

# 430 Ophthalmology Team

1<sup>st</sup> lecture:

## Ocular Manifestations of Systemic Diseases

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The slides not provided by doctor (Prof. Abu Al-Asrar's)

Sources are (doctor's notes/ 429 teamwork)

Important Notes in **red**

Doctor's notes in black

Your notes in **blue**

Titles and subtitles in this color

Highlight possible MCQs mentioned or pointed by the doctor

**Introduction:**

- Many systemic diseases can affect the eye particularly the retina, and systemic involvement of the eye can cause blinding.
- In fact, most of the cases seen are blindness unless the disease is detected early and treated aggressively.
- Most infections involve the retina microvasculature.

**1. Diabetes Mellitus:**

- The most common disease that affects the eye is diabetes, 30% of the population are diabetics and almost 30% of diabetic patients have retinopathy.
- Diabetic retinopathy (DR) is the commonest cause of legal blindness in individuals between the ages of 20 and 65 years.
- The risk of blindness is 2-5 times more in diabetics than non diabetics.
- By 20 years of diabetes, almost all patients with type 1 diabetes will develop **hemianopsia** and 6% of type 2 diabetes will have hemianopsia.
- Consider diabetes in the case of unexplained retinopathy, cataract, **new vessels on iris**, extra-ocular muscle palsy, optic neuropathy or sudden change in refractive error.
- Most important factor in development of Diabetic retinopathy is: **duration** of the disease (**non modifiable** risk factor).
- Other important **modifiable** risk factors:

1. Glycemic control:

A study was done that included only patients with type 1 diabetes, one group on tight control blood sugar with insulin pump, the other one on conventional treatment.

After 6.5 years, the study showed:

Tight control patients were protected against diabetic retinopathy, nephropathy, kidney involvement and neuropathy.

So this study shows for sure that reduction of blood sugar is very important

Also many years later after this study termination, they found that patients who were tight control and converted to conventional treatment are still yet protected.

2. Blood pressure control .
  3. Hyperlipidemia & obesity (**magnify macular edema**)
  4. **Smoking** .
  5. **Pregnancy (accelerates progression)**
- There's a strong association between nephropathy and diabetes.

- Retinopathy is a microangiopathy: disease of microvasculature of the retina involving the capillary arterioles and venules, the same pathogenesis as microangiopathy is seen in the CNS and kidneys.

### 1.1 The Retina:

- The most important structure affected by DM.

**Pathophysiology:** 2 major changes that occur in the retina:

1st: the first early change is break down of the blood retinal barrier (which is formed by the tight junctions between the endothelial cells and capillaries) → early loss of pericytes and early loss of tight junction proteins between endothelial cells → vessels leak fluid, blood and lipoproteins → retinal edema → visual loss (edema of the macula is one of the common causes of visual impairment among patients with diabetes).

- Can happen long before detachment
- Due to loss of pericytes, microaneurysms develop
- Hemorrhages can occur (flame-shaped)

2nd: the second change is progressive occlusion of retinal microvasculature → ischemia and hypoxia (The retina is metabolically reactive, so how does it react to hypoxia? by releasing angiogenic molecules like vascular endothelial growth factor and others which will lead to vascular hyper permeability) → leakage → neovascularization → angiogenesis (occur by proliferation of endothelial cells and migration) → bleeding → vitreous hemorrhage → fibrous tissue formation (myofibroblasts will produce proteins like collagen) → traction of the retina → detachment.

**From doctor's explanation on pictures:**

- Macula is the area responsible for sharp vision.
- Focal laser will stop the leakage from microaneurysms.
- Focal laser is effective to control diabetic macular edema.
- **Central signs of retinal ischemia:**
  1. **Cotton wool spots:** a clinical sign of **retinal infarction** due to occlusion of retinal arterioles.
  2. **Hard exudates:** a sign of **leakage**, they are composed of lipoproteins and leydig macrophages.
  3. Venous changes: most important and reliable sign of retinal ischemia. (Venous bleeding means there are areas of dilations and constrictions and venous looping, if the patient has this sign they call it: severe non proliferative diabetic retinopathy).
- **Signs of Severe non proliferative retinopathy:**
  1. Venous changes (in the form of bleeding and looping).
  2. Intra retinal microvasculature collaterals: dilations of intra retinal blood vessels in response to ischemia.
  3. Presence of multiple hemorrhages in 4 quadrants.

**Treatment:**

**Pan retinal photocoagulation:** they apply laser burns throughout the retina sparing the macula and optic nerve. (It's a destructive way of treatment but it keeps the vision of the patient).

If untreated → new vessels will develop within the optic nerve causing bleeding and vitreous hemorrhage.

They are considered emergency cases, if the patients with those signs are left untreated, 50% of them will have high risk proliferative disease within 1 year.

- New vessels: always develop from the veins (because they are darker and broader than arteries).
- When the new vessels arise from the disc → called new vessels of the optic nerve head.

**1.2 The Iris:**

- Neo-vascularization of iris (**rubeosis iridis**): a very severe complication of diabetes because those new vessels will obstruct the angle of anterior chamber leading to increase in pressure → leads to **neo-vascular glaucoma**.
- Sign of severe retinopathy.
- Treated by pan retinal photocoagulation.

**1.3 The Lens:**

- Earlier onset of senile sclerosis and cortical cataract
- May get hyperglycemic cataract due to sorbitol accumulation (rare)
- Poor glycemic control can suddenly cause refractive changes by 3-4 diopters

**1.4 THE Extra-Ocular Muscles & Optic Nerve:**

- Usually CN III infarct
- Pupils usually spared in diabetic CN III palsy but get ptosis (Why? Parasympathetic fibers run around the nerve not in it)
- May involve CN IV and VI
- Usually recover within few months
- Visual acuity loss due to infarction of optic disc/nerve

**1.5 Screening and Prevention:****• How do we prevent blindness in diabetics?**

The only way is to establish **regular screening programs** where a picture of the fundus (digital fundal photography) is taken on a regular basis, using non mydriatic fundus cameras, then the photo would be sent to a reading center which will provide certain instructions

**• Why do we need screening programs?**

**Because the patient may have a blinding disease while still asymptomatic.** The only case where the patient will have a complaint is if they develop vitreous hemorrhage, which is very late.

## 2. Grave's Disease:

Is an autoimmune condition characterized by excessive deposition of inflammatory cells, edema fluid in the orbit, extra orbital muscles and periocular tissue leading to proptosis, contraction of the levator **palpebrae superioris**, **upper** eyelid retraction ( because of sympathetic over stimulation), optic neuropathy due to increase pressure in the orbit, restriction of ocular motility due to fibrosis of extra ocular muscles.

### 2.1 Lid retraction:

- Unilateral or bilateral; upper or lower lids
- Due to **hyper stimulation of the sympathetic nervous system** and contraction + fibrosis of levator **palpebrae superioris** muscle.

### 2.2 Exophthalmos:

- Usually asymmetric; may be unilateral
- Due to and increase in the bulk of the ocular muscles and the orbital fat  
.The increase is due to infiltration by inflammatory cells
- Diagnosis: MRI/CT

### 2.3 Ophthalmoplegia:

- Restrictive myopathy is due to fibrosis of extra-ocular muscles
- Limitation of elevation is the most common finding – due to **tethering** and fibrosis of the inferior rectus.

### 2.4 Retinal and optic nerve changes:

- Compression of the globe may lead to elevation of intra-ocular pressure
- Optic neuropathy occurs either as a result of compression or due to ischemia

### 2.5 Corneal changes:

- Normally, the upper lid covers 1-2 mm of the cornea
- Lagophthalmos is the inability to close eyelids completely
- **Keratitis lagophthalmos**: is inflammation of the cornea due to dryness and formation of ulcers in the lower 1/3 of cornea during sleep because the patient can't close his eyes which lead to excessive exposure .  
-So the patient should fill the eye with lubricating ointment to prevent corneal dryness before sleep.

## 3 .Granulomatous Diseases:

### 3.1 Tuberculosis:

- Eye inflammation of uveitis secondary to tuberculosis.

**1st** most common cause of uveitis is **Vogt- koyanagi- harada disease**.

**2nd** most common cause of uveitis is **Tuberculosis**.

**3rd** most common cause of uveitis is **Behcet's disease**.

- Tuberculosis can mimic any type of eye inflammation.
- Whenever you see a patient with uveitis→ rule out tuberculosis.

- Diagnosed by: history and tuberculin skin test (usually 15 mm or more in duration).
- It's a common disease in the kingdom.
- It can cause granulomatous inflammation manifested as *\*(30:18 minutes from record ----- keratic precipitates on the cornea)\**, iris nodules, inflammation of the vitreous, cystoid macular edema, retinal vasculitis (Eale's disease), choroiditis (inflammation of the choroidal granulomas).

### From doctor's explanation on pictures:

- It presents as multiple nodules (granulomas) in the anterior chamber.
- If the patient has vasculitis it will manifest as whitish exudate inflammation around the blood vessels and hemorrhages.
- **Tuberculosis can cause the most aggressive retinal vasculitis** that can lead to blindness if left untreated.
- But: Remember that you can have TB uveitis **without pulmonary TB** or any other
- TB affects the eye in 2 ways:
  - Direct infection: **choroidal granuloma** (appears as pinkish nodules).
  - Type 4 hypersensitivity immune reaction to tuberculin protein causes **retinal vasculitis**

(appearance: whitish vessels; "sheathing").

- ***Suspect TB in a patient with eye inflammation who has been receiving steroids for long time without benefit.***
- Treatment: TB responds only to anti-tuberculosis drugs and needs a long course of treatment (6-9 months) ± a short course of steroids.

## 3.2 Syphilis:

- Important cause of uveitis
- It's a rare cause of eye inflammation in our country.
- More prevalent in Western countries due to higher prevalence of HIV infection.

### Ocular features:

**a) Congenital :** *(due to infection during 3rd trimester; if infection occurs in 1st trimester → abortion)*

- 1) Interstitial keratitis
- 2) Chorioretinitis

### **b) Acquired:**

- 1) Ocular chancre
- 2) Iridocyclitis
- 3) Interstitial keratitis
- 4) Chorioretinitis
- 5) Neuro-ophthalmic manifestations

Any patient with uveitis rule out syphilis → by doing **VDRL test** and fluorescent treponemal antibody absorption test (FTA-Abs).

### 3.3 Sarcoidosis:

- Sarcoidosis is a multisystem disease characterized by non-caseating granulomatous infiltration of affected tissues.
- Patients may present with pulmonary, ocular, joint or reticuloendothelial system manifestations
- The most common cause of uveitis in Japan & **Blacks** (not common here).

#### Ocular features:

- 1) Lid margin and conjunctival granuloma
- 2) Acute iridocyclitis
- 3) Chronic granulomatous iridocyclitis
- 4) Peripheral retinal periphlebitis
- 5) Choroidal granulomas
- 6) Retinal granulomas
- 7) Optic nerve granulomas
- 8) Retinal vasculitis: less aggressive than T.B

#### • Diagnosis by:

- CT chest
- Trans-bronchial lavage (biopsy) or liver biopsy.
- Angiotensin converting enzyme: usually elevated
- Serum lysozyme: usually elevated
- Liver Function Tests

#### From doctor's explanation on pictures:

- Causes granulomatous uveitis.
- **Mutton fat keratic precipitate**: accumulation (whitish deposits) of inflammatory cells in the cornea (diagnostic) → indicates granulomatous inflammation.
- **Posterior synechiae** (adhesions): between the iris and the lens, it's a complication of chronic inflammation.
- Vasculitis

- On x ray: Hilar lymph adenopathy.

#### Causes of granulomatous inflammation of the eye:

1. Sarcoidosis 2. Tuberculosis 3. Multiple sclerosis (usually seen in women) 4. Syphilis 5. Herpes 6. CMV 7. Vogt-koyanagi-harada disease

- So if there are granulomas + synechiae → granulomatous inflammation.

- But large granulomas are either due to sarcoidosis or tuberculosis.

Note: **\*another sign of sarcoidosis (41 mins)\***

- **Treatment**: unlike T.B, granulomatous uveitis due to sarcoidosis responds well to corticosteroids.

### 3.4 Toxoplasmosis:

- Most common cause of **infectious uveitis**.
- Common in Brazil (they found that the organism is transmitted by drinking water). Some European countries like France (they eat raw meat which increases the risk of toxoplasmosis).
- Typically causes **necrotizing retinitis**.

**1) Etiology:** Toxoplasma gondii, obligate intracellular protozoan parasite

#### 2) Congenital:

- If the mother is infected for the first time during 1st trimester, the pregnancy will be terminated because the baby won't survive.
- If the mother is infected during 3rd trimester, the baby will present with congenital toxoplasmosis with:
  1. Convulsions
  2. Chorioretinitis
  3. Intracranial calcifications

#### 3) Acquired: either by:

1. Reactivation of old lesion of retinitis ( if develops near old scar).
2. New infection:

It may lead to blindness because of severe toxoretinitis involving the macula.

#### 4) Treatment:

It's sensitive to many antibiotics: clindamycin, azithromycin, minocycline, sulfonamides, co tri moxazole pyrimethamine (Daraprim).

For patients with recurrent attacks of toxoretinitis (because the lesion develops from an old scar due to its reactivation): prophylactic treatment: co tri moxazole, 6 mg twice a week .

### 4. Viral: Rubella:

- Maternal rubella during the 1st trimester causes serious congenital anomalies.

#### • Features:

1. Eyes: small eyes (microphthalmos), cataracts (most common), glaucoma, retinopathy
2. Ears: deafness
3. Heart: congenital anomalies

- **It's rare in our country.**



## Multisystem Autoimmune:

### 5.1 Systemic Lupus Erythematosus (SLE):

- Features: butterfly rash, pericarditis, Raynaud's, renal disease, arthritis, anemia, and CNS signs
- **Ocular features:**  
Most important and most common is **retinopathy** that occurs only during active disease, "flare-ups" and affects the cornea causing corneal melting.
- **Findings:** **Cotton wool spots** and large areas of infarction and ischemia in the peripheries (signs of arteriolar occlusion), intra retinal hemorrhage
- **Diagnosis:** elevated ESR, antibodies: anti-nuclear antibodies (ANA), anti-double-stranded DNA antibodies, anti-phospholipid antibodies, low complements 3 and 4.
- If the patient has Anti-Phospholipid Antibodies, anti lupus antibodies and anticardiolipin antibodies → high risk of retinopathy.
- **Anti-Phospholipid Antibody Syndrome:** recurrent thromboembolism, recurrent abortions, +ve anti-phospholipid antibodies → produces any kind of retinal vascular occlusive disease.

### 5.2 Rheumatoid Arthritis (RA):

Seropositive, rheumatoid factor.

#### Ocular features:

- 1) Keratoconjunctivitis sicca
  - 2) Scleritis, lead to melting of the sclera
  - 3) Keratitis
  - 4) Melting of the cornea
- Dryness of the cornea and conjunctiva because it destroys the accessory lacrimal glands and it's diagnosed by **Rose Bengal staining** (shows dead and devitalized tissue as well as tissue that is inadequately protected by mucin)
  - The scleritis may lead to **scleromalacia perforans**: thinning of the sclera, it's common in western countries. This can lead to uveal tissue herniation and perforation of the globe.

### 5.3 Ankylosing Spondylitis (AS):

Seronegative

#### Ocular features:

**Acute recurrent non-granulomatous iridocyclitis.**

non-granulomatous means : no mutton fat , no iris nodules, limited to the anterior segment of the eye.

- History: **young man** with acute recurrent non-granulomatous anterior uveitis
- Ask if he has **lower back pain** which is worse in the morning and decrease in the evening.

• **Diagnosis:**

1. **HLA B27** detection → acute recurrent non-granulomatous anterior uveitis
2. x-ray of sacroiliac joints.

**Other conditions associated with HLA B27 positivity that can cause recurrent non-granulomatous anterior uveitis:**

1. Inflammatory bowel disease
2. Reiter's Syndrome(Reactive arthritis)
3. Psoriatic arthritis

## 5.4 Juvenile Chronic Arthritis:

The disease tends to affect the eye causing uveitis, mostly anterior uveitis.

**Types:**

- 1) Systemic onset "Still's disease" ( the child presents with *fever, lymphadenopathy, rash & pericarditis*) →

Uveitis is extremely **rare**

- 2) Polyarticular onset (*5 joints or more*) → Uveitis is fairly **rare**

- 3) **Pauciarticular** (oligoarticular) onset (*4 joints or less; esp. elbow, knee, & wrist*) → the risk to develop uveitis is high. **20% develop uveitis.**

**Risk factors:**

1. **Girls are more prone** than boys (x3).
2. If the child develops the disease **before the age of 4**, the risk of eye involvement is high.
3. Associated with **positive antinuclear antibodies (ANA)**; increases the risk of eye involvement.
4. Oligoarticular type.

- Referral to a pediatric ophthalmologist is necessary as soon as the diagnosis is made, because uveitis may be asymptomatic and this can lead to blindness due to cataract and glaucoma, they need aggressive treatment to control the inflammation.

## 5.5 Behcet's Disease:

- **HLA B51** association.

- Common in areas of the "Ancient Silk Road" it extends from the Mediterranean up to the Far East passing by Japan, China, and Korea. It has a genetic predisposition, **very rare** in Caucasians (Europe). Most common and prevalent in **Turkey**.

- **Diagnosed clinically:** recurrent **oral ulcers (aphthous ulcers)** they are very painful and **2** of the following:

- Recurrent Genital ulcers

- Skin lesions
- Eye inflammation. Uveitis (severe, occasionally with **hypopyon** (present in about 30% of patients with Behcet's Disease), which is **pus** collection in anterior chamber)
- Positive Behcet's test

Behcet's disease is a very aggressive type of eye inflammation and a blinding disease if not treated; it causes severe **occlusive retinal vasculitis** (most important destructive complication) leading to atrophy of the retina, **venous occlusions** and hemorrhages.

#### Treatment:

Corticosteroids combined with immunosuppressive therapy, for example: cyclosporine, azathioprine (Imuran), mycophenolate.

If no response: biological treatment: **infliximab (anti  $\alpha$ -TNF)** it changes the management of the disease and saves the vision of the patient. It's also very effective in Rheumatoid arthritis and inflammatory bowel disease.

### 5.6 Sjogren's Syndrome:

- Autoimmune disease. Causes **dryness**.
- Involvement of salivary glands leading to dryness of the mouth.
- Involvement of bronchial epithelium
- Involvement of vaginal epithelium
- **Ocular features:** keratoconjunctivitis sicca : dryness of the conjunctiva.

### 5.7 Vogt- Koyanagi- Harada Syndrome:

- Disease of Pigmented individuals (**common here in the Kingdom** but rare in the white population in Europe and Caucasians)
- Cutaneous signs
- Neurological signs
- **Ocular features:** Anterior and posterior uveitis

-Multisystem and Autoimmune disease with **HLA DR4** association.

- **Most common cause of eye inflammation especially in the kingdom.**

#### • T-lymphocytes attack melanin containing structures:

- Skin → vitiligo
- Hair → alopecia (white hair)
- Lashes → poliosis (white lashes)
- Meninges → severe headache, meningitis
- Inner ear → tinnitus, deafness

- Eye → uveitis
  - When the choroiditis is exudative → ( accumulation of fluid under retina) → serous **retinal detachment**
  - Irregular pupil (not rounded) due to **synechiae**.
- The inflammation could be granulatamatus leading to **Mutton fat keratic precipitates** (due to anterior uveitis)

### Treatment:

Should be very early in the acute phase by **large doses of systemic steroids** for at least 1 year + **immunosuppressive** therapy like mycophenolate mofetil (Cellcept) and cyclosporin, to prevent permanent visual loss.

Prognosis: visual recovery is not always complete → residual depigmentation of the fundus

## 5.8 Giant-Cell Arteritis:

- One of the top emergencies in ophthalmology.
- The patient comes to the emergency room because of sudden loss of vision.
- Autoimmune vasculitis of large and medium sized arteries
- More common in **elderly >60 years**
- **Features: Sudden visual loss** due to ischemic anterior- posterior optic neuropathy (infarction of optic nerve); due to occlusion of the small circulation supplying the optic nerve, disc will be **pale and swollen**, and other features:
  - Pain over the temporal artery
  - Jaw claudication (pain with chewing)
  - Scalp tenderness (gangrene of the scalp may occur)
  - Polymyalgia rheumatica (muscular pain, esp. neck, shoulders and hips)
  - Constitutional symptoms
- **Diagnosis:** Erythrocyte Sedimentation Rate (ESR: very high), C reactive protein (CRP: high), **temporal artery biopsy (gold standard)**.
- **Treatment:** immediately and urgently with **large doses of systemic steroids** to **prevent visual loss in the other eye** (the affected eye will be **irreversibly damaged** at the time of presentation).

## 6. Hereditary Metabolic Disorders: Wilson's Disease:

- Also called "hepatolenticular degeneration".
- Pediatric disease.
- Deficiency of alpha-2 globulin ceruloplasmin (copper binding protien) → abnormal copper metabolism, this will allow copper metabolism in the tissues.

• So copper will deposit:

1. In the **cornea** at the level of descemet's membrane in the peripheral part (brownish ring) → (**Kayser-Fleischer ring**).
2. In the **lens** → (**green sunflower cataract**)
3. In the liver → cirrhosis
4. In the basal nuclei

## 7. Heritable Connective Tissue Disorders: Marfan's Syndrome:

### Ocular features:

- 1) **Lens subluxation** (**Ectopia lentis**) (important; usually superiorly and nasally)
  - 2) Angle anomaly
  - 3) Glaucoma
  - 4) Hypoplasia of the dilator muscle
  - 5) Axial myopia
  - 6) Retinal detachment
- Rare syndrome due to fibrillin-1 gene mutation on chromosome 15; autosomal dominant
  - Features: increased length of long bones, esp. fingers and toes (arachnodactyly) +
    - Scanty (little) subcutaneous fat
    - Relaxed ligaments
    - Congenital heart disease
    - Deformities of the spine and joints

### What are the other causes of lens subluxation (Ectopia lentis) :

1. Trauma
2. Homocysteinemia
3. Hyperlysinemia
4. Weill–Marchesani syndrome: is a rare, genetic disorder characterized by short stature, broad head (**brachycephaly**) and other facial abnormalities; hand defects and distinctive eye abnormalities. The eye manifestations typically include unusually small, round lenses of the eyes (spherophakia), which may be prone to dislocating.

## 8. Hematologic: Sickle Cell Disease:

- Sickled RBC's will occlude the peripheral retinal circulation → retinal ischemia → **neovascularization** (angiogram will show area of ischemia and new vessels) → vitreous hemorrhage and tractional retinal detachment
- Not seen very frequently.
- Treatment: (as in diabetes) focal laser ± vitrectomy

## 9. Vascular: Hypertensive Retinopathy:

### • Ocular features:

- Stage 1: Attenuation of arteries (↓ diameter) and increase light reflex , sometimes referred to as “copper/silver wiring” .  
*Copper wire arterioles* where the central light reflex occupies most of the width of the arteriole and *Silver wire arterioles* where the central light reflex occupies all of the width of the arteriole, due to sickening of the walls of arteries.
- Stage 2: as grade 1 + Nipping of the retinal veins where they are crossed by arterioles
- Stage 3: as grade 2+ Narrowing of arterioles → breakdown of blood-retina barrier: **hard exudates, hemorrhages, macular star and retinal edema.**  
If severe → signs of capillary occlusion: **cotton wool spots**
- Stage 4: **Optic disc edema** (bilateral = papilledema) → blurring of vision and temporary visual loss

## Summary: (from 429):

**Structure:** Conjunctiva, Cornea, and Sclera

Disease	Manifestation
Grave's disease	Keratitis lagophthalmos
Tuberculosis	Phlyctenular keratoconjunctivitis, interstitial keratitis
Sarcoidosis	Lid margin & conjunctival granulomas Mutton-fat keratic precipitates
Syphilis (congenital & acquired)	Interstitial keratitis
Rheumatoid arthritis	Keratoconjunctivitis sicca, scleritis & scleromalacia perforans
Sjögren's syndrome	Keratoconjunctivitis sicca
Vogt-Koyanagi-Harada syndrome	Keratic precipitates
Wilson's disease	Kayser-Fleischer ring

## Structure: Lens

Disease	Manifestation
Diabetes mellitus	Earlier onset of senile cataract, hyperglycemic cataract Sudden change in refractive error
Rubella	Cataract
Marfan's syndrome	Lens subluxation (superiorly & nasally)
Wilson's disease	Green sunflower cataract

### Structure: Uveal Tract & Retina

Disease	Manifestation
Diabetes mellitus	Rubeosis iridis
Tuberculosis	Uveitis (most common cause), retinal vasculitis
Sarcoidosis	Acute iridocyclitis, chronic granulomatous iridocyclitis Retinal periphlebitis, choroidal & retinal granulomas
Syphilis	Iridocyclitis, chorioretinitis
Toxoplasmosis	Posterior uveitis (most common cause)
Rubella	Glaucoma, retinopathy
SLE	Retinal artery occlusive disease
Ankylosing spondylitis	Anterior uveitis "iridocyclitis" (non-granulomatous)
Juvenile chronic arthritis	Uveitis w/pauciarticular type
Behçet's disease	Uveitis (w/hypopyon), retinal vasculitis, RVO
Vogt-Koyanagi-Harada	Anterior and posterior uveitis, retinal detachment
Marfan's syndrome	Glaucoma, retinal detachment
Sickle Cell Disease	Retinal ischemia & neovascularization ± vitreous hemorrhage

### Structure: Optic Nerve

Disease	Manifestation
Diabetes mellitus	Optic neuropathy (ischemic)
Grave's disease	Optic neuropathy
Sarcoidosis	Optic nerve granulomas
Giant cell arteritis	Ischemic optic neuropathy