REVIEW

RULA A. HAJJ-ALI, MD
Department of Rheumatic and Immunologic Disease, Center for Vasculitis Care and Research, The Cleveland Clinic Foundation

CAREEN LOWDER, MD, PhD
Cole Eye Institute, The Cleveland Clinic Foundation

BRIAN F. MANDELL, MD, PhD
Vice-Chairman of Medicine for Educational Affairs; Department of Rheumatic and Immunologic Diseases, Center for Vasculitis Care and Research, The Cleveland Clinic Foundation; Editor-in-Chief, *Cleveland Clinic Journal of Medicine*

Uveitis in the internist's office: Are a patient's eye symptoms serious?

ABSTRACT

Uveitis is an inflammatory process that may affect one or several specific areas of the eye. But when a patient presents to an internist with eye symptoms, be it photophobia, "floaters," or red eye, the diagnosis is not always clear. If the diagnosis of uveitis is made, internists must search for an underlying cause, such as infection or an autoimmune disease.

KEY POINTS

Many systemic and regional diseases can cause ocular inflammation. It is critical to rule out infectious disease as the cause of uveitis, because giving immunosuppressive therapy to someone with infective uveitis can be disastrous.

Infectious causes of uveitis include toxoplasmosis, cytomegalovirus, herpes simplex virus, tuberculosis, and syphilis.

Systemic inflammatory causes include sarcoidosis, juvenile idiopathic arthritis, inflammatory bowel disease, and HLA-B27-associated diseases, especially ankylosing spondylitis and reactive arthritis.

If the cause of uveitis is not infectious, treatment includes corticosteroids, given either topically, by periocular injection, or systemically. Immunosuppressive therapy may be required to limit steroid use.

This paper discusses therapies that are not approved by the US Food and Drug Administration for the use under discussion.

PATIENTS OFTEN PRESENT to the office with vague eye symptoms, such as photophobia, red eye, or "floaters." In most cases the symptoms are minor and do not reflect a serious problem. But in some cases, those symptoms indicate the more serious, vision-threatening condition of uveitis (intraocular inflammation).

Diagnosis of uveitis is challenging, and its diagnosis and treatment are best handled collaboratively with an ophthalmologist.

Once uveitis is diagnosed, physicians must determine whether it is caused by infection or is a sign of an underlying condition.

This article covers the causes of uveitis, how to approach its diagnosis, and recommendations for managing it.

UVEITIS IS INFLAMMATION AT ANY SITE

The uvea constitutes the middle portion of the eye between the retina and sclera. However, *uveitis* now commonly refers to intraocular inflammation at any site.

The anterior uveal tract consists of the iris. The ciliary body is the intermediate area connecting the iris to the posterior uveal portions of the choroid (**FIGURE 1**). *Anterior uveitis* refers to inflammation of the iris (iritis) or both iris and ciliary body (iridocyclitis). Inflammation of the ciliary body is termed *cyclitis*, *pars planitis*, or *intermediate uveitis*.

Posterior uveitis includes vitritis, choroiditis, retinitis, chorioretinitis, or retinochoroiditis.

Panuveitis or *diffuse uveitis* is the term used when there is both anterior and posterior uveitis.

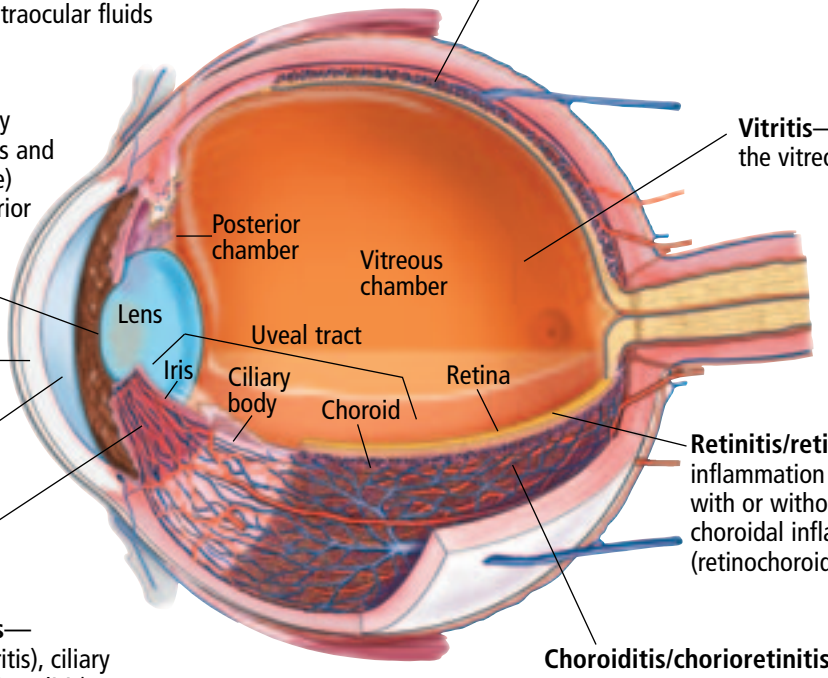
Terms used in the text

Cells and flare—findings on slit lamp examination: cells imply the presence of leukocytes within the anterior, posterior, or vitreous chambers; flare represents increased protein in the intraocular fluids

Uveitis—inflammation of the uveal tract (iris, ciliary body, choroid)

Synechiae—inflammatory adhesions between the iris and cornea (anterior synechiae) or the iris and lens (posterior synechiae)

Vitritis—Inflammation within the vitreous cavity



Retinitis/retinochoroiditis—inflammation of the retina (retinitis) with or without contiguous choroidal inflammation (retinochoroiditis)

Iritis/cyclitis/iridocyclitis—inflammation of the iris (iritis), ciliary body (cyclitis) or both (iridocyclitis)

Choroiditis/chorioretinitis—inflammation involving the choroid primarily (choroiditis), with or without contiguous involvement of the retina (chorioretinitis)

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FIGURE 1. Schematic figure of the different structures of the eye.

CLASSIFICATION OF UVEITIS

Uveitis is classified according to its:

- Anatomic location (anterior, intermediate, or posterior)
- Laterality (unilateral or bilateral)
- Onset (acute or insidious)
- Duration (self-limited, chronic, or recurrent)
- Size and distribution of keratic precipitates ("granulomatous" or "nongranulomatous") seen by slit lamp examination. Biopsy of these inflammatory precipitates is rarely performed, but older pathological studies permit the current labeling of the deposits as granulomatous or nongranulomatous on the basis of their magnified (not biopsied) appearance.

This classification helps the ophthalmologist develop a differential diagnosis.[4,5] Although many cases are idiopathic, an attempt to categorize by etiology should be made (see below),[4] ie:

- An infectious disease
- A localized specific ocular disease
- A specific systemic inflammatory disease
- A masquerade syndrome (eg, intraocular tumors).

DIFFERENT PATTERNS IN DIFFERENT POPULATIONS

Different patterns of uveitis are associated with different ages, genders, and races, mainly because of disease associations.

For example, chronic anterior uveitis is associated with pauciarticular juvenile rheumatoid arthritis, and it is more common in young girls. Acute anterior uveitis, associated with ankylosing spondylitis, is more common in men and boys and is an important cause of uveitis in the United States and the United Kingdom.

TABLE 1

Features of anterior uveitis that differentiate it from other common causes of red eye

No discharge
No itching
Redness affecting primarily the limbus (FIGURE 2)
Poorly reactive pupil
Irregularity of the pupil
Pain and photophobia
Family history of uveitis

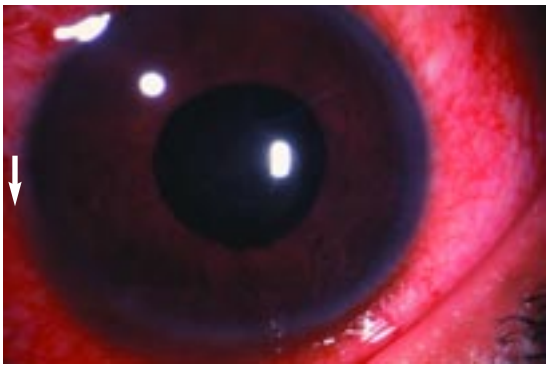

FIGURE 2. Congestion of the limbus (the junction between the cornea and the sclera) in anterior uveitis.

In Caucasians, in whom the prevalence of uveitis is approximately 17 cases per 100,000 and the peak ages are between 20 and 50 years,[1] anterior uveitis is the most common pattern.[2] In contrast, in Japanese people, posterior uveitis accounts for most cases and is a manifestation of Behçet syndrome or Vogt-Koyanagi-Harada syndrome.[3–5] Ocular sarcoidosis is more common in African Americans, while Behçet disease is much more common in Asians and in people of Middle Eastern descent.[2]

IS THIS UVEITIS?

The first question the internist must answer is whether a patient with eye symptoms has uveitis and should be referred to an ophthalmologist.

Many patients with anterior uveitis have a red eye, but other causes of a red eye that should be distinguished from uveitis include corneal inflammation (keratitis), conjunctival inflammation (conjunctivitis), blood vessel inflammation in the episclera or sclera (episcleritis and scleritis, respectively), or acute closed-angle glaucoma. TABLE 1 summarizes the signs and symptoms that help in recognizing anterior uveitis.

Patients with posterior uveitis are more likely to be pain-free but with visual changes such as floaters. The new onset of significant floaters, especially with any haziness of vision, warrants referral to an ophthalmologist.

The diagnosis of uveitis is confirmed by slit lamp examination, which can demonstrate inflammatory cells and the flare that results from protein extravasations from inflamed blood vessels into the anterior or posterior chambers.

SYMPTOMS DEPEND ON SITE

The symptoms of uveitis depend on the site of involvement.

Acute anterior uveitis frequently causes pain and photophobia associated with ciliary injection. This is the typical pattern in patients with HLA-B27-associated iridocyclitis. Initially, vision may or may not be affected.

Insidious anterior uveitis. If the onset is insidious (eg, in pauciarticular juvenile idiopathic arthritis), patients may experience no symptoms, despite inflammation and intraocular damage, until scarring, loss of vision, and cataracts occur.

Posterior uveitis causes "floaters" and hazy vision. Redness and pain are not usual features of isolated posterior uveitis, although a dull ache may be present. Involvement of the retina may produce blind spots or flashing lights (a major warning sign).

Uveitis may precede the full-blown expression of systemic disease

CAUSES OF UVEITIS: INFECTIOUS DISEASES

Although infection is an uncommon cause of uveitis, it is critical to rule out infection because giving immunosuppressive therapy to someone with infective uveitis can be disastrous.

Infectious uveitis can occur in immunocompromised or healthy people. It is usually recognized by specific findings on ophthalmologic examination in an immunocompromised patient—or after uveitis does not respond to anti-inflammatory therapy.

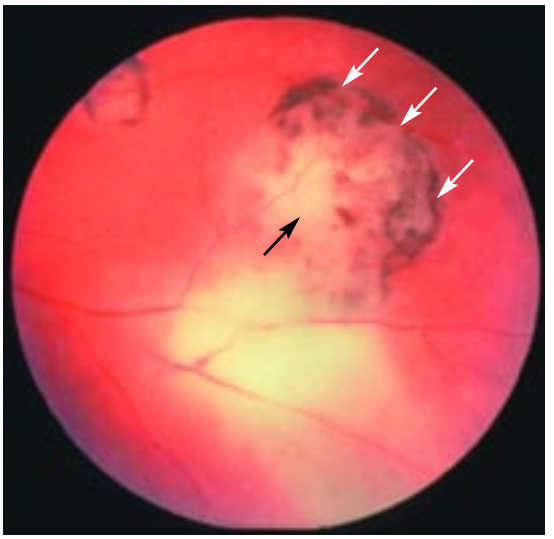

FIGURE 3. Toxoplasmosis. Note the focal area of retiniitis (white arrows) adjacent to scar area (black arrrow).

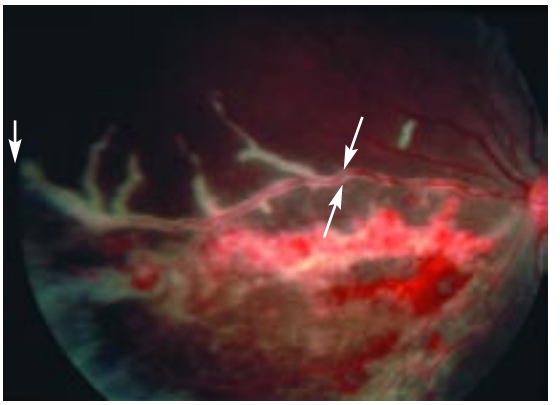

FIGURE 4. Cytomegalovirus retinitis. Note the characterisitic retinitis that progresses along the nerve fiber layer (arrows).

Inappropriate use of immunosuppressive therapy in infectious uveitis can be disastrous

Parasitic infection: toxoplasmosis

Toxoplasmosis is a common cause of retinochoroiditis (posterior uveitis) in normal and immunosuppressed patients,[6] accounting for as many as 25% of cases of posterior uveitis in the United States. Retinitis is usually prominent.[7] Most cases of acute toxoplasmic retinochoroiditis in adults are believed to be reactivations of congenital infection.

Toxoplasmosis is diagnosed by observing a focal active area of retinitis adjacent to a chorioretinal scar (FIGURE 3), with supportive serologic testing. The finding of antitoxoplasmic antibodies helps in the diagnosis but is not sufficient to confirm active disease, since seropositivity is very common in the general population.[8]

Viral infections

Cytomegalovirus infection can cause posterior uveitis (retinitis) in immunocompromised people. Patients with acquired immunodeficiency syndrome are the most susceptible, especially those with CD4 cell counts lower than 50 cells/mL.[9] The incidence has decreased in the United States since highly active antiretroviral therapy has become available.[10]

The infection is bilateral in 50% of cases. The diagnosis is made by recognizing the characteristic retinitis that progresses along the nerve fiber layers (FIGURE 4) in the setting of systemic cytomegalovirus infection, or by polymerase chain reaction studies of vitreous fluid.

Other herpesviruses that can cause retinitis include herpes simplex and herpes zoster. Herpes simplex retinitis usually occurs in immunosuppressed patients or in patients who are congenitally infected. A unique form of rapidly progressive necrotizing retinitis can occur in normal hosts as a result of various herpes infections and is known as the acute retinal necrosis syndrome.[11,12] This is associated with visual loss and can be identified by an ophthalmologist. It warrants immediate high-dose antiviral therapy.

Bacterial and treponemal diseases

Tuberculosis was once the most frequent cause of choroiditis. Now it is found in fewer than 1% of all cases of uveitis in the United States.[13,14] It should be considered as the cause of uveitis in a patient with active systemic tuberculosis.

Syphilis can cause anterior or posterior uveitis, usually during the secondary or tertiary stages of infection.[15]

Anterior syphilitic uveitis typically presents as acute unilateral iritis or iridocyclitis with involvement of the contralateral eye in half of cases (a pattern not generally found in HLA-B27-associated uveitis—see below). Posterior syphilitic uveitis can present as diffuse or localized choroiditis or chorioretinitis, most often in patients with human immunodeficiency virus infection. Half of all cases

of syphilitic posterior uveitis are also bilateral. Uveitis due to secondary syphilis often cannot be distinguished from other causes of uveitis on the basis of the ocular manifestations.

Other, rare causes of bacterial and spirochetal uveitis include leprosy, leptospirosis, cat scratch disease, Lyme disease, and Whipple disease.

CAUSES OF UVEITIS: LOCALIZED OCULAR DISEASES

Some inflammatory diseases that are confined to the eye, without systemic associations, manifest as uveitis. Patients may present to their internist, but the specific diagnosis is generally recognized by an ophthalmologist on the basis of special features on examination or by history.

Sympathetic ophthalmia is inflammation of the "sympathizing" eye that results from penetrating trauma or surgery in the contralateral ("exciting") eye. It is thought to be due to an immune response against an ocular antigen that is exposed after the trauma.[16] Early enucleation of the exciting eye improves the visual outcome in the sympathizing eye; use of systemic corticosteroids and other immunosuppressant agents has also improved the prognosis.

Birdshot choroidopathy is a bilateral posterior uveitis characterized by yellowish spots disseminated throughout the fundus at the level of the retinal pigment epithelium or choroid. Also noted are disc edema and numerous inflammatory cells in the vitreous and choroid in a birdshot appearance.

Most patients are women in middle age (mean age 50). The disease is strongly associated with HLA-A29 antigen: about 80% to 90% of patients are positive for HLA-A29, compared with 7% of the general population.[19,20]

Pars planitis is an idiopathic inflammation of the pars plana of the ciliary body, the portion of the eye between the iris and the choroid. It is known as "intermediate uveitis" when it is associated with a systemic disease such as multiple sclerosis or sarcoidosis.[17,18] Vision is usually affected, but about half of patients have a mild inflammation and a favorable prognosis.[21] Periodic remissions and exacerbations are typical.

CAUSES OF UVEITIS: SYSTEMIC INFLAMMATORY DISEASES

HLA-B27-associated diseases

Anterior uveitis is associated with the histocompatibility antigen HLA-B27. In the United States and England, where HLA-B27 is relatively common (prevalence 4%–10%), from 30% to 70% of patients with acute anterior uveitis have this antigen.[22,23]

Only half of patients with HLA-B27 and anterior uveitis have an associated systemic disease such as ankylosing spondylitis, psoriatic arthritis, reactive arthritis, or inflammatory bowel disease. Of patients with ankylosing spondylitis, 90% have HLA-B27; in reactive arthritis the prevalence is 60%. A patient with ankylosing spondylitis or Reiter syndrome has a 20% to 30% chance of developing iritis during the course of the disease.[24]

HLA-B27-associated uveitis is characterized by the acute onset of unilateral iridocyclitis with redness and photophobia. With treatment, the prognosis is good, and the inflammation usually resolves within 2 to 4 months, which permits therapy to be discontinued. Recurrences are frequent, however, and may occur unilaterally in the contralateral eye (a "flip-flop"pattern). Some patients develop synechiae (scarring).

Trauma to one eye can cause uveitis in the other

Iritis as a complication of either psoriatic or inflammatory bowel disease is less common, less well characterized, and less frequently associated with HLA-B27. Around 7% of patients with psoriatic arthritis develop uveitis, as do fewer than 5% with inflammatory bowel disease.[25] Iritis associated with ulcerative colitis is frequently unilateral and sudden in onset, but the uveitis associated with Crohn disease is much more variable and is frequently bilateral, posterior, insidious in onset, and chronic in duration.[26]

Sarcoidosis

To the internist, sarcoidosis is a chronic multisystem disease characterized by lung infiltrates, hilar adenopathy, and lesions of the eye and skin. Eye disease may be the initial or only

manifestation, and it can affect all ocular structures.

Sarcoidosis accounts for fewer than 6% of cases of anterior uveitis.[27,28] Sarcoidosis-related uveitis is bilateral in 80% of cases; approximately 85% of cases are anterior and 25% are posterior (10% are both).[29,30] Anterior sarcoidosis-related uveitis is an iridocyclitis characterized on slit-lamp examination by large "mutton-fat" keratic precipitates. The iridocyclitis can be chronic, bilateral, and recurrent and may lead to posterior synechiae formation. Posterior uveitis can be accompanied by involvement of the retinal vessels, the central nervous system, or both.[30]

Occasionally, sarcoid uveitis presents acutely with parotitis, fever, and facial nerve palsy (uveoparotid fever). Asymptomatic lacrimal gland enlargement is common and may provide a clue to the underlying disease.

The diagnosis of ocular sarcoidosis is strongly supported by the finding of sterile noncaseating granulomas on biopsy of an affected organ, most commonly the lungs or lymph nodes. Conjunctival biopsy in patients suspected of having ocular sarcoidosis may occasionally be worthwhile; the yield is increased by biopsy of clinically abnormal tissue. Computed tomography of the lungs is superior to chest radiography in demonstrating adenopathy. The angiotensin-converting-enzyme level is a nonspecific test and should not be used diagnostically.

Ophthalmologists often make the diagnosis of ocular sarcoidosis on the basis of the clinical appearance and pattern of the inflammatory disease, after excluding alternative diagnoses, in the absence of systemic findings. How often this pattern "evolves" into systemic sarcoidosis is unknown.

Uveitis is common in juvenile idiopathic arthritis

Juvenile idiopathic arthritis

Juvenile idiopathic arthritis is a group of inflammatory arthritides affecting children younger than 16 years. It can present in four different modes:

- A systemic onset characterized by fever, polyarthritis, rash, adenopathy, and leukocytosis
- A polyarticular onset in which more than four joints are involved
- A pauciarticular onset with involvement of four joints or fewer
- Spondylitis, often with an initial peripheral arthritis.

Uveitis is common in juvenile idiopathic arthritis: the prevalence can reach 20% in children with pauciarticular onset and 5% with polyarticular onset. It is extremely rare in the form with systemic onset. Most often, it occurs in young girls who have early-onset pauciarticular disease, frequently with a positive antinuclear antibody test. However, a recent study suggests that despite the classic teaching, antinuclear antibody positivity may not predict uveitis risk in patients with pauciarticular juvenile idiopathic arthritis.[31]

Uveitis is usually asymptomatic and often presents within 5 years of the onset of juvenile idiopathic arthritis. An insidious, bilateral iridocyclitis, it is often completely asymptomatic until complications and loss of vision develop.[32]

Reports from the 1970s described visual loss in 66% of patients and blindness in up to 38%.[33,34] Early detection by regular eye screening every 3 to 4 months has dramatically decreased the rate of visual impairment to 16%.[32,35]

Children with spondylitis may develop acutely painful recurrent anterior uveitis, similar to adults with HLA-B27-associated uveitis.

Behçet disease

Behçet disease, most commonly seen in the Mediterranean and eastern rim of Asia, is characterized by recurrent orogenital ulcers, uveitis, thrombosis, vasculitis, and cutaneous manifestations. Uveitis, a dominant feature of the disease, occurs in 80% of patients.[36]

Uveitis in Behçet disease typically is chronic and bilateral, and can be anterior or posterior or both. The inflammatory response in the anterior chamber may be so brisk as to elicit a visible meniscus of inflammatory cells, termed hypopyon (**FIGURE 5**). Blindness can result from a relentlessly progressive occlusive retinal vasculitis that often does not respond to aggressive immunosuppressive therapy.[37]

Vogt-Koyanagi-Harada syndrome

Vogt-Koyanagi-Harada syndrome is a presumed autoimmune disease that can cause bilateral panuveitis and acute serous retinal detachment. It is one of the leading causes of uveitis in Japan.[38] Other manifestations include alopecia, peliosis (whitening of patches of hair), sterile meningitis, and eighth cranial nerve disease.

Other systemic causes

Other causes of uveitis include tubulointerstitial nephritis,[39] Kawasaki disease,[40] multiple sclerosis,[18,41] relapsing polychondritis,[42] Sjögren syndrome,[43] Wegener granulomatosis,[44] drug or hypersensitivity reactions,[45] and Lyme disease.[46] Uveitis is rarely associated with rheumatoid arthritis or systemic lupus erythematosus.

MASQUERADE SYNDROMES

A number of noninfectious processes can be mistaken for an inflammatory process and can mimic uveitis. These "masquerade syndromes" include non-Hodgkin lymphoma, leukemia, retinitis pigmentosa, and retinoblastoma. These are often suspected when there is poor response to anti-inflammatory agents that are given to treat assumed uveitis.

Lymphomas must be considered when uveitis presents at an older age. They are typically of B-cell origin and confined to the eye and the central nervous system.[47]

Other masquerade syndromes include uveal melanoma and metastatic lesions of breast, lung, or renal origin.

COMPLICATIONS OF UVEITIS

The major sight-threatening complications of uveitis are cataracts; glaucoma; cystoid macular edema; retinal detachment; subretinal, retinal, and optic nerve neovascularization; and band keratopathy.

Cataracts occur in patients with uveitis as a direct result of inflammation—as well as treatment of the inflammation with corticosteroids. Uveitis may lead to anterior and posterior synechiae which can impede aqueous outflow and cause glaucoma. Permanent loss of vision can occur with long-standing macular edema, observed most commonly in patients with sarcoidosis, intermediate uveitis, birdshot chorioretinopathy, and retinal vasculitis.

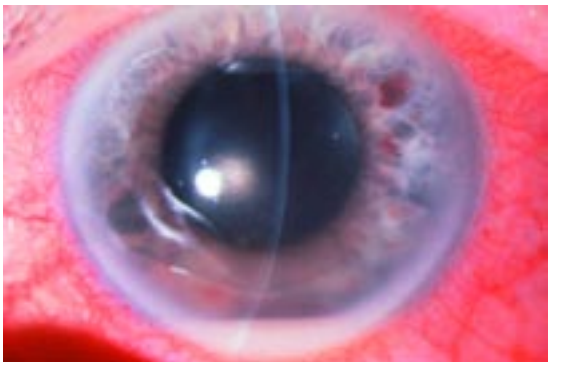

FIGURE 5. Hypopyon in Behçet disease (can also be seen in anterior uveitis of other causes).

Glaucoma may occur if the inflammatory cells and debris clog the trabecular meshwork or from posterior synechiae.

Retinal detachment occurs in patients with posterior, intermediate, or diffuse uveitis.

It is believed that aggressive reduction of all inflammation will prevent most delayed sequelae of uveitis.

APPROACH TO PATIENTS WITH UVEITIS

When uveitis is diagnosed, potential causes should be considered. A specific diagnosis for uveitis can be found in approximately 70% of cases, and a systemic disease is associated with uveitis in up to half.[48–50] Infection should be considered when uveitis develops in an immunocompromised patient, or when uveitis fails to respond to anti-inflammatory therapy. The active participation of the internist in the evaluation and management of immunosuppression in patients with uveitis is extremely helpful.

Cataracts can be due to inflammation—or anti-inflammatory treatment

If this is uveitis, is it associated with systemic disease?

The most helpful tools in the initial search for associated systemic diseases are the patient's history and the general physical examination, coupled with the information given by the ophthalmologist about the ocular pattern of the inflammation. **TABLE 2** summarizes systemic conditions and their common associated ocu-

TABLE 2

Systemic conditions and their associated ocular pattern of inflammation

SYSTEMIC DISEASE	PATTERN OF UVEITIS
Ankylosing spondylitis	Acute unilateral anterior uveitis; may "flip-flop" between eyes
Reactive arthritis	Acute unilateral anterior uveitis
Inflammatory bowel disease	Acute unilateral anterior uveitis*
Juvenile idiopathic pauciarticular arthritis	Chronic insidious bilateral uveitis
Sarcoidosis	Chronic insidious bilateral anterior or posterior uveitis, retinal involvement
Behçet syndrome	Chronic insidious bilateral anterior or posterior uveitis
Vogt-Koyanagi-Harada syndrome	Chronic insidious bilateral anterior or posterior uveitis, retinal detachment

*Uveitis associated with Crohn disease may be bilateral, posterior, insidious in onset, and chronic in duration

lar pattern of inflammation.

Once the inflammation is localized to either anterior or posterior segment, and the onset (acute or insidious) and the symmetry (unilateral or bilateral) have been established, clues from the history and physical examination can direct the diagnosis and workup (TABLE 3).

The new onset of floaters and hazy vision warrants referral to an ophthalmologist

Are there specific considerations in the uveitis workup?

The diagnostic evaluation of patients with uveitis should be tailored to fit the history and physical findings. Chest radiography, computed tomography, or both are mandatory when pulmonary symptoms are elicited. However, imaging can still be considered if there are no pulmonary symptoms and if a cause of uveitis is not obvious, since thoracic sarcoidosis is frequently asymptomatic. This approach has not been demonstrated to influence outcomes in patients with otherwise asymptomatic sarcoidosis, however.

Symptoms of spondyloarthropathy may be atypical in female patients, and radiographic evaluation of the sacroiliac joints can be helpful if this diagnosis is considered.[51] A normal sacroiliac radiograph does not exclude spondyloarthropathy, since radiographs may be normal early in the disease.[52] However, the ultimate clinical value of routine spine or sacroiliac radiographs in the absence of axial symptoms is not established.[53]

HLA typing can occasionally help determine the prognosis of anterior uveitis.

HLA-B27 is associated with both spondyloarthropathy and isolated anterior uveitis. Seventy-one percent of patients with acute-onset unilateral "nongranulomatous" (the ophthalmologic term based on the slit-lamp appearance of the eye) anterior uveitis are HLA-B27-positive.[54] HLA typing is not indicated if a patient presents with acute unilateral uveitis and the diagnosis of spondyloarthropathy is already established, however. HLA-B27 testing is also not helpful when the uveitis is posterior or bilateral, since in this setting the relation to HLA-B27 is not clear.

Testing may be most useful when a patient presents with acute unilateral anterior uveitis without a clear explanation by history and physical examination. In such cases, detecting HLA-B27 would direct the diagnosis away from sarcoidosis or syphilis and would suggest that the disease is likely to respond to intermittent local therapy with steroid drops, although it will likely recur.[24]

Typing for HLA-A29 strongly supports the

TABLE 3

Important clues to systemic inflammatory diseases

POSSIBLE DIAGNOSE	CLUES	WORKUP
Spondyloarthropathy	Asymmetric peripheral arthritis Dactylitis, enthesitis Morning back stiffness	Sacroiliac radiography HLA-B27 testing if diagnosis is unclear
Sarcoidosis	Cough, dyspnea Lacrimal gland enlargement Parotid gland enlargement	Chest radiography Computed tomography
Behçet disease	Oral or genital ulcers	Rule out infectious cause (eg, herpes viruses)
Inflammatory bowel disease	Gastrointestinal symptoms Heme-positive stools	Colonoscopy
HIV infection **Malignancy** **Cancer therapy**	Opportunistic infections Abnormal white blood cell count Thrombocytopenia	HIV testing CD40 count

diagnosis of birdshot retinopathy, a serious chronic chorioretinitis that is usually suggested by the clinical appearance of the retina.[19,20]

Antinuclear antibody testing is not recommended in cases of unexplained uveitis, because the test has poor diagnostic value for lupus (or any other specific diagnosis) in the absence of specific diagnostic concern suggested by the history, laboratory evaluation, or physical examination. A positive antinuclear antibody test in the setting of isolated uveitis does not warrant the diagnosis of systemic lupus erythematosus. Some pediatric rheumatologists use the antinuclear antibody test in young patients with pauciarticular juvenile inflammatory arthritis to help predict prognosis, but as noted, this practice has recently been questioned.[31]

Serologic tests for syphilis should be considered in patients with unexplained uveitis. Venereal Disease Research Laboratory (VDRL) testing may be negative but the fluorescent treponemal antibody absorption test is usually positive in syphilis-related eye disease.[4] This is especially important in patients infected with human immunodefieciency virus.

TREATMENT IS MULTIDISCIPLINARY

Uveitis is best managed in collaboration with an ophthalmologist. Inflammatory eye disease is a distinct subspecialty of ophthalmology, and a uveitis specialist may need to be consulted in complex cases. Often, an internist or rheumatologist manages dosing and monitors the toxicity of immunotherapy, while an ophthalmologist assesses disease activity and ocular damage, dictating the need for increased or decreased intensity of therapy.

A positive antinuclear antibody test does not establish lupus—or anything else

Treatment of infectious diseases

Viral infections, particularly cytomegalovirus infection and herpetic acute retinal necrosis, should be treated very aggressively with antiviral agents to prevent retinal damage.

Syphilitic uveitis should be treated as neurosyphilis.

Toxoplasma infection is usually treated with the combination of sulfadiazine, pyrimethamine, and folinic acid.

Corticosteroid therapy

Corticosteroids are the mainstay of therapy for noninfectious causes of uveitis; the route depends on the location of inflammation, the severity, the degree of visual disability, and the presence or absence of systemic disease.

Topical corticosteroids are used in anterior uveitis but are not recommended in posterior uveitis because of poor penetration and thus limited efficacy. The frequency of doses

depends on disease severity; hourly application may be needed at first.

Topical steroids may worsen viral or other infections and delay the appropriate therapy. Thus, it is imperative to communicate with an ophthalmologist before starting topical corticosteroid therapy.

Periocular corticosteroid injections are used for posterior disease. They have the advantage of achieving high intraocular levels of steroids while avoiding the systemic side effects of oral corticosteroids. Globe perforation, ptosis, and glaucoma are potential risks.

Systemic corticosteroid therapy, may be effective in controlling anterior uveitis, but is generally reserved for patients with bilateral disease that is refractory to local medication or for those with major ocular disability or retinitis.

Systemic or topical corticosteroids usually elicit a therapeutic response, but some inflammatory conditions do not fully respond or require unacceptably high doses and long-term use. Although untreated uveitis can cause cataracts and glaucoma, these are also recognized complications of steroid therapy.

Other immunosuppressive medications used in steroid-dependent or refractory uveitis include methotrexate, sulfasalazine, azathioprine, cyclosporine, mycophenolate, chlorambucil, and tacrolimus.[55–57] Few randomized trials of these agents have been performed. Recent reports showed promising results with anti-tumor necrosis factor agents in some forms of inflammatory uveitis.[58–59]

Immunosuppressive medications should be managed by physicians experienced in their use, given the wide range of potential toxicity, and in collaboration with an ophthalmologist skilled in the management of uveitis.

Adjunctive therapies, including mydriatic/cycloplegic agents, are used mainly to prevent adhesion of the pupillary margins to the anterior lens capsule and to relieve painful ciliary spasm.

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ADDRESS: *Brian Mandell, MD, PhD, Vice-Chairman of Medicine for Educational Affairs, NA20, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195; e-mail mandelb@ccf.org.*