RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

4th Annual National Conference

September 21–23, 2023

Key Principles in Comanaging Ocular Inflammation and Dry Eye Symptoms

Brandon Runyon, OD, FAAO
brandonrunyon@gmail.com

Financial Disclosures

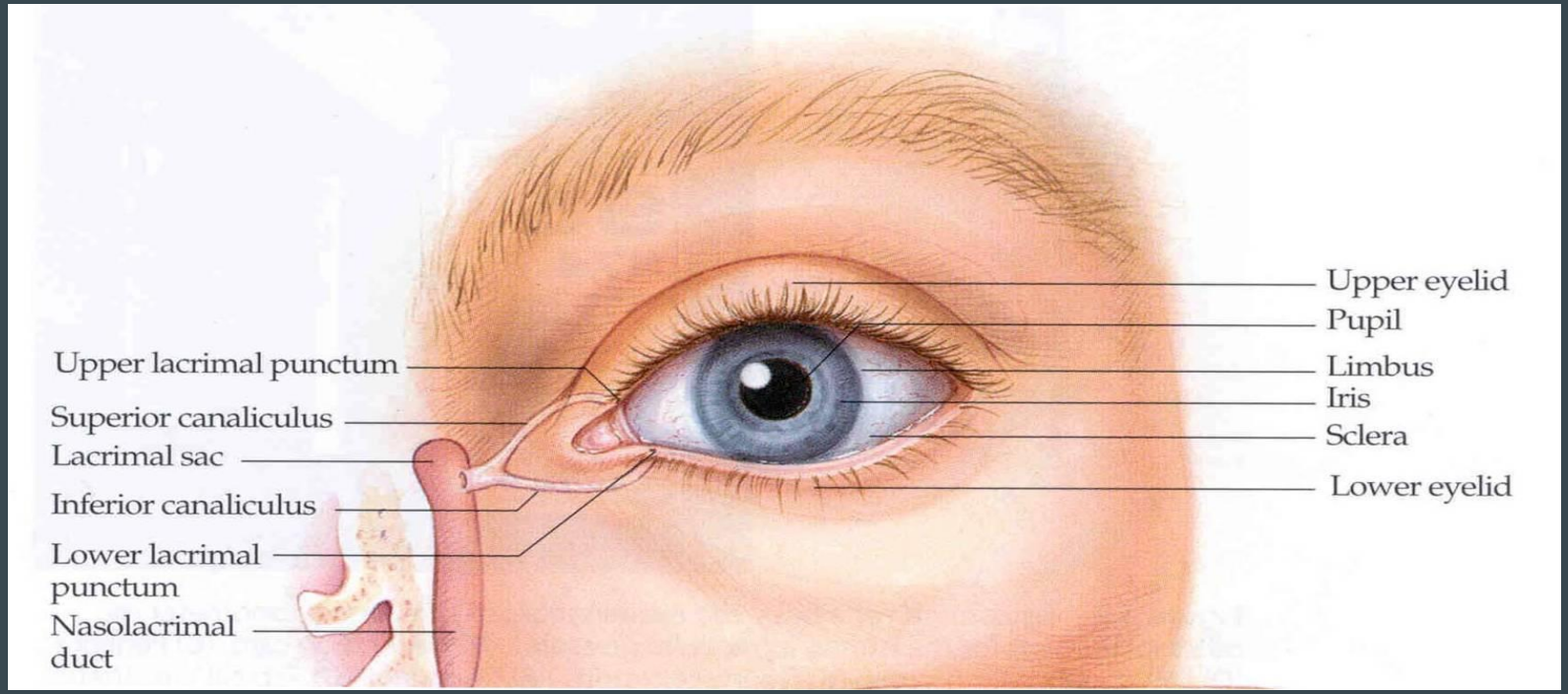
- There are no relevant financial relationships to disclose.

Objectives

1. Improve provider confidence in when to refer patients for evaluation as well as the timeliness of their referrals.
2. Understand the importance of collaboration and ongoing communication between rheumatology providers and eyecare providers regarding disease activity.
3. Enhance knowledge of uveitis diagnosis, treatment, and management.
4. Enhance knowledge of dry eye diagnosis, treatment, and management.

ANATOMY REVIEW

Gross Ocular Anatomy



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Basic Eye Anatomy

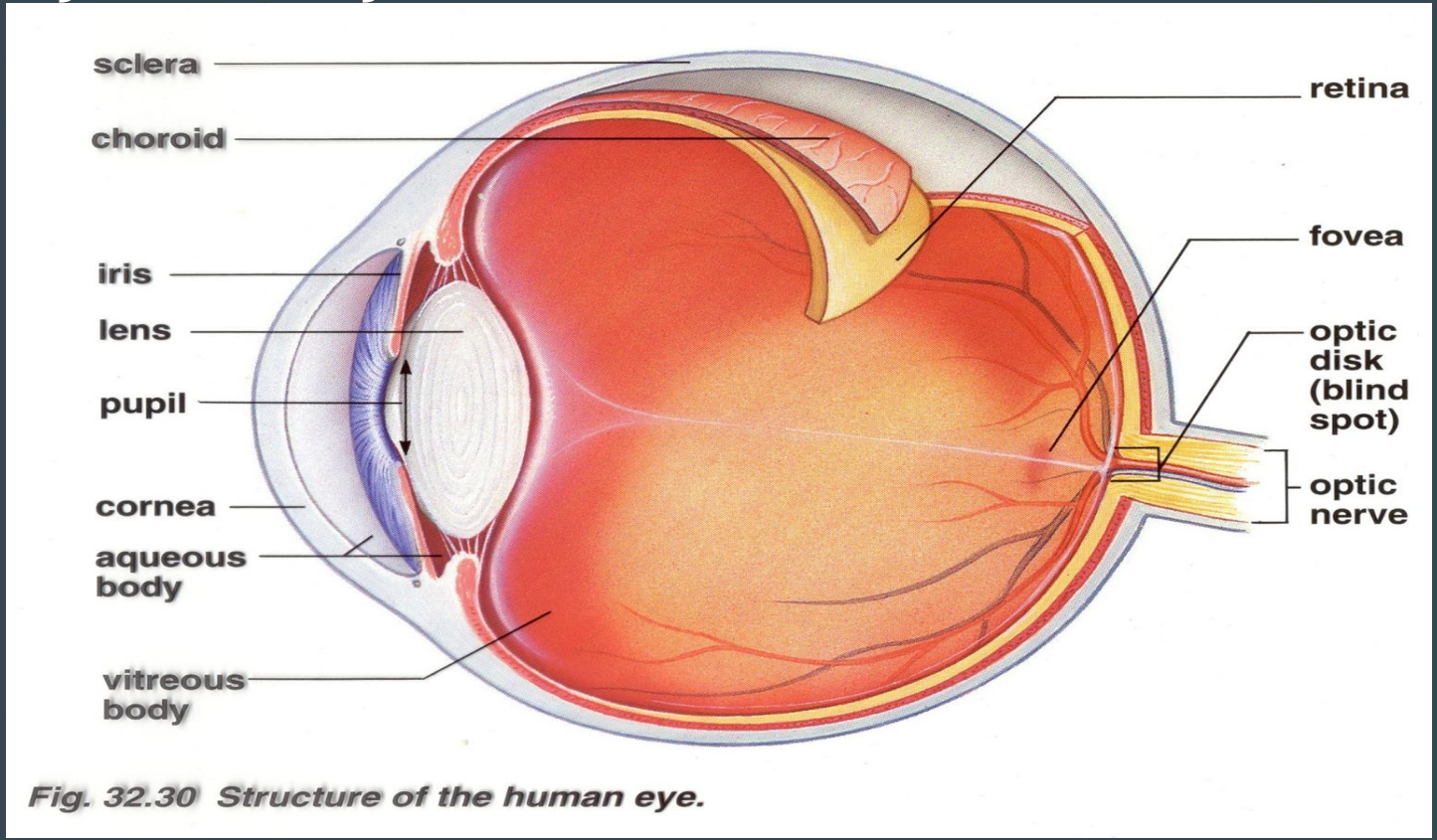
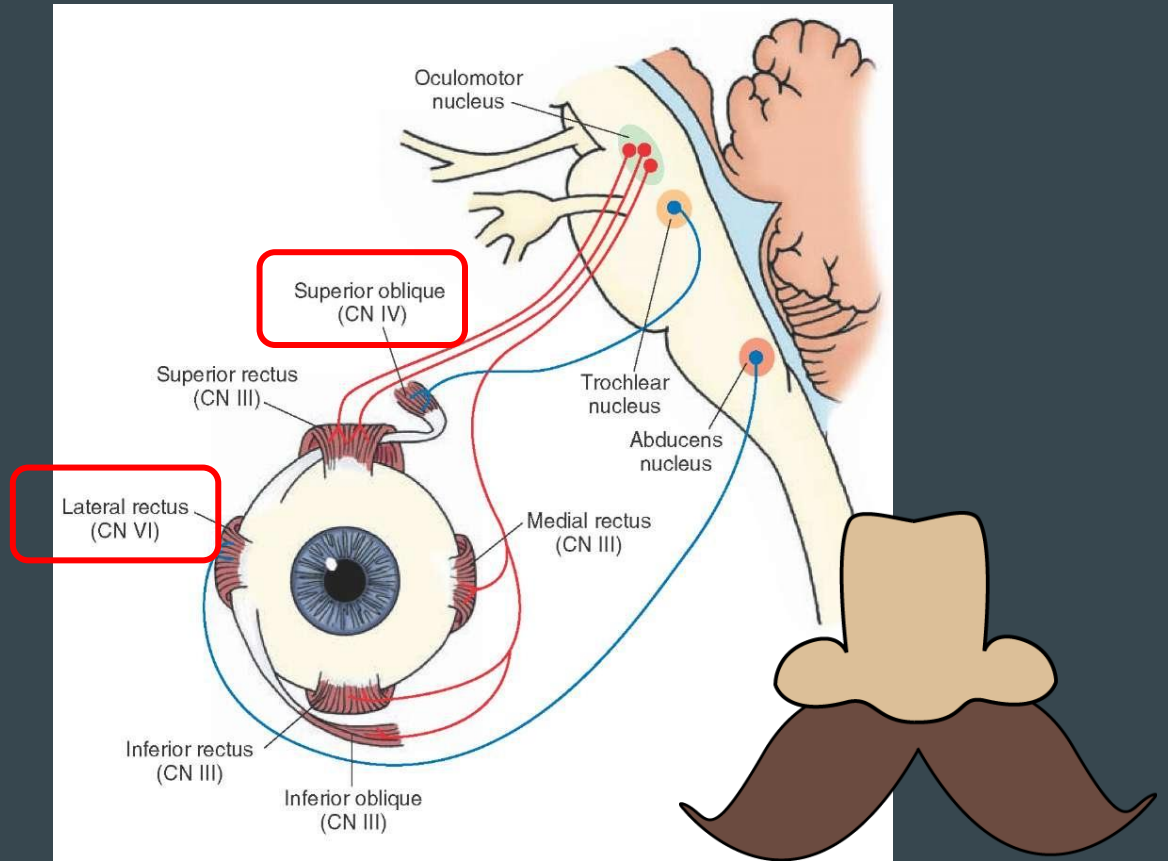


Fig. 32.30 Structure of the human eye.

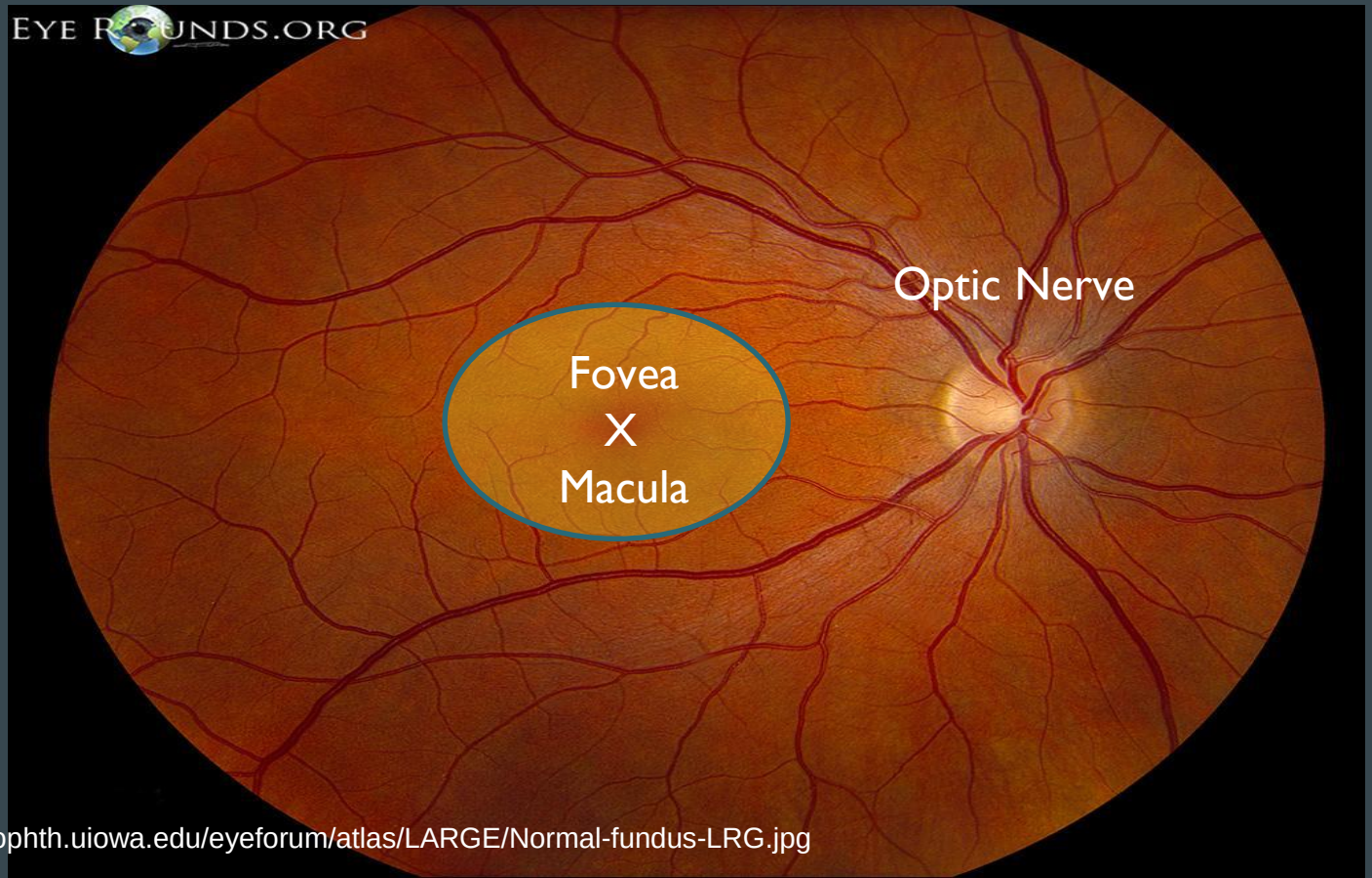
Source: http://medicalanatomy.net/wp-content/uploads/eye-anatomy-499.jpg

Extraocular Muscle Anatomy



Source: http://what-when-how.com/wp-content/uploads/2012/04/tmp15E38.jpg

Retinal Anatomy



Source: http://webeye.ophth.uiowa.edu/eyeforum/atlas/LARGE/Normal-fundus-LRG.jpg

Triaging Common Eye Symptoms

Symptom #1: Eye Pain

Eye Pain

- Nonspecific complaint
- Need more qualitative information

KEY HISTORY:

- Eyeball or eyelid?
- Sharp Pain vs. Dull Pain?
- Constant vs. Intermittent?
- Duration?
- Sudden Onset vs. Gradual?
- Redness?
- Photophobia?
- Discharge?
- Contact Lens Wear?
- Has this happened before?
- Blurred Vision?

TRIAGE PEARL: ANTERIOR UVEITIS

NOTE: this pupil likely has been dilated in office

- Red
- Aching/throbbing eye
- Tearing / Watering
- Photophobia
- Constricted Pupil
- NO MUCOID DISCHARGE
- +/- Nausea/Vomiting → High IOP

- Highly suspect if patient has condition associated with anterior uveitis (HLA-B27 related diseases are most common)

- **REFER ASAP**

Symptom #2: Red Eye

Red Eye

- Nonspecific complaint
- Need more qualitative information

KEY HISTORY:

- Constant vs. Intermittent?
- Duration?
- Sudden Onset vs. Gradual?
- Pain?
- Redness?
- Photophobia?
- Contact Lens Wear?
- Has this happened before?
- Blurred vision?

Gervasio, K. A., & Rook, T. J. (2023). *The Wills Eye Manual Office and emergency room diagnosis and treatment of eye disease*. Wolters Kluwer

TRIAGE PEARL: SCLERITIS

- Red
- SEVERE EYE PAIN
- Tearing / Watering
- Photophobia
- +/- Constricted Pupil
- NO MUCOID DISCHARGE

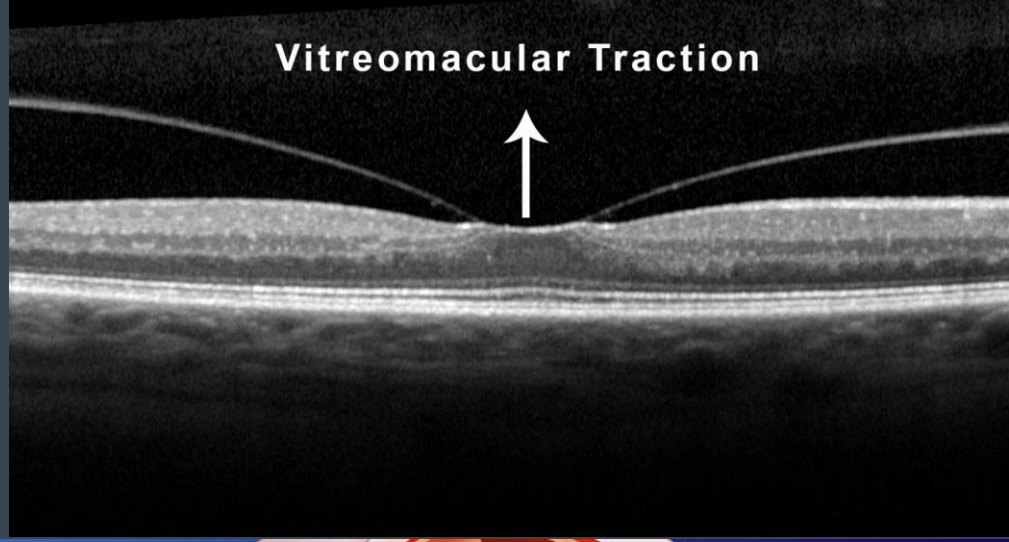
- 50% idiopathic
- ~50% autoimmune
  - RA, Sarcoid
  - Connective Tissue Diseases

- **REFER ASAP**

Symptom #3: Flashes and/or Floaters

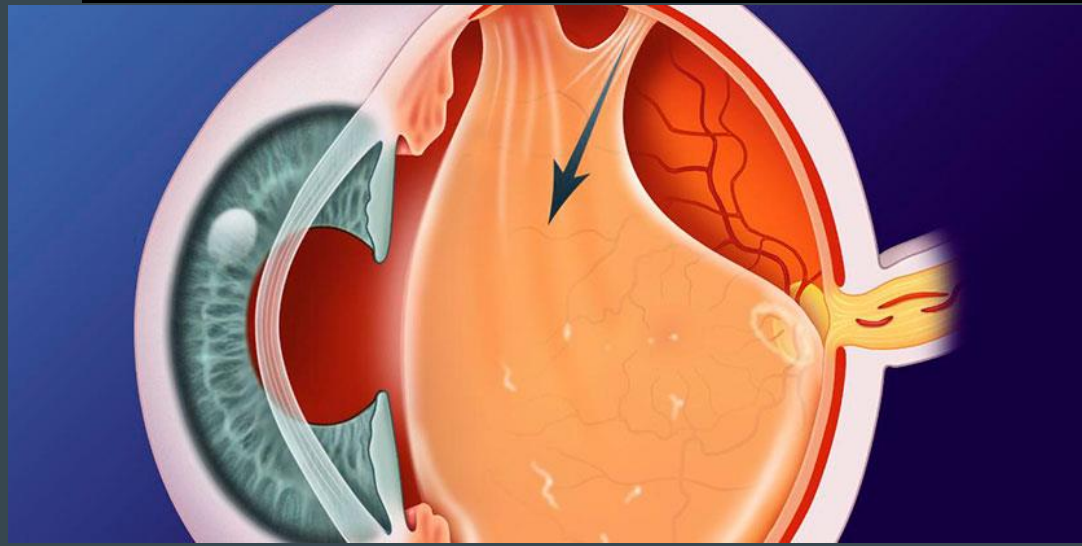
Flashes of Light

- Indicate vitreous traction on the retina and/or chorioretinal inflammation
- Usually “camera flashes,” “flickering,” or “lightning bolts” in vision
- Wide differential



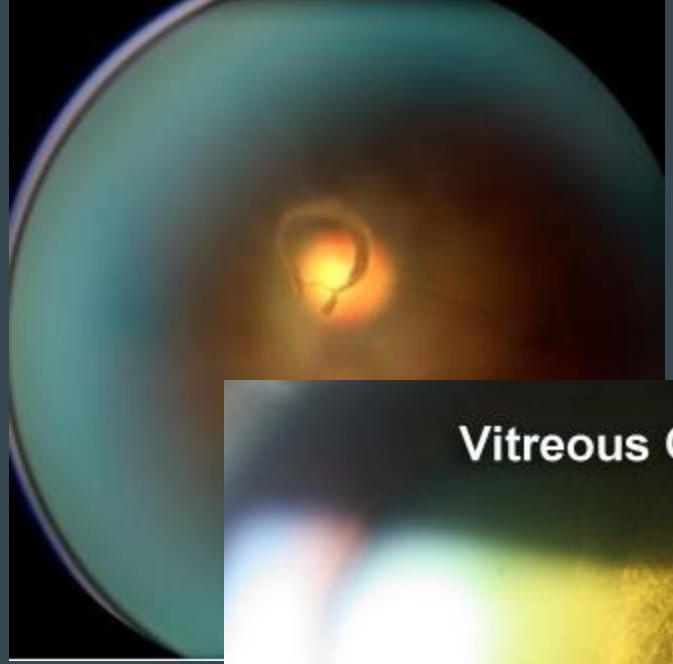
KEY HISTORY:

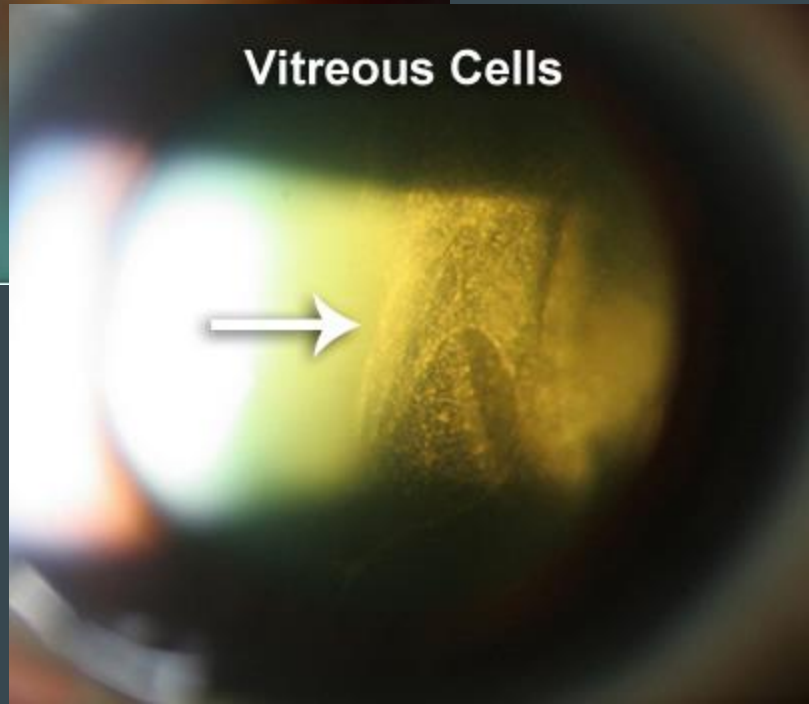
- Duration?
- Sudden Onset vs. Gradual?
- Has this happened before?
- Blurred vision?
- Floaters?



Floaters

- Commonly caused by vitreous separation from retina or vitreous degeneration
- Retinal tears or detachments
- Presence of inflammatory cells in vitreous
- Wide differential

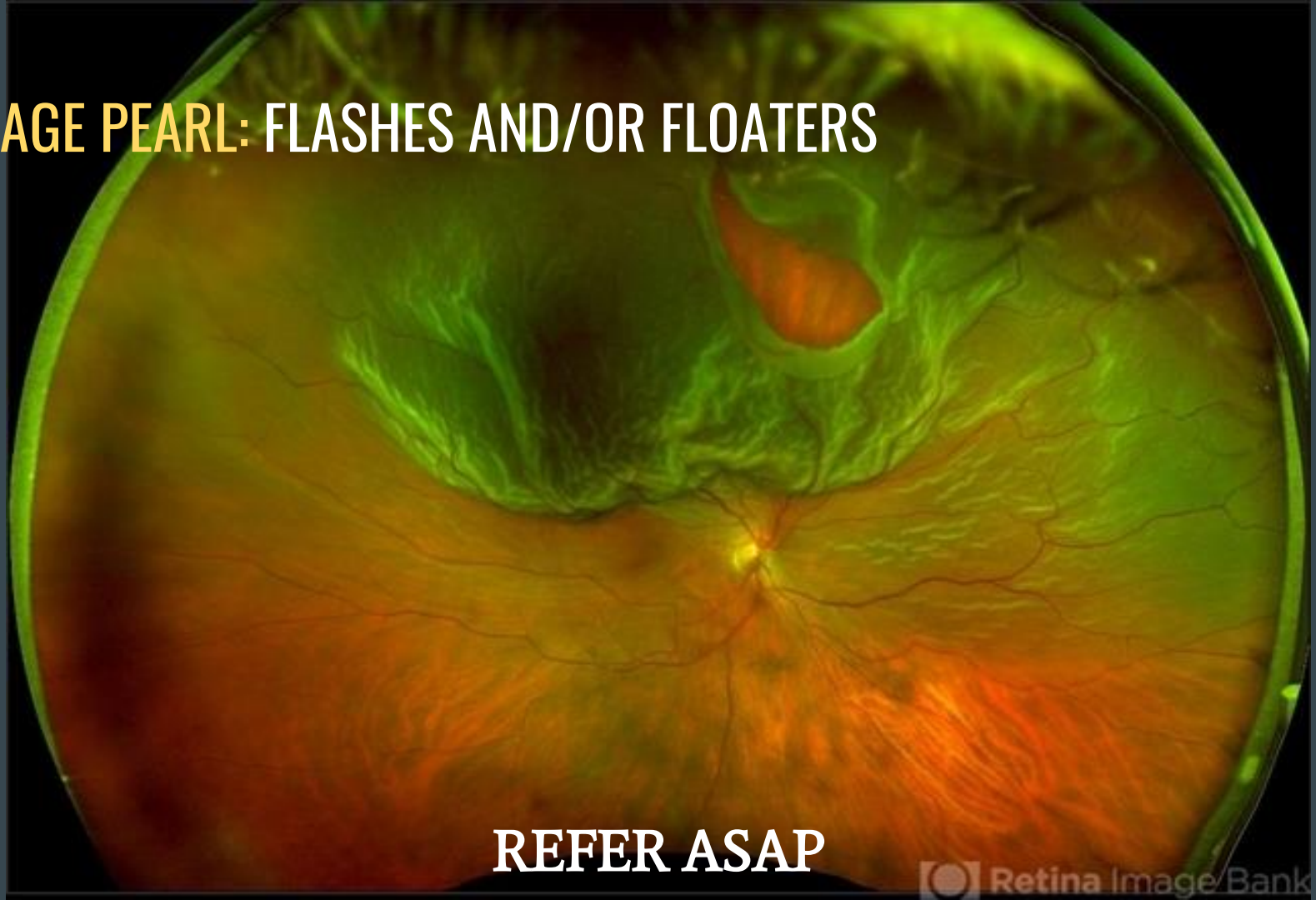




KEY HISTORY:

- Duration?
- Sudden Onset vs. Gradual?
- Has this happened before?
- Blurred vision?
- Flashes?

TRIAGE PEARL: FLASHES AND/OR FLOATERS



REFER ASAP

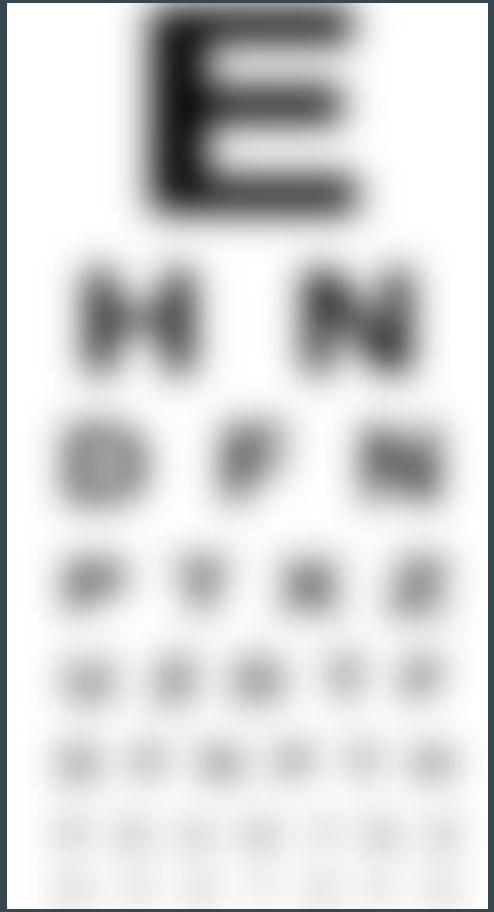
Symptom #4: Blurred Vision

Blurred Vision

- Measure a reliable visual acuity at distance in clinic
- Observe the patient during testing
- If uncorrected vision → use pinhole occluder

KEY HISTORY:

- Sudden Onset vs. Gradual?
- Duration?
- Constant vs. Intermittent?
- Has this happened before?
- Pain?



TRIAGE PEARL: PINHOLE ACUITY

- Pinhole acuity is used to differentiate refractive vision changes vs. pathological vision changes (in most cases)

- Example #1:
  Uncorrected Distance VA: 20/80
  PH acuity:
  20/25
  ******Most likely refractive change******

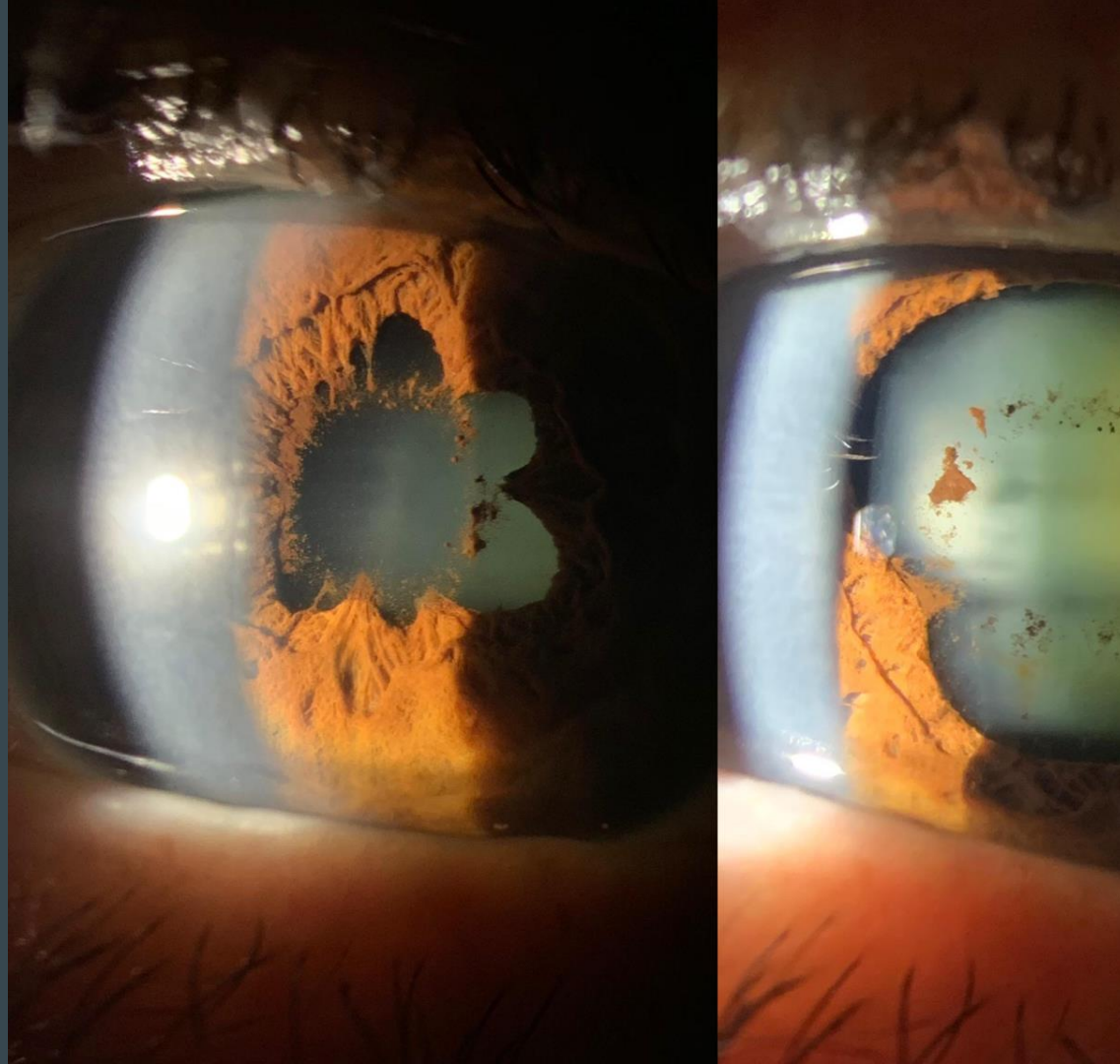
- Example #2:
  Corrected Distance VA:
  20/80
  PH acuity:
  20/40
  ******Probable PATHOLOGY******

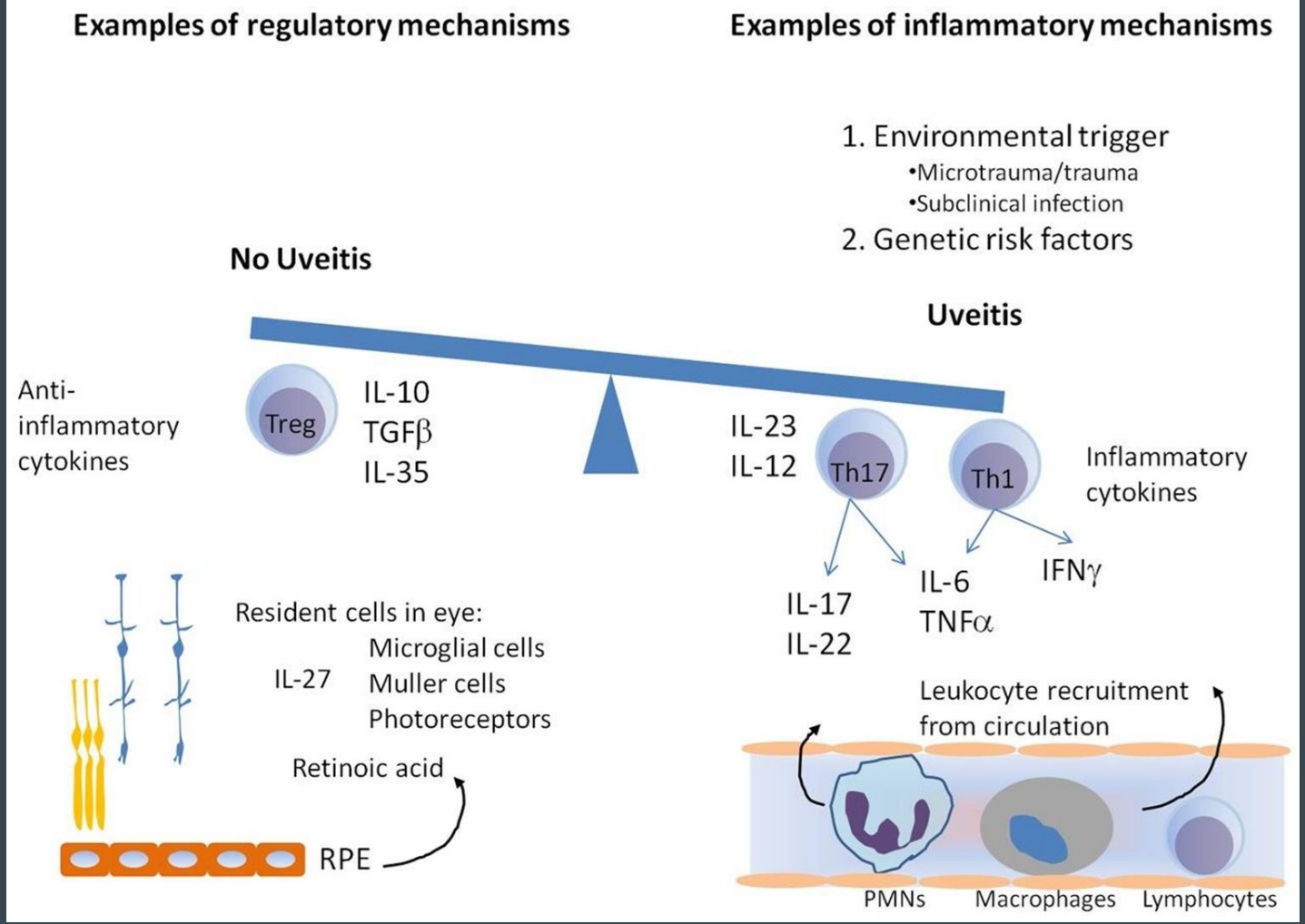
TRIAGE PEARL: SUDDEN ONSET BLURRED VISION

- CONSTANT, sudden onset blurred vision +/- PAIN → refer TODAY
- INTERMITTENT, sudden onset blurred vision +/- PAIN → less urgent

UVEITIS:

DIAGNOSIS
TREATMENT
MANAGEMENT





Lin P, Suhler EB, Rosenbaum JT. The future of uveitis treatment. *Ophthalmology*. 2014;121(1):365-376. doi:10.1016/j.ophtha.2013.08.029

PREVALENCE:
ANTERIOR >>> INTERMEDIATE, POSTERIOR & PANUVEITIS

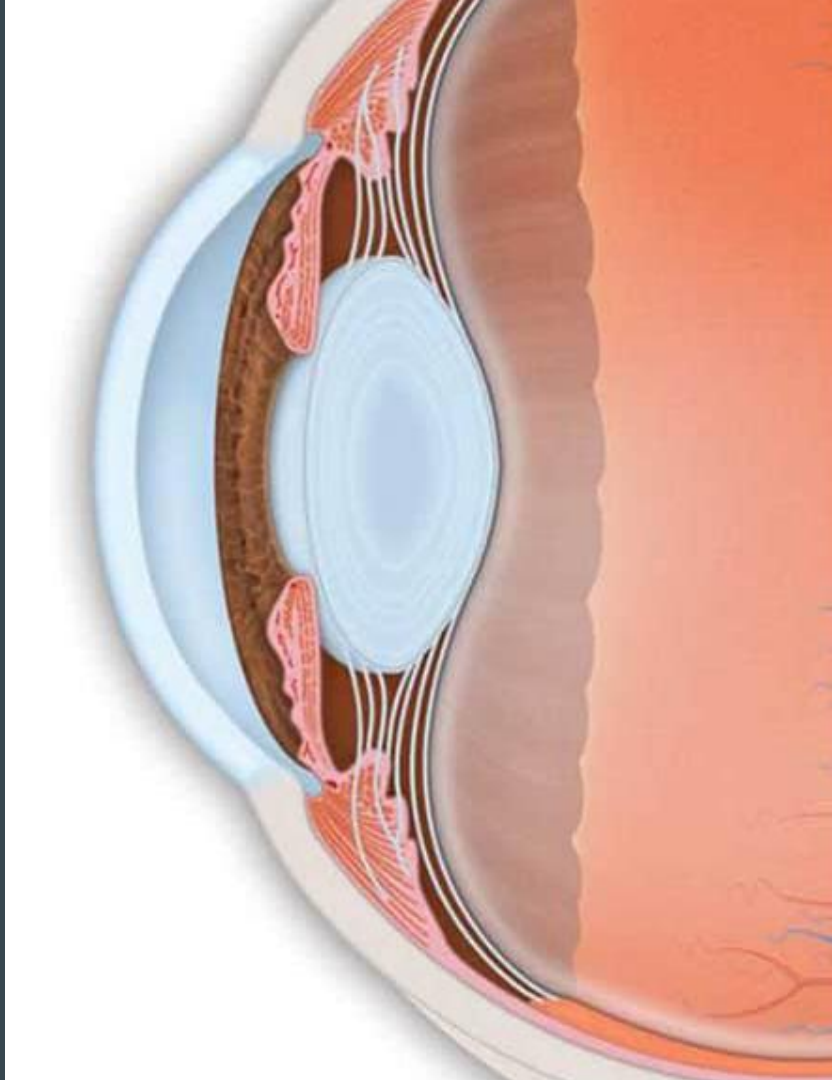
Table 1 – SUN Working Group anatomic classification of uveitis[6]

Type	Primary site of inflammation	Includes
Anterior	Anterior chamber	Iritis Iridocyclitis Anterior cyclitis
Intermediate	Vitreous	Pars planitis Posterior cyclitis Hyalitis
Posterior	Retina or choroid	Focal, multifocal, or diffuse choroiditis Chorioretinitis Retinochoroiditis Retinitis Neuroretinitis
Panuveitis	Anterior chamber, vitreous, and retina or choroid	

Jabs DA, Nussenblatt RB, Rosenbaum JT; for the 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(3):509-516.

ANTERIOR UVEITIS

- Primary site of inflammation is iris and/or ciliary body
- **SYMPTOMS:**
  - Red, painful eye
  - Photophobia
- **ETIOLOGY:**
  - Idiopathic (most common)
  - HLA-B27 diseases
  - Syphilis / other infectious
  - Other autoimmune



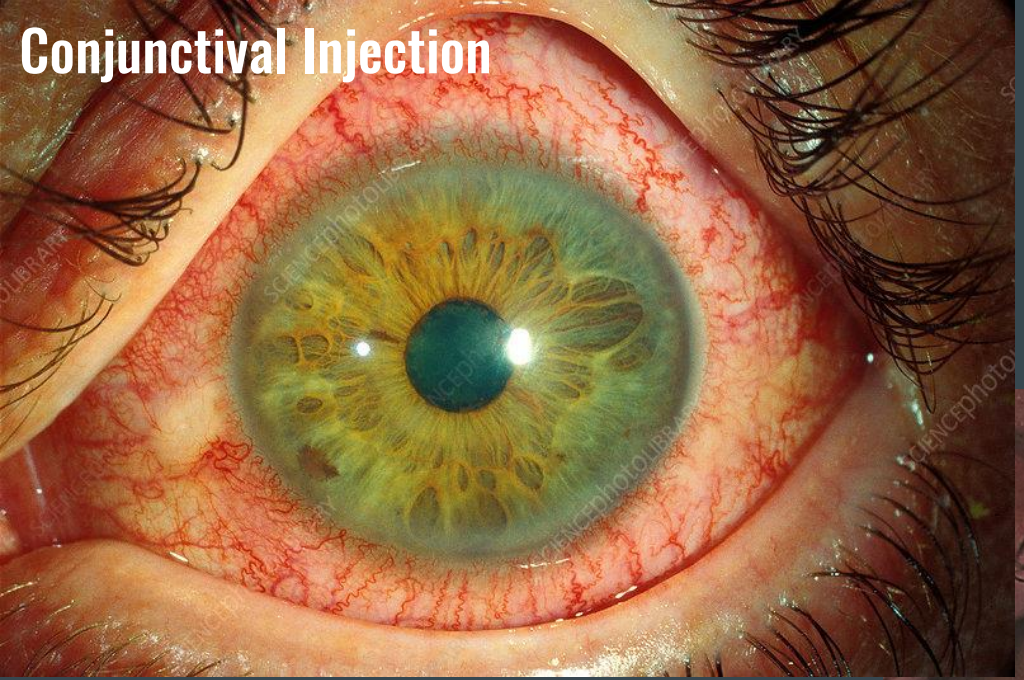
Jabs DA, Nussenblatt RB, Rosenbaum JT; for the Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the first international workshop. *Am J Ophthalmol.* 2005;140(3):509-516.

CLINICAL SIGNS

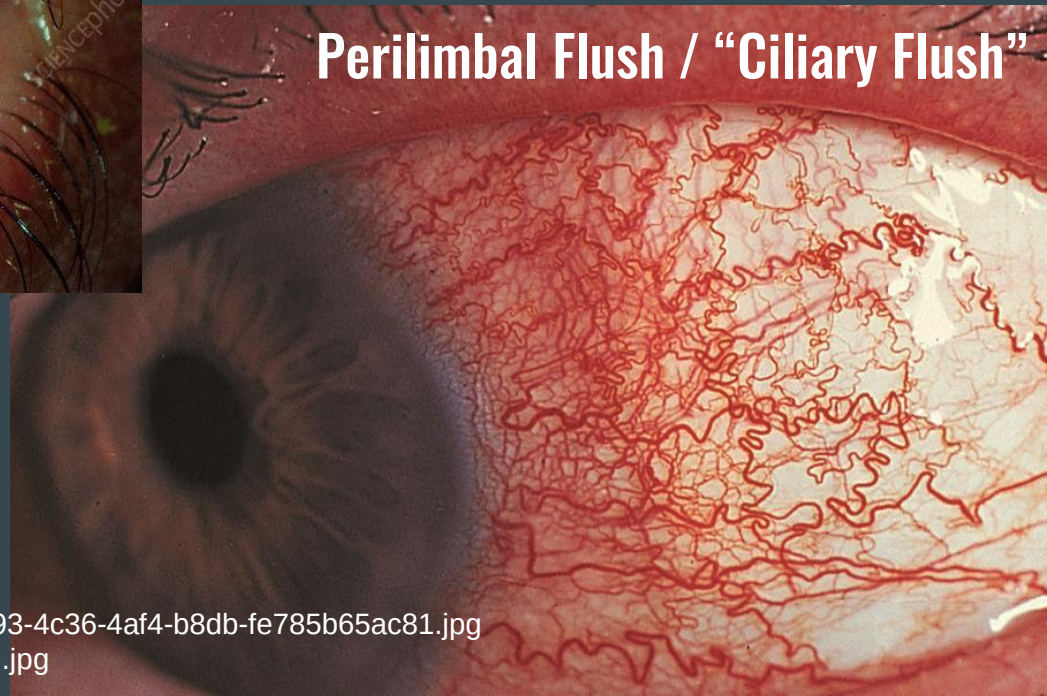
What can I see with my ophthalmoscope?

Source:https://www.welchallyn.com/content/dam/welchallyn/images/Product-Images/Physical-Exam/Eye-Exam/Ophthalmoscopes-Traditional-Direct/3-5V-Standard-Ophthalmoscope/soph_11710.jpg

Conjunctival Injection



Perilimbal Flush / “Ciliary Flush”



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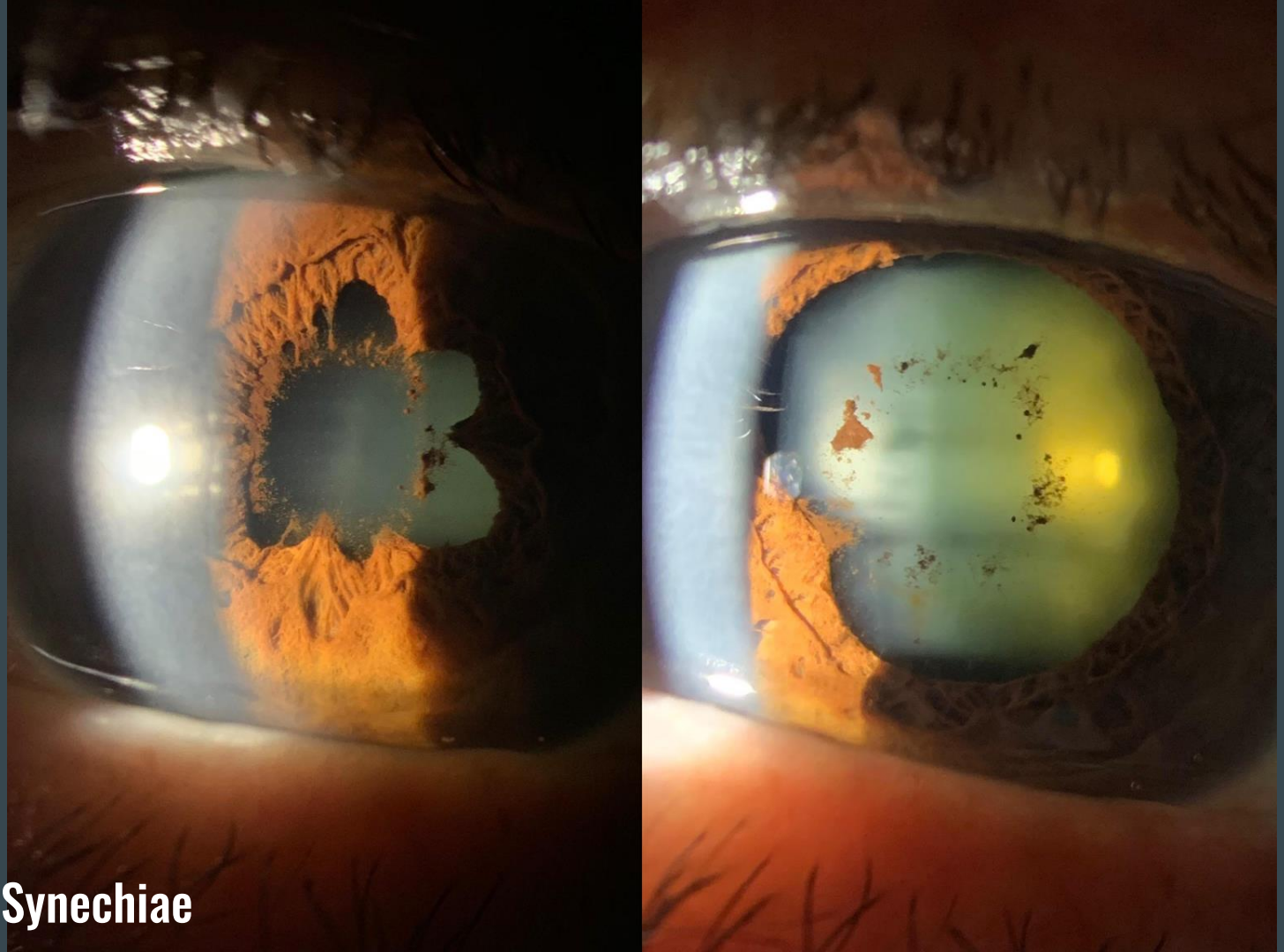
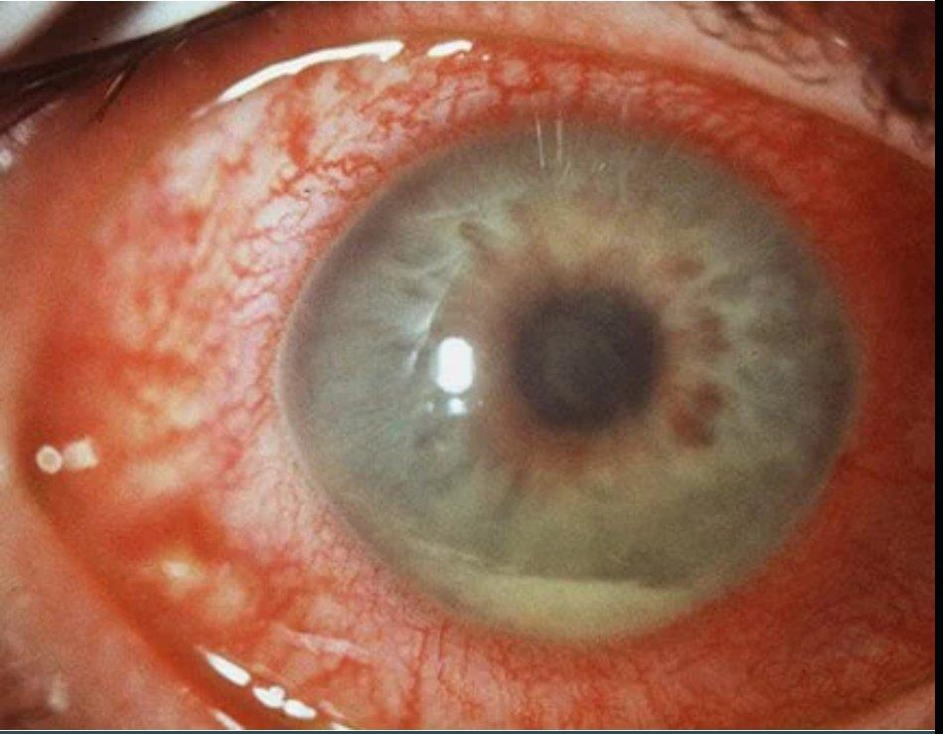
https://media.sciencephoto.com/c0/34/58/26/c0345826-800px-wm.jpg

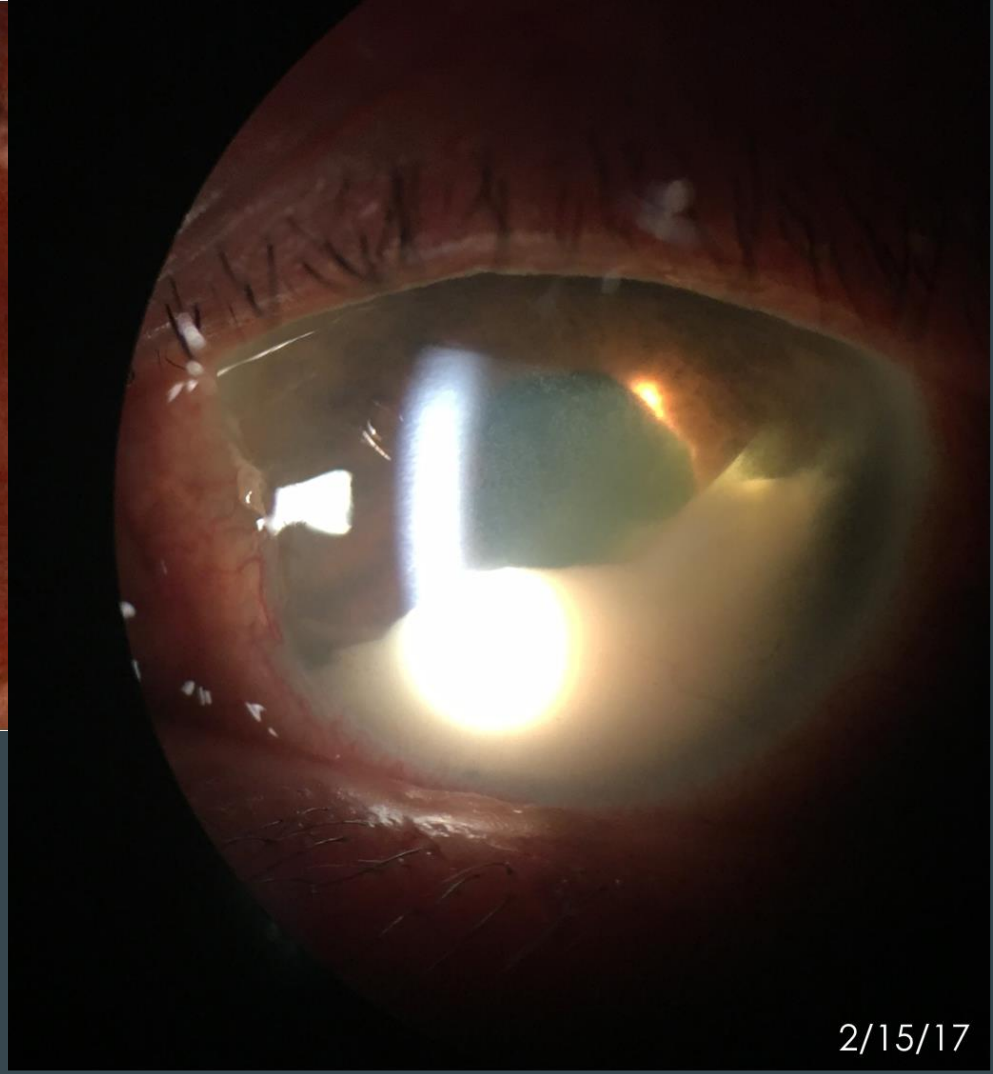


Posterior Synechiae

Anterior Uveitis

NOTE: strand of surgical debris is NOT associated with uveitis

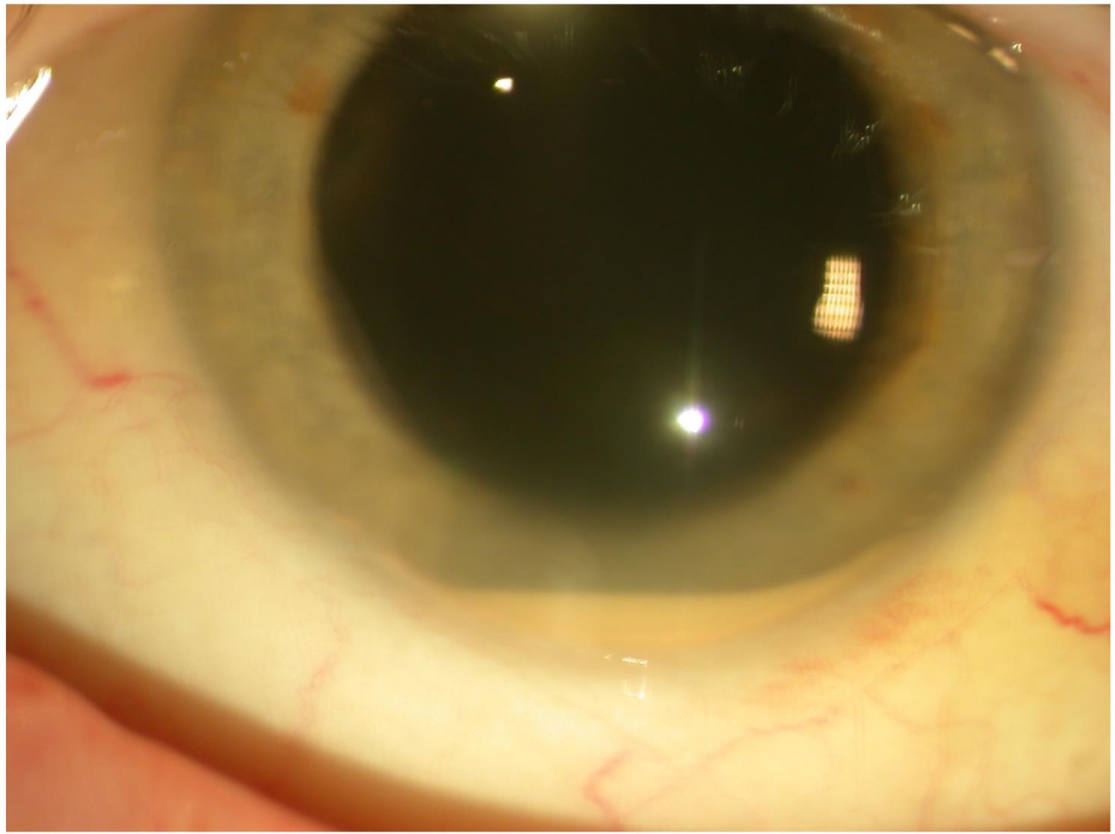




Hypopyon

2/15/17

CLINICAL PEARL: JIA/JRA-RELATED UVEITIS

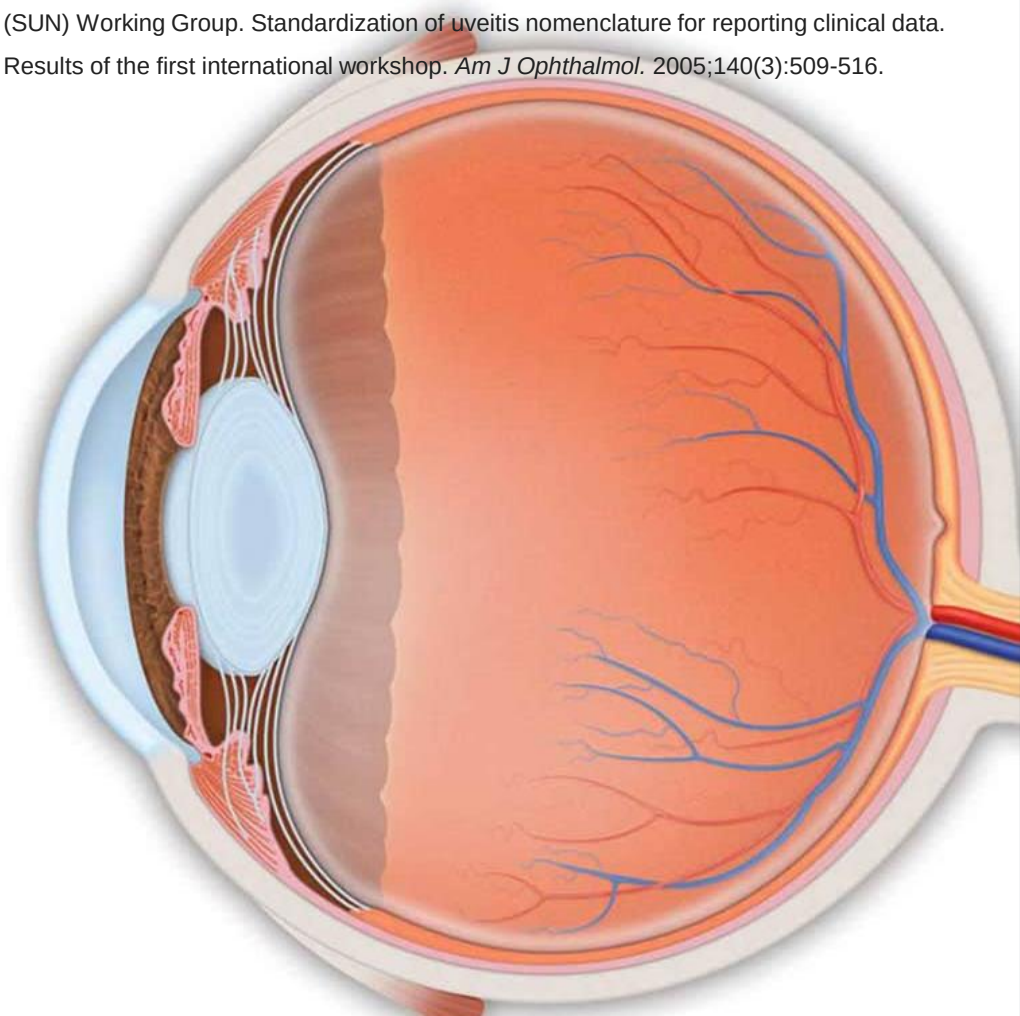


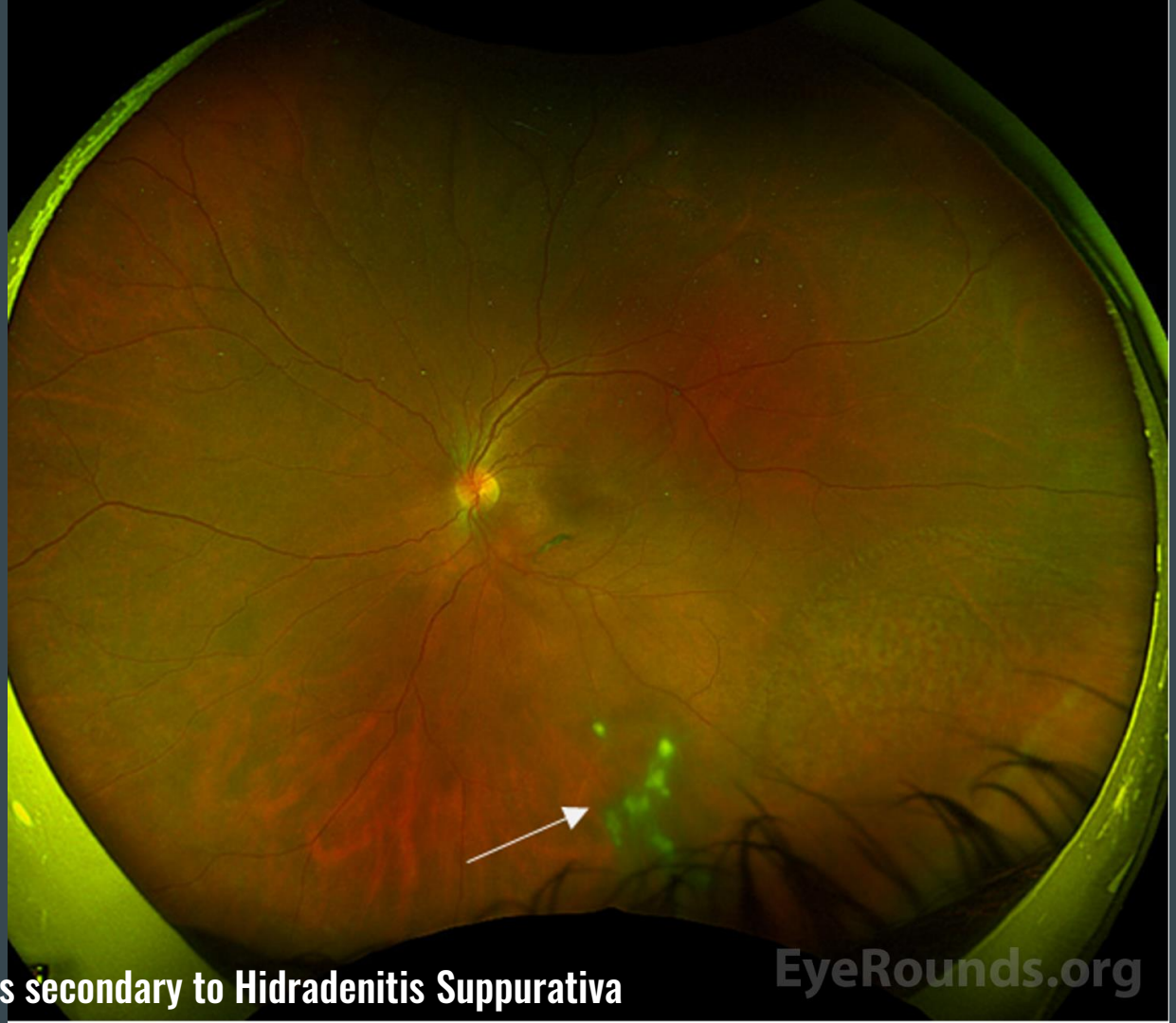
- CHRONIC
- ASYMPTOMATIC / MINIMALLY SYMPTOMATIC
- SIGHT-THREATENING
- POOR FOLLOW-UP

INTERMEDIATE UVEITIS

- Primary site of inflammation is vitreous
- **SYMPTOMS:**
  - Floaters
  - Decreased vision
  - NO PAIN
- **ETIOLOGY:**
  - Idiopathic (70% or more!)
  - Infectious
    - TB
    - Syphilis
    - Toxocariasis
  - Non-infectious
    - **MS**
    - **Sarcoid**
    - IBS
    - Sjogren's

Jabs DA, Nussenblatt RB, Rosenbaum JT; for the 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(3):509-516.



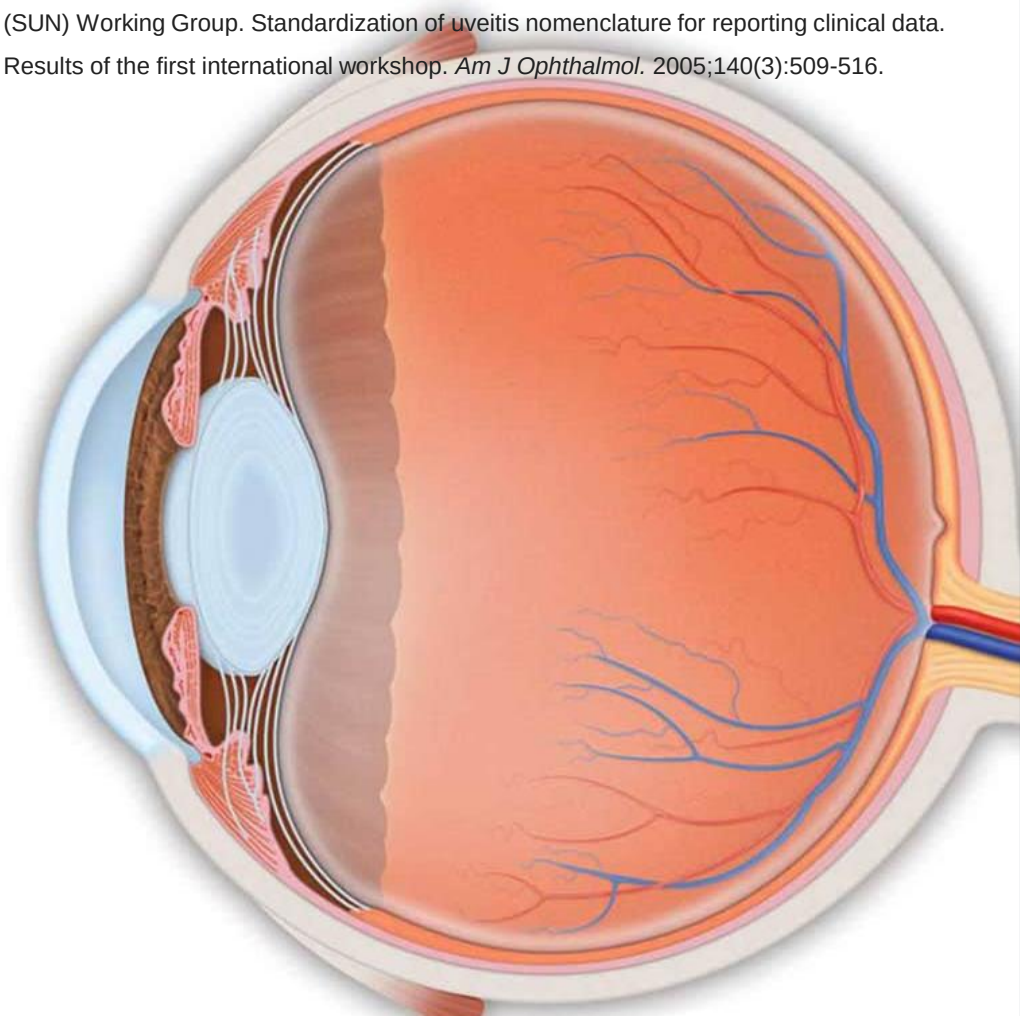


Intermediate Uveitis secondary to Hidradenitis Suppurativa

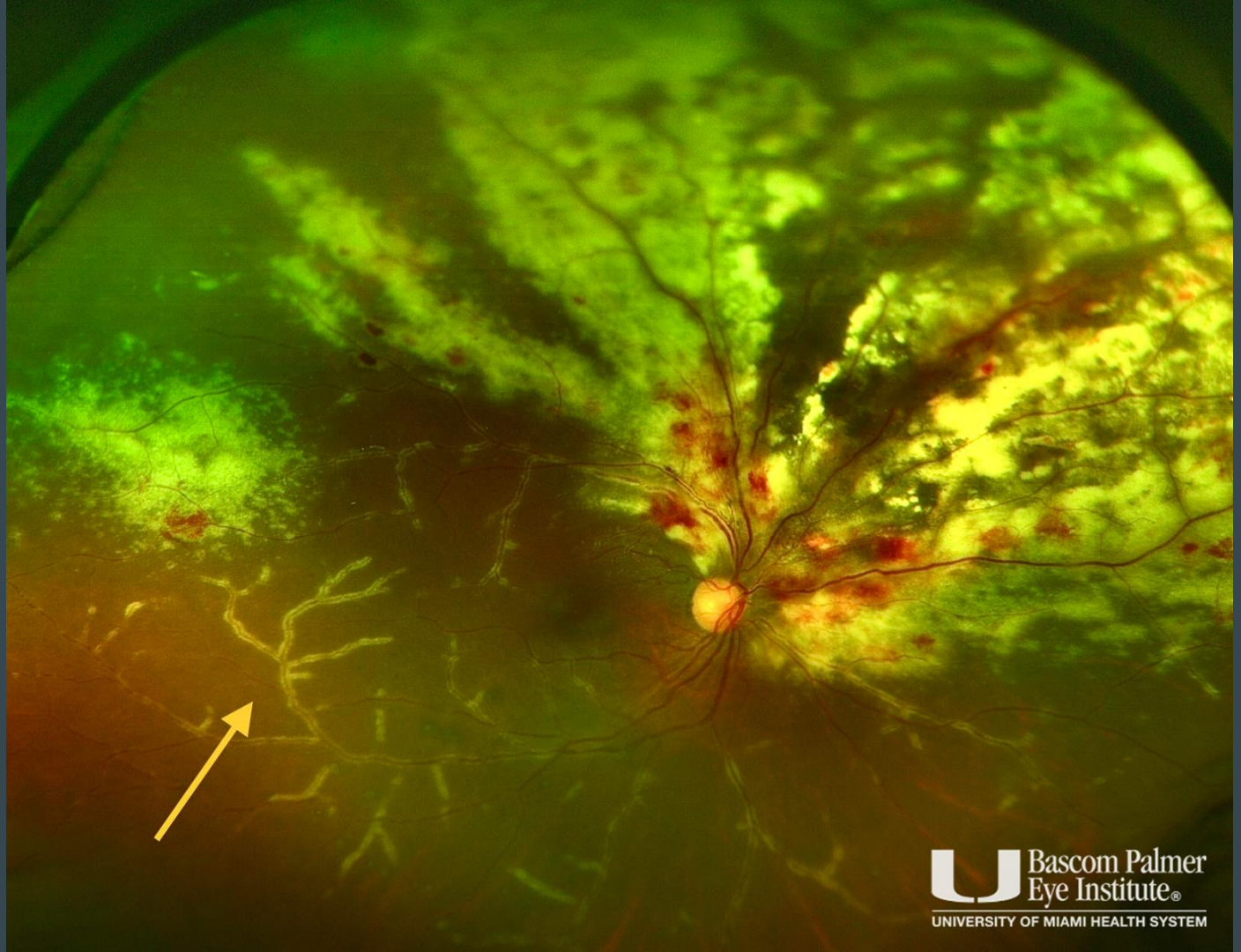
POSTERIOR UVEITIS

- Primary site of inflammation is retina and/or choroid
- **SYMPTOMS:**
  - Flashes and floaters
  - Decreased vision
  - NO PAIN
- **ETIOLOGY:**
  - Infectious (most common)
    - Toxoplasmosis
    - TB
    - Syphilis
    - Viral (CMV/HSV/Zoster/HIV)
  - Non-infectious
    - Sarcoidosis & other autoimmune
    - Other eye-specific diseases

Jabs DA, Nussenblatt RB, Rosenbaum JT; for the 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(3):509-516.

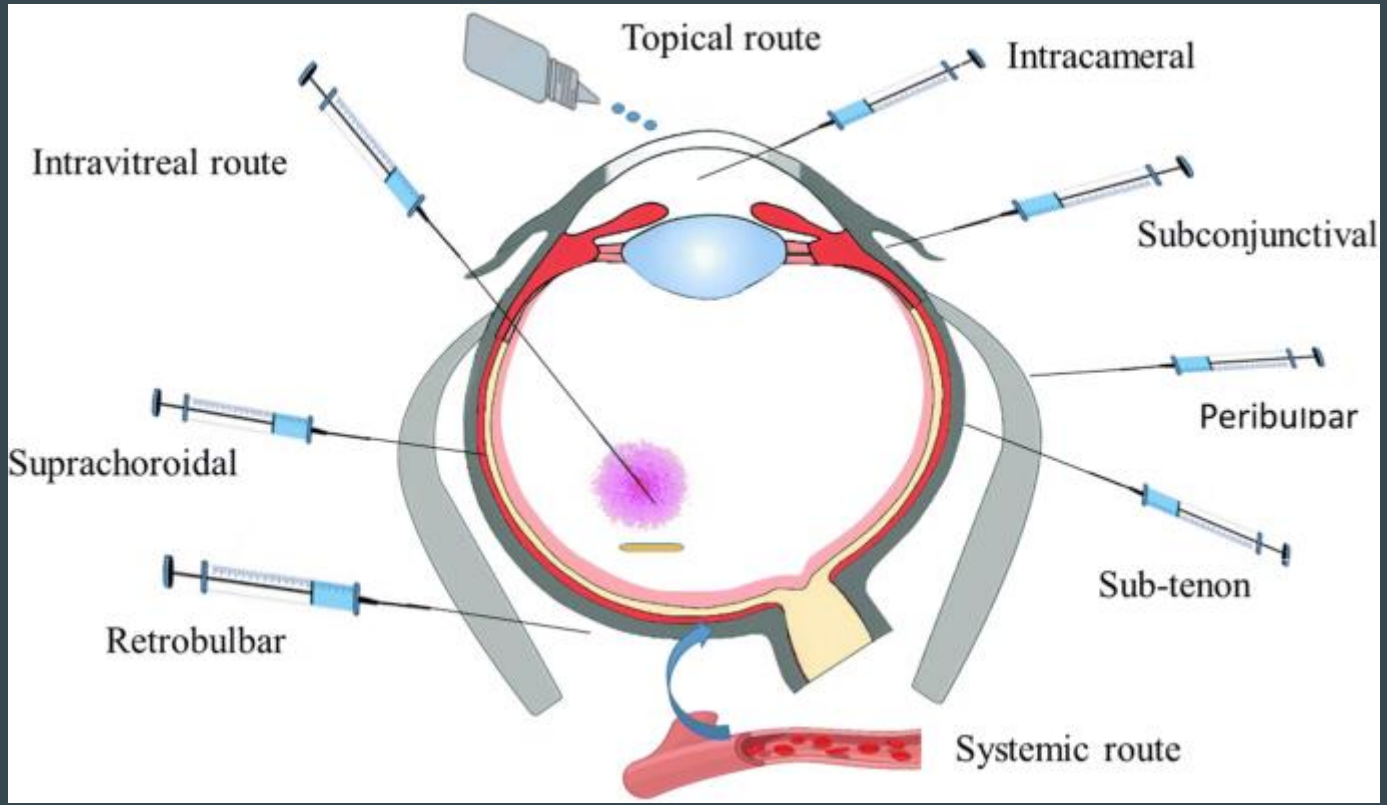


Retinal Vasculitis secondary to SLE



CMV Retinitis

TREATMENT & MANAGEMENT



Review > Surv Ophthalmol. 2016 Jan-Feb;61(1):1-17. doi: 10.1016/j.survophthal.2015.07.001. Epub 2015 Jul 9.

The Ocular Immunology and Uveitis Foundation preferred practice patterns of uveitis management

C Stephen Foster [1], Srishti Kothari [2], Stephen D Anesi [3], Albert T Vitale [4], David Chu [5], Jamie Lynne Metzinger [3], Olga Cerón [3]

Affiliations + expand

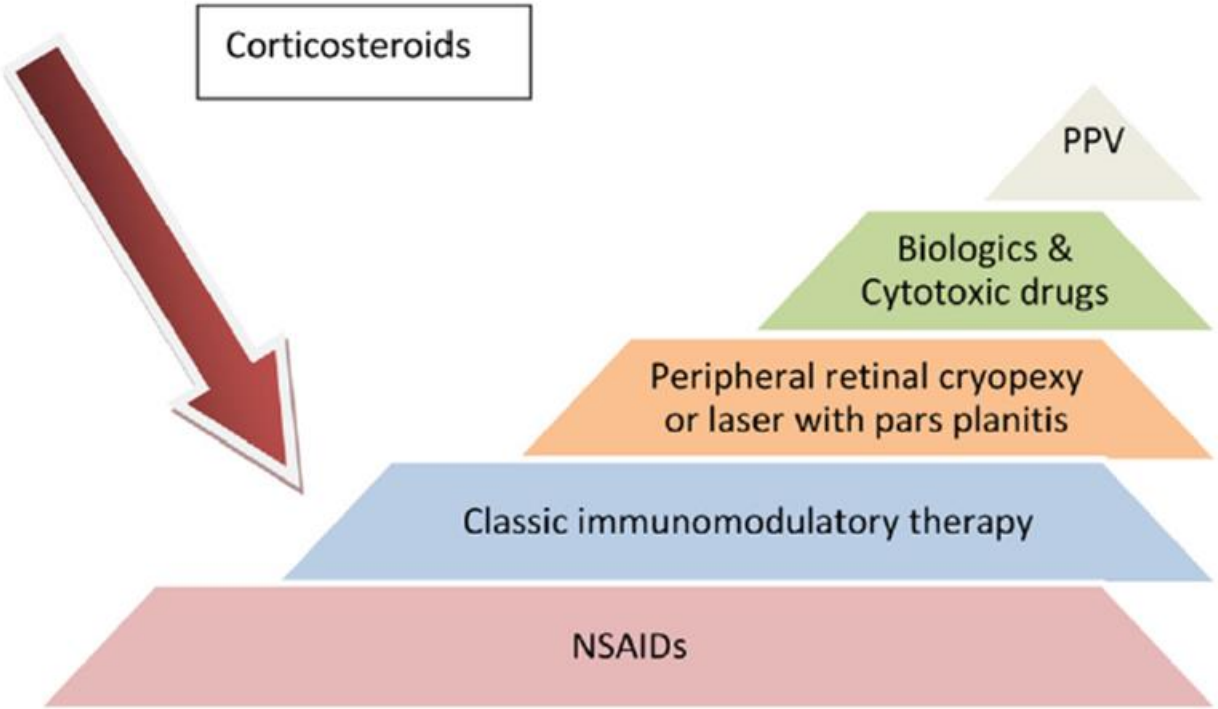
PMID: 26164736 DOI: 10.1016/j.survophthal.2015.07.001

TREATMENT GOALS

- “Topical, regional, and systemic steroids are the cornerstone of treatment”

- Goals of long term treatment:
  - Durable
  - Corticosteroid-Sparing
  - Remission of uveitis

Foster CS, Kothari S, Anesi SD, Vitale AT, Chu D, Metzinger JL, Cerón O. The Ocular Immunology and Uveitis Foundation preferred practice patterns of uveitis management. Surv Ophthalmol. 2016 Jan-Feb;61(1):1-17. doi: 10.1016/j.survophthal.2015.07.001. Epub 2015 Jul 9. PMID: 26164736.



(PPV = Pars Plana Vitrectomy, NSAIDs = Non-steroidal anti-inflammatory drugs)

Fig. 1 – The stepladder approach. PPV, pars plana vitrectomy; NSAIDs, nonsteroidal anti-inflammatory drugs.

TOPICAL TREATMENTS

- **TOPICAL STEROIDS (pink or white cap)**
  - Difluprednate
  - Dexamethasone
  - Prednisolone
  - Loteprednol
- **CYCLOPLEGICS (red cap)**
  - Tropicamide
  - Cylcopentolate
  - Scopolamine
  - Homatropine
  - Atropine

DOSAGES BASED OFF OF SEVERITY OF PRESENTATION

TABLE 2. Suggested Guidelines for the Use of Prednisone for Chronic Ocular Inflammation

Parameter	Suggested Guideline
Initial dose	1 mg/kg/day*
Maximum adult oral dose	60–80 mg/day
Maintenance dose (adult)	≤10 mg/day
Tapering schedule	Over 40 mg/day, decrease by 10 mg/day every 1–2 weeks
	40–20 mg/day, decrease by 5 mg/day every 1–2 weeks
	20–10 mg/day, decrease by 2.5 mg/day every 1–2 weeks
	10–0 mg/day, decrease by 1 to 2.5 mg/day every 1–4 weeks
Monitor	Blood pressure, weight, glucose every 3 months
	Lipids (cholesterol and triglycerides) annually
	Bone density within first 3 months and annually thereafter
Supplemental treatment	Calcium 1500 mg daily and vitamin D 800 IU daily
	Estrogens and antiresorpative agents as needed

*In selected situations, where an immediate effect is needed, some investigators will begin with intravenous methylprednisolone at a dosage of 1 gm/day for 3 days and then start oral prednisone.

Jabs DA, Rosenbaum JT, et al. *Guidelines for the use of immunosuppressive drugs in patients with ocular inflammatory disorders: recommendations of an expert panel*. Am J Ophthalmol. 2000 Oct;130(4):492-513.

Table 8 – Immunosuppressive therapy

Class	Generic name (trade name)	Initial dose (route)	Maximum dose (route)	Mechanism	Expected onset	Major indications	Representative side effects	Lab test—baseline	Lab test—follow up
Antimetabolites	Methotrexate (Folex, Mexate, Rheumatrex)	7.5–15 mg/week or 0.15 mg/kg/week (Oral/SC)	20 mg/week (PO), 50 mg/week (SC), 200 mg/week (IV)	Inhibitor of dihydrofolate reductase	3–6 weeks	Uveitis—JIA, reactive arthritis, AS, IBD, psoriatic arthritis and sarcoidosis, scleritis—reactive arthritis and RA, SO	Ulcerative stomatitis, myelosuppression (leukopenia, thrombocytopenia), GI distress, hepatotoxicity (hepatitis, cirrhosis), pulmonary toxicity, cutaneous vasculitis, fetal loss	CBC & Diff, LFTs BUN/Cr, UA	CBC & Diff—q1–4 wks, LFTs, BUN/Cr, UA—q3–6 wks
	Azathioprine (Imuran)	1 mg/kg/day (PO—q.d./b.i.d.)	3 mg/kg/day (PO)	Alters purine metabolism	1–3 months	Scleritis—RP, OCP, JIA iridocyclitis, ABD, GPA, SLE, SO, VKH, sarcoidosis, pars planitis, Reiter's syndrome—iridocyclitis	Myelosuppression (leukopenia, thrombocytopenia), GI distress, hepatitis, infections, pancreatitis, ?Cancer	CBC & Diff, LFTs, BUN/Cr, TPMT activity	CBC & Diff—q1–4 wks, LFTs, BUN/Cr—q3–6 wks
	Mycophenolate mofetil (Cellcept), Mycophenolate sodium (Myfortic)	1 g (PO—divided dose), Sodium—360 mg	3 g (PO—divided dose) Sodium—760 mg (PO) on an empty stomach	Inosine monophosphate dehydrogenase inhibitor (purine synthesis)	2 weeks–3 months	Scleritis, methotrexate nonresponsive noninfectious uveitis in adults and children, adjuvant to cyclosporine in ABD and BSRC	GI distress, neutropenia, infection	CBC & Diff, LFTs, BUN/Cr	CBC & Diff—q1–4 wks, LFTs, BUN/Cr—q3–6 wks

Foster CS, Kothari S, Anesi SD, Vitale AT, Chu D, Metzinger JL, Cerón O. The Ocular Immunology and Uveitis Foundation preferred practice patterns of uveitis management. Surv Ophthalmol. 2016 Jan-Feb;61(1):1-17. doi: 10.1016/j.survophthal.2015.07.001. Epub 2015 Jul 9. PMID: 26164736.

							blurred vision		
Adjuvants	Bromocriptine (Parlodel)	1.25–7.5 mg/day (PO—divided)	10 mg/day (PO)	Prolactin inhibitor		Adjunct to cyclosporine, iridocyclitis, thyroid ophthalmopathy	Postural hypotension, GI distress		
	Ketoconazole (Nizoral)	200 mg/day (PO—divided)	400 mg/day (PO—divided)	Inhibition of sterol metabolism		Adjunct to cyclosporine	Hepatotoxicity, endocrine abnormalities, GI distress		
	Colchicine	1 mg (PO—divided)	1.8 mg/day (PO—divided)	Microtubule formation inhibitor		ABD	GI distress, myelosuppression, neurotoxicity	CBC & Diff, LFTs, BUN/Cr, UA	CBC & Diff, LFTs BUN/Cr, UA—q3mnth
	Adalimumab (Humira)	40 mg/every other week (SC)	40 mg/week (SC)	Fully humanized Ig1 monoclonal anti-TNFα antibody	1–2 weeks	Adjuvant in ocular inflammatory disorders secondary to RA, JIA, AS, psoriatic arthritis and plaque psoriasis, VKH, BSRC, orbital pseudotumor	Sepsis, injection site reactions, demyelinating disorder, anaphylaxis, drug induced lupus, secondary malignancies	CBC & Diff, LFTs, tuberculin testing, hepatitis B (if at risk)	CBC& Diff, LFTs—qvisit, tuberculin testing—q1 yr, hepatitis B (if at risk)—several months after therapy
	Infliximab (Remicade)	5–20 mg/kg/day (IV) Loading dose 0, 2, 4 weeks × 6 months after steroid-free remission has been achieved. Then taper off with 3 infusions at 6, 8, 10, 12 week interval each, before withdrawal	20 mg/kg (IV)	Chimeric IgG1κ anti-TNFα monoclonal antibody with a human constant and mouse variable region	1–2 weeks	Refractory ABD, uveitis and scleritis secondary to JIA, AS, GPA, sarcoidosis, Crohn's disease, CIST-resistant uveitis	Tuberculosis reactivation, invasive fungal and opportunistic infections, nonmelanoma skin cancer, and secondary malignancies	CBC & Diff, LFTs, ANA, Tuberculin testing, hepatitis B (if at risk)	CBC & Diff, LFTs—qprior each infusion, ANA—q3mnth, tuberculin testing, hepatitis B (if at risk)—q1 yr
	Abatacept (Orencia)	500–1000 mg (IV—Wt based), 125 mg (SC)		Recombinant soluble fusion protein consists of extracellular domain of human CTLA-4 linked to modified Fc portion of human IgG1		Recalcitrant JIA uveitis	Drug induced lupus, thromboembolism, tuberculosis reactivation, hepatitis B reactivation, demyelinating disorders, lymphoma, and solid tissue cancers	CBC & Diff, LFTs, ANA, Tuberculin testing, hepatitis B (if at risk)	CBC& Diff, LFTs qprior each infusion, ANA—q3mnth, tuberculin testing, hepatitis B (if at risk)—q1 yr

Foster CS, Kothari S, Anesi SD, Vitale AT, Chu D, Metzinger JL, Cerón O. The Ocular Immunology and Uveitis Foundation preferred practice patterns of uveitis management. Surv Ophthalmol. 2016 Jan-Feb;61(1):1-17. doi: 10.1016/j.survophthal.2015.07.001. Epub 2015 Jul 9. PMID: 26164736.

COMANAGEMENT PEARLS: THE ROLE OF EYECARE PROVIDERS

- Clinical evaluation and monitoring of uveitis
- Initial Lab Workup?
- Acute and Chronic Topical Medication Management
- Short-term oral steroids PRN
- Office Procedures
- Recommendation for elevation of therapy to chronic systemic agents
- Communicating:
  - Classification of Uveitis (anterior, posterior, etc.)
  - Active or Inactive
  - Relevant Labs
  - Relevant Systemic History
  - Frequency of episodes

COMANAGEMENT PEARLS: THE ROLE OF RHEUM PROVIDERS

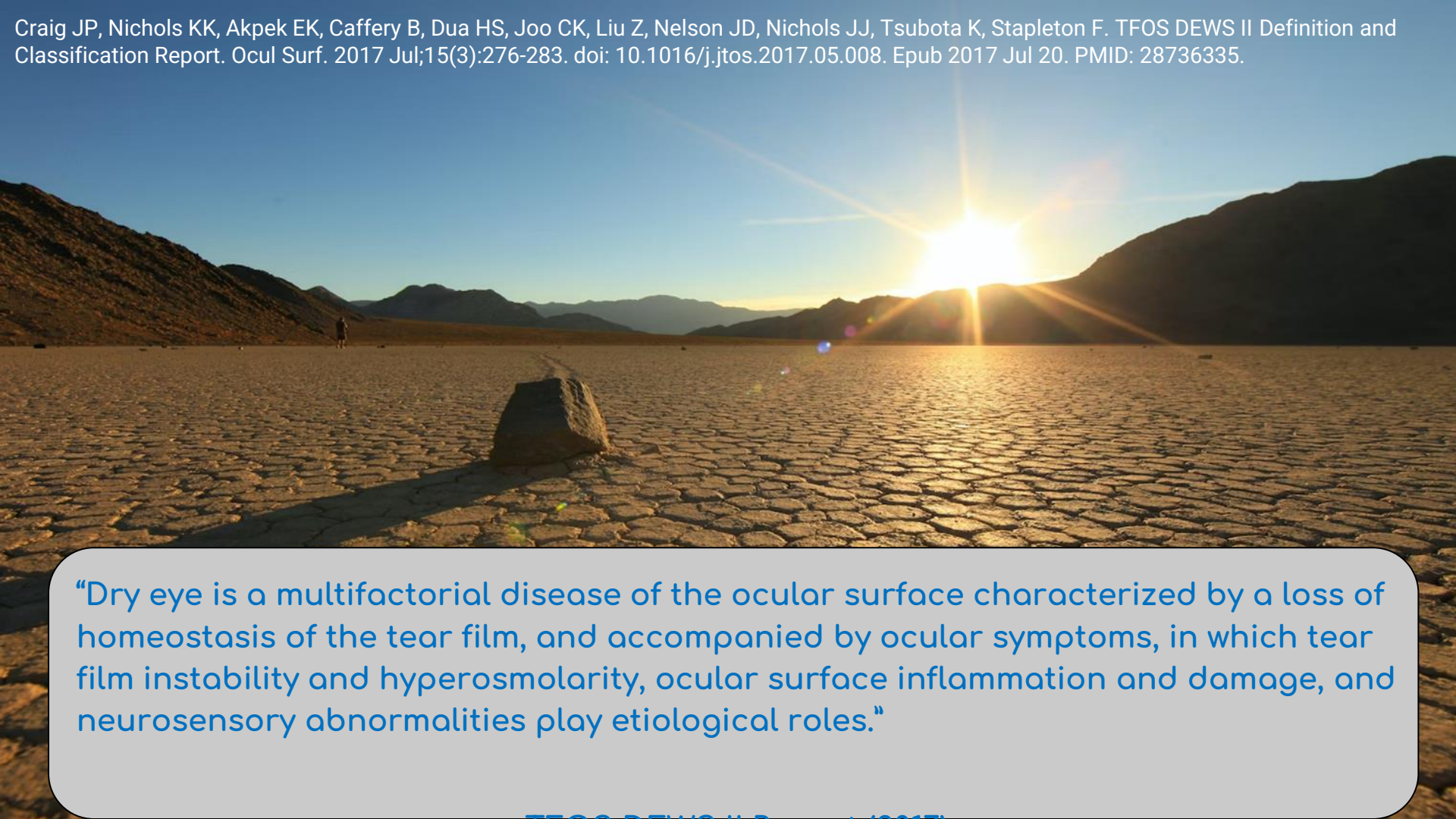
- Focused systemic workup and additional labs
- Starting chronic immunomodulatory therapy
- Monitoring for side effects of immunomodulatory therapy

- Communicating:
  - Med changes
  - New flares/symptoms
  - Any concerns

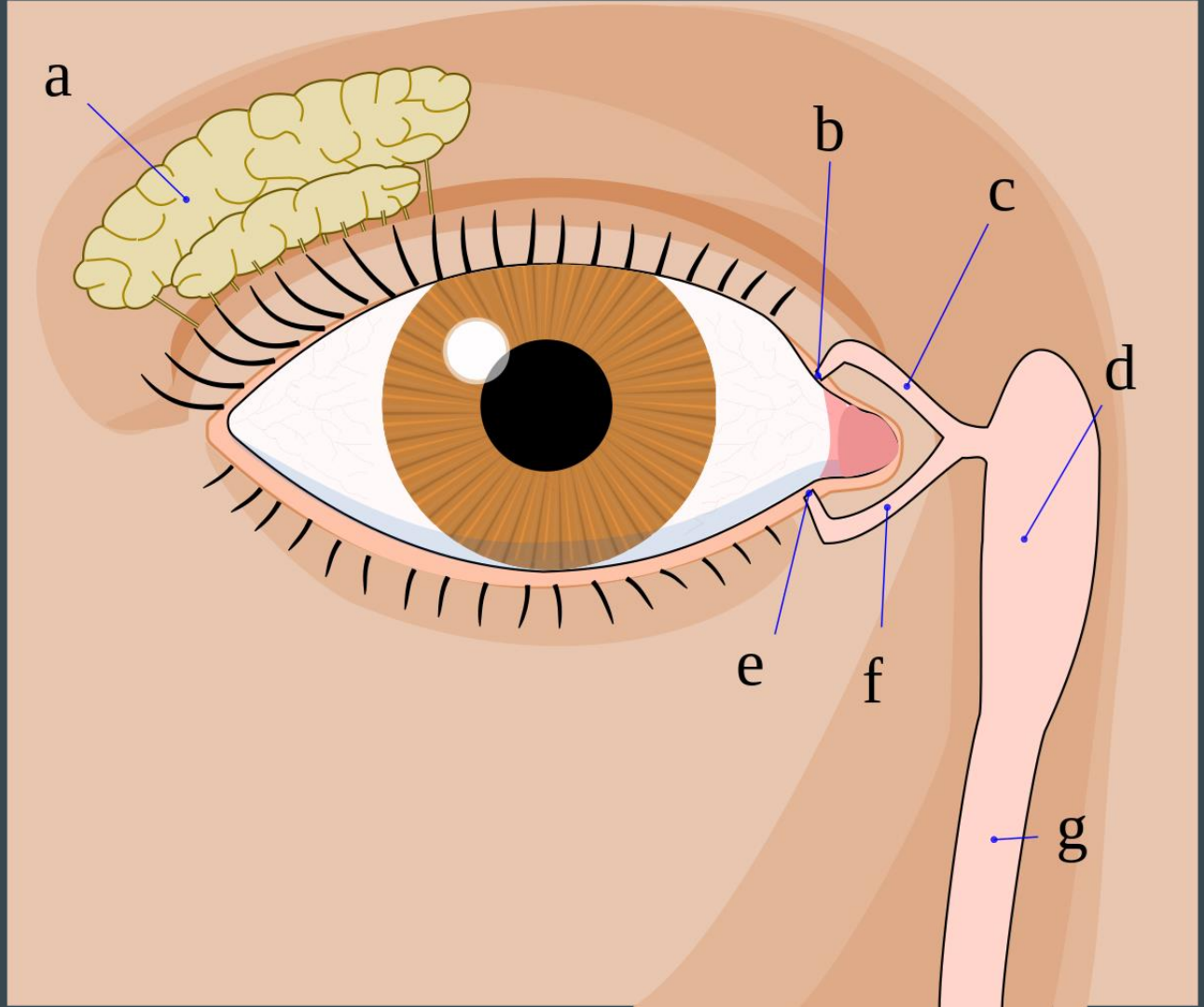
DRY EYE SYNDROME:

DIAGNOSIS
TREATMENT
MANAGEMENT

Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo CK, Liu Z, Nelson JD, Nichols JJ, Tsubota K, Stapleton F. TFOS DEWS II Definition and Classification Report. Ocul Surf. 2017 Jul;15(3):276-283. doi: 10.1016/j.jtos.2017.05.008. Epub 2017 Jul 20. PMID: 28736335.



"Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."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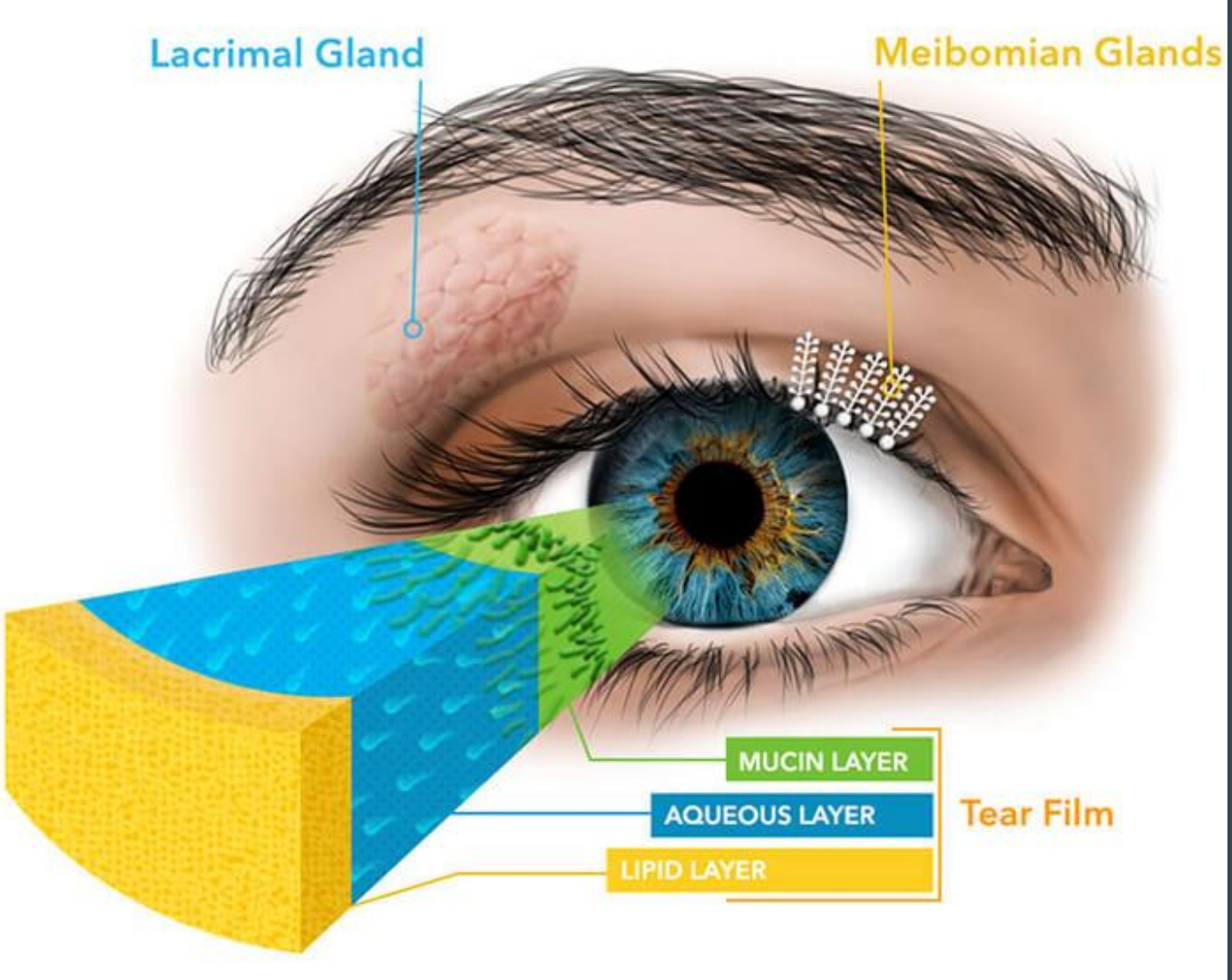
Lacrimal Gland
Meibomian Glands
MUCIN LAYER
AQUEOUS LAYER
LIPID LAYER
Tear Film

Dry Eye Syndrome

- Tears are made of three components:
  - Water component (lacrimal gland)
  - Oil component (meibomian glands)
  - Mucin (sugar) component (conjunctival goblet cells)

- Multiple Etiologies:
  - Systemic Diseases
  - ***Rheumatoid Arthritis / Sjögrens*** cause chronic inflammation and dysfunction of the lacrimal gland resulting in dry eye symptoms (can be **severe**)
  - Medications can affect dryness as well
  - Diuretics, allergy medications
  - Hormonal changes
  - Pregnancy, menopause, etc.

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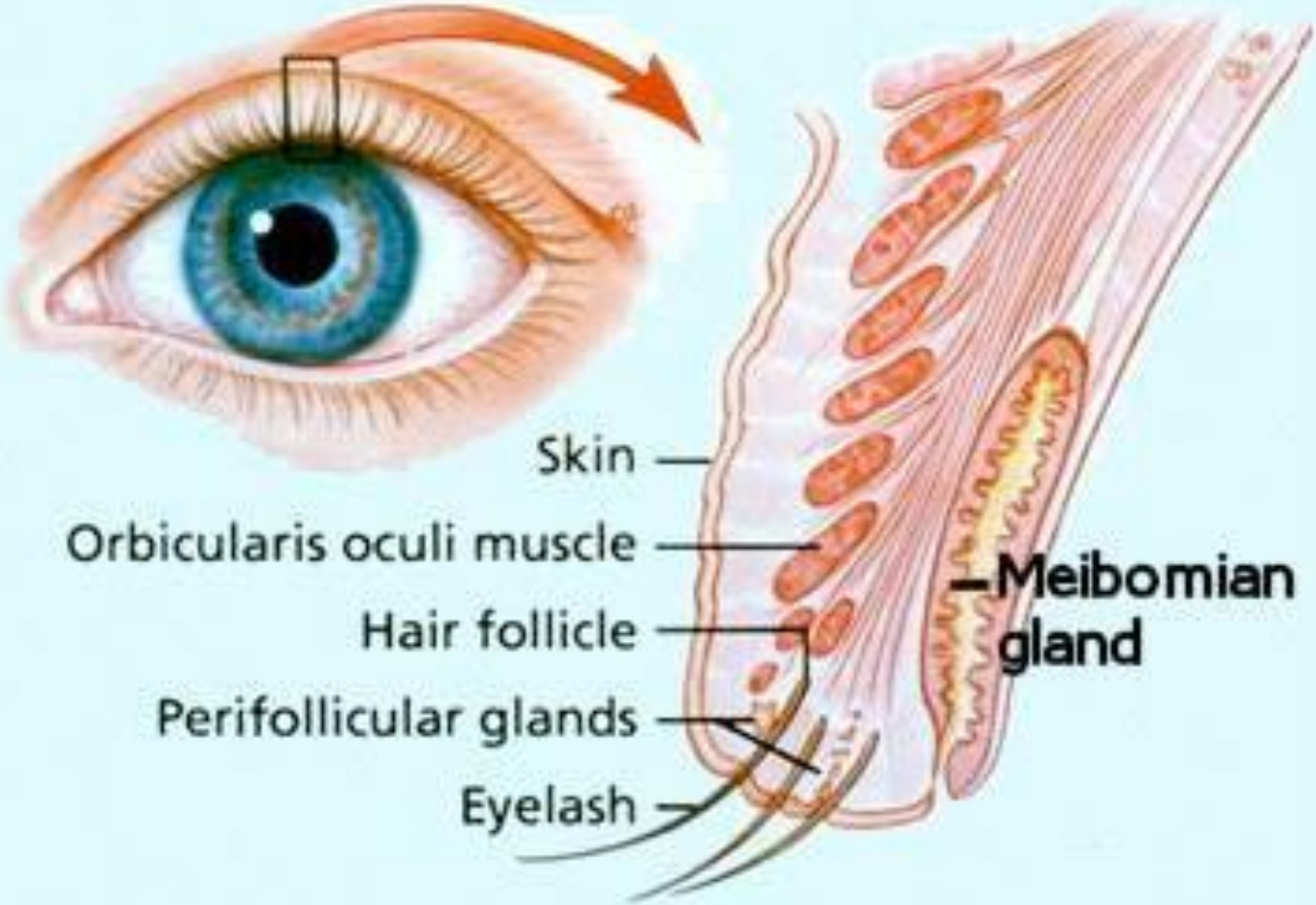

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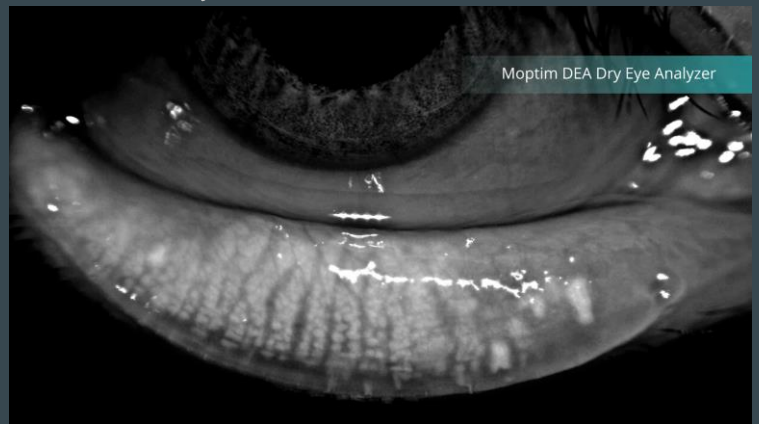
s://www.phxdryeye.com/s/cc_images/teaserbox_708594704.jpg?t=1543651691

DRY EYE CLASSIFICATION

Evaporative Dry Eye

- Most common form of dry eye
- Atrophy and/or dysfunction of meibomian glands (“MGD”)
- Many factors



Aqueous Deficiency

- Less common
- Inflammation and subsequent scarring of lacrimal gland results in decreased tear production and volume
- Autoimmune dry eye

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DRY EYE TREATMENT

- Artificial Tears
- Heated Eye Mask
- Eyelid wipes and sprays
- Steroid eye drops
- Steroid-sparing dry eye medications
  - Cyclosporine variations
  - Xiidra (lifitegrast ophth sol)
  - Tyrvaya (varenicline nasal spray)
  - Miebo (perfluorohexyloctane ophth sol)
- Amniotic Fluid Eye Drops
- Amniotic Membranes
- Scleral Contact Lenses
- In-Office Procedures
  - Lid Procedures (Lipiflow, iLux, TearCare)
  - Punctal Plugs / Cautery
- Autologous Serum
- Oral secretagogues

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ARTIFICIAL TEARS

- Preservative-free tears are generally better (often in vials or labeled PF)
  - PF Refresh with Mega 3 (vials)
  - PF Systane Complete (PF bottle)
  - Ivizia (PF bottle)

- Preserved tears generally come in a bottled formulation
  - Refresh Tears
  - Systane Complete
  - Soothe XP

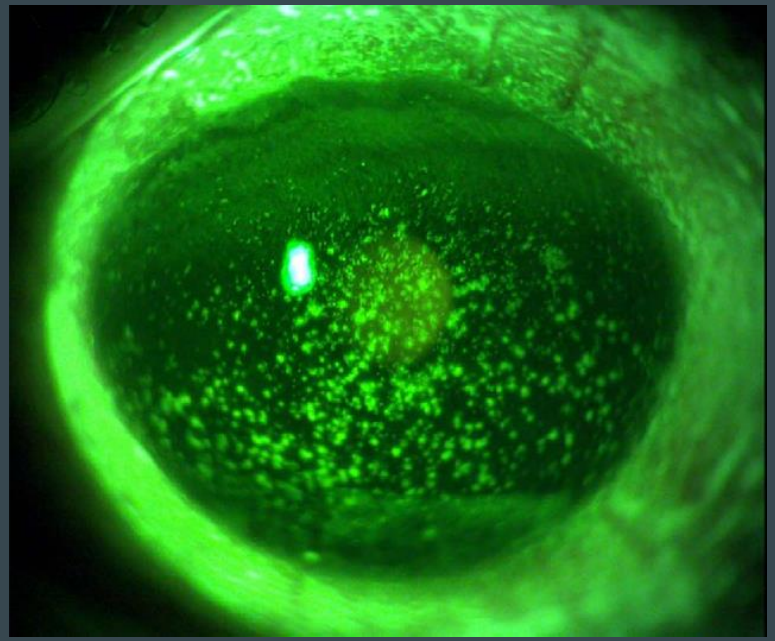
- *Artificial tears treat symptoms, NOT the underlying cause...*

WHAT IS THE ROLE OF CYCLOSPORINE?

- Steroid-free agent
- Average of 3-6 months to full effect
- Blocks T-cell infiltration and release
- Blocks release of inflammatory cytokines

On the ocular surface:

- Decreased inflammation
- Improved tear retention
- Increased tear production
- Improves conjunctival goblet cell density



COMANAGEMENT PEARLS: THE ROLE OF EYECARE PROVIDERS

- Clinical evaluation and monitoring of dry eye
- Initial Lab Workup?
- Acute and Chronic Topical Medication Management
- Office Procedures
- Recommendation for rheumatology evaluation in cases of suspected systemic etiologies (RA, Sjogren's, etc.)
- Communicating:
  - Severity of Dry Eyes
  - Relevant Labs
  - Relevant Systemic History

COMANAGEMENT PEARLS: THE ROLE OF RHEUM PROVIDERS

- Focused systemic workup and additional labs
- Starting chronic systemic therapy when appropriate (oral pilocarpine?)
- Monitoring for side effects of chronic systemic therapy

- Communicating:
  - Med changes
  - New flares/symptoms
  - Any concerns

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Canyon de Chelly National Monument

Chinle, AZ