Ocular Manifestation of Systemic diseases

Objectives:

- Not given.

[Color index : Important | Notes | Extra]

Resources: Slides+434team+Notes

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Diabetic Retinopathy:

- DR (Diabetic Retinopathy) is the **most common cause of blindness in the age of 20-65.**
- Systemic diseases involved in Retina can lead to blindness..
- The most common disease that involves the eye (particularly Retina) is DIABETES.
- DM can cause **retinopathy, acute angle closure glaucoma, cataract and III, IV and VI cranial nerve palsy**.
- Most common ocular manifestation is **retinopathy**.
- Almost in all people with type 1 diabetes mellitus. '**Due to early onset**'.
- Microvascular complications correlate significantly with DM.
- Hypertension, obesity and the control of blood sugar are risk factors that could be modified.
- Diabetic retinopathy is most common microvascular complication of DM and can lead to retinal degeneration.
- Because diabetic retinopathy often goes unnoticed until vision loss occurs, people with diabetes should get a comprehensive dilated eye exam at least once a year.
- **Diabetic macular edema is a consequence of diabetic retinopathy that causes swelling in the area of the retina called the macula**.
- Controlling diabetes—by taking medications, staying physically active, and maintaining a healthy diet—can prevent or delay vision loss.
- The only means of preventing blindness due to diabetic retinopathy is through **screening and early treatment.**
- Once the person diagnosed with type 2, they must see an ophthalmologist immediately "because we don't know when did it start". But in Type 1 check after 5 years "because the onset is known".
- The risk of blindness is about 25 times greater in diabetic than in non-diabetics.
- The incidence of Diabetic retinopathy is related more to the **duration of diabetes** than to any other factor.

❖ Ocular Manifestation:

1. **Iris:** Rubeosis iridis (neovascularization in iris) "**May lead to Neovascular glaucoma**"
2. **Lens:** Cataract (Glucose levels affects osmolarity => the lens gets opacified)
3. **Uvea:** Iridocyclitis (another term of uveitis)
4. **Retinopathy**: **Most common one.**
5. **Optic neuropathy.**
6. **3rd, 4th, 6th nerves palsies.**

❖ Risk Factors:

1. **Duration of diabetes:** The longer the duration of diabetes, the more risk of DR.Non-Modifiable risk factor.

   It's well known that after 15-20 years of diabetes, almost all of T1DM will have some sort of retinopathy, and 60% of T2DM will have some sort of retinopathy.

2. **Poor control of diabetes**: Raised HbA1c is associated with an increased risk of PDR (Proliferative diabetic retinopathy).

   Recent studies showed that well controlled diabetes will protect the patient from retinopathy, microvascular diseases, nervous system, and the kidneys. However, blood sugar control has its complications, frequently hypoglycemia, and for those patients with retinopathy they will have temporary worsening of retinopathy that will resolve eventually. the most interesting part of the study is that the patient who had controlled diabetes during the study had a protected retina and blood vessels, although they stopped controlling their diabetes after the study(controlling blood glucose levels particularly in early stages of the disease), and that what's called the metabolic memory!!.

3. **Pregnancy**
4. **Hypertension:** should be rigorously controlled (<140/80 mmHg).

   Control BP = Control DM (Poor control of both HTN & DM is destructive for the retina).

5. **Nephropathy**: Renal transplantation may improve DR.
6. **Others**: **Hyperlipidemia**, smoking, cataract surgery, obesity and anemia.
   - Use of **Fenofibrate** is protective agent for the retina.
   - Hb A1c shouldn't be reduced more than 6%, because they found that decreasing Hb A1c more than 6% will increase the mortality rate from cardiovascular diseases.
   - ➔ So blood lipids should be controlled in addition to Hb A1c and HTN in order to protect the retina.

   Diabetic patients are more prone to have cataract, inflammation, retinopathy, optic neuropathy (as a part of involvement of the nervous system), and the patient may present with paralysis of the 3rd, 4rth, and the 6th CNs.
   How would we prevent DR?? By implantation of National screening Program.

❖ RETINAL CHANGES: (Pathogenesis)

- DR has two main component:

1. **Neuro degeneration** (not many people knew about it, however, it's now been confirmed that early in the course of DR without the presence of any vascular disease the retinal neurons die. there are many pathways for that).
2. **Microvascular disease** which can lead to catastrophic loss of vision.
   - As result of the retinal ischemia the iris can develop neovascularization called Rubeosis iridis and neovascular glaucoma.
   - there are two major changes occur in microvascular disease of DR.

   ➔ **First** thing that occurs very early in the disease is the break of blood retinal barrier, the capillaries of the retina are lined by endothelial cells with tight junctions on the basement membrane and supported by cells that called pericytes, those tight junctions are lost in DR, and the basement membrane is diseased and the pericytes are lost, all of those changes will eventually lead to leakage and accumulation of fluids in macula which will cause edema of the macula and then visual loss.

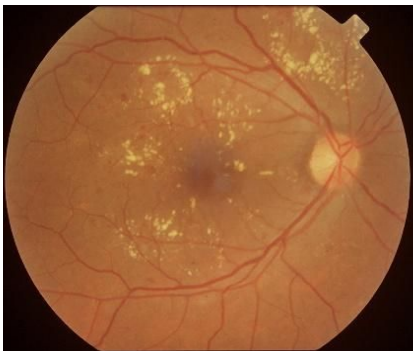
➔ **Second** thing occurs is the progressive occlusion of retinal capillaries and arterioles, leading to hypoxia and ischemia which will enhance induction and activation of transcriptional factor like HIF-1-alpha -> angiogenic molecules (VEGF).

- Retina is very active tissue, thus it will react during ischemia by the secretion of angiogenic factors (there are many, however the most famous is the vascular endothelial growth factor) this will induce neovascularization (new vessels are fregil weak and leaky, which make it easily ruptured).
- Neovascularization is the cause of formation of the fibrous tissue around the new vessels. Neovascularization along with the fibrosis can cause bleeding in the eye and the patient present with loss of vision, or it causes traction of the retina causing traction retinal detachment. This is called erative retinopathy.

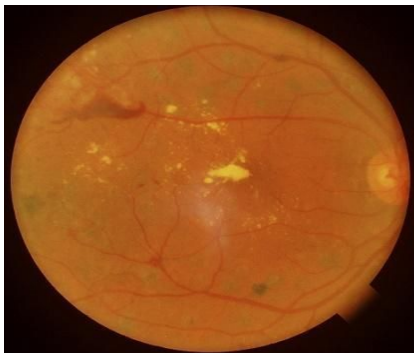
- **Changes:**

1. **Hard exudates** on the retina and macular edema resulted from the leakage of and lipoproteins "yellow spots".
2. Microaneurysms **'blots and dots'**.
3. Soft exudates '**cotton-wool spots**' "white spots".
4. Venous changes: beading vs looping (**The most reliable signs of retinal ischemia in diabetic retinopathy**).
5. Hemorrhage if neovascularization results in weak vessels and easy to break.
6. Neovascularization.

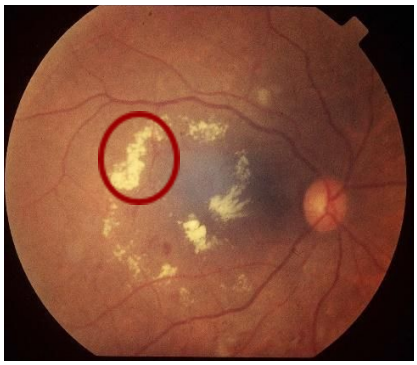
Hard Exudate and Hemorrhage



Hemorrhage

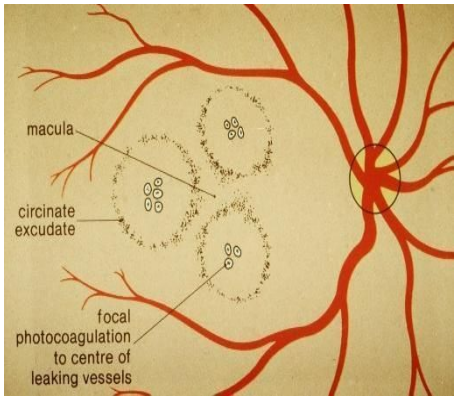


Hard Exudate



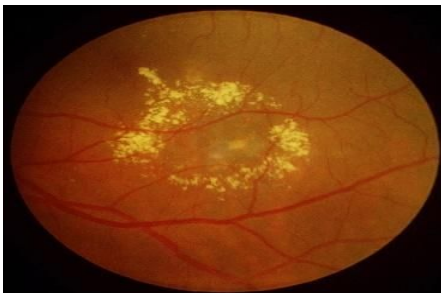
★ This is a patient with Macular edema: you can see the retinal veins and arteries. Veins are darker and broader than the arteries. So when there is leakage the capillaries will leak two components. Fluids that will cause hard exudates, which composed of **lipoproteins and lipid laden macrophages.** You can see also, small red dots, those are **microaneurysms**, which are part of retinopathy, and are leaky. **Treatment** of leaky microaneurysms is by **laser photocoagulation** and we inject Anti-VEGF in those patient to help in the effectiveness of laser treatment .

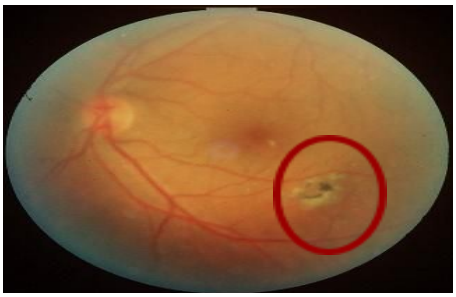
Photocoagulation: we use focal laser to treat the leaking microaneurysms, and when the leak stopped the hard exudates will be cleared. Currently in severe cases of macular edema we use in addition injections of drugs in the vitreous cavity to block the secretion of the growth factors (to decrease the hyper permeability). Like bevacizumab which used also in metastatic colorectal cancer, and ranibizumab.



Circinate exudate: when blood vessels leak it will result in Exudates and hemorrhages AROUND the source of leaking.

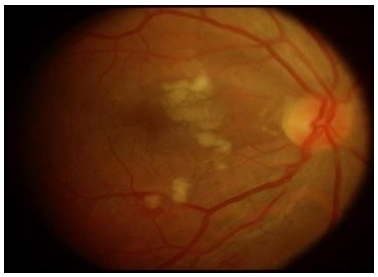
A B

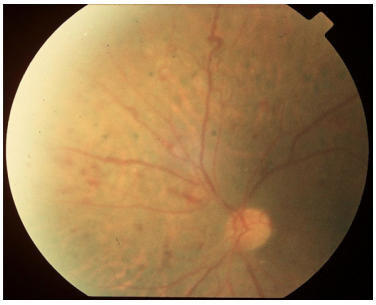




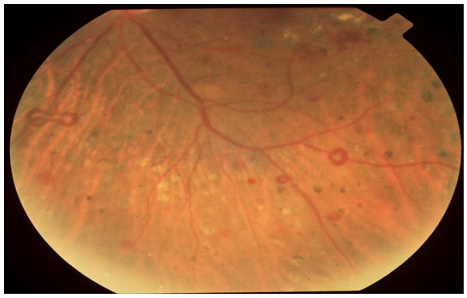
- ★ **(A)** Young diabetic patient **with large ring of hard exudates**, and in the center you can see the **laser scar** that we applied.
- ★ **(B)** Same patient **6 months** post later therapy, with a complete clearance of the hard exudates with permanent laser scar (Scar from the laser at the lower right)*
- ★ If there is extensive exudates and hemorrhages, PRP "panretinal photocoagulation" is done (the whole periphery gets cauterized except the posterior pole). results in loss of rods >> loss of vision at night.

★ **cotton wool spots. Which represents infarction of the retina,** because of occlusion of retinal arterioles. They are different from hard exudate in the cause and the clinical picture. Veins are always darker and broader than arteries White patch result of infarction of retina (sign of ischemia) occlusion of retinal arteriole

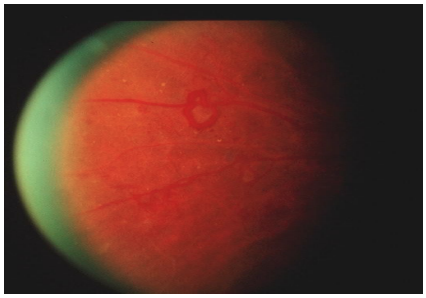




There is hemorrhage, neovascularization at the optic disk, neovascularization in the retina, venous looping at the top "NEEDS PRP"



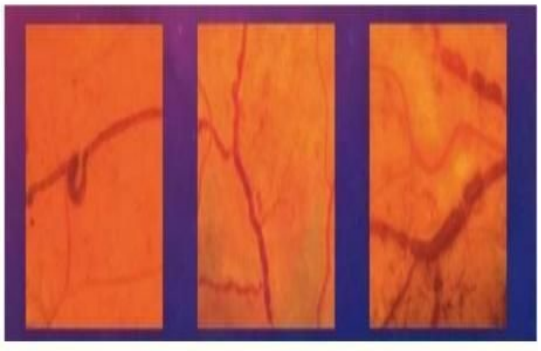
Venous looping



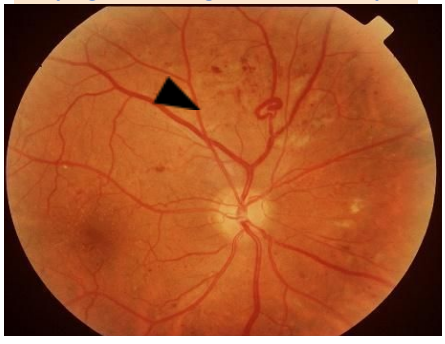
Venous looping

VENOUS CHANGES

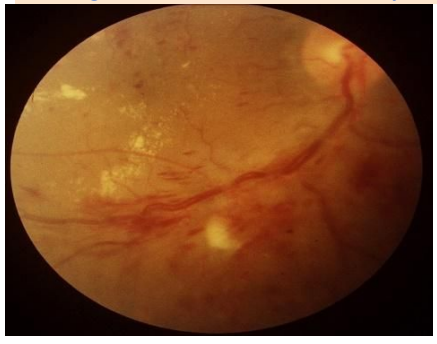
- Looping, Beading, Segmentation (sausage like)



Looping,hemorrhage, cotton wool spots



Bleeding, hard exudate, cotton wool spots.



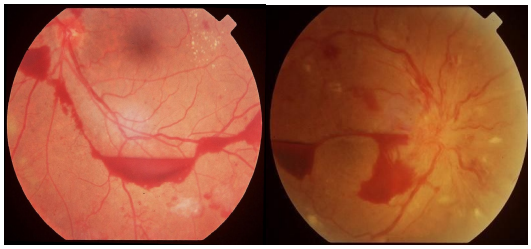
★ **Venous changes is considered the most important predictor of retinal ischemia.** The veins are usually darker and broader than the arteries. However, in retinal ischemia the veins will be **looped (tortuous) (omiga sign) and beaded. Looping is the Most predictable sign of new vascularization**

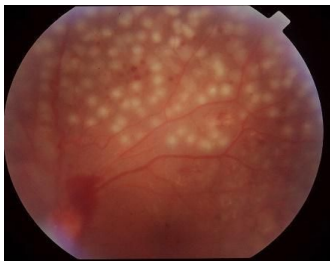
➔ In Severe nonproliferative diabetic retinopathy: Does not cause hemorrhage (no new vessels); we see only sign of ischemia.

➔ Presence of intra retinal hemorrhage in four quadrants with tortuous engorged veins very important sign of severe ischemia

★ Hemorrhage from the new vessels is an emergency cases for **laser photocoagulation. "subhyaloid hemorrhage"**

Bleeding and cotton wool spots in right Pic





★ Laser scars from pan-retinal photocoagulation everywhere except the macula and disc + Intraretinal Hemorrhage (It's a common feature in diabetic retinopathy)

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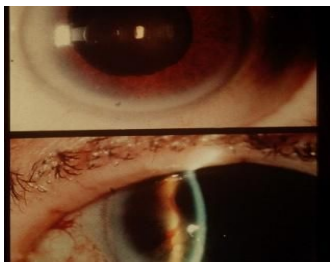


★ Patient with iris neovascularization will develop neovascular glaucoma which is very difficult type of glaucoma to be controlled, and frequently will lead to blindness.

Rubeosis iridis

Non-Proliferative Diabetic Retinopathy:

- **Mild NPDR:** (Control blood sugar) Microaneurysm only.
- **Moderate NPDR:** (Control blood sugar) Microaneurysms – retinal haemorrhages - circumstances exudates – cotton wool spots – minimal intraretinal microvascular anomalies (arterio-venous shunt) – minimal venous changes (looping and beading).
- **Severe NPDR** :(Control blood sugar + **Consider panretinal laser coagulation** **45% of patient will develop new vessels**).
- All of the above + severe intraretinal microvascular anomalies (arterio-venous shunt) – severe venous changes (looping and beading).

  At this stage, Patient should receive laser Panretinal photocoagulation.

- **SO the Signs of Retinal Ischemia are:** (Patient is at high risk to develop new vessels):

  - **Cotton wool spots** (less important sign and not used in the classification of non-PRD).
  - **Venous changes** (**The most reliable signs of retinal ischemia in diabetic retinopathy**).
  - **Intraretinal microvascular abnormalities (IRMA):** are arteriolar– venular shunts that run from retinal arterioles to venules, thus bypassing the capillary bed and are therefore often seen adjacent to areas of marked capillary hypoperfusion.

  * Dilated telangiectatic capillaries **Intraretinal Hemorrhage:** The extent of involvement is a significant marker of the likelihood of progression to proliferative diabetic retinopathy.

  - **Diabetic macular edema "DMO":**

  The hard exudate is in the center of the macula (can cause a loss of central vision). It's a sign of macular edema.

  Nowadays, Optic coherence tomography (OCT) is used to diagnose early macular edema even in patients with very mild edema that you can't see it.

  Treatment:

  1- Focal laser photocoagulation: Treatment of micro aneurysms with laser (After 6 months there will be a scar from the laser treatment but no hard exudate).

  ➔ Very effective in controlling diabetic macular edema.

2- Intravitreal injection of anti-VEGF agents (anti- vascular endothelial growth factor)

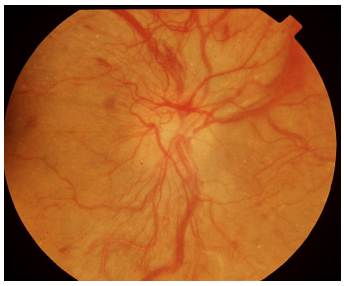
Ranibizumab or Bevacizumab, in addition to laser, we frequently inject Intravitreal injection of anti-VEGF agents to help control diabetic macular edema. * Diabetic retinopathy patients have progressive macular vascular occlusion, which will cause ischemia of retina (hypoxia).

Proliferative Diabetic Retinopathy:

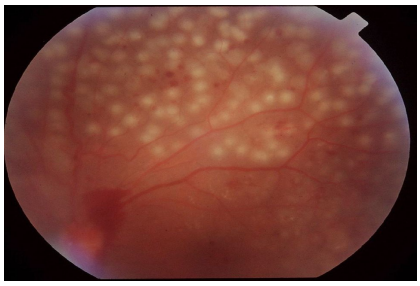
- More aggressive new vessels can arris from optic nerve head. Although it can be originate from outside the optic nerve head
- hemorrhage from the new vessels is an emergency cases for laser photocoagulation
- **New vessels at the disc (NVD):** describes neovascularization on or within one disc diameter of the optic nerve head.
- **New vessels elsewhere (NVE):** describes neovascularization further away from the disc; it may be associated with fibrosis if long-standing.
- **New vessels on the iris (NVI):** also known as **rubeosis iridis**, carry a high likelihood of progression to **neovascular glaucoma.**

- **Treatment:**
  1. Pan-retinal photocoagulation. We apply laser all around the retina sparing the macula and the optic nerve. This will result in regression of the new vessels and protecting the patient from bleeding or traction retinal detachment.
  2. Intravitreal anti-VEGF injection

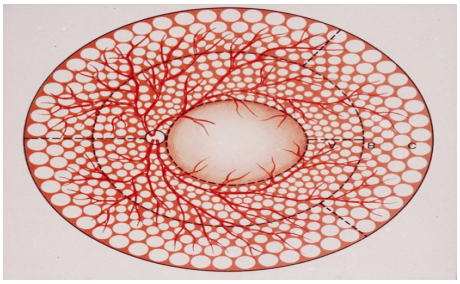
- **Complications of Retinal photocoagulation**:
  - Anterior segment complications such as corneal or lenticular opacification
  - Transient visual loss.
  - Photocoagulation of the fovea.
  - Macular edema.
  - Hemorrhage.
  - Choroidal Effusion
  - Color vision alterations. Visual field defects and night vision problems.
  - Hemeralopia.

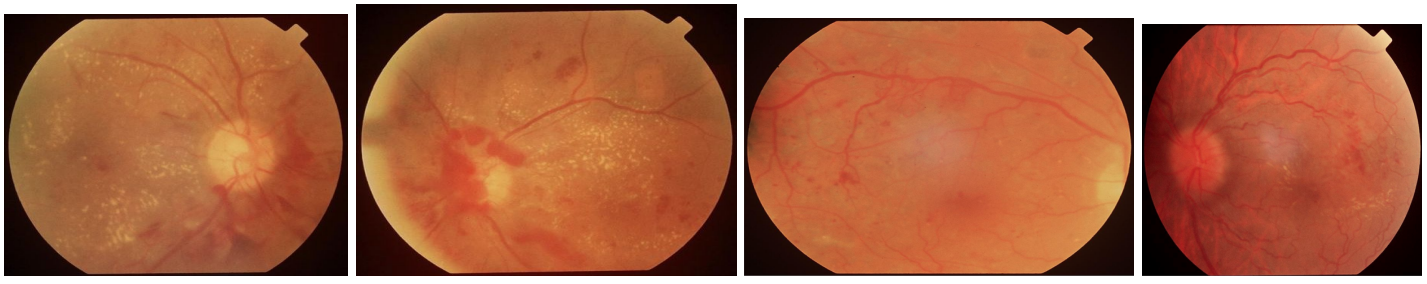


Extensive abnormalities
PRP, the more aggressive => inside (large and tortuous blood vessels with neovascularization)



Laser scars





Neovascularization, hemorrhages, exudates.

- **THE THREE MOST COMMON CAUSES OF INTRAOCULAR INFLAMMATION IN THE KINGDOM:**

1) Vogt–Koyanagi–Harada (VKH) syndrome.

2) Tuberculosis.

3) Behçet disease.

Grave's Disease:

Most common cause of **both bilateral and unilateral proptosis** in an adult.

- **Pathogenesis:**
  - Autoimmune disease characterized with serum IgG antibodies bind to TSH receptors in the thyroid and causes overstimulation and high thyroid hormone production.
  - Autoimmune antibodies infiltrate eye, cause inflammation of extraocular muscles and associated with increased secretion of glycosaminoglycans and osmotic imbibition of water.

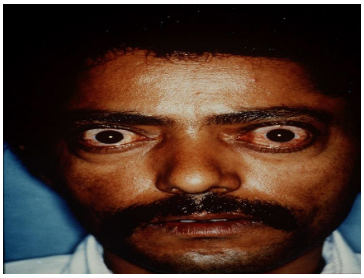
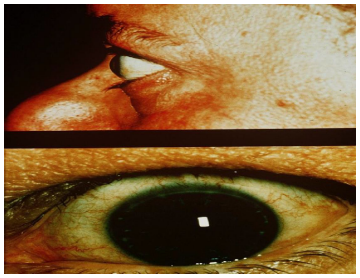
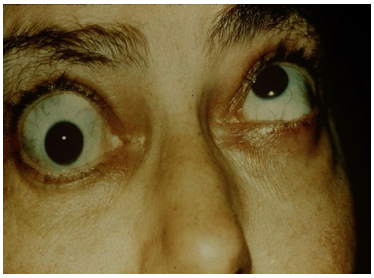
- **Risk factors:** **Smoking (most important)** – family history
- **Systemic manifestation**: Pretibial myxedema, heat intolerance, weight loss etc…
- **Ocular manifestation:**

  Proptosis and exophthalmos, Lid retraction, Lid lag, restrictive thyroid myopathy, infiltrative ophthalmopathy, dysthyroid optic neuropathy, chemosis, exposure keratopathy, ophthalmoplegia.
- **Investigations:**

1- Thyroid function test: High T3, T4 and low TSH

2- Visual evoked potential: **To exclude Optic neuropathy.**

- **Treatment:**
  1. Anti-thyroid medications or Thyroid ablation with radioactive iodine (**for disease itself**)
  2. Steroid, lubricants and eye protection before sleep (**for eye symptoms**)
  3. If there is **restrictive myopathy** surgical intervention is required


Proptosis, lid lag, red eye, ophthalmoplegia due to exposure keratopathy (dry eyes).

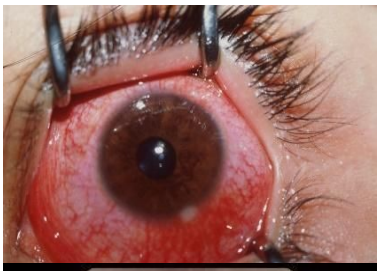
Tuberculosis:

- TB is a chronic granulomatous infection usually caused in humans by **Mycobacterium tuberculosis**.
- TB is primarily a pulmonary disease but may spread by the bloodstream to other sites; ocular involvement (TB can involve any part of the eye) commonly occurs without clinically overt systemic disease.
  Extrapulmonary TB when you have an eye infection without pulmonary infection in 60% of cases.
- Tubercles uveitis is an important cause of blindness (second most common cause of uveitis in KSA)
- TB can present with granuloma in the eye.
- TB may be indolent and the first manifestation in the eye.

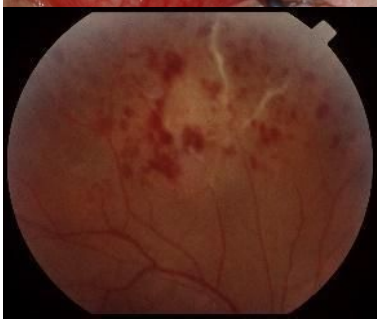
  Can be: 1. Direct infection 2. Immune response to tubercular protein

- **Ocular manifestation:**
  - **Phlyctenular keratoconjunctivitis** (small, circumscribed lesions at the corneal limbus) - Interstitial keratitis – Vitritis - Choroidal granuloma.
  - **Retinal vasculitis 'Eales disease'.**
  - **Anterior uveitis (Granulomatous uveitis):** causes blindness if not treated.
  - TB is the second most common cause of uveitis in KSA, after Vogt- koyanagi-Harada disease, and the third cause is Behçet disease.
  - Can involve anterior uvea, posterior uvea, or all the uvea and called panuveitis.
  - Granulomatous inflammation that is the disposition of mutton-fat keratic precipitate, iris nodules, infiltration of the choroids, and retinal vasculitis. These are the most important manifestation of TB in the eye.
  - **Mutton-fat keratic precipitation:** collection of inflammatory cells on the corneal endothelium appear large with yellowish color.
    (can be seen as white dot inferiorly, mostly due to staph but could be caused by TB).

★ A 16 y/o patient, many members of the family are having tuberculosis. She presented with pinkish granulomas in the angle of anterior chamber, which is due to TB. **Phlyctenular keratoconjunctivitis**



★ This picture shows **retinal vasculitis "the white vessel above" due to TB infection**. It's white because it has perivascular inflammatory infiltrates, also when there is vasculitis there will be leakage of blood and there is intraretinal hemorrhage.

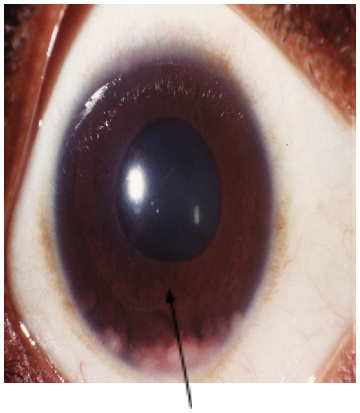


- **Investigations:**
  - First you should take a good history.(family history or history of exposure will increase the chance that the eye inflammation is caused by TB).
  - **CXR** to roll out that the patient has previous infection in the chest.
  - We rely more to tuberculin skin test, if it was strongly positive, 15 mm or more induration, this will support the diagnosis.
    1. **PCR** and the interferon-gamma release assay (**IGRA**).
    2. Aqueous or vitreous sampling rarely yields demonstrable (smear – acid-fast bacilli on Ziehl–Neelsen staining – or culture – Lowenstein–Jensen medium).

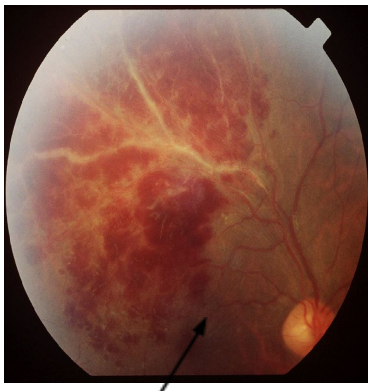
- **Treatment:**

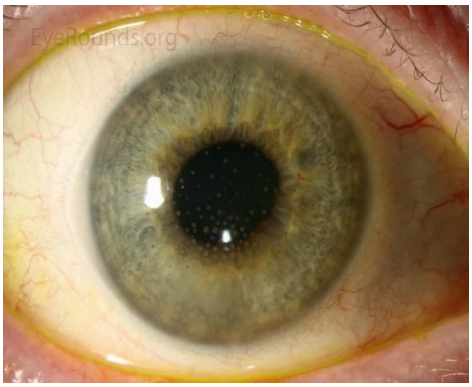
  1. **Prolonged Anti-TB therapy** *multi-drug therapy (4 drugs in 2 months, then continue for 6 months with 2 drugs)
     - Isoniazid (with Vitamin B6 (pyridoxine) to prevent the development of peripheral neuropathy), rifampicin, pyrazinamide and ethambutol
     - Ethambutol can cause optic neuropathy
  2. **Topical and systemic steroids** may be used concomitantly to reduce inflammation- induced damage.

Mutton-fat keratic precipitation



Retinal vasculitis





★ **Tubercles granuloma**
★ **Occlusive retinal vasculitis due to TB**

Syphilis:

- Can affect the uvea causing uveitis. any patient with uveitis has to undergo routine syphilis checkup.
- Although,we do routinely a syphilis serology test for any patient who present in our institute with uveitis, because syphilis is used to be a great imitator (mimics many types of inflammations), it's rare in KSA.

➔ Could be either congenital syphilis 'transplacental infection' or acquired.

- **Congenital syphilis:**
  - Interstitial Keratitis
  - Chorioretinitis
- **Acquired syphilis:**
  - Ocular chancre.
  - Iridocyelitis. inflammation of the iris and ciliary body
  - Interstitial Keratitis.
  - Chorioretinitis.
  - Neuro-ophthalmic (nerve palsies, optic neuritis).

Rubella:

Transplacental transmission could lead to congenital abnormalities.

- **Ocular manifestation:**
  - Congenital Cataract and Glaucoma
  - Microphthalmia (small eye)
  - Pigmentary retinopathy: salt and pepper.
  - Anterior uveitis: unresponsive to steroids.
  - This children can also have deafness and heart disease

    They use VERY big glasses. they us hearing aid also.

Sjogren's syndrome:

- **Sjogren's syndrome is an autoimmune disease involve the salivary glands, bronchial epithelium and vagina.**
- **Systemic manifestation:**
  - Dryness of skin and mouth and arthralgia and polyneuropathy.
- **Ocular manifestation:**
  - keratoconjunctivitis sicca (KCS) "dryness of eye"
- **Investigation:**

1. Schirmer tear test
2. Positive Rose Bengal staining (for keratoconjunctivitis sicca"
3. ANA, RF positive
4. Associated with **HLA-B8/DR3**

Sarcoidosis:

- It's the most common cause of uveitis in japan.(they name it the disease of increase hiyagen).
- It is a chronic disorder of unknown cause, manifesting with **non- caseating granulomatous inflammatory foci**.
- Will Cause granulomatous uveitis, retinal vasculitis, also it can involve the optic nerve head.
- Common in Japan, Hypothesis> due to high level of hygiene.
- Eye lesions:
  - Lid margin and conjunctival granuloma
  - Acute iridocyclitis
  - Chronic granulomatous iridocyclitis
  - Peripheral retinal periphlebitis
  - Choroidal granulomas
  - Retinal granulomas
  - Optic nerve granulomas

❖ Systemic manifestation:

- **The triad**: erythema nodosum - bilateral hilar lymphadenopathy – polyarthralgia.
- Could be the same as TB manifestation

❖ Ocular manifestation:

- **Candle-wax exudate in the retina**
- **Optic nerve, Retinal, Choroidal Lid margin and conjunctival granulomas.**
- **Mutton-fat keratic precipitates**

❖ Investigations:

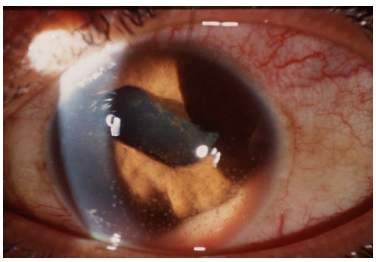
1. **Tuberculin skin test**: negative in sarcoidosis
2. **Chest X-ray:** showing bilateral hilar lymphadenopathy (BHL) (DIAGNOSTIC)
3. **Elevated serum ACE levels and/or elevated serum lysozyme**
4. **Abnormal liver enzyme tests**

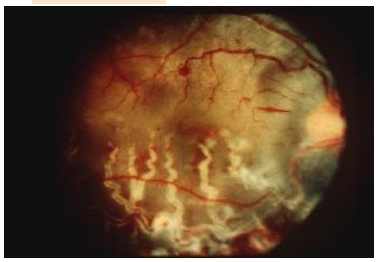
   Biopsy should be taken to confirm the diagnosis, if we were in doubt.

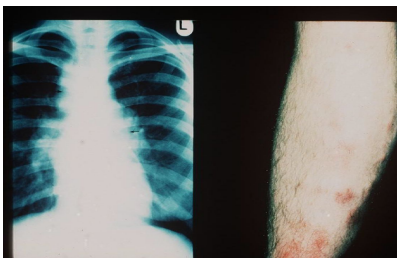
❖ Treatment:

- Steroid and NSAIDs.

candle wax

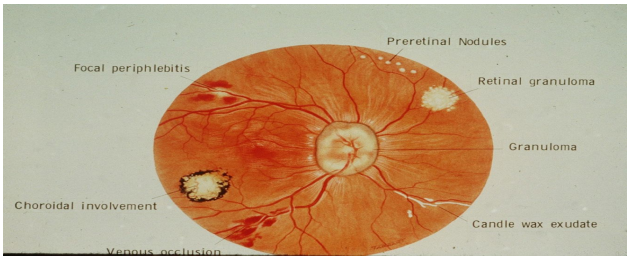






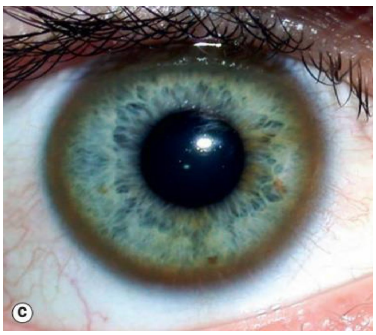
★ A young male at presentation he had sarcoidosis proven by biopsy. the FIRST picture shows deposition of inflammatory cells at the back of the cornea (Keratic participates, seen as dots below), they are large in sarcoidosis (it also called granulomatos participate, or mutton- fat keratic precipitate). distorted pupils caused by synchia (as a result of inflammation there will be adhesions between the iris and the pupil and the lens, and you can see a lot of iris pigments on the lens). retinal vasculitis. Hilar lymphadenopathy In X-ray. erythema nodosum in the last picture.

Granulomatous inflammation: TB, Sarcoidosis, syphilis, Vogt- koyanagi-Harada, Multiple sclerosis.



Wilson's Disease (hepatolenticular degeneration):

- A rare condition involving the widespread **abnormal deposition** of **copper** in tissues. It is caused **by a deficiency of alpha 2 ceruloplasmin**, the major copper-carrying blood protein.



Systemic manifestation:

- Liver disease.
- Basal ganglia dysfunction.
- Psychiatric disturbances.

Ocular manifestation:

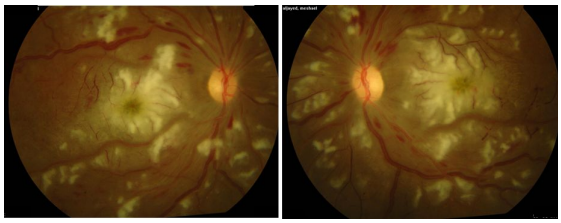
- **Kayser-Fleischer ring**: consists of a brownish-yellow zone of fine copper dusting in peripheral descemet membrane detected with gonioscopy (Important sign). Brown ring in cornea
- **Green sunflower cataract. Deposition in lens**

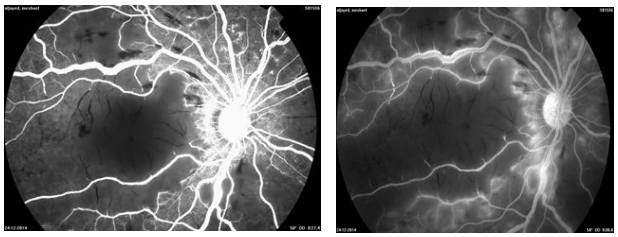
Treatment:

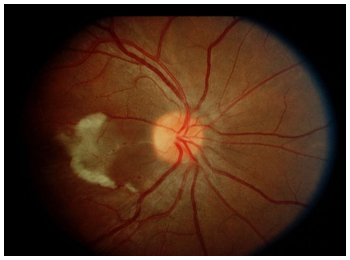
- Penicillamine.

Systemic Lupus Erythematosus:

- Autoimmune disease characterized by increased **Anti-DNA, ANA, antiphospholipid antibodies and decreased C3 & C4.**
  Retinal pathology most common eye part to be affected cotton wool spots and vasculitis.
- If it was active and not controlled definitely it will affect the retina and may cause blindness.
- the presence of ANA and antiphospholipid antibodies will increase the chance of retinal disease.
- SLE retinopathy there will be a lot of infarction of the retinal tissue due to vessels occlusion by microthrombosis> cotton wool spots.
- **Senario: young lady with <u>Bilateral</u> <u>multiple cotton wool spots</u> Always think of SLE.**







Inflammation of retinal arterial and infection
Must follow up due to the treatment "hydroxychloroquine"

Fluorescence geography

Marfan's syndrome:

Introduction:

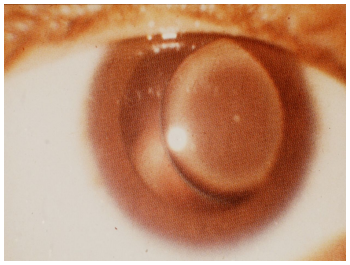
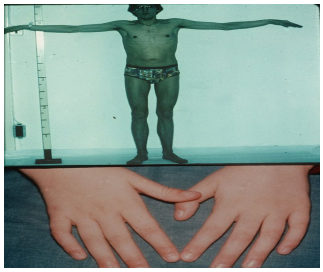
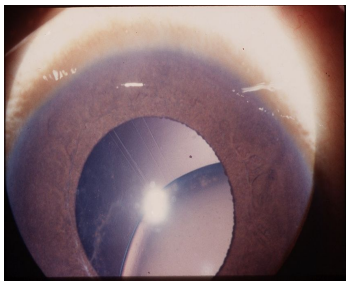
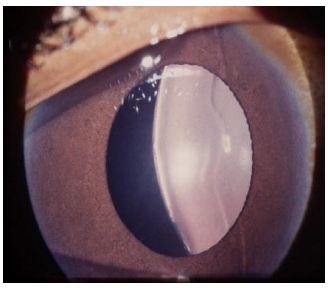
It is an autosomal dominant disease.

Systemic manifestation

- **Arachnodactyly (Long fingers)** .
- Heart diseases.
- Bone deformities

Ocular manifestation:

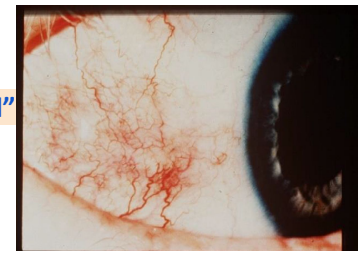
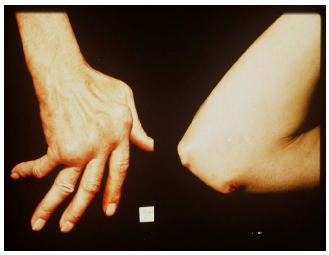
- **Lens subluxation**: due to weakness of the lens zonules.most important feature *In the picture*
- **Retinal detachment**
- **Axial myopia**
- **Angle anomaly lead to glaucoma**
- **Hypoplasia of the dilator M**

Rheumatoid Arthritis:

Ocular manifestation:

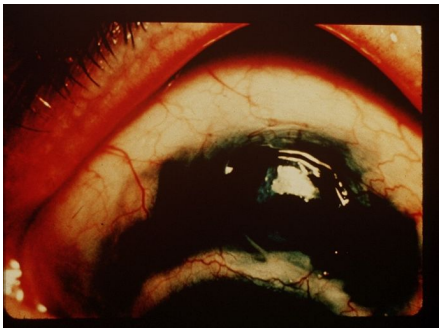
- **keratoconjunctivitis sicca (K.C.S => Severe dry eye "because autoimmune disorders attack the lacrimal gland" => may processed to corneal melting, thus susceptible to infections.)**
- **keratitis**
- **scleritis leading to melting sclera**
- **in the right picture: radial deviation, swollen fingers and nodules in the elbow.**

Investigation:

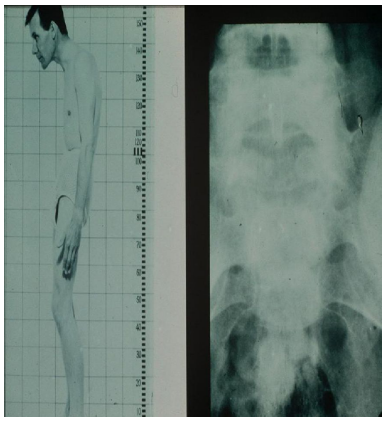
1. Positive Rose Bengal staining (for keratoconjunctivitis sicca)
2. RF positive.

★ Severe secularities with melting of sclera or scleromalacia perforans (black area is the cornea)



Ankylosing Spondylitis:

- Ankylosing spondylitis (AS) is characterized by inflammation, calcification and finally ossification of ligaments and capsules of joints with resultant bony ankylosis of the axial skeleton.
- it tend to increase in winter!
- as soon as you see young patient in the ER with **acute** recurrent alternating **unilateral non-granulomatous uveitis (fine dust)**, we always think of ankylosing spondylitis.
- It called: HLB27 associated uveitis
- patients with HLB27 associated uveitis can present either without systemic manifestations, or with systemic manifestations like psoriasis,Rieter disease، IBD, and spondylitis.



Systemic manifestation:

- Pain and stiffness in the lower back with limitation of movement.
- Calcification of spinal ligaments gives rise to a **'bamboo spine'.**

Ocular manifestation:

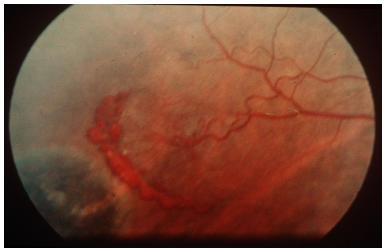
- Acute recurrent **non- granulomatous** anterior uveitis
- Complications? synchia.

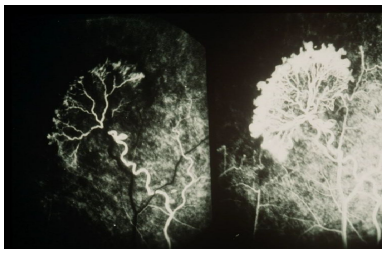
Investigations:

1. **HLA-B27-positive**
2. **X-ray: sacroiliac joints shows juxta-articular osteoporosis in the early stages** .

Sickle Cell Disease:

- Retinopathy due to sickling of RBC causing peripheral vascular occlusion of the circulation and **neovascularization in the periphery**. Looks like "Sea fans"
- Occlusion of peripheral retinal vessels > peripheral retinal ischemia> Neovascularization> traction retinal detachment /vitreous hemorrhage.
- ★ Picture on the left is early fluorescein angiogram shows massive ischemia, and on the right is delayed fluorescein angiogram which shows a big patch of complete filling of the new vessels with leakage around it(new vascular tufted filled with fluorescein)
- SCD retinopathy is differentiated from Diabetic retinopathy by the location of the new vessels, DR will be around the center, while SCD retinopathy in the periphery.
- treated by laser for the ischemic peripheral retinal.





Ocular features:

- Conjunctival comma-shaped capillaries.
- Retinal changes: arterial occlusions, neovascular Patterns, capillary closure.

Juvenile Chronic Arthritis:

- It is defined as **arthritis of unknown etiology** that begins **before the age of 16 years and persists for at least 6 weeks.**
- **Most common cause of anterior uveitis in children** in western countries.

Risk factors of the disease are:

- Female gender child, if the child developed the arthritis before the age of 4 y/o, and if the child is ANA positive.

Systemic manifestation:

A. **Pauciarticular form:** four or less joints are affected **(associated with 20% uveitis)** (it's a blainding disease in children).
B. **Polyarticular form:** five or more joints are affected. **(rare uveitis).**
C. **Still's disease:** fever, episodic erythematous maculopapular rash, lymphadenopathy and hepatosplenomegaly. **(extremely rare uveitis).**

Ocular manifestation:

- Chronic non-granulomatous uveitis
- Band keratopathy
- Posterior synechiae

Investigations:

1. **Anti-ANA antibodies:** will be positive in majority of pauciarticular type.
2. **Rheumatoid factor:** positive in some polyarticular type.
3. **HLA-B27:** it will be positive in some patient.

Treatment:

- Topical and systemic Steroid and mydriatic agent to prevent posterior synechiae.

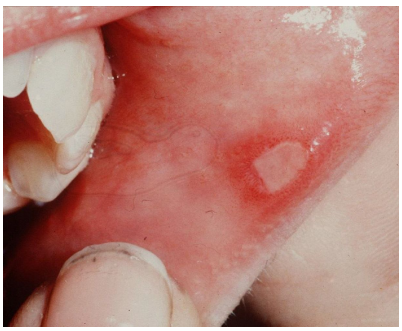
Leprosy (Hansen's Disease):

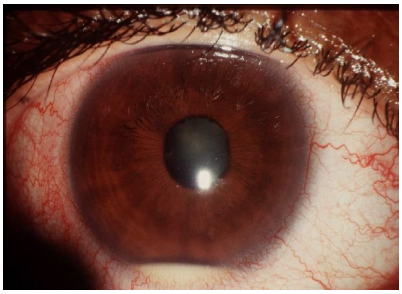
Ocular involvement is more common in the lepromatous type.
Signs: Facial nerve affection, Loss of the lateral portions of the eyebrows and eyelashes (Madarosis), Interstitial keratitis and Iritis.

Reiter's Syndrome:

A triad: 1-Urethritis, 2-Conjunctivitis and 3-Seronegative arthritis.
Ocular features: Conjunctivitis, Keratitis and Iridocyclitis.

Behçet's Disease:





clinical diagnosis: International criteria are:having a painful recurrent mouth ulcers + two of the following: eye inflammation, genital ulcer, skin lesions, and positive pathergy test.

Systemic manifestation:

- Vasculitis
- Recurrent aphthous oral ulcers
- genital ulceration
- skin lesion

Ocular manifestation:

- Anterior nongranulomatous uveitis
- Transient hypopyon usual presentation(contains polymorph leukocytes> highly activated in Behcet)
- Retinal vasculitis + white patches of retinitis
- Optic disc hyperemia
- ★ Accumulation of inflammatory cells in anterior chamber (Hypopyon)
- ➔ Most common cause of blindness in patient with behcet disease is recurrent occlusive retinal vasculitis (if it's not controlled the patient will have retinal atrophy and end up with loss of vision)

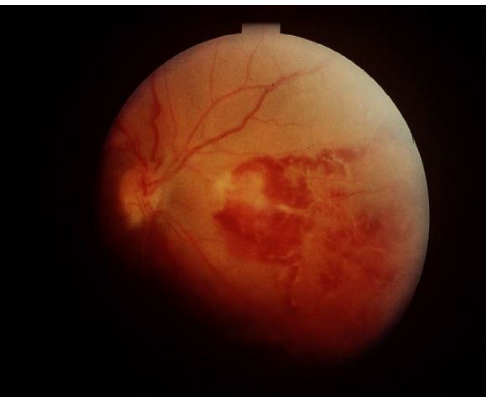
Investigations:

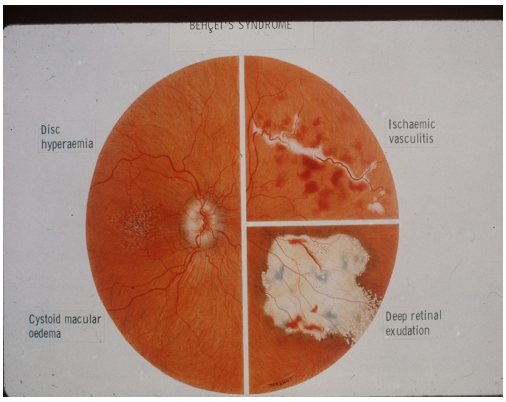
1- HLA-B51 is positive

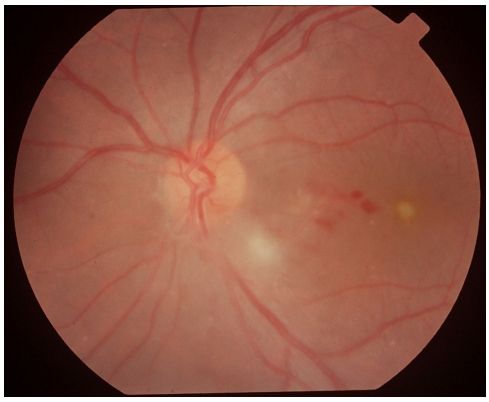
2- Pathergy test: pustule 24–48 hours after a sterile needle prick

Treatment:

- Steroid for a short time then Cyclosporine
- **Anti-Alpha tumor necrosis agents "infliximab"And adalimumab(humira)** if case is resistant it protect from blindness (Behcet patients have high levels of Alpha tumor necrosis agents in the eye)



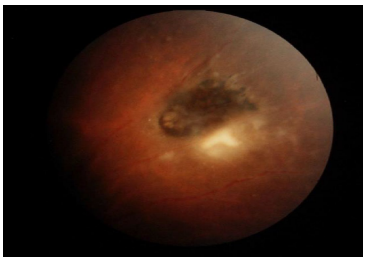


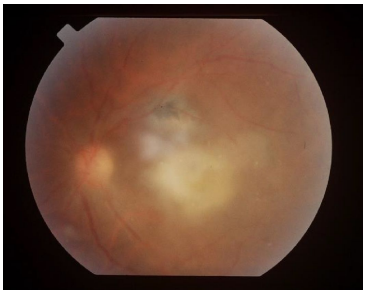


Toxoplasmosis:

- Toxoplasmosis is caused by Toxoplasma gondii after eating raw meat (obligatory intracellular protozoan parasite)
- Can be congenital: in the **third trimester**

A





B

Systemic manifestation:

- Congenital: Convulsions and intracranial calcification and chorioretinitis.
- Acquired disease is usually due to reactivation of old lesions. manifest manly as necrotising, inflammation of retina (retinitis).

Ocular manifestation:

- posterior uveitis
- Macular lesion
- Retinochoroiditis ”fluffy white with pigmented scar”
- Unilateral floaters, blurring and photophobia.

Investigations: PCR and serology

Treatment:

Clindamycin and Sulphonamides, Pyrimethamine (Daraprim) steroids.

★ **(B)** Retinal scar with reactivation of toxoplasmosis. >will lead to blindness if it involved the macula.

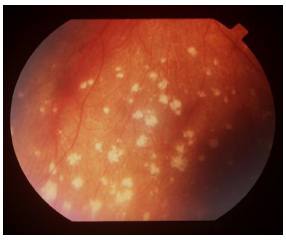
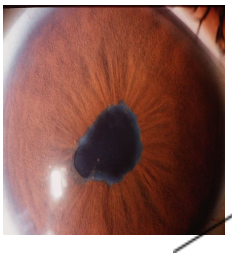
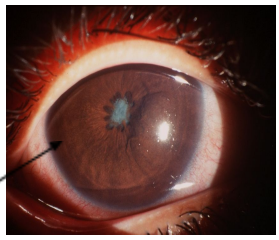
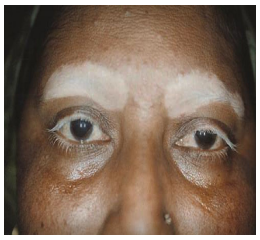
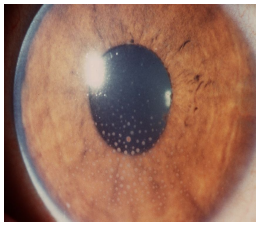
★ **(A)** Old scar (black area) and new lesion on top (white area).

Vogt- koyanagi-Harada disease:

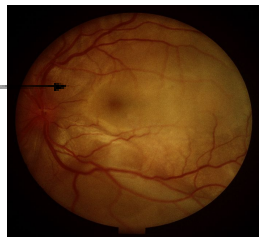
- Idiopathic Multisystem, autoimmune disease directed against melanocyte-containing tissues such as the uvea, ear and meninges.
- **Most common cause of uveitis in the kingdom of Saudi Arabia**

Systemic manifestation: If you treat early after the onset of eye inflammation you can prevent these manifestations

- Alopecia
- Vitiligo
- **Poliosis**: absence or decrease melanin in head hair, eyebrows or eyelashes.
- Deafness and vertigo
- Meningismus patient present with headache
- Neurological and cutaneous signs.
- pigmented individuals.

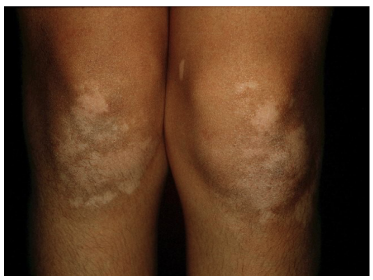
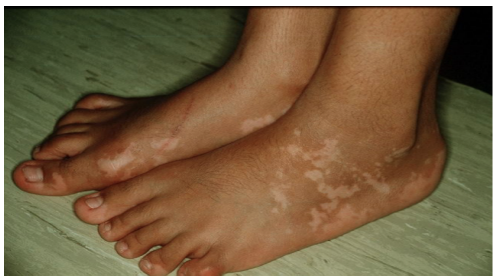
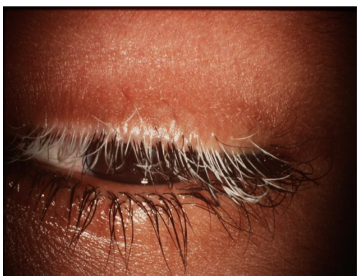






★ Synched and cataract
★ Mutton fat keratic precipitate
★ Retinal detachment with collect of fluid
★ Keratic precepitates in the first picture from the right



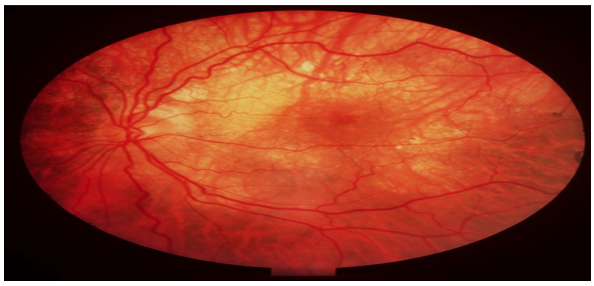
Ocular manifestation:

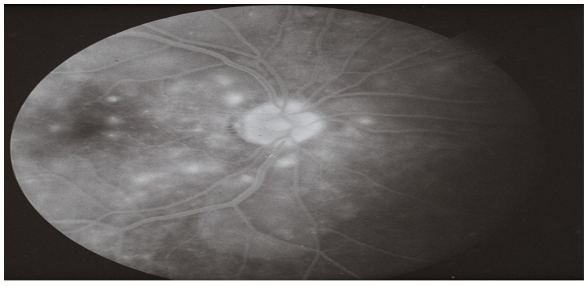
- Bilateral **granulomatous** anterior uveitis
- Bilateral multifocal posterior uveitis
- Dalen–Fuchs nodules
- 'sunset glow' fundus
- Mutton - fat keratic precipitates, chronic manifestation.
- Acute phase manifested as inflammation of the choroid with exudative retinal detachment(accumulation of fluids under the retina)

sometimes there is white pigmentation on different parts of the body.

white eyelashes





Sunset glow fundus or orange fundes “if VKH is not treated” => it affects the retinal pigment layer

starry sky appearance

Investigations:

1. Associated HLA-DR1 and HLA-DR4
2. Lumbar puncture if diagnosis uncertain; CSF shows a transient lymphocytic pleocytosis, and melanin-containing macrophages.

Treatment:

- High-dose steroid or infliximab in case of steroid resistance

Complications:

1. Glaucoma
2. Cataract
3. Choroidal neovascularization.
4. Subretinal fibrosis.
5. Retinal atrophy.

Hypertensive Retinopathy:

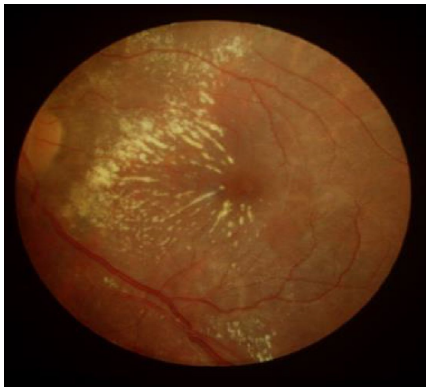
- common in KSA

Ocular manifestation:

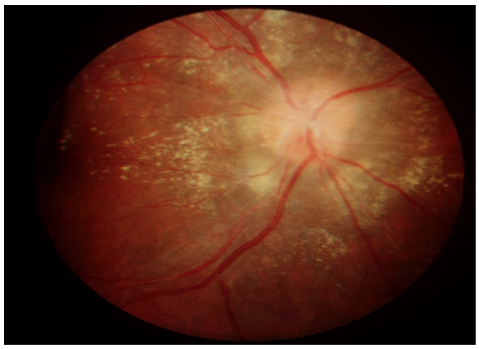
- Keith-wagener grouping:
  - **Stage I & II:** arteriolar attenuation (**silver wire and copper wire in the artery**) and increased light reflex coming out of the blood vessel due to diseased blood vessels wall.
  - **Stage III:** Cotton-wool spots due to retinal arterioles occlusion, Hard exudate due to leakage, **Macular star,** hemorrhage, retinal edema.
  - **Stage IV:** All the above + Edema of optic disc.
- Ischemic choroidal infacts (Elsching's spots):
  - Retinal arterial macroaneurysm.

Treat systemic disease first

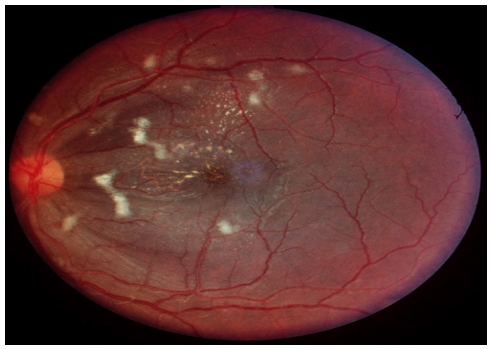
Picture shows:



- ★ artery with white wall due to sickness of the arterial wall. copper wire is the reddish part of the artery.
- ★ Hard exudates which is very typical HTN retinopathy. It has radial Fan shaped distribution or confirmation, and this unique arrangement is due to the presence of hinly nerve fiber layer in the macula, which is arranged radially.
- ★ artery crossing over the vein, this is called nipping, or arteriovenous crossing changes (the crossing of the sclerosed artery over the vein will cause constriction, attenuation, and tapring of the vein)
- ★ Optic nerve head swelling/Sliver wire arteries/ Copper wire arteries



massively swollen disk exudates
cotton wool spots



silver wiring vessels above

Giant cell Arteritis:

- Affect medium and large vessels. Anterior ischemic optic neuropathy is divided into two types: Arteritic, Non-Arteritic.
- Is a serious disease because it can lead to irreversible blindness due to ischemic optic neuropathy. By occluding the circulation supplying the optic nerve.
- Disease of people over 60 y/o. Affects medium and large blood vessels, and it can cause sudden visual loss. can be associated with central retinal arterial occlusion (CRAO), cotton wool spots, anterior segment necrosis, oculomotor palsy, and cortical blindness.

➢ **Non-arteritic anterior ischaemic optic neuropathy (NAION):** more common, caused by occlusion of the short posterior ciliary arteries resulting in partial or total infarction of the optic nerve head. Patient complains of sudden painless monocular visual loss; this is frequently discovered on awakening, suggesting a causative role for nocturnal hypotension.

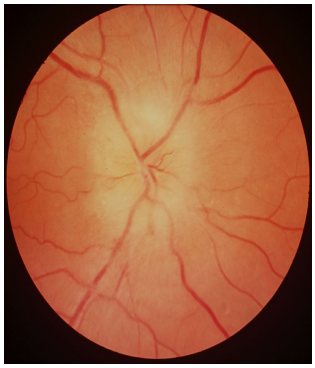
➢ **Arteritic anterior ischaemic optic neuropathy (AAION):** Caused by giant cell arteritis (GCA). About 50% of patients with GCA have polymyalgia rheumatic (PMR)" pain and stiffness in proximal muscle groups, typically the shoulders and biceps, that is worse on waking , scalp tenderness and **jaw claudication**".

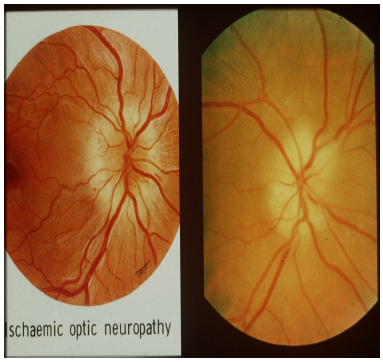
Risk Factors:

- **Old age, Females, smoking, low body mass index and early menopause.**

Investigations: to confirm the diagnosis

1. Erythrocyte Sedimentation Rate 'ECR' (Check esr first if it is high then start steroids and arrange for biopsy).
2. CBC
3. temporal artery biopsy.





Ocular manifestation:

1. Ocular motor palsies, including a pupil-involving third nerve palsy,
2. Sudden, profound unilateral visual loss
3. Amaurosis fugax and anterior ischemic neuropathy.
4. strikingly pale 'chalky white' edematous disc "characteristic".

Treatment:

- If the diagnosis is confirmed, patient should treated urgently with systemic corticosteroids. To prevent the involvement of the other eye, because the risk on the other eye is very high.
- **High-dose of steroid**.

Picture shows:

★ A giant cell arteritis patient that present with gangren over the scalp.

★ the patient present with sudden loss of vision in this eye(typical clinical picture of ischemic optic neuropathy), you dilate the pupil and you looked to the fundus, you see (the picture)pale optic nerve with undefined margins, and the disc is swelled.

★ Admission is required in such patients, because it's a life threatening disease, and this might be the first manifestation.