Case 1

- 32 year old Caucasian policeman
- Pain, redness, photophobia OS 7 days
- On prednisolone acetate Q2hrs for 3 days
- No improvement
- VA 20/20 OD, 20/200 OS
The differential diagnosis in this case includes all of the following except:

1. HLA-B27 uveitis
2. Syphilis
3. Endogenous endophthalmitis
4. Fuchs iridocyclitis
5. Syphilis
DDX severe, acute iritis with hypopyon

- **Infectious**
  - ARN
  - Metastatic endophthalmitis
  - Post-operative endophthalmitis
  - Syphilis

- **Non-infectious**
  - HLA B-27
  - Idiopathic
  - Behcet’s disease
Case 1

- No ocular surgery or trauma
- No previous episodes
- Healthy, no meds
- ROS: low back pain, worse in morning or after inactivity
- Family history: ulcerative colitis in mother
- IOP 10, fundus normal, other eye normal
Case 1

- **Work-up:**
  - HLA-B27 positive
  - FTA-ABS negative

- **Diagnosis:** HLA-B27 acute iridocyclitis, possible ankylosing spondylitis

- **Treatment**
  - Pred Forte hourly
  - Short course of PO prednisone
  - Refer to rheumatology
Intracameral TPA 25 μ


20 minutes

45 min
Classification of uveitis

- Anatomic
- Onset and course (acute vs. chronic)
- Granulomatous vs. non-granulomatous
- Infectious vs. non-infectious
- Isolated ocular disease vs. associated with systemic disease
Anatomic classification of uveitis

- Based on site of inflammation
- Not structural complications, such as CME or disc edema

AJO 2005;140(3):509-516
Which of the following is never present in anterior uveitis

1. Anterior chamber cells
2. Choroidal granulomas
3. Anterior vitreous cells
4. Cystoid macular edema
5. Posterior synechiae
Anatomic classification

- Anterior uveitis
  - Primary site of inflammation is anterior chamber
  - Iritis
  - Iridocyclitis
    - Cells in anterior vitreous
Anatomic classification

- Intermediate uveitis
  - Primary site of inflammation is vitreous
  - Includes pars planitis (idiopathic)
Anatomic classification

- Posterior uveitis
  - Primary site of inflammation is retina or choroid
  - Choroiditis, chorioretinitis, retinochoroiditis, retinitis
Anatomic classification

- Panuveitis
  - No predominant site of inflammation
  - Inflammation in anterior chamber, vitreous and retina and/or choroid
  - Do not consider structural complications such as CME or neovascularization
Classification of uveitis: timing

- **Onset**
  - Sudden
  - Insidious

- **Course**
  - Limited – less than 3 months
  - Persistent – greater than 3 months
Characterization of uveitis

- **Acute**
  - Characterized by sudden onset and limited duration
  - e.g. HLA-B27-associated

- **Recurrent**
  - Repeated episodes activity separated by period of inactivity, off treatment, of > 3 months

- **Chronic**
  - Persistent uveitis
  - Relapse with cessation of therapy

AJO 2005;140(3):509-516
Classification of uveitis

- Granulomatous vs. non-granulomatous
  - Descriptive rather than histopathological
Non-granulomatous

- Small KP
- May have Koepppe nodules (small)
- No Busacca nodules
- DDx includes HLA-B27, sarcoidosis, Herpes, Fuchs’ iridocyclitis, TINU
**Granulomatous**

- Mutton fat KP (may leave “ghost KP”)
- Large Koepppe nodules
- Busacca nodules
- DDx includes sarcoidosis, VKH, Herpes, Toxoplasmosis
Granulomatous iris nodules
Granulomatous iris nodules
Granulomatous KP
Granulomatous iritis
Granulomatous KP

Hyalinized (ghost) KP

Corneal edema

Pigmented old KP
Koeppe nodules

Synechiae form at nodules
Classification of uveitis

- **Infectious**
  - Toxoplasmosis
  - Herpes (including ARN and PORN)
  - Syphilis
  - TB
  - Endophthalmitis
    - Post-op or post-trauma
    - Metastatic

- **Non-infectious**
  - Immune mediated
  - Malignant masquerades
  - Non-malignant masquerades
Anterior uveitis: symptoms

- **Acute**
  - Sudden onset
  - Pain, redness, photophobia
  - Definite start date
  - Self-limited

- **Chronic**
  - Insidious onset
  - Asymptomatic
  - Floaters, decreased vision
  - History often less precise
  - Long duration
Anterior Uveitis: Signs

- **Acute**
  - Limbal injection
  - KP
  - AC reaction (may have hypopyon)
  - Posterior synechiae, PAS
  - IOP often low

- **Chronic**
  - Usually no injection
  - KP
  - AC reaction
  - Posterior synechiae, PAS
  - IOP often high
Acute iridocyclitis

- Idiopathic
- HLA-B27 related
  - Ankylosing spondylitis
  - Reactive arthritis
  - Psoriatic arthritis
  - Inflammatory bowel disease
  - Isolated uveitis
- Behcet’s disease
- Herpetic
- Tubulointerstitial nephritis and uveitis syndrome (TINU)
- Hypersensitivity
  - Drug induced
  - Post-infectious
Uveitis

- History is of paramount importance
  - Previous episodes
  - Trauma
  - Systemic diseases
  - ROS
  - Medications
    - eg bisphosphonates/scleritis
Ankylosing spondylitis

- 80% male
- 96% HLA-B27 +
- More common in Caucasians
- Low back pain, stiffness, worse after inactivity
Ankylosing spondylitis

- 25% have ocular involvement
- Acute anterior uveitis
- Unilateral, may alternate between eyes
Reactive arthritis

- **Triad**
  - Urethritis
  - Arthritis
  - Conjunctivitis

- **65% HLA-B27 positive**
  - 97% positive if have uveitis

- Possible triggers: Chlamydia, Shigella, Salmonella, Yersinia

- Other findings: scaly skin rash (keratoderma blennorrhagicum), circinate balanitis
Reactive arthritis

- Uveitis often very severe, fibrinous
Inflammatory bowel disease

- Uveitis more common in UC than Crohn’s disease
  - UC: 5 – 12%
  - Crohn’s: 2%
- Also chronic iridocyclitis, CME, retinal vasculitis, scleritis
- Uveitis may precede bowel disease
- Increased incidence of uveitis in patients without IBD but with family history of IBD
HLA-B27

- 6-14% Caucasian population
- 0-4% African American population
- 1.3% of the HLA-B27+ population will develop ankylosing spondylitis
Theories as to how HLA-27 causes spondyloarthritis

- HLA-B27 presents a bacterially derived 'arthritogenic peptide'
- Misfolding or homodimerization of HLA-B27 heavy chains results in a pro-inflammatory response
- HLA-B27-positive individuals have deficient intracellular killing of arthritogenic organisms
- HLA-B27 itself, due to sequence homology with bacterial proteins, becomes autoantigenic
All of the following are characteristic of Behcet’s disease except

1. Fibrinous iritis
2. Oral ulcers
3. Hypopyon uveitis
4. Erythema nodosum
5. Genital ulcers
Behcet’s disease

- Recurrent, painful oral and genital ulcers
- Silk route countries
- HLA B5, B51
- Pan-uveitis with retinal vasculitis
Behcet’s disease: diagnostic criteria

- Recurrent oral ulceration plus two other findings
  - Recurrent genital ulceration
  - Ocular inflammation
  - Skin lesions
  - Positive pathergy test

International Study Group for Behcet’s Disease - 1990
Behcet’s Ulcers
Behcet’s Disease: anterior segment

- Hypopyon uveitis
  - Hypopyon is short-lived
  - Less pain than with HLA B-27 hypopyon
  - Shifting
  - No fibrin
Behcet’s disease

- Posterior segment disease
  - Arteritis
  - Vascular occlusions
  - Retinitis

- Usually require systemic immunosuppression
Herpes simplex iritis

- May occur in absence of corneal disease
- Often more FB sensation than pain
- KP
  - Fine, stellate, throughout cornea
  - Mutton-fat
- IOP may be high acutely
- Iris atrophy
  - Patchy or diffuse
- Dilated pupil
  - (CJO 2009;44: 314-316)
- Often becomes chronic
Herpetic iritis

Intra-iris hemorrhage
Herpes simplex iritis

- Live virus in AC
- HEDS study
  - Small numbers, benefit of oral ACV — “trend towards significance”
- Oral antivirals
  - Acyclovir 200-400 mg PO 5/day
  - Famcyclovir (Famvir) 500 mg PO TID
  - Valacyclovir (Valtrex) 1 gram PO TID
- Topical steroids/antivirals
- Dilators
- May be very difficult to taper topical corticosteroids
Herpes zoster iritis

- VZV in V₁
- IOP may be high
- Very often chronic
- Oral antivirals
- Topical steroids
- Dilators
TINU

- Tubulointerstitial nephritis and uveitis syndrome
- Young patients
- More common in females
- Usually bilateral
- Acute, recurrent or chronic
- Non-granulomatous anterior or pan-uveitis
- Increased urinary $\beta$-2 microglobulin
- Renal biopsy
Chronic iridocyclitis

- Idiopathic
- JIA
- Fuchs
- Sarcoidosis
- TINU
**JIA uveitis**

- White, quiet eye
- Asymptomatic
- Usually bilateral

**Complications**
- Band keratopathy
- Posterior synechiae
- Cataract
- Glaucoma
- Hypotony
JIA uveitis

- Most common if:
  - ANA positive
  - Female
  - Pauci or monoarticular at presentation
  - Younger age at onset of arthritis
JIA uveitis

- Uveitis activity and severity not related to activity of joint disease
- Most develop after onset of arthritis
- Highest risk within 4 years of onset of arthritis, most within 7 years
Screening for uveitis in JIA patients

- High risk group
  - Pauci or monoarticular arthritis
  - ANA positive
  - Onset < 6 years of age
  - Disease duration < 4 years
  - Screen every 3 – 4 months (EUA if necessary)
Screening for uveitis in JIA patients

- **Moderate risk**
  - Onset after age 6
  - ANA negative
  - ANA positive, disease duration > 4 years
  - Screen Q 6 months

- **Low risk**
  - Systemic onset
  - ANA negative, onset after age 6
  - Joint disease (no eye disease) for more than 7 years
  - Screen yearly
Worse prognosis

- More severe ocular involvement at presentation
- Longer duration of uveitis
- Female sex
- Younger age at disease onset
- Uveitis diagnosis prior to arthritis diagnosis
Fuchs heterochromic iridocyclitis

- Fuchs iridocyclitis
- 2-3% of patients with uveitis
- Often under-diagnosed and over-treated
- 3rd – 4th decade of life
- Unilateral in > 90%
- No gender predilection
FHI symptoms

- Asymptomatic/ incidental finding
- Decreased vision (cataract)
- Floaters
- Do not present with pain and photophobia
FHI signs

- Diffuse iris stromal atrophy
  - Loss of crypts, iris detail
- Small white KP
  - Classically stellate
  - Throughout cornea
- Low grade cell and flare
- No synechiae
- Often have small iris nodules
FHI signs

- Cells and opacities in the anterior vitreous
- Abnormal vessels in angle (Amsler sign)
- Normal fundus
  - Rare CME (cataract surgery)
  - Association with retinal scars (toxoplasmosis)
FHI signs

- **Heterochromia**
  - Not required for diagnosis
  - Up to 10% bilateral
  - May be harder to see in dark irides
  - Light eyes appear bluer
  - Brown eyes may appear darker
Glaucoma in 30%
- Often resistant to medical therapy

Cataract in 70 – 100%
- PSCC
- Do well with standard phaco/PCIOL

Inflammation doesn’t usually require treatment

Require follow-up to monitor for elevated IOP, nerve damage
Differential diagnosis

- Herpetic iritis
- Sarcoid uveitis
  - KP may be seen throughout cornea
  - Elevated IOP
  - (Often bilateral, synechiae, granulomatous, retinal/choroidal involvement)
- Posner-Schlossman
  - Unilateral
  - Elevated IOP, early, acute, symptomatic
  - Recurrent acute rather than chronic
- Toxoplasmosis
  - KP
  - Elevated IOP
  - (active retinitis, vitritis)
- Any chronic uveitis with iris atrophy
## FHI vs Herpes

<table>
<thead>
<tr>
<th>FHI</th>
<th>Herpetic iritis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chronic</strong></td>
<td><strong>May have acute onset</strong></td>
</tr>
<tr>
<td><strong>Usually unilateral</strong></td>
<td><strong>Usually unilateral</strong></td>
</tr>
<tr>
<td><strong>Eye usually quiet</strong></td>
<td><strong>Redness, discomfort</strong></td>
</tr>
<tr>
<td><strong>Iris atrophy – anterior stroma, diffuse</strong></td>
<td><strong>Iris atrophy – pigment epithelium with TID Patchy or diffuse</strong></td>
</tr>
<tr>
<td><strong>KP: Diffuse stellate</strong></td>
<td><strong>KP : Diffuse stellate, central granulomatous</strong></td>
</tr>
<tr>
<td><strong>High IOP – usually late</strong></td>
<td><strong>High IOP – early</strong></td>
</tr>
<tr>
<td><strong>No synechiae</strong></td>
<td><strong>Synechiae</strong></td>
</tr>
<tr>
<td><strong>Pupil usually normal</strong></td>
<td><strong>Irregular pupil, often dilated</strong></td>
</tr>
</tbody>
</table>
FHI and Rubella

- Elevated intraocular antibodies to rubella in 52 of 52 tested patients with FHI (modified Goldman-Witmer coefficient)
- Many also had positive reverse transcription polymerase chain reaction (RTPCR) for rubella virus, (i.e. active viral replication)

Quentin CD, Reiber H. Am J Ophthalmol 2004;138:46-54
FHI and Rubella

- Rubella Ab in aqueous in 13/14 FHI patients (Goldman-Witmer)
- Negative titers for HSV, VZV and T.Gondii

de Groot-Mijnes JD, de Visser L, Rothova A. Am J Ophthalmol 2006;141:212–214
FHI and rubella: epidemiologic evidence

- Decrease in incidence of FHI in US since Rubella vaccination in 1969
- 65% reduction in FHI in patients born 1959-1968 compared to earlier
- Further 40% drop in FHI in patients born 1969-78
- Foreign born FHI increased from 24% to 55%

FHI and CMV

- Aqueous paracentesis on 104 patients with unilateral uveitis with high IOP
  - 23 (22.8%) had + CMV PCR, - herpes simplex, herpes zoster, T. gondii
  - 18 had exam consistent with Posner-Schlossman syndrome
  - 5 FHI
  - 14 confirmed active viral replication with RT-PCR

Sarcoid uveitis

- Classically granulomatous iridocyclitis
  - Mutton fat KP
  - Iris nodules
- May also be non-granulomatous
- Usually bilateral
- Most often chronic, but may begin with acute disease
- Frequent posterior segment involvement
- ROS: skin, pulmonary, joints
- May occur without apparent systemic disease
Biopsy proven sarcoid uveitis at UIC

- 63 patients 1989 - 2009
  - 62% African-American, 30% Caucasian
  - 68% female

- African-American patients
  - Presented at earlier age
  - 8% presented > age 50
  - More likely to have granulomatous anterior segment inflammation (p=0.0006)

- Caucasian patients
  - Older: 67% presented > age 50 (p=0.0001)
Biopsy proven sarcoid uveitis at UIC

- ACE elevated in 40%
- Lysozyme elevated in 42%
- At least one marker was elevated in 58%
- CXR consistent with sarcoidosis in 69% (n=36 pts)
- CT chest consistent with sarcoidosis in 100% of tested patients (n=19 pts)
- Combination of serum markers and chest imaging increased the percentage of patients positively identified to 69-93%
Sarcoid KP
Iris Crystals

Russell Body

IgG crystal
Familial juvenile systemic granulomatosi

- **Blau syndrome**
  - (Arthrocutoanouveal granulomatosi)
  - Arthritis, skin lesions & eye findings
- Eye findings similar to sarcoidosis
- Do not have pulmonary findings
- Autosomal dominant
- CARD 15/NOD2 mutation (also linked to Crohn’s disease)
Anterior uveitis work-up

- Work-up required if:
  - Bilateral
  - Severe
  - Recurrent
  - Granulomatous
  - Posterior segment involvement
  - Positive review of systems
# Work-up of iridocyclitis:

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
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<tbody>
<tr>
<td>- HLA B27</td>
<td>- ANA in children</td>
</tr>
<tr>
<td>- CXR +/- CT chest</td>
<td>- CXR</td>
</tr>
<tr>
<td>- FTA-ABS</td>
<td>- Consider CT chest</td>
</tr>
<tr>
<td>- ACE/lysozyme</td>
<td>- ACE/lysozyme</td>
</tr>
<tr>
<td>- Consider Lyme titers if appropriate</td>
<td>- FTA-ABS</td>
</tr>
<tr>
<td>- Consider Urine $\beta$-2 microglobulin, esp if bilateral simultaneous onset</td>
<td>- PPD</td>
</tr>
<tr>
<td></td>
<td>- Urine $\beta$-2 microglobulin</td>
</tr>
<tr>
<td></td>
<td>- ? Lyme titers</td>
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</table>
Treatment of acute anterior uveitis

- **Topical corticosteroids**
  - Pred Forte (prednisolone acetate 1%), hourly (or more) if severe
  - Durezol (difluprednate emulsion 0.05%), QID (or more)

- **Dilators**
  - e.g. homatropine 5% BID
  - Pain relief
  - Break acute synechiae
  - Prevent development of new synechiae
  - Longer lasting agent if dark irides, shorter if light

- Avoid depot steroids if first attack (caution re endophthalmitis)

- May need oral steroids
Treatment of chronic iridocyclitis

- Topical steroids – less frequent than for acute
- May need chronic dilators
- Depot steroids
  - e.g. subtenon triamcinolone acetonide
    - TRIESENCE™ (triamcinolone acetonide injectable suspension) 40 mg/mL (Alcon)
    - Kenalog 40 mg/ml. Not formulated for intraocular use
- Oral steroids
  - Avoid long term use
- Immunosuppressive/immunomodulatory agents
Treatment of chronic iridocyclitis

- Use lowest dose of anti-inflammatory agents to prevent sequelae but decrease risk of glaucoma
- Concept of chronicity
  - “chronic disease is chronic”
- Treatment may be long term
- Patients often asymptomatic
- Compliance a major issue
Anterior uveitis

- History is of paramount importance
  - Previous episodes
  - Trauma
  - Systemic diseases
  - ROS
  - Medications

- Acute and chronic diseases are treated differently
Anterior uveitis

- Remember infectious etiologies
- Examine the fundus
  - Posterior segment disease can present with pain, redness, AC reaction