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Wills Eye Manual

Sections

Chapter 12

UVEITIS

12.1 Anterior Uveitis (Iritis/Iridocyclitis)

Symptoms

• **Acute:** Pain, redness, photophobia, consensual photophobia (pain in the affected eye when a light is shone in the fellow eye), excessive tearing, decreased vision.

• **Chronic:** Decreased vision (from cataract, vitreous debris, cystoid macular edema (CME), or epiretinal membrane [ERM]) and floaters. May have periods of exacerbations and remissions with few acute symptoms (e.g., juvenile idiopathic arthritis [JIA]).

Signs

Critical. Cells and flare in the anterior chamber, ciliary flush, keratic precipitates (KP):

• Fine KP (“stellate;” typically covers entire corneal endothelium): Herpes simplex or varicella zoster virus, cytomegalovirus (CMV), Fuchs heterochromic iridocyclitis (FHIC).

• Small, nongranulomatous KP (NGKP): Human leukocyte antigen (HLA)-B27-associated, trauma, masquerade syndromes, JIA, Posner–Schlossman syndrome (glaucomatocyclitic crisis), drug-induced. Granulomatous uveitides such as sarcoidosis can present with NGKP; the reverse rarely occurs.

• Granulomatous KP (large, greasy, “mutton-fat”; mostly on inferior cornea): Sarcoidosis, syphilis, tuberculosis (TB), JIA-associated, sympathetic ophthalmia, lens-induced, Vogt–Koyanagi–Harada (VKH) syndrome, and others.

Other. Low intraocular pressure (IOP) more commonly seen (secondary to ciliary body hyposecretion), elevated IOP can occur (e.g., herpetic, lens-induced, FHIC, Posner–Schlossman syndrome), fibrin (e.g., HLA-B27 or endophthalmitis), hypopyon (e.g., HLA-B27, Behçet disease, infectious endophthalmitis, rifabutin, tumor), iris nodules (e.g., sarcoidosis, syphilis, TB), iris atrophy (e.g., herpetic, oral fourth generation fluoroquinolones), iris heterochromia (e.g., FHIC), iris synechiae (especially HLA-B27, sarcoidosis), band keratopathy (especially JIA in younger patients, any chronic uveitis in older patients), uveitis in a “quiet eye” (consider JIA, FHIC, masquerade syndromes), CME **(See Figure 12.1.1)**.

Differential Diagnosis

• Intermediate or panuveitis with spillover into the anterior chamber: Mainly floaters and decreased vision, positive fundoscopic findings (**SEE 12.3, POSTERIOR UVEITIS**).

• Traumatic iritis. **SEE 3.5, TRAUMATIC IRITIS.**

• Posner–Schlossman syndrome: Recurrent episodes of very high IOP and minimal inflammation. **SEE 9.8, GLAUCOMATOCYCLITIC CRISIS/POSNER–SCHLOSSMAN SYNDROME.**

• Drug-induced uveitis (e.g., rifabutin, cidofovir, sulfonamides, pamidronate, systemic fluoroquinolones [especially moxifloxacin], some chemotherapeutic drugs).

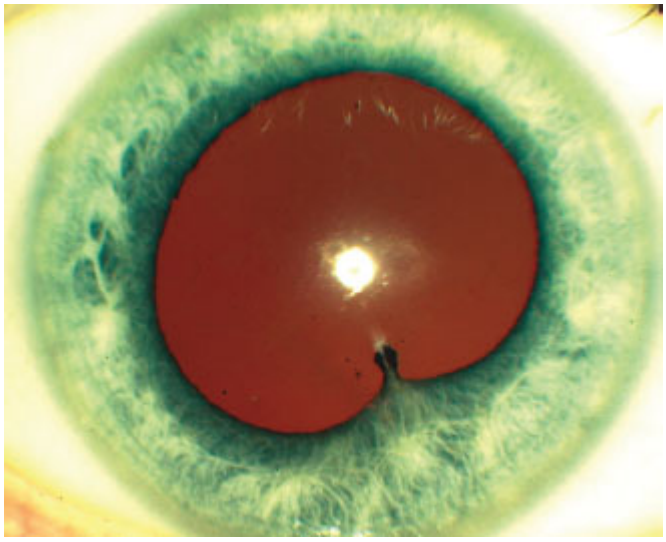

Figure 12.1.1. Anterior uveitis with posterior synechiae.

• Sclerouveitis: Uveitis secondary to scleritis; typically presents with profound pain and tenderness to palpation. **SEE 5.7, SCLERITIS.**

• CLARE (contact lens-associated red eye): Red eye, corneal edema, epithelial defects, iritis with or without hypopyon; hypoxic subepithelial or stromal infiltrates may be present.

• Infectious keratouveitis: Corneal infiltrate is present. **SEE 4.11, BACTERIAL KERATITIS.**

• Infectious endophthalmitis: History of recent surgery or penetrating trauma, pain, hypopyon, fibrinous anterior chamber reaction, vitritis, decreased vision, red eye; may have endogenous source with fever, elevated white blood cell count. **SEE 12.13 TO 12.16, ENDOPHTHALMITIS SECTIONS.**

• Schwartz–Matsuo syndrome: Pigment released from a chronic retinal detachment clogs the trabecular meshwork, resulting in elevated IOP.

• Tumor: Retinoblastoma in children, intraocular lymphoma in elderly, metastatic disease in all ages, and others.

• Pseudouveitis from pigment dispersion syndrome. Other findings include Krukenburg spindle and iris transillumination defects. Pigment cells in the AC are smaller than white blood cells.

Etiology

• Idiopathic (roughly half of all anterior uveitis has no identifiable cause or disease association).

• HLA-B27-associated uveitis: Systemic associations include ankylosing spondylitis, reactive arthritis (Reiter syndrome), psoriatic arthritis, inflammatory bowel disease.

NOTE: Bilateral recurrent alternating anterior uveitis is very characteristic of HLA-B27 uveitis.

• Lens-induced uveitis: Immune reaction to lens material, often secondary to incomplete cataract extraction, trauma with lens capsule damage, or hypermature cataract. **SEE 9.12, LENS-RELATED GLAUCOMA**.

• Postoperative iritis: Anterior chamber inflammation following intraocular surgery. Endophthalmitis must be considered if severe inflammation and pain are present. **SEE 12.14, CHRONIC POSTOPERATIVE UVEITIS.**

• Uveitis–Glaucoma–Hyphema (UGH) syndrome: Usually secondary to irritation from an intraocular lens (IOL) (particularly a closed-loop anterior chamber lens or single-piece lens in ciliary sulcus). **SEE 9.16, POSTOPERATIVE GLAUCOMA.**

• Behçet disease: Young adults, acute shifting hypopyon, iritis, aphthous ulcers, genital ulcerations, erythema nodosum, retinal vasculitis (arteries and/or veins) and hemorrhages, may have recurrent episodes.

• Lyme disease: May have history of a tick bite and rash. **SEE 13.3, LYME DISEASE.**

• Anterior segment ischemia: Flare out of proportion to cellular reaction. Pain. Secondary to carotid insufficiency, tight scleral buckle, or previous extraocular muscle surgeries.

• Tubulointerstitial nephritis and uveitis (TINU) syndrome: Rare, usually bilateral nongranulomatous uveitis in children and young adults, female predilection.

• Other rare infectious etiologies of anterior uveitis: Mumps, influenza, adenovirus, measles, Chlamydia, Leptospirosis, Kawasaki disease, rickettsial disease, Chikungunya virus, and others.

Chronic

• JIA: Usually occurs in young girls; may be painless and asymptomatic with minimal injection. Often bilateral. Iritis may precede the typical pauciarticular arthritis (four or fewer joints involved). Positive antinuclear antibody (ANA), negative rheumatoid factor, and increased erythrocyte sedimentation rate (ESR) most commonly seen. Associated with glaucoma, cataracts, band keratopathy, and CME. Uveitis may occur in polyarticular and rarely in systemic JIA (Still disease).

• Chronic iridocyclitis of children: Usually occurs in young girls; is similar to JIA in signs and symptoms but lacks arthritis.

• FHIC: Few symptoms, diffuse iris stromal atrophy often causing a lighter-colored iris with transillumination defects and blunting of the iris architecture. Gonioscopy may reveal fine vessels that cross the trabecular meshwork, typically without posterior synechiae. Fine KP over the entire corneal endothelium, mild anterior chamber reaction. Vitreous opacities, glaucoma, and cataracts are common, but macular edema and posterior synechiae are absent.

• Sarcoidosis: More common in African Americans and Scandinavians. Usually bilateral; can have extensive posterior synechiae and conjunctival or iris nodules. **SEE 12.6, SARCOIDOSIS.**

• Herpes simplex/varicella zoster: Diffuse KP, increased IOP, and iris atrophy. History of unilateral recurrent red eye, occasionally history of skin vesicles. Corneal scars associated with decreased corneal sensation may be present.

• Syphilis: Anterior and intermediate uveitis most common. May have a maculopapular rash, iris roseola (vascular papules on the iris), and interstitial keratitis with ghost vessels in late stages. Inflammation of any ocular structure may occur. Placoid chorioretinitis is virtually pathognomonic. Neurosyphilis can cause meningismus. **SEE 12.12, SYPHILIS.**

• Tuberculosis: Positive protein derivative of tuberculin (PPD) and/or interferon-gamma release assay (IGRA) (e.g., QuantiFERON-TB Gold), typical chest radiograph findings (helpful but not necessary for diagnosis; most TB uveitis occurs in patients without pulmonary TB), occasionally phlyctenular or interstitial keratitis, sometimes signs of posterior uveitis. **SEE 12.3, POSTERIOR UVEITIS.**

• Others: Leprosy, brucellosis, etc.

Work-Up

1. Obtain a thorough history and review of systems **(Tables 12.1.1 and 12.1.2)**. Specifically ask about fevers, chills, cough, shortness of breath, joint pain/swelling/stiffness, diarrhea, blood in urine/stool, skin rashes, and oral or genital ulcers.

 **NOTE:** Autoimmune diseases are less common in the very young and very old—consider masquerades.

2. Complete ocular examination, including an IOP check, gonioscopy, and a dilated fundus examination. The vitreous should be evaluated for cells.

3. A laboratory work-up may be unnecessary in certain situations:

• First episode of a mild, unilateral, nongranulomatous uveitis with a history and examination that is not suggestive of systemic disease.

• Uveitis in the setting of known systemic disease such as sarcoidosis or the use of medicines known to cause uveitis (e.g., rifabutin).

• Clinical findings are classic for a particular diagnosis (e.g., herpetic keratouveitis, FHIC, toxoplasmosis).

4. In all other situations requiring laboratory or diagnostic testing, performing a targeted work-up is recommended. If too many tests are ordered unnecessarily, a portion of them may come back false-positive and confuse the diagnosis. **See Table 12.1.3.** However, if a patient presents with bilateral, granulomatous, or recurrent uveitis without a suspected diagnosis, our practice is to at least evaluate for sarcoidosis, syphilis, and TB (in at-risk patients). Consider additional work-up as needed based on history and examination.

• Rapid plasma reagin (RPR) or venereal disease research laboratory test (VDRL). Also need confirmatory test such as fluorescent treponemal antibody absorption (FTA-ABS) or treponemal-specific assay (e.g., microhemagglutination assay [MHA-TP]) given RPR and VDRL may be falsely negative.

Table 12.1.1 Epidemiology of Anterior Uveitis

Age:	**Infants**	**Children**	**Young Adults**	**Elderly**
	TORCH infections, retinoblastoma	JIA, toxocariasis, toxoplasmosis	HLA-B27, Fuchs hetero-chromic iridocyclitis, pars planitis, idiopathic	Lymphoma or other masquerades, serpigi-nous choroidopathy, birdshot retinocho-roidopathy, ARN
Sex:	**Female**	**Male**		
	JIA, SLE	Ankylosing spondylitis, reactive arthritis		
Race:	**Caucasian**	**African-American**	**Mediterranean, Asian, Middle Eastern**	**Asian, Native American**
	HLA-B27, MS, white dot syndromes	Sarcoidosis, SLE	Behçet disease	VKH syndrome

Table 12.1.2 Review of Systems

Musculoskeletal	
Arthritis	Behçet disease, Lyme disease, SLE, HLA-B27, relapsing polychondritis, JIA
Heel pain	Reactive arthritis, HLA-B27
Pulmonary	
Asthma	Sarcoidosis, TB, granulomatosis with polyangiitis
Pneumonia	Cytomegalovirus, AIDS, aspergillosis, SLE, sarcoidosis, granulomatosis with polyangiitis
Ear–Nose–Throat	
Auditory	VKH, sympathetic ophthalmia
Gastrointestinal	
Diet/hygiene	Poor handwashing (toxoplasmosis and toxocariasis); raw or undercooked meat and game (toxoplasmosis and cysticercosis); unpasteurized milk (brucellosis and TB)
Diarrhea	Whipple disease, ulcerative colitis, Crohn disease
Oral ulcers	Behçet disease, reactive arthritis, ulcerative colitis, herpes, sarcoidosis
Genitourinary	
Genital ulcers	Behçet disease, reactive arthritis, syphilis
Hematuria	Polyarteritis nodosum, SLE, granulomatosis with polyangiitis, TINU
Urethral discharge	Reactive arthritis, syphilis, chlamydia

Skin	
Erythema nodosum	Behçet disease, sarcoidosis
Maculopapular rash on palms and soles	Syphilis
Erythema chronicum migrans	Lyme disease
Lupus pernio (purple malar rash)	Sarcoidosis
Psoriasis	Psoriatic arthritis
Vitiligo and poliosis	VKH
Shingles	Varicella zoster
Pets	
Puppy	Toxocariasis
Cat	Toxoplasmosis
Social History	
Drug abuse	Candida, HIV/AIDS
Venereal disease	Syphilis, HIV/AIDS, reactive arthritis

Table 12.1.3 Suggested Diagnostic Work-Up for Anterior Uveitis

Ankylosing spondylitis	HLA B27, SI joint films, rheumatology consult
Reactive arthritis	HLA B27, SI joint films (if symptomatic), swab for *Chlamydia*
Psoriatic arthritis	HLA B27, rheumatology and/or dermatology consult
Lyme disease	Lyme antibody immunofluorescent assay (e.g., ELISA)
Juvenile idiopathic arthritis or any suspect uveitis in children	Rheumatoid factor, antinuclear antibodies, HLA-B27, radiographs of affected joints, urinalysis and renal function tests, rheumatology consult
Sarcoidosis	Chest radiograph and/or chest CT, PPD or IGRA, ACE, lysozyme
Syphilis	RPR or VDRL, FTA-ABS or treponemal-specific assay; HIV testing if positive
Ocular ischemic syndrome	Intravenous fluorescein angiography, carotid Doppler studies

• PPD and/or IGRA.

• Chest radiograph or chest CT to rule out sarcoidosis and pulmonary tuberculosis.

• Angiotensin-converting enzyme (ACE) ± lysozyme (questionable utility).

• Lyme antibody (consider in endemic areas).

• HLA-B27 (in acute unilateral or bilateral alternating anterior uveitis; especially if hypopyon present).

• Anterior chamber paracentesis for polymerase chain reaction (PCR) testing for suspected herpes virus-associated anterior uveitis (CMV, herpes simplex, varicella zoster).

NOTE: In children with uveitis, it is recommended to perform ANA, RF, HLA-B27, urinalysis and renal function tests. Evaluation for systemic disease by a pediatric rheumatologist may be warranted (e.g., JIA, TINU).

Treatment

1. Cycloplegic (e.g., cyclopentolate 1% t.i.d. for mild to moderate inflammation; atropine 1% b.i.d. to q.i.d. for severe inflammation).

2. Topical steroid (e.g., prednisolone acetate 1%) q1-6h, depending on severity of inflammation. Most cases of moderate to severe acute uveitis require q1–2h dosing initially. Difluprednate 0.05% may allow less frequent dosing than prednisolone acetate. Consider a loading dose (prednisolone acetate 1% one drop every minute for 5 minutes) or fluorometholone 0.1% ophthalmic ointment at night. If the anterior uveitis is severe, unilateral, and is not responding to topical steroids, then consider periocular repository steroids (e.g., 0.5 to 1.0 mL subtenon injection of triamcinolone 40 mg/mL). **SEE APPENDIX 10, TECHNIQUE FOR RETROBULBAR/SUBTENON/SUBCONJUNCTIVAL INJECTIONS.**

NOTE: Periocular use of triamcinolone is off-label and must be discussed with patients. A trial of topical steroids at full strength for several weeks may help identify patients at risk of a significant IOP increase from steroids. Additionally, periocular depot steroids should be used with extreme caution in patients with scleritis because of possible scleral melting.

3. If there is no improvement on maximal topical and repository steroids, or if the uveitis is bilateral and severe, consider systemic steroids, or immunosuppressive therapy. Consider referral to a uveitis specialist and rheumatologist.

 **NOTE:** Prior to initiating systemic steroids or periocular depot steroids, it is important to rule out infectious causes.

4. Treat secondary glaucoma with aqueous suppressants. Avoid pilocarpine. Glaucoma may result from:

• Cellular blockage of the trabecular meshwork. **SEE 9.7, INFLAMMATORY OPEN ANGLE GLAUCOMA.**

• Secondary angle closure from synechiae formation. **SEE 9.4, ACUTE ANGLE CLOSURE GLAUCOMA.**

• Neovascularization of the iris and angle. **SEE 9.14, NEOVASCULAR GLAUCOMA.**

• Steroid-response. **SEE 9.9, STEROID-RESPONSE GLAUCOMA.**

5. If an exact etiology for the anterior uveitis is determined, then additional ocular and/or systemic management may be indicated.

• Ankylosing spondylitis: Often requires systemic anti-inflammatory agents (e.g., NSAIDs such as naproxen). Consider consulting rheumatology, physical therapy, and cardiology (increased incidence of cardiomegaly, conduction defects, and aortic insufficiency).

• Inflammatory bowel disease (IBD): Often benefits from systemic steroids, sulfadiazine, or other immunosuppressive agents. Obtain a medical or gastrointestinal consult.

• Reactive arthritis (previously known as Reiter syndrome): If urethritis is present, then the patient and sexual partners are treated for chlamydia (e.g., single dose azithromycin 1 g p.o.). Obtain medical and/or rheumatology or urology consult.

• Psoriatic arthritis: Consider a rheumatology and/or dermatology consult.

• Glaucomatocyclitic crisis: **SEE 9.8, GLAUCOMATOCYCLITIC CRISIS/POSNER–SCHLOSSMAN SYNDROME.**

• Lens-induced uveitis: Usually requires removal of lens material. **SEE 9.12, LENS-RELATED GLAUCOMA.**

• Herpetic uveitis: Herpes simplex typically requires topical or oral antivirals and steroid drops for non-epithelial corneal disease. Herpetic iridocyclitis benefits from topical steroids and systemic antiviral medications (e.g., acyclovir/valacyclovir); topical antivirals are ineffective for uveitis due to poor intraocular penetration. **SEE 4.15, HERPES SIMPLEX VIRUS AND 4.16, HERPES ZOSTER OPHTHALMICUS/VARICELLA ZOSTER VIRUS.**

• UGH syndrome: **SEE 9.16, POSTOPERATIVE GLAUCOMA.**

• Behçet disease: **SEE 12.7, BEHÇET DISEASE.**

• Lyme disease: **SEE 13.3, LYME DISEASE.**

• JIA: Steroid dosage is adjusted according to the degree of anterior chamber cells, not flare. Prolonged cycloplegic therapy may be required. Consult rheumatology or pediatrics as systemic steroid therapy or immunomodulatory therapy is often needed. Regular follow-up is essential as

flares may be asymptomatic; recurrent or chronic disease can lead to irreversible damage and various sequelae including synechiae, glaucoma, CME, and cataract formation.

 **NOTE:** Cataract surgery in patients with JIA-associated uveitis has a high complication rate. Avoid cataract surgery if possible until patient is inflammation-free for at least 3 months. An IOL may be placed in select circumstances.

• Chronic iridocyclitis of children: Same as JIA.

• FHIC: Usually does not respond to or require steroids (a trial of steroids may be attempted, but they should be tapered quickly if there is no response); cycloplegics are not necessary.

 **NOTE:** Patients with FHIC usually do well with cataract surgery, however they may develop a hyphema (i.e., Amsler sign).

• Sarcoidosis: **SEE 12.6, SARCOIDOSIS.**

• Syphilis: **SEE 12.12, SYPHILIS.**

• Tuberculosis: Refer the patient to an internist, infectious disease specialist, or public health officer for consideration of systemic treatment. Patients with ocular TB frequently have no pulmonary disease but still require systemic four-drug antituberculous therapy. Concomitant oral steroids may be necessary.

Follow-Up

1. Every 1 to 7 days in the acute phase, depending on the severity; every 1 to 6 months when stable.

2. At each visit, the anterior chamber reaction and IOP should be evaluated.

3. A vitreous and fundus examination should be performed for all flare-ups, when vision is affected, or every 3 to 6 months. Macular edema is a frequent cause of decreased vision even after the uveitis is controlled; optical coherence tomography (OCT) can be very useful diagnostically.

4. If the anterior chamber reaction has resolved, then the steroid drops can be slowly tapered with intermittent examinations to ensure that the inflammation does not return during the taper (usually one drop per day every 3 to 7 days [e.g., q.i.d. for 1 week, then t.i.d. for 1 week, then b.i.d. for 1 week, etc.]). Steroids are usually discontinued following the taper when the anterior chamber does not have any cellular reaction. Occasionally, long-term low-dose steroids every day or every other day are required to keep the inflammation from recurring. Punctal occlusion techniques may increase potency of drug and decrease systemic absorption. The cycloplegic agents also can be tapered off as the anterior chamber reaction improves and no new posterior synechiae are noted.

 **NOTE:** As with most ocular and systemic diseases requiring steroid therapy, the steroid should be tapered. Sudden discontinuation of steroids can lead to severe rebound inflammation.

12.2 Intermediate Uveitis

Symptoms

Painless floaters and decreased vision. Minimal photophobia or external inflammation. Most often bilateral and classically affects patients age 15 to 40 years.