JAMA | Review

Uveitis in Adults
A Review

Panayiotis Maghsoudlou, PhD; Simon J. Epps, MBBS; Catherine M. Guly, MBChB; Andrew D. Dick, MD

IMPORTANCE Uveitis is characterized by inflammation of the uvea—the middle portion of the eye composed of the iris, ciliary body, and choroid—causing eye redness, pain, photophobia, floaters, and blurred vision. Untreated uveitis may cause cataracts, glaucoma, macular edema, retinal detachment, optic nerve damage, and vision loss.

OBSERVATIONS Uveitis predominantly affects individuals aged 20 to 50 years. Anterior uveitis affects the iris and ciliary body (41%-60% of cases); intermediate uveitis affects the pars plana (attachment point of vitreous humor) and peripheral retina (9%-15%); posterior uveitis involves the choroid and/or retina (17%-23%); and panuveitis involves all uveal layers (7%-32%). Uveitis is classified as noninfectious or infectious, with toxoplasmosis, herpes, tuberculosis, and HIV comprising 11% to 21% of infectious cases in high-income countries and 50% in low- and middle-income countries. Incidence and prevalence of uveitis are influenced by genetic factors (eg, human leukocyte antigen–B27), environmental factors (eg, air pollution), and infection rates. In the US and Europe, 27% to 51% of uveitis cases are idiopathic, and 37% to 49% are associated with systemic disease, such as axial spondyloarthritis. Treatment goals are to induce and maintain remission while minimizing corticosteroid use to reduce corticosteroid-related adverse effects. Infectious uveitis requires systemic antimicrobial treatment. Active inflammatory disorders associated with uveitis should be treated by the appropriate specialist (eg, rheumatologist). Treatment for uveitis depends on subtype; anterior uveitis is treated with topical corticosteroids, and mild intermediate uveitis may be monitored without initial treatment. Patients with moderate to severe intermediate uveitis, posterior uveitis, and panuveitis are at high risk of sight-threatening complications and require systemic and/or intravitreal corticosteroids and immunosuppressive agents. For posterior uveitis, first-line therapy with disease-modifying antirheumatic drugs such as methotrexate achieved remission of inflammation in 52.1% (95% CI, 38.6%-67.1%) of patients, and mycophenolate mofetil controlled inflammation in 70.9% (95% CI, 57.1%-83.5%). In patients who do not improve or worsen with first-line therapy, adalimumab extended time to treatment failure to 24 weeks vs 13 weeks with placebo and reduced frequency of treatment failure from 78.5% to 54.5% ($P < .001$).

CONCLUSIONS AND RELEVANCE Uveitis is characterized by inflammation of the uvea and primarily affects adults aged 20 to 50 years. For noninfectious anterior uveitis, corticosteroid eyedrops are first-line treatment. For posterior noninfectious uveitis, disease-modifying antirheumatic drugs are first-line therapy; biologics such as adalimumab are second-line treatment for patients with inflammation refractory to treatment. Uveitis caused by systemic infection should be treated with antimicrobials, and local or systemic steroids may be used depending on the severity of uveitis and the specific microorganism.

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Supplemental content

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Author Affiliations: Academic Unit of Ophthalmology, Translational Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom (Maghsoudlou, Dick); Regional Ocular Inflammatory Service, Bristol Eye Hospital, Bristol, United Kingdom (Maghsoudlou, Epps, Guly); School of Cellular and Molecular Medicine, University of Bristol, Bristol, United Kingdom (Dick); UCL Institute of Ophthalmology, London, United Kingdom (Dick); National Institute for Health and Care Research Moorfields Biomedical Research Centre, London, United Kingdom (Dick).

Corresponding Author: Andrew D. Dick, MD, UCL Institute of Ophthalmology, 11-43 Bath St, London EC1V 9EL, United Kingdom (a.dick@ucl.ac.uk).

Uveitis affects 38 to 714 per 100 000 people worldwide, is reported to be associated with 3% to 10% of vision impairment in the US and Europe, and has been reported to be associated with up to one-fourth of cases of blindness in low- and middle-income countries (based on studies, many of which are almost 30 years old).[1] In a retrospective analysis of US insurance claims (1998-2012), 5% of patients with noninfectious intermediate uveitis, posterior uveitis, or panuveitis developed blindness or low vision over 5 years.[2] Uveitis involves inflammation of the uvea, which consists of the iris, ciliary body, and choroid. Symptoms include eye redness, pain, photophobia, floaters, and blurred vision. Prompt ophthalmologic evaluation is needed to assess severity, determine etiology, and initiate treatment.

Uveitis has various etiologies, including autoimmune diseases (eg, multiple sclerosis [1%])[1]; systemic immune-mediated inflammatory diseases (eg, sarcoidosis [2%-17%])[3-7] and autoinflammatory diseases (rare genetic disorders affecting the immune system, such as Blau syndrome); infections (including tuberculosis [1%-13%], syphilis [1%-4%], HIV [1%-14%], and toxoplasmosis [5%-7%])[8-10]; and adverse reactions to medications (eg, immune checkpoint inhibitors, <0.5%).[11-14] Masquerade syndromes are ocular conditions with intraocular infiltrating cells, such as lymphoma (1%-5%).[15] There is geographic variation in the etiology and presentation of uveitis due to variation in the prevalence of risk factors such as infections, air pollution, and tobacco smoking and of genetic variables.[16,17] The underlying cause of uveitis is unidentified in 27% to 51% of cases (*idiopathic uveitis*).[5,11,18-20]

This review summarizes current evidence regarding epidemiology, pathophysiology, diagnosis, and treatment of uveitis in adults.

Methods

MEDLINE and Embase were searched (January 1, 2000, to March 1, 2025) using keywords and MeSH headings related to epidemiology, pathophysiology, diagnosis, management, and prognosis of uveitis. We prioritized articles according to study quality (randomized trials and larger studies), novel findings, and clinical applicability. Of 2995 articles retrieved, 107 were included, consisting of 23 randomized clinical trials, 18 cohort studies, 17 cross-sectional studies, 26 narrative reviews, 8 meta-analyses, and 15 evidence-based guidelines.

Discussion

Epidemiology

Uveitis may occur at any age (**Table 1**) but presents most frequently (60%-80% of cases) in young and middle-aged adults (aged 20-50 years).[1,18,21] Uveitis is more common in females than males (57% of cases are among women),[22] particularly in patients with multiple sclerosis (75% female), juvenile idiopathic arthritis (50%-80% female), and sarcoidosis (55%-64% female).[23] However, uveitis associated with human leukocyte antigen (HLA)–B27 is more common in men (male to female ratio, 1.5:1). In the US and Europe, 37% to 49% of uveitis cases are associated with systemic disease such as axial spondyloarthritis.[5-7,11-13,18]

Among patients with uveitis who are evaluated for associated conditions, 11% to 21% of cases are caused by infection in high-income countries, compared with up to 50% in low- and middle-income countries.[1,8] Toxoplasmosis-related (5%-7%) and herpes-related (5%-15%) uveitis are the most common infectious causes of uveitis in high-income countries,[3,4,6] with tuberculosis-related (8%-13%) and HIV-related (10%-14%) uveitis more prevalent in low- and middle-income countries.[9,10,24,25] In Japan, Vogt-Koyanagi-Harada disease, an autoimmune disease that affects melanin-rich tissues, accounts for a higher proportion of uveitis cases (Table 1).[26,27] The most common form of uveitis in Turkey is Behçet disease (30%), a chronic, autoimmune multisystem inflammatory disorder associated with HLA-B51.[28] When compared with other regions of the world, sarcoidosis uveitis is more frequent in Europe and the US (8%-10%).[29,30]

Epidemiologic data are summarized in Table 1.[3,9,24,26-36]

Classification and Etiology

The Standardized Uveitis Nomenclature classified uveitis anatomically into 4 types, depending on the site of inflammation: anterior (iris and ciliary body), intermediate (pars plana and peripheral retina), posterior (retina and/or choroid), or panuveitis (all areas) (**Figure 1**).[8] In the US and Europe, anterior uveitis is most common (41%-60%), followed by posterior (17%-23%), intermediate (9%-15%), and panuveitis (7%-32%).[5,6,11,19,30] In countries with a lower prevalence of HLA-B27, such as Japan, the most common type is panuveitis (46%), followed by anterior (38%), posterior (13%), and intermediate (3%) uveitis.[37] Anterior uveitis is frequently unilateral (53% of cases), while intermediate, posterior, and panuveitis are typically bilateral (79%, 57%, and 75% of cases, respectively).[38]

Anterior uveitis is associated with systemic diseases such as axial spondyloarthritis (15%-50%) and tuberculosis (1%-13%) (Table 1).[39,40] Intermediate uveitis is associated with multiple sclerosis (1%-5%).[26,28,29,41] Causes of posterior uveitis include toxoplasmosis (17%-50%) and sarcoidosis (1%-9%).[18,26,28,29] Panuveitis is also associated with toxoplasmosis (1%-8%) and sarcoidosis (5%-29%).[18,26,28,29] The International Uveitis Study Group provided a clinical classification of uveitis (Table 1).[42,43]

Pathophysiology

The healthy eye possesses immune privilege, allowing it to suppress immune responses against endogenous antigens (eg, S-antigen; a protein that stops excess sensing of light) and exogenous antigens (eg, bacterial proteins). This immune privilege is maintained by the blood-retina barrier; cellular mechanisms, including regulatory T cells; and cytokine mechanisms, including transforming growth factor beta and IL-10. Noninfectious uveitis is hypothesized to result from reduced immune tolerance to retinal proteins, leading to inflammation.[44,45] In infectious uveitis, the infectious organism breaches the blood-retina barrier, and may contain proteins resembling retinal proteins (a process called antigenic mimicry), exacerbating the inflammatory response (**Figure 2**). The prevailing theory is that infectious uveitis begins with pathogen-derived antigen presentation, while noninfectious uveitis begins with ocular autoantigen presentation—both involving major histocompatibility complex class II molecules activating naive T cells. Naive $CD4^+$ T cells differentiate into Th1 and Th17 subsets on activation and migrate to the retina. These T cells release proinflammatory cytokines (eg, interferon gamma, IL-2, IL-17), triggering a cytokine cascade that recruits immune cells such

Table 1. Major Epidemiologic and Clinical Characteristics of Uveitis

Domain	Characteristics
Prevalence	38-714 per 100 000 people globally
Incidence	17-52 per 100 000 people globally
Age distribution	Most common in young and middle-aged adults (20-50 years), comprising 60%-80% of cases
	Can present at any age
Gender distribution	Overall, slightly more common in females
	Female preponderance in multiple sclerosis (75% female), juvenile idiopathic arthritis (50%-80% female), and sarcoidosis (55%-64% female)
	HLA-B27–associated uveitis more common in men (male to female ratio up to 1.5:1)
Laterality	Unilateral uveitis is at least as common as bilateral uveitis in specialist and non-specialist clinics
Types of uveitis	Classified anatomically as anterior uveitis (41%-60%), intermediate uveitis (9%-15%), posterior uveitis (17%-23%), panuveitis (7%-32%)
	Specific diseases target distinct locations, with axial spondyloarthritis predominantly anterior (91%) and multiple sclerosis typically intermediate (80%)
Symptoms	Anterior uveitis: eye pain, redness, photophobia
	Intermediate uveitis: increased floaters, painless, blurred vision
	Posterior uveitis: blurred vision, visual distortion, or asymptomatic
	Panuveitis: eye pain, redness, photophobia, blurred vision
Etiology	Infectious (11%-50% of cases):
	Endophthalmitis (an infection-driven inflammation of the entire eye): endogenous (from hematogenous spread) or exogenous (following surgery or trauma)
	Viral: herpes simplex/herpes zoster (5%-15%), cytomegalovirus (1%-5%), HIV (1%-14%) (rest of viral causes listed are rare), Chikungunya, Zika, HTLV-1, West Nile, measles, mumps, rubella, dengue, Ebola
	Bacterial: tuberculosis (1%-13%), syphilis (1%-4%), Lyme disease (<1%) (rest of bacterial causes rare), leprosy, bartonella, leptospirosis, Whipple disease (*Tropheryma whipplei*)
	Parasitic: toxoplasmosis (5%-7%), toxocariasis (<1%) (rest of parasitic causes rare), onchocerciasis, cysticercosis
	Fungal: candidiasis (<1%) (rest of fungal causes rare), aspergillosis, histoplasmosis, *Pneumocystis jirovecii*, Cryptococcus
	Noninfectious (52%-79%):
	With known systemic association: sarcoidosis, Behçet disease, Vogt-Koyanagi-Harada syndrome,[a] juvenile idiopathic arthritis, tubulointerstitial nephritis with uveitis, IgA nephropathy, multiple sclerosis, HLA-B27-associated (axial spondyloarthritis, reactive arthritis, psoriatic arthritis, inflammatory bowel disease)
	With no known systemic association: Fuchs' heterochromic uveitis, Posner-Schlossman syndrome, multifocal choroiditis with panuveitis, punctate inner choroidopathy, acute posterior multifocal placoid pigment epitheliopathy, serpiginous choroidopathy, birdshot chorioretinopathy, acute zonal occult outer retinopathy, multiple evanescent white dot syndrome, sympathetic ophthalmia, idiopathic retinal vasculitis, and neuroretinitis syndrome
	Idiopathic (27%-51%): No identifiable cause despite full workup
	Trauma (5%-20%)
	Masquerade syndromes (1%-5%):
	Neoplastic
	Nonneoplastic: ocular ischemia, Schwartz-Matsuo syndrome (anterior uveitis, increased intraocular pressure, and retinal detachment)
	Medication-induced (0.5%): Immune checkpoint inhibitors, bisphosphonates, latanoprost, rifabutin, fluoroquinolones, sulfonamides, topiramate
Geographic distribution	Low- and middle-income countries: Infections account for 50% of uveitis cases, with tuberculosis being the most common infectious cause (8%-10%)
	High-income countries: Infections account for a smaller proportion (11%-21%), most frequently herpes (10%) and toxoplasmosis (7%)
	Sarcoidosis uveitis more common in US and Europe (3%-7% of all cases)
	Behçet uveitis more common in Turkey and along historical Silk Road regions (China, Iran, Iraq, Japan, Korea, and Saudi Arabia; 25%-32% of all cases)
	Vogt-Koyanagi-Harada disease more common in China, India, Japan, and Korea (5%-8% of all cases)

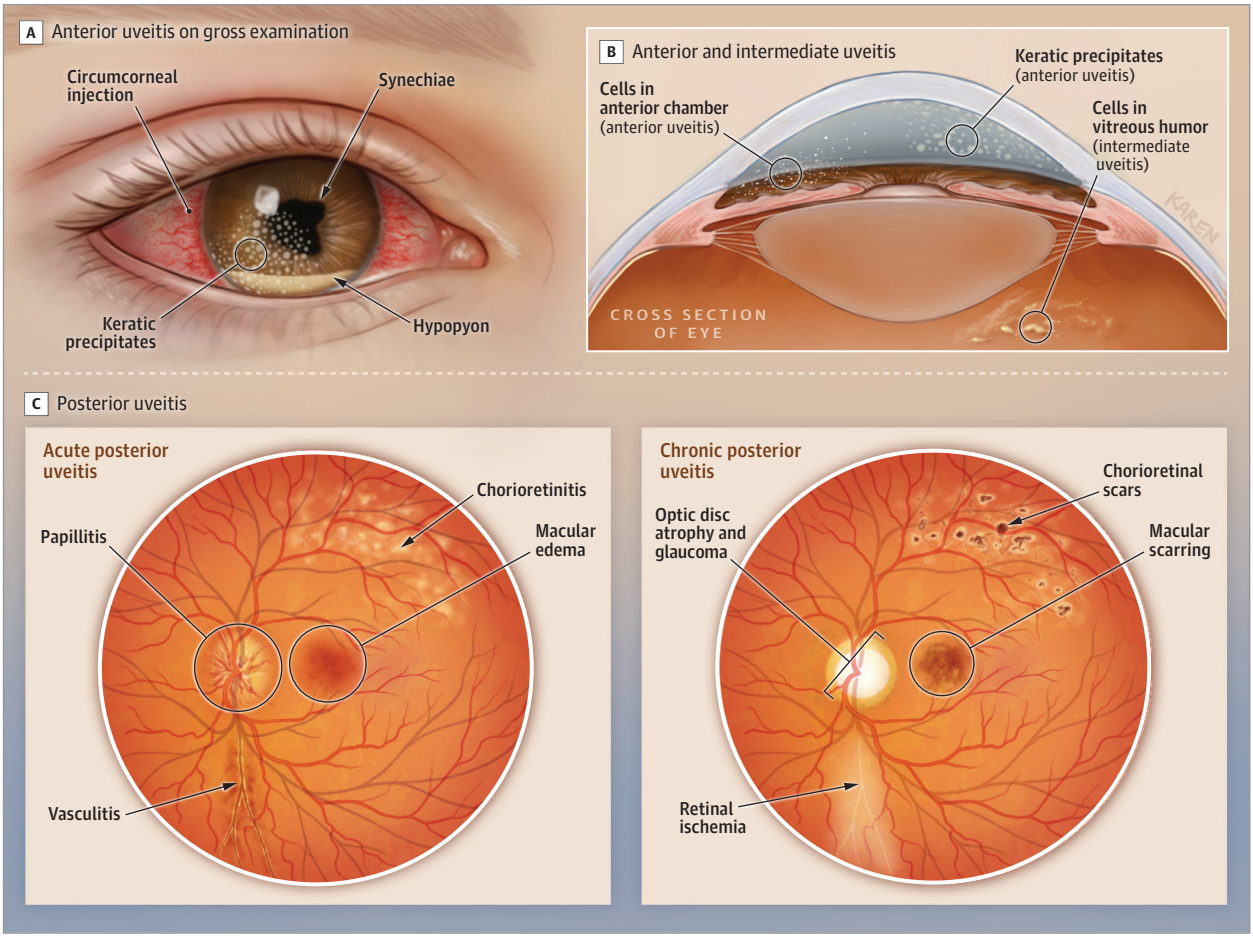
[a] Vogt-Koyanagi-Harada syndrome is a rare autoimmune disorder against melanocytes, causing bilateral panuveitis with retinal detachments, along with neurologic (meningism), auditory (tinnitus), and skin (vitiligo, alopecia, poliosis [a white streak in the hair]) signs.

as macrophages and neutrophils, leading to chorioretinitis, vasculitis, and edema.[45]

Clinical Presentation

Patients with anterior uveitis typically present with eye pain (sharp and worsened by bright light or reading) and perilimbal redness (Figure 1A). Up to 50% of patients with anterior uveitis have vision loss, defined as visual acuity letter score less than 61 in 1 study.[46] In this review, we use the Early Treatment Diabetic Retinopathy Study (ETDRS) method to determine visual acuity, in which a score of 85 equals 20/20 on the Snellen chart or LogMAR value of 0. In intermediate uveitis, patients report painless floaters and blurred vision.[41] Patients with posterior uveitis may present with vision loss if widespread or involving the macula (Figure 1C) but can be asymptomatic with peripheral retina involvement. Panuveitis manifests with symptoms from all 3 uveal regions. Patients with endophthalmitis, an infectious panuveitis, may present with sepsis (eg, fever, hypotension) with eye pain and vision loss.

Figure 1. Clinical Features of Uveitis



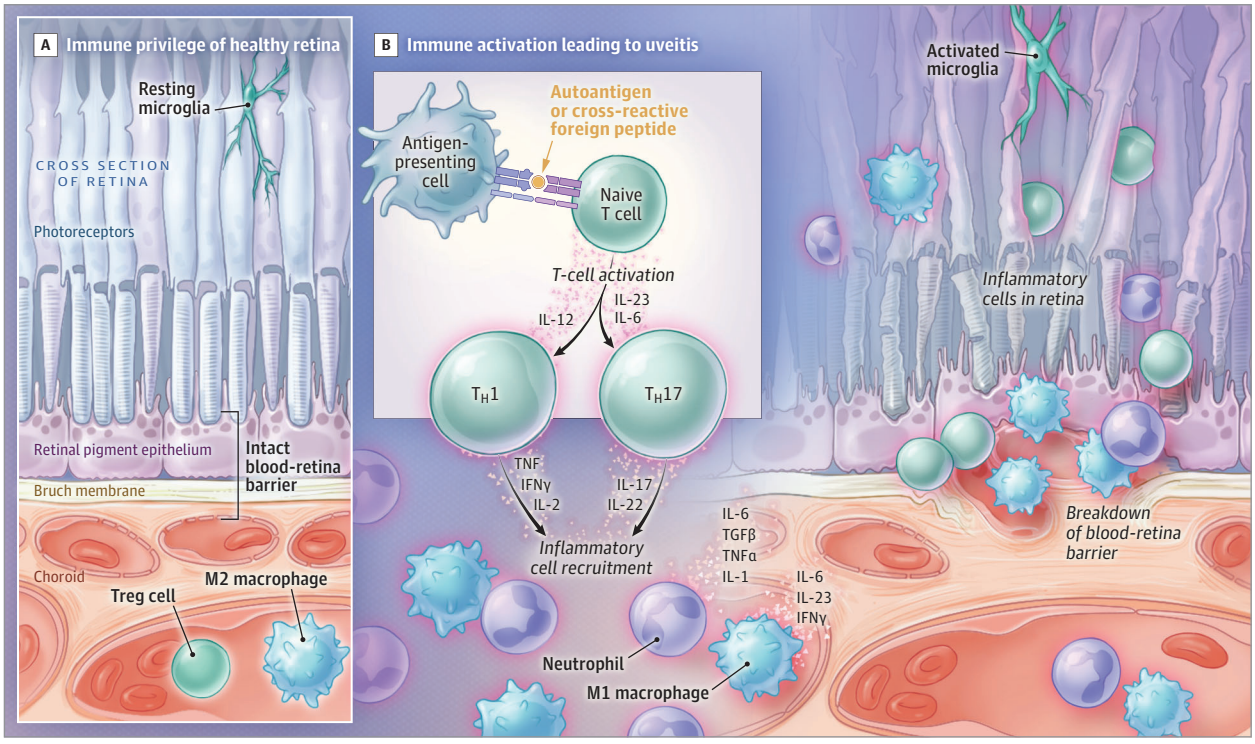
A, Anterior uveitis characteristics, including ciliary injection. The iris may develop adhesions either anteriorly to the structures of the anterior chamber angle and/or corneal posterior surface (anterior synechiae) or posteriorly to the lens (posterior synechiae), causing pupil distortion. Both forms of synechiae increase the risk of raised intraocular pressure and glaucoma. A hypopyon may be present, characterized by an accumulation of white blood cells in the inferior portion of the anterior chamber (the fluid-filled space between the cornea and iris). B, Anterior chamber cells, flare, and keratic precipitates associated with anterior uveitis. C, Features of posterior uveitis. The left panel demonstrates acute features, including optic disc swelling (papillitis), with its attendant risk of optic nerve dysfunction, which may be seen as a complication of uveitic inflammatory activity directly or secondary to hypotony (low intraocular pressure). Occlusive vasculitis, vascular sheathing (a white cuff of inflammation surrounding vessels), hemorrhages, and focal chorioretinal spots can also present with different types of uveitis. The right panel demonstrates posterior segment complications, including glaucomatous optic neuropathy. Neovascular responses, particularly in the form of choroidal neovascular macular membranes, may develop in the chronic phase. Epiretinal membrane formation on the inner surface of the macula can cause visual distortion. A variety of disease mechanisms may result in retinal detachment. Chorioretinal scarring and subretinal fibrosis may cause severe visual impairment, and has a poor visual prognosis with limited treatment options. Clinical features suggestive of infection include uveitis with corneal disease (corneal swelling), iris atrophy, or increased intraocular pressure (herpes); hypopyon with vitritis (endophthalmitis); string-of-pearls appearance to the vitreous (fungal); occlusive retinal vasculitis (tuberculosis); placoid chorioretinopathy, a flat, white plaque of inflammation (syphilis); and chorioretinitis adjacent to a pigmented chorioretinal scar (toxoplasmosis).

Assessment and Diagnosis

Patients with suspected uveitis should be referred to an ophthalmologist for diagnosis and treatment. Urgent same-day referral is necessary for vision loss or distortion, especially with eye pain and redness. Patients with visual symptoms and systemic illness (eg, fever, hypotension) should be referred to the emergency department for evaluation and treatment due to the risk of vision-threatening endophthalmitis and potentially life-threatening sepsis. Some signs of uveitis, such as posterior synechiae (iris-lens adhesions causing a distorted pupil), can be identified without specialized equipment. Direct ophthalmoscopy can identify retinitis, choroiditis, and optic disc swelling. Definitive diagnosis requires a slit lamp to examine the anterior segment of the eye and a handheld lens for the fundus (ie, indirect ophthalmoscopy). Signs of anterior uveitis on slit lamp include a cellular infiltrate in the anterior chamber and keratic precipitates (cell deposits on the posterior cornea) (Figure 1A-B). In intermediate uveitis, a cellular infiltrate appears in the vitreous humor (Figure 1B). In posterior uveitis, choroidal and/or retinal inflammation occurs in the ocular fundus (Figure 1C). **Figure 3** provides a diagnostic algorithm for patients with suspected uveitis.

Patients who initially present with unilateral anterior uveitis without signs or risk factors for infection or systemic symptoms indicating autoimmune disease (eg, joint pain and skin rash) do not

Figure 2. Uveitis Pathogenesis



The retina's immune privilege relies on the blood-retina barrier, which shields ocular tissue proteins from the systemic immune system. This protective mechanism can be compromised, leading to autoimmune reactions. Within the retina, Tregs marked by $CD4^+$, $CD25^+$, and $FoxP3^+$ identifiers contribute to immune tolerance by emitting neuropeptides and anti-inflammatory cytokines. These Tregs can suppress other T cells that have escaped elimination in the thymus during development and have the potential to react against self-antigens, producing cytokines, TGFβ, and IL-35 to reduce inflammation. Furthermore, retinal pigment epithelium and retinal cells express certain proteins on their surfaces that deactivate lymphocytes, thereby regulating ocular inflammation. Disease is typically associated with major histocompatibility complex class II molecule–mediated presentation of autoantigens or cross-reactive foreign peptides to naive T cells. Activated $CD4^+$ T cells differentiate into $CD4^+$ T_H1 and T_H17 cells that migrate to the affected tissue, recruiting inflammatory cells and producing tissue damage. T cells differentiate into $CD4^+$ T_H1 and T_H17 cells, producing IFNγ and IL-17, respectively. These facilitate the recruitment and activation of downstream cytokine release and innate inflammatory response, such as IL-6, TNF, and granzyme B (a protease involved in programmed cell death), which in turn can lead to vasculitis and edema.[21,22]

IFNγ indicates interferon gamma; TGFβ, transforming growth factor beta; TNF, tumor necrosis factor; Treg, regulatory T cell.

require additional testing. Patients with recurrent or bilateral anterior uveitis, intermediate uveitis, posterior uveitis, or panuveitis should be tested for infection (eg, syphilis) and systemic disease (eg, sarcoidosis). Figure 3 and **Figure 4** detail tests for systemic conditions. Aqueous humor and/or vitreous sampling (for microscopy and culture) should be performed if infection is suspected. Because infectious organisms are identified in only 22% to 32% of cases, a negative result does not exclude infection.[47] Additional systemic testing, particularly for syphilis or tuberculosis, is needed.

There is no international consensus on the best diagnostic approach for uveitis. Testing varies by regional infection prevalence, comorbidities, immunocompromise, and clinical presentation. Patients who are immunocompromised, especially those with HIV, require comprehensive infectious screening for both HIV-related and opportunistic infections, including cytomegalovirus and candida.

Treatment

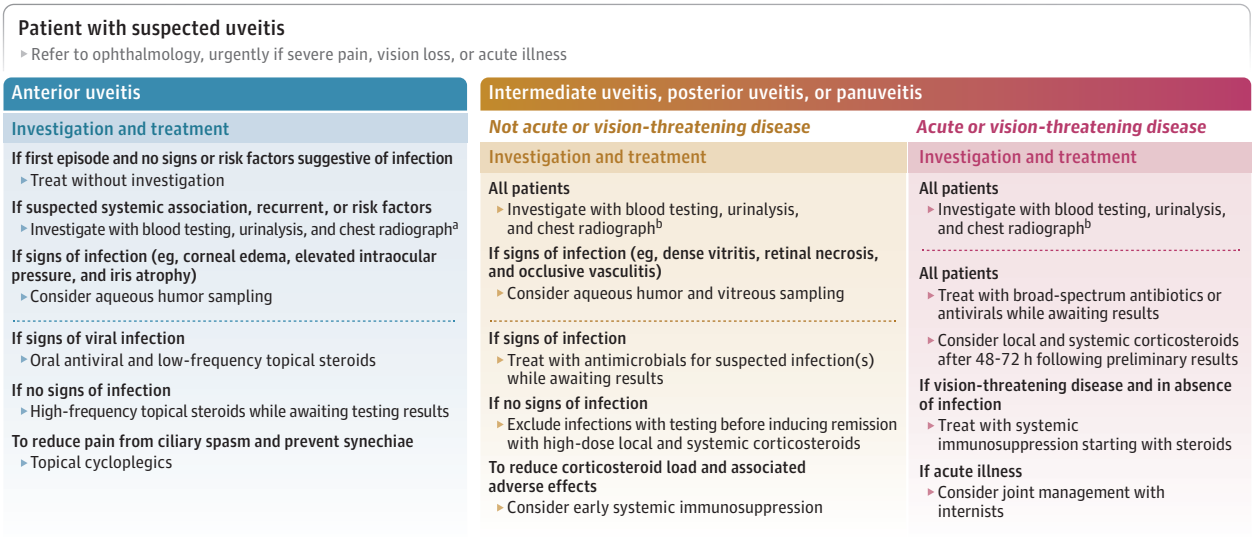
Treatment is determined by the patient's anatomical uveitis subtype, infectious exposures, age, comorbidities, country of origin, signs of infection, and sight-threatening features of uveitis (such as severe vitritis, macular edema, retinochoroiditis, and forms of uveitis carrying high risk of visual loss, eg, Behçet disease). The goal of therapy is to reduce inflammation in the uvea, thereby lowering the risk of vision loss.

Noninfectious Anterior Uveitis

Topical Corticosteroids

For noninfectious anterior uveitis, prednisolone acetate is the most commonly used first-line topical corticosteroid,[48] which is administered initially as hourly steroid drops during waking hours in the affected eye for 7 days, followed by a frequency taper. Tapering typically reduces the dose by 1 drop weekly (6 times daily, 5 times daily, etc) until discontinuation, individualized based on clinical response. A randomized trial of 78 patients with acute, chronic, and recurrent anterior uveitis compared the effectiveness of prednisolone acetate (1%) and rimexolone (1%) ophthalmic suspensions in reducing anterior chamber inflammatory cells, a marker of uveitis, as measured by slit-lamp examination at 28 days. Mean anterior chamber cell scores decreased from 1.79 to 0.13 ($P < .05$) with prednisolone and from 1.81 to 0.14 ($P < .05$) with rimexolone, both

Figure 3. Algorithm for the Initial Investigation and Management of Care for Patients With Possible Uveitis



Patients with possible uveitis will develop symptoms dependent on the anatomical location of the inflammation and should be referred to an ophthalmologist for assessment. If the patient is acutely ill or experiencing vision loss, this should be an urgent referral. The management of anterior uveitis varies depending on whether it is the first episode or recurrent. Treatment of intermediate and posterior uveitis and panuveitis varies based on whether the case is vision threatening.

[a]Blood testing including complete blood cell count, antinuclear antibody (juvenile idiopathic arthritis), angiotensin-converting enzyme (ACE)/lysozyme (biochemical markers of granulomas in sarcoidosis), human leukocyte antigen (HLA)–B27, kidney panel (creatinine and beta-2 macroglobulin levels for tubulointerstitial nephritis and uveitis syndrome), and syphilis serology. ACE is produced by epithelioid cells in granulomas, and lysozyme is a bactericidal enzyme produced by monocytes and macrophages responding to the granulomas.

[b]Blood testing including complete blood cell count, antinuclear antibody, ACE/lysozyme, HLA-B27, kidney panel, liver panel, serum calcium, C-reactive protein, interferon gamma release assay (for tuberculosis), and syphilis serology. Consider additional testing depending on clinical signs or patient population, such as HLA-B51 (Behçet disease); HLA-A29 (birdshot chorioretinopathy); HLA-DR4/DRB1*04 (Vogt-Koyanagi-Harada disease); antineutrophil cytoplasmic antibody (granulomatosis with polyangiitis); HIV, toxoplasma, Lyme, and *Bartonella* serology; serum lactate dehydrogenase level; and serum protein electrophoresis (for lymphoma).

treatments achieving clinically meaningful change. The difference between the 2 treatments was not statistically significant.[49]

Ocular Corticosteroids

Localized corticosteroid injections are used as second-line therapy for noninfectious anterior uveitis if topical corticosteroids are ineffective and when systemic treatment (such as systemic corticosteroids) is unsuitable or not tolerated.[50] However, in cases of severe uveitis, systemic corticosteroids are favored. Options include short-acting steroid injections around the eye (sub-Tenon space overlying the sclera or orbital floor; 1-2 months duration, such as triamcinolone acetonide), intermediate-acting steroid implants into the vitreous (3-6 months duration, such as dexamethasone), and longer-acting steroid implants into the vitreous (36 months duration, such as fluocinolone acetonide). A 6-month multicenter randomized clinical trial (RCT) (n = 192) of patients with uveitic macular edema reported significantly reduced macular thickness at 8 weeks with use of intravitreal triamcinolone implants (39%) and dexamethasone implants (46%) at 8 weeks compared with periocular triamcinolone implants (23%) ($P < .001$ vs baseline for all comparisons).[51] A recent RCT (n = 160) reported that suprachoroidal triamcinolone improved visual acuity by 15 or more letters in 47% of patients at 4 weeks compared with 16% with placebo ($P < .001$).[52]

Systemic Corticosteroids

Systemic corticosteroids are recommended for severe noninfectious anterior uveitis that does not improve or worsens with topical or regional corticosteroids.[53,54] Treatment typically begins with high-dose oral prednisone (1 mg/kg/d, up to 60-80 mg daily), tapering the dosage over 4 to 10 months.[53]

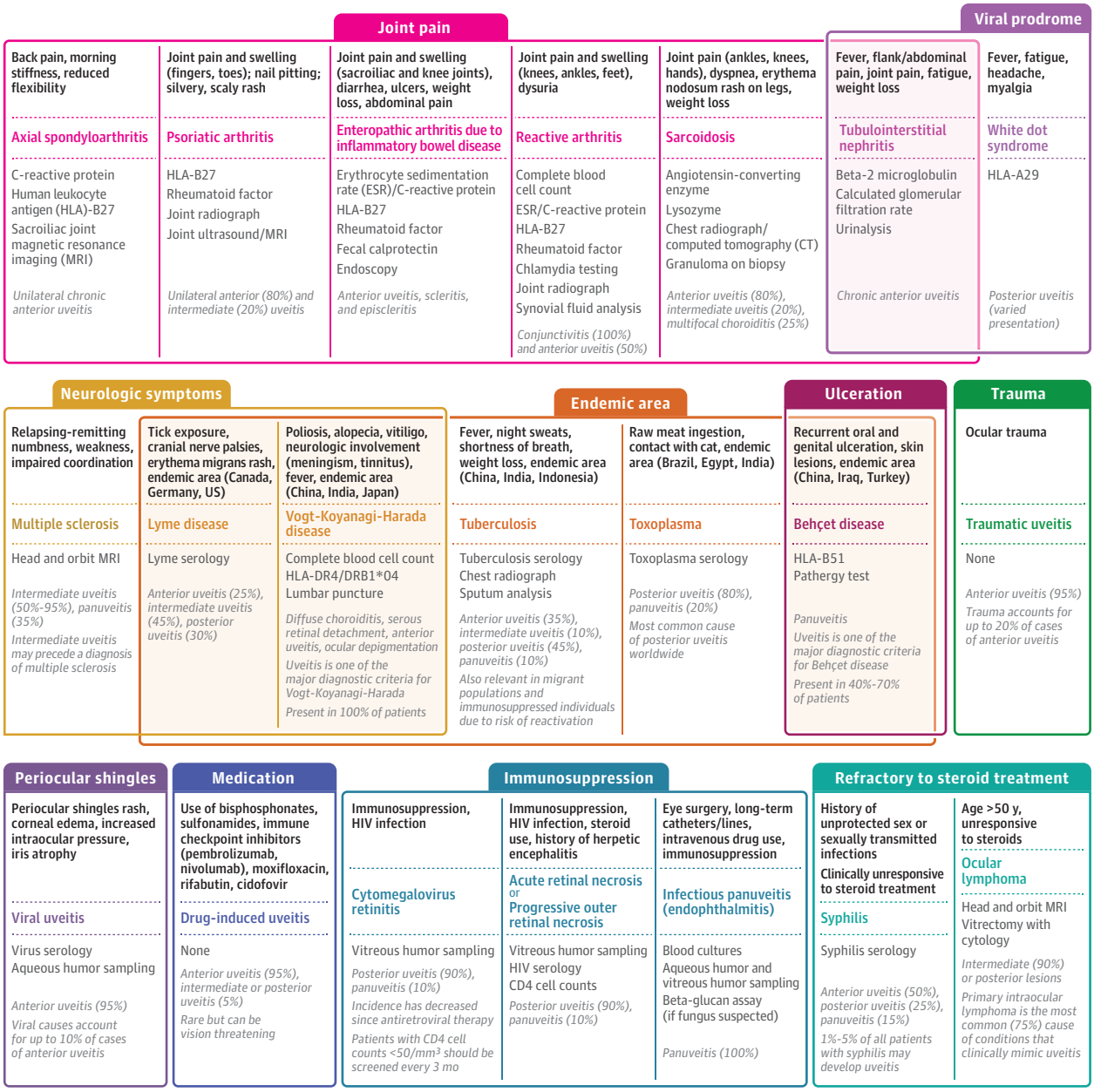
Complications Associated With Use of Ocular and Systemic Corticosteroids

Ocular hypertension, glaucoma, and cataracts can develop from prolonged topical, periocular, intravitreal implant, and systemic corticosteroid use. Up to 18% to 24% of patients treated with steroids may require cataract or glaucoma surgery.[48,55,56] Complication frequency depends on corticosteroid type, administration route, application frequency, and treatment duration. Among 192 patients with uveitic macular edema, the intravitreal dexamethasone implant had a cumulative risk of ocular hypertension at 24 weeks of 41% (95% CI, 26%-53%), comparable to intravitreal triamcinolone (30% [95% CI, 17%-40%], $P = .37$) but significantly higher than periocular triamcinolone (20% [95% CI, 9%-29%], $P = .007$).[51] In a randomized trial of 160 patients with uveitic macular edema, suprachoroidal triamcinolone and sham treatment had similar frequency of ocular hypertension (11.5% vs 15.6%) and cataracts (7.3% vs 6.3%), with no significant differences.[52]

Noninfectious Posterior Uveitis

While mild intermediate uveitis may be monitored without initial treatment, patients with moderate to severe intermediate uveitis, posterior uveitis, and panuveitis are at high risk for sight-threatening

Figure 4. Clinical Approach to Uveitis: Linking Suggestive Features, Etiologies, and Diagnostic Tests



Diagnostic approach to uveitis based on clinical features, showing key signs and symptoms that suggest specific conditions. Each box is organized into major presenting features (first row), leading to suspected conditions (second row), required confirmatory tests (third row), and epidemiological information, including prevalence and anatomical patterns (bottom row). Common presentations include joint symptoms, neurological manifestations, and viral prodromes; risk factors include endemic exposures and immunosuppression.

complications and require systemic and/or intravitreal corticosteroids and immunosuppressive agents.

Systemic Corticosteroids

Systemic corticosteroids are typically used to achieve remission in patients with noninfectious posterior uveitis, regardless of the cause (Figure 3). For vision-threatening conditions, such as Behçet disease or Vogt-Koyanagi-Harada syndrome, high-dose intravenous methylprednisolone (1 g once daily for 3 days) may be prescribed.[53] Long-term use of systemic corticosteroids, especially at doses exceeding 7.5 mg daily of prednisone, is associated with risks including hyperglycemia and osteoporosis. The SITE retrospective cohort study (N = 9263) examined treatment outcomes for ocular inflammation. Among 47 patients with noninfectious uveitis, 57% (95% CI, 33%-83%) attained complete remission of inflammation within 1 month after receiving intravenous methylprednisolone (500-1000 mg once daily up to 3 days), followed by tapering dose of oral prednisone over 4 to 10 months.[53,57] Treatment aims for rapid remission, verified by resolution of uveitis findings on eye examination and imaging (eFigure in the Supplement).[53] An RCT that

Box. Commonly Asked Questions About Uveitis

What Are the Most Common Causes of Uveitis Worldwide?
In high-income countries, 52%-79% of uveitis cases are noninfectious (systemic diseases such as axial spondyloarthritis account for 37%-49%). Infectious causes of uveitis such as tuberculosis and toxoplasmosis are common in low- and middle-income countries, accounting for up to 50% of cases. In 27% to 51% of all cases worldwide, no specific cause can be identified (idiopathic uveitis).

Which Symptoms Suggestive of Uveitis Should Prompt Referral to Ophthalmology?
Individuals with symptoms of uveitis, such as eye redness, pain, photophobia, floaters, or blurred vision, should be referred to ophthalmology. An urgent same-day referral is needed for patients with sudden vision loss or visual distortion with eye pain or redness. Patients with uveitis and signs and symptoms of systemic illness (eg, fever, hypotension) require emergency care.

What Are the First-Line Treatments for Infectious and Noninfectious Uveitis?
For infectious uveitis, treatment should target the underlying infection (such as antibiotics for tuberculosis, antiviral medications for herpes) often combined with corticosteroids. For noninfectious uveitis, treatment varies by uveitis location. Anterior uveitis should be treated with topical corticosteroid drops. First-line treatment for posterior uveitis is DMARDs such as methotrexate; biologics such as adalimumab are second-line therapy if uveitis persists or worsens despite initial treatment with DMARDs.

DMARD indicates disease-modifying antirheumatic drug.

included 255 patients with noninfectious intermediate, posterior, and panuveitis reported that those treated with systemic therapy (corticosteroids and/or disease-modifying antirheumatic drugs [DMARDs] and/or biologics) had clinically meaningful improvements in visual acuity over 7 years, gaining 7.2 letters compared with those receiving fluocinolone acetonide implants (95% CI, 2.1-12) ($P < .01$).[58-60]

Disease-Modifying Antirheumatic Drugs

Evidence-based guidelines recommend systemic corticosteroids in combination with DMARDs as first-line therapy for noninfectious posterior uveitis to control severe/persistent inflammation and decrease the risk of complications (**Box**).[61,62] DMARDs alone can be used for patients with contraindications to or intolerance of corticosteroids. Dosing, adverse effects, contraindications, and effect of DMARDs and biologics are listed in **Table 2**.

In the SITE cohort of patients with noninfectious uveitis (N = 168), 52.1% (95% CI, 38.6%-67.1%) of patients with posterior or panuveitis and 74.9% (95% CI, 56.1%-90.3%) of patients with intermediate uveitis receiving weekly methotrexate achieved control of inflammation (defined as complete suppression of inflammation on examination sustained for 28 days or more) at 12 months.[63] Additionally, 40% to 50% of patients taking methotrexate maintained control of inflammation with a prednisone equivalent dose of 10 mg or less daily. Approximately 15% of patients discontinued methotrexate due to lack of efficacy and another 15% discontinued it due to adverse effects such as gastrointestinal upset or bone marrow suppression.[63]

In the SITE study, among 145 patients with noninfectious uveitis, treatment with mycophenolate mofetil was associated with control of inflammation (defined as no inflammatory activity on ocular examination) at 12 months in 70.9% (95% CI, 57.1%-83.5%) of patients with posterior or panuveitis and 76.7% (95% CI, 49.1%-95.6%) of patients with intermediate uveitis.[64] An open-label, multicenter RCT of 41 patients with noninfectious intermediate uveitis reported a lower relapse rate over 15 months with use of prednisone plus mycophenolate mofetil compared with prednisone alone (40.9% vs 78.9%, $P < .05$).[65]

In an RCT of patients with Behçet disease (N = 73), among those without eye involvement at the start of the study (N = 25), 8.3% in the azathioprine group developed uveitis, compared with 61.5% in the placebo group ($P < .01$).[66] Additionally, among patients with Behçet syndrome who already had eye involvement (N = 48), azathioprine reduced recurrent uveitis episodes (4% vs 65.2%, $P < .001$). In the SITE cohort of patients with noninfectious uveitis (N = 91), azathioprine was associated with complete control of inflammation on ocular examination at 6 months in 69% (95% CI, 41%-93%) of patients with intermediate uveitis, 44% (95% CI, 28%-64%) of those with posterior or panuveitis, and 24% (95% CI, 10%-52%) of those with anterior uveitis.[67]

In the SITE study of noninfectious uveitis of all etiologies (N = 373), cyclosporine was associated with controlled inflammation at 1 year on ocular examination in 51.7% (95% CI, 42.6%-61.6%) of patients with posterior or panuveitis and 51.8% (95% CI, 40.4%-64.2%) of patients with intermediate uveitis.[68] In an RCT of 70 patients with Vogt-Koyanagi-Harada disease, recurrence or worsening of uveitis at 1 year was reported in 15.0% (95% CI, 3%-27%) of patients receiving cyclosporine plus oral prednisone, compared with 25.0% (95% CI, 11%-39%) receiving intravenous steroid pulse followed by oral prednisone.[69] The absolute risk difference between groups was −10.0% (90% CI, −27.0% to 6.0%), meeting the predefined noninferiority margin of 20.0% ($P = .001$ for noninferiority).

Biologics

For patients with poorly controlled noninfectious posterior uveitis despite treatment with DMARDs, biologic therapy is second-line treatment,[61,62] with adalimumab having the strongest evidence of effectiveness.[70-77]

Adalimumab was approved by the US Food and Drug Administration (FDA) in 2016 to treat adults with noninfectious uveitis (Table 2).[70,71] The VISUAL placebo-controlled RCTs compared the efficacy of adalimumab in patients with noninfectious posterior uveitis.[70,71] In the VISUAL I trial (N = 217 with active noninfectious intermediate uveitis, posterior uveitis, or panuveitis despite prednisone for >2 weeks), time to treatment failure (defined by new lesions, persistent inflammation, or vision loss ≥15 letters after week 6) was 24 weeks with adalimumab vs 13 weeks with placebo (hazard ratio, 0.50 [95% CI, 0.36-0.70]).[70] However, adalimumab was associated with higher rates of adverse events such as reduced visual acuity and fatigue (1052.4 vs 971.7 per 100 person-years) and serious adverse events such as pneumonia and demyelination (28.8 vs 13.6 per 100 person-years) compared with placebo.[70] In the VISUAL II trial (N = 226 with inactive noninfectious intermediate,

Table 2. Disease-Modifying Antirheumatic Drugs and Biologics for Uveitis

Category/drug	Population	Design	Effect size	Adult dose and administration	Adverse effects	Monitoring	Contraindications/ cautions	Special considerations
Disease-modifying antirheumatic drugs								
Antimetabolites								
Methotrexate	168 Patients with noninfectious uveitis	Retrospective cohort study	Control of inflammation at 12 mo: Anterior uveitis: 67.2% (95% CI, 56.7%-77.3%) Intermediate uveitis: 74.9% (95% CI, 56.1%-90.3%) Posterior/panuveitis: 52.1% (95% CI, 38.6%-67.1%) Patients stopping medication for any reason (32%), adverse effects (18.1%), ineffectiveness (15.4%)	7.5-25 mg/wk	Embryofetal toxicity, gastrointestinal reaction (10%), bone marrow suppression (2%), hepatoxicity (15%), interstitial pneumonitis, opportunistic infections	Complete blood cell count, kidney panel, liver panel	Contraindication in pregnancy, breastfeeding, alcoholism or liver disease, immunodeficiencies, blood dyscrasias Caution in active infection	Considered first-line alongside mycophenolate mofetil Subcutaneous administration more effective that oral administration
Mycophenolate mofetil	145 Patients with noninfectious uveitis	Retrospective cohort study	Control of inflammation at 12 months: Anterior uveitis: 72.4% (95% CI, 52.4%-89.2%) Intermediate uveitis: 76.7% (95% CI, 49.1%-95.6%) Posterior/panuveitis: 70.9% (95% CI, 57.1%-83.5%) Patients stopping medication for any reason (34%), adverse effects (12%), ineffectiveness (9.7%)	1-1.5 g Twice daily	Embryofetal toxicity, gastrointestinal reaction (20%), bone marrow suppression (2%), hepatoxicity (20%), malignancies (lymphoma and skin), opportunistic infections	Complete blood cell count Mycophenolate levels can be measured for patients not responding to therapy	Caution in pregnancy, breastfeeding, blood dyscrasias, active infection	Considered first-line alongside methotrexate
	42 Patients with noninfectious intermediate uveitis	RCT (prednisone and mycophenolate vs prednisone)	Relapse rate at 15 months: 40.9% (mycophenolate) vs 78.9%					
Azathioprine	91 Patients with noninfectious uveitis	Retrospective cohort study	Control of inflammation at 12 mo: Anterior uveitis: 34.6% (95% CI, 15.2%-66.7%) Intermediate uveitis: 89.8% (95% CI, 63.6%-99.4%) Posterior/panuveitis: 59.7% (95% CI, 40.9%-79.3%) Patients stopping medication for any reason (68%), adverse effects (24%), ineffectiveness (15%)	150-200 mg Once daily	Gastrointestinal reaction (10%), bone marrow suppression (5%), hepatoxicity (4%), hypersensitivity syndrome (rash and arthralgia)	Complete blood cell count	Contraindication in pregnancy, previous alkylating agents (cyclophosphamide, chlorambucil)	Consider thiopurine methyltransferase (TPMT) testing before starting azathioprine, as reduced TPMT activity can lead to severe bone marrow toxicity
	73 Patients with Behçet disease	RCT (placebo-controlled)	Episodes of uveitis: In patients with preexisting uveitis: 65.2% (placebo) vs 4% (azathioprine) In patients with no preexisting uveitis: 61.5% (placebo) vs 8.3% (azathioprine)					

(continued)

Table 2. Disease-Modifying Antirheumatic Drugs and Biologics for Uveitis (continued)

Category/drug	Population	Design	Effect size	Adult dose and administration	Adverse effects	Monitoring	Contraindications/ cautions	Special considerations
Calcineurin inhibitors								
Cyclosporine	70 Patients with Vogt-Koyanagi-Harada disease	RCT (cyclosporine + oral prednisone vs intravenous + oral prednisone)	Recurrence rate at 12 mo: 15.0% (95% CI, 3%-27%) for combination therapy vs 25% (95% CI, 11%-39%) for prednisone	1.5 mg/kg Twice daily	Nephrotoxicity (4%), hypertension (3%), hepatotoxicity (1.5%), gum hyperplasia (1%), skin cancer	Complete blood cell count, kidney panel, blood pressure Cyclosporine trough levels can be measured for patients not responding to therapy	Contraindication in uncontrolled hypertension, kidney disease, malignancy	
	373 Patients with noninfectious uveitis	Retrospective cohort study	Control of inflammation at 12 mo: Anterior uveitis: 54.3% (95% CI, 40%-69.9%) Intermediate uveitis: 51.8% (95% CI, 40.4%-64.2%) Posterior/panuveitis: 51.7% (95% CI, 42.6%-61.6%) Patients stopping medication for any reason (49%), adverse effects (13%), ineffectiveness (7%)					
Biologics								
TNF blockers								
Adalimumab	217 Adults with active noninfectious posterior segment uveitis	RCT (placebo-controlled)	Treatment failure (new inflammatory lesions, anterior chamber or vitreous inflammation, or worsening of visual acuity): 54.5% (adalimumab) vs 78.5% (placebo)	40 mg Subcutaneously every 2 wk	Infusion reactions (20%), gastrointestinal reaction (15%), hepatotoxicity (10%), demyelination, increased risk of malignancy and infection (including tuberculosis, hepatitis B)	Complete blood cell count, kidney panel, liver panel Ongoing vigilance for serious or opportunistic infections Repeat tuberculosis serology and chest radiography if pulmonary symptoms occur Consider brain MRI in cases of neurologic symptoms compatible with demyelinating disorders Antiadalimumab antibodies can be measured for patients not responding to therapy	Initiation contraindicated during an active infection Caution during infection (stop if serious), caution for hepatitis B carriers (reactivation may occur), caution for demyelinating disease and heart failure (may worsen)	First-line biologic with the strongest evidence in both adults and children
	226 Adults with inactive noninfectious posterior segment uveitis	RCT (placebo-controlled)	Treatment failure (new inflammatory lesions, anterior chamber or vitreous inflammation, or worsening of visual acuity): 39% (adalimumab) vs 55% (placebo)					
	114 Children with active juvenile idiopathic arthritis-associated uveitis	RCT (placebo-controlled)	Treatment failure (persistent or worsening intraocular inflammation, lack of improvement, development or worsening of coexisting ocular conditions, or protocol deviations such as ineligible medications or prolonged suspension of the trial regimen): 27% (adalimumab) vs 60% (placebo)					
	31 Children with chronic juvenile idiopathic arthritis-associated uveitis	RCT (placebo-controlled)	Reduction of inflammation by 30% determined by laser flare photometry, with no worsening on slit-lamp examination: 56.3% (adalimumab) vs 20% (placebo)					

(continued)

Table 2. Disease-Modifying Antirheumatic Drugs and Biologics for Uveitis (continued) (continued)

Category/drug	Population	Design	Effect size	Adult dose and administration	Adverse effects	Monitoring	Contraindications/ cautions	Special considerations
Golimumab	93 Patients with axial spondyloarthritis and recurrent uveitis	Prospective study	Episodes of uveitis: 11.1 per 100 person-years (12 mo before golimumab) vs 2.2 per 100 person-years (12 mo after); 80.2% reduction	50 mg Subcutaneously monthly	Hepatotoxicity, bone marrow suppression, infusion reactions (2%), hypertension (2%), demyelination, increased risk of malignancy and infection (including tuberculosis, hepatitis B)	Complete blood cell count, kidney panel, liver panel Ongoing vigilance for serious or opportunistic infections Repeat tuberculosis serology and chest radiography if pulmonary symptoms occur Consider brain MRI in cases of neurologic symptoms compatible with demyelinating disorders	Initiation contraindicated during an active infection Caution during infection (stop if serious), caution for hepatitis B carriers (reactivation may occur), caution for demyelinating disease and heart failure (may worsen)	
Certolizumab	115 Patients with axial spondyloarthritis and recurrent uveitis	Prospective study	Episodes of uveitis: <1: 100% (Before treatment) vs 20.2% (2 y after) >1: 59.6% (Before treatment) vs 11.2% (2 y after) >3: 17.9% (Before treatment) vs 0% (2 y after)	200 mg Subcutaneously every 2 wk	Hepatotoxicity, bone marrow suppression, gastrointestinal reaction, infusion reactions, demyelination, increased risk of malignancy and infection (including tuberculosis)	Complete blood cell count, kidney panel, liver panel Ongoing vigilance for serious or opportunistic infections Repeat tuberculosis serology and chest radiography if pulmonary symptoms occur Consider brain MRI in cases of neurologic symptoms compatible with demyelinating disorders	Initiation contraindicated during an active infection Caution during infection (stop if serious), caution for hepatitis B carriers (reactivation may occur), caution for demyelinating disease, blood dyscrasias, and heart failure (may worsen)	

(continued)

Table 2. Disease-Modifying Antirheumatic Drugs and Biologics for Uveitis (continued) (continued)

Category/drug	Population	Design	Effect size	Adult dose and administration	Adverse effects	Monitoring	Contraindications/ cautions	Special considerations
JAK inhibitor								
Filgotinib	74 Patients with noninfectious posterior segment uveitis	RCT (placebo-controlled)	Treatment failure (new inflammatory lesions, anterior chamber or vitreous inflammation, or worsening of visual acuity): 37.5% (filgotinib) vs 67.6% (placebo)	200 mg By mouth	Major cardiovascular events, malignancy, venous thromboembolism, serious infections (adverse effects currently considered as class-effect from tofacitinib) Embryofetal toxicity, gastrointestinal reaction (4%), bone marrow suppression (1%), nephrotoxicity, hepatotoxicity, hyperlipidemia	Complete blood cell count, kidney panel, liver panel, glucose, blood pressure High suspicion index to investigate venous thromboembolism, cardiac events, or new skin lesion Repeat tuberculosis serology and chest radiography if pulmonary symptoms occur	Avoid use in patients 65 y or older, in patients who are current or past long-time smokers, and in patients with other cardiovascular disease or malignancy risk factors, unless there are no suitable alternatives Use with caution in patients with risk factors for venous thromboembolism	

Abbreviations: JAK, Janus kinase; MRI, magnetic resonance imaging; RCT, randomized clinical trial; TNF, tumor necrosis factor.

posterior, or panuveitis controlled by 10-35 mg/d of prednisone), time to treatment failure was longer with adalimumab (median not reached [>18 months] vs 8.3 months with placebo; hazard ratio, 0.57 [95% CI, 0.39-0.84]).[71]

Golimumab, a biologic agent that blocks tumor necrosis factor (TNF), was approved by the FDA for treatment of adults with axial spondyloarthritis. A multicenter prospective study (N = 93) of patients with axial spondyloarthritis, who often experience anterior uveitis, evaluated its efficacy.[74] Comparing pretreatment and posttreatment periods, golimumab was associated with a reduction in anterior uveitis episodes from 11.1 to 2.2 per 100 person-years (rate ratio, 0.20 [95% CI, 0.04-0.91]).[74]

Certolizumab pegol, a monoclonal antibody to TNF, was approved by the FDA for treatment of adults with axial spondyloarthritis and was evaluated in an open-label trial (N = 115) of patients with axial spondyloarthritis and recurrent uveitis.[75] In the 2-year pretreatment period, all patients experienced more than 1 uveitis episode, with 59.6% experiencing more than 2 episodes of uveitis. Following 2 years of certolizumab treatment, 11.2% of patients had more than 2 episodes of uveitis ($P < .001$; pretreatment vs posttreatment).[75]

Infectious Uveitis

For patients with infectious uveitis, the primary goal is treating the underlying infection with systemic and/or local antimicrobials, guided by evidence-based guidelines. Treatment with concomitant corticosteroids depends on clinical findings (eg, vision-threatening chorioretinitis) and clinician judgment (considering disease severity, vision loss risk, corticosteroid-related risks). Corticosteroids should not be used alone in viral retinitis or toxoplasmosis because they suppress immune function without controlling pathogen replication, risking disease progression.[78]

Infectious Panuveitis (Endophthalmitis)

Treatment of infectious panuveitis (also termed endophthalmitis) varies based on whether the source of infection is exogenous (eg, surgery) or endogenous (eg, endocarditis). Exogenous cases require intravitreal antimicrobials, while endogenous cases should be treated with systemic antimicrobials plus targeted infection management (eg, abscess drainage, valve replacement). Empiric broad-spectrum antimicrobials should be initiated and the antimicrobial regimen subsequently tailored based on microbiological results. A retrospective study of 278 US patients with endogenous and exogenous endophthalmitis reported that 78.5% had gram-positive organisms (100% sensitive to vancomycin, 63.6% to ceftazidime) and 11.8% had gram-negative organisms (94.2% sensitive to ciprofloxacin, 80.9% to amikacin); the remainder were fungi.[79]

Tuberculosis

Uveitis may be caused by tuberculosis infection within the eye or as an inflammatory reaction to tuberculosis infection elsewhere in the body. The decision to start antitubercular therapy for uveitis should be based on the likelihood of active tuberculosis infection, as indicated by immunologic (eg, interferon-gamma release assay or Mantoux) and radiologic findings and the population-based prevalence of tuberculosis.[80] The World Health Organization (WHO) recommends a 6-month regimen: isoniazid/rifampicin/pyrazinamide/ethambutol for 2 months, followed by isoniazid/rifampicin for 4

months, achieving 85% success for drug-susceptible tuberculosis.[80-82] In a meta-analysis of 49 retrospective studies with 4017 participants with tubercular uveitis, complete resolution of inflammation on ocular examination and imaging was achieved in 83% (95% CI, 77%-89%) of 1812 patients, and visual acuity improved in 65% (95% CI, 51%-78%) of 542 patients.[81]

Syphilis

Syphilitic uveitis can present at any stage but is most common in secondary and late latent (after primary symptoms resolved).[83] For early syphilis, the WHO and Centers for Disease Control and Prevention (CDC) recommend a single 2.4-million-unit intramuscular benzathine penicillin dose.[84,85] For ocular syphilis, the CDC recommends daily intravenous aqueous crystalline penicillin (10-14 days)[85] and the WHO recommends weekly intramuscular benzathine penicillin (3 weeks).[84] A meta-analysis of 32 retrospective studies (670 patients) with ocular syphilis reported treatment success for improving visual acuity of 91% (95% CI, 84%-97%) with antibacterial agents alone (penicillin, ceftriaxone, tetracycline, or doxycycline), and 95% (95% CI, 91%-98%) with antibacterial agents with systemic corticosteroids.[86] Systemic corticosteroids (eg, oral prednisone [60 mg/day for 1 week then tapered]) are typically started 48 hours before antibiotics to mitigate the inflammatory response, although controlled studies are lacking.

Herpes Simplex and Varicella Zoster Viruses

There is a paucity of high-quality evidence regarding management of viral uveitis. The Infectious Uveitis Treatment Algorithm Network expert consensus (87% agreement) recommends administration of both antiviral and anti-inflammatory treatments for herpes simplex virus (HSV) and varicella zoster virus (VZV) anterior uveitis based on clinical appearance alone, without confirmatory testing. Experts advise against using topical corticosteroids alone for viral uveitis.[87,88] Antiviral treatment for HSV and VZV anterior uveitis consists of acyclovir or its prodrug, valacyclovir.[89] These medications can also be used as preventive therapy to help reduce future recurrences, which were experienced by 44.9% of patients within 10 years.[90] Although duration of prophylactic therapy should be individualized based on disease severity and recurrence history, long-term prophylaxis with oral acyclovir (400-800 mg twice daily) or valacyclovir (500 mg once daily) can be used and typically is continued for 1 year after the last episode of inflammation. The treatment of viral posterior uveitis (less common than viral anterior uveitis) combines systemic antiviral therapy with intravitreal antiviral therapy.[91]

Cytomegalovirus

No RCTs have examined treatments for cytomegalovirus (CMV)-related uveitis. A systematic review of retrospective and open-label studies of 106 patients with CMV anterior uveitis reported inflammation resolution among 90% of patients (95% CI, 74%-100%) treated with topical ganciclovir gel and 95% (95% CI, 88%-100%) with oral valganciclovir.[92] Cytomegalovirus posterior uveitis, which occurs in patients who are immunocompromised, may be treated with intravenous ganciclovir or oral valganciclovir. Patients with CMV posterior uveitis and HIV should also receive antiretroviral medications.[93,94] Foscarnet is used for CMV uveitis resistant to ganciclovir or valganciclovir.

Candidiasis

Current treatments for ocular candidiasis have not been evaluated by high-quality RCTs.[95] A trial comparing amphotericin B and fluconazole in 206 patients with candidemia reported no significant difference in symptom resolution and fungemia—79% for amphotericin B and 70% for fluconazole (P = .22).[96] The Infectious Diseases Society of America (IDSA) recommends systemic antifungal therapy for candida chorioretinitis without vitritis, with either fluconazole or voriconazole for susceptible strains of candida and amphotericin B for resistant strains.[97] For patients with macular involvement or vitritis, intravitreal amphotericin B is also recommended.[97] For patients with vitritis, vitrectomy may be considered to reduce the fungal load and excise vitreous abscesses.

Aspergillosis

For patients with uveitis due to aspergillus, IDSA recommends oral or intravenous voriconazole with either intravitreal voriconazole or intravitreal amphotericin B, along with vitrectomy.[98]

Toxoplasmosis

Systemic therapy (pyrimethamine-sulfadiazine or trimethoprim-sulfamethoxazole) is first-line treatment for ocular toxoplasmosis.[99] A systematic review of 3 RCTs (N = 227) comparing antibiotics with placebo for toxoplasma chorioretinitis reported recurrence rates over 12 to 20 months of 18.9% in the placebo group vs 4.5% in the antibiotic group (P < .001).[100] A systematic review of 2 RCTs (N = 86) comparing different systemic antibiotic regimens (trimethoprim-sulfamethoxazole vs pyrimethamine-sulfadiazine or azithromycin) reported that no antibiotic regimen was superior to others in reducing eye inflammation on ocular examination (62.8% vs 62.8%; relative risk, 1.08 [95% CI, 0.59-1.98]).[101]

Complications of Uveitis

Severe and chronic inflammation due to uveitis may cause vision-threatening complications such as cataracts (18%-49%), glaucoma (7%-56%), and macular edema (8%-10%), which can develop despite appropriate treatment (Figure 1).[55,56,102] Elevated intraocular pressure (ie, ocular hypertension) without nerve damage precedes glaucoma with optic nerve damage causing progressive vision loss. Macular edema impairs detailed central vision.

Prognosis

Infectious Uveitis

Long-term outcome data for infectious uveitis are limited. In a US study of 77 patients with infectious uveitis (most commonly, herpetic anterior uveitis and toxoplasmosis),[103] 55.8% of patients had visual acuity better than 70 letters at presentation, decreasing to 50.6% after 5 years despite treatment. In 66 patients with ocular syphilis treated with intravenous penicillin/doxycycline/ceftriaxone, 71.8% had improved visual acuity, with a mean 30-letter gain over 10 months.[104] In patients with ocular toxoplasmosis (N = 92), 21% of affected eyes had vision below 35 letters at final follow-up, with a 33.9% recurrence rate at 3 years after receipt of antibiotics.[105]

Noninfectious Uveitis

The 7-year MUST cohort of posterior uveitis (N = 177) reported that visual acuity declined annually, more in eyes with macular edema

(−1.82 vs −0.72 letters/year; $P < .01$).[106] The VISUAL III study (N = 214 with noninfectious intermediate, posterior, or panuveitis) reported that adalimumab (40 mg subcutaneously every other week) increased quiescence rates—defined as the absence of active eye inflammation—from 34% to 85% over 3 years.[107]

Limitations

This review has limitations. First, some publications may have been missed. Second, the review process lacked a systematic evaluation of evidence quality. Third, the review is limited by varying study eligibility criteria, outcome measures, and follow-up lengths, as well as lack of long-term data on the effectiveness of newer treatments.

Conclusions

Uveitis is characterized by inflammation of the uvea and primarily affects adults aged 20 to 50 years. For noninfectious anterior uveitis, corticosteroid eyedrops are first-line treatment. For posterior noninfectious uveitis, disease-modifying antirheumatic drugs are first-line therapy; biologics such as adalimumab are second-line treatment for patients with inflammation refractory to treatment. Uveitis caused by systemic infection should be treated with antimicrobials, and local or systemic steroids may be used depending on the severity of uveitis and the specific microorganism.

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Submissions: We encourage authors to submit papers for consideration as a Review. Please contact Kristin Walter, MD, at kristin.walter@jamanetwork.org.

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