Managing Uveitis: Tips for Success

ANNA K. BEDWELL, OD, FAAO, FORS
CLINICAL ASSOCIATE PROFESSOR
INDIANA UNIVERSITY SCHOOL OF OPTOMETRY
Bio

Dr. Anna Bedwell is a Clinical Associate Professor at Indiana University School of Optometry. She completed her optometry degree from IU in 2010 and a residency at the San Francisco VA in 2011. She is a fellow of the American Academy of Optometry and a member of the American Optometric Association. Dr. Bedwell, also, holds fellowship in the Optometric Retina Society, where she currently serves as the editor of their quarterly newsletter.

Disclosures: None
Tips to successful uveitis management:

1) Get a thorough review of systems
Review of Systems

**Constitution:** fever, malaise, weight loss/gain

**Dermatological:** rashes, sores, dry skin, vitiligo

**Rheumatological:** personal or family hx of autoimmune disease

**Respiratory:** shortness of breath, cough, wheezing

**GI:** stomach upset, irritable bowel, abdominal pain, diarrhea

**GU:** ulcers/sores, painful urination, discharge, hx of STD

**Musculoskeletal:** joint pain/arthritis, muscle aches

Social Hx: drug abuse?, STDs?, animal exposure? (puppies, cats/kittens)
<table>
<thead>
<tr>
<th>Condition</th>
<th>Signs/Sxs</th>
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</thead>
<tbody>
<tr>
<td>Ankylosing spondylitis</td>
<td>Male predominance, presents in early adulthood, low back/hip pain, chest pain</td>
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<tr>
<td>Reiter’s syndrome/ Reactive Arthritis</td>
<td>Young male triad = arthritis, urethritis, conjunctivitis</td>
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<tr>
<td>Juvenile idiopathic arthritis</td>
<td>Slight male predilection sacroiliitis common</td>
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<tr>
<td>IBD (ulcerative colitis and Crohn’s)</td>
<td>Generally diagnosed early adulthood Diarrhea, abdominal cramps, blood in stool</td>
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<tr>
<td>Sarcoidosis</td>
<td>AA predominance, F&gt;M Causes hilar adenopathy Cough, SOB, weight loss, night sweats, fatigue, rash on shins/ankles. May be asymptomatic.</td>
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<tr>
<td>Tuberculosis</td>
<td>Latent or active Lung granulomas on X-ray, CT cough, fever, chills, night sweats, weight loss</td>
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<tr>
<td>Syphilis</td>
<td>Acquired by sexual contact Rash (palms of hands and soles of feet), chancre sores, fever, malaise, joint pain</td>
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<tr>
<td>Toxoplasmosis</td>
<td>Caused by exposure to cats or from eating undercooked meat; consider in pt with immunocompromised state retinal lesions with adjacent vitreous haze or “headlight in the fog” sign</td>
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<tr>
<td>Rheumatoid arthritis</td>
<td>Attacks the synovium (membrane surrounding joints) Tender, swollen joints (smaller first)</td>
<td></td>
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<tr>
<td>Disease</td>
<td>Characteristics</td>
<td>Symptoms</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>------------------------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Behcet’s disease</td>
<td>M=F, diagnosed in 20s-30s, middle eastern and far east decent</td>
<td>Painful oral and genital ulcers, arthritis</td>
</tr>
<tr>
<td>Systemic lupus erythematosus (SLE)</td>
<td>F&gt;M</td>
<td>butterfly rash, malaise, fatigue, fever</td>
</tr>
<tr>
<td>Lyme disease</td>
<td>Carried by ticks</td>
<td>Early: bulls-eye rash, fever, chills, fatigue, joint aches</td>
</tr>
<tr>
<td>Granulomatosis w/ polyangiitis (formerly Wegener’s)</td>
<td>Vasculitits; causes sinus, pulmonary, kidney disease</td>
<td>scleritis&gt;uveitis, Weight loss, fatigue, fever, nose bleeds, congestion, SOB, bloody cough</td>
</tr>
</tbody>
</table>
Rashes

Syphilis
- Copper penny rash
  - typically found palms of the hands and soles of the feet.
  - found in secondary stage - 6 weeks to 6 months after exposure

Lupus
- Butterfly rash “malar”
  - Covers cheeks and bridge of nose; flat or raised
  - Rosacea is most common cause of malar rash

Lyme
- Erythema migrans
  - Circular rash that expands associated with early Lyme
  - Classic pattern is bullseye
Joint Pain

Rheumatoid arthritis (RA)
- Affects multiple joints in a bilateral and symmetric pattern
- Worse in morning
- Small and large joints
- Systemic lupus erythematosus (SLE) and polymyalgia rheumatica can have similar complaints

Spondyloarthropathies (HLA-B27 +)
- Joint paint is asymmetric
- Targets the sacroiliac joints and lower spine

Lyme
- Early disease has migratory symptoms: joint sx.resolve and then reappear in different joints
Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
Categorizing Uveitis

**Location:** anterior, posterior, intermediate, pan

**Duration:** acute, chronic, recurrent

**Laterality:** OD, OS or OU

**Type of inflammation:** granulomatous or non-granulomatous
Workup

When is it necessary?

- Recurrent
- Bilateral
- Granulomatous
Granulomatous Uveitis

Characteristics:
- Cornea: large, greasy “mutton fat” KPs
- Iris: Koeppke nodules (pupillary margin), Busacca nodules
  ↑ risk of synechiae

Etiology:
- Sarcoid
- TB
- Syphilis
- Lyme disease
Nongranulomatous Uveitis

Characteristics:
- Cornea: smaller KPs
- Iris: less risk of synechiae

Etiology (acute presentation):
- Non-specific to particular autoimmune disease
- Heavy flare and fibrin -> think HLA B27

Other:
- JRA (chronic)
- Fuch’s heterochromic (chronic)
- Trauma/postoperative
- Herpetic/viral
Lab Work

Complete blood count w/ differential (CBC)
  ◦ Useful to determine pts general health status

C-reactive protein (CRP)
  ◦ Nonspecific marker for inflammation

Erythrocyte sedimentation rate (ESR)
  ◦ Nonspecific marker for inflammation
<table>
<thead>
<tr>
<th>Test:</th>
<th>Conditions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiotensin-converting enzyme (ACE)</td>
<td>Sarcoid</td>
</tr>
<tr>
<td>Human leukocyte antigen B27 (HLA-B27)</td>
<td>Spondyloarthopathies: Ankylosing spondylitis, reactive arthritis/Reiter’s syndrome, Crohn’s disease, psoriatic arthritis</td>
</tr>
<tr>
<td>Purified protein derivative (PPD)</td>
<td>TB</td>
</tr>
<tr>
<td>QuantiFERON-TB gold</td>
<td>TB</td>
</tr>
<tr>
<td>Antinuclear antibody (ANA)</td>
<td>SLE, scleroderma, juvenile arthritis, polymyosistis, IBD, psoriasis, Sjögren’s syndrome</td>
</tr>
<tr>
<td>Rheumatoid factor (RF)</td>
<td>Rheumatoid arthritis, Sjögren’s syndrome</td>
</tr>
<tr>
<td>RPR, VDRL, FTA-ABS</td>
<td>Syphilis</td>
</tr>
<tr>
<td>ELISA or Western blot for Lyme</td>
<td>Lyme disease</td>
</tr>
<tr>
<td>SS-A, SS-B</td>
<td>Sjögren’s syndrome</td>
</tr>
<tr>
<td>ANCA</td>
<td>Vasculitis (ie GPA/Wegner’s), ulcerative colitis</td>
</tr>
<tr>
<td>HLA-B5</td>
<td>Behcet’s</td>
</tr>
<tr>
<td>Toxoplasma IgG/IgM</td>
<td>Toxoplasmosis</td>
</tr>
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</table>
HLA B27

- Human leukocyte antigens (HLAs) are proteins on WBCs
- 6% of the population is HLA-B27 positive
  - +HLA B27 persons have much higher risk of developing spondyloarthropathy

**HLA-B*27 Disease Association**

<table>
<thead>
<tr>
<th>Disease</th>
<th>% HLA-B*27 Positive</th>
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</thead>
<tbody>
<tr>
<td>Ankylosing spondylitis</td>
<td>88%–96%</td>
</tr>
<tr>
<td>Acute anterior uveitis</td>
<td>40%–70%</td>
</tr>
<tr>
<td>Reactive arthritis (Reiter’s syndrome)</td>
<td>40%–80%</td>
</tr>
<tr>
<td>Aortic regurgitation (with cardiac conduction abnormality)</td>
<td>67%–88%</td>
</tr>
<tr>
<td>Inflammatory bowel disease (with sacroiliitis)</td>
<td>33%–75%</td>
</tr>
<tr>
<td>Psoriatic arthritis (with sacroiliitis)</td>
<td>40%–50%</td>
</tr>
<tr>
<td>Undifferentiated spondyloarthropathies</td>
<td>70%</td>
</tr>
</tbody>
</table>

https://www.labcorp.com/tests/related-documents/L1187
Lab testing for syphilis

Non-treponemal tests:

◦ Rapid plasma regain (RPR)
◦ Venereal disease research lab (VDRL)
  ◦ Tests for antibodies to *Treponema pallidum*
  ◦ Reflection of disease activity and response to therapy
  ◦ (+) in primary and secondary; (-) in tertiary or latent and after treatment
  ◦ RPR easier to run and cheaper
  ◦ False positives can be seen in viral infections, lymphoma, TB, CT disease, pregnancy, autoimmune diseases
Lab testing for syphilis

**Treponemal tests:**
- Fluorescent treponemal antibody absorption test (FTA-ABS)
  - Detects presence of the bacteria; regardless of stage (unless very early, first few weeks) or if pt has been successfully treated
  - Less sensitive in HIV+ patients
- Other treponemal tests:
  - Microhemagglutination-Treponema pallidum (MHA-TP)
  - Treponema pallidum particle agglutination assay (TP-PA)
  - Treponema pallidum hemagglutination assay (TPHA)
Imaging

Granulomatous
- Chest X-ray -> rule out sarcoid, TB
- May need chest CT

Non-Granulomatous, +HLA-B27
- X-ray of the sacroiliac (SI) joints is useful for ankylosing spondylitis
  - Causes chronic inflammation of the spine and SI joints
- MRI can pick up earlier involvement if high suspicion with clear X-ray
Design your own lab orders. It makes life easier.
Case example

48 year old AA female

CC: presents for urgent care with blurred vision R eye x 2 weeks, mild redness, mild discomfort, seen at immediate care 3 days ago given moxifloxacin drops with no improvement

Medical Hx: seizure disorder (controlled on keppra)

Ocular Hx: none

ROS: +cough x 2 months
Exam Findings

BCVA: **20/30- NIPH OD**, 20/20 OS

Pupils: irregular, fixed OD; reactive OS

Slit lamp:
- Lids/lashes: clear OU
- Conj: **2+ diffuse injection OD**, clear OS
- Cornea: **fine, diffuse KPs**, clear OS
- Iris: **synechiae, nodules OD**, clear and flat OS
- A/C: **deep with 2+ cell, 2+ flare OD**, clear OS

Goldmann IOP: 20/19

Dilation (1% tropicamide, 5% homatropine):
- Vitreous: **1+ cell OD**, Cl OS
- Retina: normal, (-)snowbanking
Koeppe nodules
A/P

Assessment: acute mostly anterior, **granulomatous** uveitis OS
ROS: +cough

Plan: start pred forte 1% q1h OS, cyclopentolate 1% BID OS
D/C moxifloxacin
Order labs: CBC, ESR, ACE, PPD, ANA, FTA-ABS, HLA-B27, chest X-ray
Follow up course

Lab results: elevated ACE, ESR

Chest X-ray: suspicion for sarcoid, confirmed on chest CT

Started on oral steroids for sarcoid

OD uveitis responded well to topical steroids, synechiae broke with cycloplegic
Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
3) Dilate!
Why Dilate?

Dilation is **essential** to diagnose posterior uveitis and CME

Opportunity to instill cycloplegic -> make the patient feel a little better
Posterior Uveitis

**INFECTIOUS**
- Toxoplasmosis
- Toxocariasis
- Tuberculosis
- Syphilis
- Bartonella
- Viral (HSV, VZV, CMV)

**NON-INFECTIOUS**
- Sarcoid
- White dot syndromes (APMPPE, MEWDS, MFC etc)
- Diffuse unilateral subacute neuroretinitis (DUSN)
- Retinal pigment epithelitis (Krill's disease)
Infectious Posterior Uveitis

Parasitic

- **Toxoplasmosis**
  - Most common cause of posterior uveitis
  - Usually diagnosed by clinical picture (“headlight in fog”) rather than lab testing
  - Tx: Bactrim + oral steroids

- **Toxocariasis**
  - Parasitic disease from dog/cat roundworm
  - Central or peripheral granuloma with overlying vitritis
  - Cause of leukocoria in children

- **DUSN (diffuse unilateral subacute neuroretinitis)**
  - Nematode infiltrates subretinal space

Inactive toxocariasis
Active Toxoplasmosis

Chorioretinitis with overlying vitritis “headlight in fog”

Often located near inactive scar
Infectious Uveitis

Bacterial
- Cat scratch disease
  - *Bartonella henselae*
  - Transmitted by scratch, lick or bite from infected cat (usually kitten)
  - **Neuroretinitis** (optic nerve edema + macular star) +/- ant chamber rxn, vitritis
- Syphilis
  - *Treponema pallidum*, spirochete
  - anterior or posterior uveitis, optic nerve involvement highly suggestive for neurosyphilis
- Tuberculosis
  - *Mycobacterium tuberculosis*
  - Characterized by caseating granulomas
  - Optic nerve can be involved in ocular TB
- Lyme disease
  - *Borrelia burgdorferi*, spirochete
  - Optic neuritis, neuroretinitis can occur in the early and disseminated stages
  - Regarded as CNS involvement; IV antibiotic therapy
Infectious Uveitis

Viral

- Herpes family (HSV, VZV, CMV)
- Anterior uveitis:
  - Viral associated with elevated IOP (from trabeculitis) and iris atrophy; +/- corneal findings
  - KPs can have non-granulomatous or granulomatous appearance
  - Recurs in same eye

Clinical Pearl: Viral uveitis can be tricky to recognize. Clinical suspicion should be high for viral if elevated IOP at onset of sx and/or presence of iris atrophy (sectoral or diffuse).
Infectious Uveitis

Viral

- Posterior - rare
  - Immunocompromised patients
    - CMV retinitis – less common now with modern HIV treatment
    - Progressive outer retinal necrosis (PORN)
      - VZV > HSV
  - Immunocompetent
    - Acute retinal necrosis (ARN)

PORN: AC tap positive for VZV
CME

- Common cause of decreased vision and vision loss in uveitis
- More likely to occur with intermediate or posterior inflammation
- Assoc with formation of ERM
- Can be difficult to tx as it may persist even though inflammation is controlled

Tx options:
- Corticosteroids
  - Topical, oral, injection, implants
- NSAIDs
- Oral CAI
- Anti-VEGF (if inflammation is otherwise controlled)
- ERM peel (if contributing factor)
Benefit of cycloplegia

- Break/prevent synechiae
- Reduce patient discomfort
- Stabilize blood-aqueous barrier
  - Reduces cell and flare

Options:

Atropine (most potent): 0.5, 1, 2%
Scopolamine: 0.25%
Homatropine: 2, 5%
Cyclopentolate: 0.5, 1, 2%

Often limited supply in pharmacy
Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
3) Dilate!
4) Don’t fear the steroids
Steroids in Anterior Uveitis

Hit hard with steroids from the start.

Minimum initial dosage: q2h while awake (pred acetate)

Don’t taper until AC clear or significantly improved!! Then taper slow, some over weeks-months.

Failure to respond to topical therapy alone may indicate need for oral steroids or immunosuppressants
Steroids in Uveitis

PredForte (prednisolone acetate) 1%
  ◦ Suspension
  ◦ Generic often works just as well as brand

Durezol (difenuprednate) 0.05%
  ◦ Emulsion – does not need to be shaken
  ◦ Stronger than PF – can be dosed half as often as PF
  ◦ Cons: causes steroid response (more often than pred), cost

Overnight coverage if needed:
  ◦ FML ung
  ◦ Lotemax ung
Injectables

Triamcinolone acetonide injectable suspensions:
- Kenalog - periocular
- Triesence

Sustained drug delivery options:
intravitreal implants approved to treat chronic non-infectious post uveitis, dissolve over months
- Ozurdex – 0.7 mg dexamethasone
- Retisert - 0.59 mg fluocinolone acetonide
- Yutiq - 0.18 mg fluocinolone acetonide - effect lasts 30-36 months

Risks: glaucoma (many requiring glaucoma surgery); inevitable cataract development
Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
3) Dilate!
4) Don’t fear the steroids
5) **But watch the IOP**
**IOP in Uveitis**

**Mechanisms for glaucoma development:**
- **Acute blockage of the TM with cellular uveitic debris**
- **Steroid response**
  - Causes outflow resistance in the TM
  - Usually occurs 2-4 weeks into tx
- **Chronic damage to the TM from uveitis**
  - Peripheral anterior synechiae formation -> secondary angle closure
  - Posterior synechiae -> iris bombe -> secondary angle closure

Can be multifactorial.
Uveitic Glaucoma

**Treatment for elevated IOP:**
- Treat the inflammation
- First choice to lower IOP: β-blocker, CAI, α-agonist (or combo)
- Avoid prostaglandins if possible
- Start steroid taper if uveitis controlled
- Some may go on to need glaucoma surgery, particularly in chronic cases

*10-20% of uveitis develops glaucoma*
Tips to successful uveitis management:

1) Get a thorough review of systems
2) Know when and what labs to order
3) Dilate!
4) Don’t fear the steroids
5) But watch the IOP
6) Consider atypical causes
Other uveitis...

**Posner-Schlossman Syndrome (PSS)** – mild uveitis with elevated IOP
- IOP is often > 40 mmHg and out of proportion to the degree of ocular inflammation, does not cause synechiae
- Presumably trabeculitis with spillover to ant chamber
- Evidence now supports links to CMV>HSV, VZV
  - Tx: oral antiviral + topical steroid

**Fuch’s heterochromic uveitis** – chronic, mild uveitis in minimally symptomatic or asymptomatic pts
- Diffuse stellate KPs
- May result in heterochromia (lighter iris in the involved eye)
- Linked to rubella

**UGH syndrome** (triad of uveitis, glaucoma and hyphema)
- Caused by a malpositioned PC IOL
- Can occurs months – years after surgery
UGH Syndrome

Images courtesy of Dr. Larissa Krenk
Case example

82 year old AA female

**CC:** +intermittent pain and redness OD

**Medical Hx:** DM, HTN, depression, low thyroid

**Ocular Hx:** poor vision from a CRVO about 8 years ago OD, POAG OU, cataract surgery OS

**Meds:** Clonazepam, Sertaline, Levothyroxine, Clopidogrel, Amlodipine, Crestor, Novolin

**Ocular Meds:** Travatan Z OS, Combigan OD
Exam findings

BCVA: LP OD, 20/20 OS

Pupils: Fixed-non reactive pupil OD, reactive OS

Slit lamp:
- Lids/lashes: clear OU
- Conj: 2+ diffuse injection OD, clear OS
- Cornea: diffuse pigmented KPs OD, clear OS
- Iris: synechiae OD, clear OS
- A/C: Deep chamber with 3+ cell, 2+ flare OD, clear OS

Goldmann IOP: 14/14

Gonio: open to SS 360 OU
Exam findings

Dilation:
- Lens: 4+ NS/3+ PSC/2+ cortical OD, PC IOL OS
- No view beyond lens OD; fundus normal OS

B-scan: retina intact OD
Assessment

82 year old female with chronic, anterior uveitis with posterior synechiae OD

ROS: (-) ulcers, cough, joint pain, rashes
Age atypical for onset of autoimmune related uveitis

Diagnosis: phacolytic uveitis due to hypermature cataract

Treatment: patient was managed short-term with topical steroids and cycloplegic until cataract surgery was arranged
Other Uveitis.... Phacolytic

**Phacolytic Cataract** – hypermature cataract that is leaking protein material

**Phacolytic or Lens Induced Uveitis** - an immunologic response to the leaking protein
  - Pathogenesis is still poorly understood
    - A clear lens leaks small amounts of protein

**Phacolytic Glaucoma** - proteins and inflammatory mediators can also clog up the trabecular meshwork, causing elevated IOP and glaucoma

**Treatment** – decrease inflammation and IOP if needed and then proceed to cataract surgery
The End

Questions: abedwell@indiana.edu