Uveal Tract

Out-lines:

1 Anatomy and physiology of uveal tract.

2 Uveitis nomenclatures.

3 Approach to patient with uveitis.

4 treatment and complications.

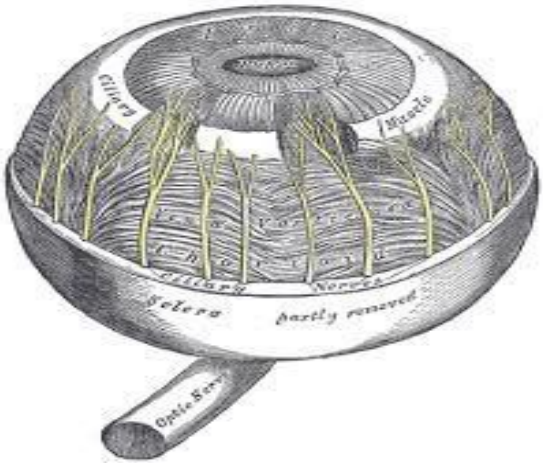
Anatomy and physiology:

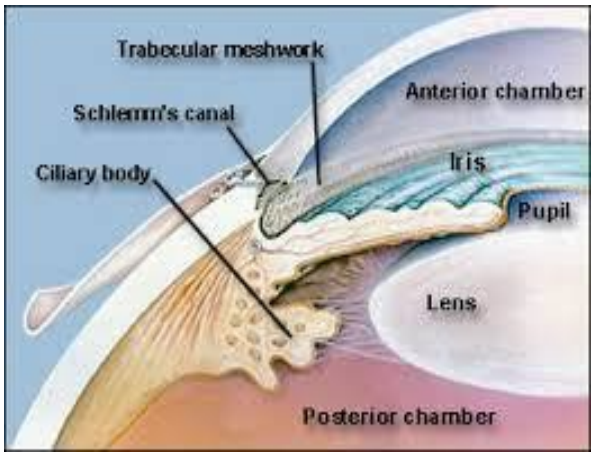
Uveal tract / **Anatomy**

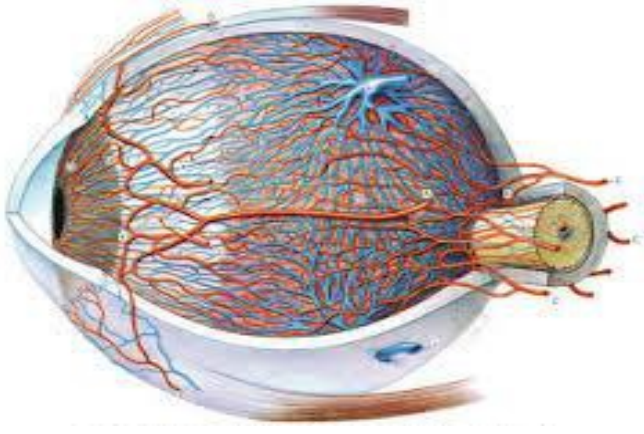
1 Iris.

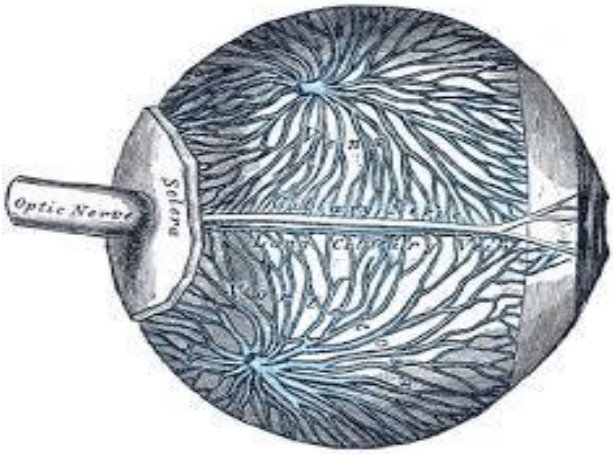
2 Ciliary body.

3 Choroid.



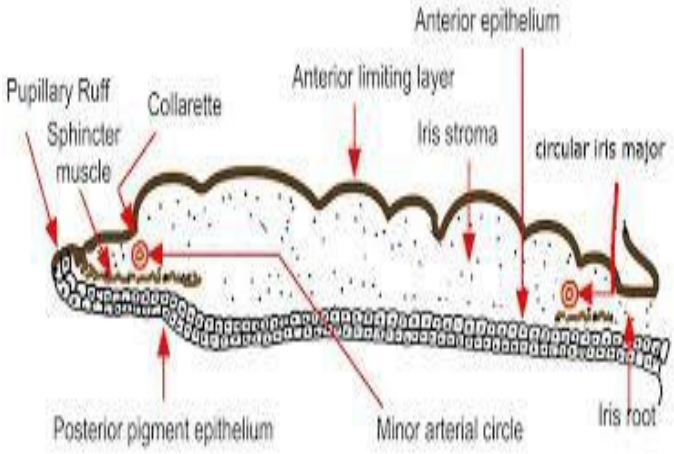


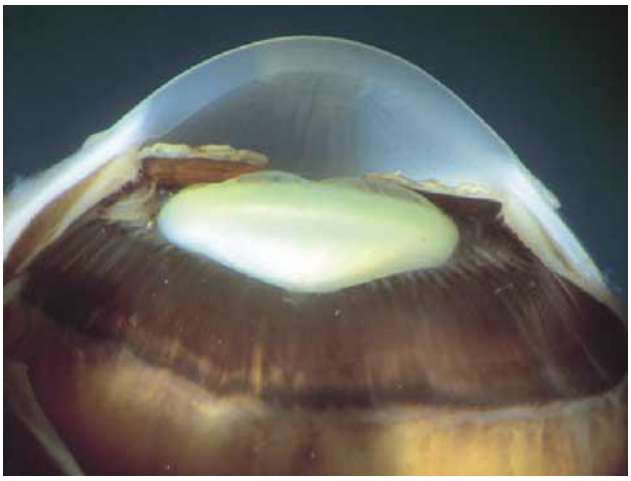




Arterial system: Long and short ciliary arteries

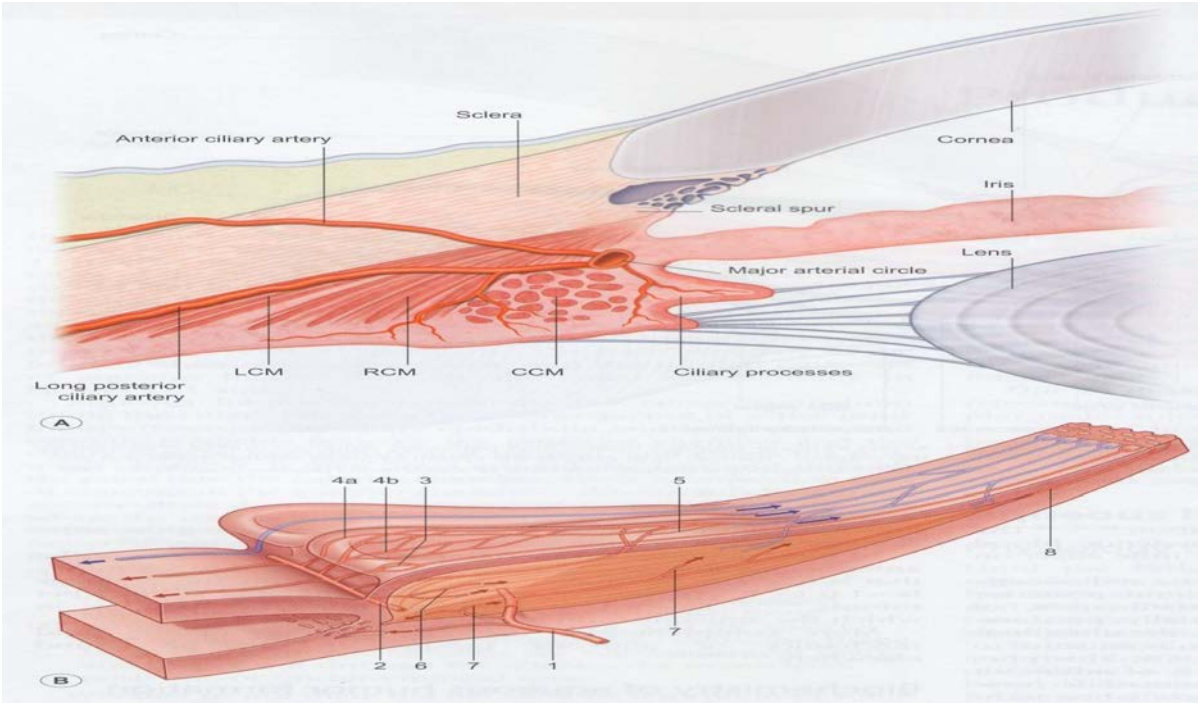
Venous system: vortex veins

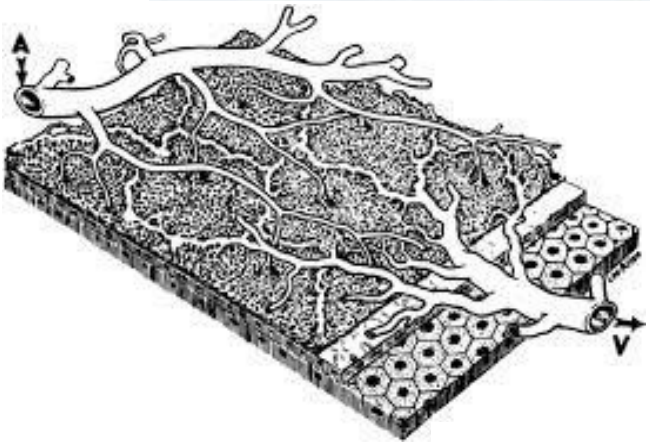




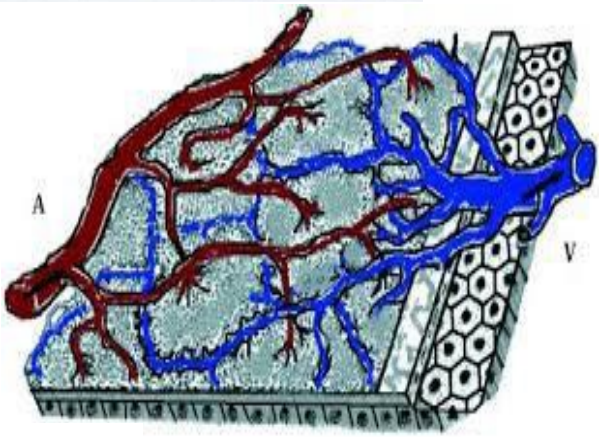
Iris

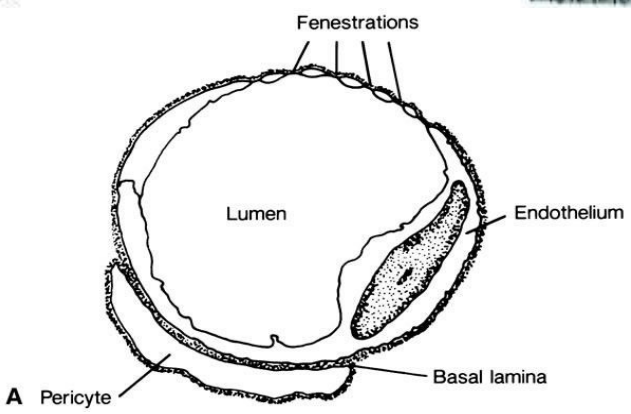
Blood supply of uveal tissue:





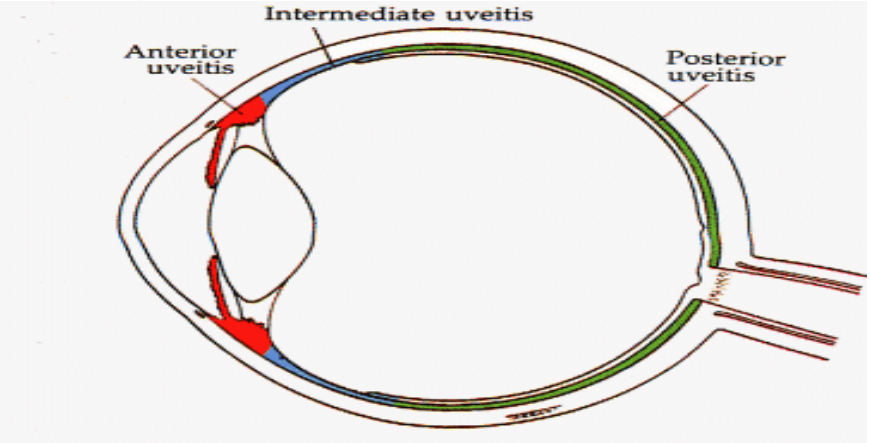
Choroid





Uveitis:

- The uvea is the intermediate vascular layer of the eye which comprise the iris, ciliary body and choroid.
- Uveitis: inflammation of uveal tract.
- The term uveitis refers to a group of inflammatory disorders affecting the uvea, the middle layer of the eye. Endogenous or associated with a systemic disease, noninfectious uveitis accounts for approximately 75% of total cases comprising of a heterogeneous group of inflammatory conditions. The incidence of uveitis in the general population is between 17 and 52 cases per 100,000 habitant per year with prevalence of 0.1%. People aged 20-50 years are commonly affected. Uveitis are responsible for about 10% of legal blindness in developed nations, and are more than 35% of patients with uveitis represent significant visual loss in at least one eye. These data reveal the magnitude of the epidemiologic, diagnostic, and therapeutic problem posed by the uveitis, as well as healthcare cost generated. So, both for diagnosis and, especially, for the proper treatment, close cooperation between ophthalmologist, rheumatologist and general practitioners are required in order to correctly classify the pattern of uveitis and associated co-morbidities to establish the most appropriate therapeutic scheme.
- Anterior uveitis: subdivided into iritis and iridocyclitis.
- Intermediate uveitis: inflammation predominantly involving the vitreous.
- Posterior uveitis: involve funds posterior to the vitreous base.
- Panuveitis: entire uveal tract inflammation.
- Panophthalmitis: involve entire globe with orbital extention.
- Uveitis may be acute,incidoius, limited or persistant. The coarse may be acute, recurrent or chronic if it is more than 3 months.



Approach to patient with uveitis:

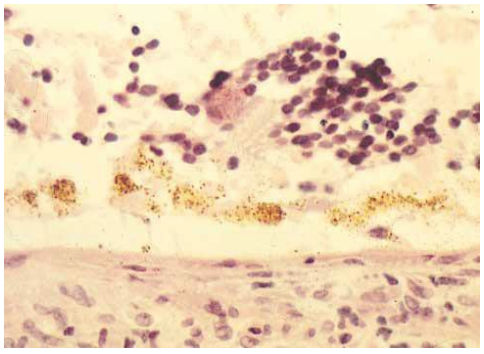
1 History.

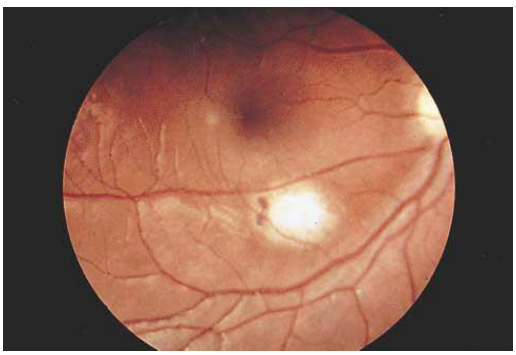
2 Investigations.

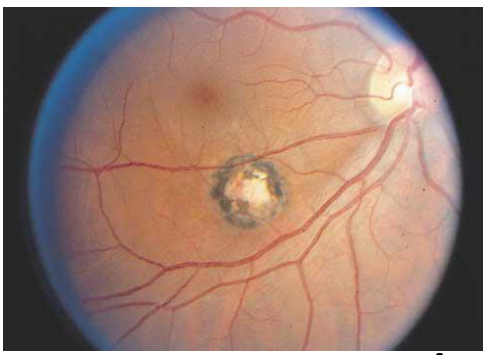
3 Treatment.

History:

- Age of presentation is very important, e.g. uveitis associated with juvenile idiopathic arthritis (JIA) is typically affects children.
- HLA B27 associated uveitis and Behcet syndrome usually affect young adults.
- Sepiginous choroditis affect 5^{th}-7^{th} decade of life.
- Past ocular history e.g. previous ocular trauma would point to sympathetic ophthalmia.
- Past medical history: exposure to infectious agent e.g. Tuberculosis and syphilis.
- History of raring pits: in toxoplasmosis.
- Toxoplasmosis may affect any age group.
- Hygiene and dietary habits: e.g. toxoplasmosis (uncooked meat).







Investigations:

- Generally not necessary in single attack if:

➢ Mild unilateral acute anterior uveitis without suggestion of possible underlying cause.

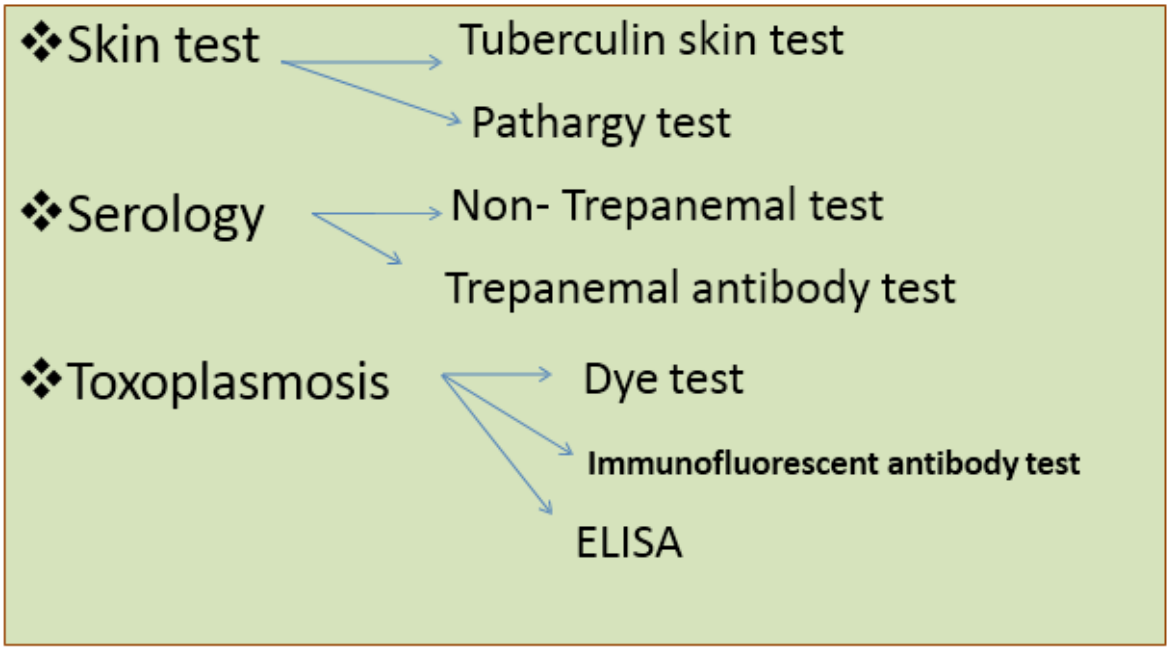
➢ Specific Uveitis entities e.g. sympathetic ophthalmia.

➢ When systemic diagnosis compatible with Uveitis

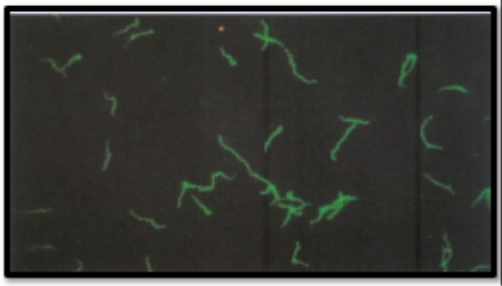
➢ **Indications for investigation:**

1. Recurrent granulomatous anterior uveitis.
2. Bilateral case.
3. Systemic manifestations without specific diagnosis.
4. Confirmation of suspected ocular picture.

➢ **Investigations:**

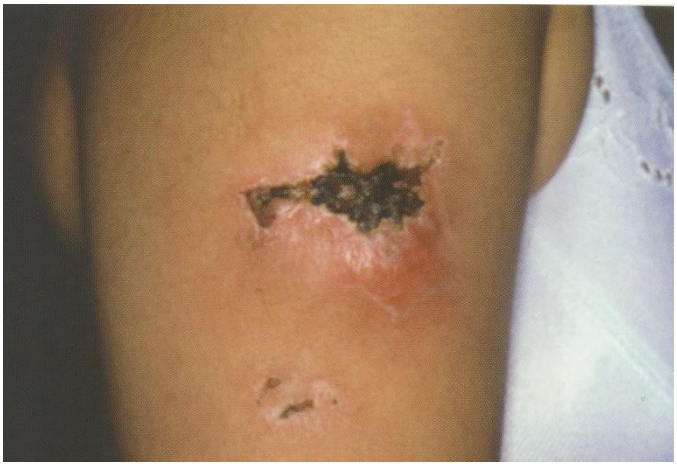


Serology for syphilis

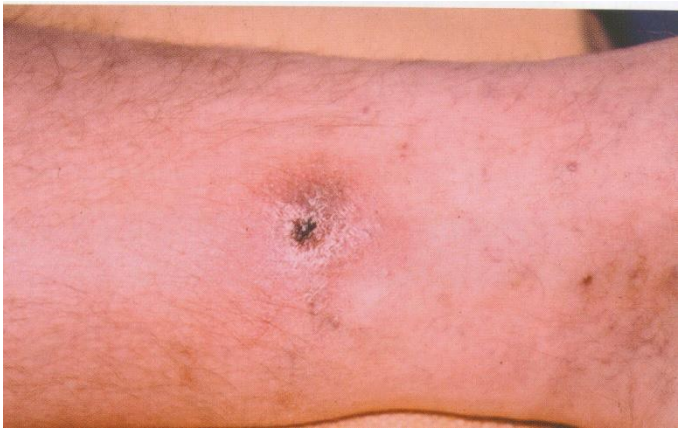


- Non- Trepanemal test
- Trepanemal antibody test

Investigations: Skin tests

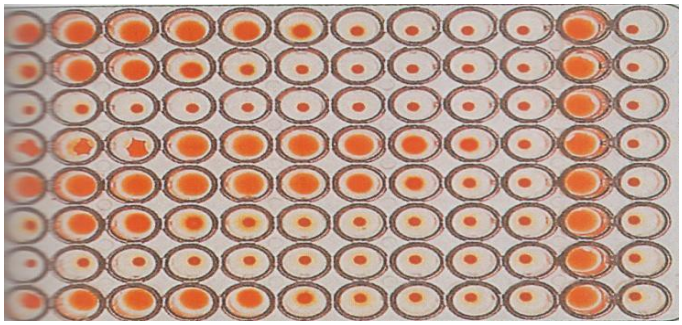


❖ **Tuberculin skin test**

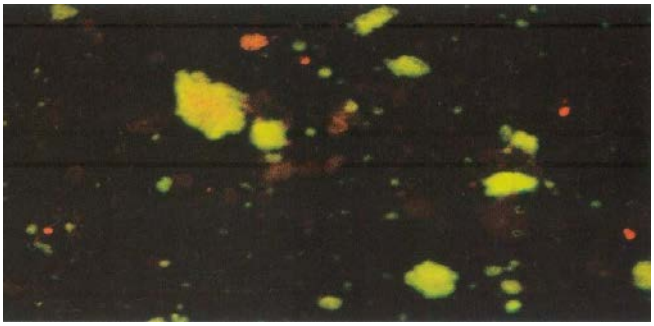


❖ **Pathargy test**

Serology: for toxoplasmosis

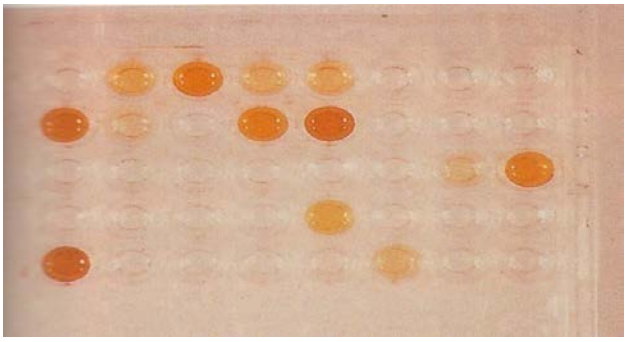


❖ **Dye test**



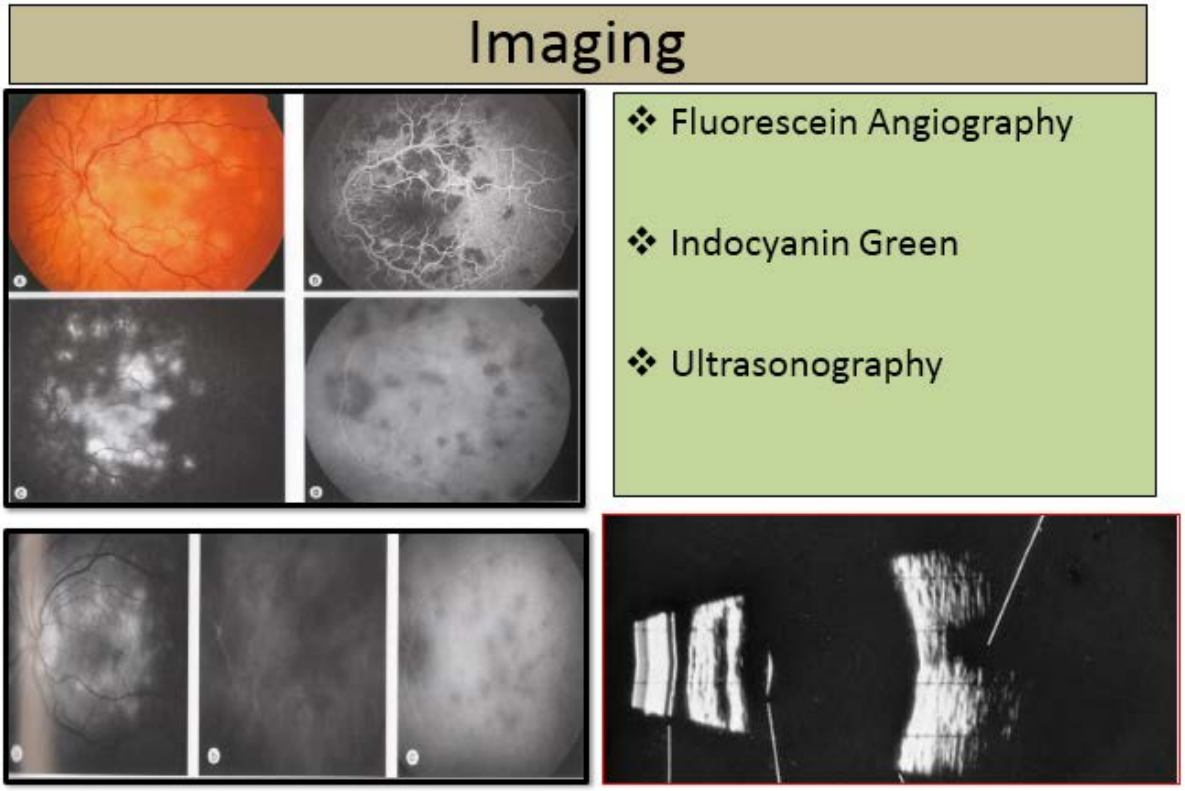
❖ **Immunofluorescent antibody test**

❖ **ELISA**



- ❖ HLA tissue typing
- ❖ Imaging:
  - o Flurescein Angiography
  - o Indocyanin Green
  - o Ultrasonography

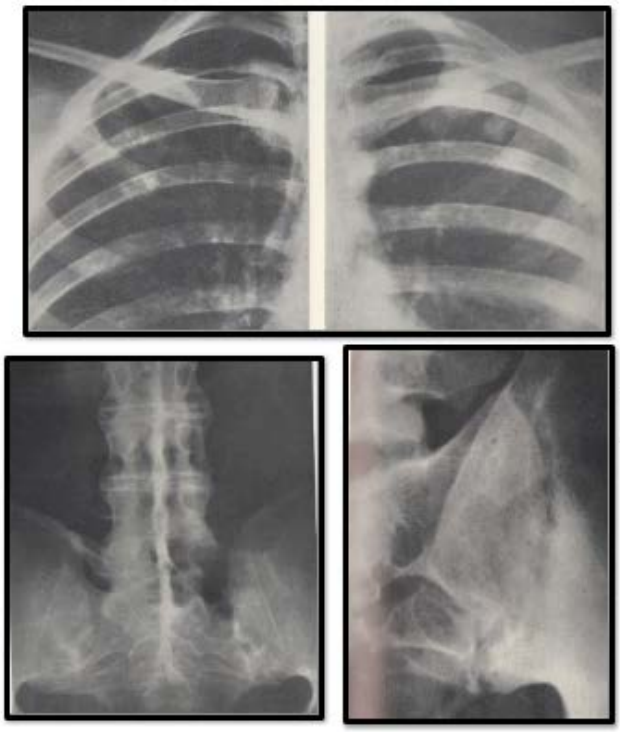
- ❖ **Biopsy:**
  - o conjunctival and lacrimal gland for Sarcoidosis.
  - o Aqueous sample with PCR for viral retinitis.
  - o Vitreous biopsy for endophthalmitis & intraocular Lymphoma



- ❖ Retinal and choroidal biopsy
- ❖ Radiology: chest X-ray, T.B and sarcoidosis Sacroiliac joint, spondyloarthropathy CT and MRI of brain and thorax.
- ❖ Antinuclear antibody (ANA)for JIA.

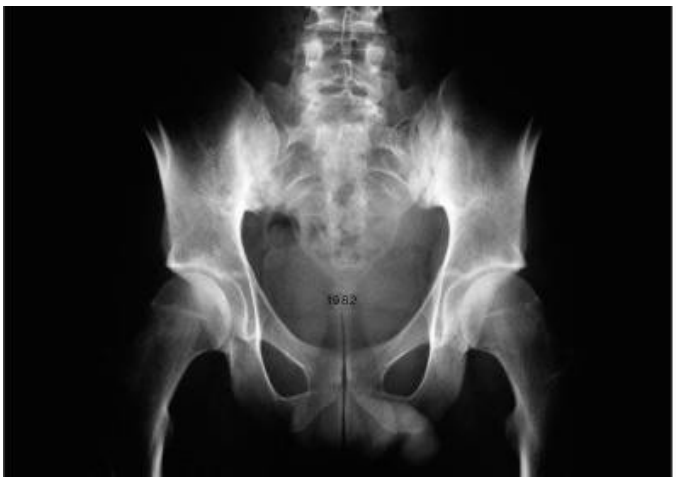
❖ Enzyme assay → Angiotensin converting enzyme(ACE),for sarcoidosis,T.B & leprosy.
→ lysosomes for sarcoidosis

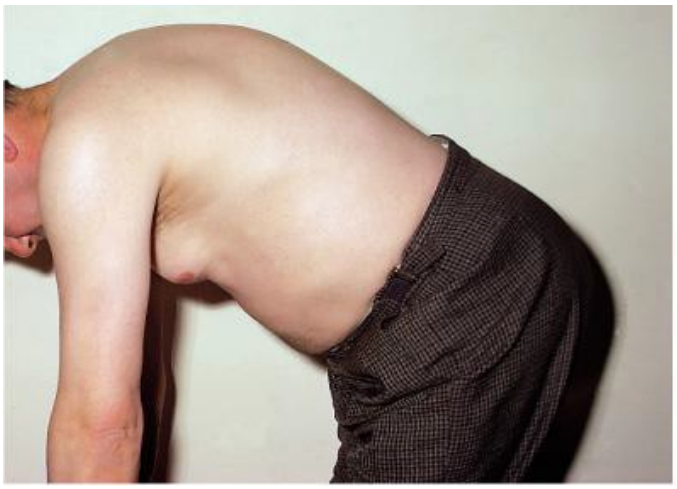
Radiology:



- chest X-ray:
  Pulmonary T.B and sarcoidosis
- Sacroiliac joint:
  spondyloarthropathy .
- **CT and MRI of brain and thorax.**

Limitation of lumbo-sacral spine movement:





Acute Anterior uveitis:

- Anterior uveitis is the most common form of uveitis. Acute anterior uveitis (AAU) is the most common form of anterior uveitis, accounting for three-quarters of cases.
- It's easily recognized due to severity of symptoms, which force the patient to seek medical attention.

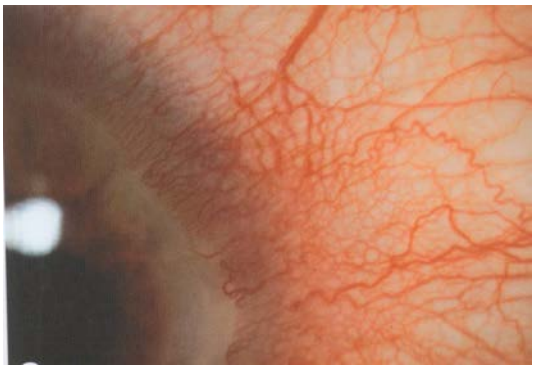
Clinical features:

Symptoms:

- Presentation is typically with sudden onset of unilateral pain, photophobia and redness, which may be associated with lacrimation.
- Acute anterior uveitis (AAU) is the most frequent form and usually requires only topical treatment with steroids and mydriatic. However, it is a cause of disability when flares are frequent or when tends to become chronic.
- Sulphasalazine and methotrexate have demonstrated a reduction in the number of flares and better control of inflammatory activity in cases of chronicity.
- Other patterns of uveitis with involvement of intermediate and posterior segments have a worse prognosis

Signs of uveitis:

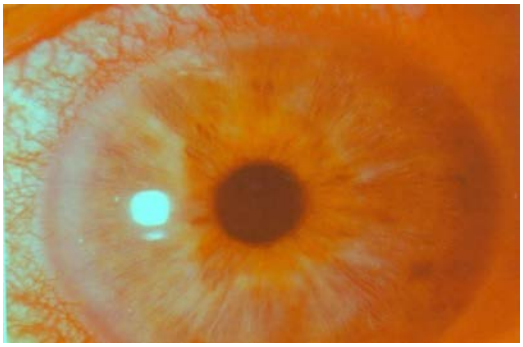
- Visual acuity: is usually good at presentation, except in very severe cases with hypopyon.
- Ciliary (circumcorneal) injection has a violaceous hue.



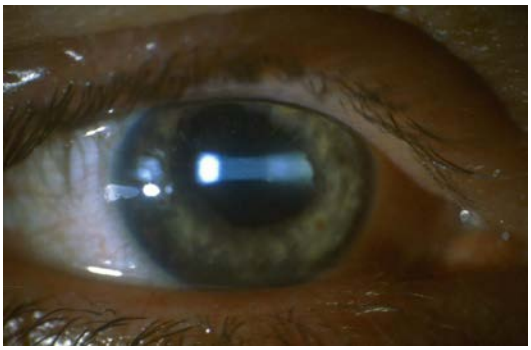
Infectious causes and masquerade syndromes should always be excluded before considering an immune-mediated mechanism, since therapeutic scheme is completely different. Some infectious causes, such as toxoplasmosis, herpes, syphilis and tuberculosis could produce uveitis and, frequently, clinical signs indistinguishable from those produced by immune-mediated uveitis. Some malignancies, especially CNS lymphoma,

can also simulate uveitis, postoperative and drug-induced uveitis must be discarded.

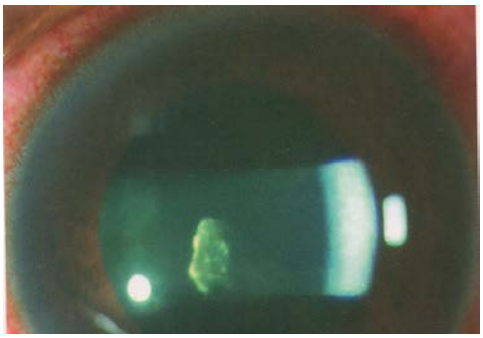
- Miosis due to sphincter spasm may predispose to formation of posterior synechiae unless the pupil is dilated.



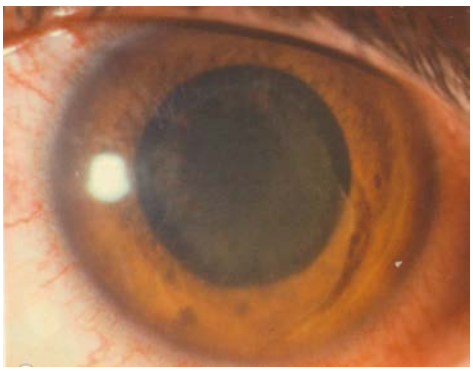
- Aqueous cells indicates disease activity and their number reflects disease severity.



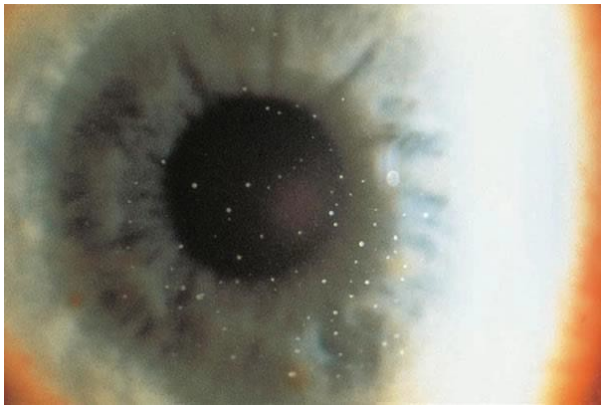
- Anterior vitreous cells indicate iridocyclitis.



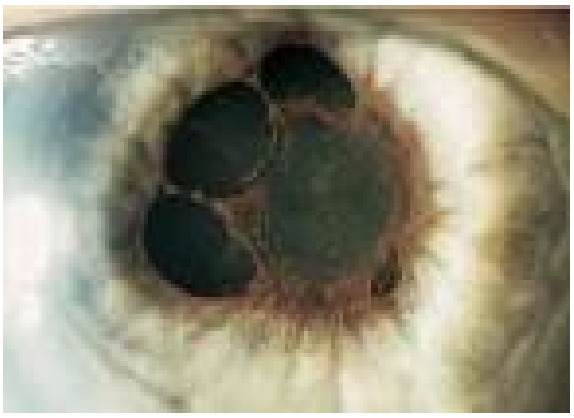
- Aqueous flare reflects the presence of protein due to break down of blood aqueous barrier.

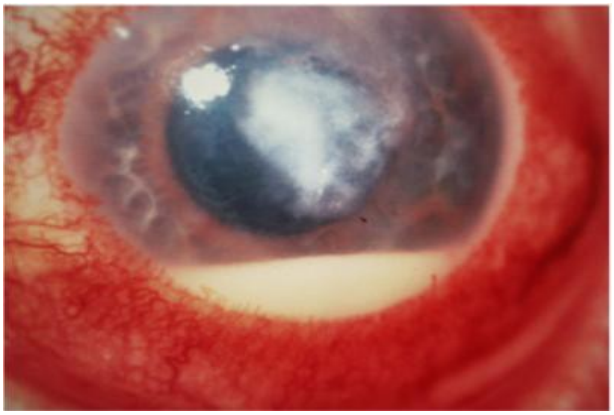


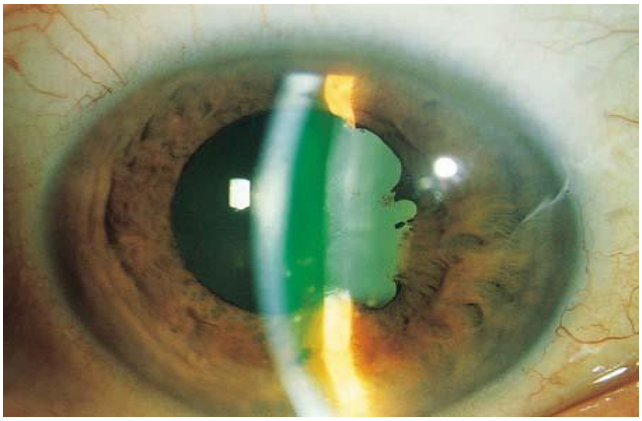
- Endothelial dusting may be myriads of cells is present early and gives rise to a “dirty” appearance and true keratic precipitates usually appears only after a few days and are usually non-granulomatous.



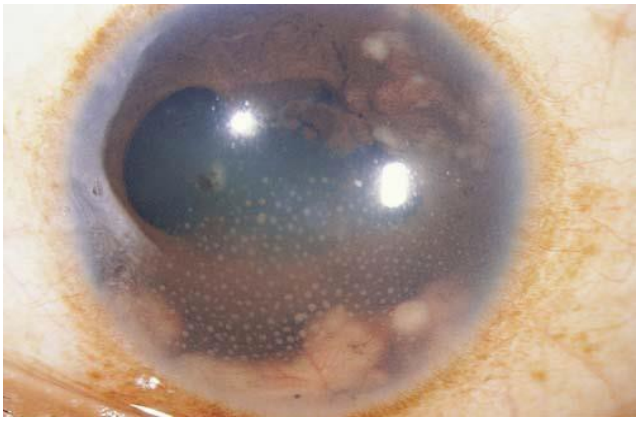
- Hypopyon is a feature of intense inflammation in which the cells settle in the inferior part of anterior chamber and form a horizontal level.
- Dilated iris vessels .
- Posterior synechiae may develop quite quickly and must be broken down before they become permanent.







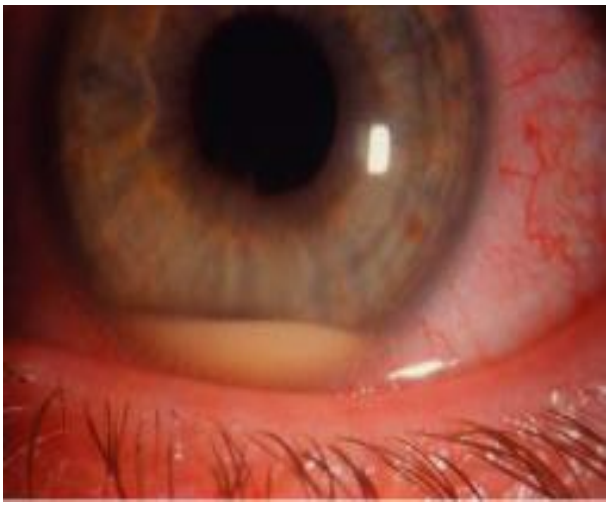
Posterior synechiae



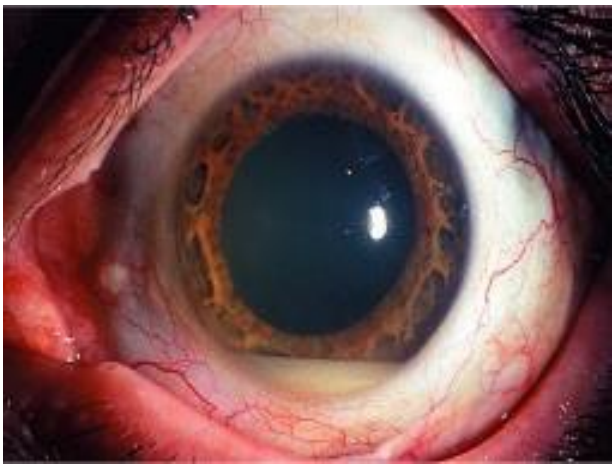
Keratic precipitate

- Low IOP is the rule as a result of reduced secretion of aqueous by ciliary epithelium.

  Occasionally ,the IOP may be elevated (hypertensive uveitis) in herpetic uveitis and toxoplasma retinitis.



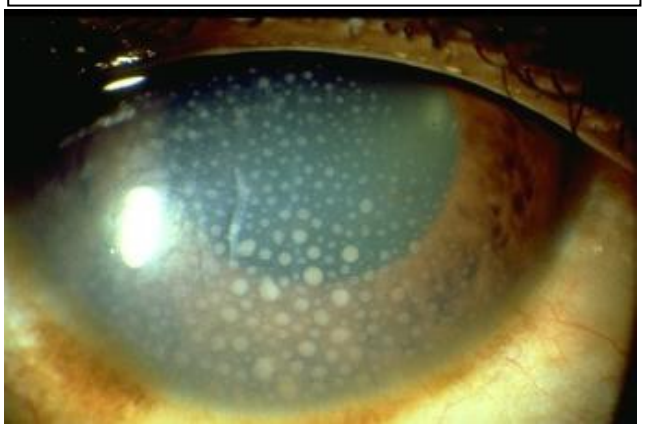
- In AAU associated with HLA-B27,the hypopyon has a high fibrin content which makes it dense, immobile and slow to adsorb.
- In patients with BehÇet syndrome, the hypopyon has minimal fibrin content and there fore shifts according to patient head position and may disappear quickly.

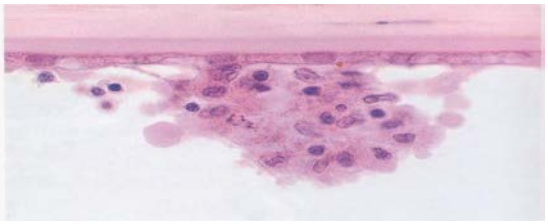


- Hypopyon associated with blood occurs in herpetic infection and in eyes with associated rubeosis iridis.

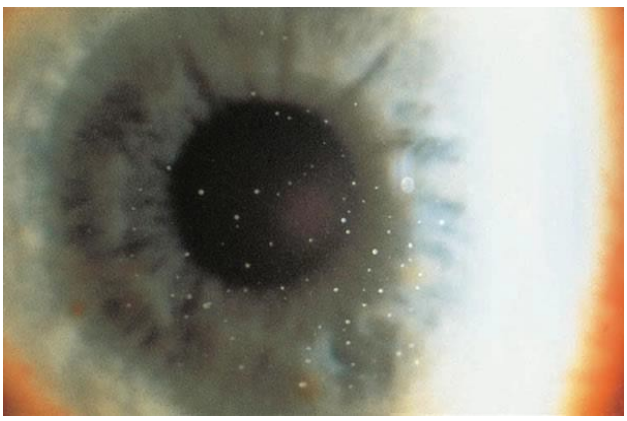
Keratic precipitates KPs:

Granulomatous uveitis Mutton fat KPs





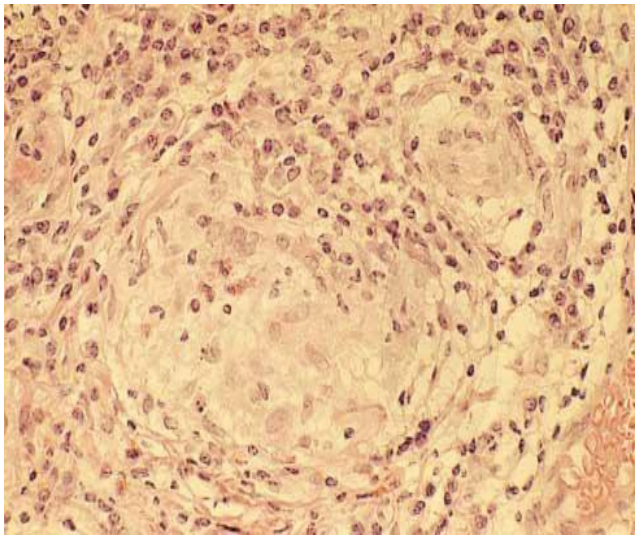
Non-granulomatous uveitis



Granulomatous inflammation:

- **Definition:**

Chronic granulomatous inflammation is a proliferative inflammation characterized by a cellular infiltrate of epithelioid cells (and sometimes inflammatory giant cells, lymphocytes, plasma cells, polymorphonuclear leukocytes (PMNs), and eosinophils.



epithelioid cells in the inflammatory nodules

Granulomatous uveitis:

Causes:

1 Chronic sarcoidosis.

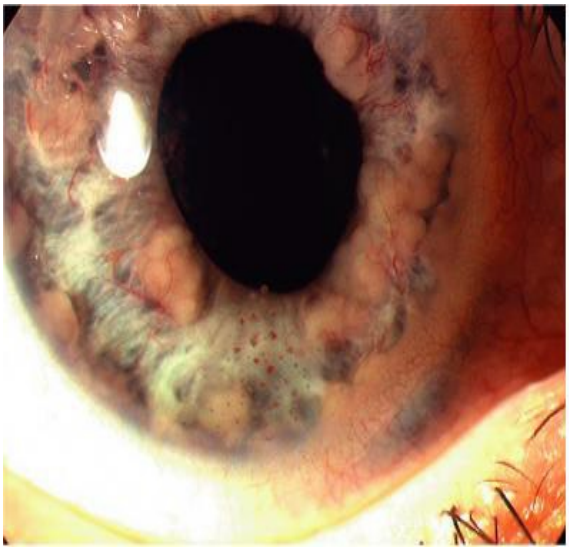
2 Sympathetic ophthalmia.

3 Voket-Koyanaki Harada syndrome.

4 Infection: T.B, syphilis, toxoplasmosis.

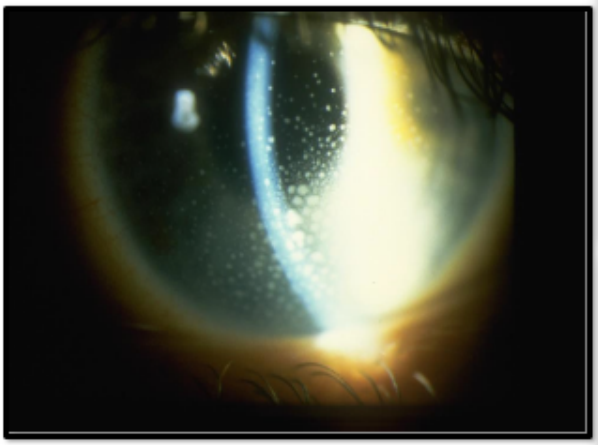
5 phacoantigenic uveitis.

6 Multiple sclerosis.

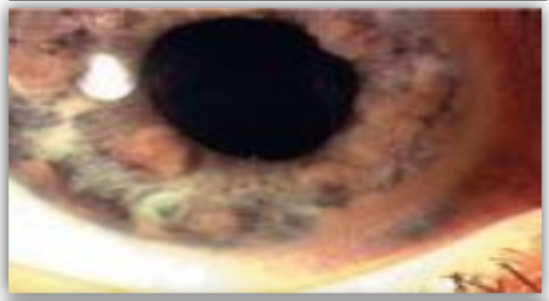


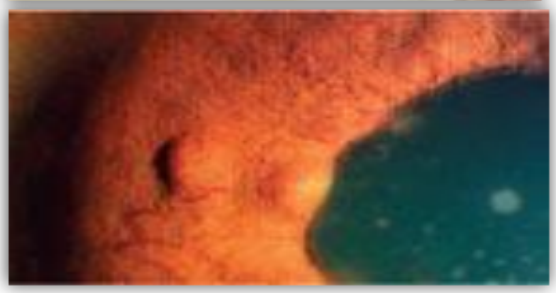
Granulomatous uveitis

Mutton fat keratic precipitates KPs



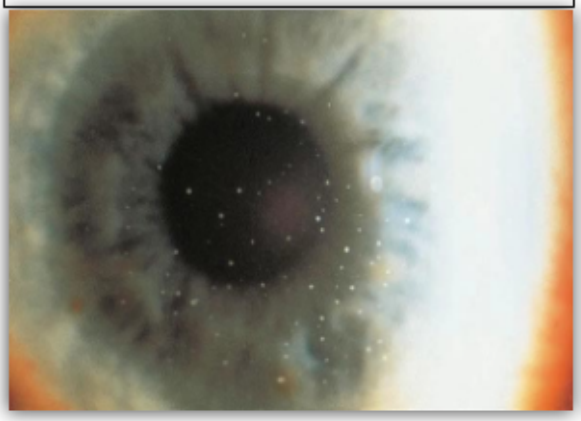
Iris nodules



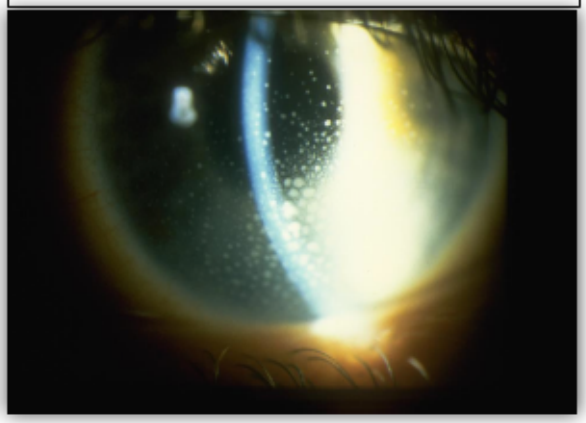


Keratic precipitates KPs

Non-granulomatous uveitis

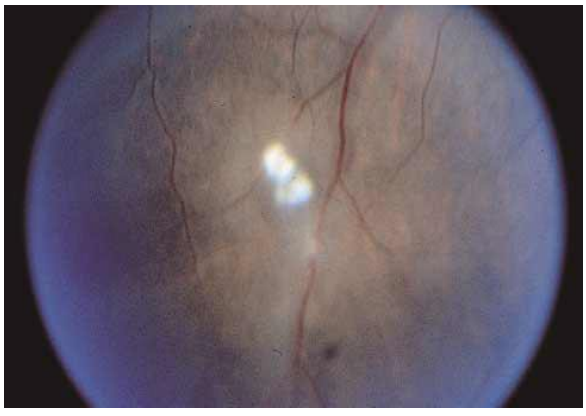


Granulomatous uveitis
Mutton fat KPs

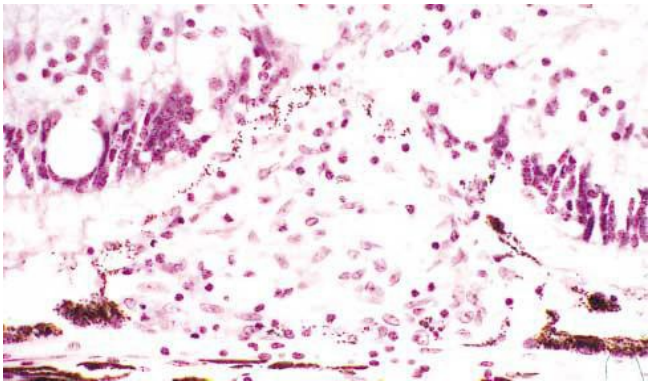


Sarcoidosis:

- Sarcoidosis. **White cellular masses ("balls")** are seen in the vitreous compartment on the surface of the inferior



- neural retina, along with early

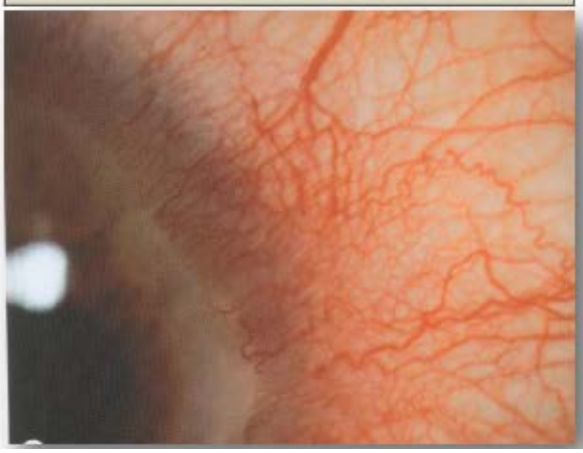


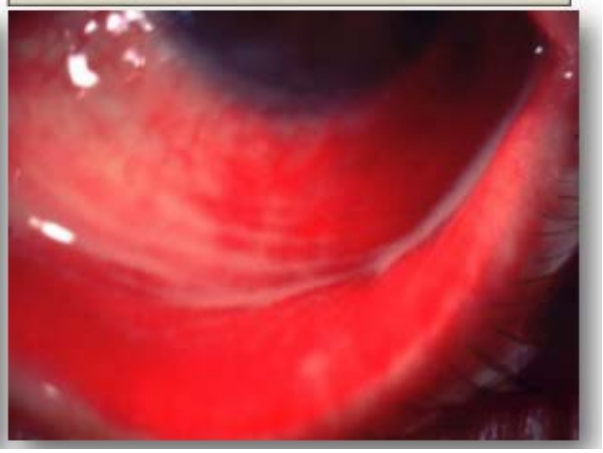
“candle wax drippings.”

- Candle wax drippings are caused by perivascular retinal granulomatous infiltration.
- White balls are caused b y accumulations of granulomatous inflammation in the vitreous.
- large Dalen–Fuchs nodule is seen in this case of sarcoidosis.

What is the difference between conjunctivitis and uveitis?

Iritis: redness maximum at limbus	Conjunctivitis : redness maximum at fornix





Comparison between acute iritis and conjunctivitis

Features	Acute conjunctivitis	Acute Iridocyclitis
• Onset	Gradual	Gradual
• Discharge	Mucopurulant	Watery
• vision	Good	Impaired
• Tenderness	Absent	Marked
• Congestion	superficial conjunctival	Deep ciliary
• Pupil	Normal	Small and irregular
• Media aqueous flare	Clear	Hazy due to
• Area of maximum redness	Fornix	Ciliary (limbal)

Masquerade Syndromes:

- Defined as those conditions that includes, as part of their clinical findings, the presence of intraocular cells but not due to immune- mediated uveitis entities.

Masquerade Syndromes:

- A- Non- neoplastic syndromes
- B- Neoplastic syndromes
- **non-neoplastic Masquerade syndromes:**

1 Retinitis pigmentosa.

2 Ocular ischemic syndrome.

3 Chronic Rhegmatogenous retinal detachment.

4 Intraocular foreign body.

5 Pigment dispersion syndrome.

- **Neoplastic masquerade syndromes:**

1 Primary CNS Lymphoma.

2 Secondary to systemic lymphoma.

3 Secondary to leukemia, Uveal melanoma, Retinoblastoma, Juvenile Xanthogranuloma and metastatic tumors.

General Principles and Treatment Strategies:

- Before starting treatment, a number of consideration should be

taken into account:

1 The majority of patient with uveitis can modify significantly the coarse of their illness if they receive proper early treatment.

2 It is recommended to work in Multi-disciplinary Units to facilitate handling of the drugs used and early detection of side effects.

3 Infectious cause and masquerades syndromes should always be excluded before considering an immune- mediated mechanism.

4 Macular edema is the main cause of vision loss in uveitis patient.

5 Always analyze what is the cause of poor vision in a specific case. Is it reversible? Are there other causes of poor vision,

Treatment:

- Mydriatics (short and long acting):
- To promote comfort.
- To break down recently formed synechiae.
- To prevent formation of posterior synechiae.
- Topical steroid;
- Intensive therapy, once inflammation controlled, gradual therapy.
- Locally injected or systemic corticosteroids and/or immunosuppressive drugs are usually required in sight – threatening immune mediated uveitis with involvement of posterior segment to halt the course of the disease.

Treatment consist in:

1- Phase of induction of remission using high-dose of systemic corticosteroids administered orally or by means of intravenous infusion.

2- Phase of maintenance of the long-term control of inflammatory activity, at this stage, the dose of corticosteroids is gradually reduced until withdrawal, and if necessary immunosuppressant′s are added.

Biological therapies, are promising therapeutic options in refractory patients as a rescue therapy; However, there is clinical

evidence of use of these powerful drugs as first line therapy in selected cases.

Steroids:

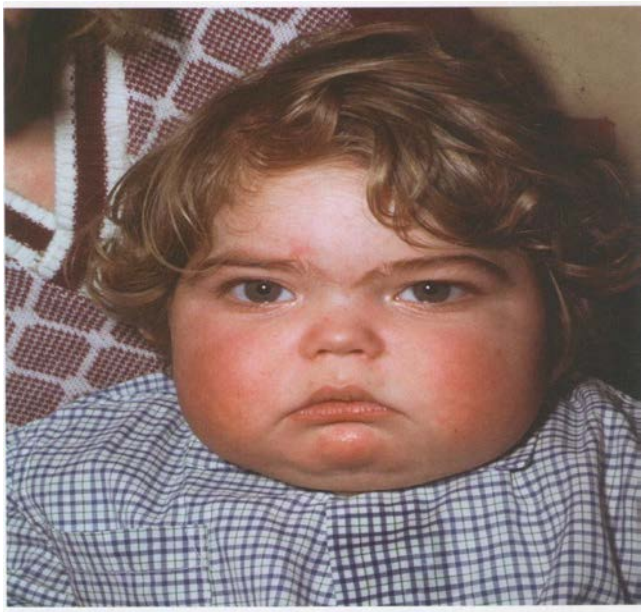
- Systemic steroid.
- Periocular steroids.
- Intraocular steroid.
- Slow release implant.

Due to high efficacy of corticosteroids, it is administered by different routes, are the drugs of choice in the induction of remission. However, in many cases corticosteroids are not enough to sustained control of the inflammation in long term. In other situations, the control of the inflammatory activity is not maintained when trying to reduce the dose of corticosteroids, or side effects of treatment are not tolerable.

In these cases, immunosuppressive treatment for maintenance of remission is necessary. It is necessary to maintain immunosuppression for long time, in order to achieve a stabilization of inflammatory parameters and avoid relapse and new flares.

Multidisciplinary units (ophthalmologist with internist or rheumatologist) have been developed to achieve a close follow-up both at the level of efficacy and early detection of side effects, allowing better management and control of these therapies.

Be aware of steroid side



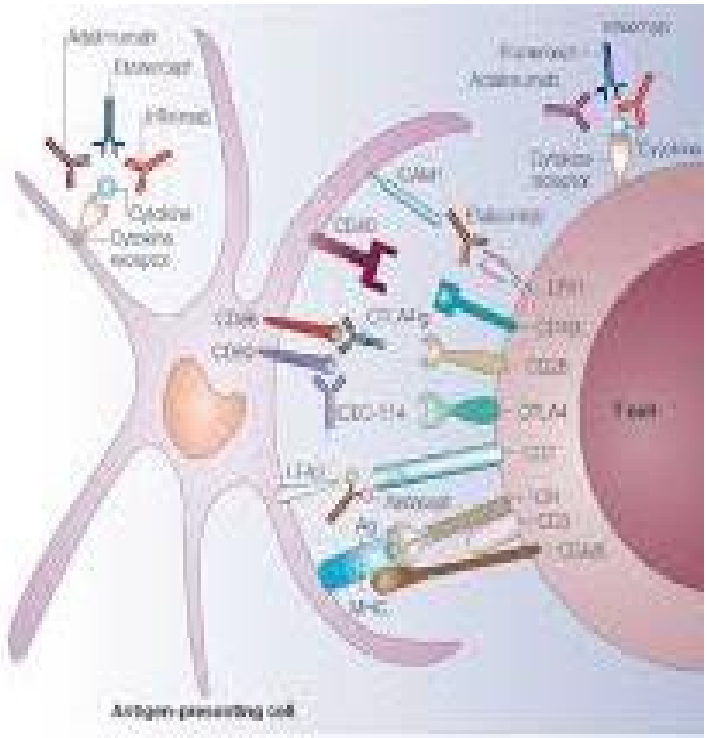
Antimetabolites:

- **Steroid spearing therapy and for sight threatening uveitis.**
- Azathioprine, Methotrexate.

Biological agents

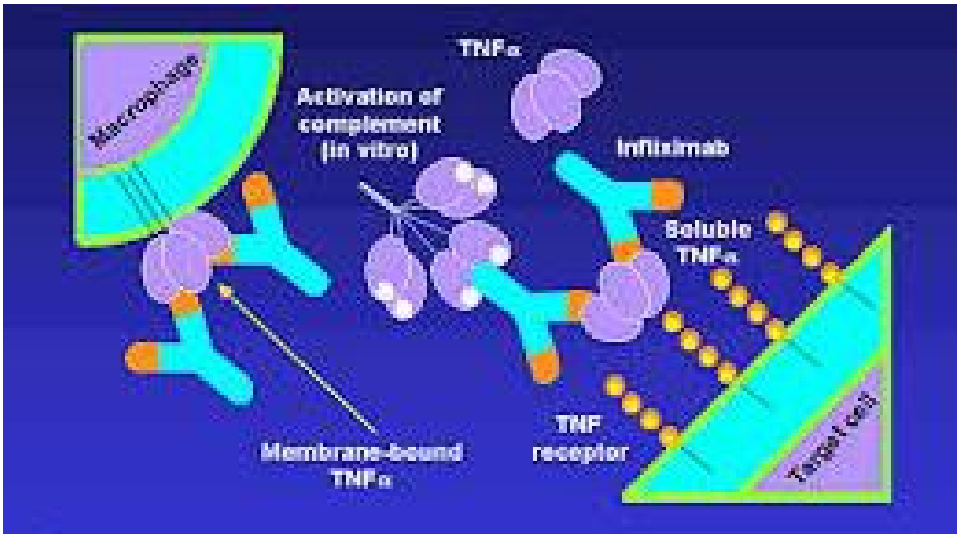
Tumour necrosis factor alpha therapy TNF-α inhibitor.	Potential complications
• **Infliximamb:** 3-10 mg/kg loading dose and then every 4-8 weeks IV. • **Adalimumab:** 40 mg weekly or every 2 weeks SQ. • **Etanercept:** 25 mg twice a week or 50 mg once a week SQ.	• Infusion reaction (Infliximamb only). • increased risk of serious infections(including TB). • Malignancy/lymphoproliferative/ lupus like syndrome. • Congestive heart failure • Headache • Rash. • GI upset.

Immune modulation



TNF-α and its receptors

Infliximamb

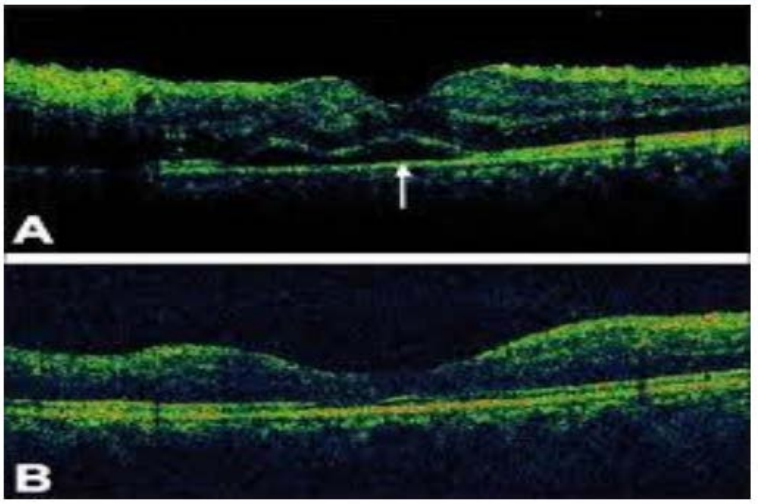


Infliximamb given as infusion IV

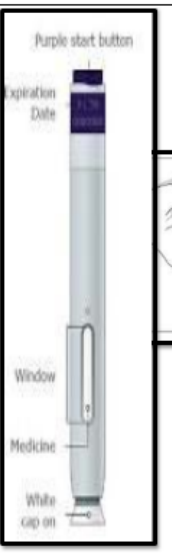
OCT: macular edema

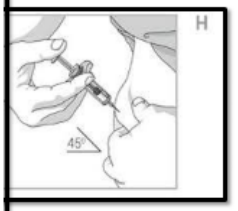
A: before injection.

B: After injection.

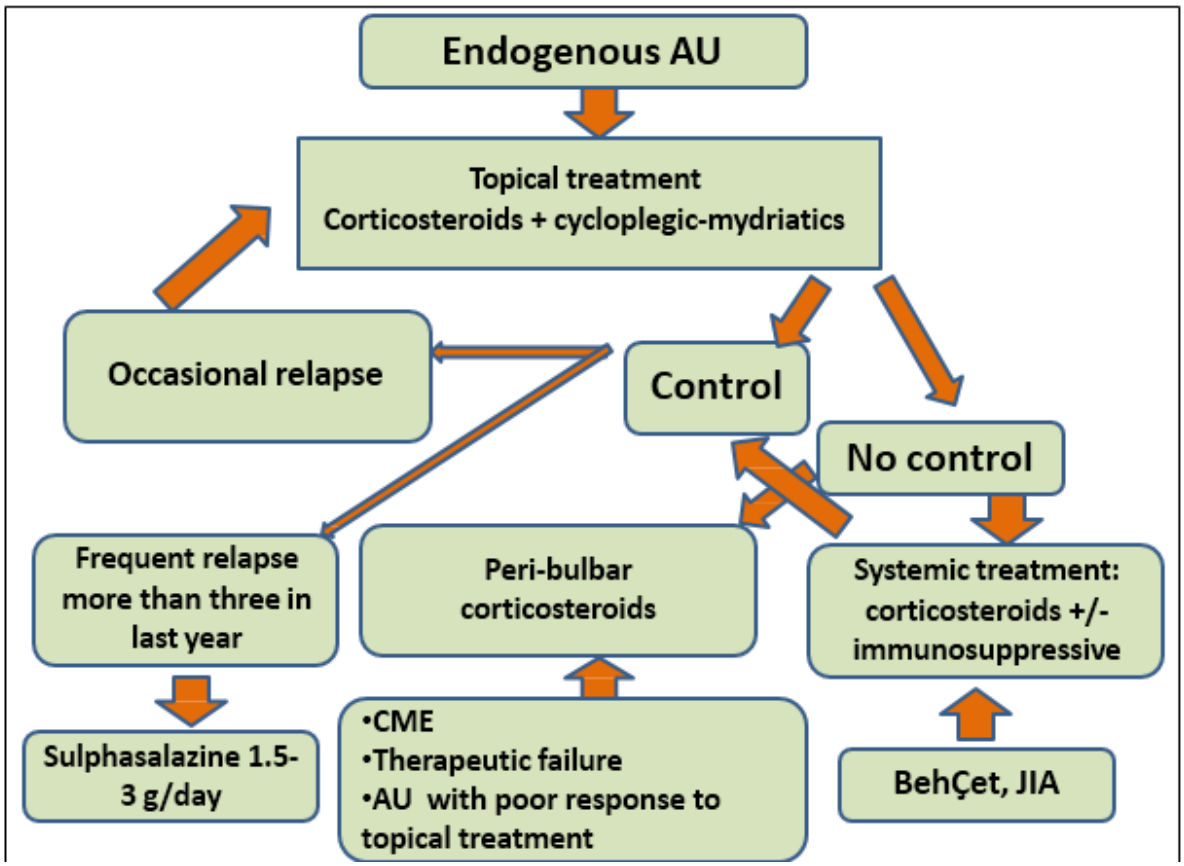


Adalimumab

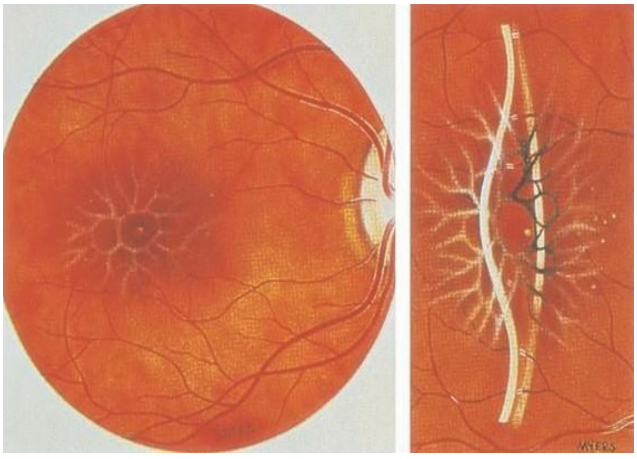




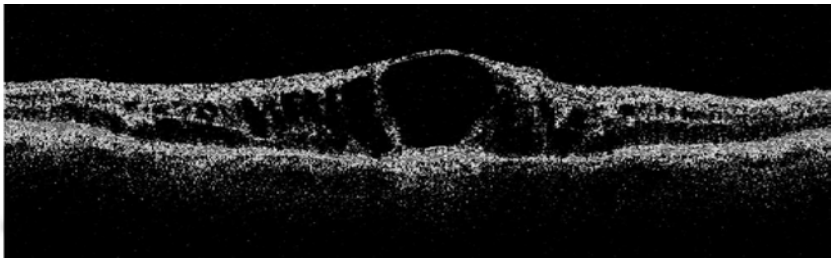
Therapeutic algorithm in Endogenous anterior uveitis



Complications of uveitis Cystoid macular edema (CME):



- Fluid accumulation in outer Plexiform and inner nuclear layers of retina with formation of cyst like changes.
- Find out what factors, as well as inflammation, may be influencing the visual loss of the patient and their reversibility.



- There can be co-morbidities such as glaucoma, persistent vitreous opacities, cataract or macular ischemia that have their particular management. It also kept in mind that some lesions are irreversible (macular or optic atrophy, advanced glaucoma…) before starting

immunosuppressive treatment with iatrogenic potential risk in eyes without the possibility of visual recovery.

- The most frequent causes of loss of visual acuity in those with uveitis is **macular edema (ME**). When ME is chronic produces lesions in the retinal photoreceptors, which can potentially be irreversible. For this reason, early and appropriate treatment is essential.
- We must always consider is a general attitude of zero tolerance to inflammation. Sustained inflammation, even in low grade, can cause severe structural damage.