Ophthalmology Technician conference 2018

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

UVEITIS

Kelly Mitchell, MD

Uveitis Definitions:

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Uvea (*Latin = grape*)

Middle pigmented, vascular layer: iris, ciliary body and choroid (the layer between retina & Sclera)

Itis (Latin = inflammation)

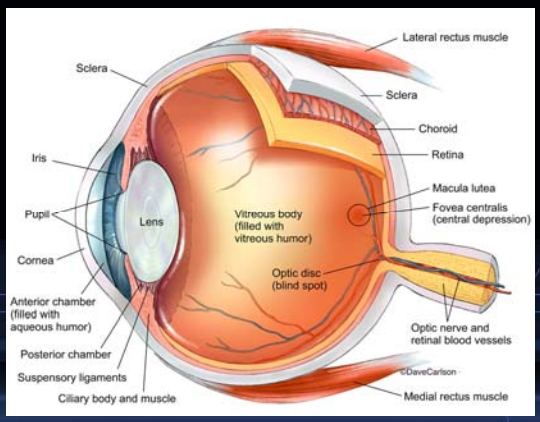
Uveitis can and frequently does involve adjacent structures: Cornea, sclera, vitreous retina, optic nerve

Uveitis Definitions:

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Uvea (*Latin = grape*)

Middle pigmented, vascular layer: iris, ciliary body and choroid (the layer between retina & Sclera)



Uveitis Classification:

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

(Historically: Anatomy, Clinical Course, Etiology, Histology)

SUN **S**tandardization of **U**veitis **N**omenclature Working Group **2005**

Etiology
- Noninfectious/ autoimmune
- Infectious

Basic 4 anatomical classifications of Uveitis (focus of inflammation)

1. Anterior	A/C	iriits/iridocyclitis/keratouveitis
2. Intermediate	Vitreous	Pars planitis/posterior cyclitis/hyalitis
3. Posterior	Retina and Choroid	retinitis, choroiditis, neuroretinitis,
4. Panuveitis	A/C//Vitreous// Retina & Choroid	

Uveitis Classification:

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

SUN **S**tandardization of **U**veitis **N**omenclature Working Group **2005**

Onset:	Sudden/Insidious	
Duration:	Limited	less than 3 months
	Persistent	more than 3 months
Course:	Acute	sudden onset and limited duration
	Recurrent	repeated episodes with periods of inactivity greater than 3 months
	Chronic	Episodes & relapse less than 3 months
Remission:	Inactive disease for greater than 3 months after stopping TX	

Uveitis Classification:

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

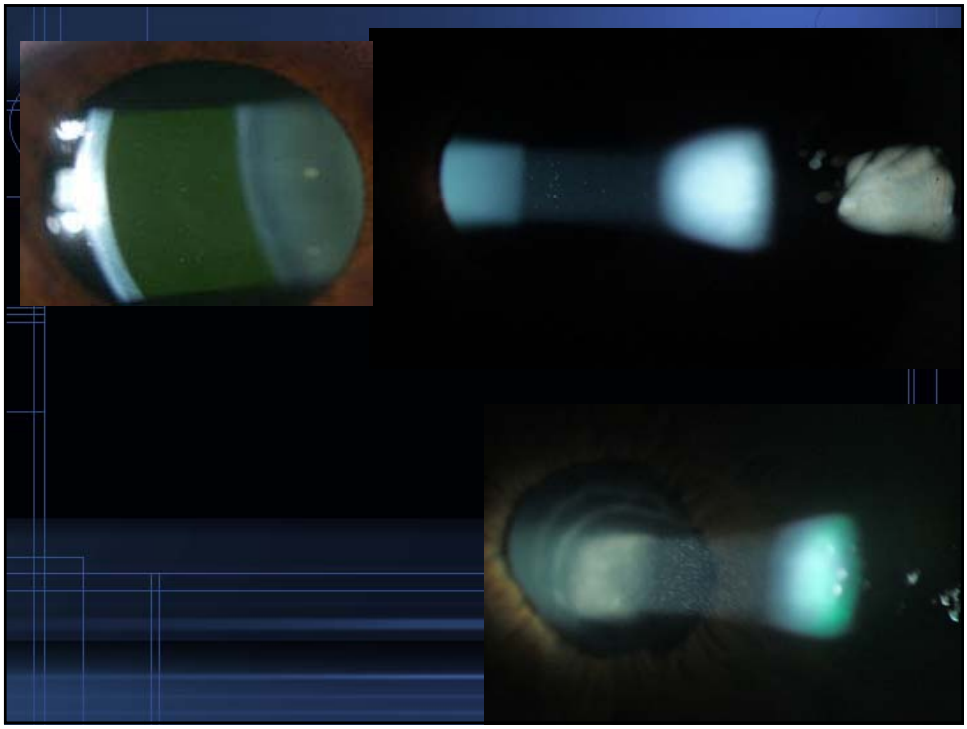
SUN **S**tandardization of **U**veitis **N**omenclature Working Group **2005**

Anterior Chamber Cells

1X1mm high mag. & high intensity light count the cells

Grade	Cells in field
0	<1
0.5+	1-5
1+	6-15
2+	16-25
3+	26-50
4+	>50

(divide beam ½ if easily over 10 or 20 can help with speed/accuracy)



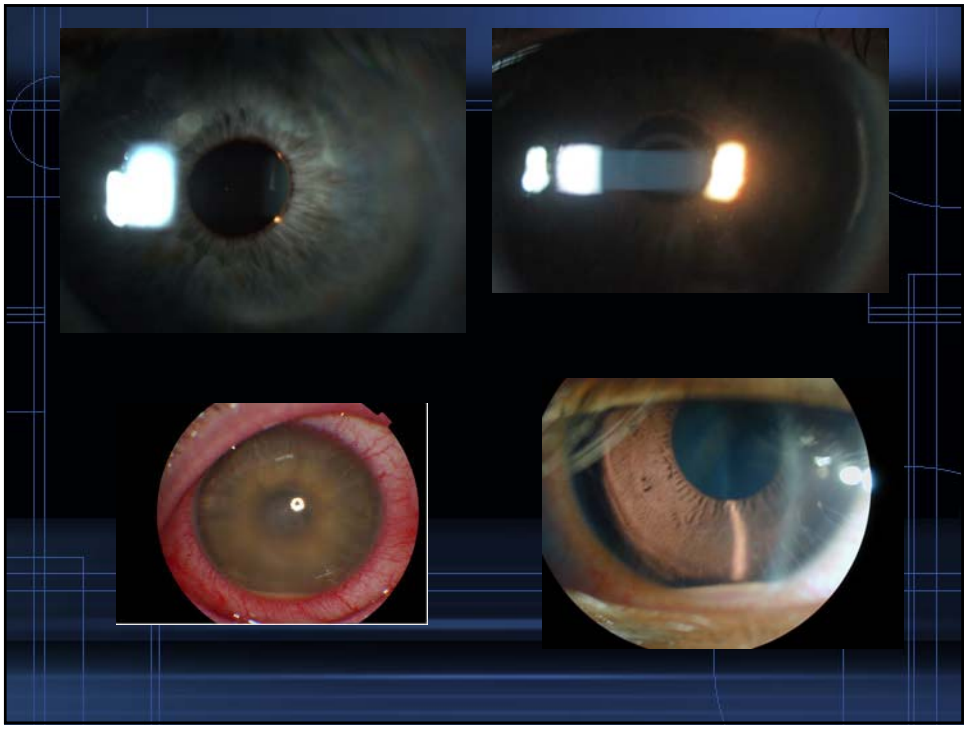
Uveitis Classification:

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

SUN **S**tandardization of **U**veitis **N**omenclature Working Group **2005**

Anterior Chamber Flare

Grade	
0	none
1+	faint
2+	Moderate (but iris and lens clear)
3+	Marked (iris and lens hazy)
4+	Intense (fibrin or plasmoid aqueous)



Uveitis Classification:

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Vitreous Haze (better indicator of disease activity)

NIH/SUN grading Indirect exam with 20D lens

0 = No Flare,
1+ = Clear disc and vessels but hazy NFL
2+ = Disc outline clear, but hazy vessels
3+ = Only Disc visible with blurred margins and detail,
4+ = NO view of Disc

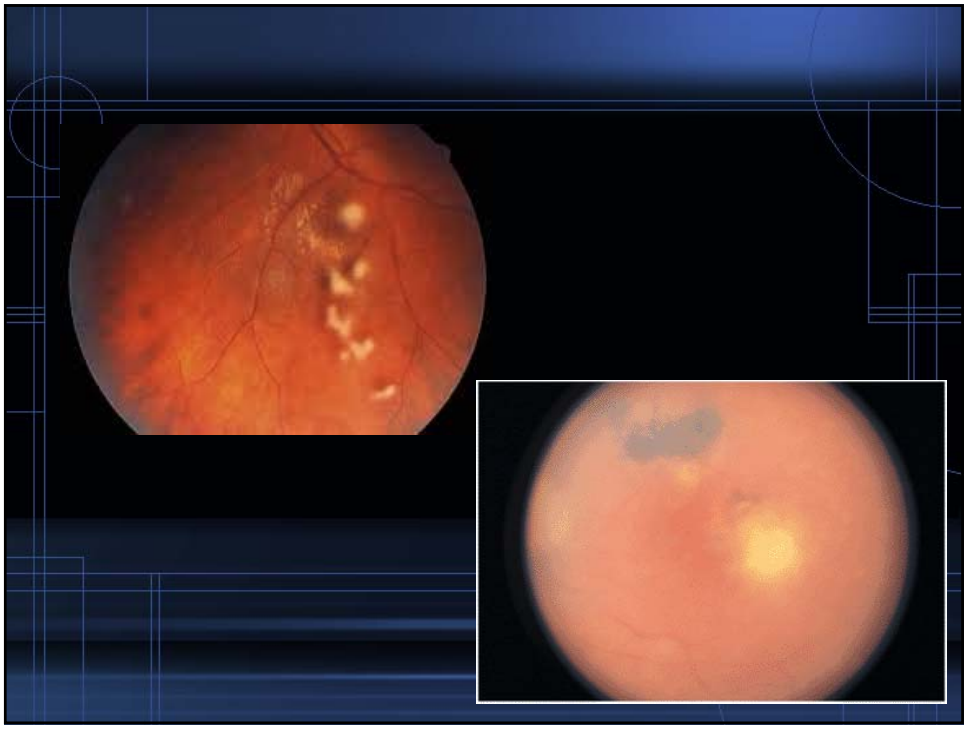
Vitreous Cell (no current SUN consensus)

1X0.5mm high mag. & high intensity light count the cells

Cells in vitreous strands are likely inactive, those is clear moving fluid active

0 =	0
0.5+	1-5
1+ =	6-10
2+ =	11-20
3+ =	21-50
4+ =	>50

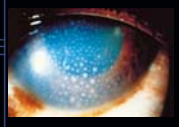
(divide beam ½ and double if hard to count)



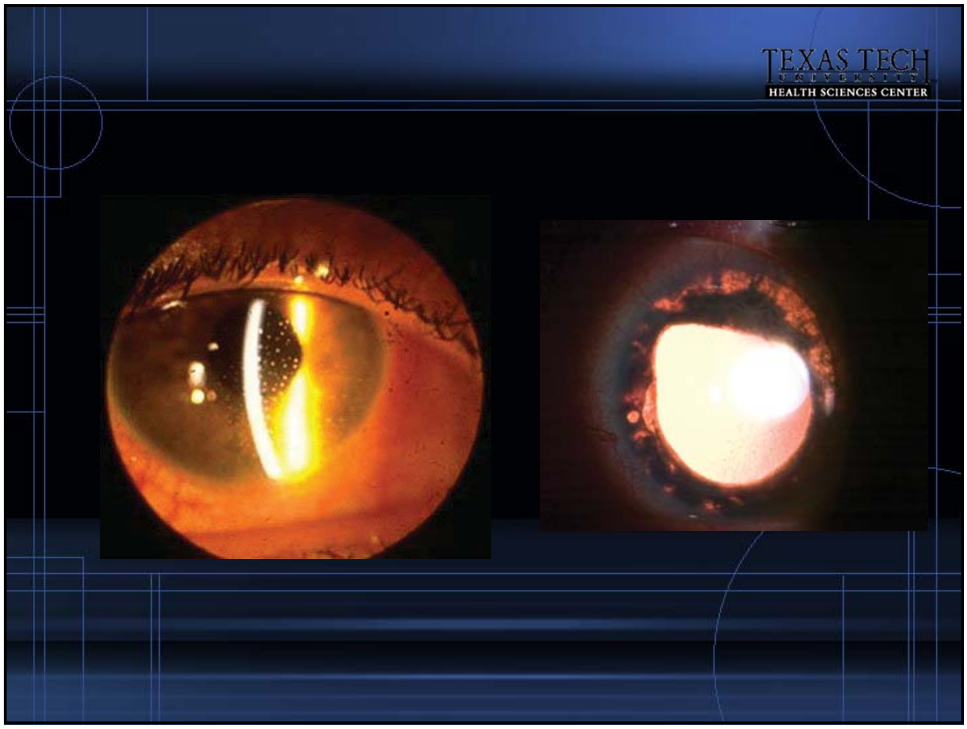
How (and why) Classify inflammation?

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

1. Granulomatous or Nongranulomatous
   - Based on Appearance of precipitates on corneal endothelium
     1. Granulomatous KP
        1. Less common, but more useful
           1. Larger, yellowish, glassy or greasy appearance = Mutton or meat Fat keratic precipitates, may have serrated borders, collections of plasma cells, lymphocytes and giant cells
           2. **Useful because can give diagnostic clue:**
              Sarcoidosis,, Lens induced uveitis,Vogt-Koyangi-Harada (VKH), Syphilis, TB, Uveitis associated with MS, IOFB, Sympathetic Ophthalmia



     2. Nongranulomatous KP
        1. More common, less useful
           1. Fine, white colored collections of plasma cells
           2. Can be seen in any form of uveitis



Herpes Uveitis

- Anterior Uveitis is the most common type of uveitis over 80%
- Herpes simplex or Herpes zoster cause 5-10% of anterior uveitis and is the most common cause of anterior infectious uveitis.
- Suggestive Clinical Picture:
- Active Skin lesions
- Active keratitis and/or corneal anesthesia
- Nearly always unilateral
- SLE:
- active keratitis/scaring/or normal cornea
- Usually granulomatous
- Iris atrophy or synchie
- Can have elevated IOP

Herpes Uveitis

TEXAS TECH HEALTH SCIENCES CENTER

Diagnosis:

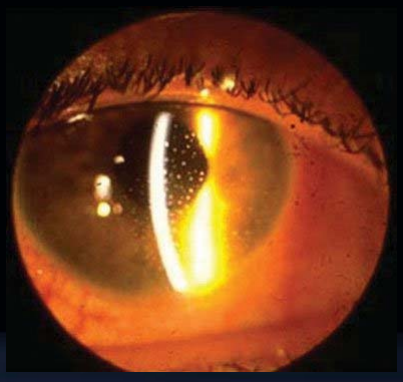
Usually Clinical, but can confirm with A/C tap of fluid for PCR or culture

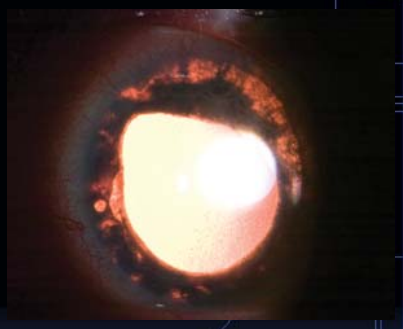
Treatment:

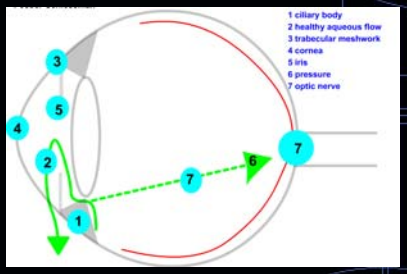
1. Topical Steroids and cyclpplegia
2. Oral Acyclovir
3. As needed IOP lowering drops

Herpes Related Uveitis

TEXAS TECH HEALTH SCIENCES CENTER







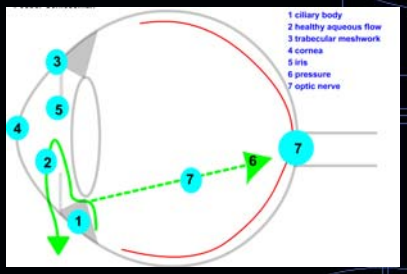
Glaucomatocyclitic crisis
Posner Schlossman

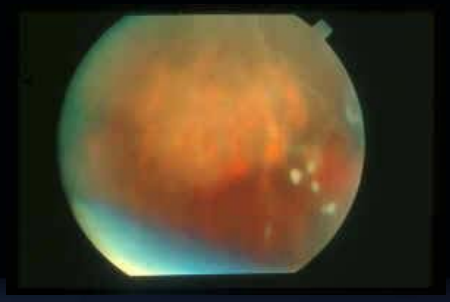
Clinical Picture/SLE:
Adults, unilateral
Mild, non-granulomatous anterior uveitis
Patchy iris atrophy or loss of iris color
PSC cataract
MARKEDLY ELEVATED IOP

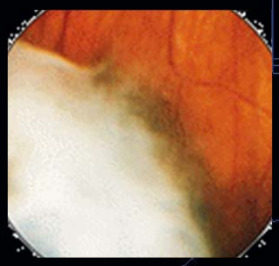
Pathology/associations:
Elevated levels of protoglandins cause increase in Aqueous production
Inflammation causes scaring in TM which decreases aqueous drainage
Associations with Rubella virus//toxocariasis//toxoplasmosis

Treatment
1. Control IOP (meds or surgery)
2. If needed cataract surgery
3. Usually steroids not used long-term

Glaucomatocyclitic crisis
Posner Schlossman







What is Intermediate Uveitis?

1. IU is defined by inflammation concentrated in the anterior vitreous and the vitreous base overlying the ciliary body and peripheral retina-pars plana and accounts for 15% of all cases of uveitis
    1. Anterior vitreous cells are seen
        1. The cells aggregate = ***snowballs***
        2. These aggregates coalesce = ***snowmen***
        3. Inflammatory exudate from the pars plana or snowballs or snowmen falling onto the pars plana = ***snowbanking***
            1. Usually associated with more severe disease
    2. Retinal phlebitis may occur
    3. Anterior cells may occur
        1. These are usually spillover from the vitreous

What is Pars Planitis?

Pars Planitis is IU of unknown cause making up 85-90% of the cases of IU

- It is the most common type of IU, but is a DX of exclusion
- Age range 5-40
    - Bimodal: 5-15 years and 20-40 years
- Men = women
- Associated with HLADR15
    - Coding for one of the two HLA-DR2 subtypes
        - MS is associated with HLA-DR2

What are the Clinical Findings of Pars Planitis?

- 80% bilateral, often asymmetric
- Children:
  - Redness, photophobia, discomfort, a/c reaction
- Teenagers and adults:
  - More insidious, usual complaint is floaters
    - Spillover a/c reaction
    - Vitreous cells: snowballs
    - Inferior peripheral retinal vessel sheathing (phlebitis)
    - **CME (10%) most common cause of ↓ acuity**
    - NVE of snowbanking in 5-10%
      - Can evolve into VH, tractional RD or RRD (10%)
    - PSC cataracts (15%) and ERMs (5-10%)

IU associated with MS

- 15% of IU eventually develop MS
  - Preceding MS, by 5-10 years
- Patients with MS
  - IU or retinal periphlebitis may be seen in 5-20%
    - Not associated with optic neuritis, systemic exacerbations or disease severity
    - IU is milder in MS patients
      - CME less common, treatment less frequently needed
      - Interferon TX of MS does not appear to effect IU
- IU and MS patients share HLA-DR2 haplotype

What in the Differential Diagnosis and work up of Pars Planitis?

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

DDX:

- Syphilis, Lyme, Sarcoid, IU associated with MS, and toxocariasis, in older patient remember intraocular lymphoma

W/U:

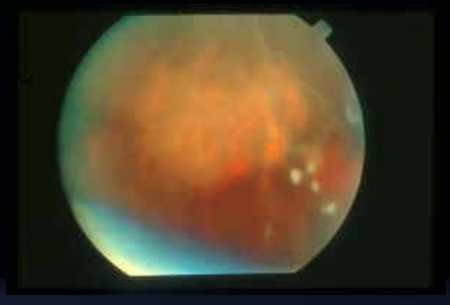
- Presence of Clinical Findings
- R/O: Sarcoid, Lyme, Syphilis, toxocarasis

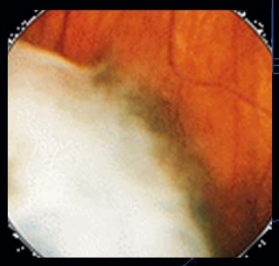
Clinical Course:

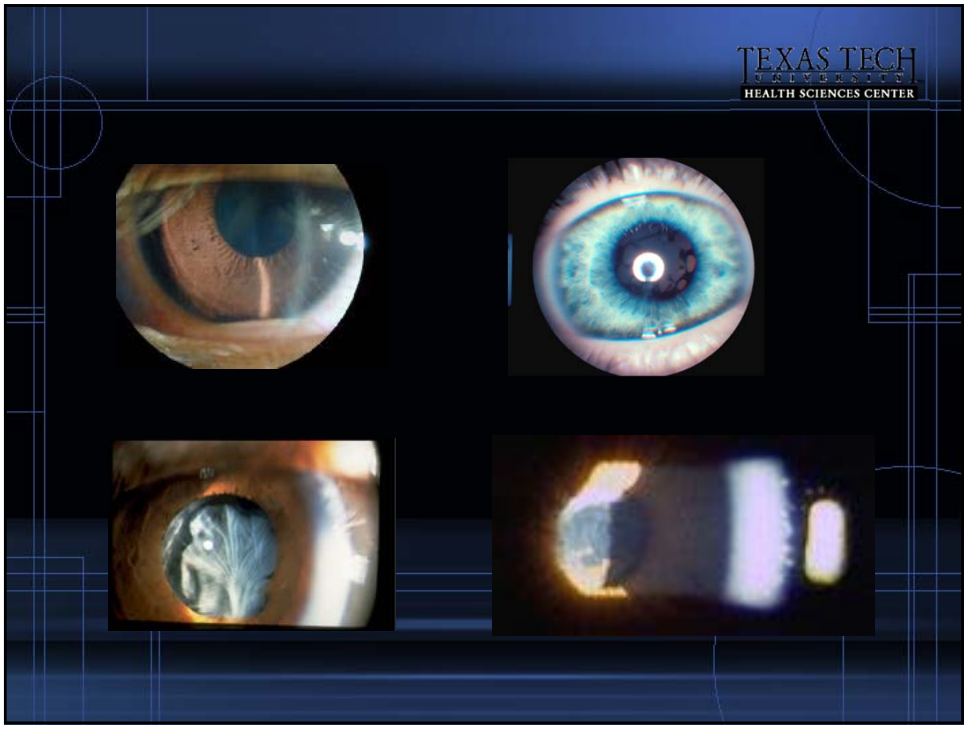
- 10% short mild course, 30% smoldering up and down course, 60% have mild but chronic course

Pars Planitis

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER







Uveitis associated with Juvenile Rheumatoid Arthritis

TEXAS TECH HEALTH SCIENCES CENTER

Juvenile Rheumatoid Arthritis (JRA)

- **Most common disease associated with iridocylitis in children. JRA has three types**
- 20% have Systemic onset (Still Disease).
  - Age under 5, fever, rash, lymphadenopathy, and hepatosplenomegaly.
  - Joint involvement is minimal or absent initially
  - Eye disease rare – less than 6%
- 40% have Polyartiuclar onset
  - Five or more joints involved within 6 weeks
  - Eye disease uncommon – 7-14%
- 40% have Pauciarticular onset
  - Four or less joints involved within 6 weeks (some have no joint symptoms)
  - Type 1: girls under five ANA+ chronic uveitis in 25%
  - Type 2: older boys, 75% are HLA-B27+, usually acute and recurrent rather than chronic

Uveitis associated with Juvenile Rheumatoid Arthritis

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

JRA associated Uveitis

- Risk factors for uveitis: female, pauciarticular, ANA+, most are RHF –
- Eye findings: OFTEN WHITE & QUIET
  - OFTEN FOUND ON ROUTINE EXAMS
    - Fine KP, cell and flare, posterior synechiae cataract, band keratopathy
  - Symptoms due occur in some: pain, photophobia and ↓ VA

These findings or history in children = workup for JRA, ANA testing and referral to PCP comfortable with this type of evaluation or to Rheumatologist that sees children.

Uveitis associated with Juvenile Rheumatoid Arthritis

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Management – Medical

- Topical Steroids mild cases short course
  - Treat for cell only, watch for complications
    - Pupil dilation important even with flare, use short acting dilator QHS to prevent synechiae
- Periocular steroids
  - Children go to OR for this
- Systemic steroids
  - Should be managed by **PCP → pediatrician**
    - All must be vigilant for systemic and ocular complications
- Systemic immunosuppresion
  - Managed by pediatrician or pedi rheum or pedi ocologist or adult rheum
    - Weekly methotrexate can be PO or IM

Uveitis associated with Juvenile Rheumatoid Arthritis?

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Management – Surgical

- Cataracts
  - Inflammation controlled for 3 months
  - This will be a challenging surgery
    - To it do well or refer to someone who can
    - Ideal Referral Surgeon (may not be typical cataract-jock)
      - Good with parents and kids
      - Comfortable with uveitic cataracts
      - Surgery will likely be done in hospital
  - Role of IOL??? This is evolving
    - young with active **no**, older and controlled **yes**
- Glaucoma
  - Medical first:
    - Beta blocker, diamox ok, no alphagan in the very young
  - Surgery last:
    - May have to be done with inflammation in order to control IOP
    - Filters with anti-metabolite or valve/tubes

Uveitis associated with Juvenile Rheumatoid Arthritis?

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

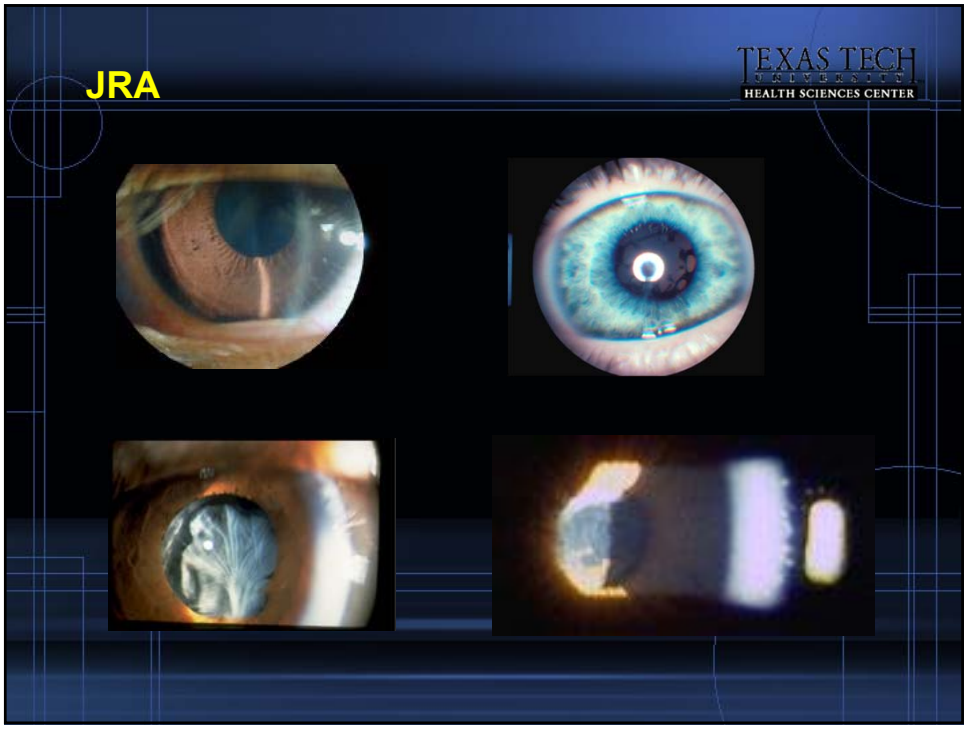
Management – Surveillance

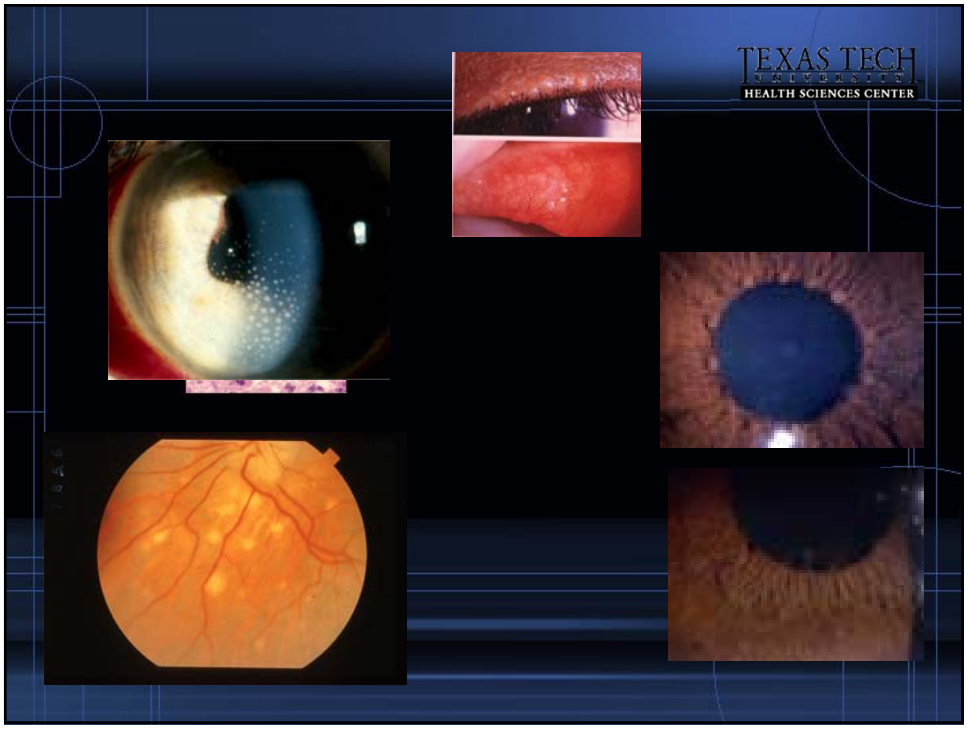
- Patients with JRA (girls, ANA +, pauciarticular)
  - Tables (AAP and AAO)
  - **Keys: less than 7, pauciarticular disease, and ANA+**

Table 7-1 Recommended Screening Schedule for JRA Patients Without Known Iridocyclitis

JRA Subtype at Onset	Age of Onset <7 Years[1]	Age of Onset ≥7 Years[2]
Pauciarticular		
+ANA	Every 3–4 months[3]	Every 6 months
−ANA	Every 6 months	Every 6 months
Polyarticular		
+ANA	Every 3–4 months[3]	Every 6 months
−ANA	Every 6 months	Every 6 months
Systemic	Every 12 months	Every 12 months

[1] All patients are considered at low risk 7 years after the onset of their arthritis and should have yearly ophthalmologic examination indefinitely.
[2] All patients are considered at low risk 4 years after the onset of their arthritis and should have yearly ophthalmologic examinations indefinitely.
[3] If no uveitis 4 years after onset of arthritis, should have ophthalmologic examination every 6 months.


JRA
TEXAS TECH
HEALTH SCIENCES CENTER


TEXAS TECH
HEALTH SCIENCES CENTER

Uveitis associated with Sarcoidosis

- Sarcoidosis accounts for 3-10% of all uveitis
- 15-50% of patients with sarcoidosis have uveitis
- Sarcoidosis is a systemic disease
  - 10x more common is blacks
  - Primarily thoracic (90%), but can effect brain, bones, joints, liver
    - Uncommon in young children, but skin/joint >> chest findings
  - Key pathological lesion
  - noncaseating epitheloid cell granuloma or tubercle
    - Epitheloid cell is a polyhedral mononuclear histiocyte
    - Tubercle = epitheloid cells + multinucleated giant cells of Langhans type (nuclei at the periphery in an incomplete circle + rim of lymphocyctes

Uveitis associated with Sarcoidosis

- Possible genetic link:
  - Increased HLA-DRB1 in biopsy proven cases
- Presence of peripheral anergy
  - Due to depression in delayed-type hypersensitivity
  - However, at the target organ site (eye)
    - Active T-lymphocyte (CD^{4+}) and MΦ response leading to granuloma

Uveitis associated with Sarcoidosis

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Acute Systemic Sarcoidosis and iridocyclitis

- Löfgren syndrome
  - Erythema nodosum, febrile arthropathy, bilateral hilar adenopathy, acute iritis
  - responsive to systemic steroids
- Heerfordt Syndrome (uveoparotid fever)
  - Uveitis, parotitis, fever and facial palsy

Chronic Sarcoidosis

- 2 years duration, thoracic findings, chronic uveitis
- Thoracic/pulmonary disease major cause of morbidity
- Mortality is 5-10% (neurosarcoidosis)

Uveitis associated with Sarcoidosis

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Eye Findings

- Skin involvement is common
  - Orbital and eyelid granulomas
- Conjunctival nodules
- Lacrimal gland infiltration cause of dry eye

Uveitis

- Can involve all structures
- May begin as acute nongranulomatous but 60% become chronic granulomatous

Uveitis associated with Sarcoidosis

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Main Uveitic Findings

- Mutton-fat KP
- Koeppe and Busacca iris nodules
- Snowballs in the inferior anterior vitreous

Other findings

- Corneal: nummular infiltrates & endothelial opacification
- Angle: posterior and anterior synchiae

Posterior Segment findings – less common than A/C

- Retinal and choroidal granulomas usually ¼ DD in size
- Irregular nodules along venules = *candelwax drippings* or *taches de bougie*
- Retinal periphelbitis presents as sheathing
- CME is common
- Disc edema, NVD,NVE can occur

Uveitis associated with Sarcoidosis?

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

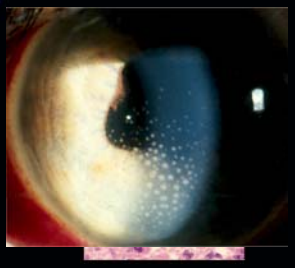
Diagnosis

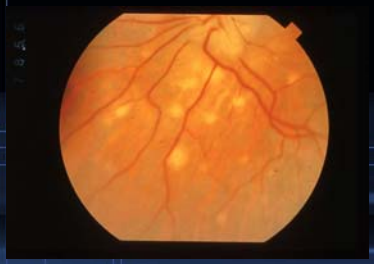
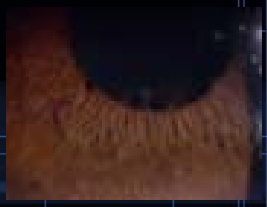
- Because of its variety of presentation and frequency, it should be considered in every case of uveitis
- If suspicion is strong
- CXR best screening test (positive in 90%) or CT
- Lysozyme, ACE are supportive but not diagnositic
- If clinical picture is strong and above are inconclusive consider
- Gallium scan of head and neck especially used with ACE
  - Steroid treatment make this unreliable
- Biopsy is useful especially of conjunctival or lacrimal nodules, which are easier than bronchial sample

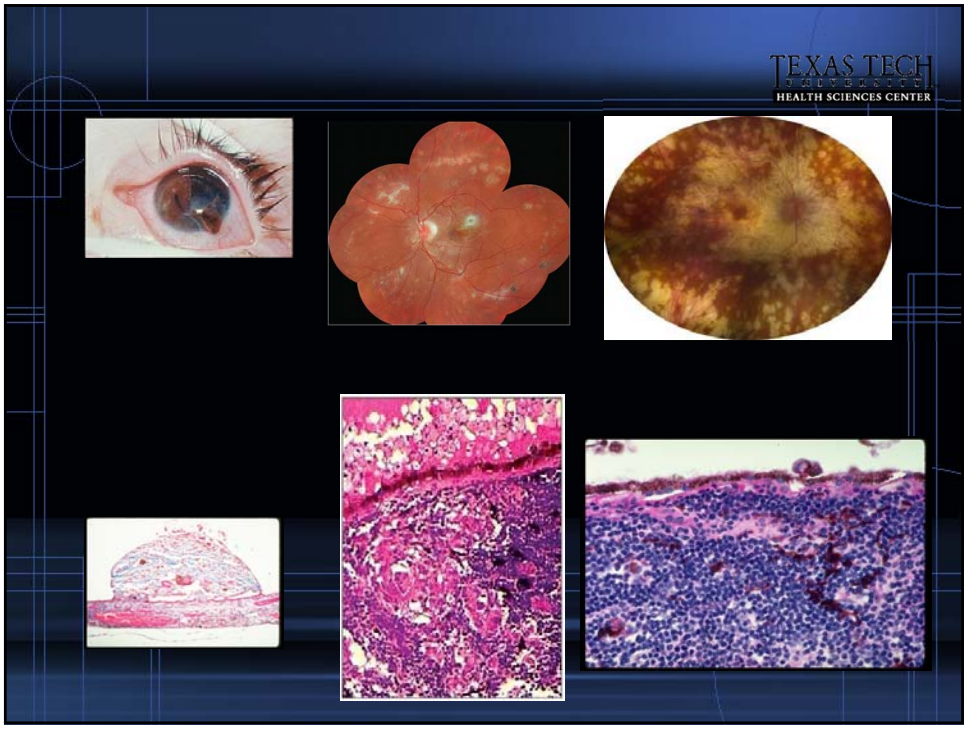
Uveitis associated with Sarcoidosis?

1. Treatment
   1. Steroids: (Topical, Periocular and Systemic)
   2. Systemic immunosuppresion
      1. MTX or azathioprine, cellcept, infliximab
   3. Remember it is a systemic dz, so get PCP involved in evaluation and management of systemic effects

Sarcoidosis





Sympathetic Ophthalmia

Sympathetic Ophthalmia (SO)

- Rare bilateral, nonnecrotizing granulomatous after injury/surgery to one eye ***(the exciting eye).*** Followed by a latent period and the development of uveitis in the uninjured eye ***(the sympathizing eye)***
- Lower incidence because we are better surgeons
  - Better wound closer and techniques (more enucleations vs eviscerations)
- Cause of SO is not known, but theories include:
  - Hypersensitivity to melanin and melanin-associated protein
  - An infectious causal agent
  - Sensitivity to retinal S antigen or retinal or uveal proteins
- Possible Genetic risk:
  - HLA-DR4, HLA-DRw53, HLA-DQw3
  - In UK and Japan also see HLA-DRB1*04 and HLA-DQB1*04
  - These and VKH are nearly the same

Sympathetic Ophthalmia

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Incidence

- 0.2-0.5% in nonsurgical trauma
- 0.01-0.03% in surgical trauma
- Vitrectomy has now emerged as the main surgical risk for the development of SO
  - 1980's 0.01-0.06%
  - Now may be as high as 0.06-0.12%
    - Makes sense
    - Better surgical care of ocular trauma
    - Greater number of PPV cases
    - Both trauma and non-trauma
  - Risk factors:
  - Old: males, children, elderly
  - Newer: no difference in the sexes, lower in kids, still high in the elderly
    - Increased history of previous eye surgery and trauma
  - Timing of onset
  - Traditional: 80% in 3 months, 90% in one year
  - Recent: 30% in 3 months, 50% in one year

Sympathetic Ophthalmia

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Histopathological Features

- Diffuse granulomatous uveal involvement
- Absence of reaction at the choriocapillaris
- Phagocytosis of uveal pigment by epithelioid cells
- Extension of the granulomatous process into scleral canals and the optic disc

Clinical Features, **asymmetrical bilateral panuveitis worse in exciting eye**

- Unaffected eye
  - Can occur within10 days after injury or surgery, slight redness, mild photophobia, mild problems with near vision
  - Progression to panuveitis
    - Mutton fat KP, iris nodules, PAS, vitritis, choroidiits, ERD, papillitis
- Injured or operated eye
  - Early Panuveitis,

Sympathetic Ophthalmia

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

Diagnosis

- Bilateral uveitis following trauma or surgery → **Think SO**
  - Inflammation may occur between 10 days to 50 years following the triggering event, but usually within the year

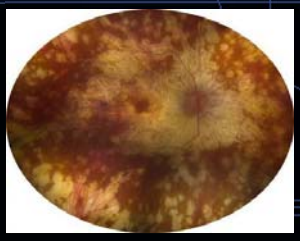
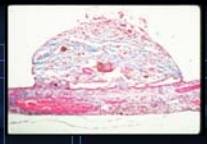
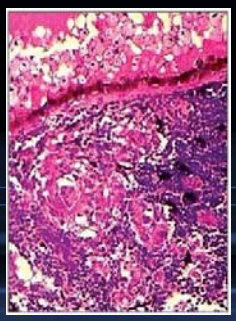
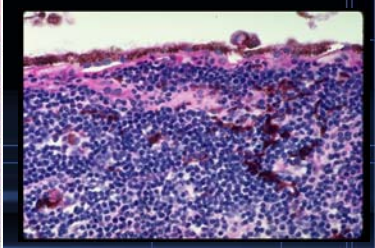
Management

- The course of SO is chronic with frequent exacerbations
  - Topical, systemic or periocular steroids
  - Cycloplegia
  - May need antimetabolite level immunsuppression: cyclosporin
- Overall current treatment for SO is effective and results in good vision over many years
- **Removal of blind exciting eye within two weeks of event has been shown to decrease risk of SO or if eye becomes blind after SO develops removal may decrease severity of SO,**
- *However, if exciting eye still sees (even LP) most will leave eye because of effective treatment of SO*
- *Prognosis is reasonable with 50% of patients having 20/40 in at least one eye*

Sympathetic Ophthalmia

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER



Uveitis and Closing Pearls

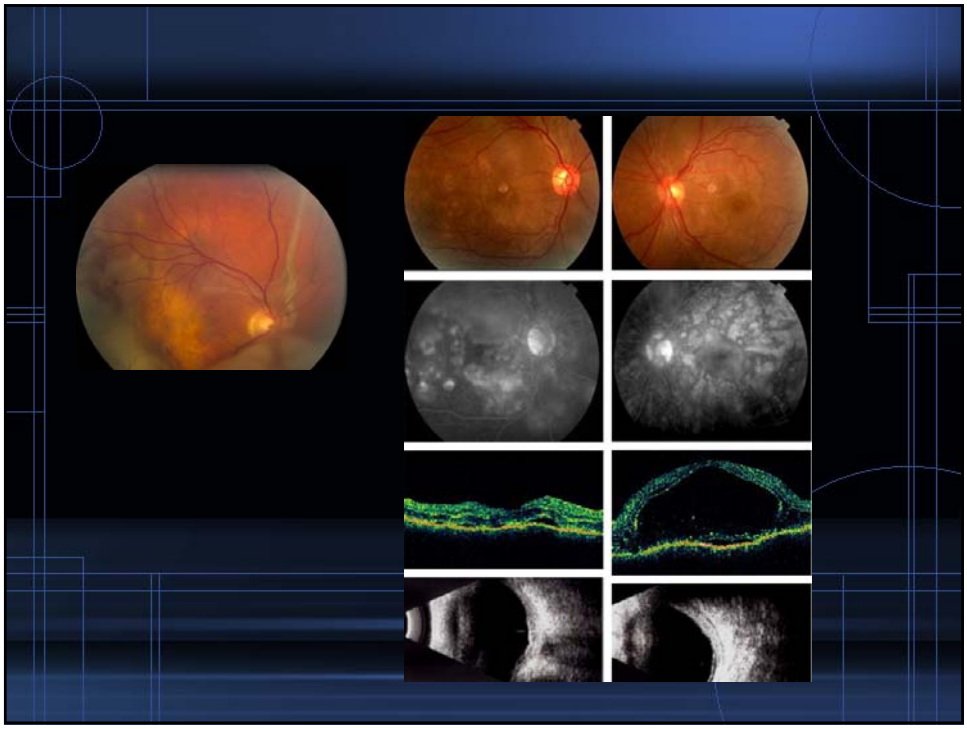
TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

When seeing a patient with Uveitis:

1. Could it be an **infection**?
2. Could it be caused from a **systemic** disease?
3. With **Initial** Treatment decisions:
    1. Deal with **inflammation & IOP**
4. With **chronic** treatment decisions
    1. Deal with **Inflammation**
    2. Deal with the **side effects** of the **medication** to TX the inflammation (toxicity and IOP)
    3. Deal with the **IOP** from uveitis or meds to treat uveitis
    4. Deal with **side effects** of **uveitis**
        1. **Eye:** cataracts and glaucoma
        2. **Systemic:** uveitis or TX of uveitis

Questions??

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER



Vogt-Koyangi-Harada (VKH) Disease

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

1. Rare cause of Panuveitis even among the mostly commonly effected groups
   1. Asian & american Indian's between 30-50 years of age
   2. Dark skinned people: hispanics
2. Cause not known
   1. However, reaction to melanin-associated protein, melanocytes or RPE
3. Overall the bilateral granulomatous panuveitis resembles SO, however these patients have no history of ocular injury or surgery

VKH – 4 Phases

1. Prodromal
    1. Flu symptoms
    2. CNS signs: nuchal rigidity, seizures, coma, loss of consciousness, paralysis, optic neuropathy, CSF → transient pleocytosis
    3. Skin signs in 30% of patients
        1. Alopecia, vitiligo, poliosis
    4. Hearing complaints in 30% of patients
        1. Deafness or tinnitus
2. Uveitic **(1-2 days after CNS signs)**
    1. Symptoms: photophobia, redness, blurry vsion and ocular pain
    2. Signs: bilateral a/c and vitreous cell and Exudative RD – these can be shallow and have a cloverleaf pattern around posterior pole, optic nerve head swelling

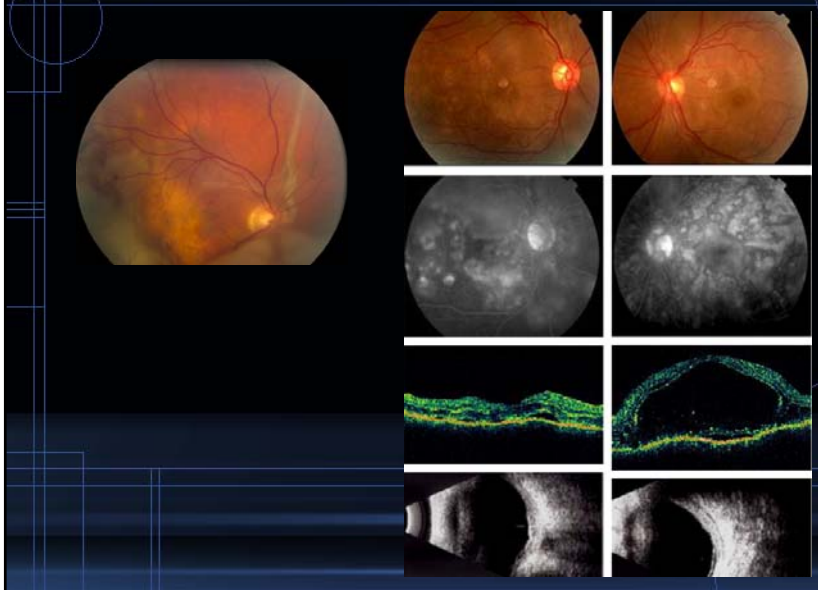
VKH – 4 Phases

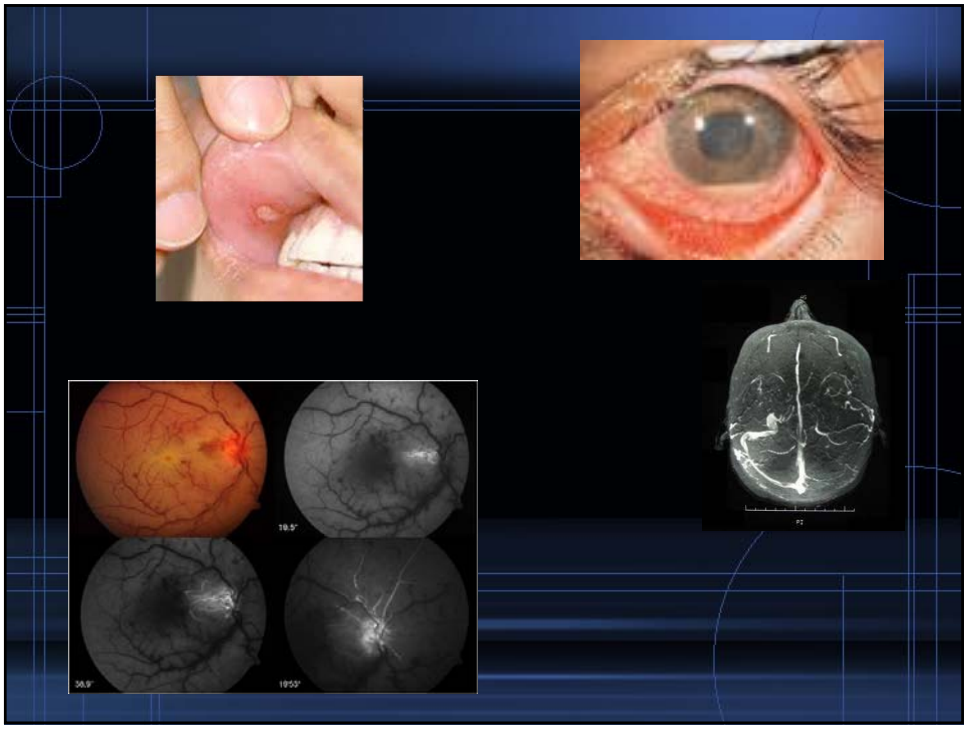
3. Chronic or convalscent
    1. Resolution of ERD and gradual depigmentation of the choroid
        1. Producing the orange-red discoloration = ***sunset-glow fundus***
    2. Discrete, round depigmented lesion develop in the inferior peripheral fundus = resolved Dalen Fuchs nodules
    3. Peripapillary atrophy can be seen
    4. Skin changes usually occur weeks to months after the beginning of the uveitic phase, but can occur at the onset
        1. Perilimbal vitiligo (Sugiura's sign) in more than 75% of cases
        2. Vitligo, alopecia, and poliosis in 30%
4. Recurrent phase
    1. Increased risk with incomplete treatment of uveitic and chronic phases
    2. Signs: granulomatous anterior uveitis: KP, iris nodules and depigmentation and atrophy
    3. Vision loss due to: Cataracts 50%, glaucoma 33%, CNVM 10%

VKH – Diagnosis and Treatment

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

1. Diagnosis based on Clinical picture
2. Consider SO
3. Work-up
    1. FA -- Multiple areas of focal leakage in early angiogram
    2. LP –lymphocytosis in pt with bilateral panuveitis is very helpful
    3. HLA- haplotyping is helpful
        1. HLA-DR1 & 4 is strongly associated (84%)with VKH in hispanics in SoCal
            1. With HLA-DR1 having a higher relative risk than HLA-DR4
        2. HLA-DRB1*04 and HLA-DQB1*04
4. Treatment
    1. Steroids: topical, periocular and systemci
        1. Taper slowly over 3 months to minimize risk of recurrent phase
    2. If steroids not effective in making eyes completely quiet, must move on to stronger immunosuppressive cyclosporine or MTX.

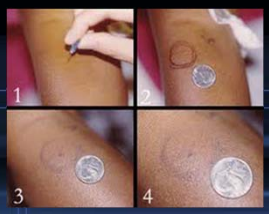




Behcet Disease (Adamantiades-Behcets)

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER

1. Chronic relapsing occlusive vasculitis
    1. Eastern Mediterranean and Pacific rim of Asia
    2. Old Silk Route established by Marco Polo
    3. Turkey: 100-300/100,000, Japan:8-10/100,000 in Japan, 0.4/100,000 in US
    4. Four classic lesion:
        1. Aphthous oral lesions
        2. Skin lesions, erythema nodosum
        3. Genitial lesions
        4. Intraocular inflammation
    5. HLA typing
        1. HLA-B51



Clinical criterion		Typical frequency in BD* (%)
1 Recurrent oral ulcers	At least 3 episodes per year. Minor aphthous, major aphthous or herpetiform ulceration.	100
2 Recurrent genital ulcers		70–80
3 Eye disease	Uveitis, retinal vasculitis, cells in the vitreous	45–75
4 Skin disease	Erythema nodosum, folliculitis, acneiform lesions outside adolescence, papulo-pustular lesions	70–95
5 Positive pathergy test	Vesicular lesion larger than 2 mm, 24-48h after skin prick with 20–22 gauge needle penetrated to 5 mm	5–75

*BD = Behçet's disease