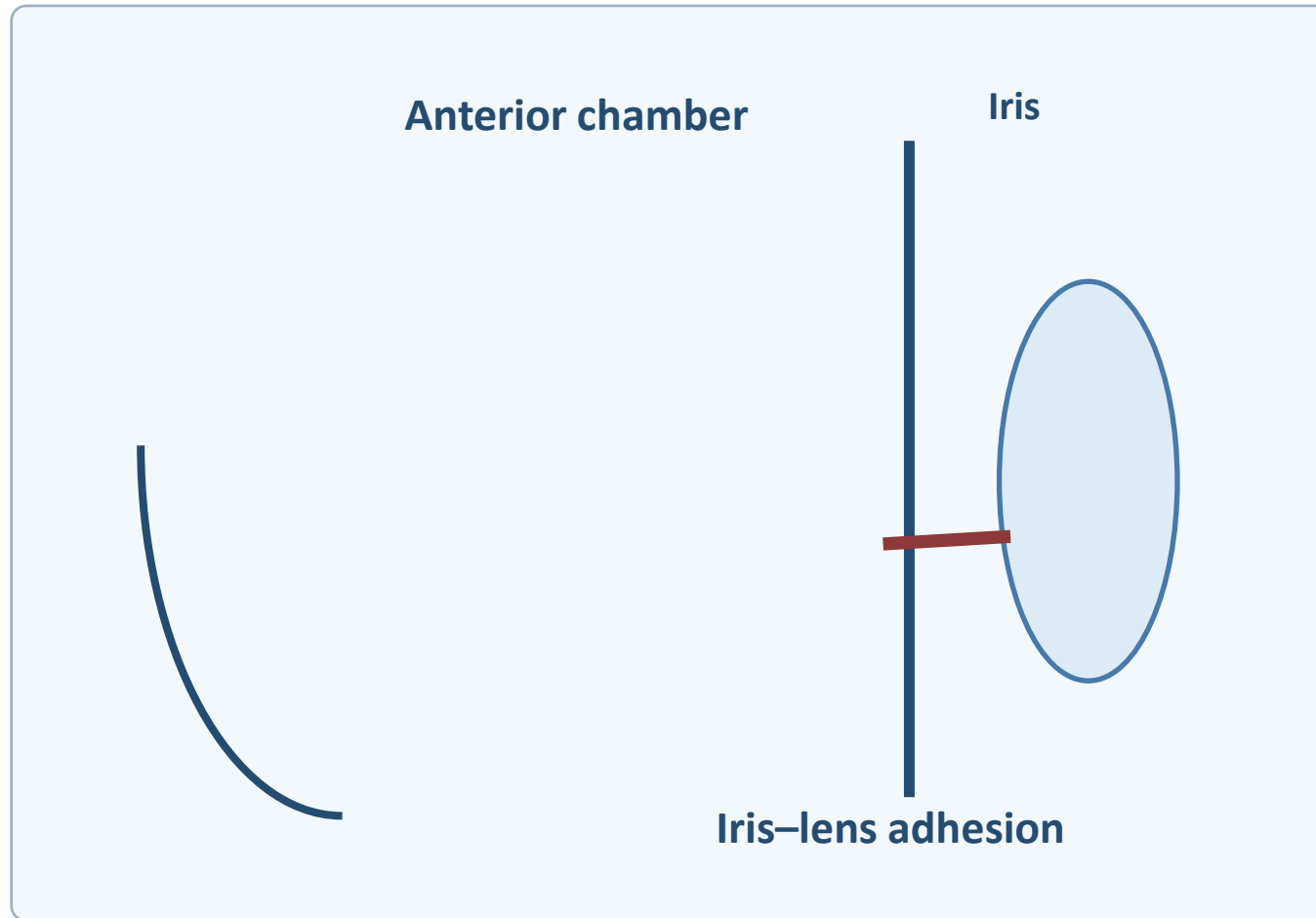
- Inflammatory cells can adhere to the posterior corneal surface.
- These visible deposits are called keratic precipitates.
- Their morphology may suggest granulomatous inflammation but does not prove an etiology.

“Mutton-fat” precipitates imply a granulomatous pattern

- Sarcoid anterior uveitis may produce large, greasy-appearing keratic precipitates.
- The precipitates evolve from an anterior-segment exudate.
- They are a characteristic clinical clue, not a stand-alone sarcoidosis diagnosis.

Synechiaie are organized inflammatory adhesions

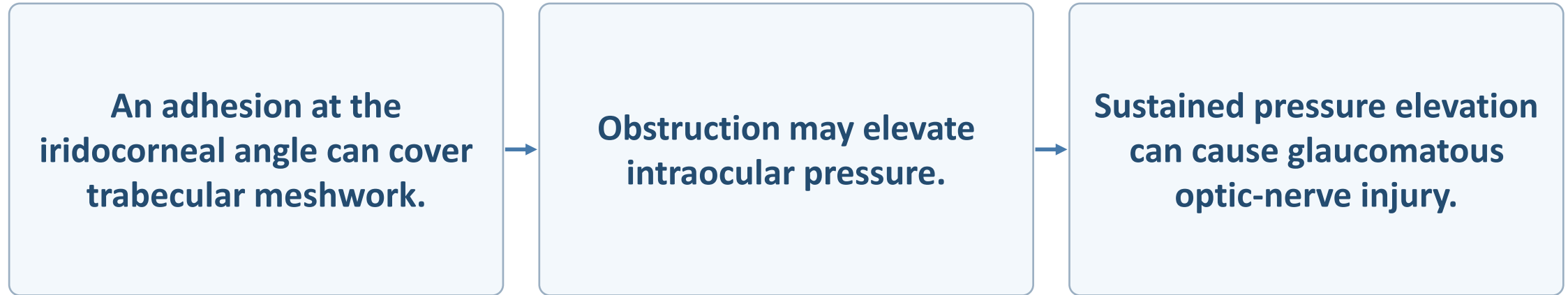
Schematic



- Anterior synechiaie: Iris adheres to cornea or angle structures.
- Posterior synechiaie: Iris adheres to anterior lens surface.
- Location determines the mechanism of subsequent visual damage.

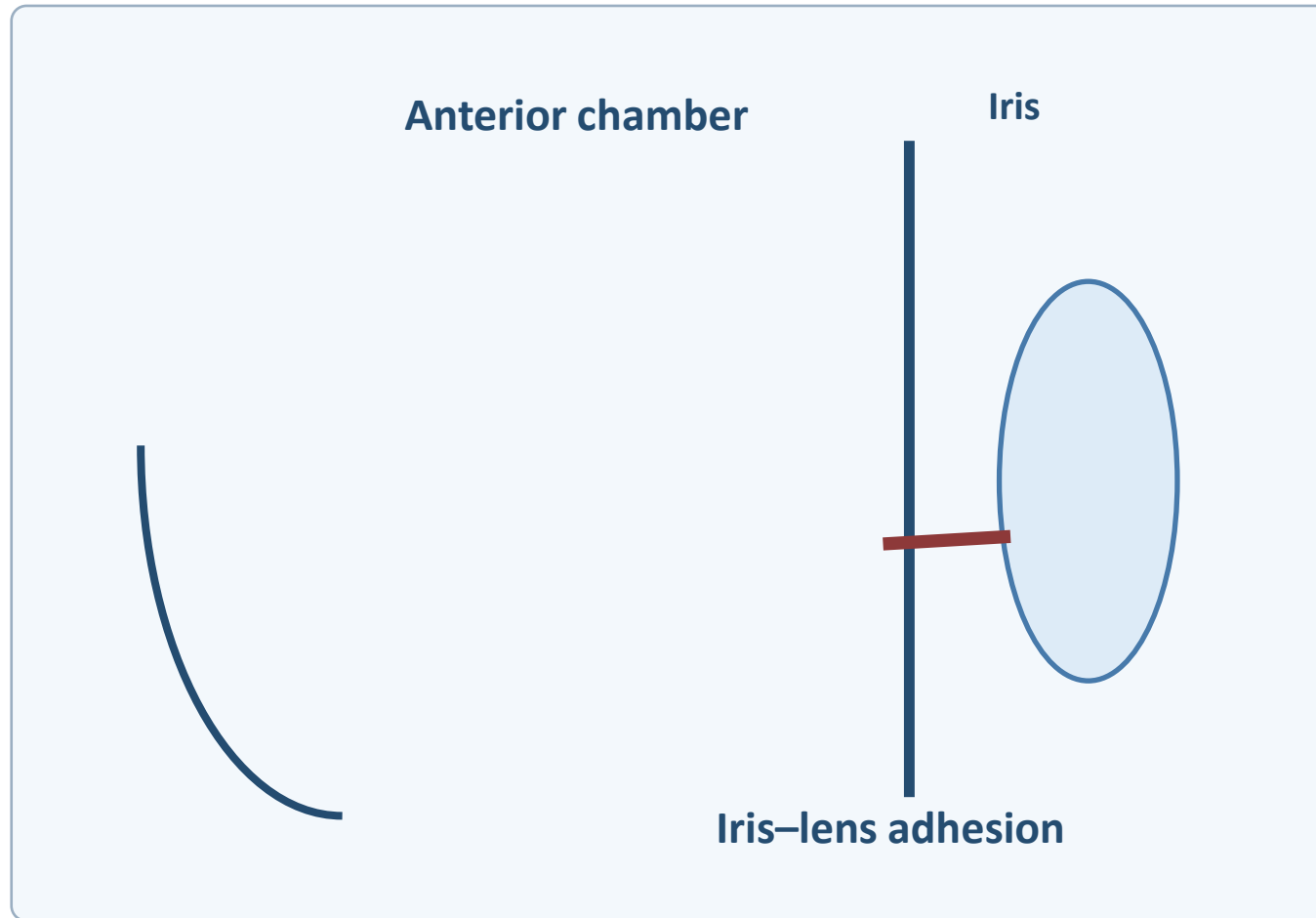
Anterior synechiae may obstruct outflow

Schematic



Posterior synechiae tether the iris to lens

Schematic



- Chronic exudate encourages iris–lens adhesion.
- Prolonged contact disrupts the normal interface of lens epithelium with aqueous humor.
- The anatomic contact can stimulate metaplastic changes in the lens epithelium.

An anterior subcapsular cataract can result

Schematic

**Posterior synechiae may
deprive adjacent lens
epithelium of aqueous
contact.**



**Fibrous metaplasia can yield
an anterior subcapsular
opacity.**



**The cataract is a secondary
structural consequence of
inflammation, not the
uveitis itself.**

Cycloplegia limits adhesion formation

Schematic

**Pharmacologic pupil dilation
and cycloplegia as measures
to reduce synechiae
formation.**



**Maintaining iris mobility
counters prolonged
apposition.**



**This is a mechanistic
complication-prevention
principle, not a complete
treatment algorithm.**

Chronic inflammation can cause band keratopathy

- Calcific band keratopathy results from calcium deposition near Bowman layer.
- Chronic uveitis as one predisposing circumstance.
- Corneal opacity then adds an anterior optical cause of impaired vision.

Anterior damage follows predictable pathways

Schematic



Sarcoidosis is a systemic granulomatous cause

- Sarcoidosis as an important cause of granulomatous uveitis.
- Ocular disease may involve anterior and posterior segments.
- Retinal signs reflect inflammation adjacent to, and within, posterior ocular tissues.

Granulomatous uveitis spans both segments

Iris / anterior chamber

Vitreous / middle segment

Choroid and retina

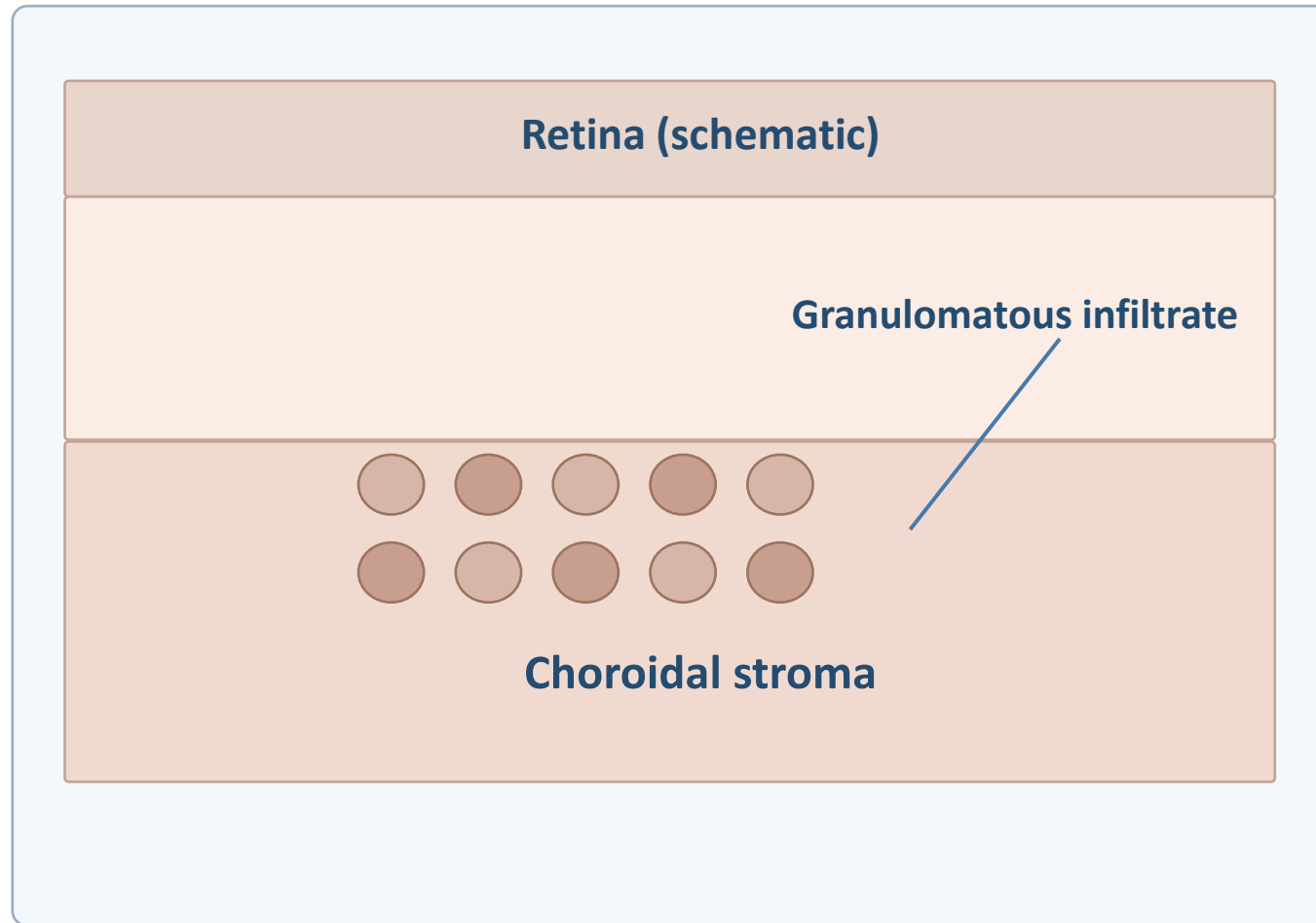
Anterior: Exudate with large keratic precipitates.

Choroid: Granulomatous infiltrates can be present.

Retina: Perivascular inflammatory changes are prominent.

Sarcoid choroiditis may contain granulomas

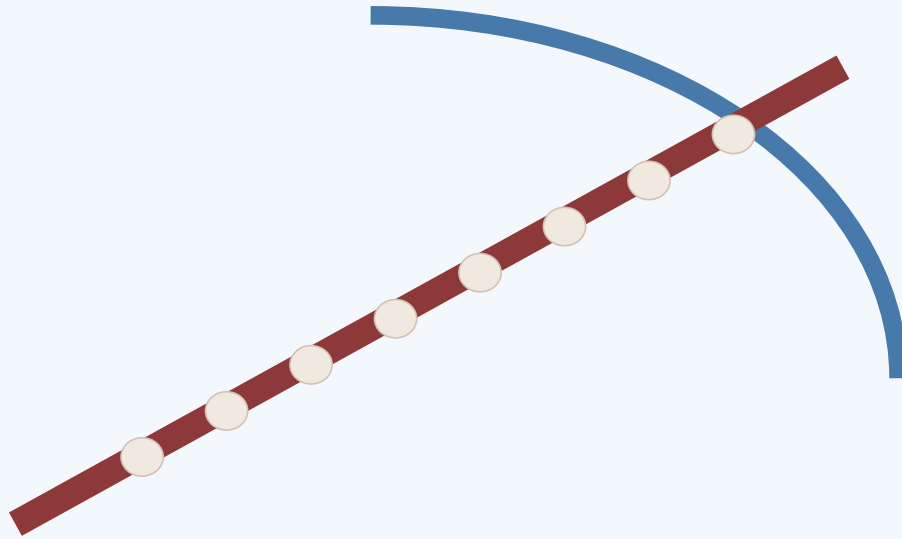
Schematic



- Granulomas can develop within the vascular choroid.
- The lesion is anatomically posterior to the retina.
- An explanatory schematic must not be confused with actual histology or fundus photography.

Retinal perivascular inflammation is central

Schematic

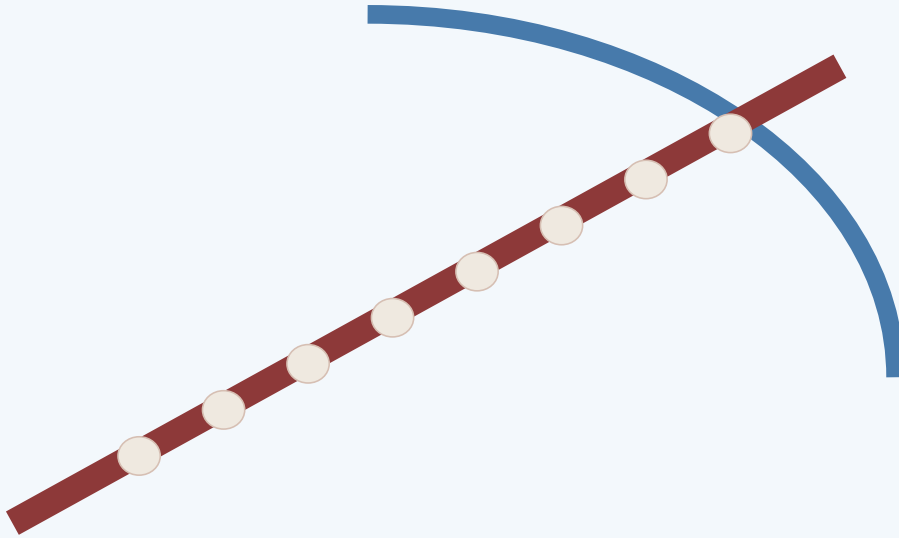


Perivenous inflammatory deposits

- Retinal vascular sheathing reflects inflammation along vessels.
- In sarcoid uveitis, perivascular inflammation may be visible ophthalmoscopically.
- The vessel-associated distribution helps distinguish it from isolated choroidal nodules.

“Candle wax drippings” describe vessel-associated exudates

Schematic

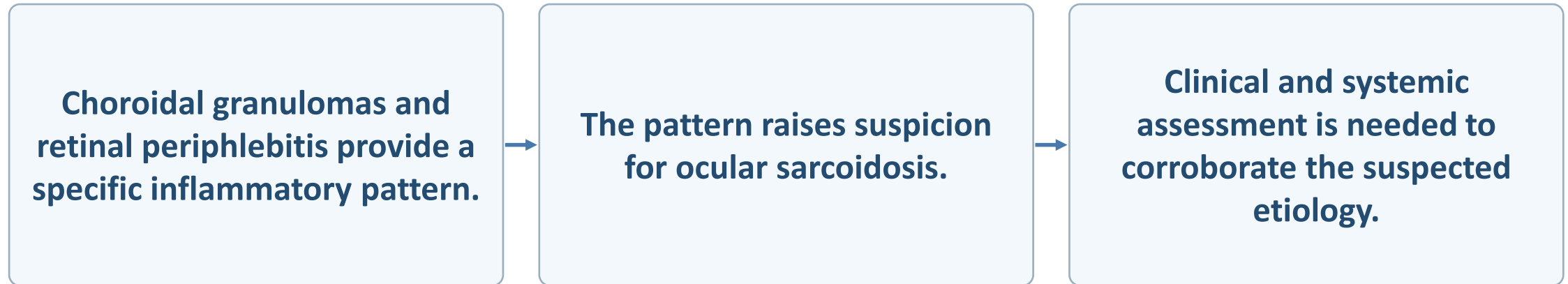


Perivenous inflammatory deposits

- Characteristic whitish perivascular deposits track along retinal veins.
- The appearance is associated with sarcoid retinal periphlebitis.
- It is a descriptive clinical sign and must be integrated with systemic and ocular data.

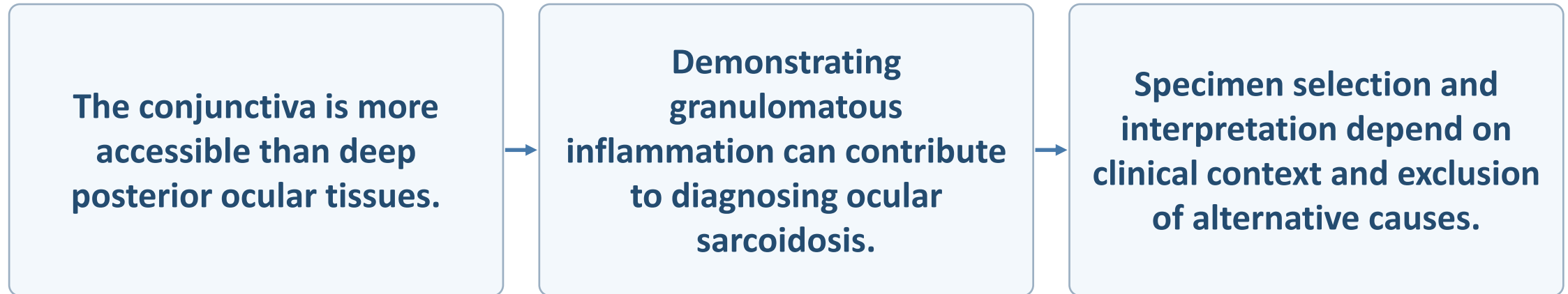
A posterior finding can inform systemic investigation

Schematic



Conjunctival biopsy may yield tissue confirmation

Schematic



Granulomatous morphology is not a unique label

Granulomatous pattern	Etiologic diagnosis
What tissue does	Why it occurs
May recur in multiple diseases	Requires contextual evidence
Not synonymous with sarcoid	Not determined by one cell type

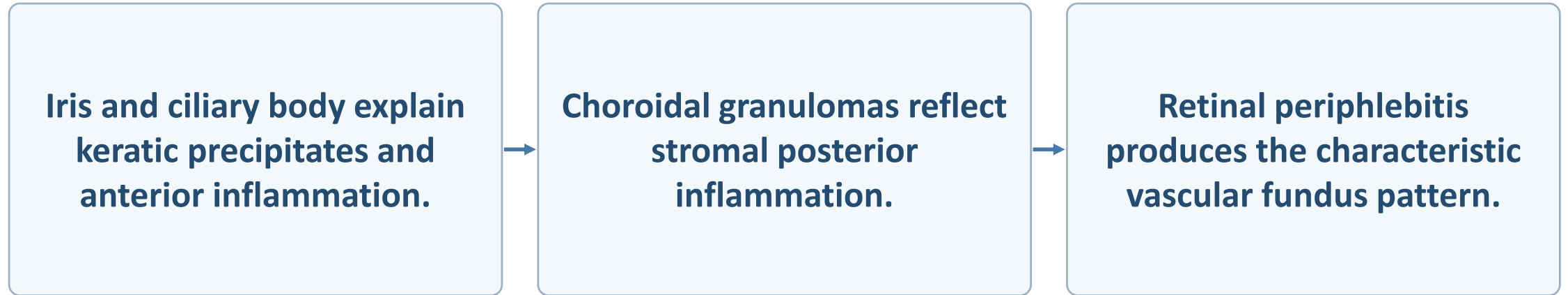
Sarcoidosis and sympathetic ophthalmia can both produce granulomatous uveitis.

The 2019 IWOS consensus emphasizes exclusion

- The revised ocular sarcoidosis framework begins by excluding other causes of granulomatous uveitis.
- It integrates characteristic ocular signs with systemic assessment and biopsy information.
- Consensus classifications support structured assessment; They do not replace clinicopathologic judgment.

Ocular sarcoid can involve more than one tissue

Schematic



Sarcoidosis: Trace the sign back to the tissue

Mutton-fat deposits → cells adhering to corneal endothelium.

Choroidal nodule → granulomatous inflammation in uveal stroma.

Candle-wax vascular sheathing → retinal perivascular inflammation.

Case: Chronic granulomatous inflammation

A patient has anterior keratic precipitates and retinal venous sheathing.

Interpretation: The combined anterior/posterior pattern is compatible with ocular sarcoidosis.

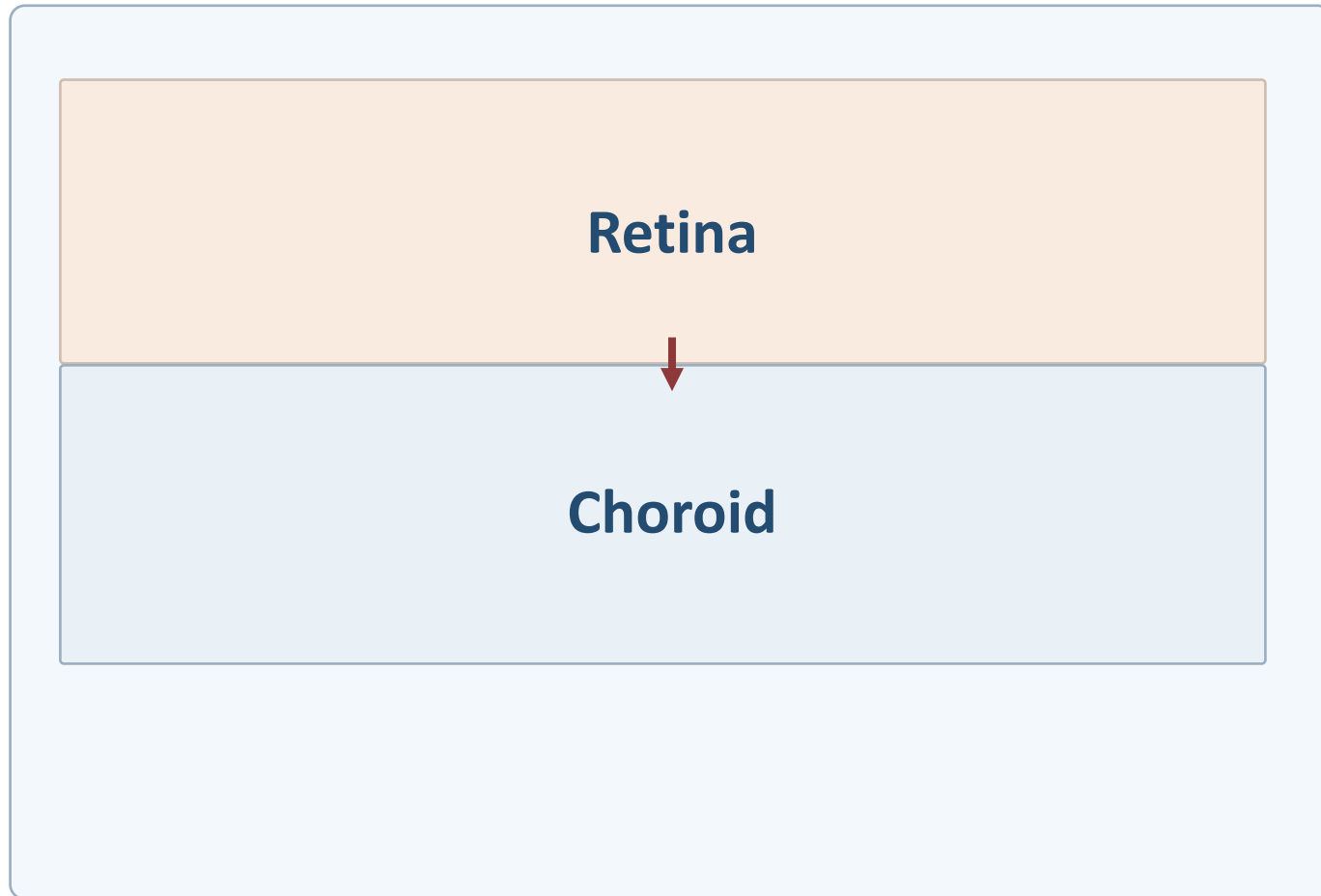
Next step: A granulomatous pattern should prompt a search for corroborating systemic evidence and alternative causes.

Sarcoidosis: What is and is not established

- Established: Keratic precipitates, choroidal granulomas and retinal perivascular inflammation.
- Not established by one ocular sign: Systemic sarcoidosis as the sole possible cause.
- Appropriate inference: Compare findings and assess for mimics before etiologic attribution.

Infectious posterior uveitis links compartments

Schematic



- Infection may involve retina, choroid or both.
- Inflammation in one compartment often accompanies inflammation in the adjacent compartment.
- Describing the primary focus and associated uveitis improves anatomic precision.

Several infectious examples

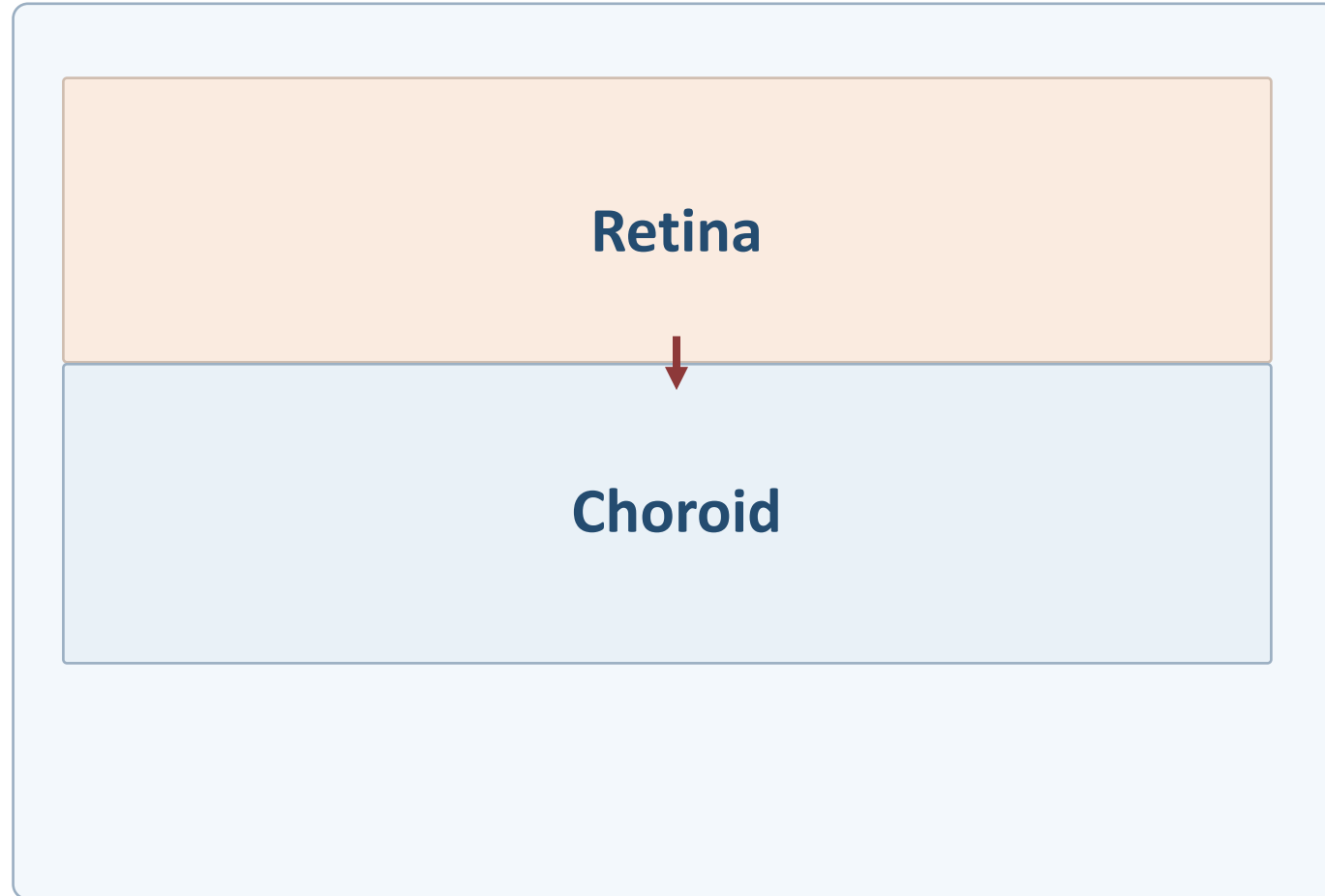
Retinal toxoplasmosis with uveitis.

Cytomegalovirus retinitis in patients with AIDS.

Pneumocystis-associated uveal infection and mycobacterial choroiditis in AIDS.

Toxoplasmosis commonly manifests as retinochoroiditis

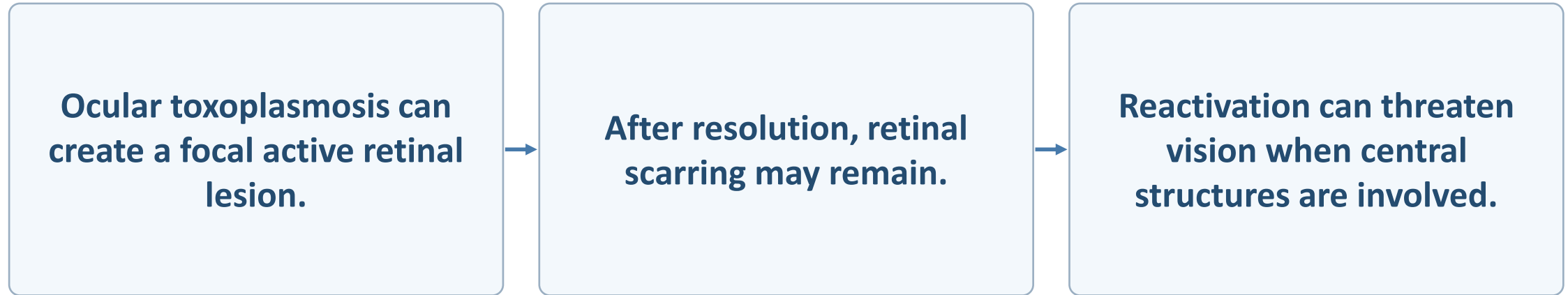
Schematic



- The retinal inflammatory focus is commonly accompanied by uveal inflammation.
- Occasional associated scleritis.
- The diagnostic target is the retinal lesion together with the surrounding ocular response.

Retinal inflammation may heal with a scar

Schematic



Toxoplasma symptoms reflect inflammatory anatomy

- Blurred or reduced vision indicates functional retinal or media involvement.
- Photophobia, ocular discomfort and redness may accompany inflammation.
- Clinical symptoms are not sufficiently specific to assign an infectious organism.

CMV retinitis is an opportunistic setting

- CMV retinitis in individuals with AIDS.
- The immune status is part of the diagnostic context.
- The textbook example emphasizes posterior retinal infection rather than isolated anterior iritis.

Pneumocystis can involve the uvea

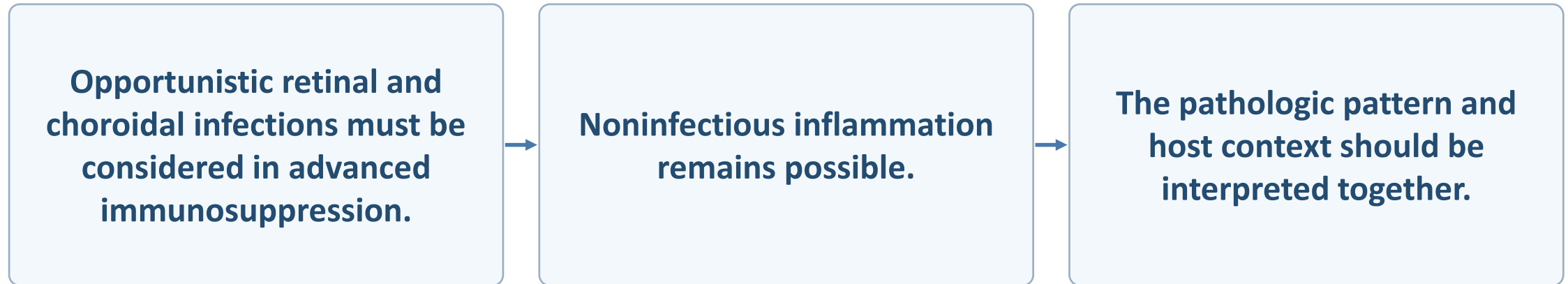
- Pneumocystis as an example of infectious uveitis.
- In patients with AIDS, the organism may produce uveal infection.
- The named organism does not imply that every uveitis in immunocompromise is infectious.

Mycobacterial infection may target the choroid

- Mycobacterial choroiditis is included among AIDS-associated ocular infections.
- A choroidal location may coexist with retinal inflammatory findings.
- Infectious granulomatous disease is an important competing explanation for posterior ocular inflammation.

Immune status changes the differential

Schematic



Do not suppress inflammation before considering infection

- Corticosteroid or immunosuppressive treatment may be appropriate in selected noninfectious uveitides.
- Unrecognized infection changes the safety of that strategy.
- Establishing infectious versus noninfectious etiology is therefore a clinically consequential distinction.

Case: Posterior inflammation in advanced AIDS

A patient with advanced HIV-related immunosuppression develops a posterior retinal lesion.

Interpretation: Robbins explicitly lists CMV retinitis and other opportunistic posterior infections.

Next step: Organism-specific evaluation is required; The anatomic term “uveitis” is insufficient.

Sympathetic ophthalmia is a bilateral panuveitis

Iris / anterior chamber

Vitreous / middle segment

Choroid and retina

The disease is noninfectious and granulomatous.

Both the previously injured and contralateral eye may be affected.

Diffuse uveal inflammation involves iris, ciliary body and choroid.

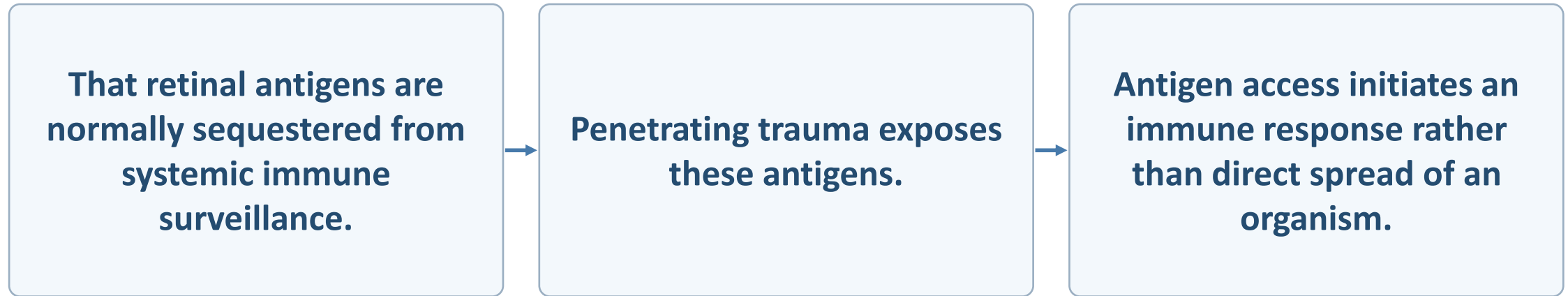
A penetrating eye injury can precede disease

Exciting eye	Sympathizing eye
Antecedent ocular injury	Fellow eye becomes inflamed
Source of antigen exposure	Immune-mediated involvement
Also may show uveitis	Often prompts recognition

Sympathetic ophthalmia can follow penetration of one globe.

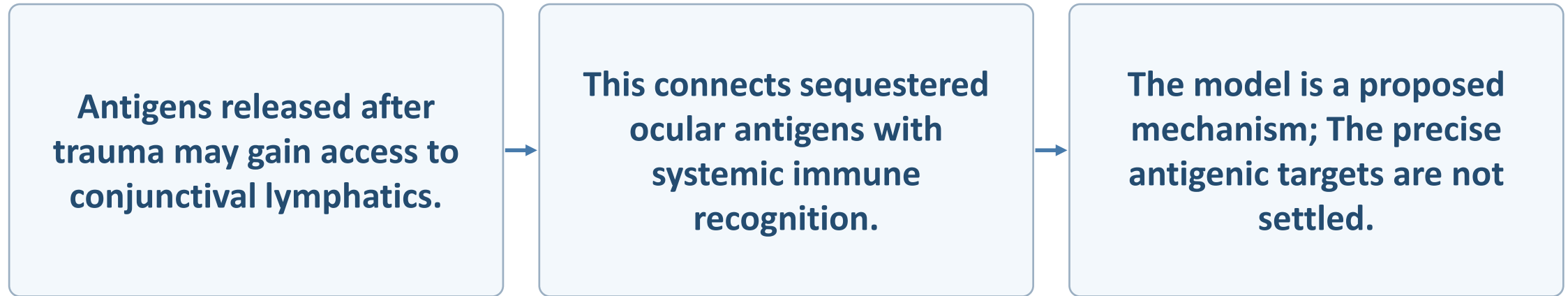
Sequestered ocular antigens can become exposed

Schematic



Conjunctival lymphatics provide an immune route

Schematic



Delayed hypersensitivity is the pathogenic model

Schematic

A delayed hypersensitivity reaction after antigen exposure.



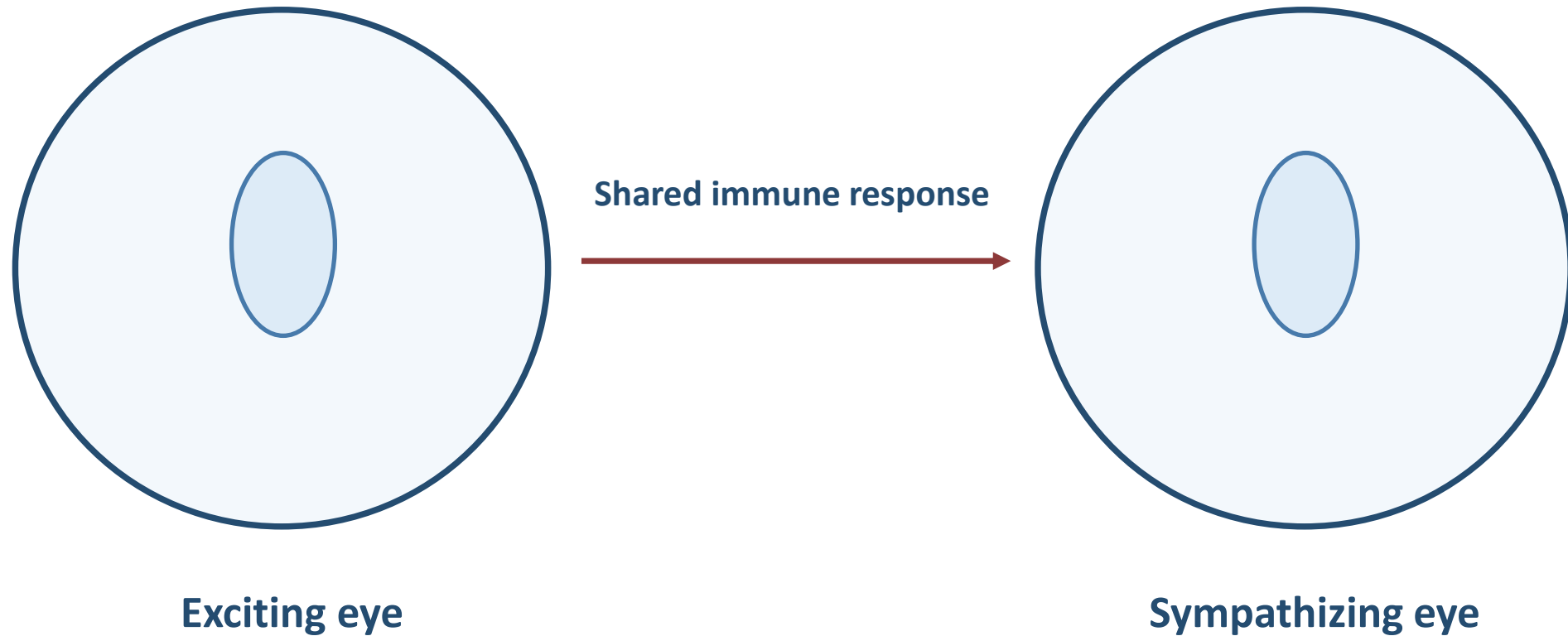
The response targets uveal tissues in both eyes.



This is a cell-mediated immune explanation for bilateral granulomatous inflammation.

Bilateral disease is not direct ocular spread

Schematic



The latency can be long

Schematic

Symptoms may begin after a short interval or many years after injury.



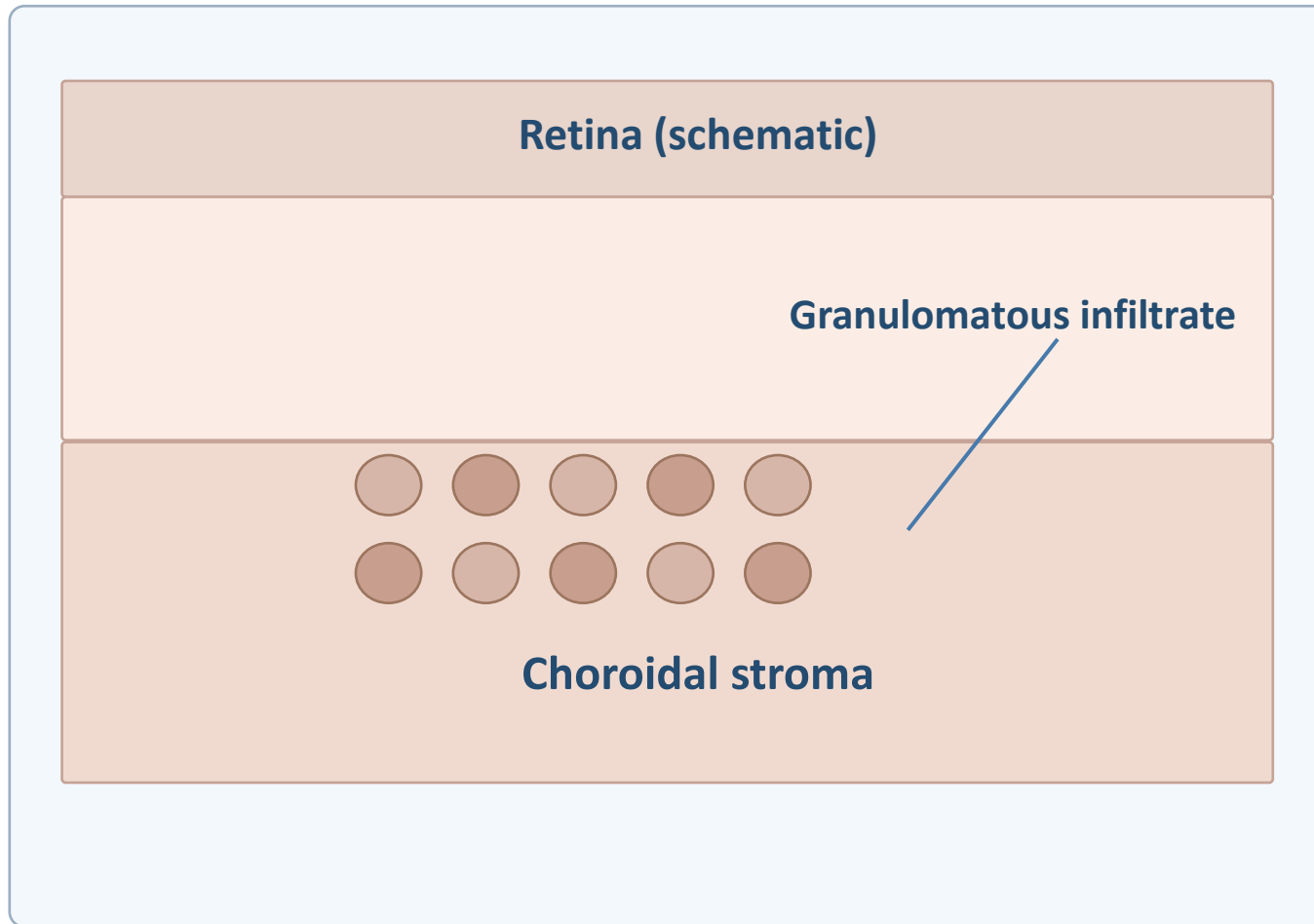
Robbins specifies approximately 2 weeks to many years.



A remote trauma history remains diagnostically relevant.

Sympathetic ophthalmia has diffuse uveal granulomas

Schematic



- Histologic inflammation may be present throughout choroid, ciliary body and iris.
- Granulomatous inflammation is the principal tissue pattern.
- A localized posterior lesion alone would not convey the full pathologic distribution.

Pigmented material may occur within granulomas

- Robbins Fig. 29.13 describes melanin pigment within uveal granulomas.
- Pigment can reflect the involved pigmented ocular tissues.
- The presence of pigment is a microscopic descriptor, not an organism or biomarker.

The inflammatory cellular mixture has a pattern

Typical reported finding	Important qualification
Diffuse uveal granulomas	Not unique to this disease
Plasma cells usually absent	Not an absolute exclusion rule
Eosinophils may be present	Variable finding

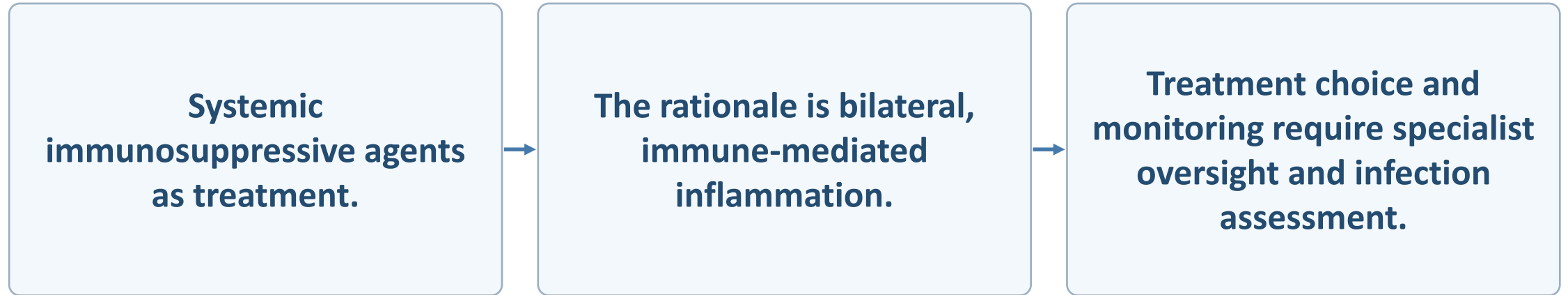
Plasma cells as typically absent.

Dalen–Fuchs nodules are an additional clue

- The sympathetic-ophthalmia review describes sub–retinal pigment epithelial nodules.
- They may correspond to yellow-white fundus spots.
- They are not obligatory or pathognomonic; This detail supplements the Robbins extract.

Treatment targets the systemic immune response

Schematic



Enucleation can supply diagnostic pathology

- A blind eye may be removed and provide tissue for examination.
- Robbins cautions that the enucleated blind eye is not necessarily the originally injured eye.
- Gross history and microscopic distribution must be interpreted together.

Compare sarcoidosis with sympathetic ophthalmia

Sarcoid-associated uveitis	Sympathetic ophthalmia
Systemic inflammatory setting	History of ocular penetration
Periphlebitis/candle-wax sign	Bilateral granulomatous panuveitis
Choroidal granulomas	Diffuse uveal granulomatous inflammation

Both may produce granulomatous anterior and posterior inflammation.

Case: Delayed inflammation of the fellow eye

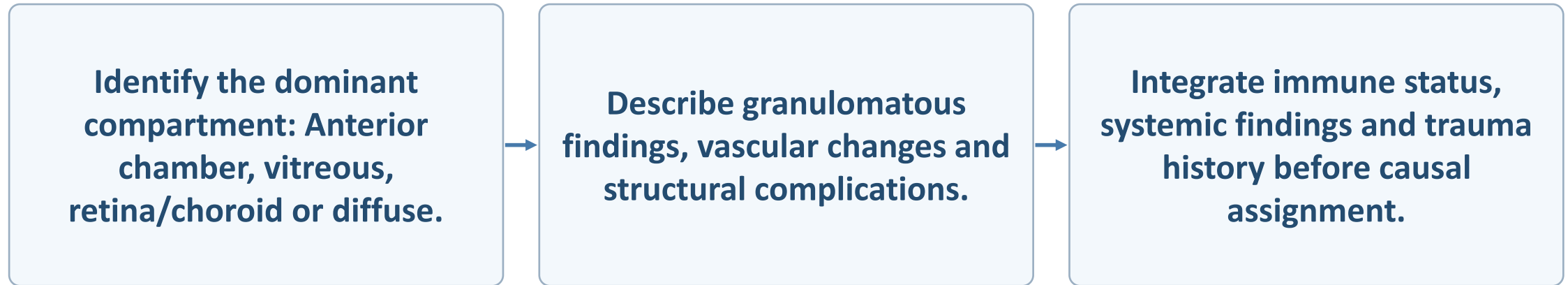
An eye develops granulomatous inflammation months after penetrating injury to the opposite eye.

Interpretation: Bilateral uveal involvement and delayed onset strongly suggest sympathetic ophthalmia.

Next step: Exclude competing granulomatous and infectious explanations before diagnosis.

A disciplined evaluation starts with localization

Schematic



Mechanism, morphology and context work together

Anterior synechiae link inflammation to impaired aqueous drainage.

Sarcoid periphlebitis links a retinal vascular sign to granulomatous disease.

Retinochoroiditis links posterior infection to adjacent uveal inflammation.

Sympathetic ophthalmia links penetrating trauma to bilateral immune disease.

Five clinicopathologic conclusions

- Uveitis is heterogeneous: Identify the involved tissue and mechanism.
- Anterior chamber exudates can create synechiae, cataract and glaucoma.
- Sarcoid produces choroidal granulomas and retinal periphlebitis.
- Infection must be considered, particularly with immunosuppression.
- Sympathetic ophthalmia is delayed bilateral granulomatous inflammation after ocular injury.

Application: Do the signs establish etiology?

A patient shows mutton-fat keratic precipitates and bilateral posterior inflammation.

Interpretation: What evidence would favor sarcoidosis rather than sympathetic ophthalmia?

Next step: What infections must be considered before initiating immunosuppressive treatment?

Selected references

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