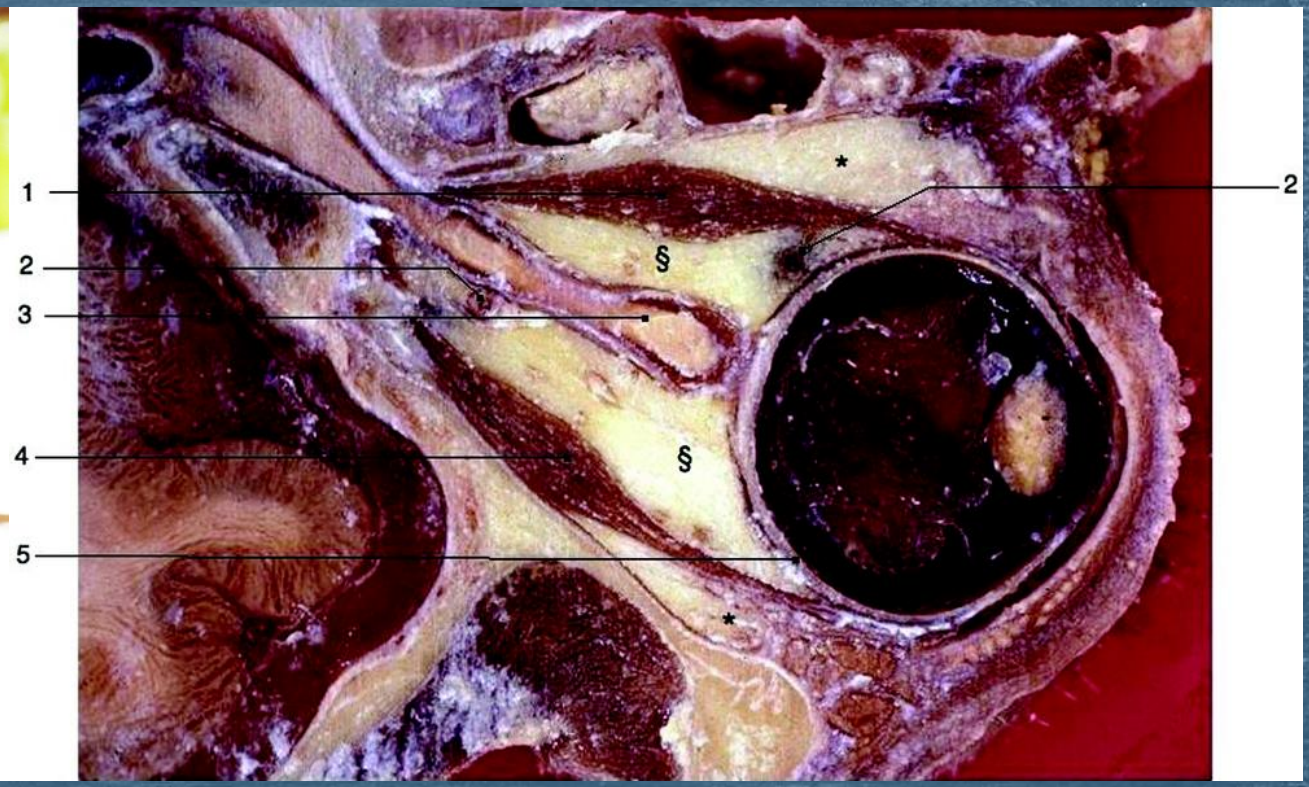
# Uveitis

# Outline

- Uveitis
  - Anatomy
  - Overview
  - Classification
  - Signs and symptoms
  - Investigations
  - Treatment
- Causes

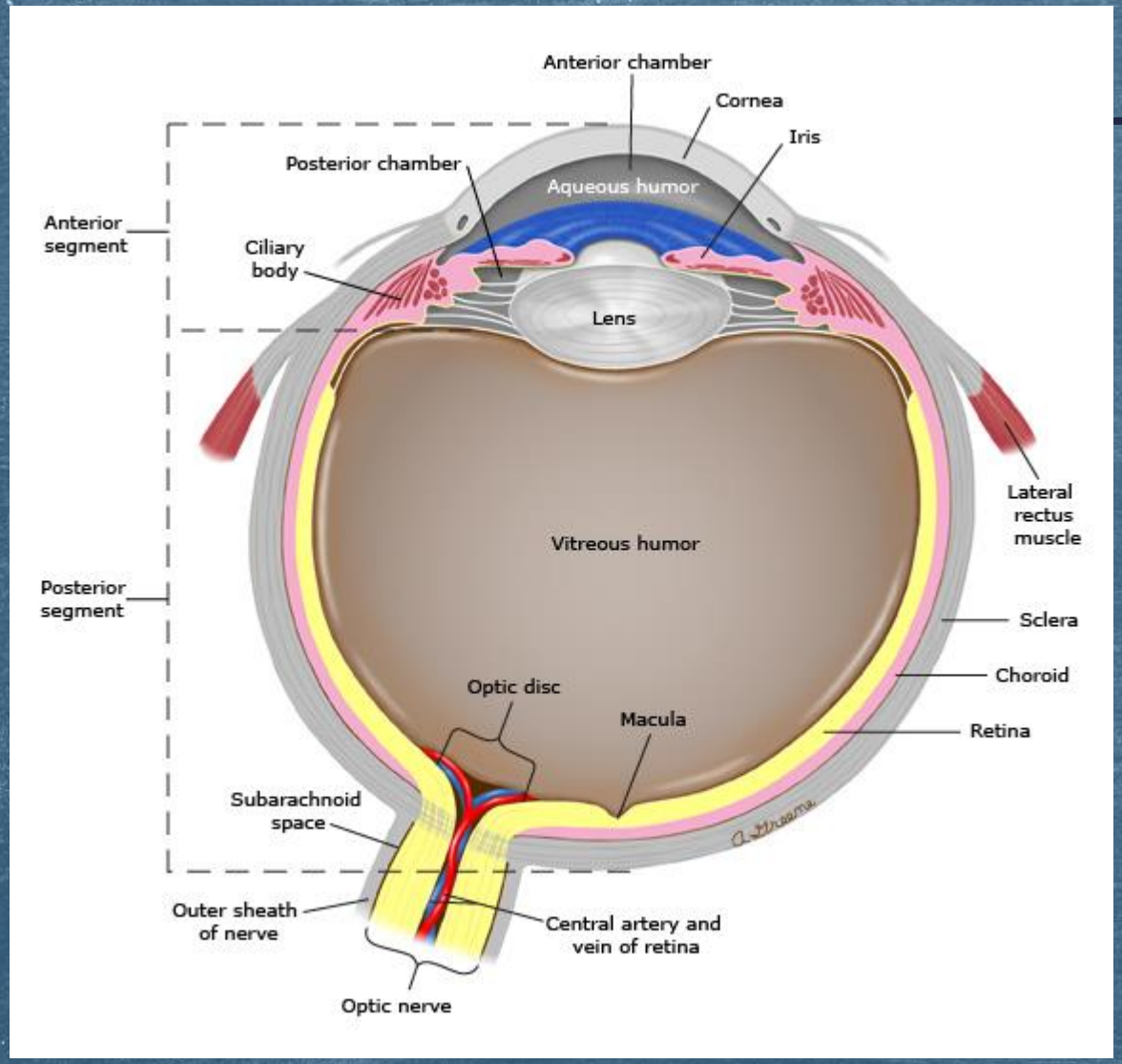
# Uva in latin = grape

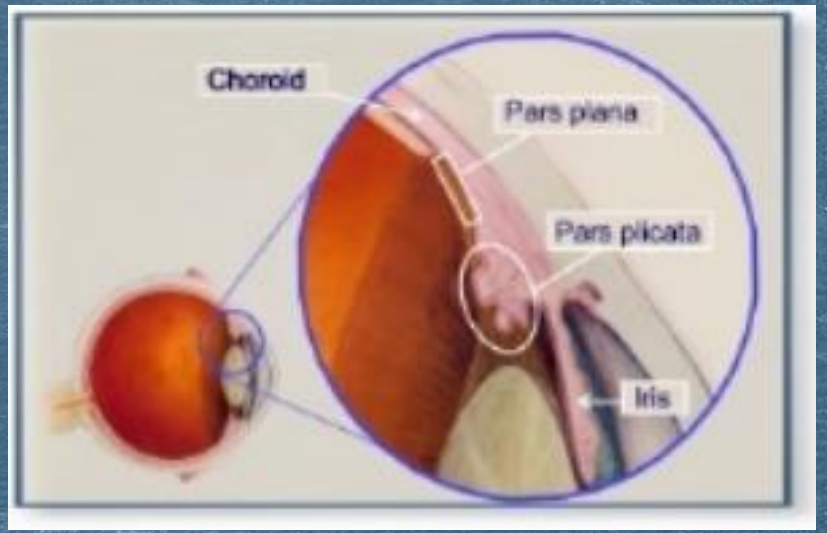
Middle vascular layer of the eye



# Uveal tract

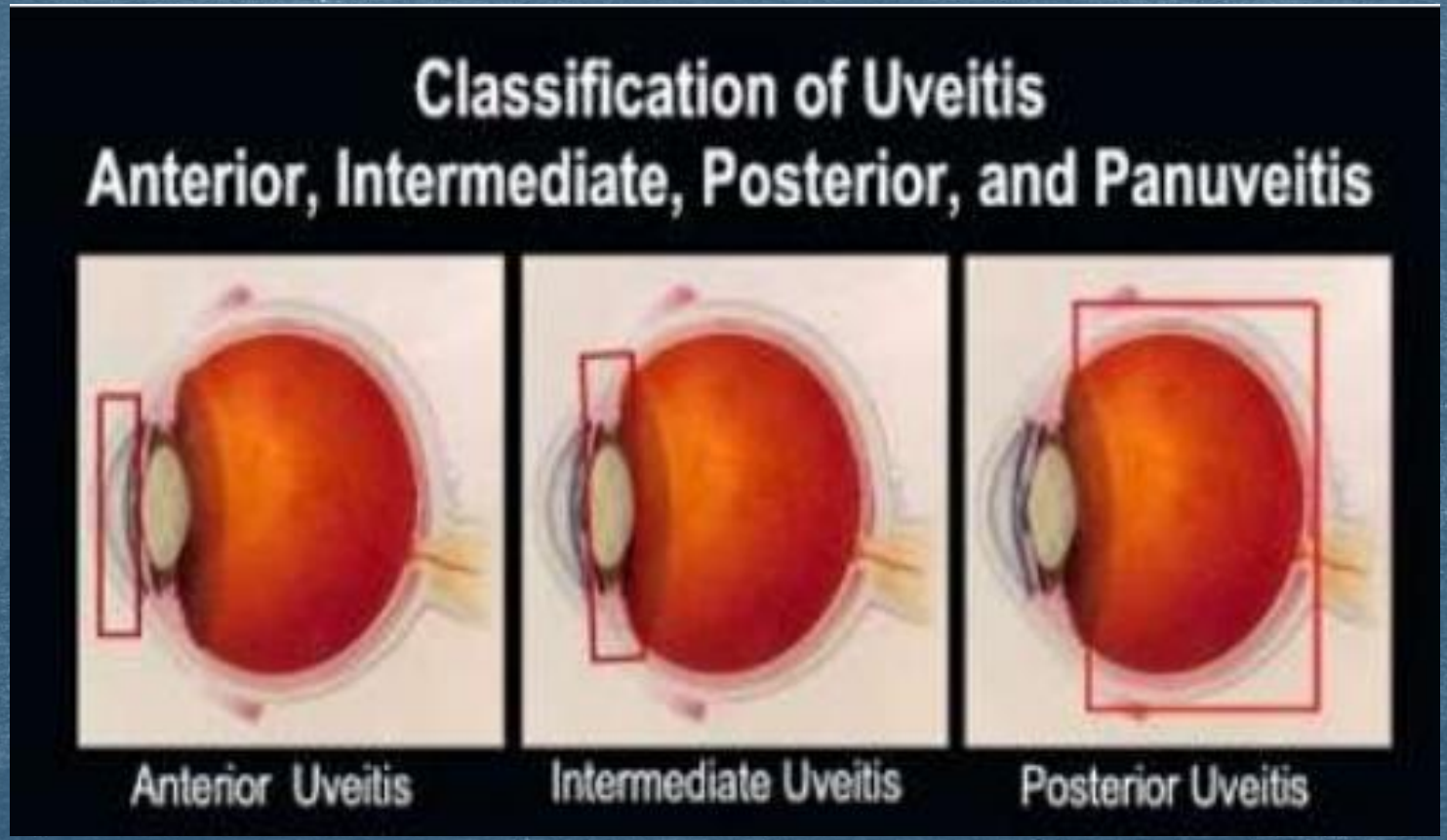
- Choroid
- Ciliary Body
- Iris


Anterior chamber
Cornea
Iris
Posterior chamber
Aqueous humor
Anterior segment
Ciliary body
Lens
Lateral rectus muscle
Vitreous humor
Posterior segment
Sclera
Choroid
Optic disc
Macula
Retina
Subarachnoid space
Outer sheath of nerve
Central artery and vein of retina
Optic nerve


Choroid
Pars plana
Pars plicata
Iris

# Uveitis

- Inflammation of the uvea



## Anterior Uveitis

1ry site : Anterior chamber

- **Includes:**
  - **Iritis**
  - **Anterior cyclitis**
  - **iridocyclytis**

## Intermediate Uveitis

1ry site : Vitreous

- **Includes:**
  - **Pars Planitis**

## Posterior Uveitis

1ry site : Choroid

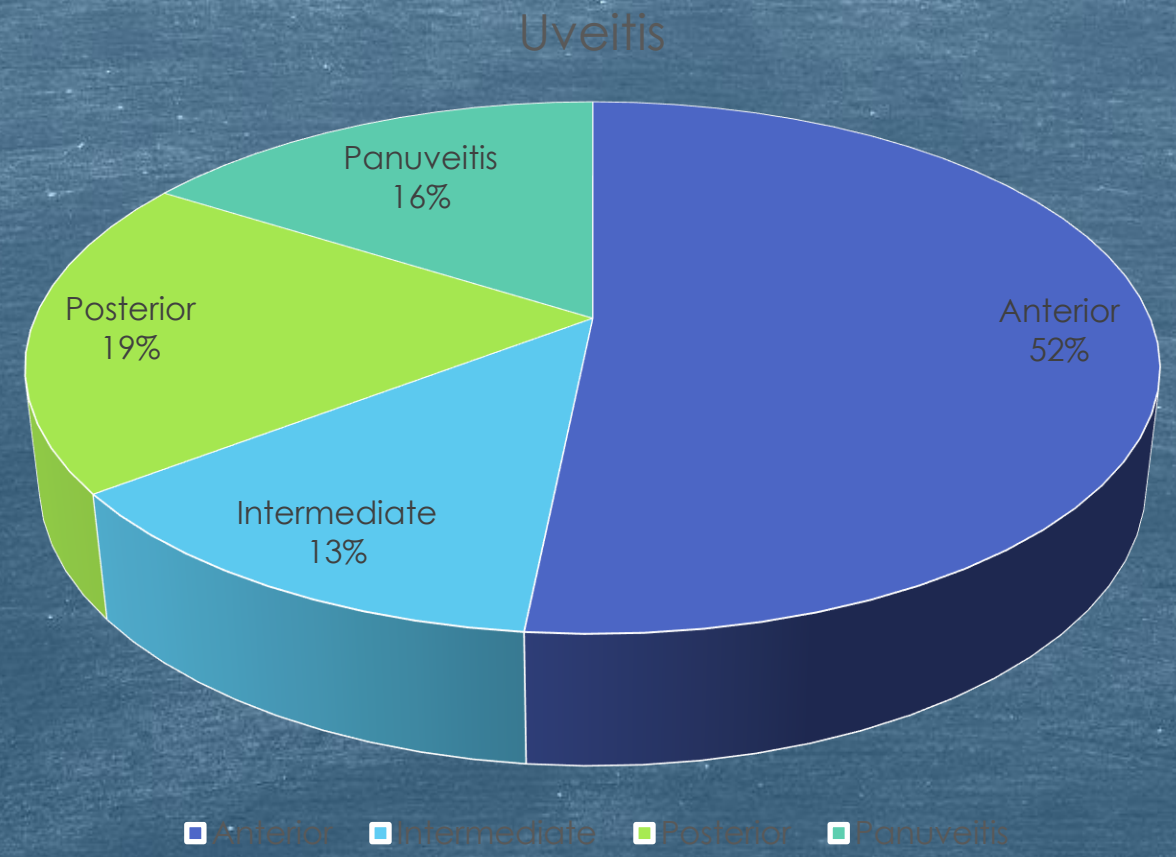
- **Includes:**
  - **Choroiditis**
  - **Retinitis**
  - **Chorioretinitis**

## Panuveitis:

# Etiology

- Infections
- Systemic Immune mediated disease
- Syndromes confined to the eye
- Idiopathic

# Epidemiology



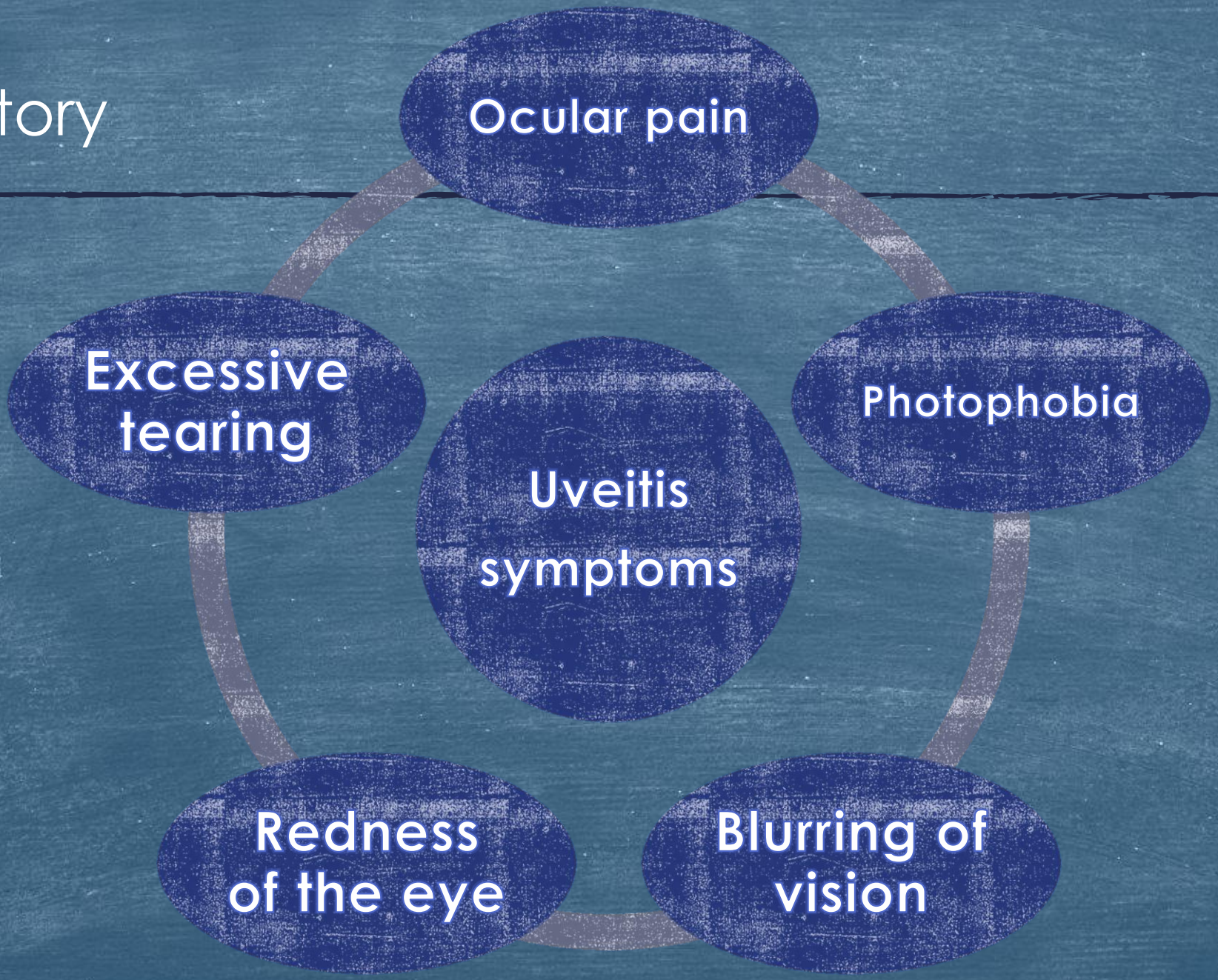
# anterior

Idiopathic (34%)
Seronegative spondyloarthropathies (10.4%)
Sarcoidosis (9.6%)
Juvenile rheumatoid arthritis (JRA) (5.6%)
SLE (4.8%)
Behçet's disease (2.5%)
AIDS (2.4%)

# posterior

***Toxoplasma* (24.6%)**
**idiopathic (13.3%)**
**cytomegalovirus (CMV) (11.6%)**
**SLE (7.9%)**
**sarcoidosis (7.5%)**

# History


Ocular pain
Excessive tearing
Photophobia
Uveitis symptoms
Redness of the eye
Blurring of vision

**Acute:** Pain, redness, photophobia, excessive tearing, and decreased vision; pain generally develops over a few hours or days except in cases of trauma

**Chronic:** Primarily blurred vision, mild redness; little pain or photophobia except when having an acute episode

**Post :** Blurred vision, floaters, less ocular pain

**Intermediate uveitis:** Similar to posterior uveitis; painless floaters and decreased vision
Minimal photophobia or external inflammation

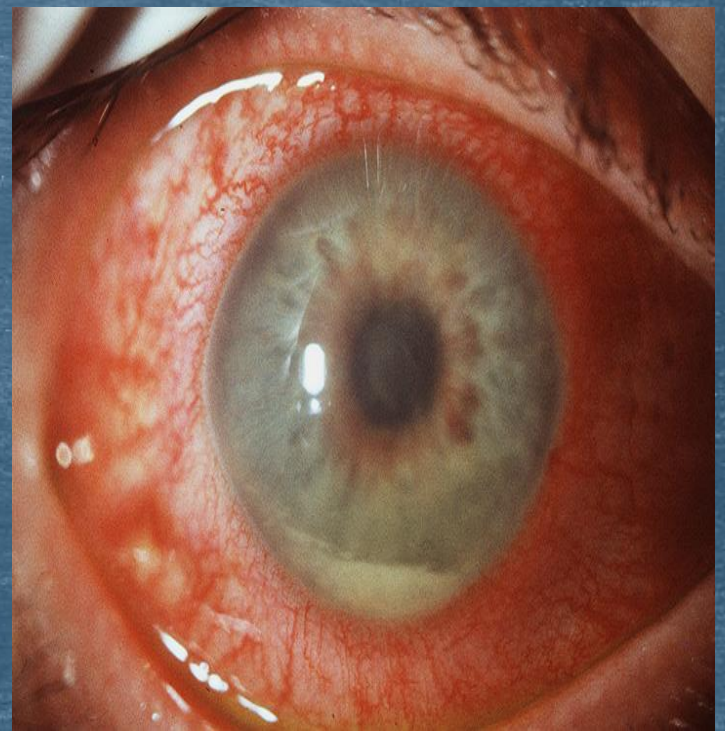
**Panuveitis:** may present with any or all these symptoms

- Carefull medical history is essential in Uveitis since 50% of patients have a systemic disease !

- Respiratory:  TB, sarcoidosis
- Skin: Behcet's, sarcoidosis ,
- Joint: ankylosing spondylitis , jeuvenile chronic arthritis , Retier's disease
- Bowel: IBD, whipple's disease
- Infectious:
  - STDs
  - TB
  - AIDS
  - fungal , metastatic infections
  - herpetic

**Signs:**

- Visual acuity may be reduced
- Inflamed eye, mostly around the limbus (ciliary injection)
- Inflammation of the iris, accompanied by increased vascular permeability, WBCs circulating in the aqueous humour of the anterior chamber can be seen with a slit lamp. Protein leaks from the blood vessels ,picked out by its light scattering properties in the beam of the slit lamp as a 'flare'



- Pupillary exam
  - Direct & consensual photophobia
  - Pupillary miosis is common.

# Signs of Anterior Uveitis:

Inflammatory reaction

- **Dilated vessels**

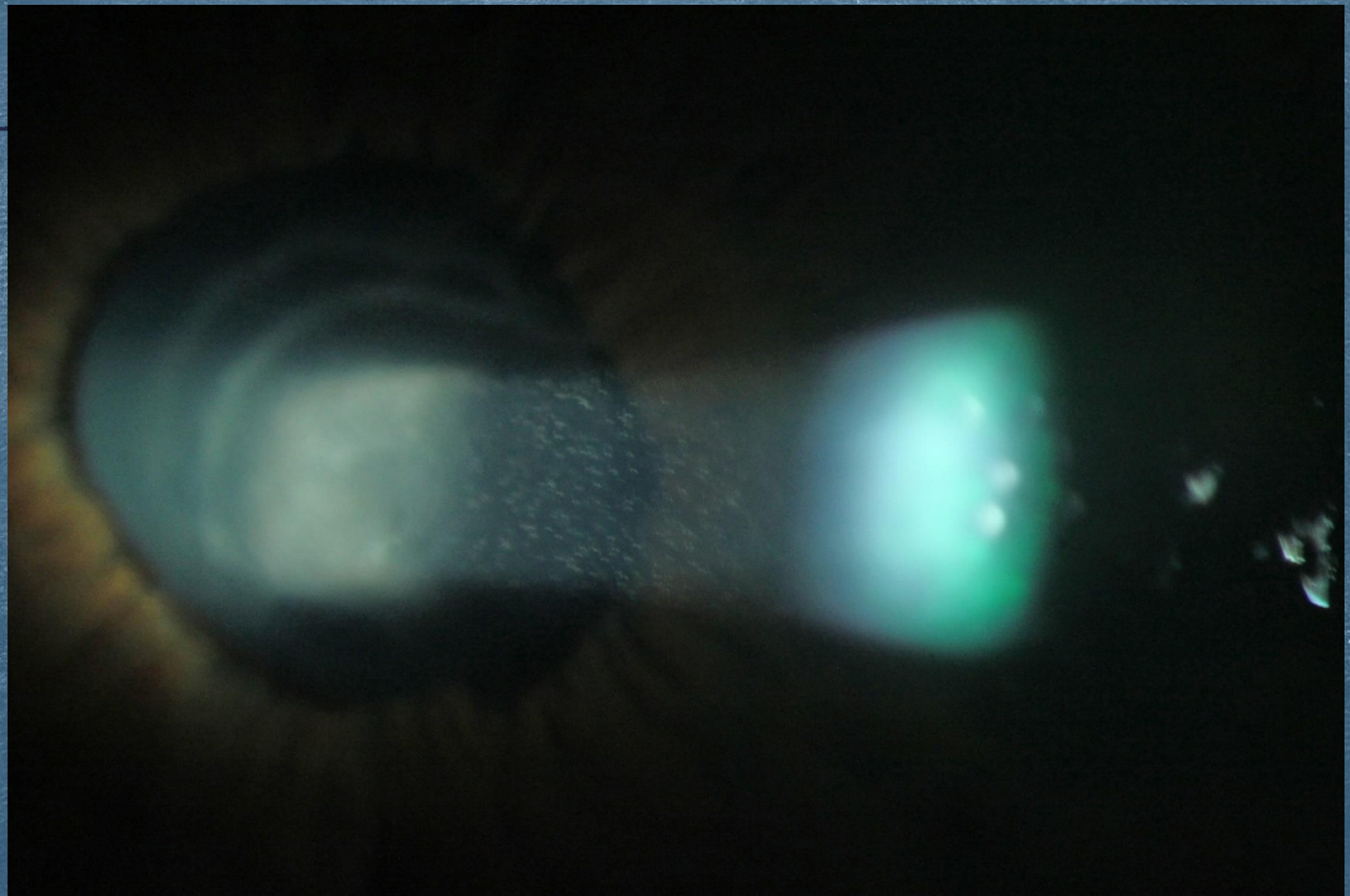
Inflammatory cells and protein exudates in the A.C

- **Aqueous cells**
- **Flare**
- **Hypopyon**

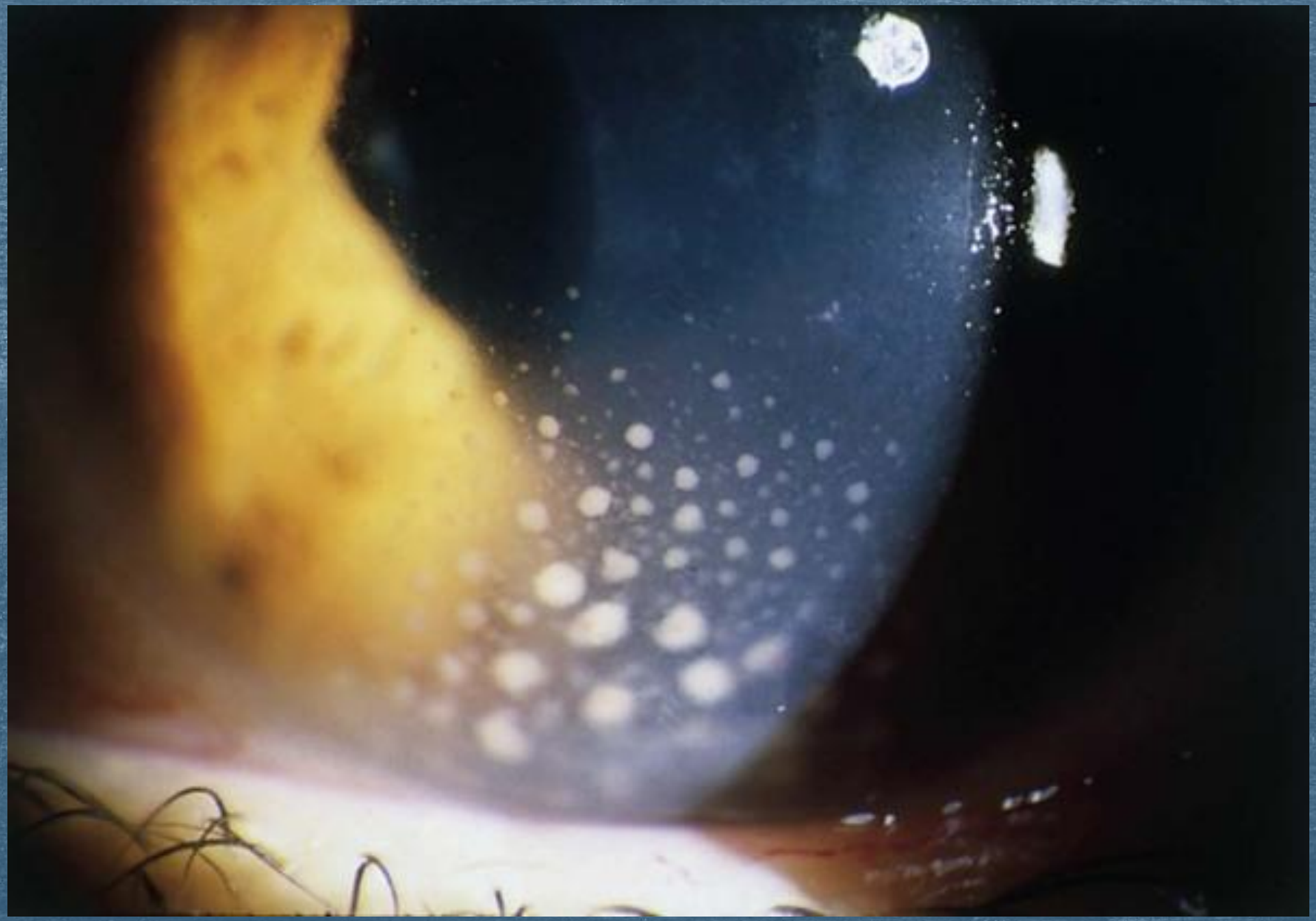
Adhesions and clumping of inflammatory cells + fibrin deposition

- **Keratitic percipitates**
- **Posterioir synechie**
- **Peripheral ant. synechie**

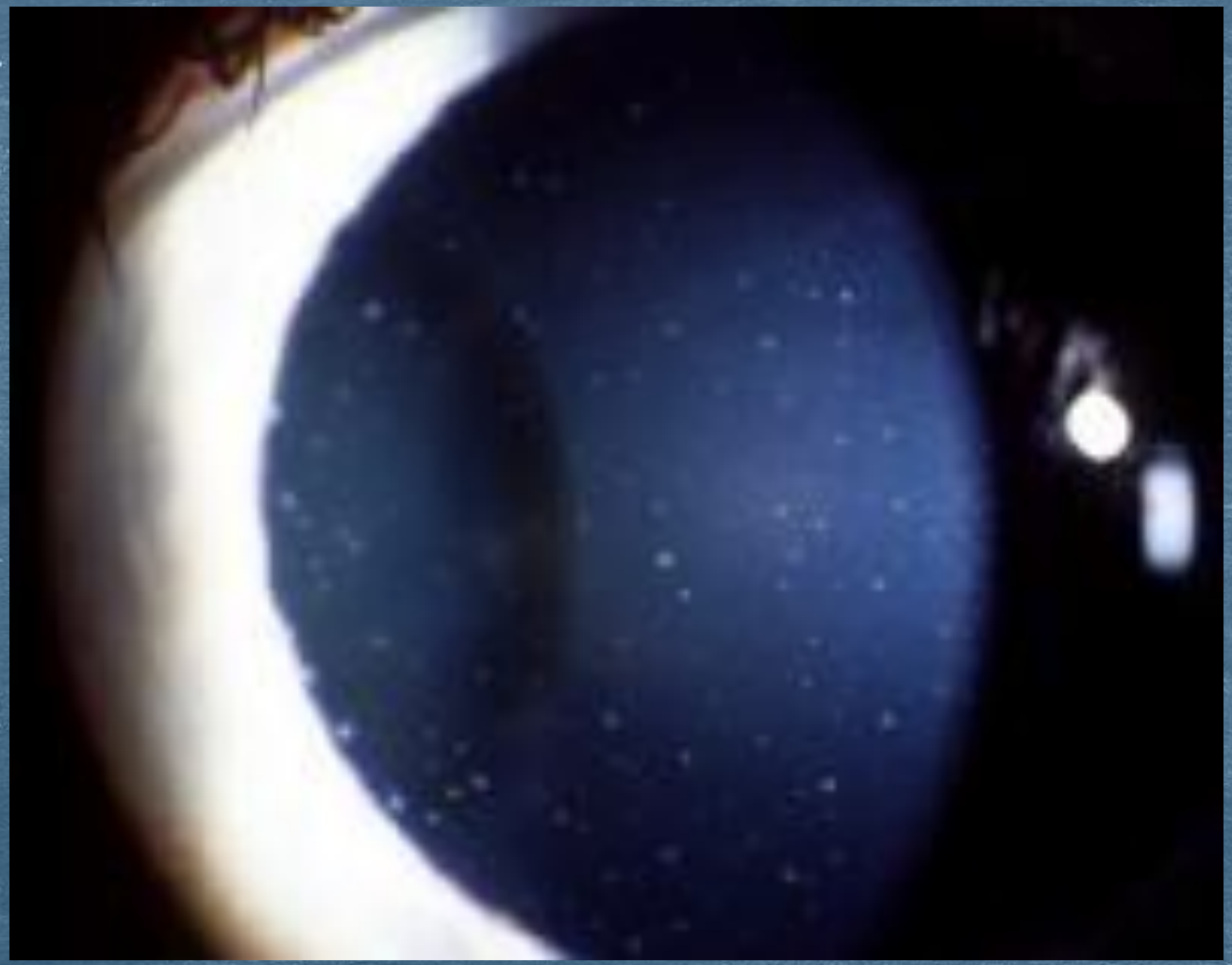
# Aqoeues cells and flare



# Keratitic Percipitates



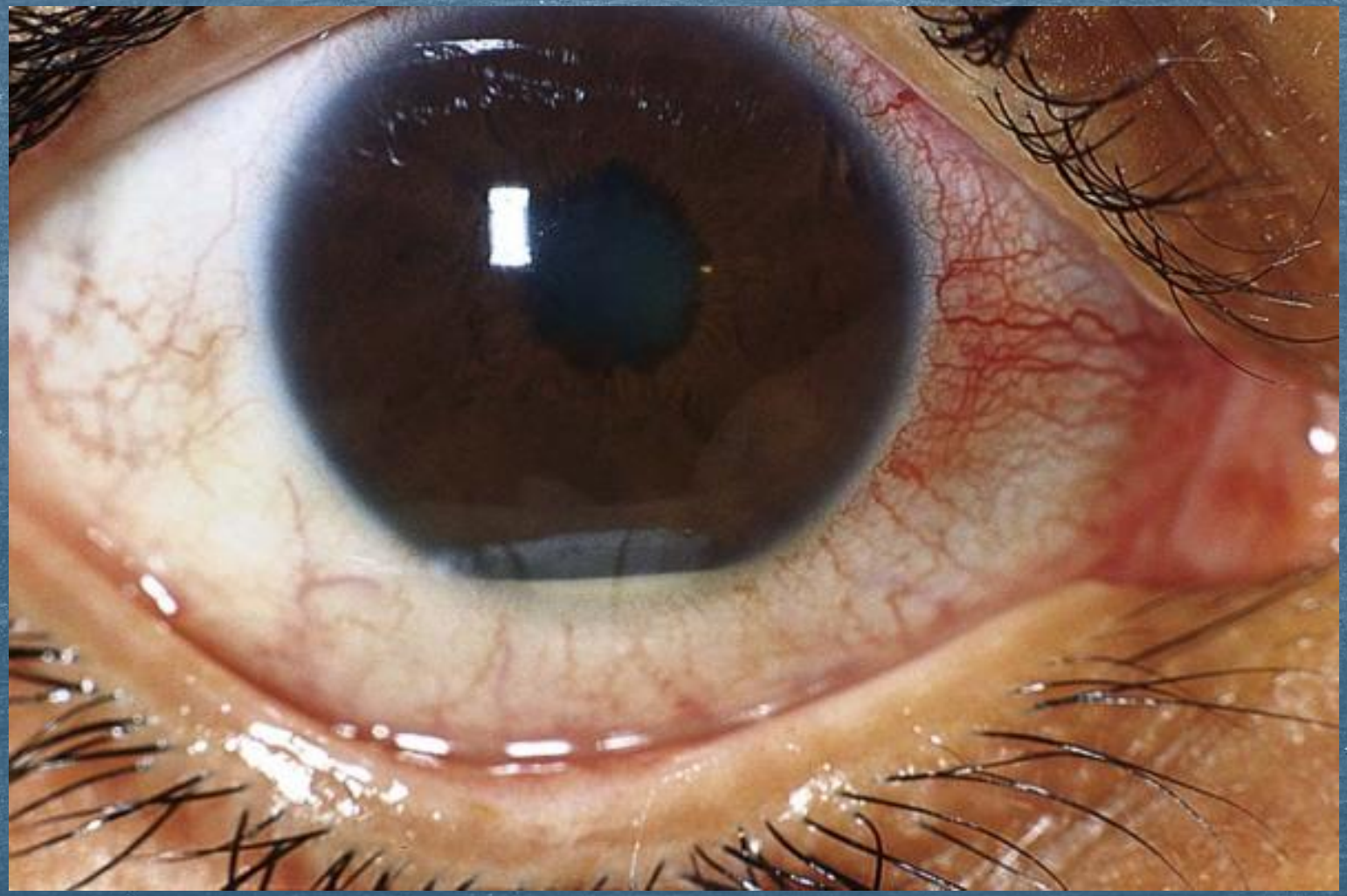
**clumped inflammatory cells on the endothelium of the cornea , esp. inferior**



Small stellate keratic precipitates with fine filaments in a patient with Fuchs heterochromic iridocyclitis.

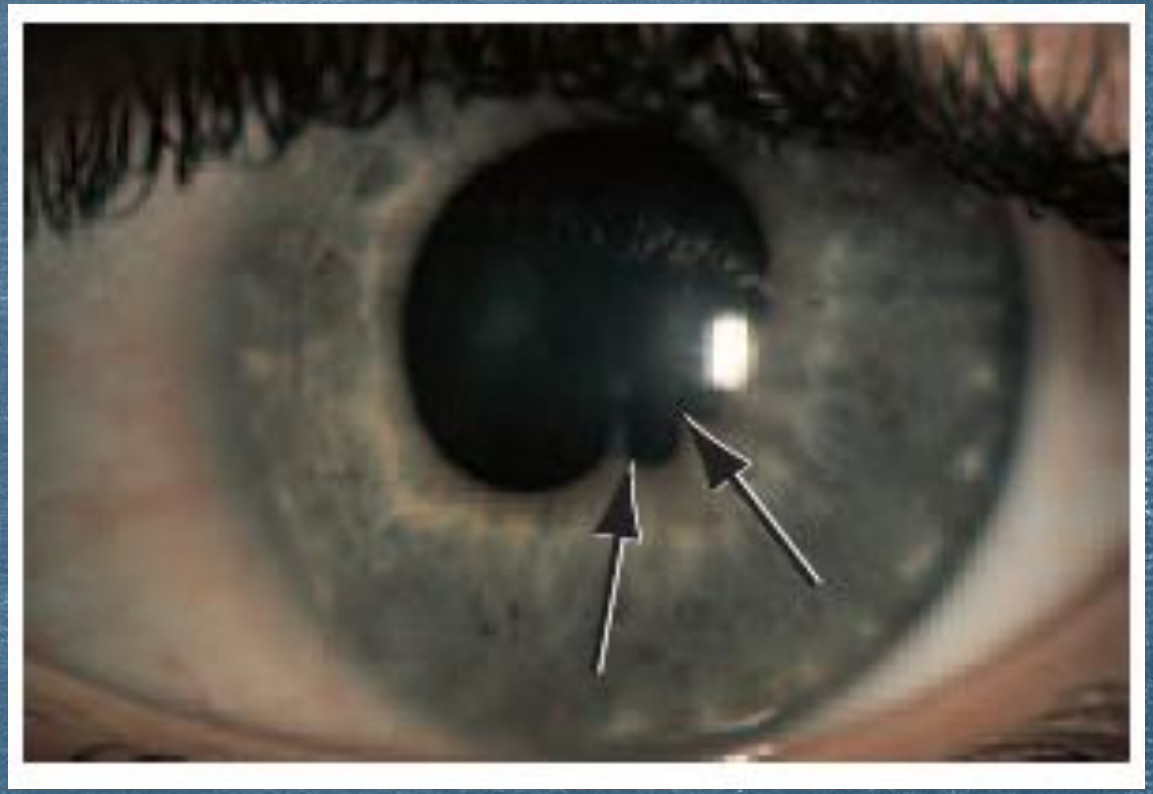
in some disorders, such as Fuchs' iridocyclitis, KPs may be present superiorly

# Hypopyon



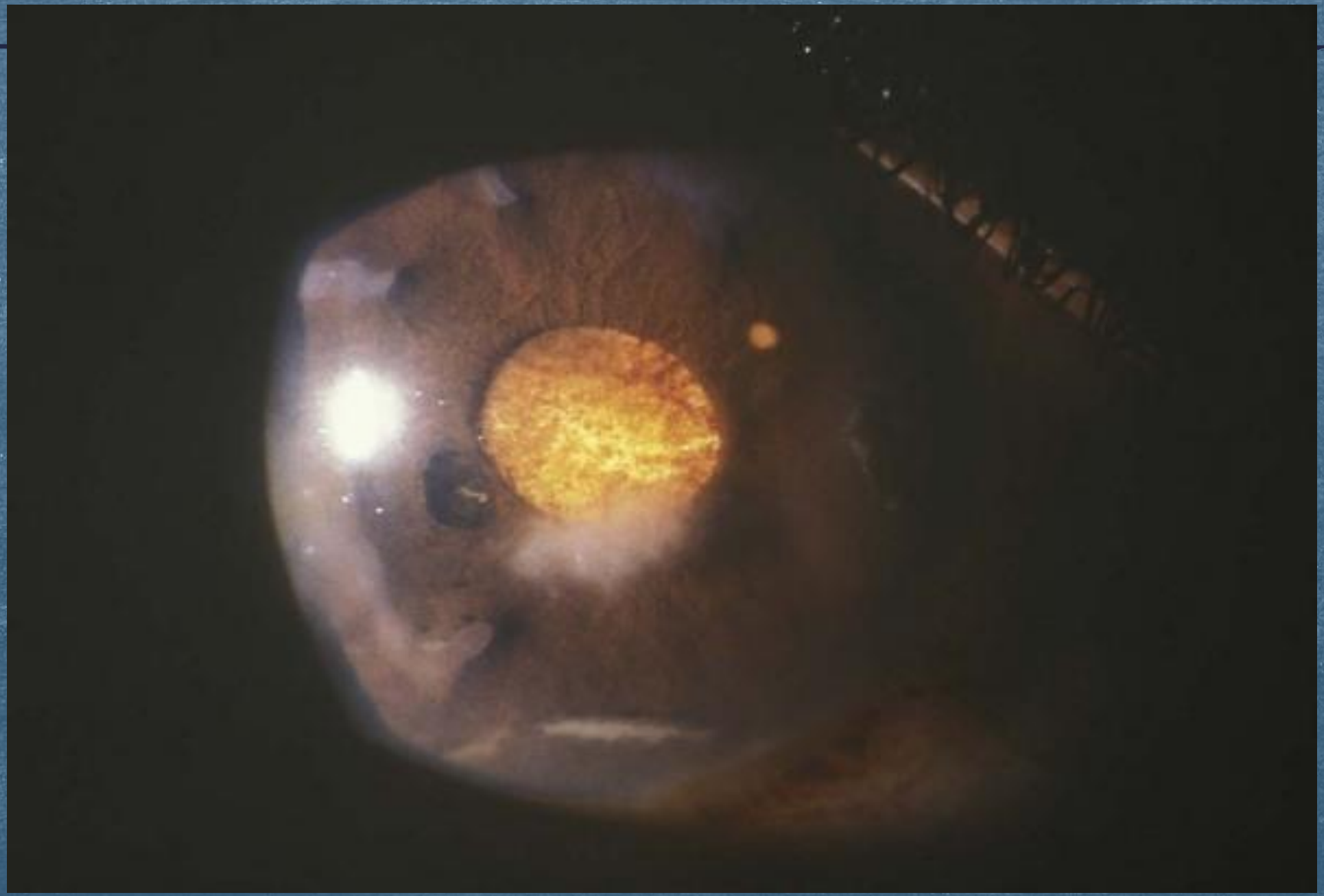
# Posterior Synechiea

iris< and lens posterior synechiea
Iris and cornea ant synechiea
Iris may adhere to the lens & bind down the pupil (**posterior synachiae) , Pupillary block glaucoma**
presence of synechiae indicates that the inflammation has been chronic or recurrent; however, these adhesions may occasionally develop within a few days in patients with severe inflammation.

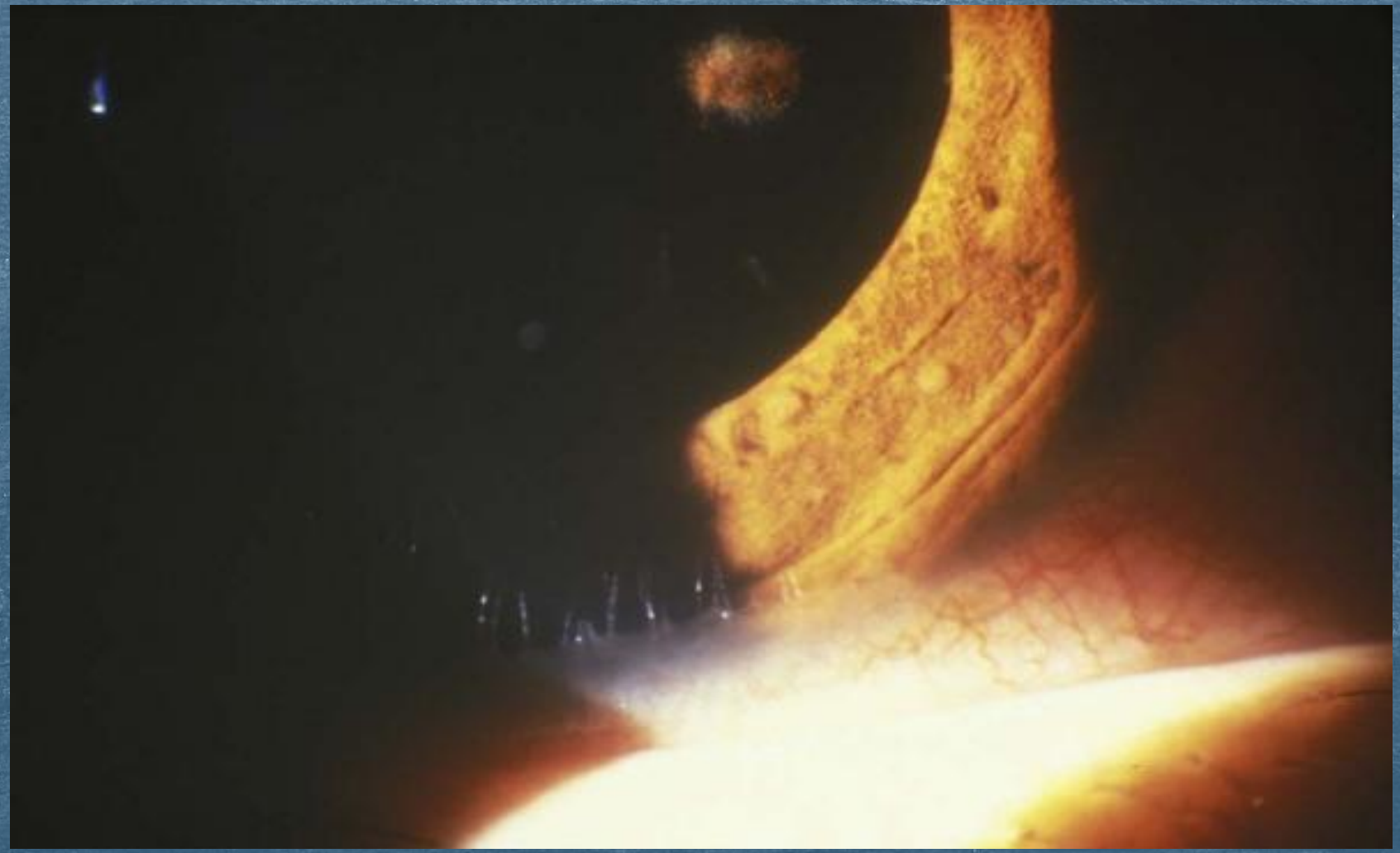


# Peripheral Anterior Synechiaea

**adhesion between the iris and the trabecular meshwork or corena may occlude the drainage angle**



# Iris nodules

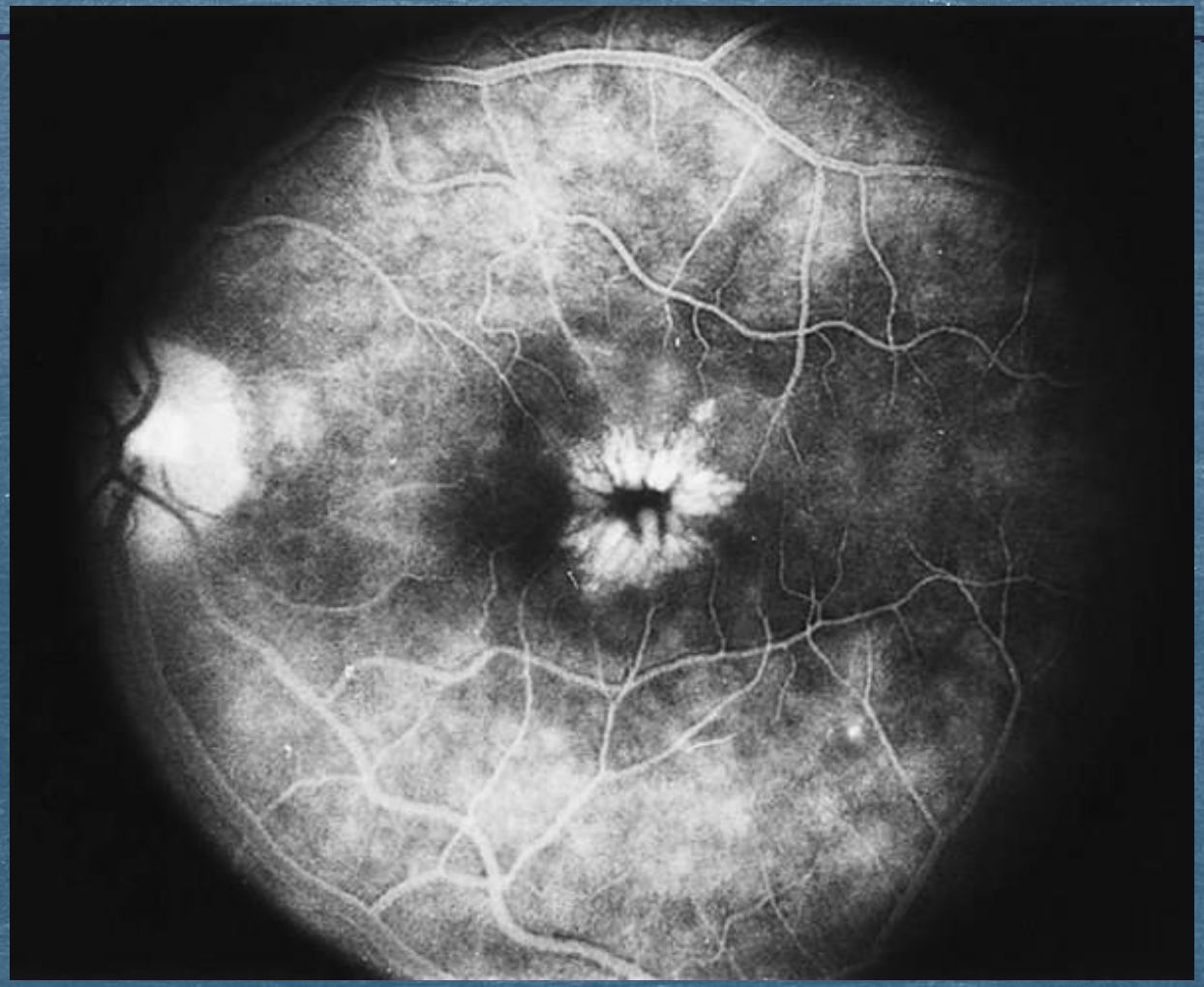


INTERMEDIATE & POSTERIOR UNEITIS

- Cells in vitreous
- Retinal or choroidal foci of inflammation
- Macular edema may be presnt

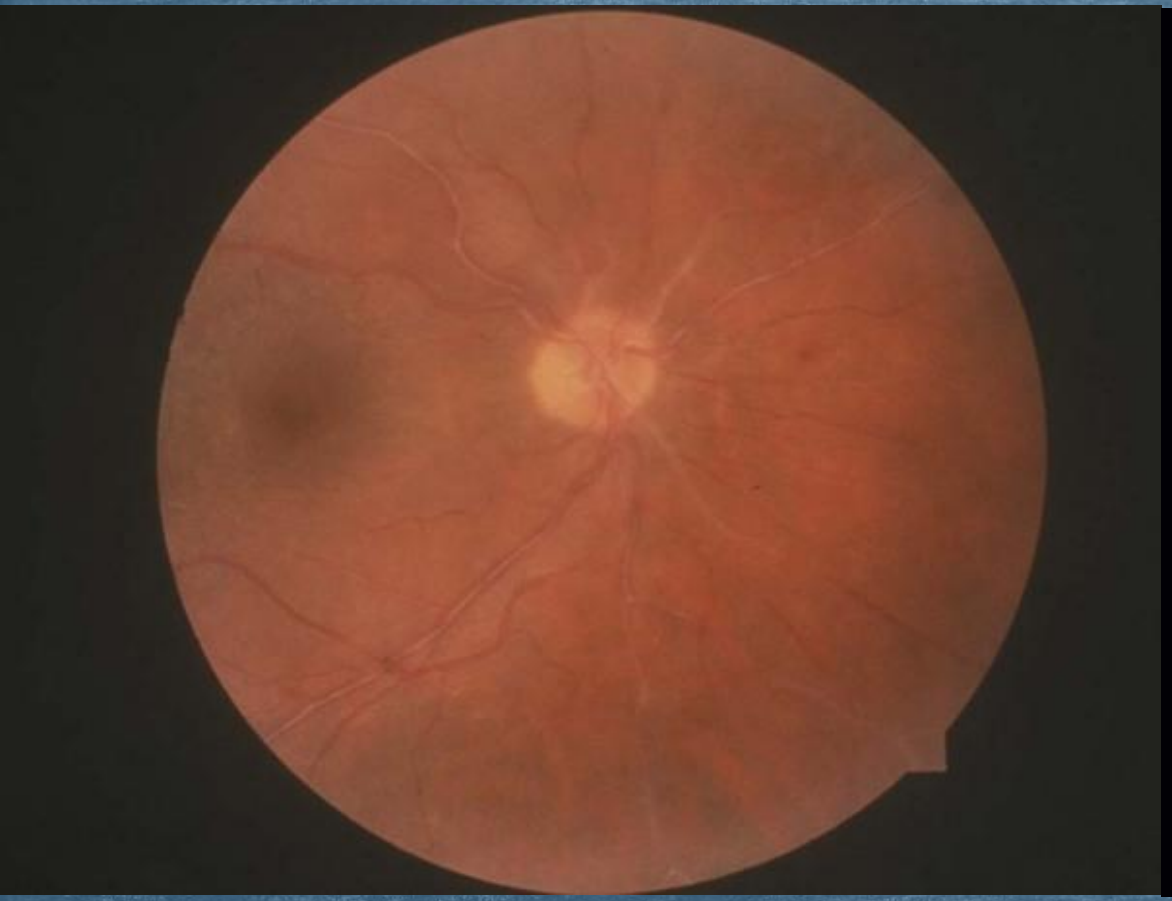
# Cells in vitreous

# Macular edema

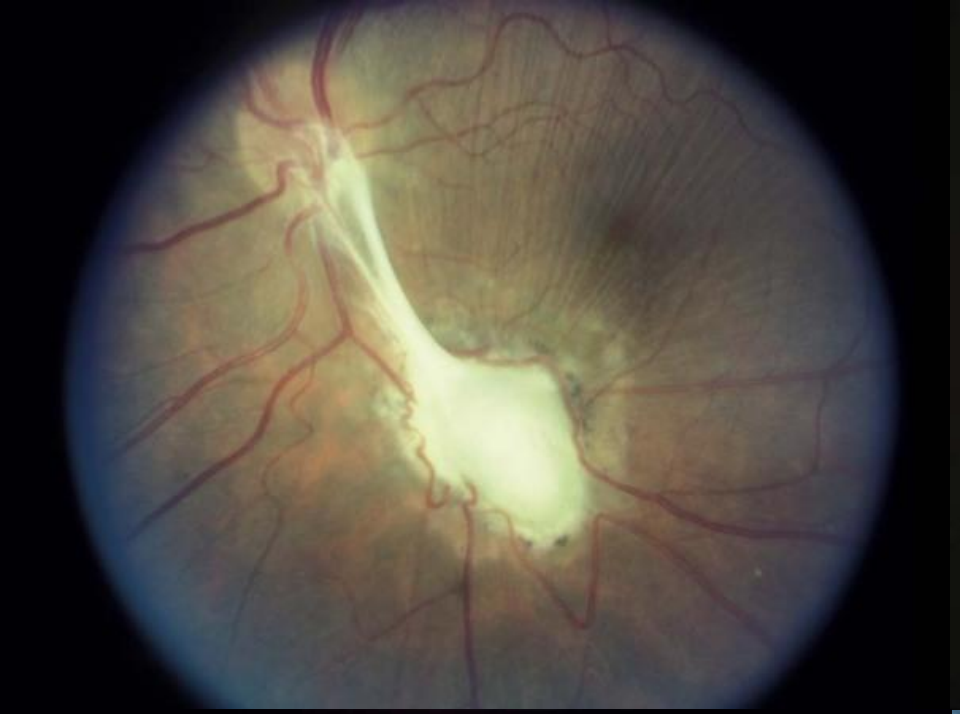


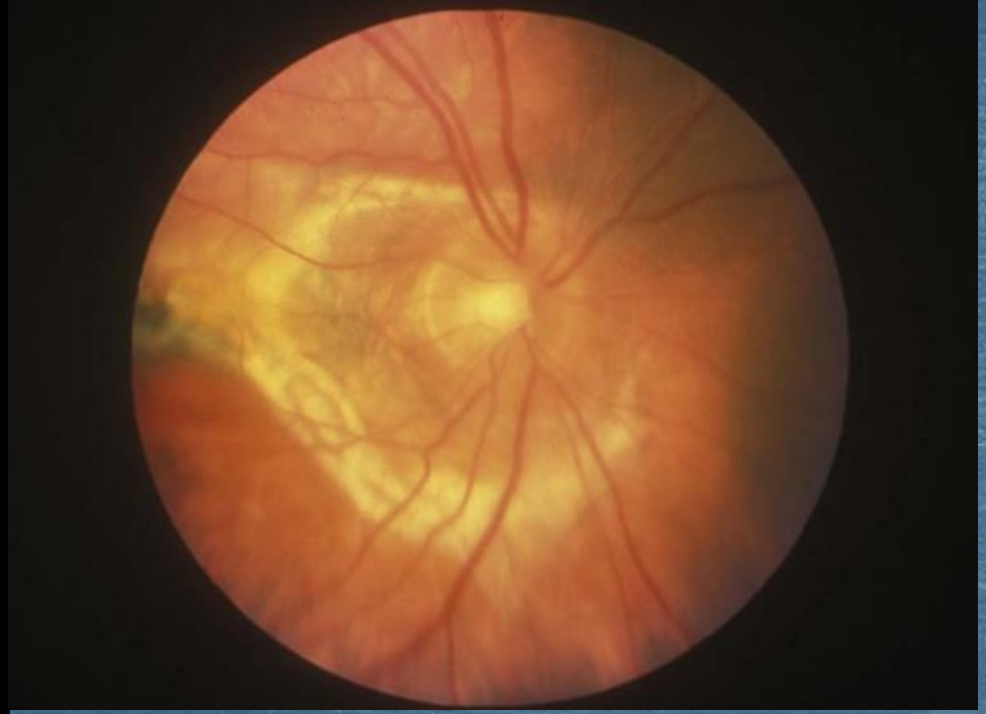
- Fluorescein angiogram demonstrating cystoid macular edema caused by pars planitis.

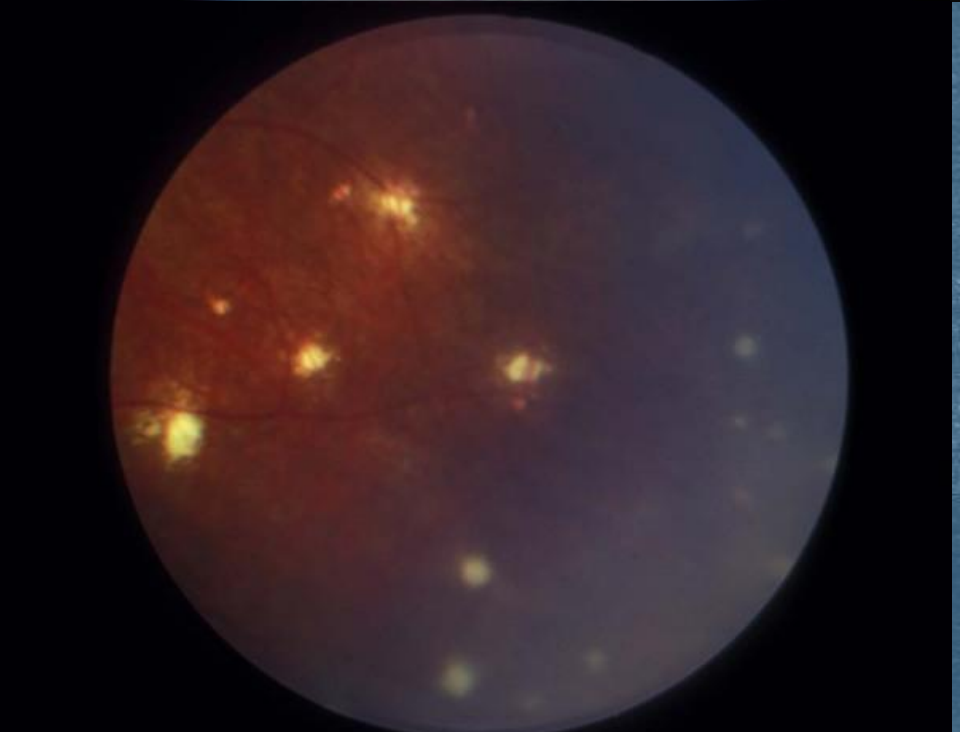
# Retinal or choroidal foci of inflammation



**Retinal vascular sheathing in patient with idiopathic retinal vasculitis.**
**Exudative retinal detachment in a patient with Vogt–Koyanagi–Harada syndrome is seen inferior to the macula**







Dense fibrotic band extends from the optic disc to the inferior vascular arcade.
Large choroidal granuloma around optic disc in a patient with sarcoidosis.
Dalen–Fuchs nodules are small, fairly discrete, yellow to white lesions that most commonly occur in the retinal periphery.
The lesions are composed of collections of inflammatory cells between the retinal pigment epithelium and Bruch's membrane.

# INVESTIGATIONS

Laboratory studies are unlikely to be helpful in cases of mild, unilateral nongranulomatous uveitis in the following settings:

- Trauma
- Known systemic disease
- A history and physical not suggestive of systemic disease

# A nonspecific workup is indicated if the hx & P/E findings are unremarkable in the presence of uveitis that is bilateral, granulomatous, or recurrent :

- CBC
- Erythrocyte sedimentation rate (ESR)
- Antinuclear antibody (ANA)
- Rapid plasma reagin (RPR)
- Venereal disease research laboratory (VDRL)
- Purified protein derivative (PPD)
- Lyme titer
- HLA-B27
- Chest radiography (to assess for sarcoidosis or tuberculosis)

- Ankylosing spondylitis : anterior uveitis , HLA-typing !!
- Sarcoidosis ; large KPs and possibly nodules on the iris , CXR, serum Ca , serum ACE
- Toxoplasmic : retinochoroiditis the focus of inflammation often occurs at the margin of an old inflammatory choroidal scar.

- A posterior uveitis may have an infectious or systemic inflammatory cause.

- Associated symptoms may also help point towards a systemic disease (e.g. fever, diarrhoea, weight loss).

# TREATMENT

This is aimed at:

- Relieving pain and inflammation in the eye;
- Preventing damage to ocular structures

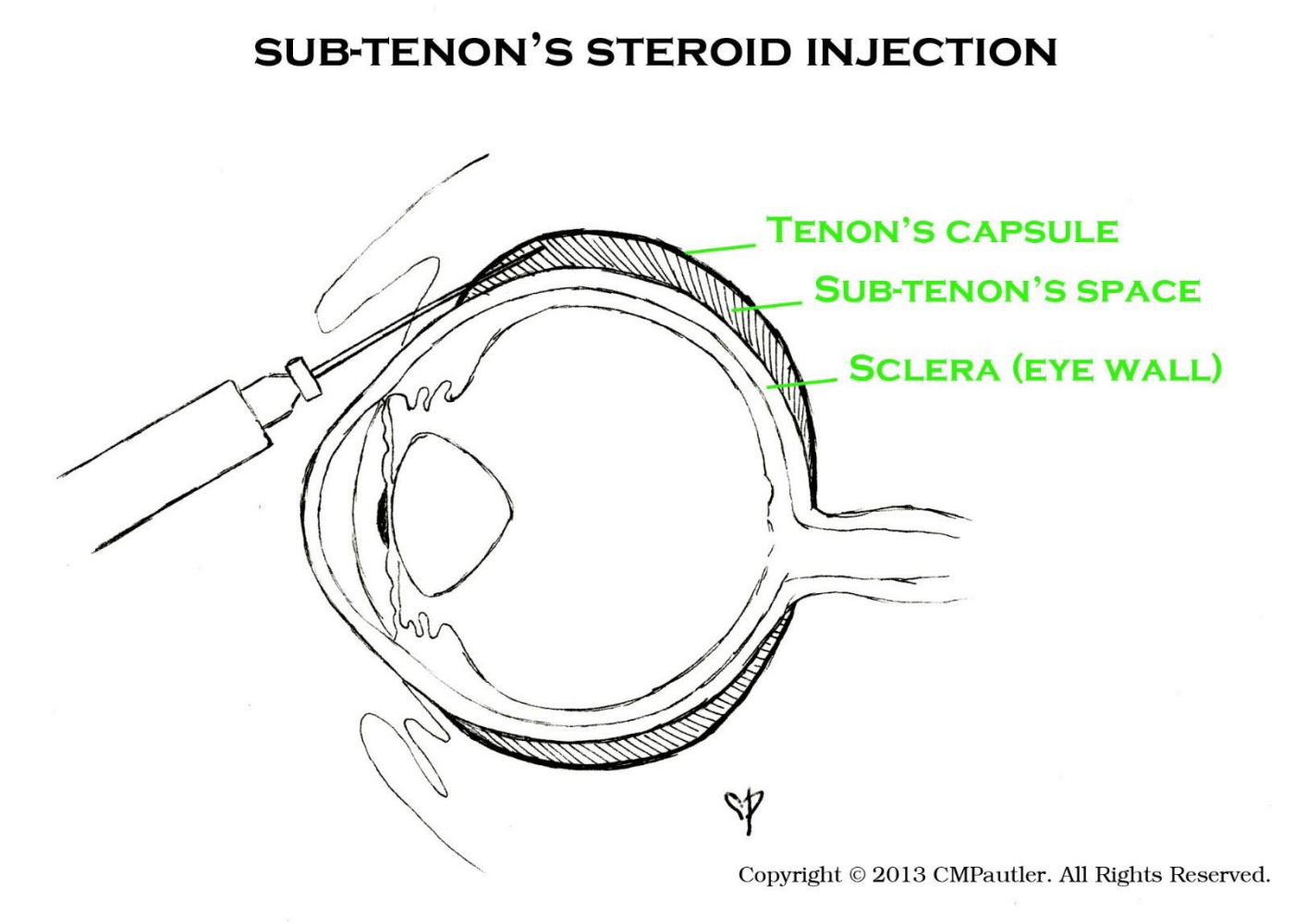
( esp. the macula & optic nerve)

- Cycloplegics (mydriatics) and corticosteroid eye drops are used to reduce pain and inflammation
- Relieves the pain from ciliary spasm and prevents the formation of posterior synechiae by separating it from the anterior lens capsule.
- By mydriatics, e.g. cyclopentolate or atropine drops (prolonged action)
- An attempt to break any synechiae that have formed should be made with initial intensive cyclopentolate and phenylephrine drops.
- A subconjunctival injection of mydriatics may help to break resistant synechiae.
- Synechiae otherwise interfere with normal dilatation of the pupil.

Steroid therapy is the mainstay of treatment.

- **Anterior uveitis** : delivered by eye drops.
- **Posterior uveitis:** treated with systemic steroids or steroids injected onto the orbital floor or into the subtenon space.

# Subtento's space



In posterior uveitis/retinitis visual loss may occur either from

- Destructive processes caused by the retinitis itself (e.g. in toxoplasma or CMV)
- Fluid accumulation in the layers of the macula (macular oedema).

- Specific antiviral or antibiotic medication may also be required.

- Some rare but severe forms of uveitis, e.g. that associated with Behçet's disease, may require treatment with other systemic immunosuppresive drugs such as azathoprine or cyclosporin. Long-term treatment may be necessary.

# SPECIFIC CONDITIONS ASSOCIATED WITH UVEITIS

# Etiology

- Infections
- Systemic Immune mediated disease
- Syndromes confined to the eye
- Idiopathic

## Representative infectious causes of uveitis

| Bacterial/spirochetal | Viral | Fungal | Parasitic (protozoan/helminthic) |
|---|---|---|---|
| Atypical mycobacteria | Chikungunya | Aspergillosis | Acanthamoeba |
| Brucellosis | Cytomegalovirus | Blastomycosis | Cystercercosis |
| Cat scratch disease | Ebola | Candidiasis | Onchocerciasis |
| Leprosy | Epstein-Barr | Coccidioidomycosis | Toxocariasis |
| Leptospirosis | Herpes simplex | Cryptococcosis | Toxoplasmosis |
| Lyme disease | Herpes zoster | Histoplasmosis | |
| Propionibacterium | HIV-1 | Pneumocystis jirovecii (PCP) | |
| Rocky Mountain spotted fever | Human T cell leukemia virus | Sporotrichosis | |
| Syphilis | Mumps | | |
| Tuberculosis | Parechovirus | | |
| Whipple's disease | Rubella | | |
| | Rubeola | | |
| | Vaccinia | | |
| | West Nile virus | | |

HIV: human immunodeficiency virus.

## Uveitis syndromes confined primarily to the eye

| |
|---|
| Acute multifocal placoid pigmentary epitheliopathy |
| Acute retinal necrosis |
| Autosomal dominant neovascular inflammatory vitreoretinopathy |
| Birdshot choroidopathy |
| Fuchs' heterochromic cyclitis (post rubella) |
| Glaucomatocyclitic crisis |
| Immune recovery (reconstitution) uveitis |
| Iridocorneal endothelial syndrome |
| Leber's neuroretinitis |
| Multifocal evanescent white dot syndrome |
| Pars planitis |
| Punctate inner choroidopathy |
| Serpiginous choroidopathy |
| Subretinal fibrosis |
| Sympathetic ophthalmia |
| Trauma |

## Systemic immune-mediated causes of uveitis

| |
|---|
| Ankylosing spondylitis |
| Behçet's disease |
| Blau syndrome |
| Crohn's disease |
| Drug or hypersensitivity reaction |
| Interstitial nephritis |
| Juvenile idiopathic arthritis |
| Kawasaki's disease |
| Multiple sclerosis |
| Neonatal onset multisystem inflammatory disease |
| Psoriatic arthritis |
| Reactive arthritis |
| Relapsing polychondritis |
| Sarcoidosis |
| Sjögren's syndrome |
| Sweet syndrome |
| Systemic lupus erythematosus |
| Ulcerative colitis |
| Vasculitis |
| Vitiligo |
| Vogt-Koyanagi-Harada syndrome |

# Seronegative Spondyloarthritis

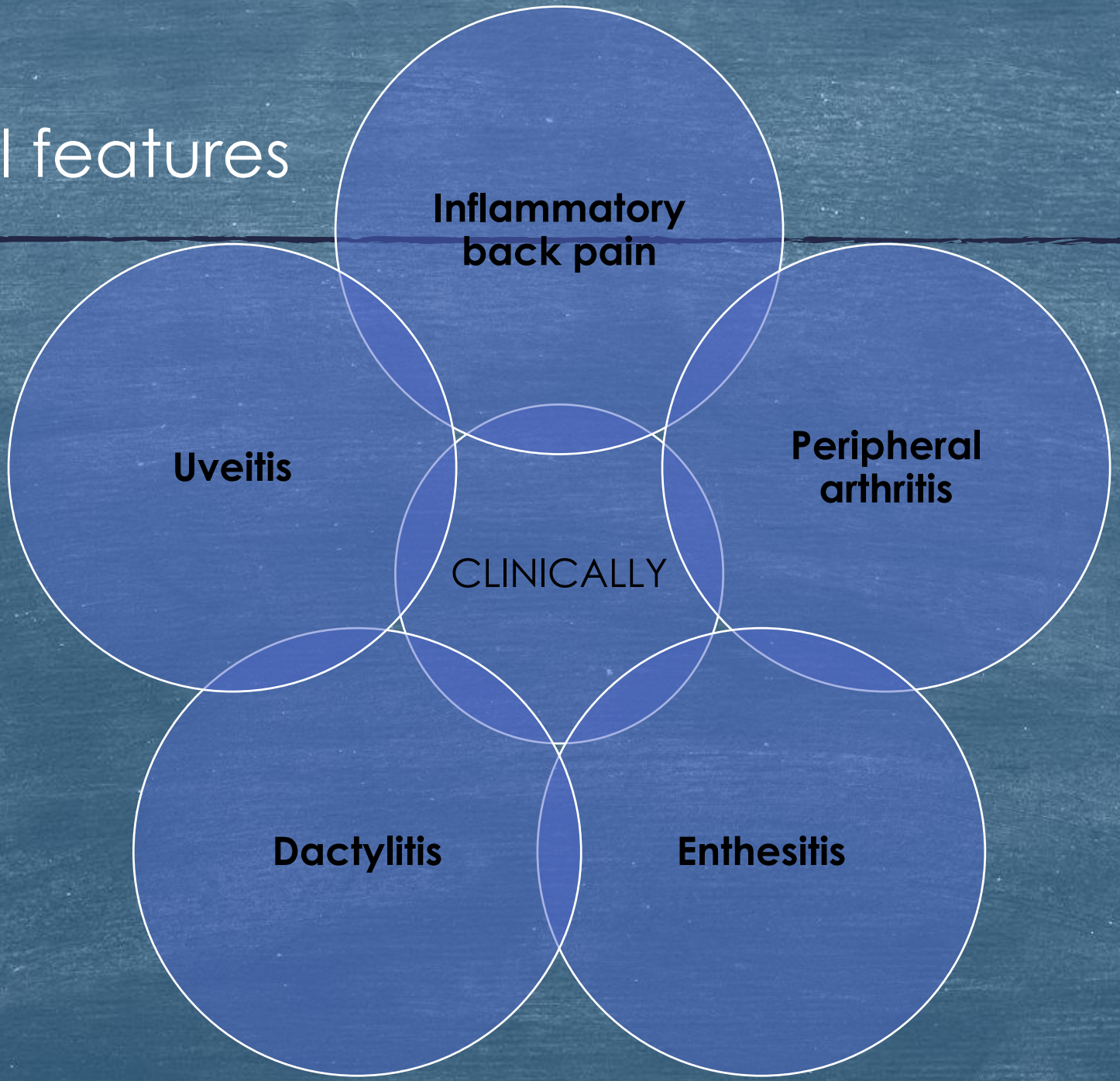
# outline

- Causes
  - Seronegative spondyloarthritis
  - Sarcoidosis
  - Juvenile chronic arthritis
  - Behcet's disease
  - Toxoplasmosis chorioretinitis
  - AIDS and HIV

| Spondyloarthritis (SpA) Epidemiology and Key Presentation Features | | |
|---|---|---|
| **Disease** | **Epidemiology** | **Other** |
| Ankylosing spondylitis | ♂:♀ = 3:1; onset in teens to mid-20s (rare after 40 y) | Progressive limitation of spine motion; "bamboo spine" |
| Psoriatic arthritis | ♂ = ♀; peak incidence 45–54 y; seen in 20–30% of Pts w/ psoriasis (*Ann Rheum Dis* 2005;64:ii14) | In 13–17%, arthritis precedes psoriasis by yrs. Does not correlate with psoriasis activity. A/w HIV. |
| Reactive arthritis | ♂ >> ♀; 20–40 y; 10–30 d s/p post-GI or GU infxn* in genetically susceptible host | Previously "Reiter's syndrome": arthritis, urethritis and conjunctivitis. Most resolve w/in 12 mo. |
| IBD-associated | ♂ = ♀; seen in 20% of IBD Pts; Crohn's > UC | Type I <5 joints: correlates w/ IBD<br>Type II >5 joints or axial disease: does not correlate w/ IBD |

*GU: *Chlamydia, Ureaplasma urealyticum*; GI: *Shigella, Salmonella, Yersinia, Campylobacter, C. diff.*

# Major Clinical features

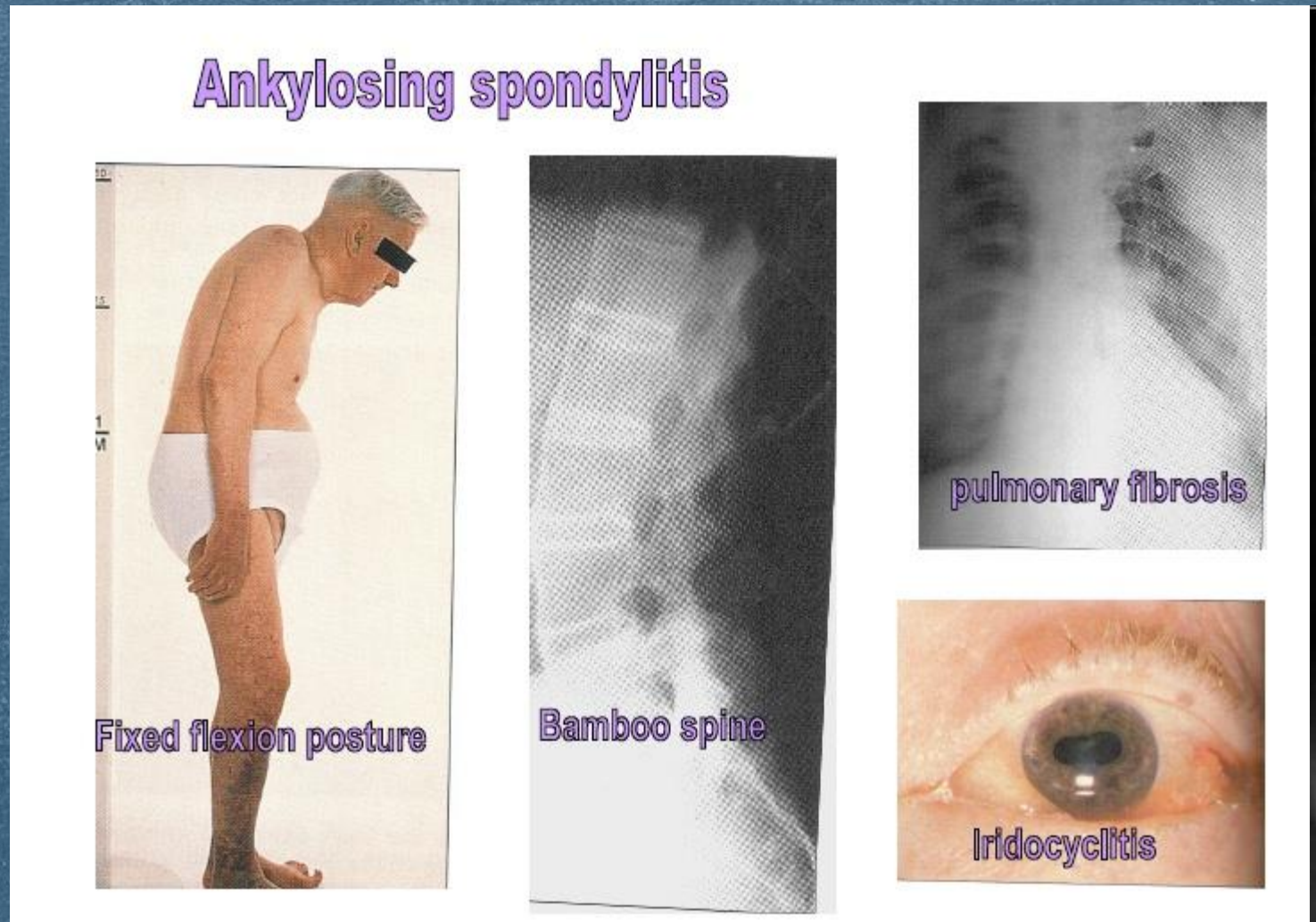


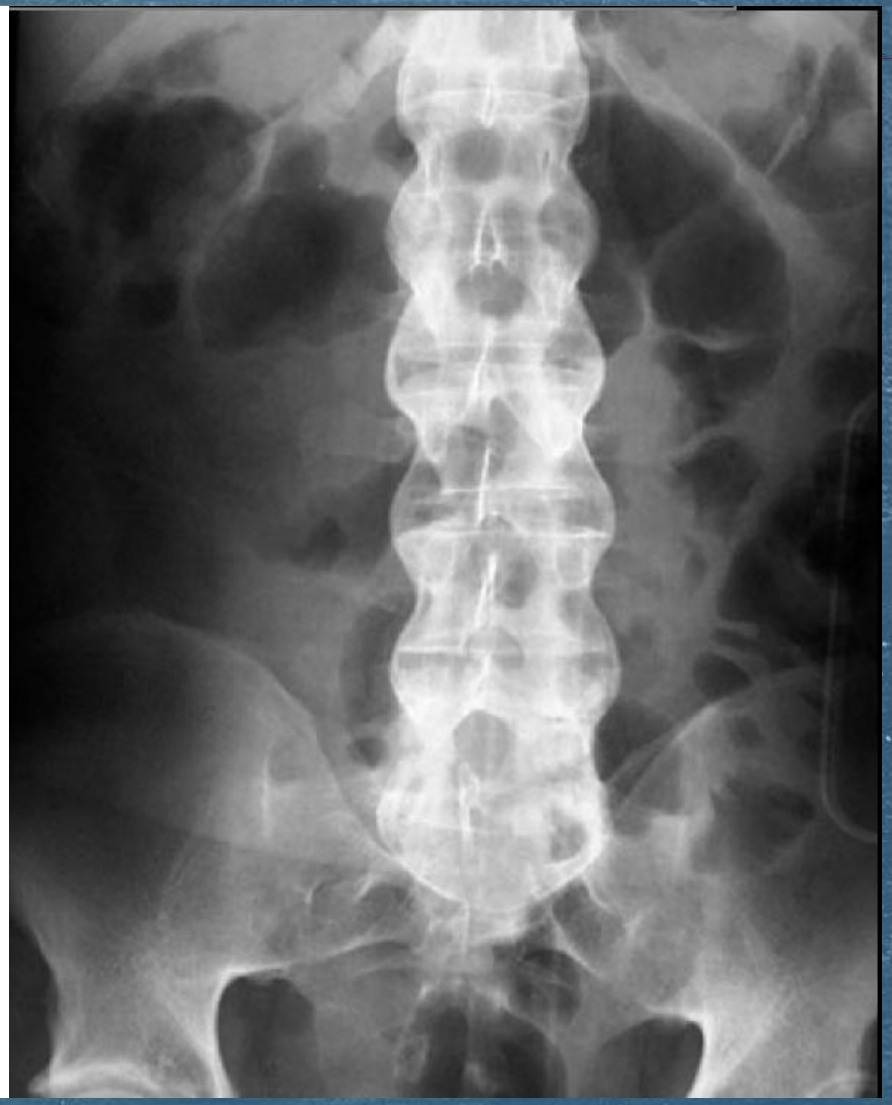
**Inflammatory back pain**: SI joints (**sacroiliitis**), apophyseal joints of spine characterized by **IPAIN** (**I**nsidious onset, **P**ain at night, **A**ge of onset <40 y, **I**mproves w/ exercise/hot water, **N**o improvement w/ rest), a.m. stiffness, *re*
*sponsive to NSAIDs*

- **Peripheral arthritis**: typically asymmetric, oligoarticular, large joints, lower > upper limb; however, can be symmetric & polyarticular (thus, mimic RA), esp. in psoriatic arthritis
- **Enthesitis**: inflammation at site of tendon/ligament insertion into bone, esp. Achilles, pre-patellar, elbow epicondyles, plantar fasciitis. **Rigidity of spine** (bamboo spine by X-ray, ankylosis due to progressive growth of bony spurs which bridge intervertebral disc).
- **Dactylitis** ("sausage digit"): inflammation of entire digit (joint + tenosynovial inflamm)
- **Uveitis**: anterior uveitis most common extra-articular manifestation; p/w pain, red eye, blurry vision, photophobia, usually unilateral

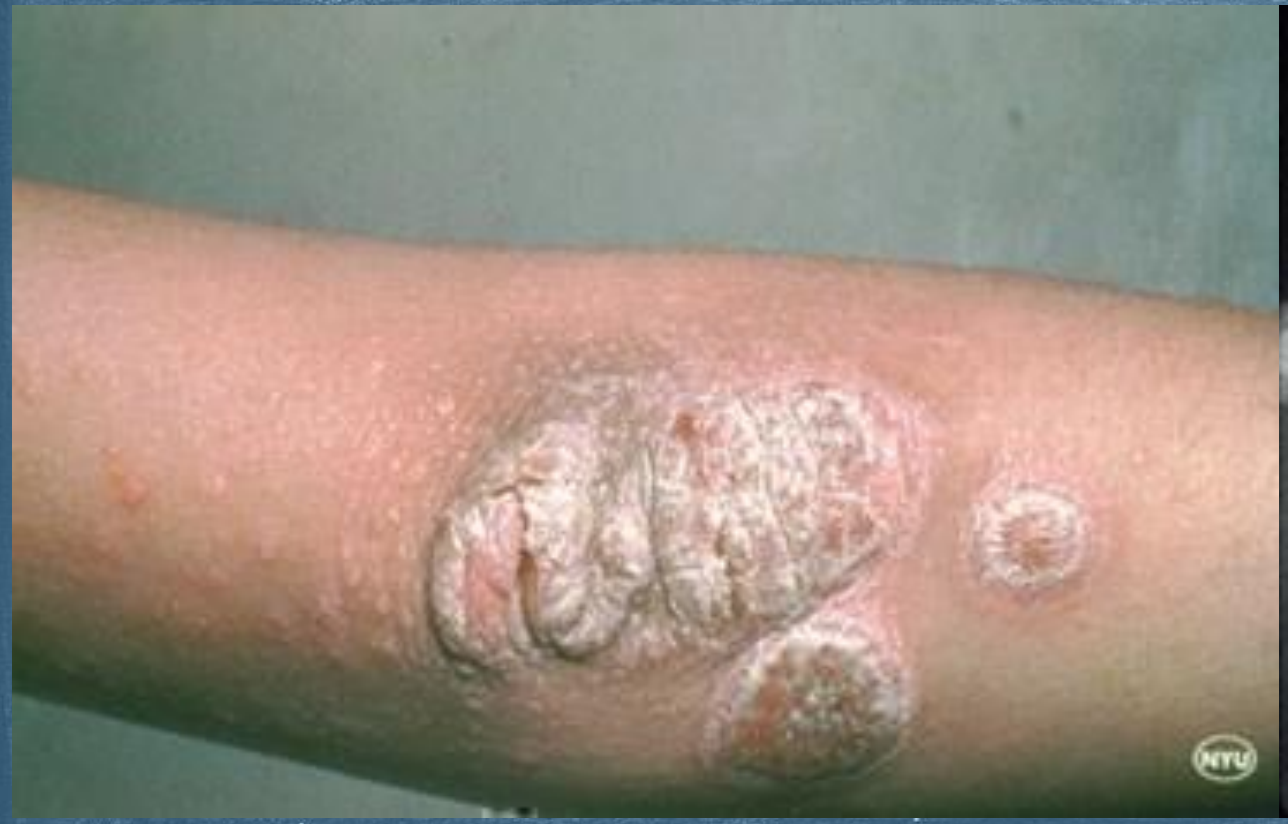
| Distinguishing Features | | | | |
|---|---|---|---|---|
| | *Axial-predom* | *Peripheral-predominant* | | |
| **Feature** | **Ankylosing spondylitis** | **Psoriatic** | **Reactive** | **IBD-assoc** |
| Axial involv. | 100% | 20–40% | 40–60% | 5–20% |
| Sacroiliitis | Symmetric | Asymm | Asymm | Symmetric |
| Periph involv. | Less common (~50%) | Frequent | Frequent | Frequent |
| Periph distrib. | Lower > Upper | Upper > Lower (see below) | Lower > Upper | Lower > Upper |
| ⊕ HLA-B27 | 80–90% | 20% | 50–80% | 5–30% |
| Enthesitis | Frequent | Frequent | Frequent | Rare |
| Dactylitis | Uncommon | Common | Common | Uncommon |
| Ocular | Uveitis in 25–40% | Conjunctivitis, uveitis, episcleritis, | **Conjunctivitis** (noninfectious), uveitis, keratitis | Uveitis |
| Skin | None | **Psoriasis**; nail pitting and onycholysis | Circinate balanitis, keratoderma blennorrhagica | *E. nodosum*, pyoderma-gangrenosum |
| Imaging | Bamboo spine (symm syndes.) | "Pencil-in-cup" DIP deformity | *Asymmetric* syndesmophytes | Periph dis. rarely erosive |
| Other | ↑ CAD; aortitis, AI, conduction defects | ↑ CAD | **Urethritis**; AI, conduction defects | |

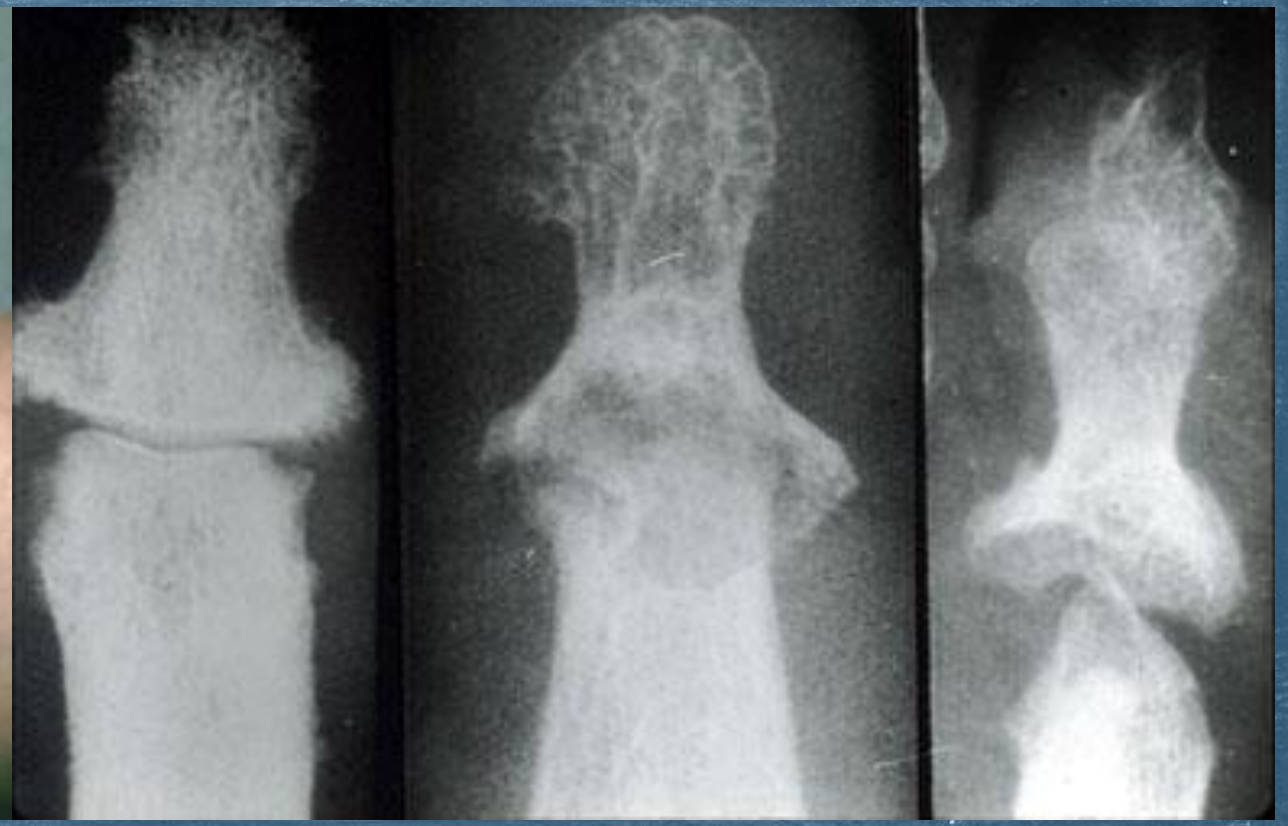
# Ankylosing Spondylitis



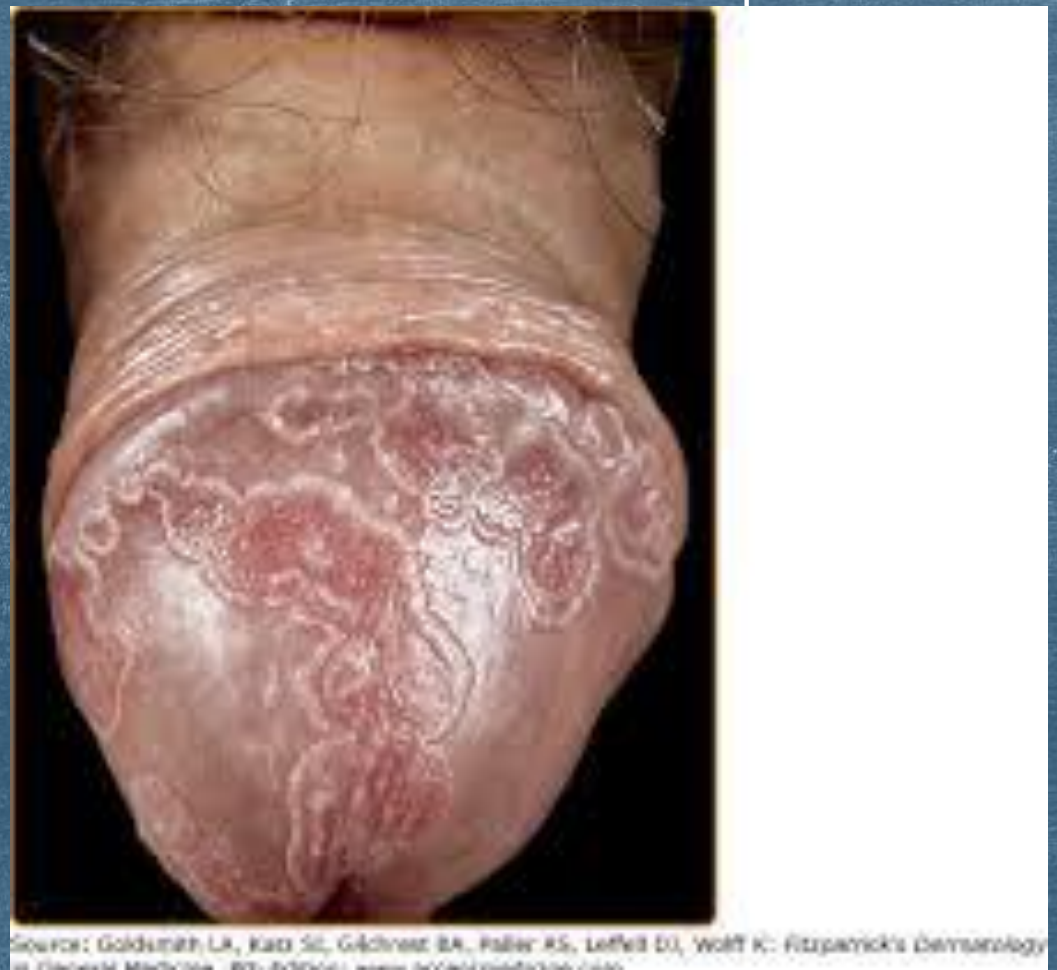
# Psoriasis

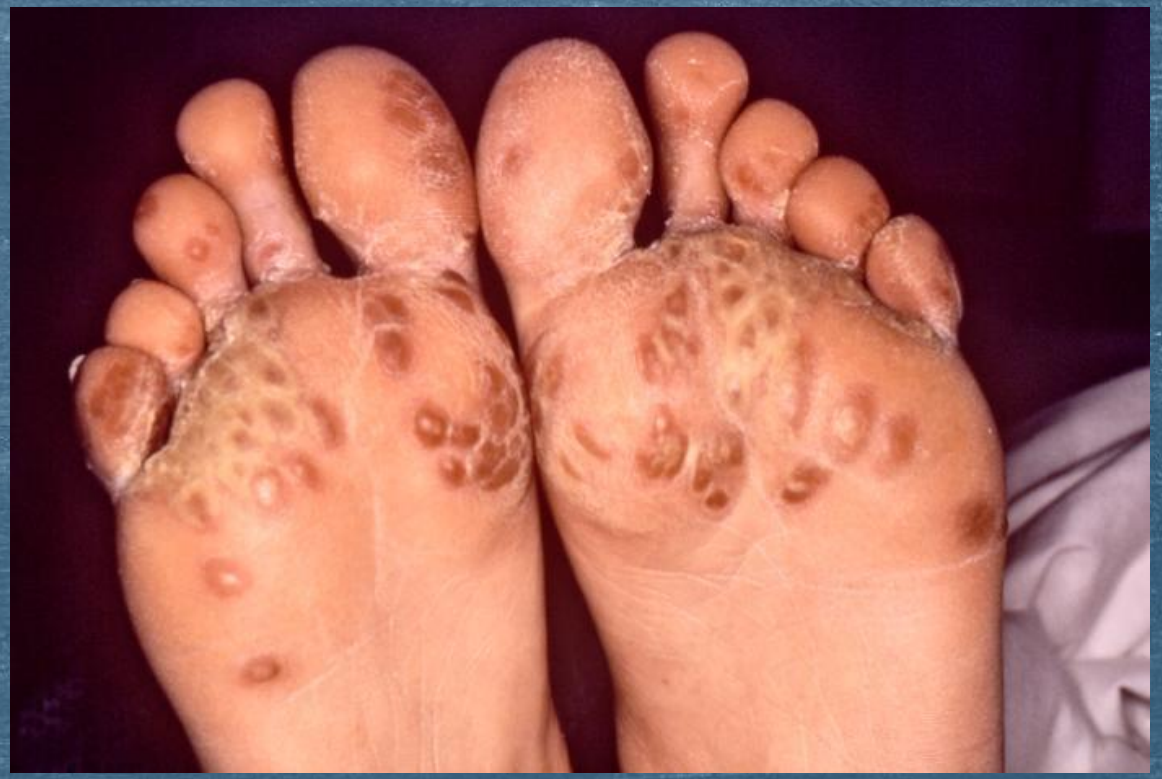


# Reactive Arthritis

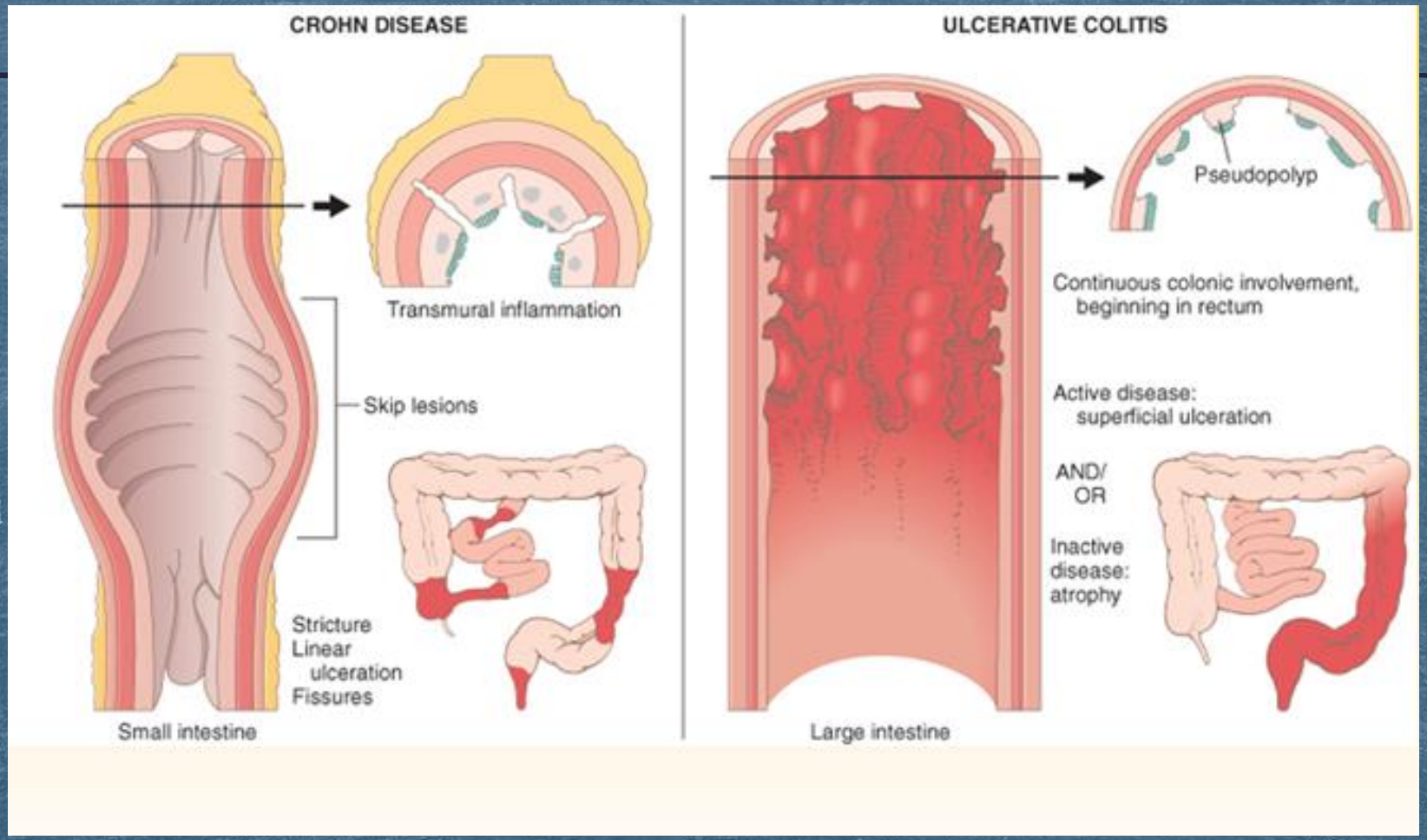
- Cant see, cant pee, cant climb a tree



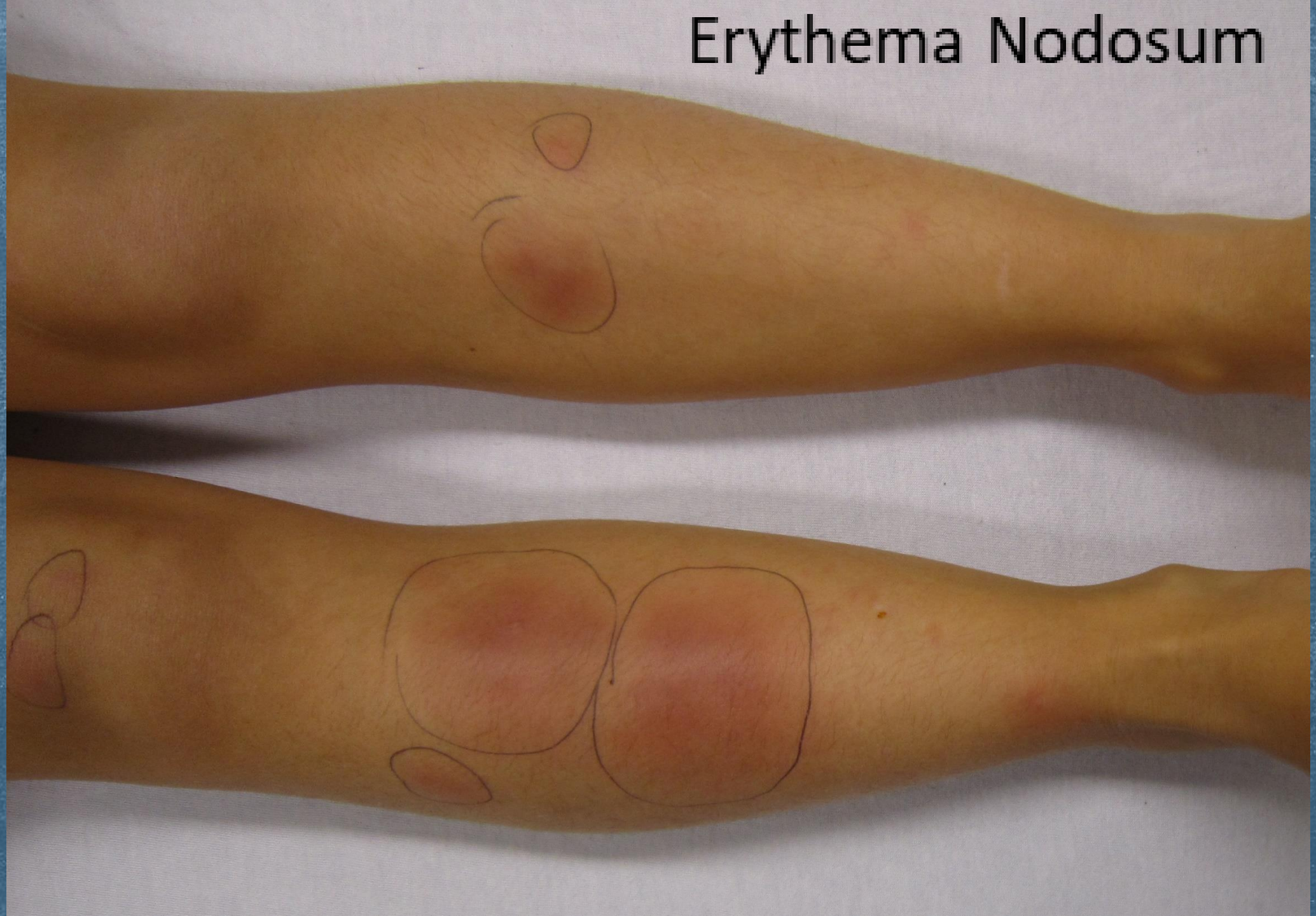


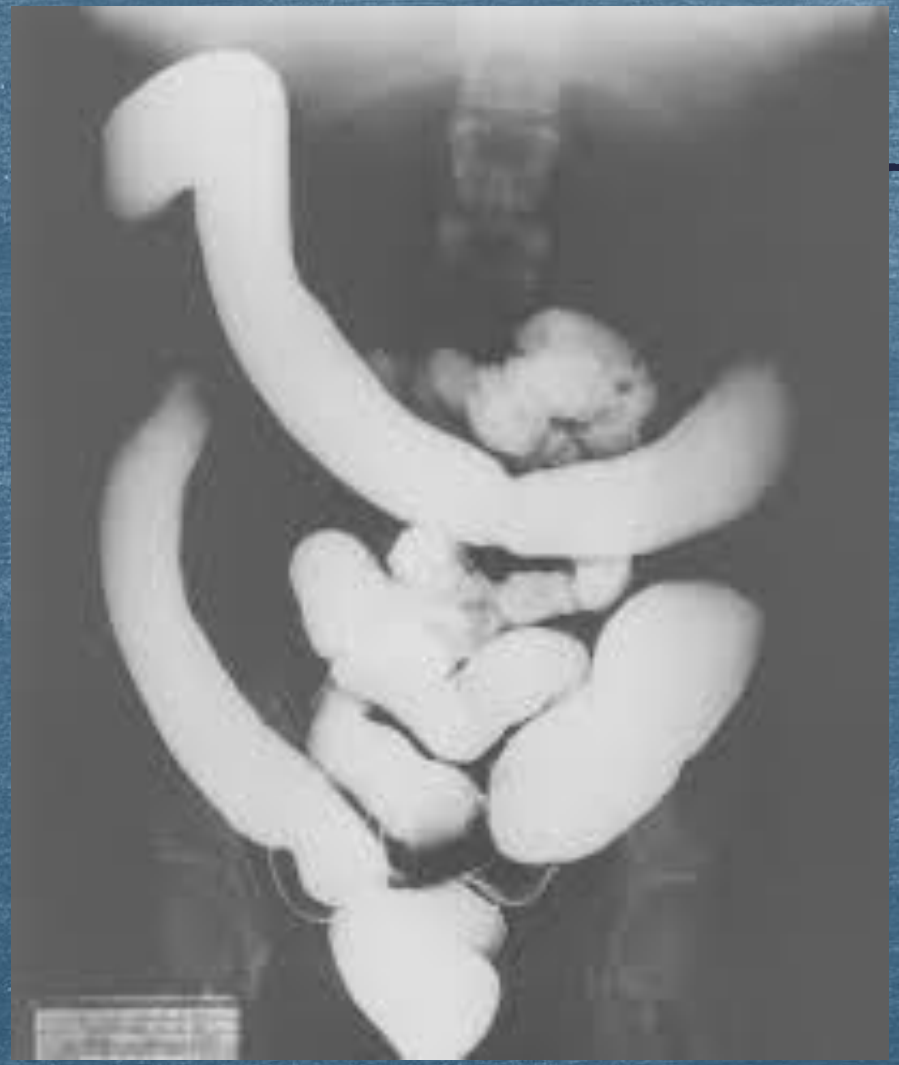
# Inflammatory bowel disease

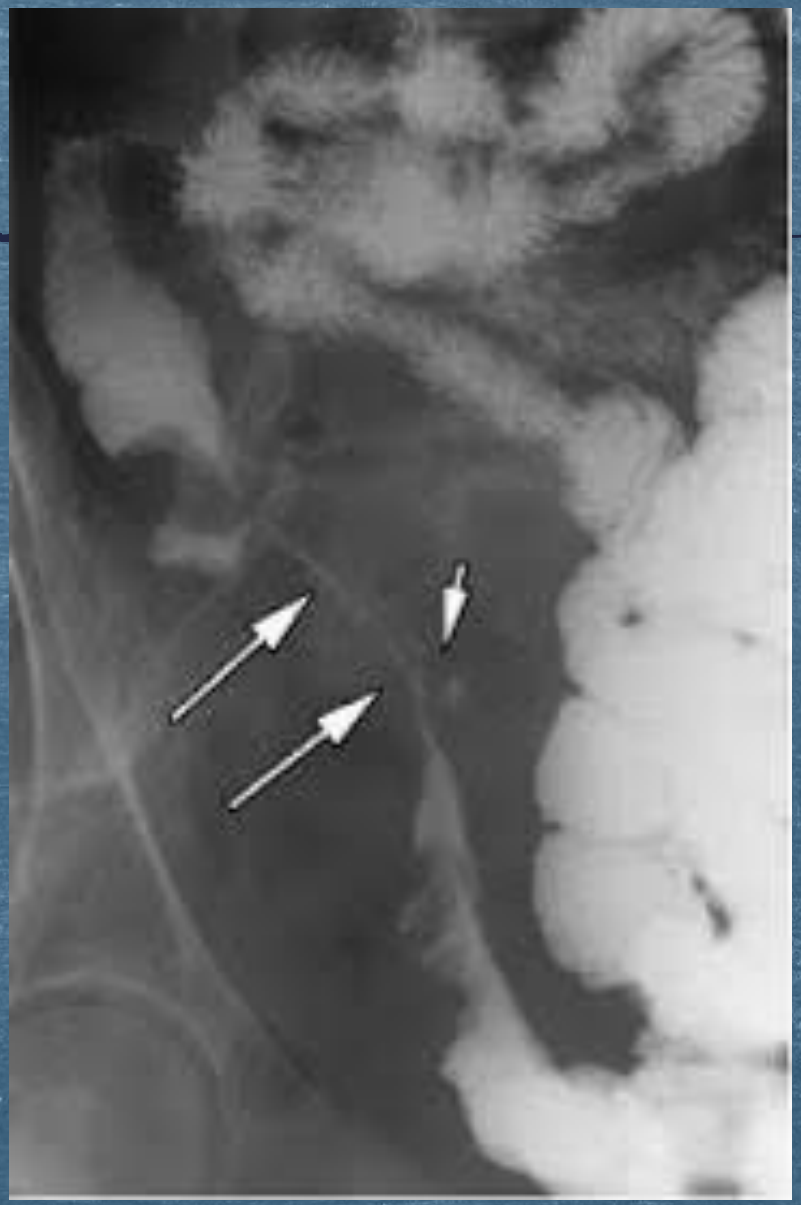
| COMPARISON OF CROHN DISEASE VERSUS ULCERATIVE COLITIS | | |
|---|---|---|
| | CROHN DISEASE | ULCERATIVE COLITIS |
| Site of origin | Terminal ileum | Rectum |
| Pattern of progression | "Skip" lesions/irregular | Proximally contiguous |
| Thickness of inflammation | Transmural | Submucosa or mucosa |
| Symptoms | Crampy abdominal pain | Bloody diarrhea |
| Complications | Fistulas, abscess, obstruction | Hemorrhage, toxic megacolon |
| Radiographic findings | String sign on barium X-ray | Lead pipe colon on barium X-ray |
| Risk of colon cancer | Slight increase | Marked increase |
| Surgery | For complications such as stricture | Curative |


CROHN DISEASE
ULCERATIVE COLITIS
Transmural inflammation
Skip lesions
Stricture
Linear ulceration
Fissures
Small intestine
Pseudopolyp
Continuous colonic involvement, beginning in rectum
Active disease: superficial ulceration
AND/ OR
Inactive disease: atrophy
Large intestine

# Erythema Nodosum



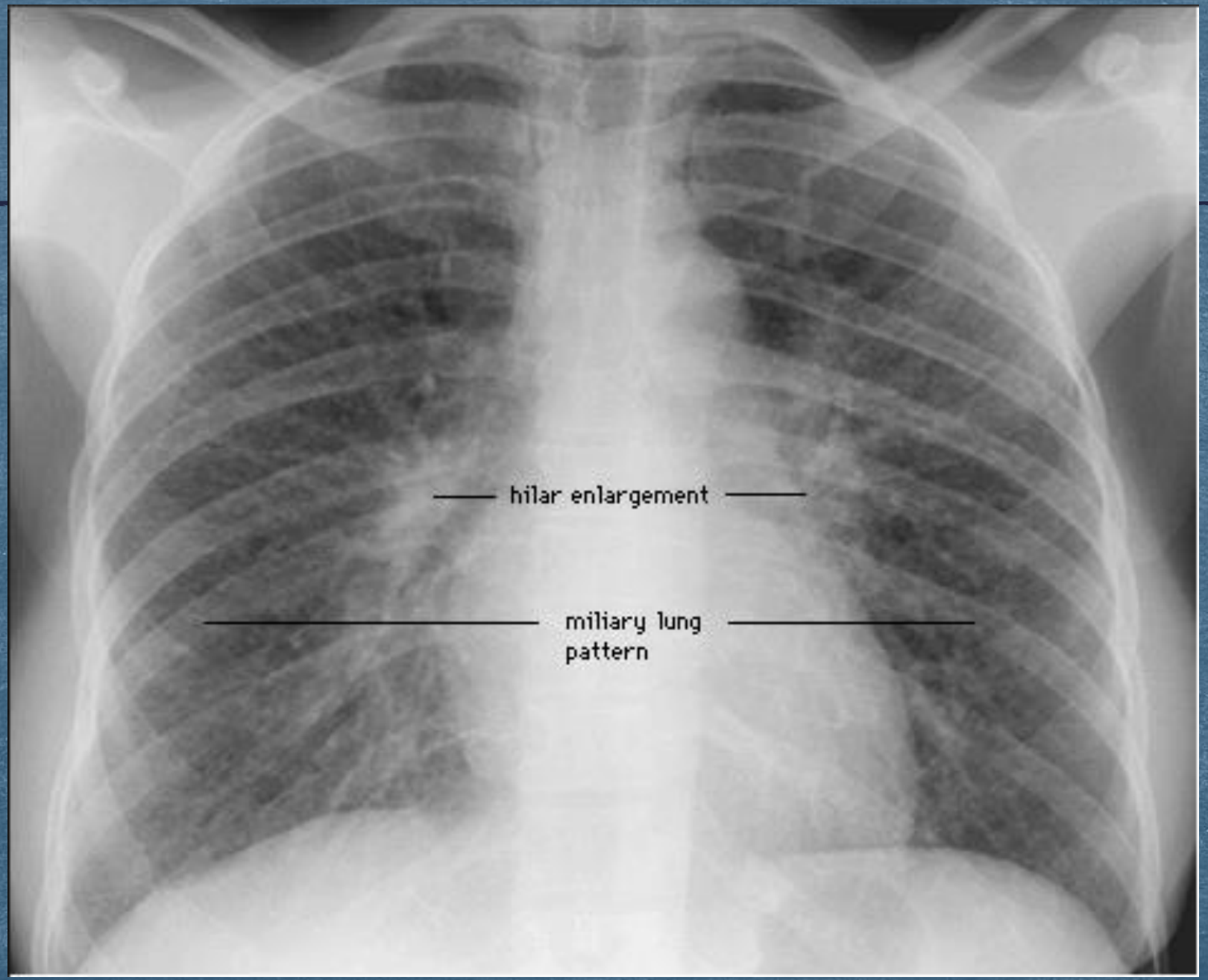




# Sarcoidosis

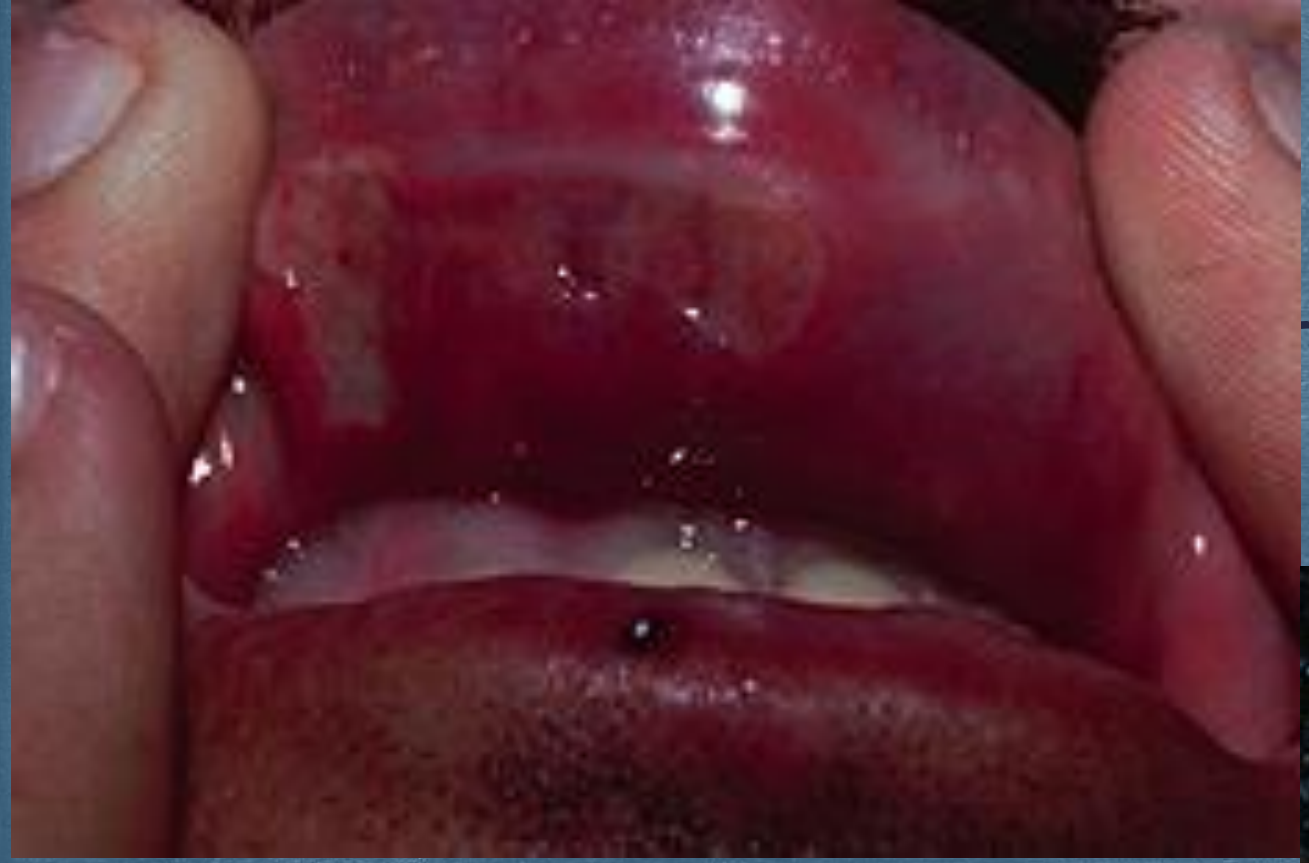
- Diagnosis
- treatment

| Clinical Manifestations of Sarcoidosis | |
|---|---|
| **Organ system** | **Manifestations** |
| **Pulmonary** | Hilar LAN; fibrosis; pulm hypertension. Stages: I = bilat hilar LAN; II = LAN + ILD; III = ILD only; IV = diffuse fibrosis. |
| **Cutaneous** (25–33%) | Waxy skin plaques<br>Lupus pernio (violaceous indurated lesions on face)<br>Erythema nodosum (red tender nodules due to panniculitis, typically on shins). Ddx: idiopathic (34%), infxn (33%, strep, TB), sarcoid (22%), drugs (OCP, PCNs), vasculitis (Behçet's), IBD, lymphoma. |
| **Ocular** (25–80%) | Anterior > posterior uveitis; ↑ lacrimal gland |
| Endo & renal (10%) | Nephrolithiasis, hypercalcemia (10%), hypercalciuria (40%)<br>Due to vitamin D hydroxylation by Mϕ |
| Neuro (10% clin, 25% path) | CN VII palsy, periph neuropathies, CNS lesions, seizures |
| Cardiac (5% clin, 25% path) | Conduction block, VT, CMP |
| Liver, spleen, BM | Granulomatous hepatitis (25%), splenic & BM gran. (50%) |
| Constitutional | Fever, night sweats, anorexia & wt loss (a/w hepatic path) |
| Musculoskeletal | Arthralgias, periarticular swelling, bone cysts |


hilar enlargement
miliary lung pattern

# Behcet disease

- **Oral ulcerations**
- **Urogenital lesions**
- **Cutaneous lesions**



# Juvenile chronic arthritis

- Seronegative
- Presents in children, either as a systemic disease with fevers and lymphadenopathy, a pauciarticular or polyarticular arthritis.
- The pauciarticular form has the higher risk of chronic anterior uveitis, particularly if the patient is positive for ANA

- **HISTORY**
- **SIGNS**

**Eye color? Cataract?**

- The anterior uveitis is chronic and usually U. A profound
- visual defect may be discovered **by chance** if the uveitis has resulted in other ocular damage. … usually **ASYMPTOMATIC**!!
- The eye is white (unusual for iritis), but other signs of an anterior uveitis are present.
- Because the uveitis is chronic, cataract may occur and patients may develop glaucoma, either as a result of the uveitis or as a result of the steroid drops used to treat the condition.
- Approximately 70% of cases show bilateral involvement.

## INVESTIGATION

- RF is negative but some patients have a positive ANA

## TREATMENT

- Ocular treatment is as previously outlined.
- Patients may be put on systemic treatment for the joint disease.
- **Screen children with juvenile arthritis regularly for uveitis as they are otherwise asymptomatic unless potentially blinding complications occur.**
- **Glaucoma can be very difficult to treat and if medical treatment fails to control pressure, it may require surgery.**

# Fuchs' heterochromic uveitis

- a rare **chronic uveitis** usually found in young adults.
- The cause is uncertain and there are no systemic associations.

## HISTORY

- The patient does not usually present with a typical history of iritis.
- Blurred vision and floaters may be the initial complaint.

## SIGNS

- A mild anterior uveitis **Glaucoma** occurs to a lesser extent
- KPs
- Vitreous body cells
- Cataract in 70%

## TREATMENT

- **Steroids are not effective** in controlling the inflammation and are thus not prescribed.
- The patients usually respond well to cataract surgery when it is required.
- The glaucoma is treated conventionally

# Toxoplasmosis

## HISTORY

- Congenital vs acquired
- The patient may complain of hazy vision, floaters, and the eye may be red and painful
- Most ocular toxoplasmosis was thought to be congenital with the resulting retinochoroiditis being reactivated in adult life.
- However, there is now evidence that it is often acquired during a glandular fever-like illness.

## SIGNS

- The **retina** is the principal structure involved with secondary inflammation

such scars are usually atrophic, with a pigmented edge

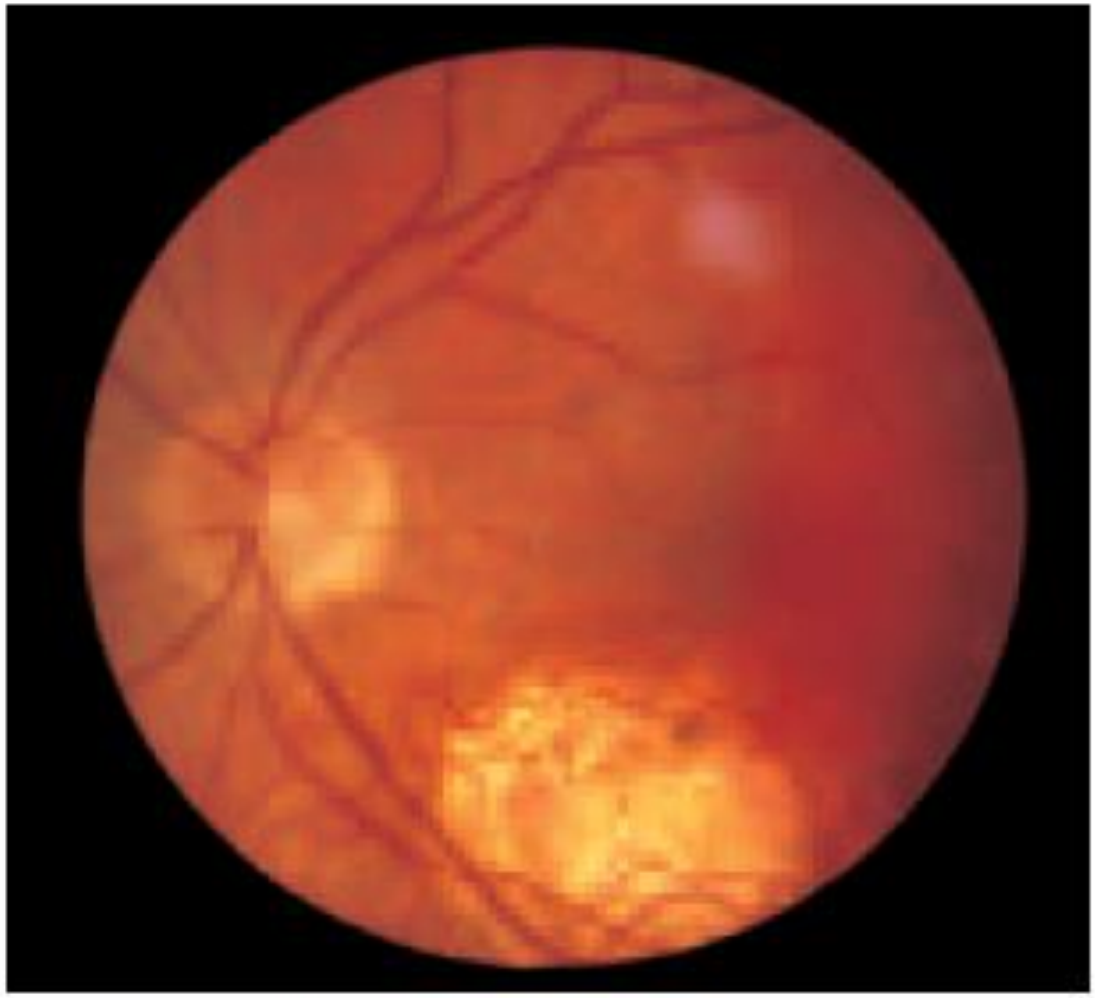
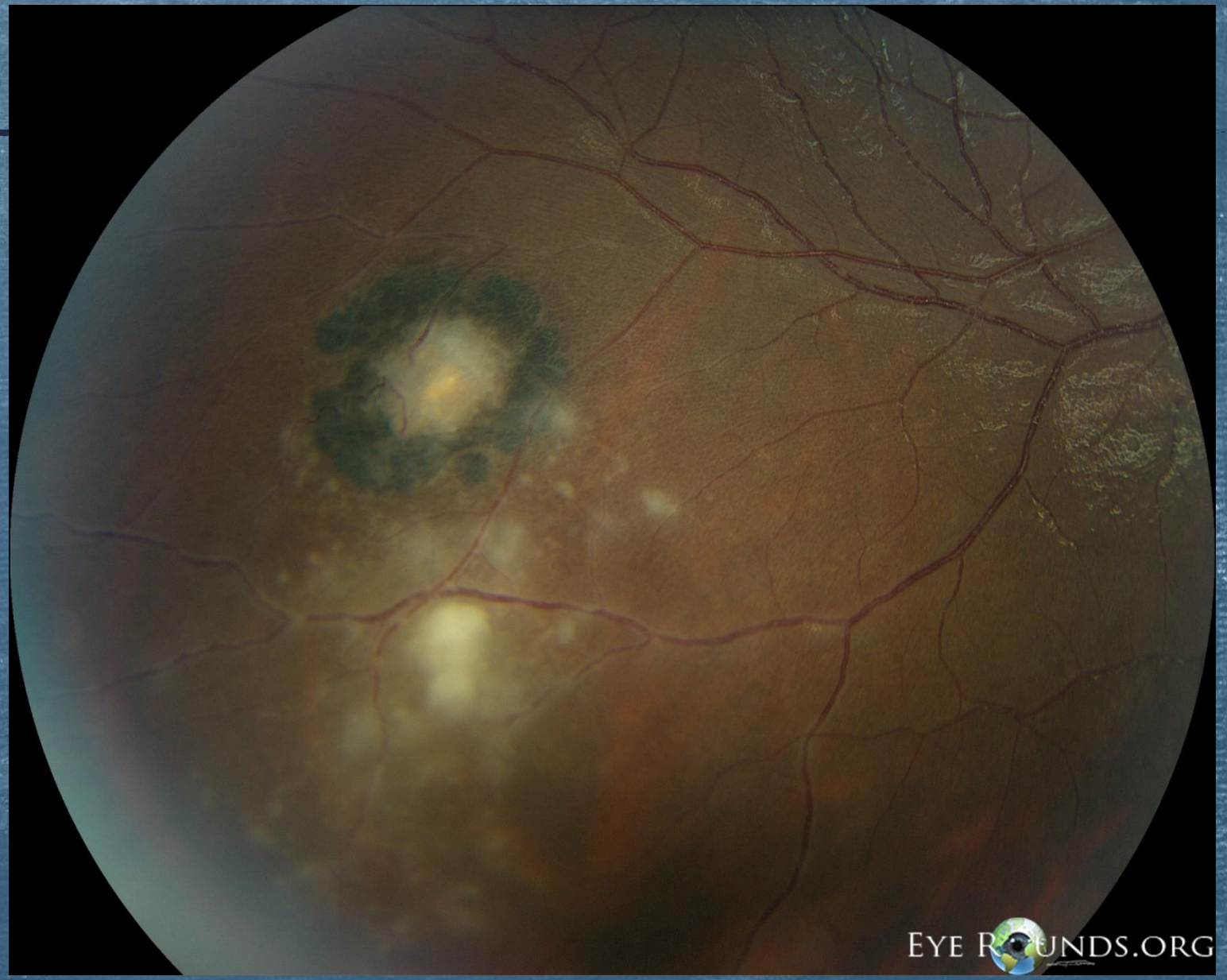


**Fig. 9.3** The appearance of an inactive toxoplasma retinitis.

An active lesion is often located at the posterior pole, appearing as a creamy focus of inflammatory cells at the margin of an old chorioretinal scar (such scars are usually atrophic, with a pigmented edge). Inflammatory cells cause a vitreous haze and the anterior chamber may also show evidence of inflammation



## INVESTIGATION

- The clinical appearance is usually diagnostic but a positive toxoplasma AB test is suggestive.
- However, a high percentage of the population have positive IgG titres due to prior infection.

## TREATMENT

- The reactivated lesions will subside but treatment is required if the macula or optic nerve is threatened or if the inflammatory response is very severe.

- Systemic steroids are administered with an antiprotozoal drugs such as clindamycin and sulphadiazenes

# Acquired immunodeficiency syndrome (AIDS) & CMV retinitis

- Ocular disease is a **common** manifestation of AIDS
- Patients develop a variety of ocular conditions:
  - **Microvascular occlusion** causing retinal haemorrhages and cotton wool spots (infarcted areas of the nerve fibre layer of the retina
  - **Corneal endothelial deposits;**
  - **Neoplasms** of the eye and orbit;
  - Neuro-ophthalmic disorders including **oculomotor palsies;**
  - **Opportunistic infections** of which the most common is **CMV retinitis,**

## Opportunistic infections

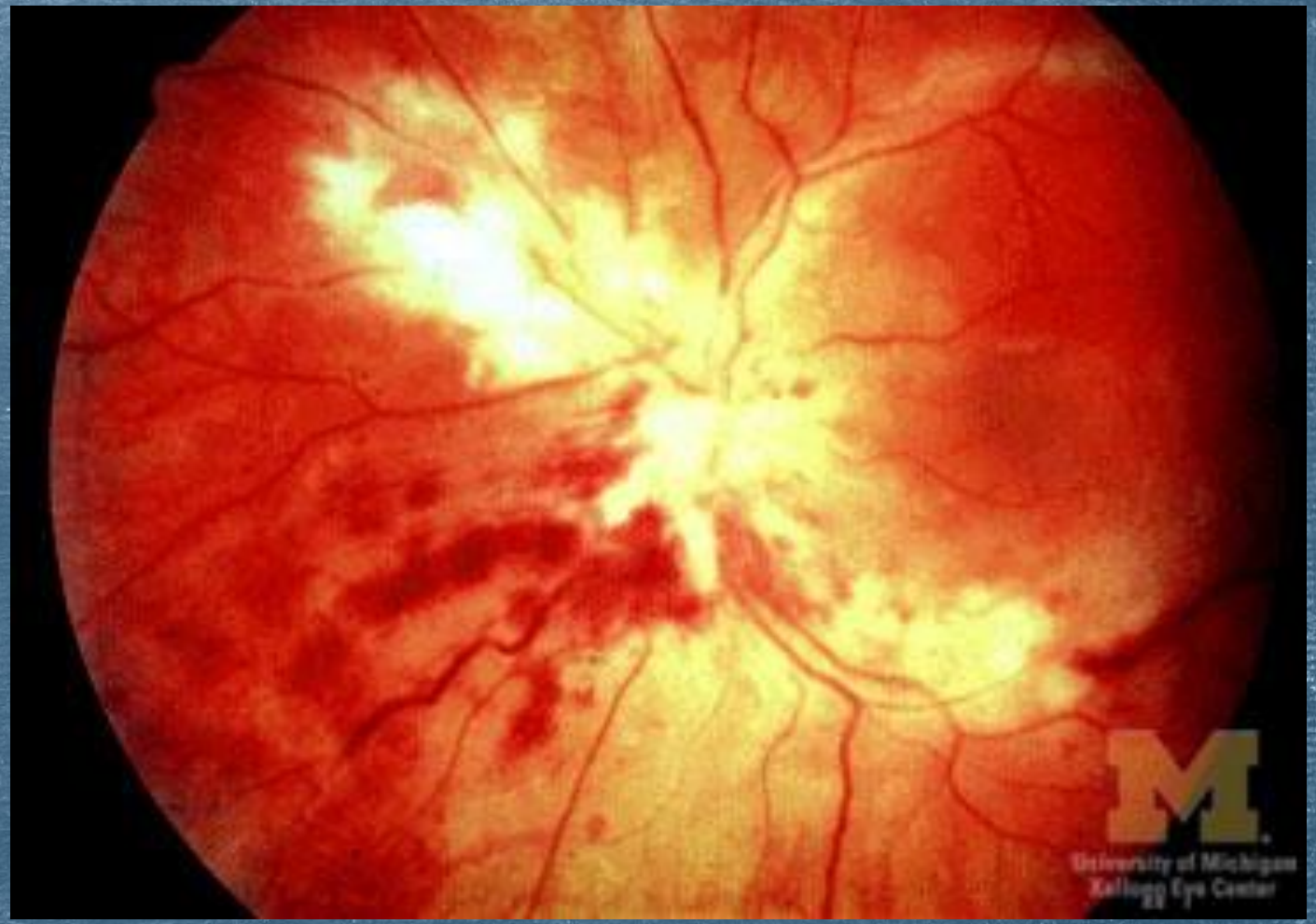
- CMV . Toxoplasmosis, herpes simplex and herpes zoster
- CD 4+ <50/ml
- more than 1/3 of AIDS pts
- HAART introduction effect

## HISTORY

- The patient may complain of blurred vision or floaters.  >>> RETINITIS

- A diagnosis of HIV disease has usually already been made, often other AIDS defining features have occurred.

You are looking at a mixture of **cotton wool spots, infiltrates, and hemorrhages**. This combination spells death for the retina. The **virus gets into the vascular endothelium, closes off blood vessels, and spreads through tissue like wildfire. The entire retina can be destroyed within weeks.This** is a moderately advanced stage. The earliest sign may be a cotton wool spot. This presents a diagnostic problem, because cotton wool spots are also a non-infectious sign of microvascular occlusion in early HIV disease. Still, any severely immunocompromised patient who develops a cotton wool spot must be presumed to have early CMV retinitis and watched carefully.
CMV retinitis may also start in the retinal periphery with infiltrates and vitreous floaters.



## TREATMENT

- Parenteral Ganciclovir or foscarnet
- Cidofivir is available for intravenous administration.
- Ganciclovir and its prodrug valganciclovir are available orally.

## PROGNOSIS

- Prolonged treatment is required to prevent recurrence

# SYMPATHETIC OPHTHALMITIS

- Mechanism
- Treatment