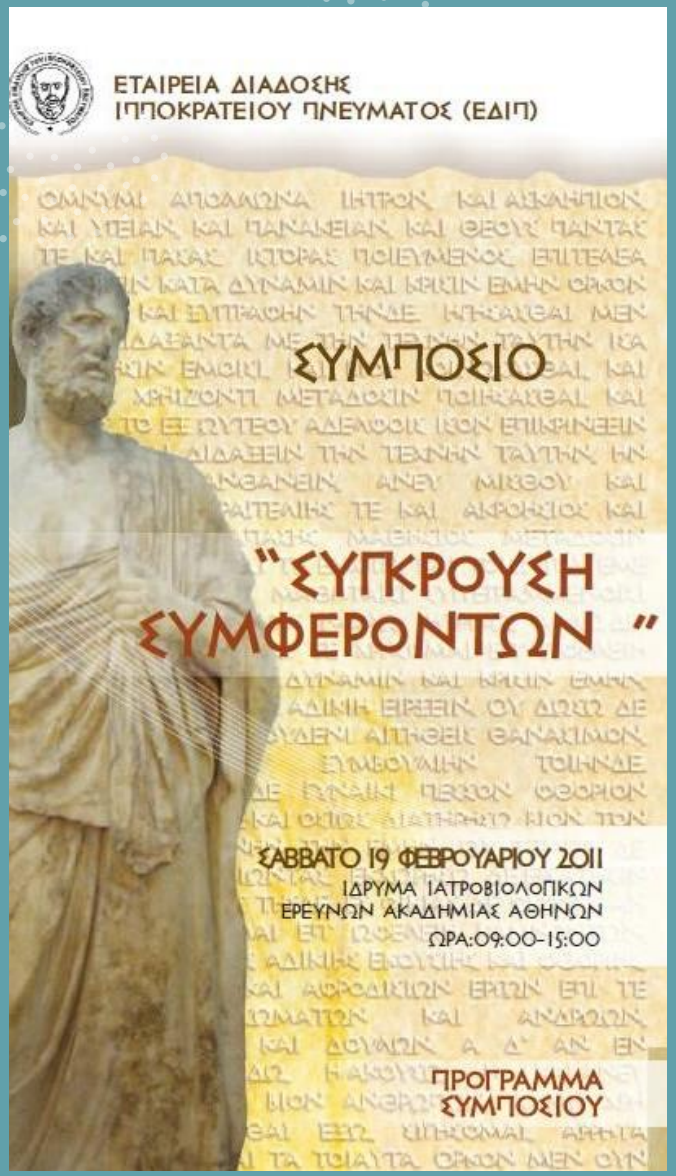
Inflammatory eye disease for rheumatologists

Ανδρέας Γ. Μπούνας
ΡΕΥΜΑΤΟΛΟΓΟΣ
ΠΑΤΡΑ

CONFLICT OF INTEREST

ΔΕΝ προβλέπεται Honorarium για την συγκεκριμένη παρουσίαση



INTRODUCTION

Σχεδόν όλα τα ρευματικά νοσήματα …

…Δυνητικά προσβάλουν το μάτι

- Το εσωτερικό (ραγοειδίτιδα)
- Εξωτερικά στρώματα (σκληρίτιδα, επισκληρίτιδα, κερατίτιδα, επιπεφυκίτιδα)
- Περιοφθαλμικές δομές (βλεφαρίτιδα)

Kelly Corbitta and Johannes Nowatzkya

Curr Opin Rheumatol 2023

Η φλεγμονή …συστηματική ή

μόνο στο μάτι

ΔΔ από λοιμώξεις, κακοήθειες,μεταβολικά νοσήματα και φάρμακα

Kelly Corbitt[a] *and Johannes Nowatzky*[a,b,c]

Curr Opin Rheumatol 2023, 35:201–212

Kelly Corbitt[a] *and Johannes Nowatzky*[a,b,c]

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The Autoimmune-mediated ocular disorders

Χρειάζονται μακροχρόνια θεραπεία

Ακόμα και επί απουσίας συστηματικής φλεγμονής !

Απαραίτητη η συνεργασία ειδικοτήτων

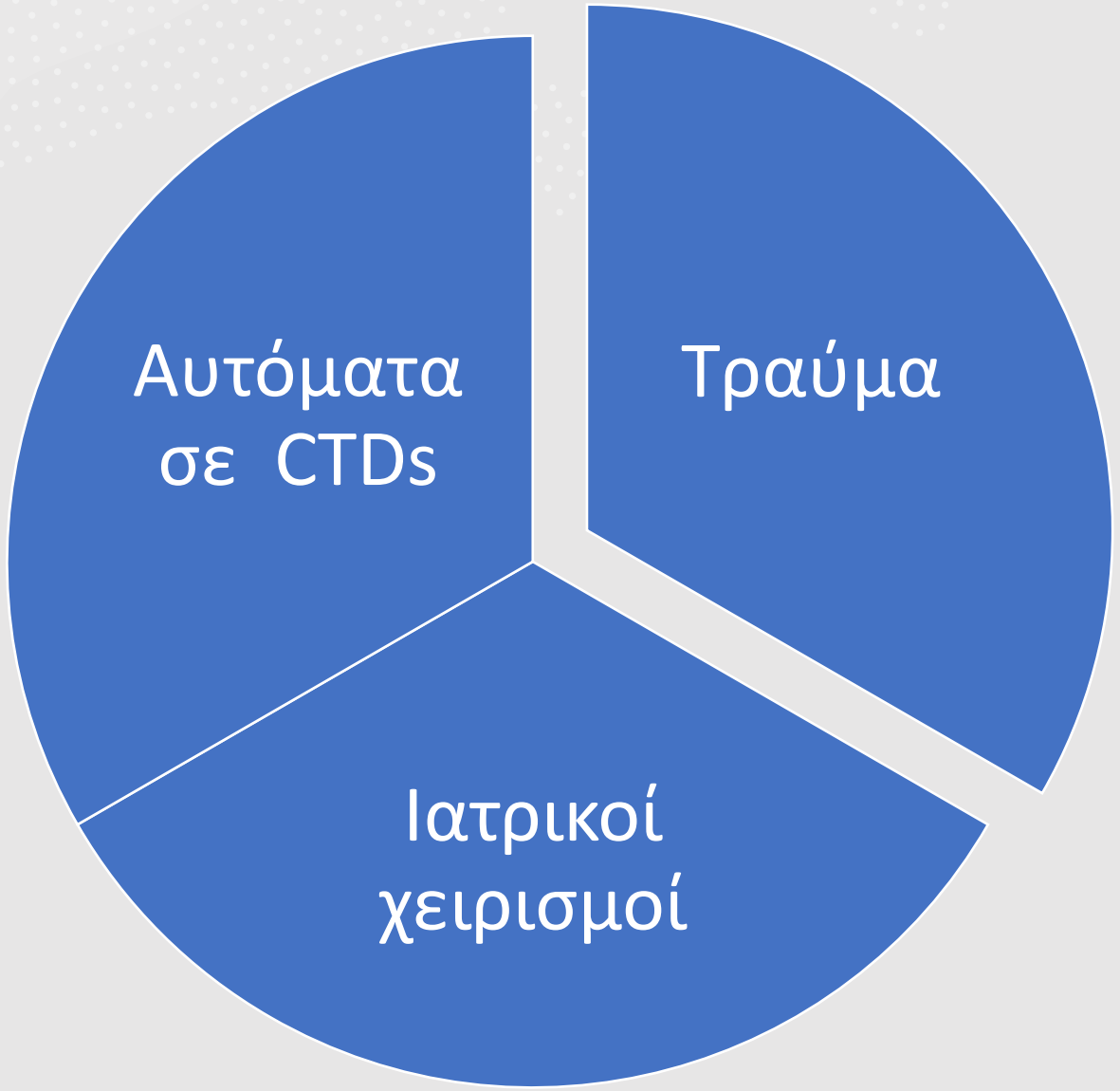
INTRAOCULAR INFLAMMATION

Δύο κύριες αιτίες

- Ραγοειδίτιδα &
- Ενδοφθαλμίτιδα

Hussain I, Ishrat S, Ching Wen Ho D, *et al.* Endogenous endophthalmitis in *Klebsiella pneumoniae* pyogenic liver abscess: systemic review and meta-analysis. Int J Infect Dis 2020; 101:259–268.

ενδοφθαλμίτιδα



Ραγοειδίτιδα

Kelly Corbitt[a] *and Johannes Nowatzky*[a,b,c]

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- η συχνότερη IOI (intraoccular inflammation)
- Αιτιολογικά ποικίλο σύνδρομο
- > 30 κλινικές οντότητες
- Δύσκολη ταξινόμηση και μελέτη

Ραγοειδίτιδες – ταξινόμιση ανάλογα με….

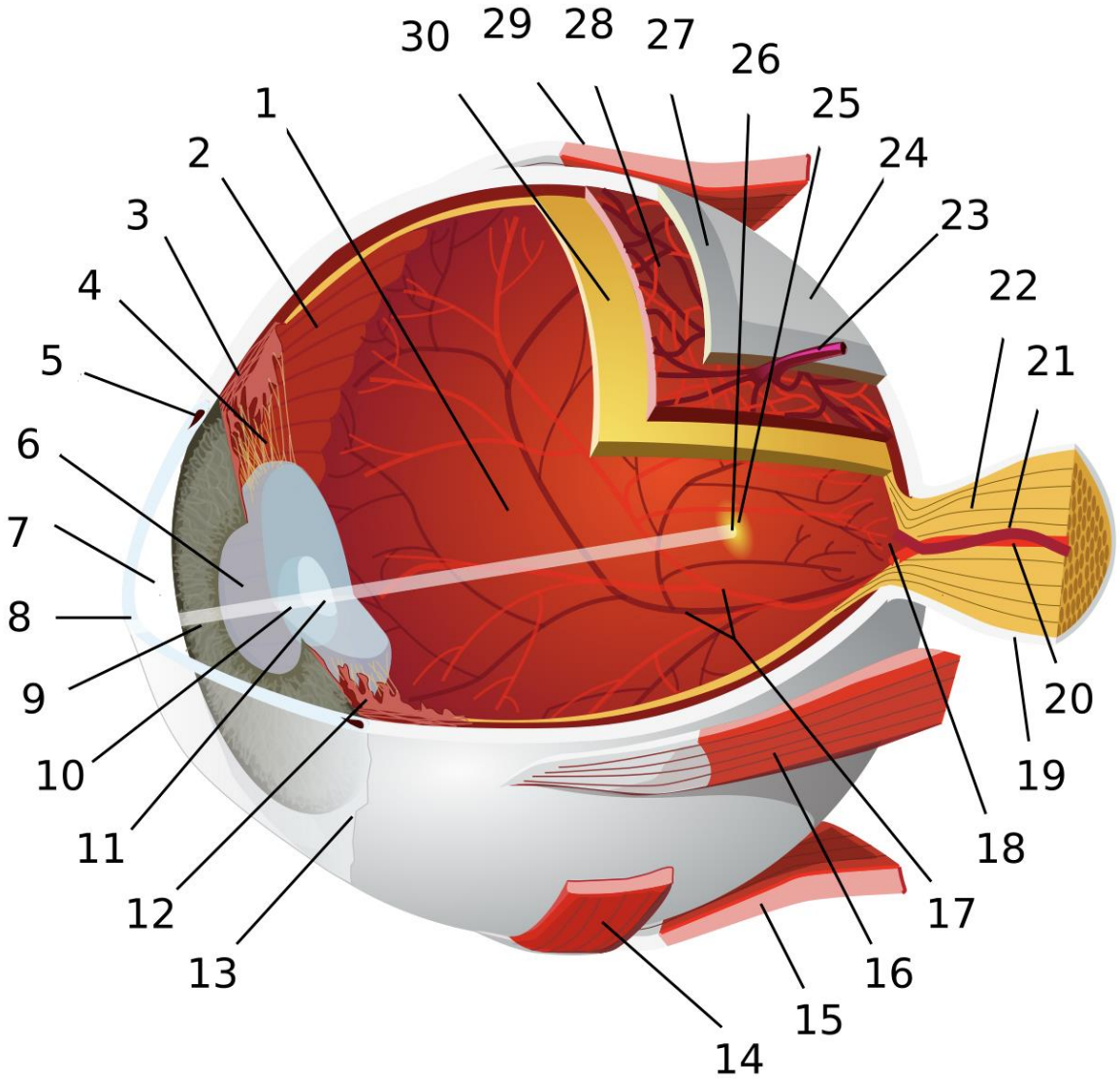
- Τμήμα του οφθαλμού (ανατομία)
- Αιτιολογία
- Both of them

The Standardization of Uveitis Nomenclature (SUN) Working Group

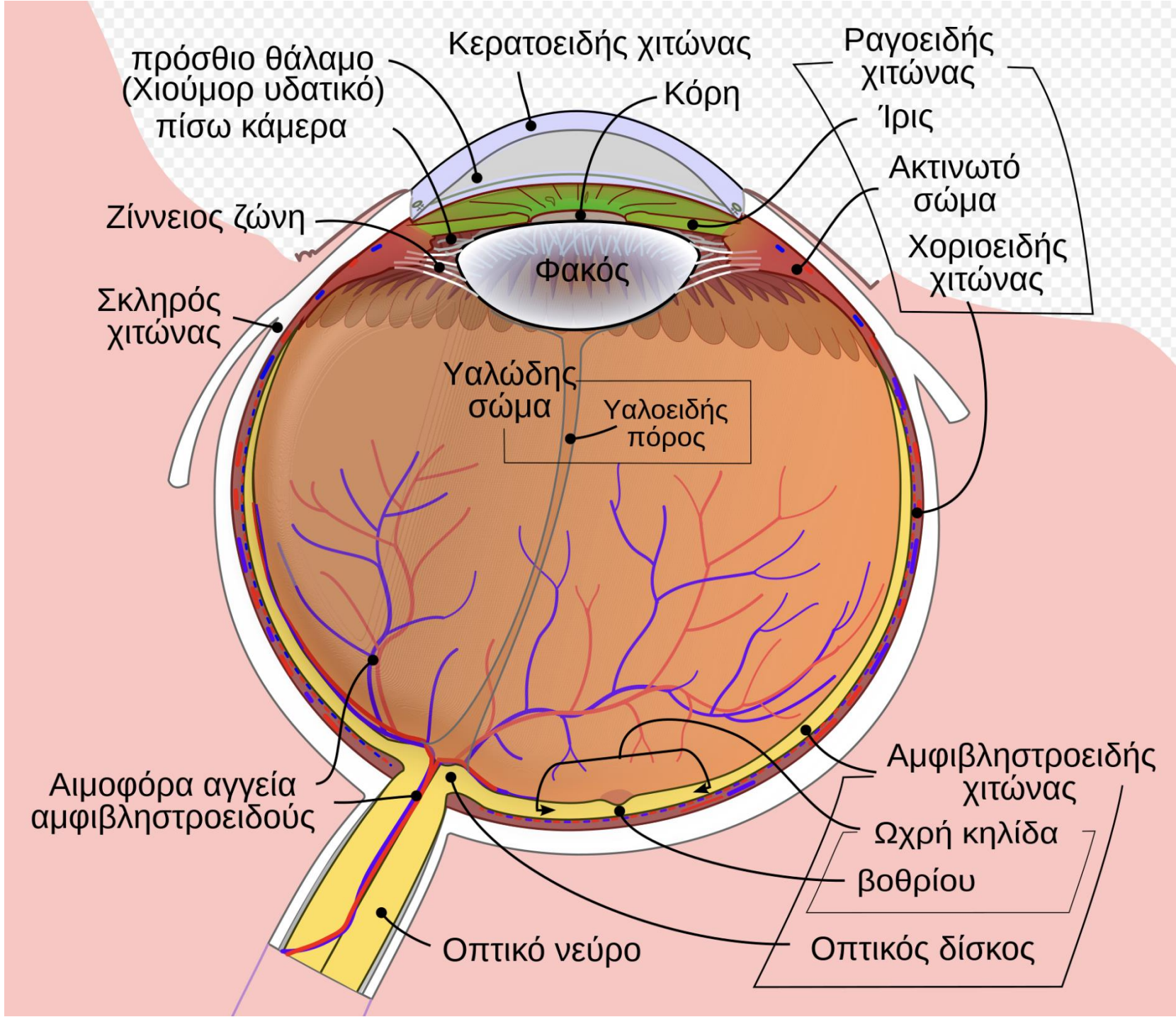
has created a widely-accepted anatomic classification system for uveitis

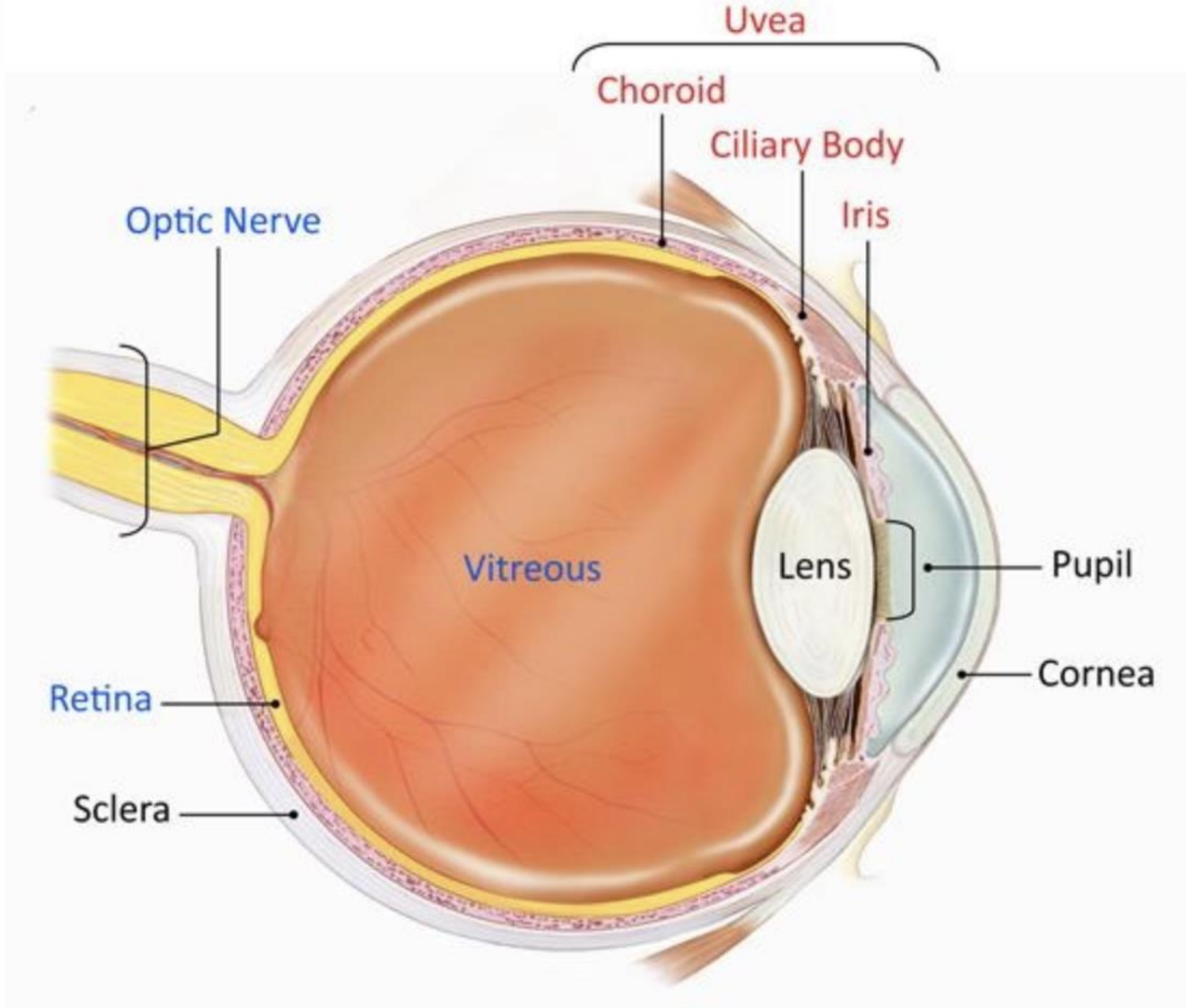
anterior
intermediate
posterior
panuveitis.

Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop. Am J Ophthalmol 2005; 140:509–516.

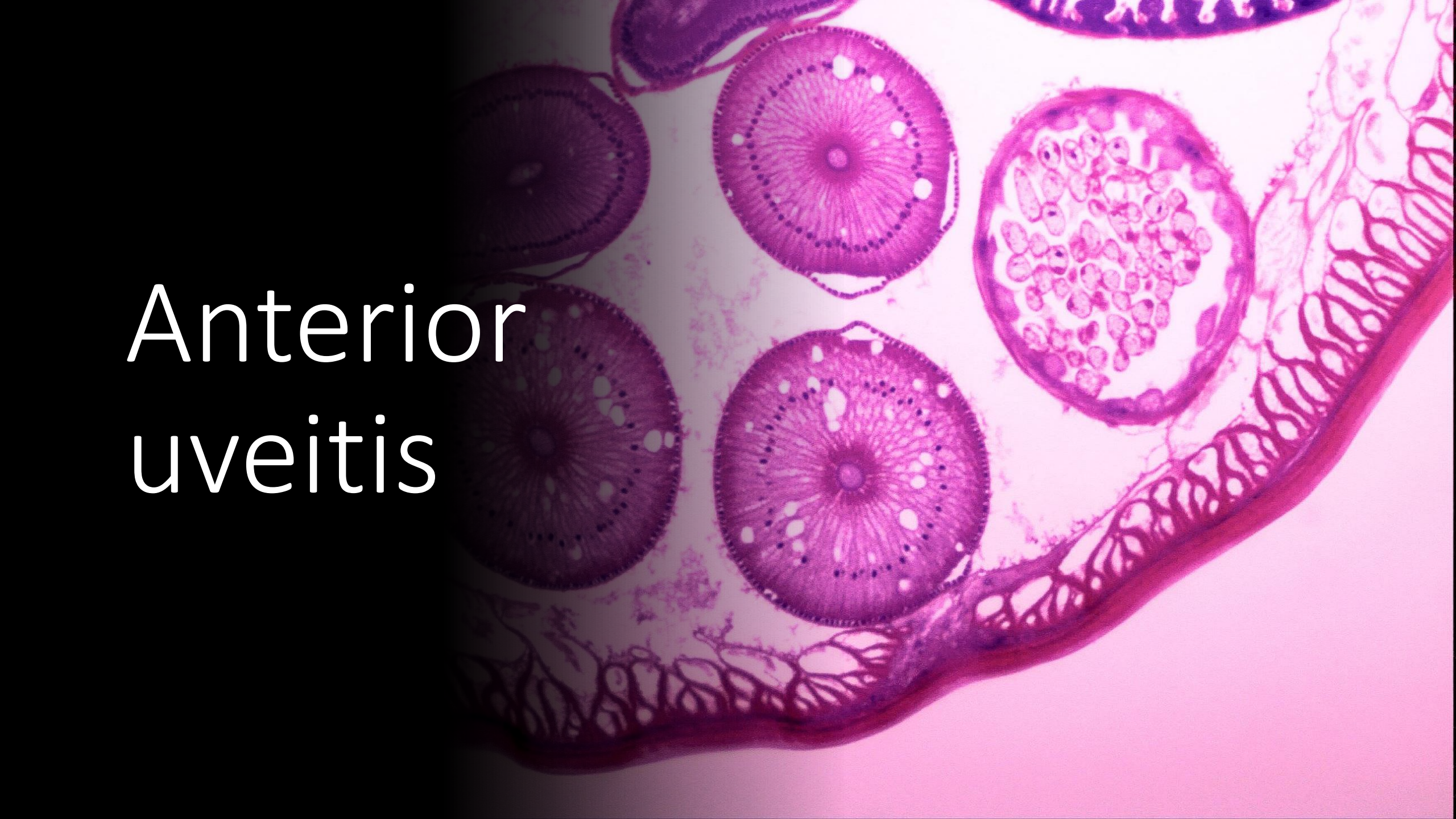


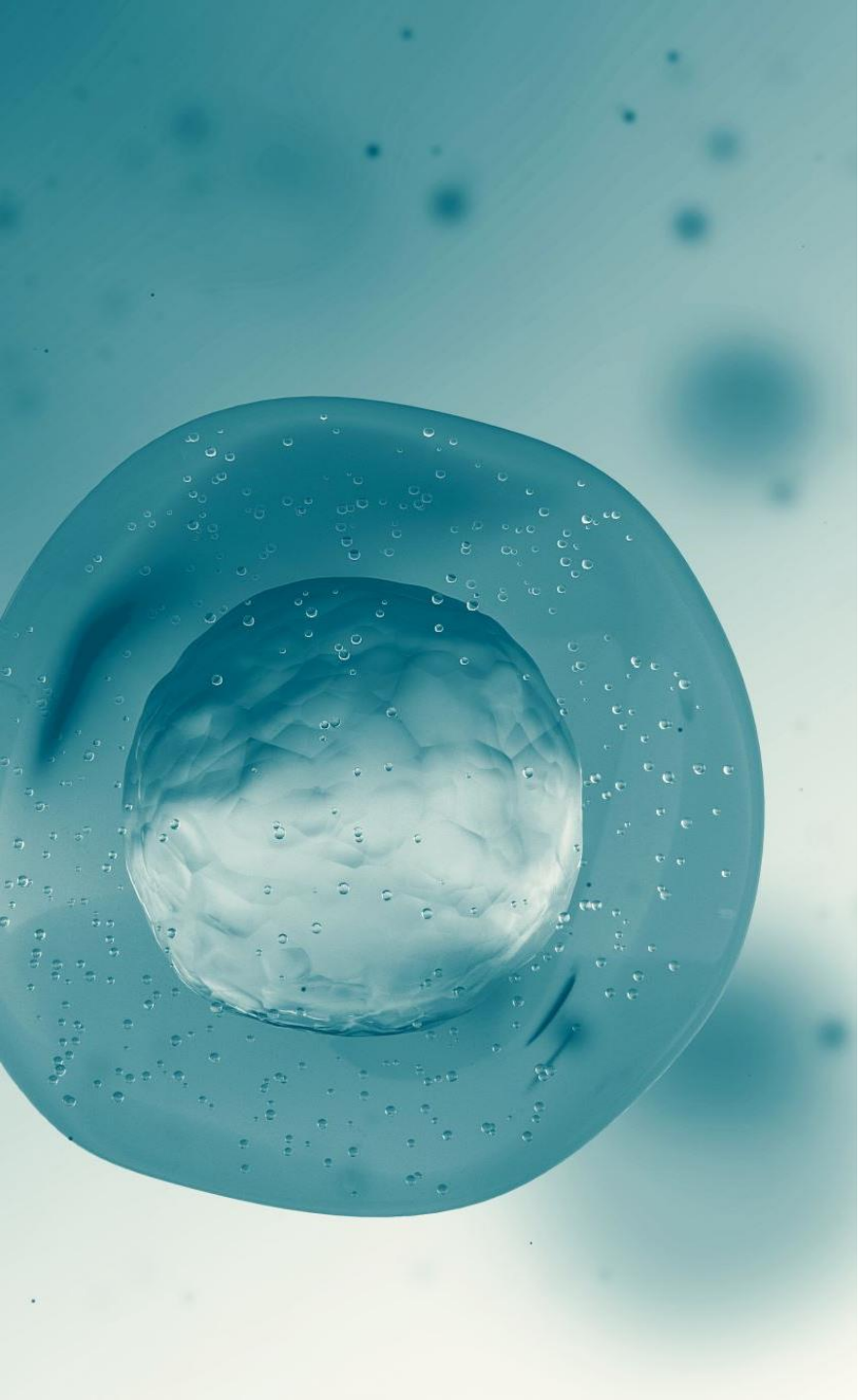
1. posterior segment
2. ora serrata
3. ciliary muscle
4. ciliary zonules
5. Schlemm's canal
6. pupil
7. anterior chamber
8. cornea
9. iris
10. lens cortex
11. lens nucleus
12. ciliary process
13. conjunctiva
14. inferior oblique muscle
15. inferior rectus muscle
16. medial rectus muscle
17. retinal arteries and veins
18. optic disc
19. dura mater
20. central retinal artery
21. central retinal vein
22. optic nerve
23. vorticose vein
24. bulbar sheath
25. macula
26. fovea
27. sclera
28. choroid
29. superior rectus muscle
30. retina


πρόσθιο θάλαμο
(Χιούμορ υδατικό)
πίσω κάμερα
Κερατοειδής χιτώνας
Κόρη
Ραγοειδής χιτώνας
Ίρις
Ακτινωτό σώμα
Χοριοειδής χιτώνας
Ζίννειος ζώνη
Φακός
Σκληρός χιτώνας
Υαλώδης σώμα
Υαλοειδής πόρος
Αιμοφόρα αγγεία αμφιβληστροειδούς
Αμφιβληστροειδής χιτώνας
Ωχρή κηλίδα
βοθρίου
Οπτικό νεύρο
Οπτικός δίσκος


Uvea
Choroid
Ciliary Body
Iris
Optic Nerve
Vitreous
Lens
Pupil
Cornea
Retina
Sclera

Anterior uveitis





Anterior uveitis.

Anterior chamber

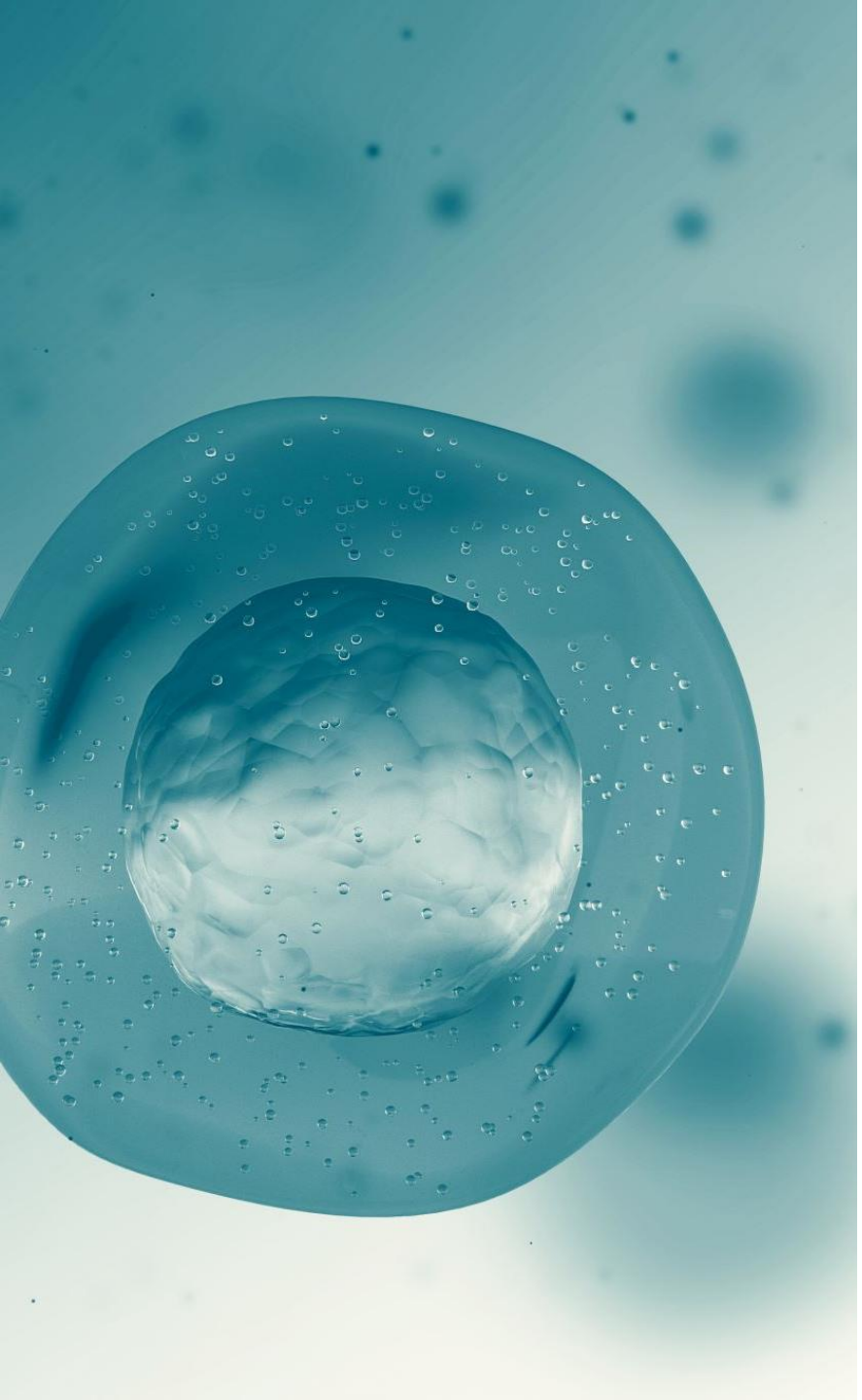
Aqueous humor

Inflammation → leukocytes (reported as ‘cells’)

and large amounts of protein (reported as ‘flare’)

0, 1+, 2+, 3+, 4+

Rosenbaum JT. The eye and rheumatic diseases. In: Firestein GS, Budd RC, Gabriel SE, *et al.*, editors. Firestein & Kelley’s textbook of rheumatology, 11th ed Elsevier; 2021. pp. 702–710.

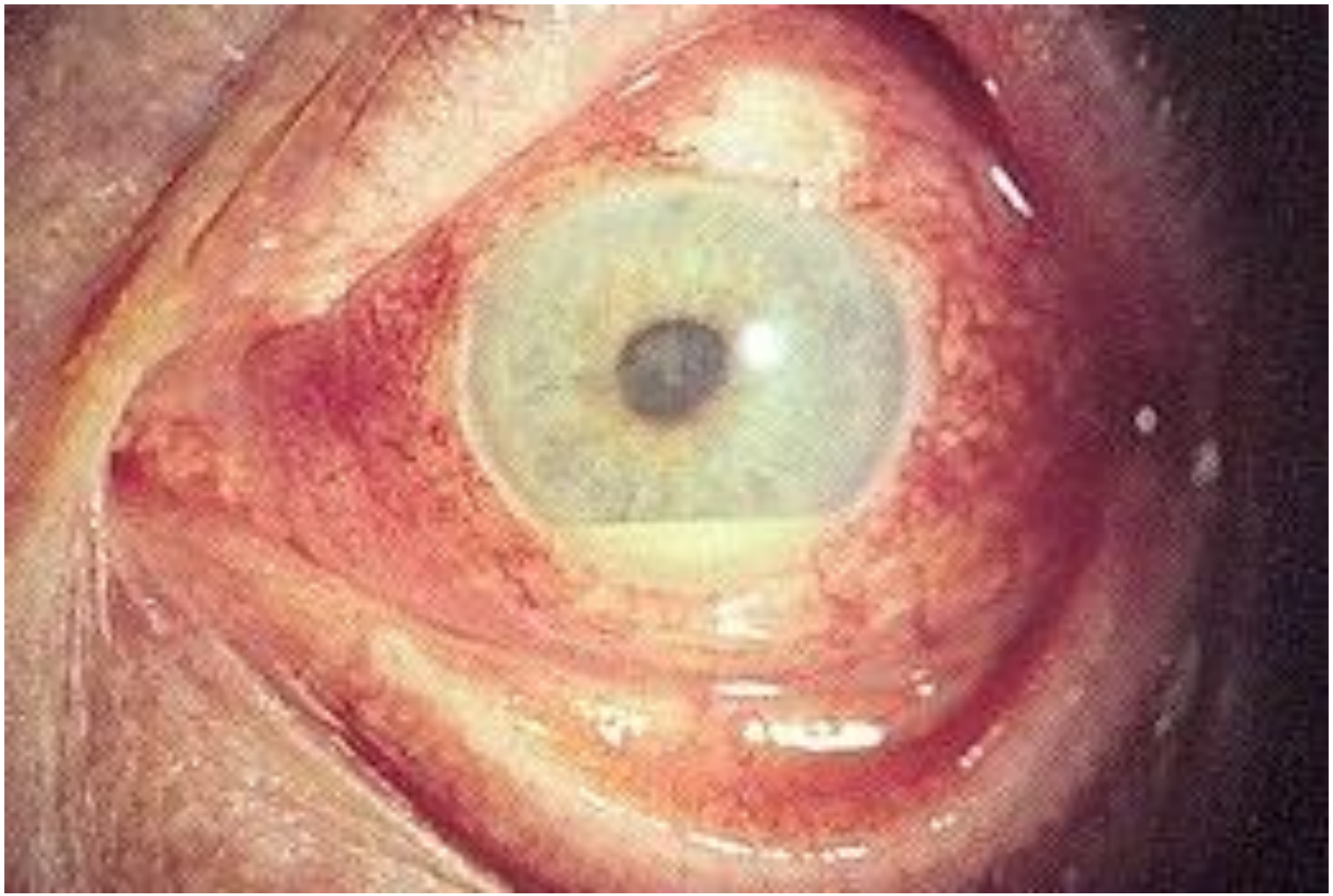


Anterior uveitis.

Other findings in the AC related to inflammation

- keratic precipitates
- iris nodules
- anterior or posterior synechiae
- hypopyon (visible sedimentation of leukocytes in the AC) and
- band keratopathy (calcium deposits across the cornea in chronic dis- ease)

Rosenbaum JT. The eye and rheumatic diseases. In: Firestein GS, Budd RC, Gabriel SE, *et al.*, editors. Firestein & Kelley's textbook of rheumatology, 11th ed Elsevier; 2021. pp. 702–710.



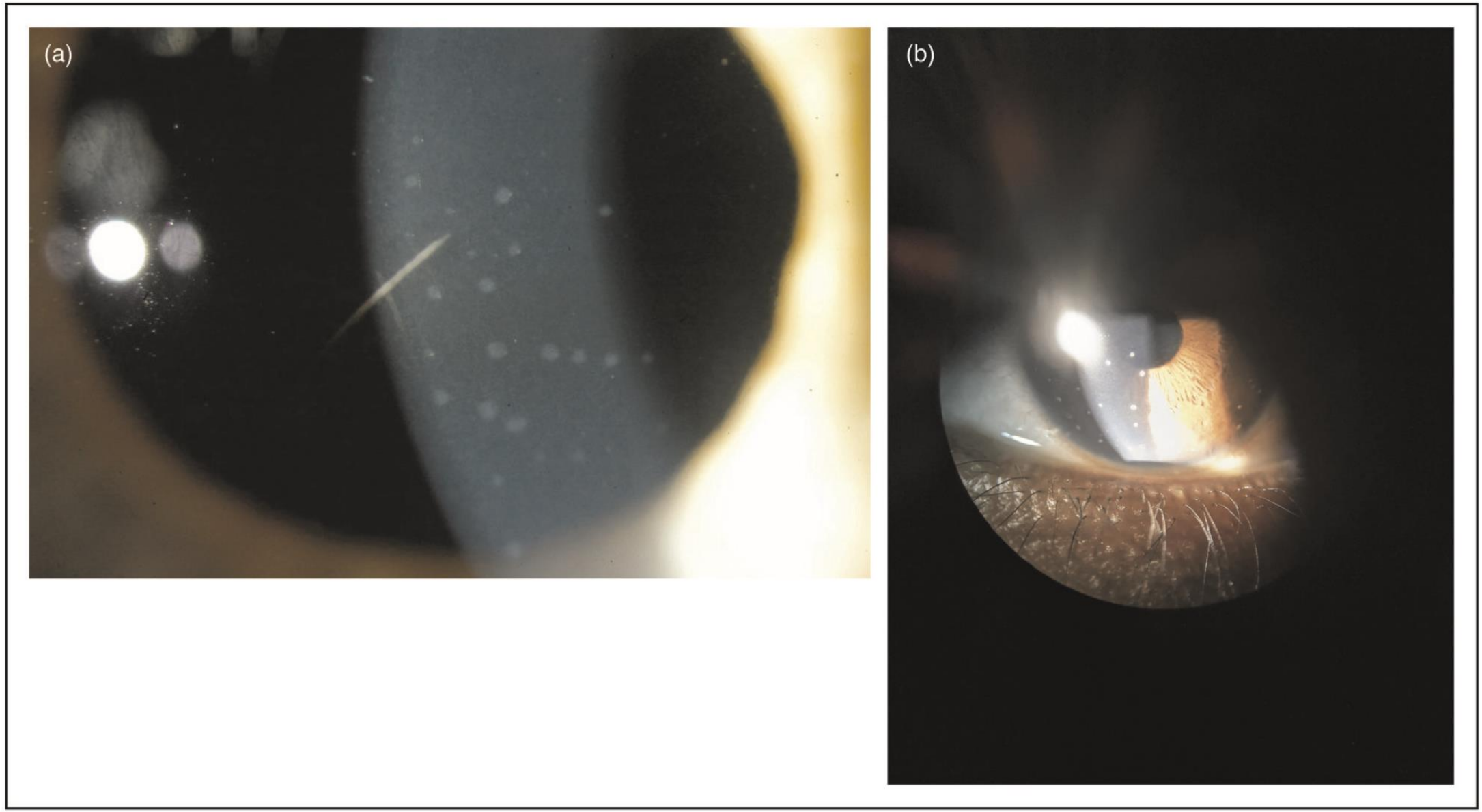


FIGURE 1. Keratic precipitates (KP) are cellular aggregates that adhere to the posterior surface of the cornea. They are frequently present in uveitis with inflammation of the anterior chamber. Large KPs define the presence of 'granulomatous' uveitis, here in an individual with idiopathic granulomatous uveitis (a) and a patient with sarcoidosis (b).

Clues to an underlying disorder

- ‘Mutton-fat’ KPs are commonly seen in sarcoidosis but exclude Behcet’s disease (BD)
- Hypopyon is typically ‘mobile’ in BD but is ‘nonmobile’ in HLA-B27-associated acute anterior uveitis
- The presence of KPs that are not fine and diffuse defines ‘granulomatous’ uveitides

Salmon JF. Uveitis. Kanski’s clinical ophthalmology. 9th ed. Elsevier; 2020; p. 423–494.

Intermediate uveitis

(Φλεγμονή του Υαλοειδούς)

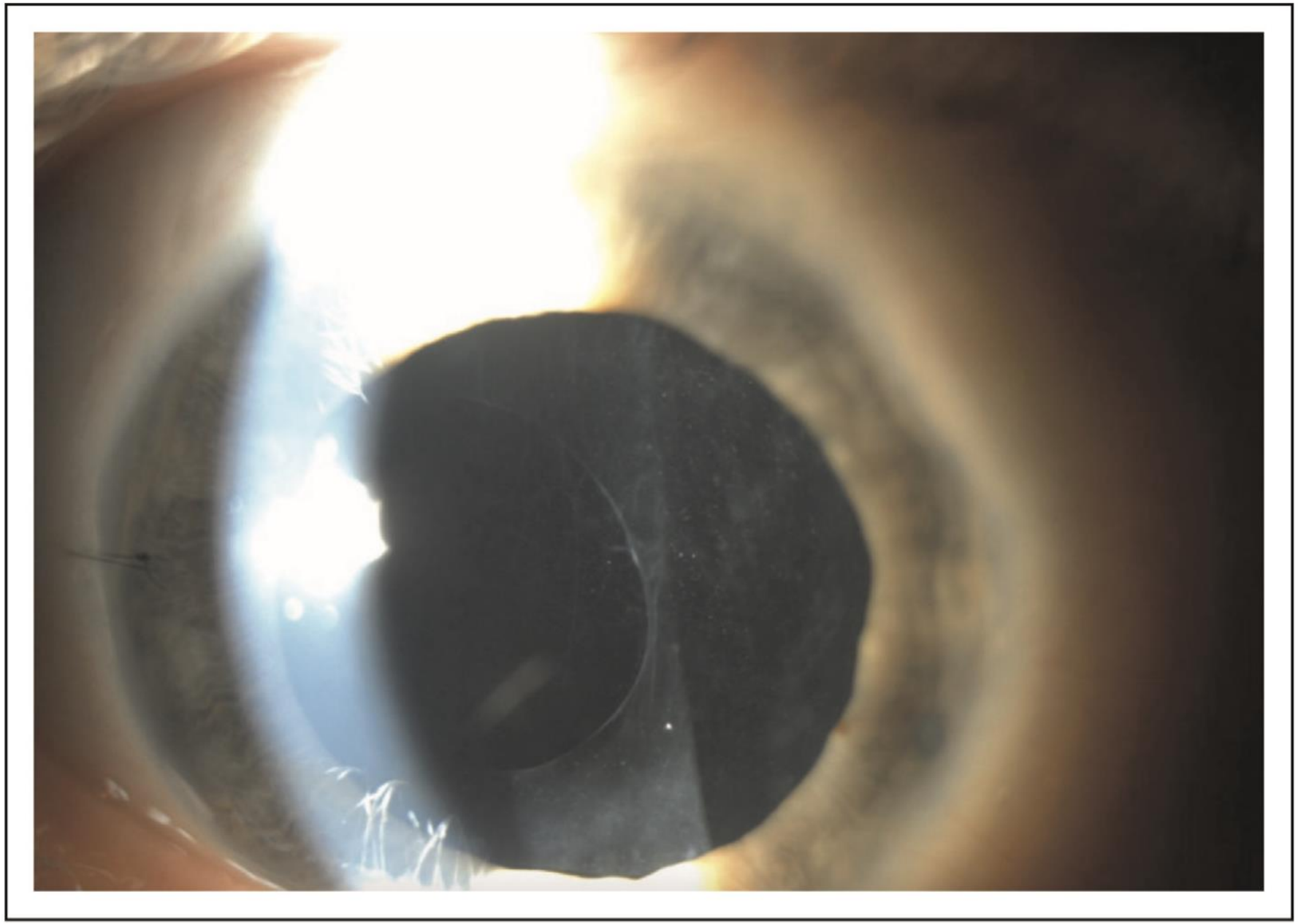
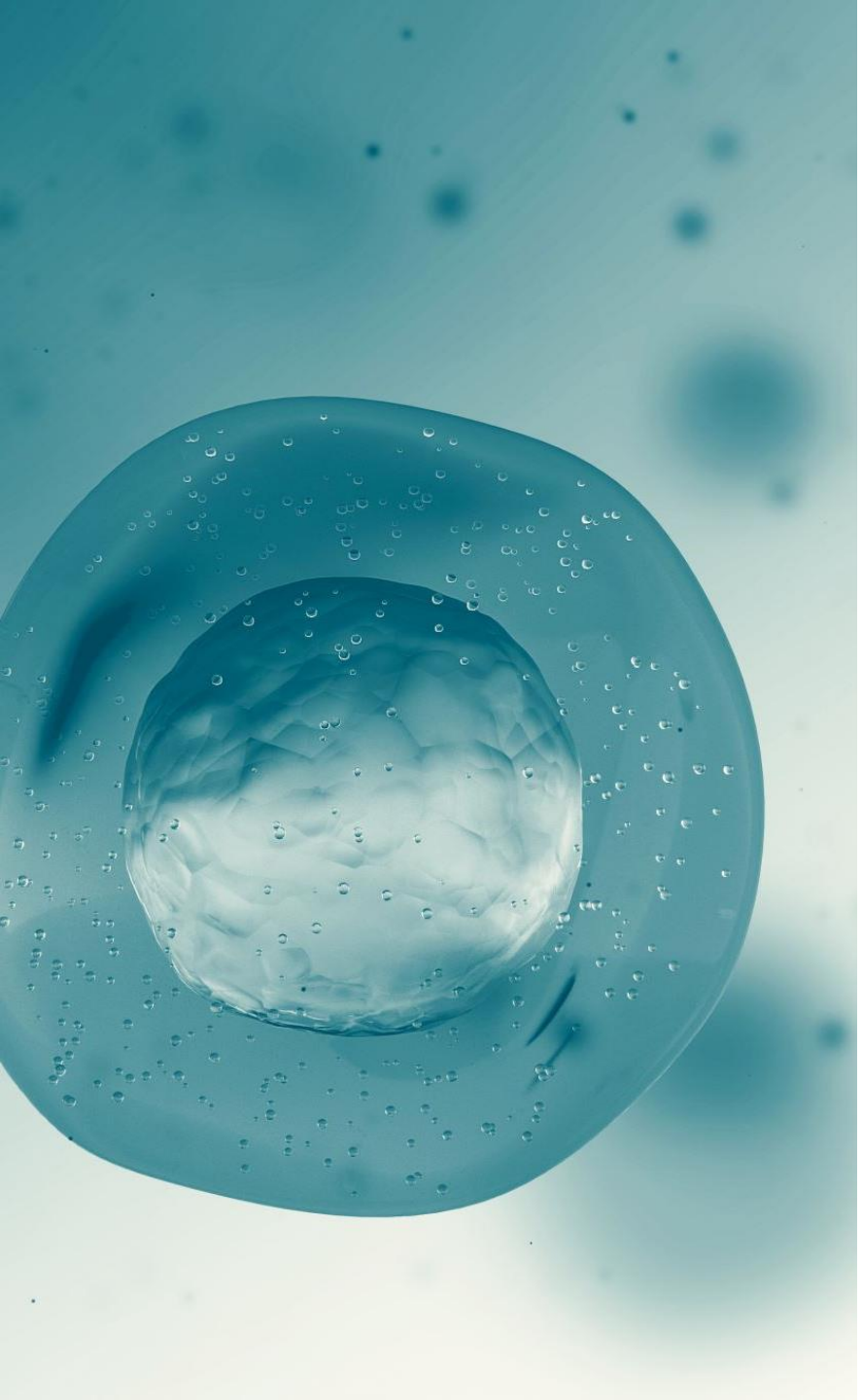


FIGURE 2. Vitritis with inflammatory cells, here affecting the anterior vitreous in a patient with intermediate uveitis.

Posterior uveitis

Οπίσθια ραγοειδίτις



Posterior uveitis.

Προσβολή

- **χοριοειδούς,**
- **αμφιβληστροειδούς ή**
- **και των δύο**

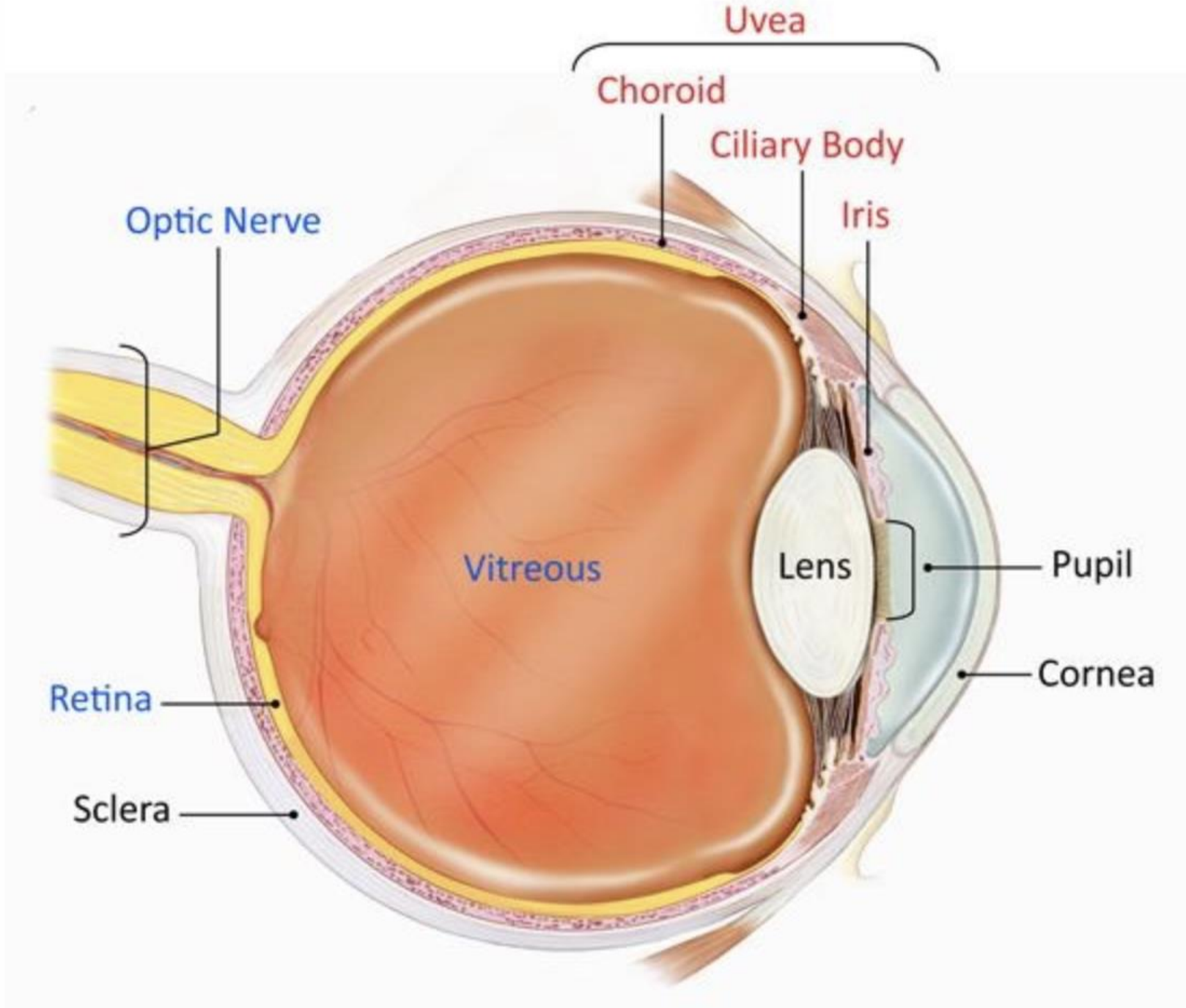
(misnomer) !!!

- Προσβολή κυρίως του αμφιληστροειδούς…
  → σε λοιμώξεις
  → σε Αδαμαντιάδη-Behcet & σαρκοείδωση

- Εδώ… ραγοειδίτις → «misnomer»

- Σε non-infectious uveitis → «spill-over phenomena»

Jabs DA, Busingye J. Approach to the diagnosis of uveitides. Am J Ophthalmol 2014; 156:228–236.


Uvea
Choroid
Ciliary Body
Iris
Optic Nerve
Vitreous
Lens
Pupil
Cornea
Retina
Sclera

- Προσβολή κυρίως του αμφιληστροειδούς…
  - σε λοιμώξεις
  - σε Αδαμαντιάδη-Behcet & σαρκοείδωση

- Εδώ… ραγοειδίτις «misnomer»

- Σε non-infectious uveitis «spill-over phenomena»

Jabs DA, Busingye J. Approach to the diagnosis of uveitides. Am J Ophthalmol 2014; 156:228–236.

ΒΥΘΟΣΚΟΠΗΣΗ

- Βασικότατη εξέταση
- disease-typical appearance

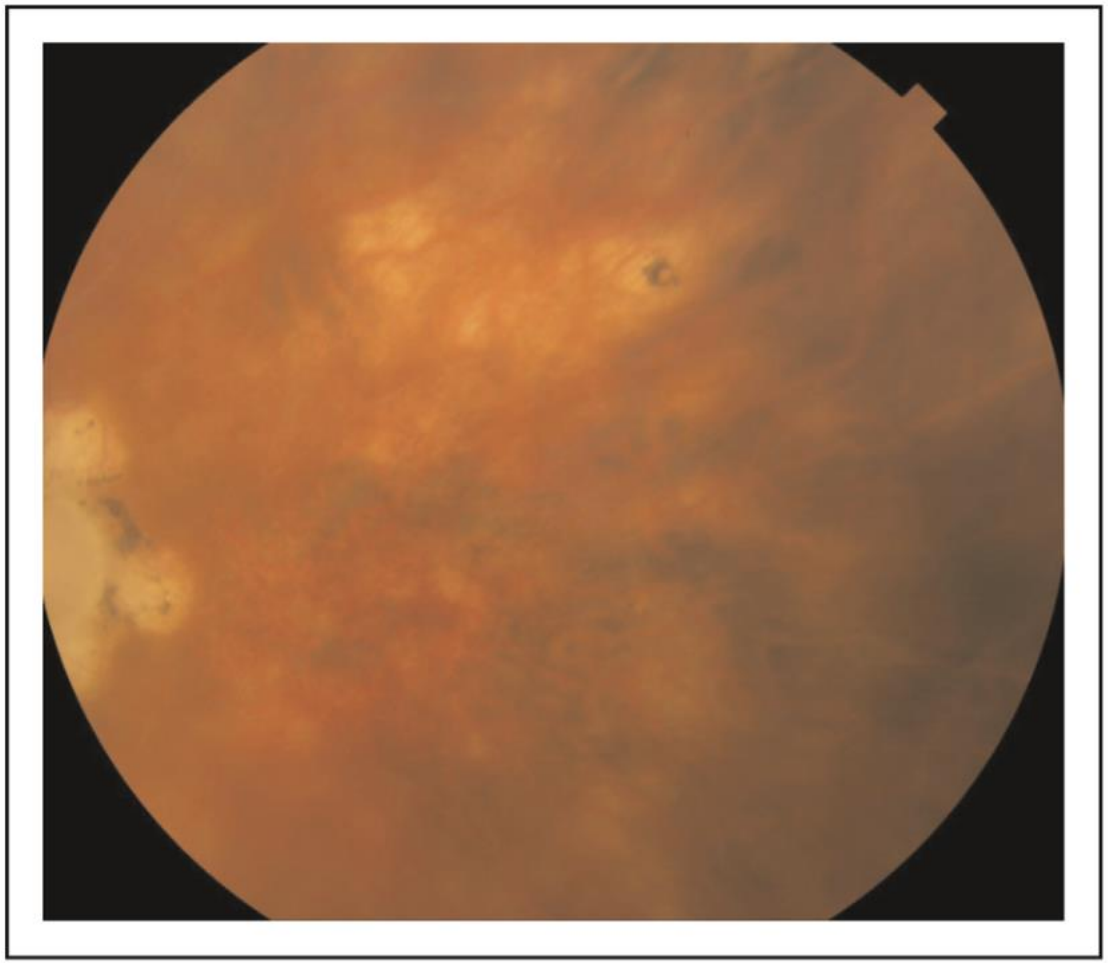
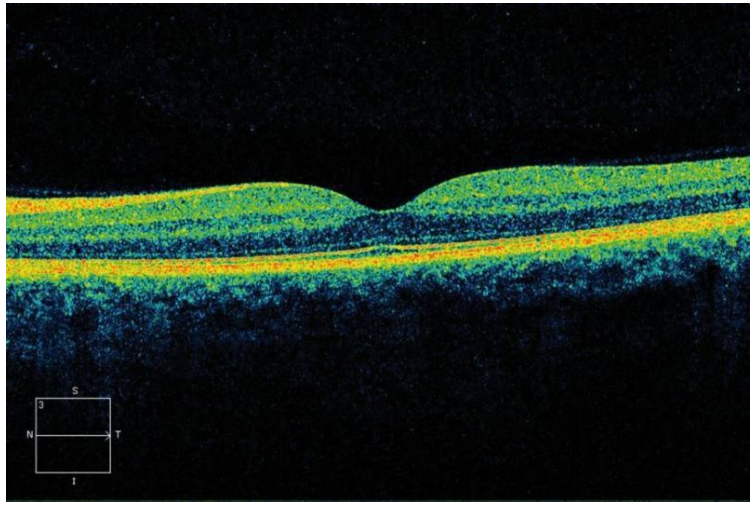


FIGURE 4. Birdshot chorioretinopathy can be diagnosed with high likelihood based on its characteristic fundus appearance. Disease progression results in retinal atrophy.

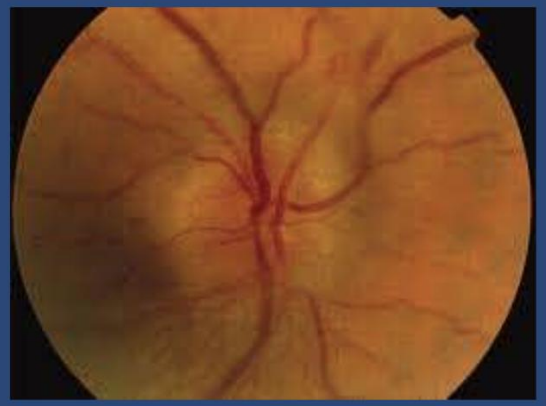
Jabs DA, Busingye J. Approach to the diagnosis of uveitides. Am J Ophthalmol 2014; 156:228–236.

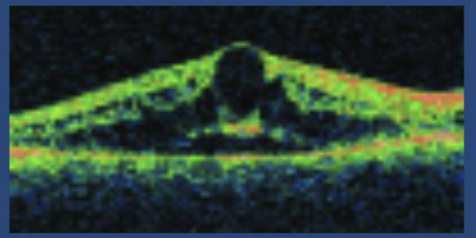
- Οίδημα οπτικής θηλής
- Η συχνότερη αιτία τύφλωσης στην ραγοειδίτιδα

- Βυθοσκόπηση
- Optical coherence tomography (**OCT**)

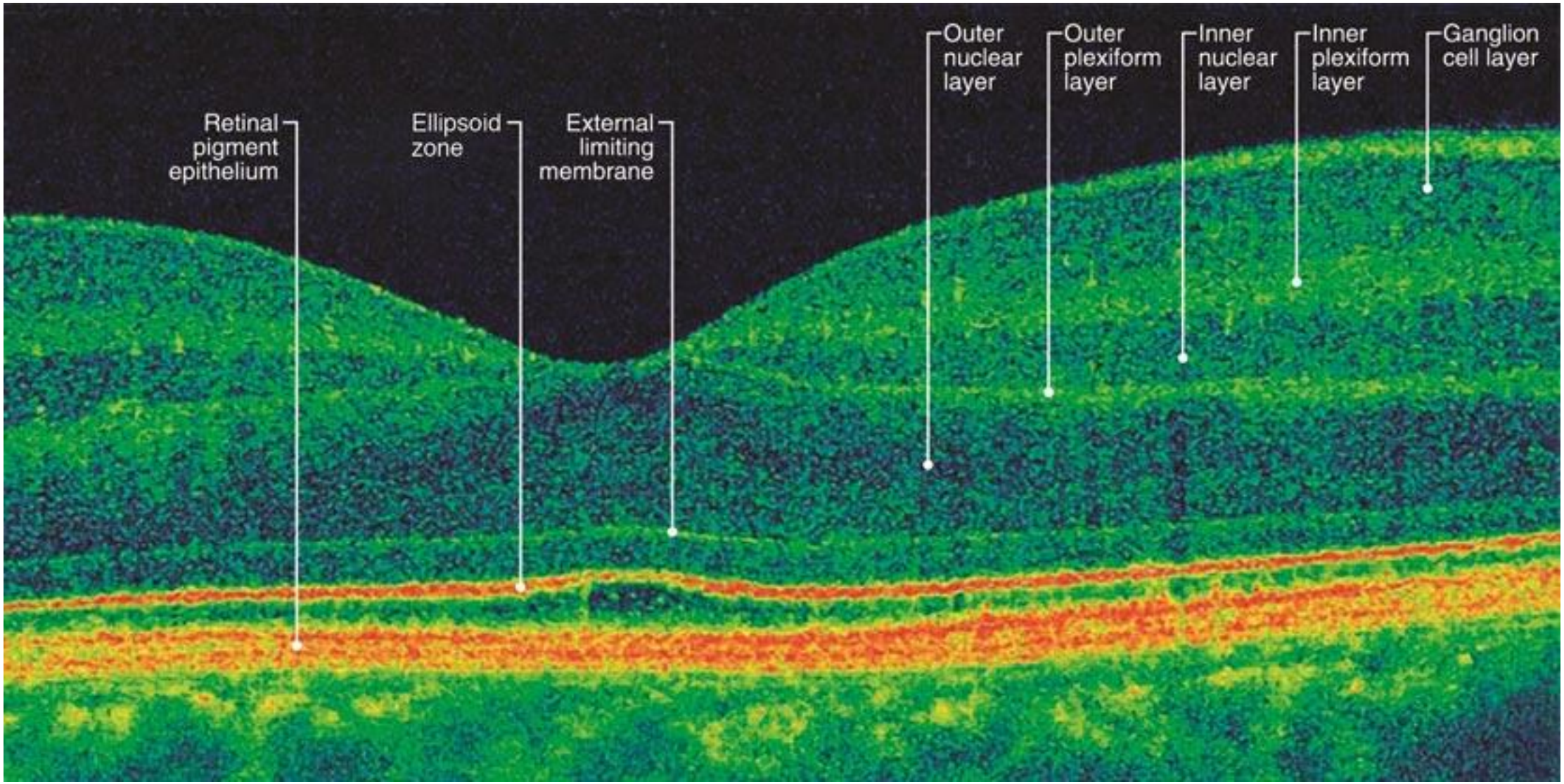


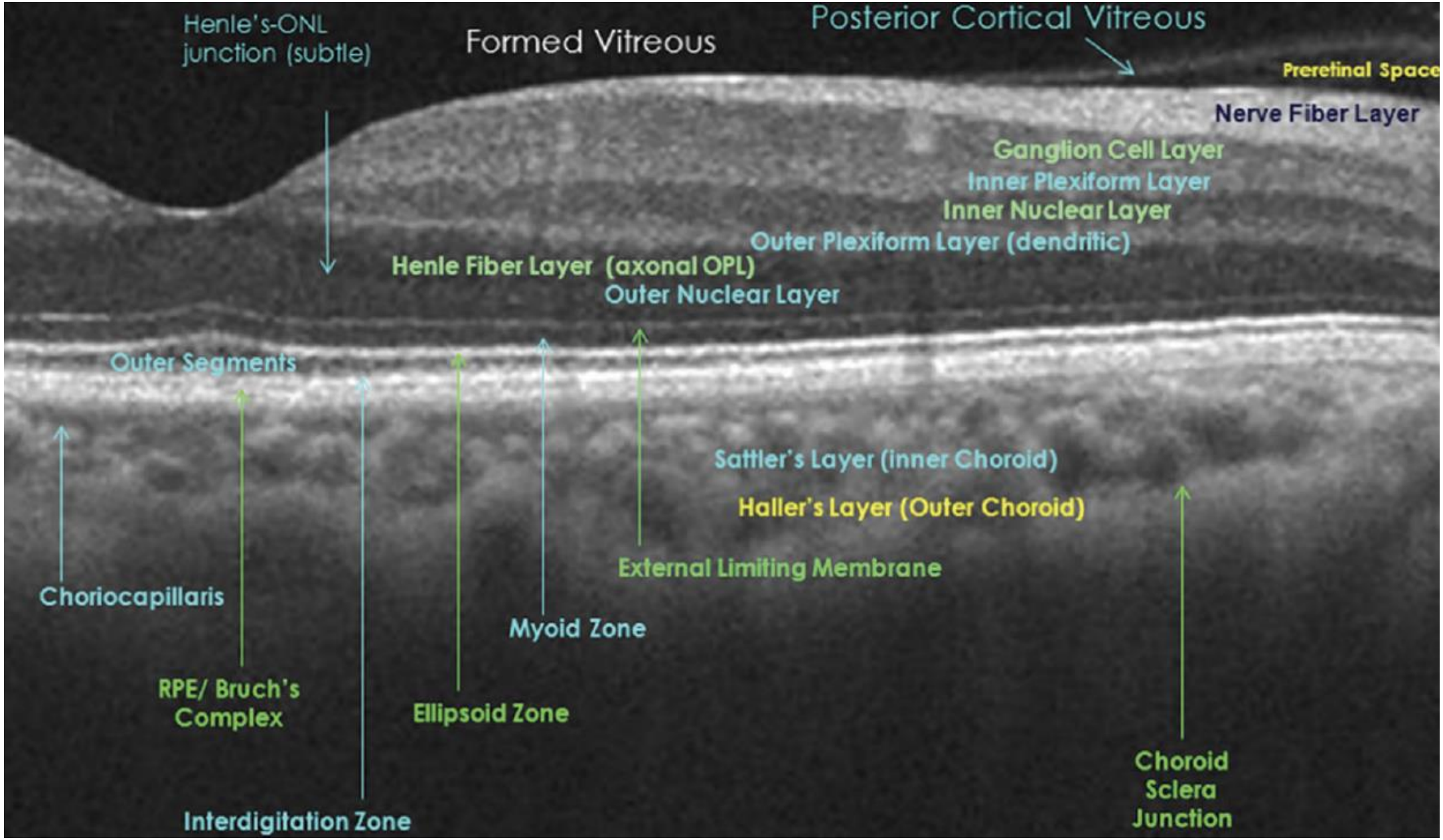
Crohn's disease



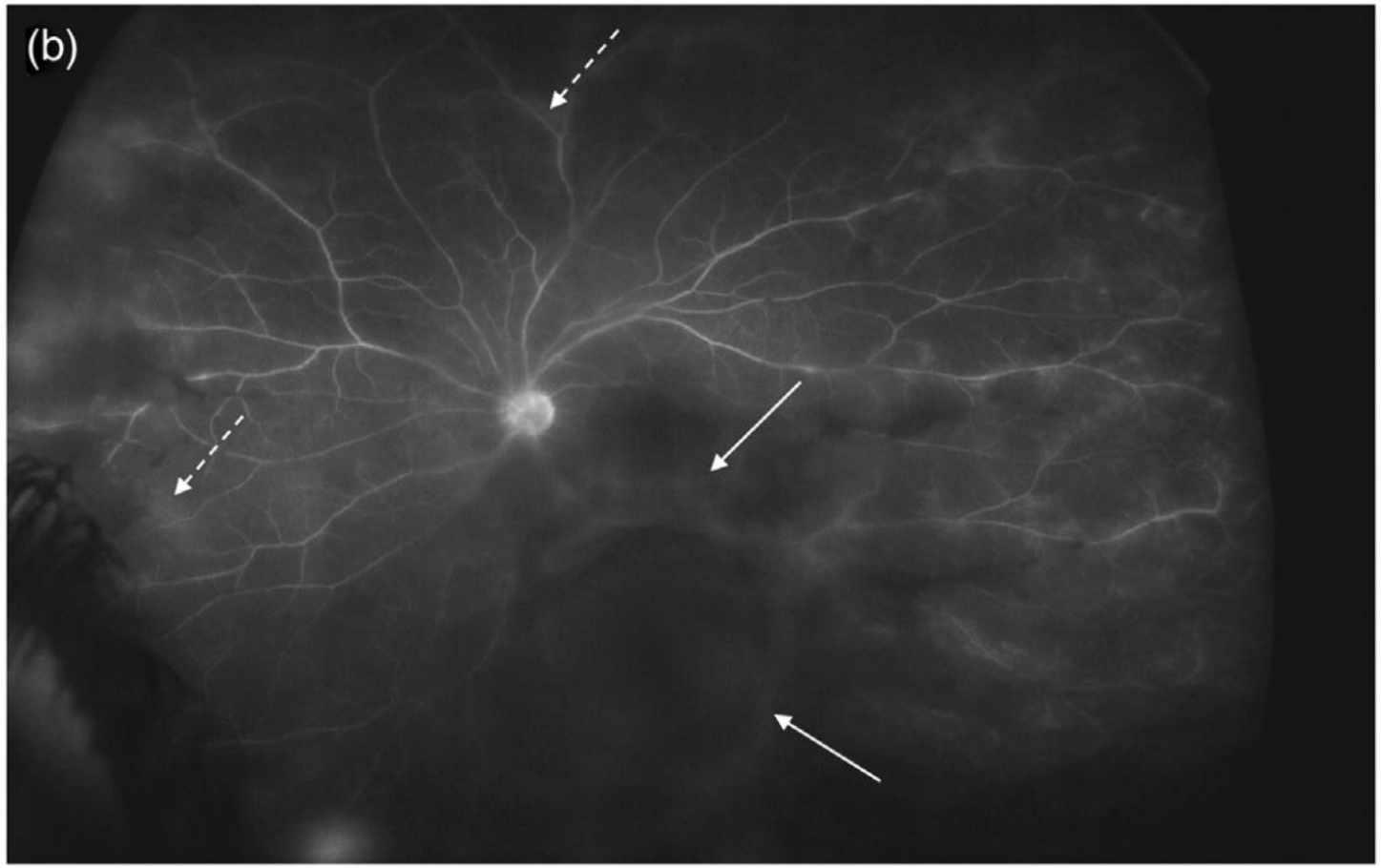


Malik A, et al. BMJ Case Rep. 2010 Concurrent macular oedema and optic neuritis in Crohn's disease with varied response to steroids. BMJ Case Rep. 2010


Retinal pigment epithelium
Ellipsoid zone
External limiting membrane
Outer nuclear layer
Outer plexiform layer
Inner nuclear layer
Inner plexiform layer
Ganglion cell layer


Henle's-ONL junction (subtle)
Formed Vitreous
Posterior Cortical Vitreous
Preretinal Space
Nerve Fiber Layer
Ganglion Cell Layer
Inner Plexiform Layer
Inner Nuclear Layer
Outer Plexiform Layer (dendritic)
Henle Fiber Layer (axonal OPL)
Outer Nuclear Layer
Outer Segments
Sattler's Layer (inner Choroid)
Haller's Layer (Outer Choroid)
External Limiting Membrane
Choriocapillaris
Myoid Zone
RPE/ Bruch's Complex
Ellipsoid Zone
Interdigitation Zone
Choroid Sclera Junction

- OCT angiography → allows visualization of the posterior pole vessels directly without injecting an intravenous dye.
- Fluorescein angiography (FA) → images the retinal vasculature better than the choroidal vasculature and can show leakage or nonperfusion



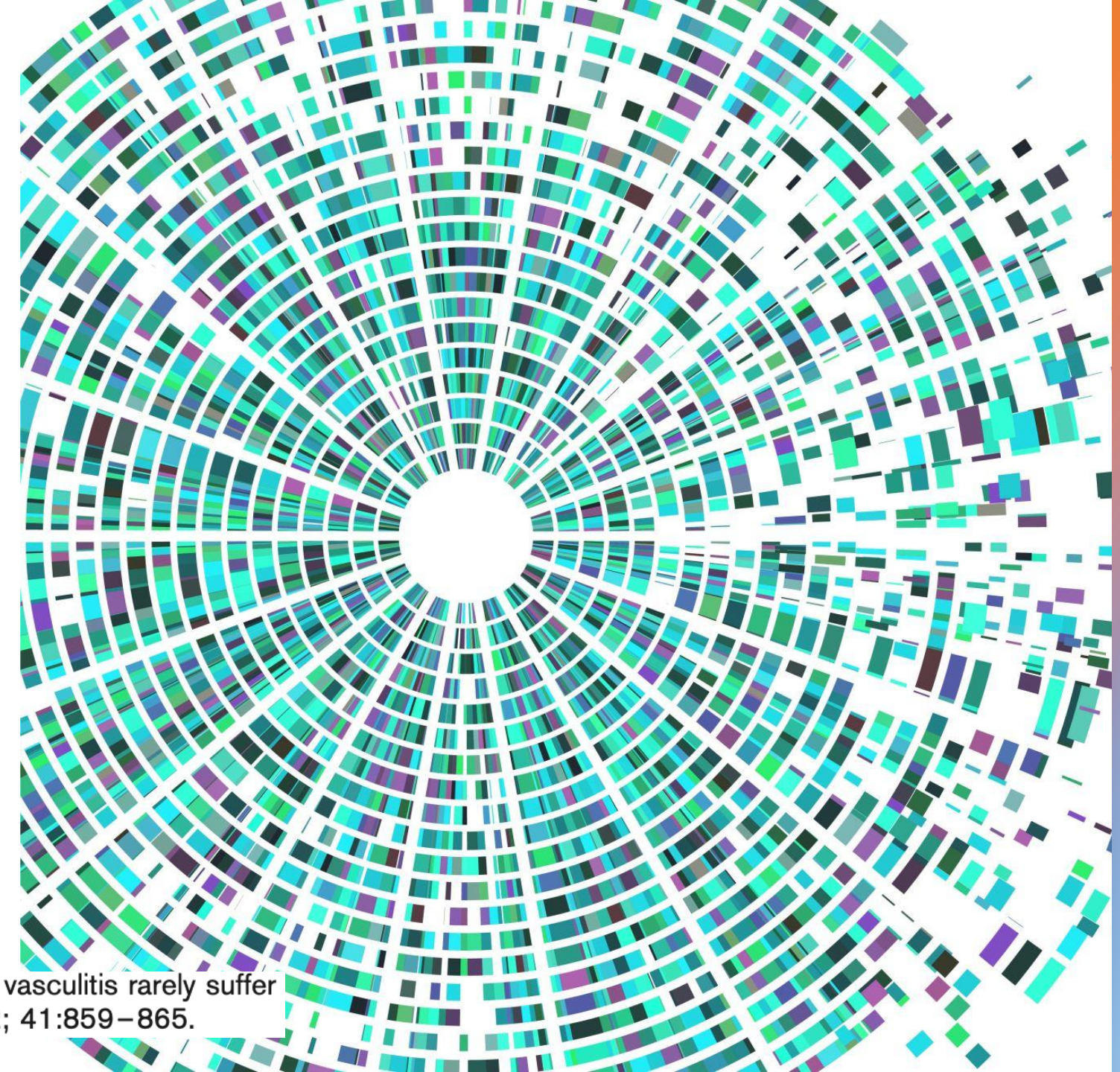
(b) Fluorescein angiography (FA)

wide-spread leakage (dotted arrows)

Associated vitritis (white arrows in b)

Retinal vasculitis

- high prevalence of BD
- Its association with systemic vasculitis is reported to be <1.5%
- Πάντοτε φλουοραγγειογραφία
- Τεκμηρίωση διάγνωσης και follow up



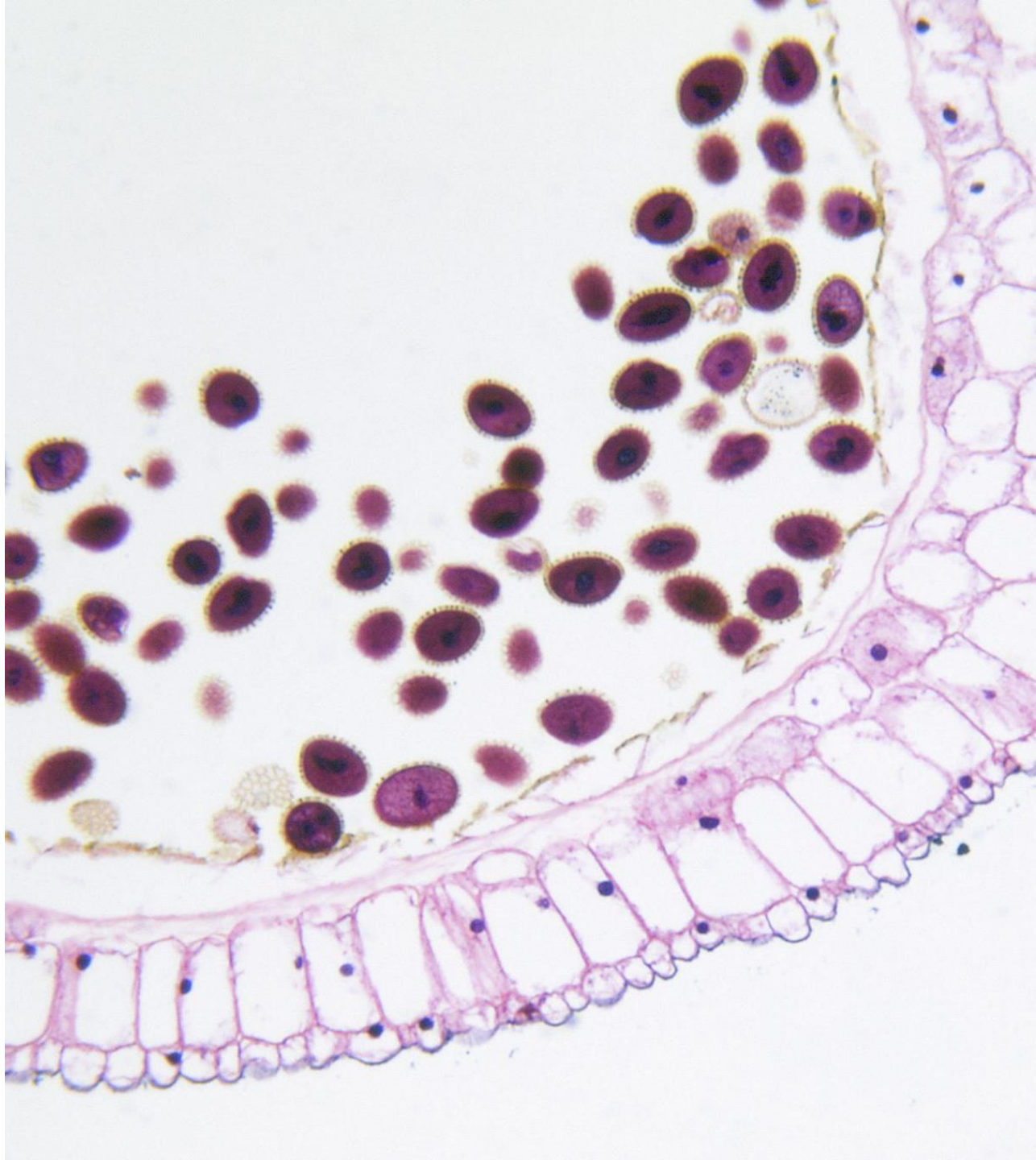
Rosenbaum JT, Ku J, Ali A, *et al.* Patients with retinal vasculitis rarely suffer from systemic vasculitis. Semin Arthritis Rheum 2012; 41:859–865.

Indocyanine green angiography (ICG

- assesses blood flow in the choroid more potently than fluorescein angiography (FA)
- indocyanine green dye is a larger molecule and leaks less from the semi-permeable choroidal vasculature.
- useful in the characterization and longitudinal monitoring of choroidal disease in uveitides, such as in VKH, Birdshot chorioretinopathy, and some forms of ocular sarcoidosis

Uveitis by etiology

ΛΟΙΜΩΔΕΙΣ



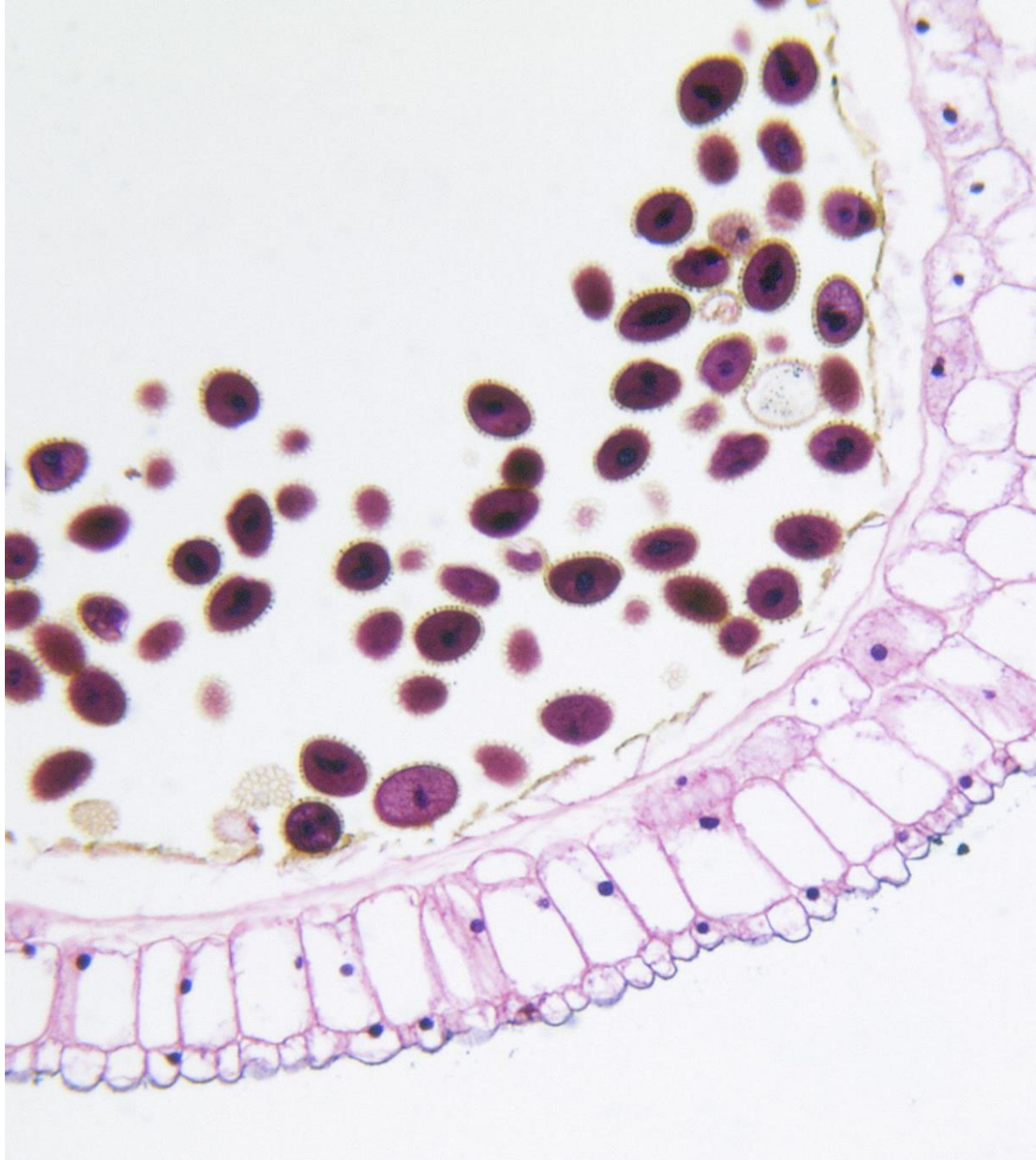
Infectious uveitides

- Πάντα στην ΔΔ
- Στον δυτικό κόσμο CMV, VZV, HSV, and toxoplasma
- στον αναπτυσσόμενο πληθώρα…
- «uveitis require an in-depth travel (e.g., Zika virus), family exposure (e.g., Tuberculosis [TB]), professional (e.g., Weil's disease/Leptospirosis), dietary (e.g., Brucella), animal exposure (e.g., Bartonella), and sexual (e.g., Syphilis, HIV) history with a complete review of systems.»

Tsirouki T, Dastiridou A, Symeonidis C, *et al.* A focus on the epidemiology of uveitis. Ocul Immunol Inflamm 2018; 26:2–16.

Uveitis by etiology

ΜΗ ΛΟΙΜΩΔΕΙΣ



HLA-B27-associated uveitis

- Συχνή
- acute anterior uveitis (AAU)
- intense inflammation of the iris
- Πόνος,φωτοφοβία,ερυθρότητα

Curr Opin Rheumatol 2023; 35:201-212

- always unilateral ή unilateral-alternative
- nonmobile hypopyon
- Σπανιότατα → και οπίσθια ραγοειδίτιδα (not vision-threatening)

Juanola X, Loza Santamaría E, Cordero-Coma M; SENTINEL Working Group. Description and prevalence of spondyloarthritis in patients with anterior uveitis: the SENTINEL Interdisciplinary Collaborative Project. Ophthalmology 2016; 123:1632–1636.

Monnet D, Breban M, Hudry C, *et al.* Ophthalmic findings and frequency of extraocular manifestations in patients with HLA-B27 uveitis: a study of 175 cases. Ophthalmology 2004; 111:802–809.

- Σε κάποιες μελέτες, 80% ασθενών με AAU …είναι *HLA-B27 (+)*
- Σε 16-40 % των AAU απουσιάζουν συστηματικά συμπτώματα SpA
- Ωστόσο μπορεί να χρειασθούν ανοσοκατασταλτικά

Burkholder BM, Jabs DA. Uveitis for the nonophthalmologist. BMJ 2021; 372: m4979.

Latkany PA, Jabs DA, Smith JR, *et al.* Multifocal choroiditis in patients with familial juvenie systemic granulomatosis. Am J Ophthalmol 2002; 134:897–904.

Rosenbaum JT. Characterization of uveitis associated with spondyloarthritis. J Rheumatol 1989; 16:792–796.

- HLA-B27(+)
- Ισχυρότερη συσχέτιση με AS
- Λιγότερο ισχυρή με IBD και PS ή PsA
- IBD με HLA-B27(-) → οπίσθια vision-threatening ραγοειδίτιδα όπως στο σ.Αδαμαντιάδη-Behcet (uveitis with retinal vasculitis)

Burkholder BM, Jabs DA. Uveitis for the nonophthalmologist. BMJ 2021; 372: m4979.

Σαρκοείδωση

- Συχνή αιτία ραγοειδίτιδας
- Οξείας ή χρόνιας
- Συνήθως αμφοτερόπλευρη
- Συχνά ενδιάμεση και οπίσθια
- vision-threatening

Latkany PA, Jabs DA, Smith JR, *et al.* Multifocal choroiditis in patients with familial juvenie systemic granulomatosis. Am J Ophthalmol 2002; 134:897–904.

Burkholder BM, Jabs DA. Uveitis for the nonophthalmologist. BMJ 2021; 372: m4979.

Sarcoid eye disease

- Συχνά…και επί απουσίας εξω-οφθαλμικών εκδηλώσεων !
- Χρήζει όμως αγωγής με ανοσοκατασταλτικά
- Ίσως η πρώτη εκδήλωση
- Α/α θώρακος σε ασθενείς με ραγοειδίτιδα (ασαφούς αιτιολογίας)

Latkany PA, Jabs DA, Smith JR, *et al.* Multifocal choroiditis in patients with familial juvenie systemic granulomatosis. Am J Ophthalmol 2002; 134:897–904.

Burkholder BM, Jabs DA. Uveitis for the nonophthalmologist. BMJ 2021; 372: m4979.

σ.Αδαμαντιάδη-Behcet (BD)

- Πρόσθεια ραγοειδίτιδα (AAU)… στα πλαίσια πανραγοειδίτιδας
- Τρέχουσας ή παλαιότερης
- AAU μόνο; → ίσως αναθεώρηση της διάγνωσης
- Ο φαινότυπος της οφθαλμικής προσβολής χρήσιμος στην ΔΔ με SpA, IBD, BD, Sarcoidosis, PS, κλπ
- Ίσως το μοναδικό διαγνωστικό κριτήριο

Δδ σε σ.Αδαμαντιάδη-Behcet

- anterior and other uveitides can present with **oral and genital ulcers** (e.g., SpA, PS, IBD)
- skin lesions that are also part of the BD spectrum (e.g., **erythema nodosum** in sarcoidosis and IBD; **pyoderma gangrenosum** in IBD; **pustular** and **genital lesions** in pustular psoriasis and IBD)

Accorinti M, Pesci FR, Pirraglia MP, *et al.* Ocular Behcet's disease: changing patterns over time, complications and long-term visual prognosis. Ocul Immunol Inflamm 2017; 25:29–36.

Abd El Latif E, Galal MAKF, Tawfik MA, *et al.* Pattern of uveitis associated with Behcet's disease in an Egyptian cohort. Clin Ophthalmol 2020; 14:4005–4014.

Juvenile idiopathic arthritis (JIA)

- a common cause of uveitis that starts in childhood but can cause life-long ocular disease.
- The prototype occurs in **ANA(+)** young **girls** with oligoarticular involvement
- Still, all children with JIA, including those without ANA, must be screened for uveitis regularly.
- JIA uveitis is often a chronic anterior uveitis that is asymptomatic until ocular complications occur.

Angeles-Han ST, Ringold S, Beukelman T, *et al.* 2019 American College of Rheumatology/Arthritis Foundation guideline for the screening, monitoring, and treatment of juvenile idiopathic arthritis-associated uveitis. Arthritis Care Res (Hoboken) 2019; 71:703–716.

multiple sclerosis-associated uveitis

- Pars planitis (intermediate uveitis) is the prototype , but MS uveitis can affect all segments of the eye.

- It is crucial to include MS in the differential diagnosis of uveitis

- uveitis can precede other clinically appreciable MS symptoms.

Curr Opin Rheumatol 2023:

- when no systemic disease is found
- Brain MRI? (MS?)
- Before TNFi treatment?

Curr Opin Rheumatol 2023:

intermediate, posterior, and panuveitis

- Συχνότερες αιτίες σε USA
- Σαρκοείδωση, IBD, VKH, Birdshot chorioretinopathy, BD
- Όλες… → συστηματικές εκδηλώσεις
- Εκτός της Birdshot chorioretinopathy

Curr Opin Rheumatol 2023:

Birdshot chorioretinopathy

- is limited to the eye, mainly to the posterior segment
- the single most strongly HLA-class I *(HLA-A29)* associated human disease known
- Απαιτείται συνήθως ισόβια ανοσοκαταστολή

Brézin AP, Monnet D, Cohen JH, Levinson RD. HLA-A29 and birdshot chorioretinopathy. Ocul Immunol Inflamm 2011; 19:397–400.

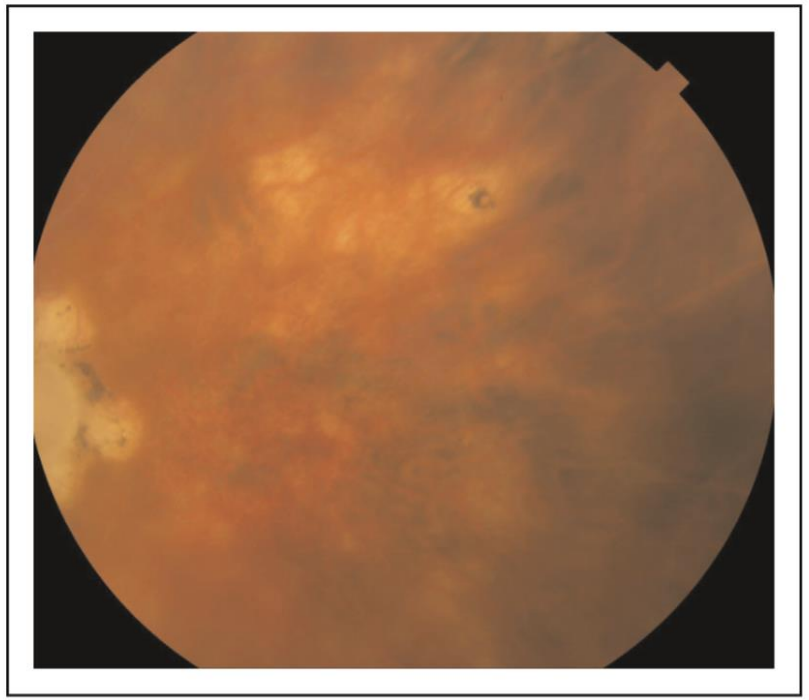
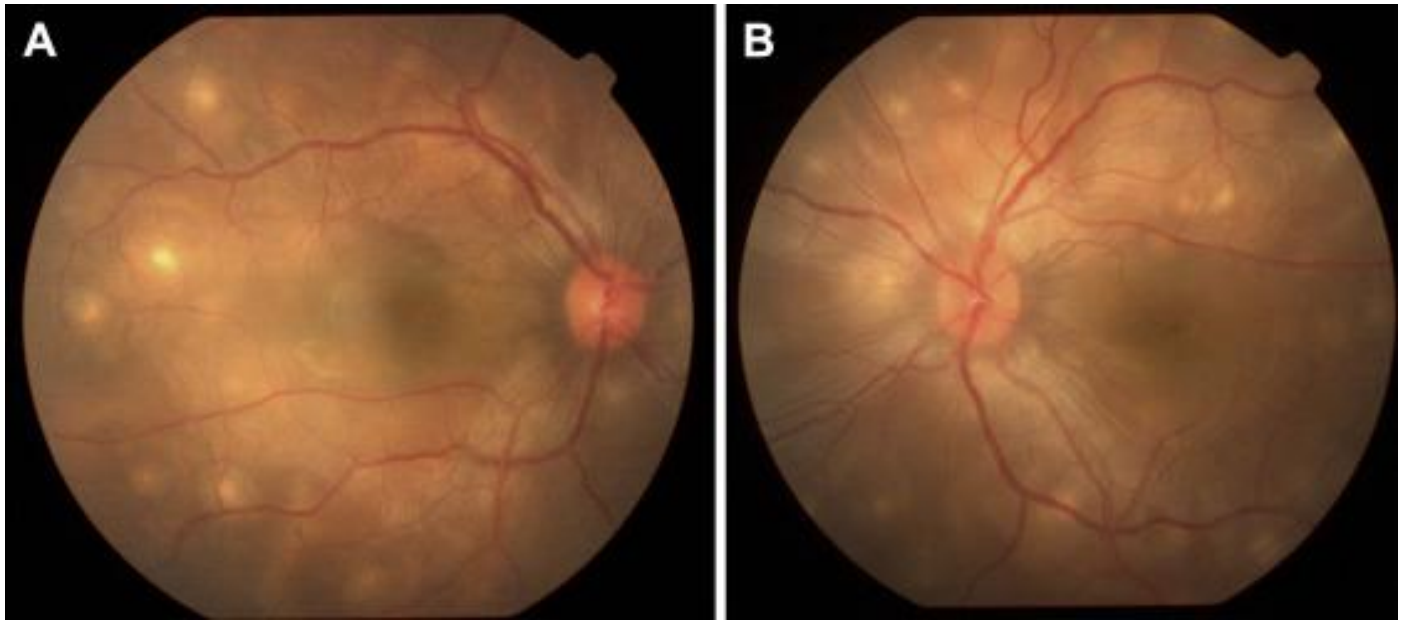


FIGURE 4. Birdshot chorioretinopathy can be diagnosed with high likelihood based on its characteristic fundus appearance. Disease progression results in retinal atrophy.

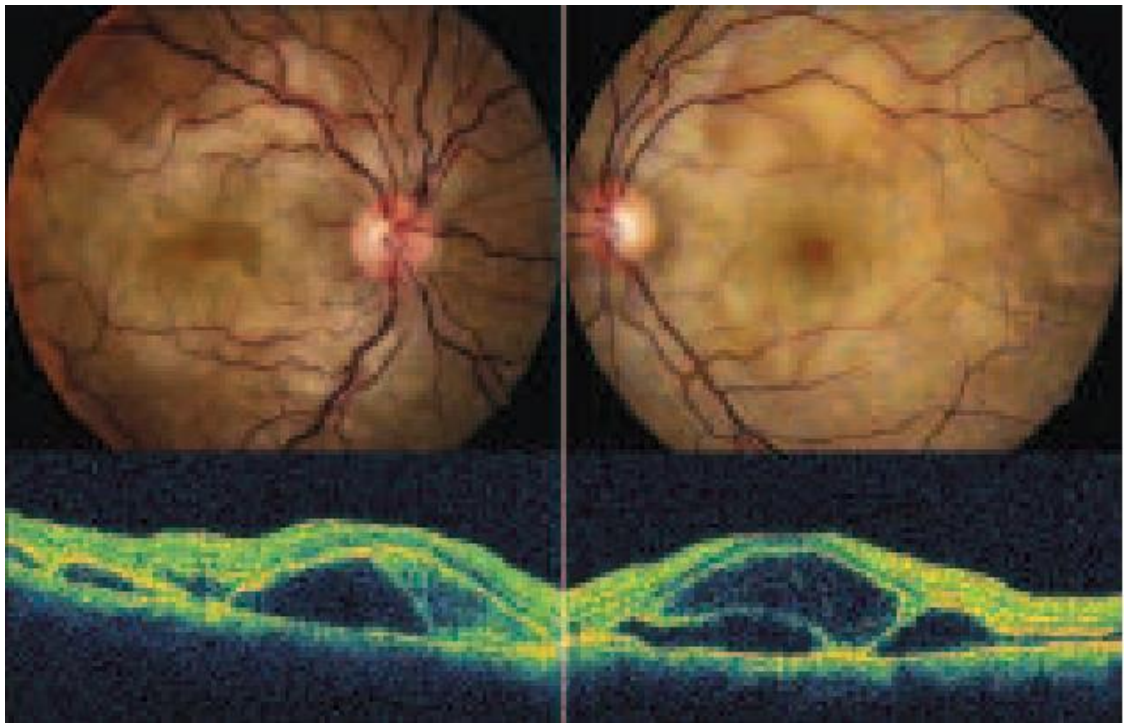
Vogt-Koyanagi-Harada syndrome (VKH)

- (VKH) is the second leading cause of uveitis in Japan after Behçet syndrome
- is manifested by bilateral posterior uveitis
- characteristic fluid accumulation beneath the retina
- leading to retinal elevation and detachment



VKH

VKH



VKH

- vitiligo,
- poliosis (loss of color from a patch of hair),
- sterile meningitis,
- alopecia, and
- eighth cranial nerve disease.

Diagnosis and classification of Vogt-Koyanagi-Harada disease.
Sakata VM, da Silva FT, Hirata CE, de Carvalho JF, Yamamoto JH
Autoimmun Rev. 2014 Apr;13(4-5):550-5. Epub 2014 Jan 15.

vision-threatening nature

- Απαιτείται γρήγορη διάγνωση &
- Άμεση έναρξη αγωγής με ανοσοκατασταλτικά
- VKH: especially in posterior uveitis or panuveitis with VKH as a prototype, where high-dose glucocorticoids, given during the first two weeks after disease onset, tapered slowly over 6 – 12 months, may achieve complete remission in some patients

Standardization of Uveitis Nomenclature (SUN) Working Group. Classification criteria for Vogt-Koyanagi-Harada Disease. Am J Ophthalmol 2021; 228:205–211.

Malignant uveitis masquerade syndromes (UMS)

- lymphoma (is the most common)
- leukemia
- melanoma
- retinoblastoma
- metastatic disease
- paraneoplastic syndromes

nonmalignant uveitis masquerade syndromes (UMS)

- retinitis pigmentosa
- retinal vasculopathies (Susac syndrome)
- ocular amyloidosis

Clues to the presence of UMS may be atypical findings on exam and ocular imaging, and inadequate responses to immunosuppression

Hsu Y-R, Wang L-U, Chen F-T, *et al.* Clinical manifestations and implications of nonneoplastic uveitis masquerade syndrome. Am J Ophthalmol 2022; 238:75–85.

Θεραπεία

- Αρχικά συνήθως στην άσηπτη ΑΑU → (Οφθαλμίατροι)→
- Τοπικά στεροειδή (για πόνο και φλεγμονή)
- Μυδριατικά (για αποφυγή συνεχειών και γλαυκώματος)

- Σε σοβαρή φλεγμονή AAU (2+ or more AC cells) → GCs συστηματικά
- Σε οπίσθια ραγοειδίτιδα 1mg/kg πρεδνιζόνης
- Ενδοφθάλμια ing GCs?

Systemic immunomodulatory therapy (IMT)

The FOCUS initiative cites as indications of systemic immunomodulatory therapy (IMT)

- acute sight-threatening disease
- persistent chronic inflammation
- posterior and macular involvement
- exudative retinal detachment
- active uveitis while taking dosing of prednisone of 0.5mg/kg or more
- relapsed disease when tapering prednisone to less than 10 mg daily steroid intolerance
- significant loss of visual acuity
- increase in vitreous haze grade 2 or more or
- relapse of cystoid macular edema

Hatemi G, Christensen R, Bang D, *et al.* 2018 update of the EULAR recommendations for the management of Behcet's syndrome. Ann Rheum Dis 2018; 77:808–818.

Without known underlying disease

IMT agents include

- mycophenolate mofetil (MMF),
- methotrexate (MTX),
- adalimumab, or
- infliximab.

Σε γνωστή υποκείμενη νόσο

Η βασική θεραπεία → κατάλληλη και για την οφθαλμική προσβολή

- **TNF inhibitors** in Behcet's and HLA- B27- associated disease
- and **methotrexate or MMF** in sarcoidosis.

TNF inhibitors

- θεραπεία εκλογής (biologic agents) σε AAU
- Adalimumab & Ifliximab (σκευάσματα εκλογής)
- Adalimumab vs Ifliximab?
- Etanercept (κατωτερότητα)

van der Horst-Bruinsma I, van Bentum R, Verbraak FD, *et al.* The impact of certolizumab pegol treatment on the incidence of anterior uveitis flares in patients with axial spondyloarthritis: 48-week interim results from C-VIEW. RMD Open 2020; 6:e001161.

- Golimumab & Certolizumab (λιγότερο μελετημένα)

Maccora I, Fusco E, Marrani E, *et al.* Changing evidence over time: updated meta-analysis regarding anti-TNF efficacy in childhood chronic uveitis. Rheumatology (Oxford) 2020; 60:568–587.

MTX vs MMF

- Παρόμοια αποτελέσματα
- Στην οπίσθια ραγοειδίτιδα MTX > MMF
- MMF πιο γρήγορο
- Παρόμοιες ανεπιθύμητες ενέργειες
- MTX μεγαλύτερες δόσεις (25mg/wk)

Karam M, Alsaif A, Al-Naseem A, *et al.* Mycophenolate versus methotrexate in noninfectious ocular inflammatory disease: a systemic review and meta-analysis. Ocul Immunol Inflamm 2022; 24:1–8.

σ.Αδαμαντιάδη-Behcet

- Levy-Clarke et al. expert panel recommendations suggest anti-TNF treatment as the first or second line for Bechet's uveitis.
- In contrast, EULAR 2018 recommendations leave this up to preference between azathioprine, anti-TNF, cyclosporine, or interferon-alpha, noting that sight-threatening disease should be treated with infliximab or interferon-alpha.
- Due to the frequently severe and vision-threatening nature of Behcet's uveitis in general and the recent unavail- ability of nonpegylated interferon-alpha, anti-TNF therapy has emerged as the first-line treatment in the United States.

Hatemi G, Christensen R, Bang D, *et al.* 2018 update of the EULAR recommendations for the management of Behcet's syndrome. Ann Rheum Dis 2018; 77:808–818.

Inflammatory eye diseases affecting the outer structures of the eye

- Conjunctivitis
- Keratitis
- Episcleritis
- Scleritis

Inflammatory eye diseases affecting the outer structures of the eye

- infectious or
- noninfectious
- systemic disease or
- be limited to the eye.

Curr Opin Rheumatol 2023;

Σκληρίτιδα vs Επισκληρίτιδας

- **Σκληρίτιδα → -** εν τω βάθει
  - vision-threatening
  - επώδυνη

- **Επισκληρίτιδα** - επιφανειακά
  - non vision-threatening
  - ανώδυνη

Σκληρίτιδα

- 38-45% των ασθενών υποκείμενο συστηματικό νόσημα
- Πρόσθια (nodular, diffuse, or necrotizing)

  ή
- Οπίσθια

Σκληρίτιδα

- Necrotizing → Scleromalacia perforans (σπάνια)

- Patients with **posterior scleritis** may have little or no anterior inflammation resulting in mild or no redness, which can make the diagnosis challenging !!!

Promelle V, Goeb V, Gueudry J. Rheumatoid arthritis associated episcleritis and scleritis: an update on treatment perspectives. J Clin Med 2021; 10:2118.

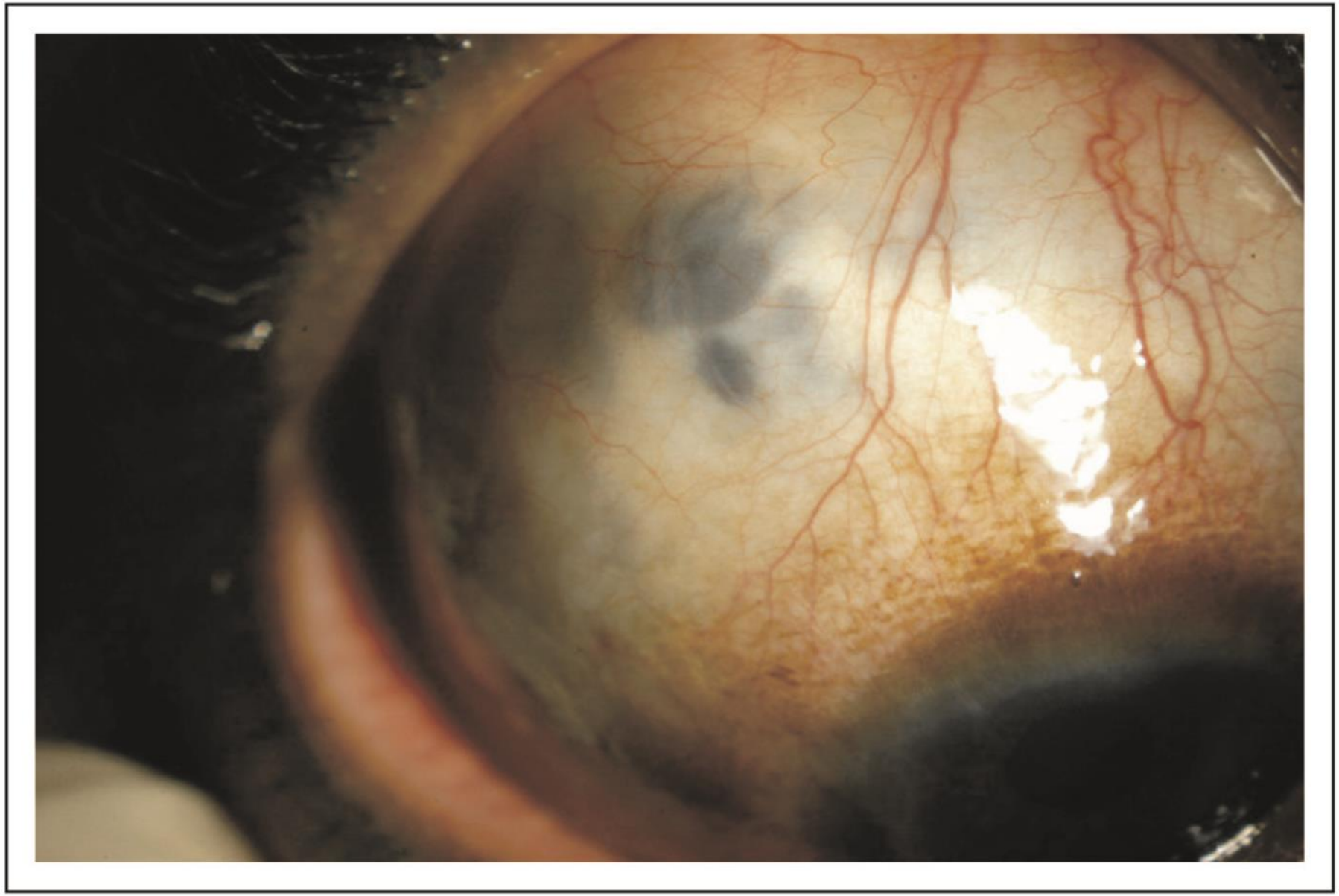


FIGURE 6. Necrotizing scleritis is a vision-threatening disease with increased risk of perforation. It can occur in rheumatoid arthritis and is one of its most severe ocular manifestations.

Σκληρίτιδα

- Φαινόμενο διάχυσης (εξω →μέσα)
- anterior scleritis → (secondary) anterior uveitis (with cells in the anterior chamber)
- posterior scleritis →(may present) with choroiditis and exudative retinal detachment → τύφλωση

Vermeirsch S, Testi I, Pavesio C. Choroidal involvement in noninfectious posterior scleritis. J Ophthalmic Inflamm Infect 2021; 11:41.

Noninfectious scleritis

- Συνήθως σε οροθετική RA και
- ANCA(+) αγγειίτιδες
- Οπωσδήποτε RF, anti-CCP, ANCA (MPO & PR3)

- Ισως το πρώτο σύμπτωμα των ANCA(+) αγγειιτίδων
- (+)anti-CCP → necrotizing Scleritis
- Patients with these antibody profiles should be treated as aggressively as severe RA or GPA patients with major organ involvement.

Vergouwen DPC, Ten Berge JC, Boukhrissi S, *et al.* Clinical relevance of autoantibodies and inflammatory parameters in noninfectious scleritis. Ocul Immunol Inflamm 2021; 30:1859–1865.

scleritis

- Other associated diseases are
- systemic lupus erythematosus
- relapsing polychondritis
- IBD
- Sjogren's syndrome
- polyarteritis nodosa
- IgG4-related disease
- IgA vasculitis
- Several medications, including bisphosphonates rarely cause

Nevares A, Raut R, Libman B, Hajj-Ali R. Noninfectious autoimmune scleritis: recognition, systemic associations, and therapy. Curr Rheumatol Rep 2020; 22:11.

Σκληρίτιδα - Θεραπεία

- 1ο επεισόδιο →ΜΣΑΦ
- Σε υποτροπή GCs
- Προσεκτική μείωση κάτω από τα 10mg/day prednisone
- (1mg μηνιαίως)
- Συχνό λάθος η γρήγορη μείωση

Nevares A, Raut R, Libman B, Hajj-Ali R. Noninfectious autoimmune scleritis: recognition, systemic associations, and therapy. Curr Rheumatol Rep 2020; 22:11.

- Patients with noninfectious recurrent scleritis and high-risk features such as necrotizing or nodular scleritis require systemic glucocorticoids and IMT

  KAI…

- bilateral disease and association with a systemic autoimmune disease such as RA or GPA

Abdel-Aty A, Gupta A, Del Priore L, Kombo N. Management of noninfectious scleritis. Ther Adv Ophthalmol 2022; 14:25158414211070879.

ΑΝΟΣΟΚΑΤΑΣΤΑΛΤΙΚΑ (IMT)

Commonly used IMT

- MTX, MMF, AZA, anti-TNF agents, rituximab, and cyclophosphamide
- A rational choice for an IMT agent considers the underlying disease or the antibody profile (RTX, MTX, and anti-TNF for anti-CCP/ RA; RTX, or AZA for ANCA-associated forms, etc.)
- Cyclophosphamide, traditionally the drug of choice for severe or necrotizing scleritis in RA, is still useful but is increasingly being replaced by anti-TNF or rituximab therapy

Promelle V, Goeb V, Gueudry J. Rheumatoid arthritis associated episcleritis and scleritis: an update on treatment perspectives. J Clin Med 2021; 10:2118.

Σκληρίτιδα

- Σε **ανθεκτικές** περιπτώσεις→→
- →→ σκέψη για **βιοψία** σκληρού χιτώνα
- →→ Αποκλεισμός **λοίμωξης**
- →→ Αποκλεισμός **κακοήθειας**

Curr Opin Rheumatol 2023:

Peripheral ulcerative keratitis

- Οξύ καταστροφικό φλεγμονώδες γεγονός…
- Δυνητικά οδηγεί σε τύφλωση
- 50% οφείλεται σε CTD
- RA 34% ιδίως anti-CCP(+)
- οπωσδήποτε αποκλεισμός σύφιλης, TB, βακτήρια, μύκητες

Hassanpour K, El Sheikh RH, Arabi A, *et al.* Peripheral ulcerative keratitis: a review. J Ophthalmic Vis Res 2022; 17:252–275.

Peripheral ulcerative keratitis (treatment)

- (Συχνά επιπλοκή της σκληρίτιδας)
- →**Ανοσοκατασταλτικά**
- Όχι μεταμόσχευση

  (ίσως σε ειδικές ανθεκτικές περιπτώσεις)

Hassanpour K, El Sheikh RH, Arabi A, *et al.* Peripheral ulcerative keratitis: a review. J Ophthalmic Vis Res 2022; 17:252–275.

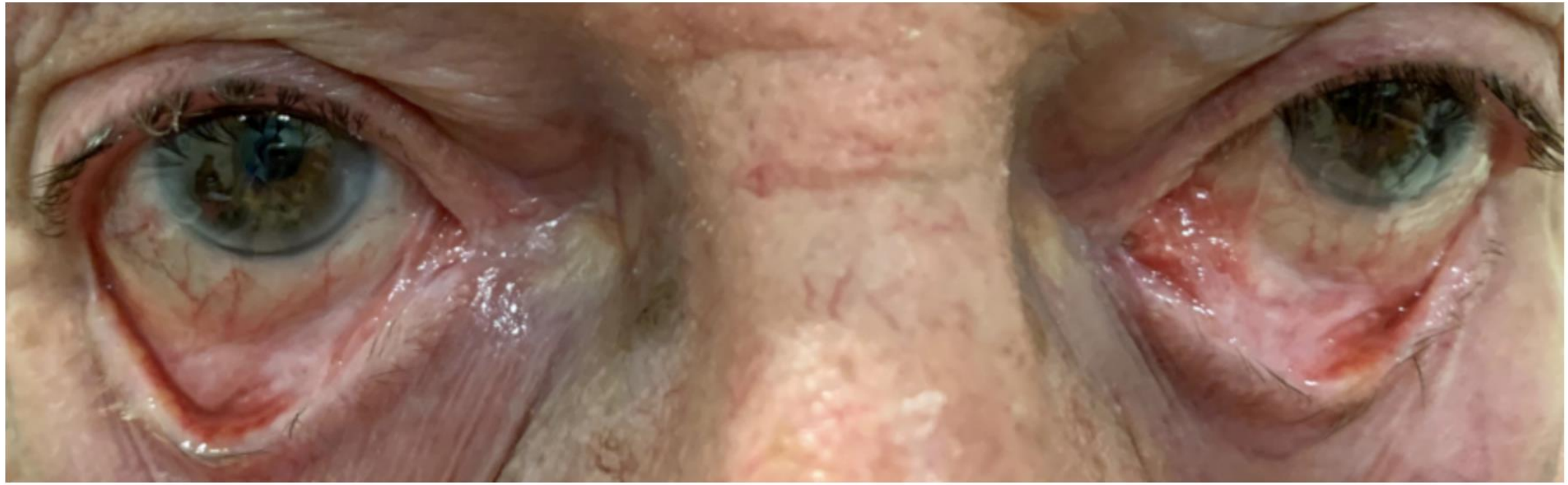
Ocular cicatricial pemphigoid
(Οφθαλμικό Ουλώδες Πεμφιγοειδές)

- Ocular cicatricial pemphigoid (OCP) is a scarring, vision-threatening process due to underlying **mucous membrane pemphigoid.**

- Επιπεφυκότας, στόμα, οισοφάγος, τραχεία, γεννητικά όργανα

- 70% μόνο στα μάτια

Ocular cicatricial pemphigoid



Ασθενής με Συμβλέφαρα και Τριχίαση λόγω Οφθαλμικού Ουλώδους Πεμφιγοειδούς

Οφθαλμικό Ουλώδες Πεμφιγοειδές

- Διάγνωση → με **βιοψία επιπεφυκότα**

- Συχνά ψευδώς αρνητικές βιοψίες

Οφθαλμικό Ουλώδες Πεμφιγοειδές

- Αποκλεισμός Σαρκοείδωσης και ANCA(+) αγγειιτίδων

- → επιθετική θεραπεία με
  high dose glucocorticoids, typically 1 mg/kg/day of prednisone

- **early addition** of steroid sparing agents. **MTX, MMF, AZA, dapsone**
  (Σε ανθεκτικές περιπτώσεις CYC, RTX)

Schmidt E, Rashid H, Maranzo AV, *et al.* European guidelines (S3) on diagnosis and management of mucous membrane pemphigoid, initiated by the European Academy of Dermatology and Venereology – Part II. J Eur Acad Dermatol Vernereol 2021; 35:1926–1948.

ORBITAL INFLAMMATION

- **Φλεγμονή βλεφάρων** (δακρυϊκοί αδένες, οφθαλμικοί μύες, οφθαλμικό λίπος)
- Θυρεοειδοπάθειες, λοιμώξεις, λεμφοϋπερπλαστικά σύνδρομα, σαρκοείδωση, GPA, Ig4-related disease
- The term **nonspecific orbital inflammation (NSOI)** indicates the absence of an identifiable cause.

ORBITAL INFLAMMATION

- Orbital imaging with **CT or MRI makes the diagnosis**
- **a biopsy may be necessary.**
- NSOI is treated with **steroids** and IMT, typically with **MTX**

ORBITAL INFLAMMATION

- Orbital inflammation in ANCA vasculitis and cases with high MPO/PR3 antibody titers in the absence of systemic manifestations is a severe disease.
- It usually requires a complete induction with glucocorticoids and RTX or cyclophosphamide, as in ANCA vasculitis with significant extra-ocular organ involvement

Lee MJ, Planck SR, Choi D, *et al.* Nonspecific orbital inflammation: current understanding and unmet needs. Prog Retin Eye Res 2021.

Συμπερασματικά

- **Every practicing rheumatologist will encounter noninfectious inflammatory eye diseases**.
- These include different forms of uveitis, scleritis, keratitis, conjunctivitis, and orbital inflammation.
- diagnose or rule out infections before accepting an autoimmune eye condition diagnosis.
- Drugs, metabolic/ endocrine diseases, and malignancies are other important causes of inflammatory eye diseases

Συμπερασματικά

- Most mimics of noninfectious ocular inflammatory diseases may initially respond to immunosuppression increasing diagnostic uncertainty and the risk of delaying vision-preserving treatment.

- For optimal care of these patients, **close communication with ophthalmology is essential.**

Kelly Corbitta and Johannes Nowatzky

Curr Opin Rheumatol 2023


THANK YOU