



Ophthalmology PG Exam Notes

1st Edition

UVEA

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I notes

(Ophthalmology PG Exam Notes)

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This is a compilation effort from my preparation notes and other sources, thus any contributions or comments are welcomed in the effort to improve this book. Therefore, feel free to e-mail me at drdpatel87@gmail.com

/ notes
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Thank you GOD

This manual is collection of the notes I made, found in books or internet while studying for the Final MD exams for ophthalmology.

I have segregated topics just like book chapters to find them back easily. Though these all might be far less then other preparation notes available, I am proud of what I have made and I feel nice to present them to my upcoming ophthalmology friends.

Good luck!

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Uvea

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Q- Approach to uveitis

DOS article

History

- 90% of diagnoses can be made on the basis of the medical history alone
- Acute or chronic
- accompanied by pain and redness, or by floaters and visual loss
- visual disability and discomfort
- **Floaters and reduced vision** are the two most common complaints of patients with inflammation of the vitreous, retina, and choroid.
- **Questionnaire** developed by **Foster and MEEI**
- Family History
- HLA associations
-

Examination

- UCVA and BCVA
 - cause of diminished vision: corneal opacity, anterior chamber inflammation, cataract, and vitreous haze
 - **improvement in near vision** can precede an improvement in distance vision by several weeks in patients with chronic macular edema
 - **Snellen eye chart**
 - ability to resolve high-contrast letters only

- not enough sensitivity if vision is poor
- no lines between 20/100 and 20/200 or between 20/200 and 20/400.
- too few letters on the lines above 20/100.
- initial improvement might be missed with use of a standard Snellen chart.
- **ETDRS chart**
 - five letters per line starting with the 20/200 line
 - every **three lines** represent a **doubling of the visual angle**
 - 20/40 to 20/20 = 20/80 to 20/40.
 - If patients cannot read the 20/200 line while sitting 4 m from the chart, they are moved to 1 m from the chart → 5/200
 - 1 and 4 m scales can be made continuous by adding 30 letters to the number read at 4 m. The scale of visual acuity is then linear and continuous from 5/200 (five letters) to 20/12.5 (95 letters).
- electronic visual acuity testing algorithm (E-ETDRS)
- **Skin:** rashes, nodules, or vitiligo
- **Pupils** and extraocular muscles:
 - Synechiae
 - Iris atrophy
 - RAPD
 - Esotropia or exotropia resulting from long-standing visual loss may develop as a result of cataract, retinal, or optic nerve disease
- **IOP:**
 - under anesthetic **without fluorescein**, done with a pneumotonometer, or preferably, performed at the end of the examination.
 - elevated intraocular pressure or hypotony can occur as a result of intraocular inflammation
- **SLE**
 - Conjunctival hyperemia: CCC

- Cornea
 - KP: aggregates of inflammatory cells
 - base-down triangle configuration generally, **diffuse in FHI**
 - **nongranulomatous**: small aggregates, neutrophils and lymphocytes
 - **'mutton-fat' or 'granulomatous'**: larger granulomatous aggregates are composed of macrophages and giant cells
 - Interstitial keratitis may be associated with **syphilis or Cogan's syndrome**
- Anterior chamber
 - anterior chamber inflammation is a convenient but somewhat indirect measure of the inflammatory reaction
 - **Cells**
 - **primarily lymphocytes** but a significant number of neutrophils may be present
 - cells represent an **index of activity** but not a direct measure of the active inflammation

CELLS Grading System

SUN-Standardization of uveitis nomenclature

<1 -0

1-5 -±

6-15 -+1

16-25 -+2

26-50 -+3

>50 -+4

- **Flare:**
- Increased protein content in the anterior chamber

- manifestation of a **breakdown of the blood-ocular barrier**
- When the slit beam is obliquely aimed across the anterior chamber, the ability to **visualize the path of the beam** is termed flare. This principle is known as TYNDALL EFFECT.
- **7 g of protein/100 mL of blood**, but only **11 mg of protein/100 mL of aqueous**.
- chronic flare alone is not a sign of active inflammation. Damaged blood vessels may be leaky for a long time after the active inflammation has resolved.

Grading of Flare

Nil	-0
Just detectable	--1
Moderate (iris and lens details clear)	+2
Marked (iris and lens details hazy)	+3
Intense (fibrinous exudate)	+4

- **Hypopyon** is a dramatic but short-lived finding in ocular inflammation that has been associated with **Behçet's disease, endophthalmitis, and rifabutin toxicity in patients with AIDS**.
 - **pseudohypopyon**, composed of tumor cells or hemorrhagic debris, can occur in some of the masquerade syndromes after vitreous hemorrhage.
 - **pink hypopyon**: *Serratia marcescens* endophthalmitis. Cytologic examination reveals no erythrocytes, and the pink color is due to the bacteria.
- Iris
 - Synechia
 - fibrovascular membrane
 - transillumination defects can be a clue to herpetic uveitis

- Iris nodules: **Koeppe nodule** develops on the pupillary border, whereas the **Busacca's nodules** occur on the iris surface, **Berlin nodule** in the angle
- Anterior chamber angle
- Lens
- Vitreous
 - Grading of vitreous cells with use of Hruby lens

Cells in Retroilluminated Field

0-1 Clear 0+

2-20 Few opacities Trace

21-50 Scattered opacities 1+

51-100 Moderate opacities 2+

101-250 Many opacities 3+

>251 Dense opacities 4+

- **vitreous haze is a better indicator** of active inflammation than are vitreous cells, because it combines the optical effect of cellular infiltration and protein leakage.
- Retina and choroid
 - Cystoid macular edema
 - Retinal vascular alterations: Vascular sheathing,
 - Retinal hemorrhages and cotton-wool spots
 - Choroidal lesions: grayish-yellow elevated masses,
- Optic nerve
 - Disc hyperemia, papillitis, or papilledema
 - Secondary glaucoma
 - Neovascularization

Differential Diagnosis

Acute or chronic uveitis

(<6 weeks, > 6 weeks)

Acute Uveitis

- Most cases of anterior uveitis: idiopathic, ankylosing spondylitis, Reiter's syndrome, Fuchs' heterochromic iridocyclitis
- Vogt-Koyanagi-Harada syndrome
- Toxoplasmosis
- White-dot syndromes: acute posterior multifocal placoid pigment epitheliopathy and multiple evanescent white-dot syndrome
- Acute retinal necrosis
- Postsurgical bacterial infection
- Trauma

Chronic Uveitis

- Juvenile rheumatoid arthritis
- Birdshot choroidopathy
- Serpiginous choroidopathy
- Tuberculous uveitis
- Postoperative uveitis (Propionibacterium acnes, fungal)
- Intraocular lymphoma
- Sympathetic ophthalmia

- Multifocal choroiditis
- Sarcoidosis
- Intermediate uveitis/pars planitis

Granulomatous or nongranulomatous

Causes of granulomatous inflammation

- Sarcoidosis
- Sympathetic ophthalmia
- Uveitis associated with multiple sclerosis
- Lens-induced uveitis
- Intraocular foreign body
- Vogt-Koyanagi-Harada syndrome
- Syphilis
- Tuberculosis
- Other infectious agents

unilateral or bilateral

Causes of unilateral uveitis

- Sarcoidosis
- Postsurgical uveitis
- Intraocular foreign body
- Parasitic disease

- Acute retinal necrosis
- Behçet's disease

Location in the Eye

IUSG Classification

International Uveitis Study Group

- **Anterior uveitis:** Iritis, Anterior cyclitis
- **Iridocyclitis:**
- **Intermediate uveitis** (formerly known as pars planitis): Posterior cyclitis, Hyalitis, Basal retinochoroiditis
- **Posterior uveitis:**
 - Focal, multifocal, or diffuse choroiditis
 - Chorioretinitis or retinochoroiditis
 - Neuroretinitis
 - Panuveitis

Tessler's classification

SUN classification

Causes of anterior uveitis

Idiopathic

Ankylosing spondylitis

Reiter's syndrome

Inflammatory bowel disease

Psoriatic arthritis

Behçet's disease

HLA-B27-associated disease

Juvenile rheumatoid arthritis

Fuchs' heterochromic iridocyclitis

Sarcoidosis

Syphilis

Glaucomatocyclitic crisis

Masquerade syndromes

Causes of intermediate uveitis

Sarcoidosis

Inflammatory bowel disease

Multiple sclerosis

Lyme disease

Pars planitis (*poorest prognosis among intermediate uveitis*)

Causes of posterior uveitis

FOCAL RETINITIS

Toxoplasmosis

Onchocerciasis

Cysticercosis

Masquerade syndromes

MULTIFOCAL RETINITIS

Syphilis

Herpes simplex virus

Cytomegalovirus

Sarcoidosis

Masquerade syndromes

Candidiasis

Meningococcus

FOCAL CHOROIDITIS

Toxocariasis

Tuberculosis

Nocardiosis

Masquerade syndromes

MULTIFOCAL CHOROIDITIS

Histoplasmosis

Sympathetic ophthalmia

Vogt-Koyanagi-Harada syndrome

Sarcoidosis

Serpiginous choroidopathy

Birdshot choroidopathy

Masquerade syndromes (metastatic tumor)

Causes of panuveitis

Syphilis

Sarcoidosis

Vogt-Koyanagi-Harada syndrome

Infectious endophthalmitis

Behçet's disease

SO

Demographics

Age (yr)	Diagnostic Considerations
<5	Juvenile rheumatoid arthritis Toxocariasis Postviral neuroretinitis (Retinoblastoma) (Juvenile xanthogranuloma) Leukemia
5-15	Juvenile rheumatoid arthritis Pars planitis Toxocariasis Postviral neuroretinitis Sarcoidosis Leukemia
16-25	Pars planitis Ankylosing spondylitis Idiopathic anterior uveitis Toxoplasmosis Sarcoidosis Acute retinal necrosis
25-45	Ankylosing spondylitis

Age (yr)	Diagnostic Considerations
	<ul style="list-style-type: none"> Idiopathic anterior uveitis Fuchs' heterochromic iridocyclitis Idiopathic intermediate uveitis Toxoplasmosis Behçet's disease Idiopathic retinal vasculitis Sarcoidosis White-dot syndromes Vogt-Koyanagi-Harada syndrome AIDS, syphilis Serpiginous choroidopathy
45-65	<ul style="list-style-type: none"> Birdshot retinochoroiditis Idiopathic anterior uveitis Idiopathic intermediate uveitis Idiopathic retinal vasculitis Behçet's disease Serpiginous choroidopathy Acute retinal necrosis
>65	<ul style="list-style-type: none"> Idiopathic anterior uveitis Idiopathic intermediate uveitis Idiopathic retinal vasculitis Serpiginous choroidopathy (Masquerade syndromes)

Factor	Disease Risks
Female	Pauciarticular juvenile rheumatoid arthritis, chronic anterior uveitis
Male	Ankylosing spondylitis, sympathetic ophthalmia
American black	Sarcoidosis
Native American	Vogt-Koyanagi-Harada syndrome
Midwestern American	Presumed ocular histoplasmosis
Japanese	Vogt-Koyanagi-Harada syndrome

Factor	Disease Risks
	Behçet's syndrome
Mediterranean ancestry	Behçet's syndrome
Central American	Cysticercosis, onchocerciasis
South American	Cysticercosis, toxoplasmosis
West African	Onchocerciasis
Intravenous drug user	Fungal endophthalmitis, AIDS
Promiscuous sexual activity	AIDS, syphilis
Frequent hiking in wooded areas	Lyme disease

Symptoms and Signs

Symptom or Sign	Possible Associated Conditions
Headaches	Sarcoidosis, Vogt-Koyanagi-Harada syndrome
Neurosensory deafness	Vogt-Koyanagi-Harada syndrome, sarcoidosis
Cerebrospinal fluid pleocytosis	Vogt-Koyanagi-Harada syndrome, sarcoidosis, acute posterior multifocal placoid pigment epitheliopathy, Behçet's syndrome
Paresthesia, weakness	Intermediate uveitis associated with multiple sclerosis, Behçet's syndrome, steroid myopathy
Psychosis	Vogt-Koyanagi-Harada syndrome, sarcoidosis, Behçet's disease, steroid psychosis, systemic lupus erythematosus
Vitiligo, poliosis	Vogt-Koyanagi-Harada syndrome
Erythema nodosum	Behçet's syndrome, sarcoidosis
Skin nodules	Sarcoidosis, onchocerciasis
Alopecia	Vogt-Koyanagi-Harada syndrome
Skin rash	Behçet's syndrome, sarcoidosis, viral exanthem, syphilis, herpes zoster, psoriatic arthritis, Lyme disease
Oral ulcers	Behçet's syndrome, inflammatory bowel disease
Genital ulcers	Behçet's syndrome, Reiter's syndrome, sexually transmitted diseases
Salivary or lacrimal	Sarcoidosis, lymphoma

Symptom or Sign	Possible Associated Conditions
gland swelling	
Lymphoid organ enlargement	Sarcoidosis, AIDS
Diarrhea	Whipple's disease, inflammatory bowel disease
Cough, shortness of breath	Sarcoidosis, tuberculosis, malignancy
Sinusitis	Wegener's granulomatosis
Systemic vasculitis	Behçet's syndrome, sarcoidosis, relapsing polychondritis
Arthritis	Behçet's syndrome, Reiter's syndrome, sarcoidosis, juvenile rheumatoid arthritis, rheumatoid arthritis, Lyme disease, inflammatory bowel disease, Wegener's granulomatosis, systemic lupus erythematosus, other connective tissue diseases
Sacroiliitis	Ankylosing spondylitis, Reiter's syndrome, inflammatory bowel disease
Chemotherapy or other immunosuppression	Cytomegalovirus retinitis, <i>Candida</i> retinitis, other opportunistic organisms

Medications possibly causing uveitis

Brimonidine

Latanoprost

Rifabutin

Terbinafine

Trimethoprim

Diagnostic Testing

Management

Medical Therapy

Corticosteroids

Gordon's dictum - "Use enough, soon enough, taper and discontinue"

Mechanism of action

- Inhibits arachidonic acid release from phospholipids
- Inhibit the transcription and action of cytokines
- Limits B-and T -cell activity.

Preparation	Antiinflammatory potency
Hydrocortisone	1.0
Cortisone	0.8
Prednisolone	4.0
Prednisone	4.0
Dexamethasone	26
Methylprednisolone	5
Triamcinolone	5
Betamethasone	33

- Topical application
- periocular injections:
 - **PST** 40 mg in 1 mL

- **anecortave acetate**, a corticosteroid that has been modified so that its **corticosteroid activity has been eliminated**, is also injected periocularly. The interest in this molecule is **related to its retardation of blood vessel growth through inhibition of endothelial cell migration**.
- **intraocular administration**
 - 2 mg of triamcinolone
 - Fluocinolone acetonide (FA) intravitreal implants
 - **Ozurdex** is a sustained-release biodegradable intravitreal implant containing dexamethasone.
 - Systemic corticosteroids remain the initial drug of choice for most patients with severe bilateral endogenous sight-threatening uveitis. **The striking exception to this rule is patients with Behçet's disease.**

Common immunosuppressive agents

Agent	Usual dosage*
Prednisone	Oral: 1-2 mg/kg/day
Methylprednisolone	IV pulse: 1 g over 1-2 h
Intraocular triamcinolone	Intravitreal: 2-4 mg
Antimetabolites	
Methotrexate	Oral: 7.5-15 mg weekly; can be given intramuscularly
Azathioprine weight/day	Oral: 50-150 mg daily, 1-1.5 mg/kg, but up to 2.5 mg/kg body
Mycophenolate mofetil	Oral: 1 g twice per day
Alkylating agents	
Cyclophosphamide	Oral: 50-100 mg daily, up to 2.5 mg/kg body weight/day
	IV pulse: 750 mg/m ² (adjusted to kidney function and white blood cell count)
Chlorambucil	Oral: 0.1-0.2 mg/kg/day
Ciclosporin	Oral: up to 5 mg/kg/day, usually given with prednisone, 10-20 mg/day
FK506	Oral: 0.10-0.15 mg/kg body weight/day
Daclizumab	IV or SC: 1-2 mg/kg

Agent	Usual dosage*
Etanercept	SC: 25 mg twice weekly; children 0.4 mg/kg twice weekly
Infliximab	SC: 3-10 mg/kg
Interferon- α	SC: $3-6 \times 10^6$ IU qd \times 1 mo, then qod; 3×10^6 IU three times per week

Include 3 main categories of therapy:

1. **Antimetabolites:** Azathioprine, methotrexate, and mycophenolate mofetil
2. **T-cell suppressors:** Cyclosporine and tacrolimus
3. **Cytotoxic agents:** Cytotoxic agents are alkylating agents and include cyclophosphamide and chlorambucil.

Most agents take several weeks to achieve efficacy; therefore, they initially are used in conjunction with oral corticosteroids. Once the disease is under control, corticosteroids can be tapered.

Azathioprine

Introduction: It is a nucleoside analog which interferes with DNA replication and RNA transcription. Decreases peripheral T- and B-lymphocyte count and reduces lymphocyte activity. Metabolism is dependent on xanthine oxidase. It may decrease proliferation of immune cells, which results in lower autoimmune activity.

Indications: Behcet disease or chronic uveitis, especially with oral corticosteroids.

Dose: 1 mg/kg/ d orally initially; not to exceed 2.5-4 mg/kg/ d

Side effects

- Causes GI upset
- Alters liver function and renal function
- Decreases the bone marrow function
- Rarely causes pancreatitis

- Increases risk of neoplasia

CBC and liver function tests should be done once every two weeks.

Methotrexate

Introduction: It is a folic acid analog and inhibitor of dihydrofolate reductase, which is the enzyme responsible for the conversion of dihydrofolate to tetrahydrofolate. It arrests DNA replication, inhibiting rapidly dividing cells (e.g. leucocytes).

Indications: It is used to treat various ocular inflammatory diseases, including vasculitis, panuveitis, intermediate uveitis, and vitritis, Behcet disease or chronic uveitis, especially with oral corticosteroids.

Dose: 7.5-12.5 mg/wk PO initially; not to exceed 25 mg/wk; folate (1 mg/ d) is given concurrently to minimize nausea

Side effects

- Increases fatigue
- Causes GI upset
- Alters liver, hematological and renal function
- Rarely causes pneumonitis

CBC and liver function tests should be done once every two weeks.

Mycophenolate mofetil

Introduction: It is a selective inhibitor of inosine monophosphate dehydrogenase, which interferes with guanosine nucleotide synthesis. It prevents lymphocyte proliferation, suppresses antibody synthesis, interferes with cellular adhesion to vascular endothelium, and decreases recruitment of leukocytes to sites of inflammation.

Indications: Various studies are ongoing to study effectivity in various inflammatory conditions.

Dose: 500 mg orally bid initially; not to exceed 1.5 g bid

Side effects

- Increases chance of infection

- Causes GI upset like nausea, vomiting and diarrhoea.
- Alters liver, haematologic and renal function
- Incidence of leucopenia, lymphoma, and non-melanoma skin cancers are reported

CBC, renal and liver function tests should be done once every two weeks.

Cyclosporine

Introduction: It binds to the cytosolic protein cyclophilin (immunophilin) of immunocompetent lymphocytes, especially T-lymphocytes. This complex of cyclosporin and cyclophilin inhibits calcineurin which under normal circumstances is responsible for activating the transcription of interleukin-2. It thus inhibits the transcription of T lymphocytes that are in the G0 and G1 phase of their cell cycle, which blocks replication and ability to produce lymphokines.

Indications: Cyclosporine can be used in cases of uveitis which are not responding to treatment with steroids.

Dose: 2.5-5 mg/kg/ d orally initially; not to exceed 10 mg/kg/ d

Side effects

- Causes gingival hyperplasia, tremors, myalgias and hirsutism.
- Nephrotoxic and Hepatotoxic
- Can lead to hypertension

CBC, renal and liver function tests should be done once every two weeks.

Cyclophosphamide

Introduction: It is chemically related to nitrogen mustards. As an alkylating agent, mechanism of action of the active metabolites may involve crosslinking of DNA, which may interfere with growth of normal and neoplastic cells. It is cytotoxic to resting and dividing lymphocytes.

Indications: The main indication is Wegner's granulomatosis. It can also be used as second line in management of cases not responding to steroids or other immunosuppressives.

Dose: 2 mg/kg/ d orally initially; not to exceed 3 mg/kg/ d

Side effects:

- Causes haemorrhagic cystitis
- Causes severe nausea, vomiting.
- It can also lead to ovarian failure and testicular atrophy.

CBC, renal, liver function tests and routine urine examination should be done once every two weeks.

Biologicals: These are monoclonal antibodies against tumor necrosis factor (TNF).

TNF alpha- Biological activities

- Induction of pro-inflammatory cytokines like IL-1, IL-6
- Enhancement of leucocyte migration
- Expression of adhesion molecules by endothelial cells and leucocytes
- Activation of neutrophil and eosinophil functional activity

Infliximab

Introduction: Infliximab is a genetically engineered fusion protein consisting of TNF receptors fused to the constant region of human immunoglobulin IgG 1. It is 75% humanised. It is a short-term immunosuppressive used in noninfectious uveitis.

Indication: Several investigator- sponsored trial and uncontrolled case series indicated that TNF antagonists, mainly infliximab is useful in ocular inflammation associated with Behcet's disease, Rheumatoid arthritis, juvenile idiopathic arthritis, Crohn's disease, Sarcoidosis, idiopathic uveitis, birdshot retinochoroiditis.

Dosage

Administered as 5-10 mg/kg- intravenous infusion. Regime (1st dose- Day 0, 2nd dose- Day14, 3rd dose- Day 42) as intravenous infusion.

Methotrexate- 7.5 mg weekly and Folic acid 5 mg daily given to reduce immunogenicity.

Mechanism of action

- Neutralises TNF-alpha activity, binds to soluble and membranous forms of TNF-alpha
- Rapid reduction of C-reactive protein

- Decreases pro-inflammatory cytokines-TNF-alpha, IL-6 & IL-1

Side effects

- Anaphylactic reaction
- Demyelination syndrome
- Infusion related reaction- hypersensitivity reaction
- Autoimmunity- Lupus like syndrome- Antibody to ds DNA

Precautions

- Immunosuppression
- Pregnancy & lactation
- Extremes of age
- Drug interactions
- Carcinogenesis, mutagenesis or impairment of fertility
- Known hypersensitivity to any murine proteins

Adalimumab

It is a completely humanised monoclonal antibody against TNF-alpha. Thus, it has the potential to cause fewer side effects like anaphylactic reaction. Its role is being studied in various uveitic conditions especially childhood uveitis.

Etanercept (Enbrel)

ENBREL was first approved 7 years ago for the treatment of moderate to severe rheumatoid arthritis (RA). It is a TNF alpha inhibitor. It binds to both soluble and cell membrane associated TNF-alpha and inhibits their binding to cell-surface TNF-alpha receptors.

Its role was studied in childhood uveitis recently. The study showed that it is not effective in uveitis associated with juvenile arthritis, in fact it can provoke uveitis.

Antiviral therapy

Mydriatic and cycloplegic agents

- helps prevent the development of posterior synechiae and, in the extreme, iris bombe
- relieves discomfort/ pain
- gives unhindered view of the media and fundus
- **avoid cyclopentolate (Cyclogyl)**, as this has been shown to be an effective chemoattractant for leukocytes.

Antitoxoplasmosis therapy

Immunostimulators

- Levamisole

Plasmapheresis

NSAIDS

Surgical Therapy

disease needs to be clinically quiescent for at least 3 months

Removal of band keratopathy

- Calcium hydroxyapatite accumulates in Bowman's membrane
- 1.7% solution of EDTA in water or saline applied to the cornea with cotton or a cellulose applicator.
- Excimer laser

Corneal transplantation

- herpetic keratouveitis

Cataract surgery

-

Glaucoma surgery

Laser treatment

Anterior Uveitis

- It accounts for around 60% of all the cases of uveitis

HLA B 27 Positive Anterior Uveitis

Uveitis in Spondyloarthropathies

Group of seronegative spondyloarthropathies include: **PAIR**

- Ankylosing spondylitis
- Reiter syndrome/Postinfectious or reactive arthritis
- Inflammatory bowel disease
- Psoriatic arthritis
- Undifferentiated spondyloarthropathy.

These conditions are associated with both acute non-granulomatous anterior uveitis and HLA B 27 positivity.

HLA B-27 Association: Human leucocyte antigen B-27 (HLA B-27) is a genome located on the short arm of chromosome 6. HLA B-27 positivity is present in around 8% of the Western population and 1% of the Asian population. But almost 50-60% of the patients with acute anterior uveitis are HLA B 27 positive.

Pathogenesis: The actual role of HLA-B27 in triggering an inflammatory response causing disease is still not precisely known. It is believed to incite the immune reaction by **molecular mimicry or acting as an arthritogenic peptide.**

Clinical Features

Symptoms

- Pain
- Photophobia
- Redness
- Blurring of vision

Signs

- Circumcorneal congestion
- Presence of fine keratic precipitates especially over the inferior part.
- Severe anterior chamber reaction, **quite often fibrin and hypopyon formation occurs.**

Natural Course

- There is a **high frequency of recurrent episodes** with a mean number of 0.6-3.3 attacks per year
- Mean duration of each episode is 4-6 weeks.
- The interval between acute attacks is about 14-25 months.
- There may also be a decrease in the frequency of uveitis attacks with increasing duration of disease.

Ankylosing Spondylitis

Ankylosing spondylitis is a chronic, usually progressive disease involving the articulations of the spine and adjacent soft tissues. The sacroiliac joints usually are affected. Involvement of the hip and shoulders commonly occurs, and peripheral joints are affected less frequently.

Epidemiology: The disease begins most often in the third decade. Males are more commonly affected. HLA B 27 positivity is found in almost 90% of the patients with ankylosing spondylitis. Almost, 1 in 4 patients with HLA B 27 positivity will develop ankylosing spondylitis or anterior uveitis.

Clinical features

Symptoms: Lower back pain and stiffness which is worse after periods of inactivity. But very often, patients might not complain of back pain.

Signs: Kyphoscoliosis

Investigations

Radiological: Radiographs of sacroiliac joints show sclerosis and narrowing of the joint space. This is followed by ligamentous ossification and osteoporosis. Both sacroiliac joints usually are involved, but findings may first appear on one side. Later on, there might be fusion of the lower vertebrae leading to loss of curvature and giving rise to 'bamboo spine' appearance.

Reactive Arthritis and Reiter's Syndrome

Reactive arthritis (ReA) refers to spondyloarthropathies following enteric or urogenital infections and occurring in individuals who are HLA-B27 positive. Reiter's syndrome is included in this category.

Reiter syndrome is described as a triad of

- Arthritis
- Nonspecific urethritis
- Conjunctivitis, often accompanied by iritis.

Epidemiology: It is generally seen in the young age group (20-40) If the disease is acquired secondary to a gastrointestinal infection, it is seen equally in both males and females. If the disease is acquired secondary to a urogenital infection, it is more common in males. Almost, 75% of the patients with reactive arthritis are HLA B 27 positive.

Pathogenesis: As described earlier, molecular mimicry is thought to be the cause for the inflammatory response. The bacteria that have been implicated include Salmonella species, Yersinia enterocolitica, Campylobacter jejuni, Chlamydia trachomatis, Chlamydia pneumoniae, Clostridium difficile, and Ureaplasma urealyticum.

Clinical features

Urethritis: The syndrome usually begins with urethritis followed by conjunctivitis and rheumatological findings.

Conjunctivitis: The conjunctivitis is usually minimal and lasts for only a few days or weeks. It is mucopurulent and papillary.

Arthritis: Arthritis begins within 1 month of infection in 80% of patients. It usually is acute, asymmetric, oligoarticular, involving predominantly the joints of the lower extremities (e.g., knees, ankles, feet, wrists). The arthritis usually is quite painful. Dactylitis or sausage digit is a diffuse swelling of a solitary finger or toe. Plantar fasciitis and Achilles tendonitis also are common. Sacroiliitis is present in as many as 70% of patients.

Other features: Punctate and subepithelial keratitis may occur rarely, leading to permanent corneal scars. Acute non-granulomatous iritis recurs frequently in this condition. It may become bilateral and chronic and may result in blindness. Mucocutaneous lesions like keratoderma blennorrhagicum, a scaly, erythematous, irritating disorder of the palms and soles of the feet, and circinate balanitis, a persistent, scaly, erythematous circumferential rash of the distal penis are known to occur.

Investigations: ReA is a clinical diagnosis without definitive laboratory or radiographic findings. The diagnosis should be considered when an acute asymmetric inflammatory arthritis or tendonitis follows an episode of diarrhoea or dysuria.

Inflammatory Bowel Disease

Ulcerative colitis and Crohn disease are associated with acute anterior uveitis. Specifically, 2.4% of patients with Crohn disease and 5-12% of patients with ulcerative colitis develop acute anterior uveitis.

Patients with uveitis and inflammatory bowel disease alone tend to be HLA B 27 negative.

Almost, 50-60% of the patients with spondyloarthropathies and inflammatory bowel disease with uveitis are HLA B 27 positive.

Psoriatic Arthritis

Psoriasis is a non-contagious disorder characterised by the presence of silvery white scales on the extensor surfaces of the body. Psoriasis precedes the onset of arthritis by months or years. Most patients have onychodystrophy, which includes onycholysis and ridging and pitting of nail beds.

Twenty-five percent of patients develop a more severe symmetrical arthritis resembling rheumatoid arthritis. The proximal interphalangeal joints and distal interphalangeal joints commonly are involved with characteristic sausage-shaped digits.

HLA B 27 positivity is present in cases where psoriatic arthritis is associated with spondylitis.

Juvenile Idiopathic Arthritis

Juvenile rheumatoid arthritis is also known as Juvenile idiopathic arthritis (JIA). JIA, as defined by the American Rheumatism Association (ARA), is the presence of arthritis (chronic, seronegative, and peripheral) before age 16 years, of at least 3 months duration, when other causes have been excluded.

Classification

It is classified as

- Oligoarticular onset jIA
- Polyarticular onset JIA
- Systemic onset jIA

Oligoarticular (Pauciarticular) Onset JIA (40-60%)

- This is common in girls (5:1).
- Peak age of onset is at age 2 years.
- Four or fewer joints are involved during the first 5 months of the disease (often asymmetric). Oligoarticular onset commonly involves the knees and, less frequently, the ankles and wrists.
- The arthritis may be evanescent, rarely destructive, and radiologically insignificant.
- Approximately, 75% of these patients test positive for antinuclear antibody (ANA). This mode of onset rarely is associated with systemic signs.
- A high risk for uveitis exists.

Polyarticular Onset JIA (20-40%)

- This is common in girls (3:1).
- Peak age of onset is at age 3 years.
- It involves 5 or more joints during the first 6 months of the disease.
- Polyarticular onset JIA commonly involves the small joints of the hand and, less frequently, the larger joints of the knee, ankle, or wrist. Asymmetric arthritis may be acute or chronic and may be destructive in 15% of patients.
- Rheumatoid factor (RF) is present in 10% of children with this JIA subgroup. It is associated with subcutaneous nodules, erosions, and a poor prognosis.
- Approximately 40% of these patients test positive for ANA. Systemic symptoms, including anorexia, anaemia, and growth retardation, are moderate.
- An intermediate risk for uveitis exists.

Systemic Onset JIA (10-20%)

- This is equal frequency in boys and girls and can appear at any age.
- Symmetric polyarthritis is present and may be destructive in 25% of patients. Hands, wrists, feet, ankles, elbows, knees, hips, shoulders, cervical spine, and jaw may be involved.

- ANA is positive in only 10% of the patients. Systemic onset is associated with fever (high in evening and normal in morning), macular rash, leucocytosis, lymphadenopathy, and hepatomegaly. Pericarditis, pleuritis, splenomegaly and abdominal pain less commonly are observed.

- A low risk for uveitis exists.

Risk Factors for Development of Uveitis in Patients with JIA

- Female gender
- Pauciarticular variety
- ANA positivity

Epidemiology: Around 10% of the cases with JIA develop uveitis.

Clinical Features

Symptoms: Patients complain of mild pain, photophobia and blurring of vision. Many a times, the patient is asymptomatic.

Signs

Conjunctiva: Most patients have no conjunctival injection even during acute exacerbations.

Cornea:

- Keratic precipitates -Small-medium, rarely mutton fat
- Patient may develop band keratopathy with time

Anterior uveitis

- Cells and flare; chronic flare (very common)
- Non-granulomatous uveitis (>90%)
- Bilateral (70-80%)
- Chronic smoldering or recurrent disease in greater than 90%

Iris: Posterior synechiae; pupillary membrane; rarely may develop Koeppe nodules

Management

It includes the use of topical steroids and use of systemic steroids in cases which are not responding to topical therapy. But, most patient have a chronic course and use of steroids can give rise to severe complications like growth retardation, hypertension and diabetes mellitus. So, steroid sparing agents like Methotrexate are being tried in these patients.

Management of cataract:

Cataract surgery is contraindicated in young patients with JIA due to the high chances of severe post-operative inflammation and cystoid macular oedema. Cataract surgery can be tried in older patients with JIA.

The following are few recommendations.

- Preoperatively the inflammation should have been absent for at least a period of three months
- Heparin coated IOL should be used
- Minimal intraoperative handling should be there
- Combined lensectomy and vitrectomy can be tried in these patients
- Post-operatively inflammation should be controlled aggressively and if required immunosuppressive therapy should be used.

Fuchs Uveitis Syndrome

Fuchs heterochromic iridocyclitis (FHI) is a chronic, unilateral iridocyclitis characterised by iris heterochromia.

Epidemiology

- It affects people between 20-60 years of age
- Males and females are equally affected.
- Nearly 2-3% of the patients with uveitis have Fuchs heterochromic iridocyclitis.

Pathogenesis

- Adrenergic dysfunction leading to iris hypopigmentation by reduced innervation to iris stromal melanocytes. Abnormal innervation to iris vasculature leads to breakdown in the blood-aqueous barrier with secondary leakage of proteins, cells, and inflammatory mediators into the anterior chamber.
- Strong association between FHI and ocular toxoplasmosis has been documented. Rubella, HSV and Toxocara canis are some of the other organisms associated with Fuch's heterochromic iridocyclitis.
- Higher interleukin 10 (IL-10) and interferon-gamma levels and lower IL-12 levels have been found in aqueous humor of patients with Fuch's heterochromic iridocyclitis compared with immune associated uveitis. These findings point to T helper (Th1) subtype response in FHI.

Clinical Features

Symptoms: The symptoms can vary from none to mild blurring of vision and discomfort.

Signs

- The classic triad of Fuch's heterochromic uveitis is heterochromia, cataract, and keratic precipitates (KPs).
- Conjunctiva and sclera: In most patients, there is no ciliary congestion or conjunctival hyperaemia.
- Cornea: Small, nonpigmented, translucent, stellate KPs with filamentous projections distributed over the entire endothelial surface is pathognomic of Fuch's heterochromic iridocyclitis. Stellate KPs can also be seen in uveitis associated with toxoplasmosis, herpes simplex, herpes zoster, and cytomegalovirus (CMV).
- Anterior chamber: There is minimal anterior chamber cells and flare. Paracentesis may result in the appearance of a filiform hemorrhage (Amsler sign).
- Iris: Heterochromia is present 75-90% cases. In unilateral cases, the hypopigmented eye is usually the affected eye. It is difficult to comment in bilateral cases (5-10%). Normally, a lighter coloured eye becomes darker when extensive loss of iris stroma occurs, exposing the darker pigment epithelial layer.
 - Iris sphincter atrophy may cause an irregular shaped pupil. White iris nodules may be seen along the pupillary border (Koeppel nodules) and in the iris stroma (Busacca nodules).
 - Fine vessels may be seen on the iris surface, especially in the angle. Neovascularisation of the iris and the anterior chamber angle (radial and circumferential) occurs in 6-22% of cases.
 - Posterior synechiae are never present. The presence of posterior synechiae should strongly suggest another diagnosis.
- Trabecular meshwork: Fine blood vessels may be seen on the trabecular meshwork. These may bleed unexpectedly when the intraocular pressure suddenly drops during surgery or paracentesis.
- Lens: Nearly, 80-90% of cases develop a posterior subcapsular cataract, which matures rapidly.
- Vitreous: Fine vitreous opacities are observed.

- Retina: The absence of cystoid macular oedema distinguishes Fuch's heterochromic iridocyclitis from other uveitis syndromes with chronic vitritis. Chorioretinal scars have been reported in some patients.
- Intraocular pressure: Secondary glaucoma is a frequent complication and can be present in 15-59% of cases.

Management

- Inflammation: *There is no need for topical steroids, as it is ineffective in controlling inflammation.*
- Cataract: The prognosis for Cataract surgery is generally good. Pre-op steroids are not required.
- Glaucoma: Medical management is sufficient most of the time. If surgery is planned, trabeculectomy with Mitomycin C or valve implant is preferred.

Posner Schlossman Syndrome (Glaucomatocyclitic Crisis)

It is characterised by recurrent episodes of unilateral uveitis associated with corneal oedema and increase in intraocular pressure out of proportion to the uveitis.

Epidemiology

- It typically affects people between the age of 20-50 yrs
- Males and females are equally affected
- Generally, only one eye is affected at one time

Pathogenesis

The exact aetiology of glaucomatocyclitic crisis is not known.

Factors that have been postulated include the following:

- Abnormal vascular process
- Autonomic defect
- Allergic condition

- Cytomegalovirus (CMV)
- Herpes simplex virus
- Variation of developmental glaucoma

Clinical Features

Symptoms

It is characterised by recurrent episodes of unilateral uveitis with elevation of IOP which is out of proportion and lasts from a period of hours to days. Patient complains of blurring of vision with haloes and sometimes pain.

Signs

Conjunctiva: The eye is quiet with no or minimal ciliary flush.

Cornea: If the IOP is above 40 mm Hg, the cornea can become edematous. Fine KP's can appear after 2-3 days of inflammation and resolve rapidly.

Anterior chamber: Minimal flare might be present and cells are generally absent.

Iris: Segmental ischaemia may be present.

IOP: It is generally elevated and in the range of 40-60 mm Hg. It is related to the number of days of uveitis and not to the severity of uveitis.

Posterior synechiae may be present.

Management

- Inflammation: Prednisolone acetate 1% drops can be started and then tapered slowly.
- Glaucoma: Medical management is sufficient most of the time. Topical beta blocker like Timolol 0.5% along with oral Diamox (Acetazolamide) is sufficient to manage the acutely elevated IOP.

Lens Associated Uveitis

Uveitis which results from immune reaction to lens material is called lens associated uveitis.

This can occur either through leakage of lens material through intact capsule as occurs in hypermature cataract or following rupture of lens capsule (traumatic or surgical).

Pathogenesis

It is thought to be an autoimmune reaction to lens protein because of altered tolerance. The first episode generally occurs insidiously but once the patient has got sensitized to the lens protein, e.g. following cataract surgery in one eye, the immune reaction occurs rapidly in the other eye following exposure to lens protein.

Clinical Features

Symptoms: Patient complains of redness, blurring of vision and pain.

Signs

- Both, granulomatous and non-granulomatous uveitis may occur.
- The anterior chamber reaction may vary from mild to severe depending on the amount of lens protein.
- Posterior synechiae formation occurs and IOP is quite often elevated.

Intermediate Uveitis

- first described as chronic cyclitis by **Fuchs in 1908**.
- clinical description: **Schepens** in 1950
- **Epidemiology**
 - **4-8%** of cases of uveitis
 - Has bimodal age distribution
 - 5-15 yrs: M>F

- 20-40 yrs: F>M
- It occurs equally in both the age groups.
- It is bilateral in 70-90% of the cases. Of which it is asymmetrical in 25% cases
- **Aetiology**
 - **Multiple Sclerosis**: In a study, 14.8% patients of intermediate uveitis had MS
 - **Lyme disease**: Caused by *Borrelia Burgdorferi* and spread by *Ixodes Dam mini*
 - **Sarcoidosis**: HTLV 1 infection: Mochizuki in his study found that 44.1% patients of IU had serology for HTLV 1
 - B Cell Lymphoma
 - Whipples Disease
 - HLA associations: HLA B 8, B 51; HLA DR 2 (Subset 15 found in 64.3% patients of IU)
HLA DR 17 ,DR-51
- **CF**
 - **Symptoms**: Floaters and blurring of vision are the most common complaints. Rarely pain, redness or photopsiae. blurred vision and/or floaters
 - DOV due to moderate vitritis and cystoid macular edema
 - **Signs**
 - minimal anterior segment inflammation (**exception** is patients with intermediate uveitis associated with **multiple sclerosis**, who typically develop a **granulomatous anterior uveitis** with formation of mutton-fat keratic precipitates.)
 - Posterior synechiae are rare and if present are broad based and difficult to break with dilatation. If posterior synechiae are present for more than 3-4 clock hours, the diagnosis of intermediate uveitis should be reconsidered.
 - Inferior vitreous snow balls. Vitreous strands.
 - Exudates may accumulate inferiorly to form snow bank.
 - The snow banks are of two types:
 - Smooth and shiny: Burned out pars planitis
 - Fluffy with attached snow halls: Active pars plani tis

- The snowbanks are commonly vascularised. These may bleed and give rise to Vitreous Haemorrhage. Peripheral retinal vasculitis is sometimes present inferiorly near the snow bank (8-30%).
- Cotton wool spots and retinal haemorrhage occur vety rarely. Seen generally after HTLV1 infection.chronic cystoid macular edema, glaucoma, inflammatory changes in the retina, and retinal detachment, VH
- Autoimmune endotheliopathy is a rare finding associated with pars planitis
- **Glaucoma: 8-10%**
- **Macular edema: 28 - 50%**
- **Features of HTL V1 Intermediate Uveitis are:**
 - **Increase in the CD4 to CD8 cells ratio**
 - Increase in the soluble IL-2
 - Increase in the IL-6 and TNF-Alpha in the aqueous humor
 - The vasculitis rather than being peripheral often affects the posterior pole
 - Cotton wool spots and haemorrhages are more common
 - Cystoid macular edema is not as common as it is acute in onset and treated before becoming chronic
- **Complications**
 - CME: Occurs in 25% of the cases
 - Macular epiretinal gliosis
 - Secondary cataract
 - Tractional retinal detachment
 - Cyclitic membrane formation: Due to massive proliferation of vascularised exudates onto and behind the posterior lens capsule. This can cause traction on the ciliary body region leading to Phthisis bulbi.
 - NVD, NVE, NVI
- **Ix**

- FFA: Detects CME. Other features include staining of the vessel wall, capillary hyperfluorescence and disc fluorescence
- UBM: Can detect the presence of exudates in the pars plana region
- ERG: Reduction in the B wave implicit time with duration of pars planitis >2 yrs
- The work up of a case of intermediate uveitis involves the routine investigations done as part of uveitis work-up and in addition work up to r/ o aetiology
 - Multiple sclerosis : MRI
 - Sarcoidosis: X-ray Chest, Serum ACE levels, Gallium Scan
 - Serum HTLV testing in patients from endemic areas like Japan and Caribbean.
- DD

Unilateral Conditions Mimicking Intermediate Uveitis

- **Coat's**: Presence of telangiectatic vessels in the periphery with presence of hard exudates might mimic IU. Even the age of presentation is similar. The presence of snowballs and snowbanks goes in favour of IU.
- **Intraocular tumours**: Retinoblastoma, malignant melanoma can disseminate into the vitreous and mimic IU. But the presence of a mass in the retina will help in distinguishing intraocular tumours from intermediate uveitis.
- **Fuch's heterochromic iridocyclitis**: Might mimic IU but the presence of stellate comma shaped KP's all over the endothelium goes in favour of Fuch's.
- **Retinal detachment**: Anterior vitreous cells might be present. But on IO, the detached retina is seen.

Unilateral/Bilateral Conditions Mimicking Intermediate Uveitis

- **Sarcoidosis**
- **Lyme's disease**: Cat scratch disease: More of retinal vasculitis and less of vitritis

Bilateral Conditions

- **Senile vitritis**: Diagnosis of exclusion. Seen in older patients. No snowballs, snowbanks, retinal vasculitis but vitritis is present.
- **Amyloidosis**: Causes vitritis but no snowbank, vasculitis or CME

- **Treatment**

- Corticosteroids
- Cycloplegics
- Immunosuppressive agents
- Surgery: cryotherapy and vitrectomy.

Intermediate uveitis is a recurrent problem, it is not possible to decrease the number of episodes of IU. The treatment is directed towards decreasing the incidence of CME which is the major cause of visual loss in these patients.

- **Role of Topical Steroids**

Topical steroids are only used when there is severe AC reaction or posterior synechiae or acute endotheliopathy. Otherwise, there is no indication for using topical steroids.

Kaplan has advised that only patients whose vision < 6/12 and who have developed CME should be treated. But, most clinicians treat if the vision has not improved at the end of 2 months even if there is no evidence of CME.

Step 1

Posterior sub-Tenon's injection of either 40 mg. Triamcinolone Acetonide or 40 mg Methyl Prednisolone every 6-8 weeks

Advantage of Triamcinolone over Methyl Prednisolone

- Smaller particle size
- Lack of carrier vehicle. The vehicle of Methyl Prednisolone causes retinal and retinal pigment epithelium scarring
- Well tolerated

Technique (Smith and Nozik)

- Ask the patient to look down.
- A 4% lidocaine soaked cotton applicator is applied over the conjunctiva.
- A 27 gauge 5/8 inch disposable needle with the bevel end up is used to enter the conjunctiva in the supero-temporal quadrant.

- The needle is moved with broad side to side movement following the curve of the globe.
- If the needle enters the sclera, the entire eyeball moves sideways with the movement of the needle.
- Once the needle has reached posteriorly, the bevel is turned downwards and the drug is injected.
- The anterior placement of the drug increases the chance of developing glaucoma and the incidence was found to be as high as 30% in one case series.
- Other complications include ptosis, globe perforation and necrotizing scleritis.

If the disease is bilateral and severe, oral steroid is added in the dose of 1 mg/kg/day.

Step 2: Cryotherapy and laser

When corticosteroids fail, either cryotherapy or laser can be applied over the snowbank.

Aaberg did a study using cryopexy and found that quiescence of disease activity was seen in 78% cases and improvement in vision in 67% cases. The potential side-effect of cryopexy includes proliferative vitreoretinopathy and Retinal Detachment.

Step 3: Vitrectomy

It is done in cases not responding to both steroids and cryo/laser. It removes the inciting antigens, clears the inflammatory cells and decreases the vitreous traction thus reducing the cystoid macular oedema.

Step 4: Immunosuppressive Therapy

Cyclophosphamide, Azathioprine, Methotrexate and Cyclosporine have all been tried in cases not responding to steroids or developing severe complications after starting steroids.

Azathioprine is commonly used. It is available as 50 mg tablets. Azathioprine 150 mg/ day is used for the first 2 months. 100 mg/day is used for the next month 50 mg/ day is used for another month

The blood Counts are Monitored. Newer immunosuppressives like Etanercept, Infliximab, Tacrolimus and Mycophenolate Mofetil are now becoming available.

Cataract Extraction in a Case of Uveitis

- The patient's eye should be quiet at least for a period of 3 months before the surgery.
- The patient should be given pre-operative oral steroids 40 mg/ day 3 days before the surgery and a posterior sub-Tenon's injection 3 days before the surgery.
- The cataract is operated by phacoemulsification and heparin coated PMMA lens is implanted.
- After, the wound is closed, peripheral pars plana vitrectomy is done and posterior capsulectomy is done.
- The chief complications of cataract surgery in these patients is the high incidence of CME and PCO formation.

Course and Outcome

Several studies have tracked the progress of the disease. Notably, Smith has found in his large series of patients 59% had a chronic course, 31% had a smoldering course with periods of exacerbations and remissions while 10% had a benign self-limited course.

The active inflammation generally persists for a period of 3 yrs and the disease burns out in a period of 5-15 yrs.

If the macula is protected for this period, most patients end up with vision better than 6/12.

Children have the worst prognosis.

pars planitis subtype

- subset of patients with intermediate uveitis when a white opacity (commonly called a **snowbank**) occurs over the pars plana and ora serrata.
- Although pars planitis probably does not represent a clinical entity distinct from intermediate uveitis, patients with pars planitis often have **worse vitreitis, more severe macular edema, and a worse prognosis** than patients with intermediate uveitis who do not have a pars plana exudate.
- inferior location of the exudate is attributed to gravity
- **diffuse phlebitis** leads to breakdown of the blood-ocular barrier and release of inflammatory cells, cytokines, and other inflammatory mediators that settle inferiorly
- snowballs are composed of **epithelioid cells and multinucleated giant cells**.

-

Panuveitis

Sarcoidosis

VKH

Behcets

1. Sarcoidosis

African Blacks

Granulomatous anterior uveitis

Vitritis, snow ball opacities

Vasculitis 'en tache de bougies' or candlewax appearance

Granulomas: Pre-retinal, Retinal, Choroidal and optic disc

Lung involvement

Skin: Lupus pernio

Investigations: X ray Chest, Serum ACE, Ca, Lysozyme

2. Vogt- Koyanagi-Harada disease

Poliosis

Suiguira's sign

Exudative detachment 'clover leaf pattern'

Sunset fundus

Vasculitis

Alopecia, Vitiligo, Meningismus

CSF pleocytosis

3. Adamantiades-Behcet's disease

Turkish, Japanese people_

Conjunctivitis, sub-conjunctival haemorrhages, filamentary keratitis

Specific Entities

Bacterial and Fungal Diseases

Spirochetal Diseases

AIDS

- HIV 1 >> 2
- sexual transmission, Intravenous drug abuse, Perinatal, needle-stick injury
- Diagnosis of HIV infection is usually made by an enzyme-linked immunosorbent assay (ELISA) and is then confirmed by a Western blot test
- Persons with HIV loads >30 000 copies/mL have an 80% likelihood of developing AIDS within 6 years. In contrast, those with HIV loads <500 copies/mL have a 5.4% chance of developing AIDS.

- most cases of **P. jiroveci pneumonia** occur when CD4+ counts fall to **<200 cells/ μ L**. Typically, **CMV retinitis** occurs when CD4+ counts are **<50 cells/ μ L**.
- HAART: many begin treatment when the CD4+ count **drops to <350 cells/ μ L** or if symptoms are present.
-

Ocular Features:

Eyelids

Molluscum contagiosum
Kaposi's sarcoma
Herpes zoster ophthalmicus
Herpes simplex virus cutaneous vesicles
Stevens-Johnson syndrome

Conjunctiva/sclera

Dry eye*
Kaposi's sarcoma
Microvasculopathy
Microsporidial conjunctivitis
Herpesvirus conjunctivitis
Scleritis

Cornea

Ulcerative keratitis
Dry eye*
Herpes simplex keratitis
Herpes zoster ophthalmicus
Microsporidiosis
Syphilitic keratitis
Tuberculosis
Gonorrhea
Lens
Cataract

Optic nerve

Optic neuropathy

Retina and choroid

Microvasculopathy (cotton-wool spots, retinal hemorrhages)*

CMV retinitis*

Acute retinal necrosis

Progressive outer retinal necrosis

Syphilis

Toxoplasmosis

Pneumocystis choroidopathy

Cryptococcosis

Mycobacterial infection

Intraocular lymphoma

Candidiasis

Histoplasmosis

Opportunistic infections

Cytomegalovirus

Pneumocystis

Mycobacterium tuberculosis

Toxoplasma gondii

Mycobacterium avium complex

Varicella-zoster virus

Cryptococcus neoformans

Coccidioides immitis

Candida

CMV Retinitis

- rarely occurring if the CD4+ count is >100 cells/ μ L and typically occurring when CD4+ counts are <50 cells/ μ L.

- reaches the eye via the bloodstream
- unusual to see more than three separate areas of CMV retinitis in an eye
- **Two types of clinical appearance**
 1. **perivascular fluffy white lesion** with many scattered hemorrhages
 2. **granular-appearing lesion** that has few associated hemorrhages and often has a central area of clearing, with atrophic retina and stippled retinal pigment epithelium
- **diagnosis**
 - based on clinical criteria.
 - PCR performed on a vitreous specimen or by culture of the virus from the vitreous or retina
- **Active CMV retinitis:**
 - faint granular border of intraretinal infiltrates that represent the new foci of viral activity in normal retina
 - **grows at approximately 250 microns per week**
 - areas that have begun to atrophy are also seen as denoted by retinal pigment epithelial stippling
- **Progression**
 1. new lesions that are not physically near an old one may form, probably by hematogenous spread
 2. old lesion spreads at its borders to involve new, previously uninfected retina
- **Treatment**
 - **ganciclovir** and derivatives, foscarnet, cidofovir, and fomivirsen.
 - Intravitreal ganciclovir implant: **1 µg of drug per hour for 8 months**
 - Current treatment: **Zone 1,2,3**

- 1971 in a report by **Urayama**
- was called **Kirisawa's uveitis**
- either sex and at any age
- **Etiology**
 - initially believed to be an autoimmune
 - experimental data support the **role of herpes virus infection** in the pathogenesis of ARN
- **CF**
 - begin with unilateral, **33% bilateral** in 1-6 weeks
 - pain, redness, floaters, and blurred vision
 - anterior uveitis with or without keratic precipitates may occur
 - **vitritis → floaters**
 - earliest retinal lesions: **small, patchy, white-yellow areas** that tend to enlarge, increase in number, and coalesce over time, in **medperiphery**
 - areas of clearing forming a **Swiss cheese pattern**
 - Retinal vasculitis
 - Optic neuropathy: Disc edema
- acute phase usually resolves in 2-3 months
- TRD/ RRD and large breaks develops
- **diagnostic criteria by American Uveitis Society**
 1. one or more foci of retinal necrosis with discrete borders in the peripheral retina
 2. rapid progression of disease if antiviral therapy has not been given
 3. circumferential spread of disease
 4. evidence of occlusive vasculopathy with arteriolar involvement
 5. prominent inflammatory reaction in the vitreous and anterior chamber
- **Differential diagnosis**

- Exogenous bacterial endophthalmitis
- Fungal endophthalmitis
- Behçet's disease
- Pars planitis
- Toxoplasmosis
- Syphilis
- Cytomegalovirus retinitis
- Sarcoidosis
- Intraocular lymphoma
- Progressive outer retinal necrosis syndrome
- **Treatment**
 - **10-14-day** course of intravenously administered **aciclovir 500 mg/m²** every 8 hours. Oral aciclovir 800 mg five times a day is then continued for an additional 6 weeks.
 - **systemic corticosteroids** such as prednisone 0.5-1.0 mg/kg can be added after the patient has received 24-48 hours of intravenous acyclovir

PORN

- Progressive outer retinal necrosis
- initially described in **immunocompromised** patients.
- **CF**
 - **rapidly progressive necrotizing retinitis** with early patchy choroidal and deep retinal lesions which progressed relentlessly until patients were left with atrophic and necrotic retinas and pale optic nerves.
 - Unlike typical ARN there is little or **no vasculitis and less vitritis**, and in many patients **posterior pole** involvement occurs early in the course of disease

- **DD:** ARN, other DD of ARN
- **Etiology:**
 - varicella-zoster virus and herpes simplex virus
- **Treatment**
 - High-dose intravenous aciclovir at a dosage of **10 mg/kg every 8 hours for 2 weeks** has also been used with inconsistent success
 - induction doses of intravenous ganciclovir and foscarnet

Toxoplasmosis

- obligate intracellular protozoan *Toxoplasma gondii*
- **50% of the adult** population is infected
- most common cause of uveitis ?? in one study
- **Organism**
 - cosmopolitan parasite
 - Humans can also be infected secondarily by **ingesting meat** (pork and lamb particularly, as well as chicken in endemic areas, but probably not beef)
 - Many antigens: **SAG 1** or p30 is most studied, **SAG 2** or p22.
- **CF**
- **Systemic**
 - **lymphadenopathy in 90%**
 - fever, malaise, and sore throat
- **Ocular**
 - **Congenital:**

- large atrophic scar, frequently in the macula
- reactivation sites will be 'satellite' lesions next to old atrophic lesions, indicative of previous toxoplasmic infections
- **Acquired**
 - organism has a propensity for neural tissue, it is important to bear in mind that the lesion classically begins in the retina
 - Scaffolding seen in vitreous of patient with severe recurrent ocular toxoplasmosis.
- **Decreased Vision**
 - vitreal inflammation
 - infection involving the macula
 - choroidal neovascularization
 - retinal vein occlusion, papillitis, and florid disc neovascularization.
- **A curious association between Fuchs' heterochromia and ocular toxoplasmosis was initially made by Toledo de Abreu**
- **Diagnosis**
 - Antibody from the aqueous of patients with chronic toxoplasmosis stained more intensely to a 28-kDa antigen, believed to be the **GRA-2 antigen**, which is expressed in both tachyzoites and bradyzoites.
 - PCR
 - Sabin-Feldman dye test
 - ELISA
- **Therapy**
 - immunocompetent person the disease is ultimately **self-limited**
 - decision to treat generally would be based on the following **criteria**
 - **A lesion within the temporal arcade;**
 - **A lesion abutting the optic nerve** or threatening a large retinal vessel;
 - **A lesion that has induced a large degree of hemorrhage;**

- A lesion that has induced enough of a vitreal inflammatory response that the **vision has dropped** below 20/40 in a previously 20/20 eye, or at least has sustained a two-line drop from the visual acuity before the acute infection;
 - A relative indication would be the case of **multiple recurrences** that develop marked vitreal condensation. Here one might be concerned that the continuation of this process might lead to retinal detachment.
- pyrimethamine, sulfadiazine and steroid
 - clindamycin, sulfadiazine, and steroid
 - trimethoprim and sulfamethoxazole

Ocular Histoplasmosis

- the only syndrome in the spectrum of ocular inflammation in which '**presumed**' has appeared in its name.
- ocular histoplasmosis syndrome is rather a distinct entity found almost exclusively in the United States
- Histoplasma capsulatum: Found in the soil, it is readily inhaled and phagocytosed.
- CF
 - White, 20-50 years of age
 - Multiple choroidal spots ('**histo**' spots): four to eight per eye, these choroidal scars are circular, depigmented, and atrophic; they have a disc diameter of 0.2-0.7 and may have a pigment clump centrally
 - CNVM
 - Peripapillary changes
 - Disciform scar
 - **No vitreous inflammatory disease**

- HLA-B7 positivity (macular disease)
- Maculopathy: RPED, CSCR,
- Treatment
 - Amphotericin B has no role in the treatment of ocular histoplasmosis
 - Corticosteroids
 - 2-mg or a 6-mg fluocinolone acetonide implant
 - intravitreal injection of anti-VEGF agents
 - Laser and PDT

Toxocara canis

- T. canis is an ascarid (i.e., a member of the Ascarididae family) that can only complete its lifecycle in the **dog**.
- Humans enter the pathway when they ingest soil, food, or other materials contaminated with the eggs.
- **Ocular manifestations**
 - average age of diagnosis is estimated to be **7.5 years** (2-31 years)
 - granuloma either in the posterior pole or in the periphery.
 - raised and whitish in color, with a width of 0.75 to 2 or 3 disc diameters
 - peripheral retinitis
 - 50% presented with a peripheral retinal granuloma and 25% as macular lesions
 - optic nerve disease (very rare)
 - endophthalmitis
- **Fuchs' heterochromia has been reported associated with this entity, just as has been noted in cases of ocular toxoplasmosis**
- **DD**

- RB (aqueous to serum LDH ratio is >1 , phosphoglucose to isomerase ratio should be >2)
- primary hyperplastic primary vitreous
- Coats' disease
- focal choroiditis from another cause, such as sarcoid
- retrolental fibroplasia.
- **Diagnosis**
 - eosinophilia and hyperglobulinemia
 - No eggs will be found in the stool
 - ELISA
- **Treatment**
 - The first is treatment with anthelmintic drugs such as **thiabendazole** or **diethylcarbamazine**
 - second is treatment with prednisone to reduce the secondary inflammatory response.
 - systemic **prednisone** (40 mg/day) with thiabendazole (2 g daily for 5 days)

Onchocerciasis

- river blindness
- one of the five major preventable causes of blindness (the others include cataract, trachoma, glaucoma, and xerophthalmia).
- tissue-dwelling parasite, the nematode **Onchocerca volvulus**.
- spread by the blackflies of the **Simulium** species
- broad belt across western and central Africa
- **CF**
 - Microfilarial infestation in the cornea: punctate keratitis; the presence of 'snowflake' opacities

- Iridocyclitis:
- glaucoma and cataract
- **Diagnosis**
- **Treatment**
 - DEC-C is microfilaricidal, and with the massive killing of these organisms a severe systemic reaction occurs (**Mazzotti reaction**).
 - **Benzimidazoles**
 - **Ivermectin**: single oral dose of 150 µg/kg

Diffuse unilateral subacute neuroretinitis (DUSN)

- **Gass in 1977: unilateral wipe-out syndrome.**
- later found to be related to a nematode in the subretinal space
- **CF**
 - scattered **recurrent** deep gray-white retinal lesions with marked loss of central acuity
 - progressive optic atrophy, narrowing of the retinal vessels, pigment epithelial stippling, and further visual field loss
 - cause destruction of the retinal outer segments, visual loss is rarely reversible.
- **Worms of two sizes**
 - **smaller** worm between **400 and 700** µm in length was seen in most patients who lived in southeastern United States
 - **larger** (**1500-2000** µm) worm has been seen in patients residing in the northern and midwestern states
- **Treatment**
 - **albendazole**, 400 mg/day for 30 days
 - can be successfully destroyed by photocoagulation

Seasonal hyperacute panuveitis (SHAPU)

- Malla and Upadhyay and colleagues in Nepal
- Unilateral, children
- contact with a **moth**
- **CF**
 - very acutely with a red eye and leukocoria with little pain
 - fibrinoid reaction in the anterior chamber, and often there is also a hypopyon
 - hypotony and a very sudden decrease in vision.
- **no systemic abnormalities.** (normal ESR and RF)

Postsurgical Uveitis

- **Day 1 to Day 30**
 - Acute aerobic bacterial endophthalmitis
 - Sterile endophthalmitis
 - Increased activity of previous uveitis
 - Phacogenic (lens-related) uveitis
 - Toxic reaction to intraocular lens
- **DAY 15 to 2 YEARS**
 - Fungal endophthalmitis
 - Propionibacterium acnes or other anaerobic endophthalmitis
 - Low virulence aerobic bacterial endophthalmitis
 - Phacogenic (lens-related) uveitis
 - Sympathetic ophthalmia
 - Toxic reaction to intraocular lens

- Iris-ciliary body irritation related to physical contact with intraocular lens
- Glaucoma drainage device
- New onset of idiopathic uveitis

Sarcoidosis

- multisystem granulomatous disease
- **adrenal glands**, which produce corticosteroids, are the only organs consistently **spared** by this disease.
- initially described as a dermatologic disease by **Hutchinson** in 1869
- **Boeck**: sarkoid → skin biopsies had a histology similar to that of sarcomas
- **Etiology**
 - Infectious, organic, and inorganic agents are possible antigens
 - **CD4+ T cells** that interact with APCs to initiate the formation and maintenance of granulomas.
 - associations between both class I antigens (HLA-B8) and class II antigens (HLA-DRB1)
- **CF**
 - respiratory symptoms
 - generalized symptoms such as fever, fatigue, or weight loss.
 - eye findings in about 25%
 - Anterior Segment
 - Acute nongranulomatous or chronic granulomatous iridocyclitis: 53% to 60%
 - Iris nodules 11%
 - cataracts in patients with chronic sarcoid uveitis is 8-17%, and the prevalence of glaucoma varies from 11% to 23%.
 - Posterior Segment

- 6-33% of patients with sarcoidosis
 - Vitritis
 - vitreal snowballs
 - macular edema
 - perivenous sheathing: **'candle wax dripping'** (en taches de bougie) along the retinal veins
 - small yellow choroidal, and retinal pigment epithelial patches of inflammation: Deep yellow choroidal lesions consistent with **Dalen-Fuchs nodules** and mottling of the pigment epithelium occur in 36%
 - optic disc swelling
 - retinal neovascularization
 - Large choroidal granulomas
 - subretinal neovascularization
 - optic neuropathy
- **DD**
 - **Blau syndrome**: in children, familial granulomatosis, arthritis, uveitis, and skin rash
 - **Diagnosis:**
 - noncaseating epithelioid cell granulomas on biopsy.
 - 90% will have an abnormal chest X-ray
 - 60% of patients with sarcoidosis have granulomas on a transbronchial lung biopsy
 - lacrimal gland biopsy
 - serum ACE levels are elevated in 60-90%
 - Serum lysozyme levels may also be elevated
 - Kveim skin test:
 - gallium scan:
 - **Mx**

- The mainstay of therapy for both systemic and ocular sarcoidosis is **corticosteroids**.
- Anterior segment disease may be managed with topical or periocular corticosteroid injections. Systemic therapy is typically required for bilateral posterior segment uveitis. Other immunosuppressive agents such as **methotrexate and infliximab** have demonstrated therapeutic benefit in the management of sarcoidosis and should be considered early for patients with chronic sarcoidosis requiring prolonged steroid therapy. **Cyclosporine and etanercept do not appear to have benefit in the treatment of sarcoidosis.**
- The glaucoma should be treated medically with aqueous suppressants for as long as possible.
- Argon laser trabeculoplasty is frequently ineffective.
- Laser iridotomy and surgical iridectomy are the treatments of choice for patients with pupillary block.
- If the intraocular pressure remains uncontrolled, surgical intervention with either a filtering procedure or a tube shunt is required.
- Surgical success is improved if the intraocular inflammatory disease can be controlled prior to the surgical procedure.

Sympathetic Ophthalmia

- bilateral granulomatous uveitis that occurs after either intentional or unintentional penetrating trauma to one eye.
- **0.19% post trauma**
- **0.015% post intraocular surgery**
- trauma to one eye (the exciting eye) will result in an inflammatory response not only in that eye but also in the contralateral eye (the sympathizing eye)
- 80% of patients some 3 months after injury to the exciting eye and in 90% within 1 year of trauma
- CF

- acute anterior uveitis: granulomatous, with mutton-fat keratic precipitates
- moderate to severe vitritis
- Dalen-Fuchs nodule:
 - Not pathognomonic
 - multiple white-yellow lesions in the periphery
- Swelling of the disc
- subretinal neovascularization
- Sequelae
 - Secondary glaucoma and cataract
 - retinal and optic atrophy
 - Disc neovascularization
- Ix
 - FA: initial **blockage of Dalen-Fuchs nodules** with **ultimate hyperfluorescence** of the lesion
 - ICG: pattern of hypofluorescence in the intermediate phase of the angiogram, followed by a fading, and the second was a hypofluorescent pattern that persisted throughout the course of the study
 - **High level of serum β 2-microglobulin**
 - strong association between HLA-DR4, DRw53, and Bw54 haplotypes and both VKH and sympathetic ophthalmia
 - cellular immune response to both **S-antigen and interphotoreceptor retinoid-binding protein (IRBP)**
- **One of the classic findings in both sympathetic ophthalmia and the Vogt-Koyanagi-Harada syndrome is the preservation of the choriocapillaris.**
- Treatment
 - Enucleation of an injured eye before the sympathizing eye becomes involved is the only known way
 - at least 1-1.5 mg/kg of **prednisone** or equivalent on a daily basis.

- **ciclosporin** as a second-line drug
- Surgery for either glaucoma or cataract

VKH

- Vogt-Koyanagi-Harada syndrome (VKH)
- **Mohammad-al-Ghafari**: disease with poliosis, neuralgias, and hearing changes
- **Alfred Vogt**: 1906:
- **Koyanagi** in 1929
- **Harada** in 1926, described an essentially posterior uveitis with an exudative retinal detachment associated with a *pleocytosis in the cerebrospinal fluid (CSF)*.

Clinical Features

- Systemic findings
 - prodromal stage: in which the patient may complain of headache, orbital pain, stiff neck, and vertigo. There may also be a fever.
 - CNS: Lumber puncture shows pleocytosis in 84%
 - auditory difficulties: Dysacusia in 74%
 - Skin Lesion:
 - sensitivity to touch of both hair and skin 72%
 - Vitiligo and poliosis: 63 - 90%
 - Alopecia: 70-73%
- Ocular findings
 - granulomatous uveitis, with mutton-fat keratic precipitates on the corneal endothelium
 - Perilimbal vitiligo (**Sugiura's sign**)

- Nodules may be noted on the pupillary margin, as well as in the iris stroma
- Glaucoma
- swelling of the optic nerve head is seen early in 87%
- retinal edema
- exudative nonrhegmatogenous retinal detachment
- **Dalen-Fuchs nodules**
- Neovascularization of the retina and optic nerve
- Subretinal neovascularization of the macula
- 'sunset glow' appearance to the fundus: characteristic depigmentation of the posterior portion of the globe occurs
- **blond fundus**: mottled appearance as well as a profound loss of pigment

Revised criteria for diagnosis of VKH

- Complete VKH: Criteria 1-5 must be present
 - Incomplete VKH: Criteria 1-3 and either 4 or 5 must be present
 - Probable VKH (isolated ocular disease): Criteria 1-3 must be present
1. No history of penetrating ocular trauma or surgery preceding the initial onset of uveitis
 2. No clinical or laboratory evidence suggestive of other ocular disease entities
 3. Bilateral ocular involvement
 - a. Early manifestations: Evidence of diffuse choroiditis → focal areas of subretinal fluid bullous serous retinal detachments
 - b. Late manifestations: suggestive of prior presence of 3a, Ocular depigmentation
 4. Neurological/auditory findings
 - a. Meningismus
 - b. Tinnitus
 - c. Cerebrospinal fluid pleocytosis
 5. Intergumentary finding

- a. Alopecia
- b. Poliosis
- c. Vitiligo

- Investigations

- FA

- multiple pinpoint areas of leakage are noted at the level of the RPE
 - large confluent area of leakage
 - late leakage of the disc
 - early choroidal stromal vessel hyperfluorescence and hypofluorescent dark dots.
 - fuzzy vascular pattern to the large stromal vessels and disc hyperfluorescence.

- ERG

- EOG

- OCT

- troughs of RPE undulations
 - Choroidal folds

- Therapy

- Medical management

- Corticosteroids

Behcet's Disease

AAO/ Kanski

CRITERIA OF THE INTERNATIONAL STUDYGROUP 1990

1. Recurrent oral aphthous ulcers; Small or large aphthous or herpetiform ulcerations, recurring at least 3 times in a 12 month period

Plus 2 of the following:

2. Recurrent genital ulcers: Aphthous ulcerations or scarring
3. Eye lesions: Anterior uveitis, posterior uveitis or cells in vitreous on slit lamp examination or retinal vasculitis observed by an ophthalmologist
4. Skin lesions: Erythema nodosum, pseudofolliculitis, papulopustulous lesions or acneiform papules in postadolescent patients without steroid treatment
5. Positive pathergy testing: Intracutaneous stick with 21G needle on the forearm (inside), read physician after 24-48 h

Retinal Vasculitis

- Retinal vasculitis is an inflammatory disease of the blood vessels of the retina that may be associated with primary ocular conditions or with inflammatory or infectious diseases in other parts of the body (systemic diseases). It has been defined as the vascular leakage and staining of vessel walls on fluorescein angiography, with or without the clinical appearance of fluffy, white perivascular infiltrates in an eye with evidence of inflammatory cells in the vitreous body or aqueous humor
- **primary causes**
 - (a) Localized to the eye
 - Idiopathic
 - Intermediate uveitis of the pars planitis type

- Frosted branch angiitis
- Idiopathic retinal vasculitis, aneurysms and neuroretinitis (**IRVAN**)
- (b) Involving the eye and other organs (primary systemic associations)
 - Giant cell arteritis
 - Takayasu arteritis
 - Polyarteritis nodosa
 - Wegener's granulomatosis
- **secondary vasculitis**
 - a) Localized to the eye:
 - Ocular sarcoidosis
 - Birdshot chorioretinopathy retinal vasculitis
 - Necrotic herpetic retinopathies (herpes simplex, varicella zoster virus)
 - Toxoplasmic retinochoroiditis
 - Tuberculosis
 - DUSN (Diffuse unilateral subacute neuroretinitis)
 - Primary ocular lymphoma
 - (b) Associated with systemic involvement
 - Sarcoidosis
 - Behçet's disease
 - Multiple sclerosis
 - Systemic lupus erythematosus (SLE)
 - Spodylarthritis with HLA-associated uveitis
 - Inflammatory bowel diseases
 - Relapsing polychondritis
 - Tuberculosis
 - Syphilis

- Lyme disease
- Viral (Cytomegalovirus, HIV, West Nile)
- CF
 - The classic symptom of retinal vasculitis is a painless decrease in vision. Other symptoms may include floaters from accompanying vitritis, a blind spot from ischemia-induced scotomas, metamorphopsia (change in shape of an object) in case of macular involvement or altered color perception. Retinal vasculitis can also be asymptomatic.
 - Retinal examination typically reveals sheathing (a whitish-yellow cuff of material surrounding the blood vessel) of the affected retinal vasculature associated with variable vitritis (inflammatory cells behind the lens in the vitreous body). It involves noncontiguous portions of the vessel. Inflammation may involve retinal arteries, veins or capillaries, but peripheral venous involvement is commonly recognized 2. Arterioles are preferentially involved in syphilis 3,4. The location and appearance of vascular lesions may have a limited diagnostic utility. "Candle-wax drippings" seen as dense, focal, nonocclusive periphlebitis are associated with sarcoidosis, but its appearance is neither pathognomonic nor present in all patients with the disease. The occlusive phlebitis of Behçet's syndrome tends to manifest in the posterior pole, although peripheral retinal vasculitis may occur. Presence of a choroiditis lesion (active or healed) underlying the retinal vessels is a common observation in vasculitis of tubercular origin. Additional evidence of ocular inflammation such as cells in the aqueous humor may accompany retinal vasculitis.
 - Narrowing of the retinal blood vessels, vitreous hemorrhage, and new blood vessel growth are present as complications of retinal vasculitis.
- Ix
 - Optical coherence tomography
 - Ultrasonography
 - Indocyanine green angiography
 - Ultrasound biomicroscopy
 - Few laboratory studies that should be done in all patients with isolated retinal vasculitis are:
 - Full blood counts
 - Erythrocyte sedimentation rate

- Mantoux test
- Chest X-ray to rule out sarcoidosis or tuberculosis (Computed tomography if required)
- Syphilis serology (Treponema pallidum hemagglutination test)
- suspecting a specific etiology
 - Toxoplasmosis serology
 - HIV
 - Lyme disease serology
 - X-ray of sacro-iliac joint
 - C-reactive protein
 - Serum Angiotensin-Converting-Enzyme
 - Human leukocyte antigen (HLA) typing
 - ANA, ANCA
- MX
 - Corticosteroids
 - Immunosuppressive agents
 -
 - Immunosuppressive therapy is usually a treatment of last resort, but there is little evidence that it is beneficial for the long-term retention of vision in severe idiopathic retinal vasculitis. The use of immunosuppressive agents in retinal vasculitis is generally reserved for patients with bilateral disease whose vision has fallen below 20/40 in the better eye. **Occlusive vasculitis in patients with Behcet's syndrome is the one form of uveitis for which most authorities agree that immunosuppressive drugs are the treatment of first choice.** They are best administered by an internist experienced in their use, with monitoring of treatment effect by an ophthalmologist, indicating the importance of a team approach. The ones commonly used in ocular inflammations include azathioprine, cyclophosphamide, methotrexate (MTX), mycophenolate mofetil, and cyclosporine.
 - Other indications of immunosuppressive therapy in retinal vasculitis may include chronic inflammation that is not responding to the primary conventional

- corticosteroid therapy; multiple relapses of inflammation, in the same or other eye, or both eyes; or intolerance or contraindications to systemic corticosteroids.
- These agents are started after an informed consent from the patient. The clinician should discuss extensively with the patient regarding the risks of secondary malignancy and gonadal dysfunction. Before starting any immunosuppressive drug, all patients are evaluated to rule out contraindications to treatment, such as hemoglobin, blood cell counts (leucocytes and platelets) and abnormal liver or renal function tests. While receiving these medications, the patients are monitored every four weeks for laboratory tests including blood cell counts, bilirubin, liver enzymes, and serum creatinine.
 - Identification of non infectious systemic associations warrants initiation of specific therapy, besides the conventional corticosteroids. Management of some of the common specific causes of retinal vasculitis is discussed below.
 - Behcet's disease: Behcet's disease is a systemic immune-mediated vasculitis of unclear origin. Although the vasculitis associated with Behcet's disease responds well to systemic corticosteroids that also delays the time to blindness in patients with posterior segment involvement, but it does not alter the long-term outcome. Further, majority of patients with ocular Behçet's disease present with multiple relapses of inflammation. The long-term consequences of corticosteroids are unacceptable and they are not always suitable as a monotherapy for maintaining remission of vasculitis due to adverse side effects. Often it becomes necessary to add immunosuppressive drug as a steroid-sparing agent.
 - Cyclosporine A (3-5 mg/kg/day) and Azathioprine (2.5 mg/kg/day) are known to effectively control intraocular inflammation, to maintain visual acuity, and to prevent onset or progression of eye disease in ocular Behcet's disease. Despite aggressive immunosuppressive treatment, the visual prognosis of ocular BD remains generally poor⁸. Recently, novel biologic drugs, including interferon- α and tumour necrosis factor (TNF)- α -antagonists have been introduced in the treatment of ocular Behcet's disease with very promising results and seem for the first time to improve the prognosis of the disease^{9,10}. Unfortunately, these new drugs are very expensive and therefore they may be not universally available in countries with a low economic status.
 -
 - Sarcoidosis: Retinal vasculitis in sarcoidosis is less common than anterior uveitis and vitreitis¹¹. Systemic corticosteroids (Prednisolone 1 mg/kg/day) are the mainstay of treatment. When associated panuveitis is also present, topical corticosteroid and cycloplegic are given. The oral corticosteroids are tapered over 8-10 weeks by 5-10 mg per week depending upon the clinical response, in

consultation with the pulmonologist. Few authors have reported the use of low-dose Methotrexate (MTX) in refractory cases of panuveitis¹².

- Retinal vasculitis may be caused directly by various infectious agents; in the majority of such cases specific antimicrobial therapy is available. It may be an antibiotic, antiparasitic or an antiviral drug administered for appropriate duration, with or without corticosteroids.
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- Tuberculosis: Tuberculosis is a common cause of retinal vasculitis in our experience. Once a diagnosis of presumed tubercular vasculitis is made, 4-drug anti-tubercular therapy including Isoniazid- 5 mg/kg/day, Rifampicin-450 mg/day (if body weight < 50 kg and 600 mg/day if body weight > 50 kg), Ethambutol 15 mg/kg/day, and Pyrazinamide 25-30mg/kg/day is initiated under the supervision of an internist, and continued for 3-4 months. Oral corticosteroids are administered in the standard dose of 1 mg/kg body weight per day, to be tapered depending upon the clinical response. The patients are monitored for any liver toxicity. Thereafter, Rifampicin and Isoniazid are used for another 9-14 months. Pyridoxine supplementation is given to all patients receiving anti-tubercular therapy till cessation of therapy. Anti-tubercular therapy has shown to significantly reduce recurrence of inflammation
- associated choroiditis. Healed choroiditis scars are typically seen in tubercular retinal vasculitis.
-
- Toxoplasmosis: The most commonly used combinations are Clindamycin and corticosteroids; or Pyrimethamine, Sulfadiazine and corticosteroids. Oral corticosteroids are used to limit the damaging effects of inflammation. Recommended regimen includes tablet Clindamycin 300 mg four times daily (3-4 weeks) along with tablet Septran-DS 960 mg daily (960 mg sulfamethoxazole and 160 mg trimethoprim) for 3-4 weeks. Oral corticosteroids (1-1.5 mg/kg/day) are started 48 hours after starting antitoxoplasma therapy, and tapered according to the clinical response. Other drugs that have been used in ocular toxoplasmosis are Atovaquone and Spiramycin.
-
- Syphilis: Penicillin remains the standard treatment for ocular syphilis. The recommended regimen for treatment of ocular syphilis is the same as that for neurosyphilis, i.e, intravenous crystal penicillin G 12-18 Million Units/day for 10-14 days, followed by supplementary intramuscular penicillin G 2.4 Million Units

weekly for 3-4 weeks. If the patient is allergic to penicillin, then oral tetracycline 500 mg four times a day for 4-6 weeks is a good alternative.

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- Lyme disease: Lyme borreliosis greatly mimics syphilis and can cause false-positive readings on both specific and non-specific tests for syphilis. Patients with Lyme uveitis are treated as if they had neuroborreliosis. Intravenous therapy with either ceftriaxone, 2 g daily for adults (50 to 100 mg/kg/day for children) for 21 days; or penicillin G, 20 million units daily, or 0.25 to 0.5 million units/kg/daily for children. Doxycycline, 100 mg twice daily, is a good alternative in adults with less severe infection but contraindicated in children, pregnant or breastfeeding women. Some patients with severe ocular inflammation may require concomitant oral prednisone (0.5 to 1.0 mg/kg/day) because of the possibility of paradoxical worsening (Jarisch-Herxheimer reaction). But steroids should not be used without appropriate antibiotic cover.
-
- Surgical therapies such as laser photocoagulation or vitrectomy are generally not indicated except in the management of persistent neovascularization (new vessel growth) or in cases of bleeding into the vitreous or glaucoma., epiretinal membrane, tractional retinal detachment threatening the macula, combined tractional and rhegmatogenous retinal detachment and a densely opacified vitreous.
-

Eales Disease

- Eales' disease is an idiopathic retinal periphlebitis that primarily affects the peripheral retina in young adults. Retinal changes are characterized by periphlebitis, peripheral non-perfusion and neovascularization leading to visual loss. The disease afflicts people worldwide but for unknown reasons is more common in the Indian subcontinent. Eales' disease appears to be an immunologic reaction that may be triggered by an exogenous exposure.
- Etiopathogenesis
 - Mycobacterium tuberculosis DNA has been detected by polymerase chain reaction, in the vitreous of such patients. However, the role of mycobacterium genome in the pathogenesis is yet to be ascertained.

- Retinal S-antigen and Interphotoreceptor Retinoid Binding Protein plays a role in the etiopathogenesis of this condition.
- An extraneous agent results in the exposure of normally sequestered uveitopathogenic antigens of the immune system, leading to an immune response in the eye that may initiate the disease process.
- Oxidative stress plays an important role in the pathogenesis of Eales' disease.
- Retinal photoreceptors and platelets have been shown to be an easy target of oxidants because of high proportion of polyunsaturated fatty acids. The decreased membrane fluidity in platelets suggests alterations in the physiological events, which may result in alterations in functioning of retinal photoreceptors.
- The natural course of Eales' disease is quite variable with temporary and even permanent remission in some cases and relentless progression to blindness in others.
- CF
- Classification
- *Charmis*
- IX
 - MANTOUX
 - CHEST X-RAY
 - VDRL
 - ESR
 - ANCA ANA CRP
 - ACE , SERUM CA LEVEL
 - SEROLOGY TITRE FOR TOXOPLASMA
 - HIV
 - COMPLETE HAEMOGRAM , BT CT

- Hb Electrophoresis
- FFA to r/o
- Active or healed vasculitis
- CNP area
- NVD, NVE
- ? Macula
- OCT to r/o
- CME Epiretinal membrane, subclinical macular hole
- USG to r/o RD and PVD status
- Mx
 - Active Vasculitis
 - Systemic steroids up to 2 mg/kg of prednisolone have been advocated in the active phase. These can be tapered over 6-8 weeks.
 - Subtenon injections of triamcinolone have also been used in a dose of 0.5-1 ml (40mg/ml).
 - The use of antimetabolites has been reported in one eyed patients and in central disease. Low dose oral methotrexate pulse therapy (at a dose of 12.5 mg/week) for 12 weeks has been reported recently but needs more evaluation
 - IF VIREOUS HAEMORRAGE
 - Treat other eye
 - Rest
 - Look for cells and flare
 - MONITOR
 - visual acuity
 - IOP
 - Ant segment- cells and flare
 - OCT - before and after treatment

- FFA - after 6-8 weeks and look for dye leakage
- Role of ATT
 - Clinical suspects- massive infiltration, nodule formation and obliteration of venous segment give 450 isoniazid and 300 ethambutol x 9 months
- PHOTOCOAGULATION
 - Never treat active vasculitis
 - NVE - moderately overlapping burns
 - NVE raised - anchoring and feeder vessels
 - Gross CNP - sectoral
 - NVD - PRP
- ARC
 - Small undilating pupil
 - Media hazy due to cataract
 - Vitreous haemorrhage
 - Adjunct to photocoagulation
- TIME FOR SURGICAL INTERVENTION
 - Study demonstrated the importance of early vitrectomy for persistent haemorrhage.
 - delaying vitrectomy is believed to allow the development of cystoid macular edema, macular scar and macular pucker.
 - Operate between 3 to 6 months
 - INDICATION
 - Nonresolving vitreous haemorrhage
 - TRD involving posterior pole
 - Multiple vitreous membranes with or without TRD
 - Combined TRD and RRD
 -

- GOOD PROGNOSIS FACTOR
 - >Fewer episodes and
 - shorter duration of vit haemorrhage
 - >PVD is completed
 - >Prior photocoagulation
- BAD PROGNOSIS
 - Multifocal attachment
 - TRD Rare inv. macula
-

Masquerade Syndromes

White Spot Syndromes- WSS

- inflammation and dysfunction of the outer retina, retinal pigment epithelium, choroid, or a combination
- differential diagnosis:

- granulomatous diseases, such as sarcoid, tuberculosis, sympathetic ophthalmia; masquerade syndromes like syphilis and intraocular lymphoma; infectious etiologies including toxoplasmosis, pneumocystis chorioidopathy; and other entities such as presumed ocular histoplasmosis, and Behçet disease
- CF
 - Blurred vision, photopsias, visual field changes, floaters, and changes in contrast sensitivity
- Unilateral or Bilateral
- Can be asymmetric
- Etiology
 - Autoimmune: birdshot chorioretinopathy, AZOOR, MEWDS

Birdshot Retinochoroidopathy

- Ryan and Maumenee in 1980
- Gass in 1981 who called it vitiliginous chorioretinitis.
- lesions are scattered around the optic disc and radiate to the equator in a “shotgun” pattern.
- fits into the broad scheme of ‘white-dot syndromes’ However this disorder seems to have better-defined boundaries
- 0.6-1.5% of patients referred to tertiary centers for uveitis, or 6-7.9% of patients with posterior uveitis
- HLA-A29*02 subtype is most commonly associated with BCR
- Pathogenesis
 - Unknown
 - Inflammation appears to be a primary feature
- CF
 - blurred vision, floaters, and photopsias
 - Severe nyctalopia despite normal visual acuity

-
- **OCULAR EXAMINATION FINDINGS**
- Quiet anterior chamber
- Vitreal inflammation but no snowbanking
- Retinal vascular leakage and cystoid macular edema
- Deep circular cream-colored lesions, mostly in the posterior pole and surrounding areas
- Bilateral
- Low to moderate risk of subretinal neovascularization
- **Supportive findings include:** HLA-A29 positive, retinal vasculitis, and CME
- **exclusion criteria include:** presence of significant keratic precipitates, posterior synechiae, or diagnosis of infectious, neoplastic, or inflammatory disease that may cause multifocal choroidal lesions.
- **ADDITIONAL TESTS**
 - Abnormal electroretinogram and electrooculogram findings
 - Evidence of retinal autoimmunity
 - HLA-A29+
- **Ix**
 - **FFA:**
 - hypofluoresce in the early phase and there can be diffuse hyperfluorescence in the late phases
 - increased transit time, leakage from retinal vasculature leading to CME, optic disc hyperfluorescence
 - **ICGA**
 - In the active disease, the birdshot lesions appear hypofluorescent during the intermediate phase
 - Late in the ICGA, there is diffuse choroidal hyperfluorescence
 - **OCT**
 - CME

- FAF
 - clinical choroidal lesions did not always correspond to the FAF defects suggests that the choroid and RPE may be affected independently
- ERG
 - negative ERG pattern: greater decrease in b-wave amplitude versus a-wave amplitude
- EOG
 - Decreased Arden ratios, representing RPE dysfunction
- Visual field
 - peripheral constriction, enlarged blind spot, central or paracentral scotomas, and generalized diminished sensitivity
- Treatment
 - **Corticosteroids** have been the mainstay of treatment. Oral, sub-Tenon's, intraocular, and most recently sustained release fluocinolone acetonide
 - *Immunosuppressive therapy*
 - Cyclosporine has been used as it inhibits T lymphocytes and prevents S-Ag-induced experimental uveitis
 - Antimetabolites such as azathioprine, mycophenolate mofetil, and methotrexate
 - alkylating agents cyclophosphamide and chlorambucil
 - **Daclizumab**, a monoclonal antibody against the alpha-subunit of the IL-2 receptor of T cells, has recently been found to have value in treating BCR
 -

Placoid diseases

- APMPPE, SC, RPC, PPM

Acute posterior multifocal placoid pigment epitheliopathy APMPE

- 1968 by Gass
- M = F
- 20 and 50 with the mean age of onset being 26
- **Pathogenesis**
 - Gass: abnormalities were primarily at the level of the **RPE**
 - Van Buskirk: alternate theory **that choroidal perfusion was the primary problem** and that the hypofluorescence seen with angiography was due to lack of perfusion of the choriocapillaris
 - Fishman: **diffuse RPE process** was implicated in the acute phase of the disease. It also confirmed the transitory nature of this process as the EOG could normalize
- **CF**
 - rapid onset of central vision loss that may be described as blurred vision, paracentral scotoma, metamorphopsia, “spots” in the vision, and photopsias
 - bilateral >> unilateral
 - multiple round and confluent cream colored, flat lesions with indistinct margins scattered in the posterior pole.
 - **Lesions are not found anterior to the equator**
 - The placoid lesions tend to clear centrally initially leaving hypopigmentation. Later there is mild pigment mottling
 - improvement of the visual symptoms within 2-4 weeks
 - relatively good prognosis
- **Ix**
 - **FFA**
 - early phase as nonfluorescent
 - Later in the angiogram there is a progressive, irregular staining of the lesions
 - As the process becomes inactive, hyperfluorescence corresponding to window defects in the RPE develops and staining is no longer evident
 - **ICGA**
 - Acute lesions show early hypofluorescence

- As the disease heals, the hypofluorescence in the late phase becomes less defined and smaller
- support to the theory of choroidal ischemia as an underlying factor in the pathogenesis of APMPE
- OCT
 - mild hyperreflective area above the RPE in the photoreceptor layer corresponding to the placoid lesions
- FAF
 - centrally there was intense hyperautofluorescence, and the depigmented halo was hypoautofluorescent, implying atrophy
- The electroretinogram is normal to minimally subnormal.
- EOG: abnormal light:dark ratios suggesting a diffuse RPE problem
- **Systemic associations**
 - cerebral vasculitis
 - meningo-encephalitis
 - stroke
 - CN VI palsy
-

Serpiginous choroiditis

- Aka
 - helicoid peripapillary chorioretinal degeneration
 - geographic helicoid peripapillary choroidopathy GHPC
 - geographical choroidopathy
- disease of healthy individuals
- 30 and 70

- M >> F
- higher prevalence of **HLA-B7**
- **Pathogenesis**
 - Autoimmune: S-antigen
 - Infectious: VZV and HSV, candida ??
 - Vascular
 - degenerative
- CF
 - asymptomatic until the lesions affect the fovea
 - bilateral but asymmetric presentation
 - classic, 80%
 - geographic patches of gray or creamy yellow placoid lesions in the peripapillary region.
 - progresses in a centrifugal manner with finger-like or serpentine projections
 - chronic → chorioretinal atrophy, subretinal fibrosis, and RPE clumping
 - Macular serpiginous choroiditis, 20%
 - no difference in the lesions except for location.
 - generally a poorer prognosis
 - nongranulomatous anterior uveitis
 - CNV, which affects 13-20% of eyes, vein occlusions, retinal vasculitis, usually a periphlebitis, CME, and bilateral full-thickness macular holes
 - multiple recurrences at intervals of months to years
- Ix
 - FFA
 - hypofluorescence during the early phase
 - ICGA
 - better staging of SC

- better identification of the active lesions
- persistence of choroidal activity even when the signs of retinal activity had disappeared
- OCT
 - retinal atrophy with disruption of the photoreceptor layers in affected area
- **Systemic associations:** Crohn's disease, SLE, celiac disease, and extrapyramidal dystonia
- Treatment
 - Steroids
 - Immunosuppressant's

Relentless placoid chorioretinitis RPC

- In 2000 by Jones and colleagues
- resembling both APMPE and serpiginous choroiditis
- CF
 - sudden painless blurring, metamorphopsia, floaters, or can be asymptomatic.
 - bilateral posterior creamy-white lesions at the level of the RPE
 - hallmark of this disease is the eventual presence of **numerous** (>50 to hundreds) lesions with involvement **anterior and posterior to the equator**
- Ix
 - FFA, ICGA, FAF, OCT
-

Persistent placoid maculopathy PPM

- resembles macular serpiginous choroiditis but differs in its clinical course and visual prognosis
- CNV is a common feature of PPM, and usually the major cause of visual loss.

Progressive subretinal fibrosis and uveitis syndrome PSFU

- also known as diffuse subretinal fibrosis syndrome
- young, healthy, and myopic
- CF
 - unilateral decreased vision, floaters, possibly photopsias, scotomas, and metamorphopsia.
 - Numerous small (100-500 μm) yellow spots are seen at the level of the choriocapillaris, RPE, and deep retina

AZOR Complex

Gass has used the term AZOR complex to encompass the following entities: MEWDS, multifocal choroiditis, punctate inner choroidopathy (PIC), acute idiopathic blind-spot enlargement, acute macular neuroretinopathy, acute annular outer retinopathy, and AZOR (acute zonal occult outer retinopathy).

Multiple evanescent white dot syndrome MEWDS

- acute, multifocal, usually **unilateral** retinopathy affecting young adults
- female predominance (75%).
- mean age of 27 years
- **Pathogenesis**
 -

- CF
 - acute onset of blurred vision in one eye
 - blind spot or “spots” in their periphery correlating to a temporal scotoma.
 - small (100-200 $\mu\mu$) white spots are seen at the level of the RPE or deep retina
 - mostly concentrated in the paramacular area, usually sparing the fovea itself
 - classic macular appearance is a **granularity**
 - Mild iritis may be present. Vitritis may be seen but is often absent
 - usually a self-limited disease
 - recovery of visual function occurs over several weeks (3-10 weeks)
- Ix
 - FFA
 - early and late hyperfluorescence of the white dots in a wreath-like pattern; diffuse, but patchy, late staining at the level of the RPE and retina; and disc capillary leakage
 - ICGA
 - no abnormalities of large choroidal vessels in the early phase
 - hypofluorescent lesions are evident in the late phase
 - OCT
 - dome-shaped reflective lesion in the subretinal space was seen corresponding to a clinical white dot
 - disturbance in the photoreceptor inner/outer segment (IS-OS) junction
 - FAF
-

Punctate inner choroidopathy PIC

- disease of young, relatively healthy, myopic women
- CF
 - scotomas were the presenting complaint in 91% of patients, followed by blurred vision (86%), photopsias (73%), floaters (69%), metamorphopsia (65%), and decreased peripheral vision (26%).
 - Most (85%) presented with unilateral symptoms
 - gray or yellow, small round lesions are seen scattered throughout the posterior pole
- Ix
 - FFA
 - hyperfluorescent in the arterial phase or may appear as blocked fluorescence
 - ICGA
 - hypofluoresce in the early, middle, and late phases of ICGA
 - OCT
 - associated with CNV, outer retinal irregularity
 -

Multifocal choroiditis and panuveitis

- Dreyer and Gass coined the term multifocal choroiditis and panuveitis
- Caucasian myopic women
- 20-60 years
- CF
 - decreased central vision, photopsias, floaters, metamorphopsia, paracentral or temporal scotomas, ocular discomfort, and photophobia
 - yellow round or oval lesions, ranging in number from one to scores
 - 50 to 1000 μm

- posterior pole, peripapillary region, and midperiphery
- can also be arranged in **linear scars parallel to the ora**
- become atrophic with a variable amount of pigment (“**punched out**” appearance).
- The peripapillary region may have a characteristic subretinal fibrosis that has been described as a “**napkin ring**” configuration
- mild to moderate anterior uveitis
- Ix
 - FFA
 - acute phase, the clinical lesions appear hypofluorescent
 - CNV may be present in the peripapillary or macular
 - ICGA
 - hypofluorescent round spots that may be far more numerous than seen on clinical examination
 - OCT
 - RPE irregularity corresponding to a clinical lesion
 -

Acute zonal occult outer retinopathy AZOOR

- linked to the white spot syndromes although it has no white spots
- predominance of Caucasians
- predominance of women
- young
- CF
 - abrupt onset of a scotoma related to outer retinal dysfunction

- photopsias
- area of involvement will show retinal atrophy and mottling
- area of involvement is often peripapillary but usually the central vision is good unless a scotoma extends to the fovea.
- may resemble sectoral retinitis pigmentosa, DUSN
- Ix
 - FFA
 - window defects and abnormalities at the level of the pigment epithelium become apparent
 - ICGA:
 - normal or may show hypofluorescence
 - OCT
 - absence or irregularity of the IS-OS photoreceptor line
 - VF
 - Scotomas (usually peripheral and temporal) develop often in continuity with the optic disc

acute annular occult outer retinopathy

Patients develop a scotoma with a grey-white line in the fundus between normal retina and involved retina. This line of activity fades. The areas of involvement subsequently may show evolution similar to AZOOR with RPE changes and retinal thinning.

Acute idiopathic blind spot enlargement AIBSE

- sudden onset of photopsias and a temporal scotoma involving the blind spot.
- primarily young women
- CF
 - Loss of vision
 - blurring, awareness of a loss of part of their visual field, or “looking through a film

- photopsias, swirling movement within a scotoma, colored lights, or after “flash bulb” phenomena
- normal fundus and normal optic disc appearance
- Afferent pupillary defects and dyschromatopsia
- Photostress recovery has been noted to be prolonged
-

Acute macular neuroretinopathy AMN

- young, healthy women in the second to fourth decades
- CF
 - decreased vision and paracentral scotomas. A viral prodrome or drug use
 - several small lesions are seen surrounding the fovea at the level of the outer retina
 - round, oval, or petaloid
 - unilateral or bilateral
 - several days after the development of scotomas
- Ix
 - FFA ICGA normal
 - OCT
 - high reflectivity band corresponding to the retinal pigment epithelium-choriocapillaris complex
 - distortion of the IS-OS junction and focal thinning of the outer retina

