

Review

Ocular Involvement in Systemic Infections: An Overview of Clinical Manifestations

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Abstract

Infectious diseases constitute a major public health concern and a leading cause of morbidity and mortality worldwide. The eye, by virtue of its rich vascularity and unique immunological microenvironment, is susceptible to involvement by a broad spectrum of bacterial, viral, fungal, and parasitic systemic infections, which may lead to diverse ocular and visual manifestations through direct pathogen invasion, immune-mediated mechanisms, or complications of therapy. Notable systemic infections with potential ocular involvement include tuberculosis; the spirochetal illnesses syphilis, Lyme disease, and leptospirosis; brucellosis; cat-scratch disease; leprosy; infective endocarditis; human immunodeficiency virus, cytomegalovirus, West Nile virus, and adenovirus infections; rubeola; dengue fever; candidiasis; cryptococcosis; aspergillosis; mucormycosis; toxoplasmosis; malaria; onchocerciasis; and cysticercosis. Ocular manifestations can serve as early diagnostic clues to underlying systemic infections, whereas, conversely, systemic features can help interpret ocular findings. Effective investigation and management of systemic infections benefit from a multidisciplinary approach, in which ophthalmologists can contribute substantially and help optimize both visual and overall health outcomes.

Keywords: ocular manifestations; ocular infections; uveitis; systemic infections; infectious diseases; multidisciplinary care

1. Introduction

Infectious diseases constitute a major public health concern worldwide, contributing substantially to morbidity, disability, and mortality, with a disproportionate impact on low- and middle-income countries [1]. In 2019, infectious syndromes accounted for approximately 13.7 million fatalities and rivaled the mortality of neoplasms and ischemic heart disease [2]. Notably, the three infections with the greatest global disease burden that year, each responsible for over 50 million disability-adjusted life years, were tuberculosis, malaria, and human immunodeficiency virus (HIV) infection [3], all of which represent recognized causes of ocular disease [4–6].

The eye, because of its rich vascularity and unique immunological microenvironment, is susceptible to involvement by a wide spectrum of systemic infections, which may give rise to variable ocular and visual manifestations arising through diverse mechanisms. Careful examination of the anterior and posterior segments of the globe as well as

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the ocular adnexa in patients with suspected systemic infections can therefore provide crucial diagnostic clues, facilitating early diagnosis and prompt initiation of treatment, which are vital for successful resolution of the infection and prevention of severe ocular sequelae [7,8].

Although prior reviews have addressed the topic of ocular manifestations of systemic infections [7–10], most were published in the previous century and do not reflect more recent advances in the field. The present review aims to provide an updated, consolidated resource that integrates current evidence, explicitly pairing ocular findings with their accompanying systemic features. In doing so, ocular findings are framed both as clues that may point to an underlying systemic infection and as features that can themselves be interpreted in light of accompanying systemic manifestations, with the goal of supporting timely diagnosis.

2. Methods

We conducted a thorough literature search across multiple databases, including MEDLINE, Web of Science, and Embase, from inception to March 2026, in order to identify articles investigating ocular manifestations that may occur throughout the clinical course of systemic infections. To this end, we utilized the terms “eye,” “ocular,” “ophthalmic,” “ophthalmologic,” “systemic infections,” “systemic infectious diseases,” “tuberculosis,” “syphilis,” “Lyme disease,” “leptospirosis,” “brucellosis,” “cat-scratch disease,” “bartonellosis,” “leprosy,” “Hansen’s disease,” “infective endocarditis,” “human immunodeficiency virus,” “HIV,” “acquired immunodeficiency syndrome,” “AIDS,” “cytomegalovirus,” “CMV,” “rubeola,” “measles,” “West Nile virus,” “dengue virus,” “adenovirus,” “candidiasis,” “cryptococcosis,” “aspergillosis,” “mucormycosis,” “toxoplasmosis,” “malaria,” “onchocerciasis,” and “cysticercosis.” To ensure comprehensive coverage of the available literature, this search of bibliographic databases was complemented by manually tracing the references (backward snowballing) and citations (forward snowballing) of pertinent studies.

Our inclusion criteria comprised peer-reviewed articles of any study design (such as original research, case reports, case series, and reviews) that reported clinical, epidemiological, diagnostic, or pathogenetic information relevant to ocular involvement in any of the systemic infections listed above. Articles were excluded if they were written in a language other than English. Among studies meeting the eligibility criteria, those that were most relevant to the aims of our review were included in our study. While we primarily focused on recently published articles, older studies with notable findings that influenced subsequent research in the field were also considered. Findings from the included studies were organized into separate sections corresponding to each major pathogen class.

3. Results

Patients with systemic infections may exhibit various ophthalmologic manifestations alongside clinical features related to other organ systems. Potential mechanisms through which ocular involvement may be observed in the context of systemic infections include direct pathogen invasion, immune-mediated mechanisms, or complications of therapy [10] (Figure 1).

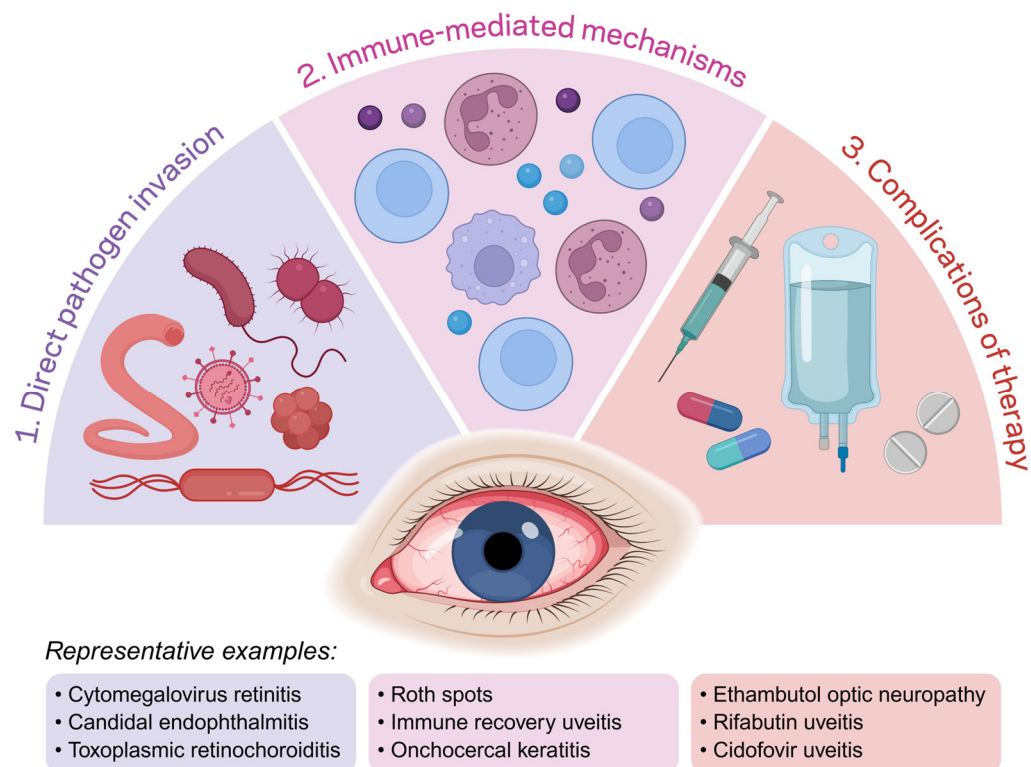


Figure 1. Pathogenic mechanisms through which ocular involvement may occur throughout the clinical course of systemic infections, along with representative clinical examples. Created in BioRender. Kanavos, T. (2026) <https://BioRender.com/yv0gd23>.

In clinical practice, the relationship between ocular and systemic findings can inform diagnostic reasoning in both directions: ophthalmological findings may serve as clues to an underlying systemic infection, while, conversely, systemic manifestations may help interpret ocular presentations (Figure 2). This bidirectional reasoning underscores the value of a multidisciplinary approach in which ophthalmologists and other specialists collaborate to ensure timely diagnosis and optimal management of patients with systemic infectious diseases.

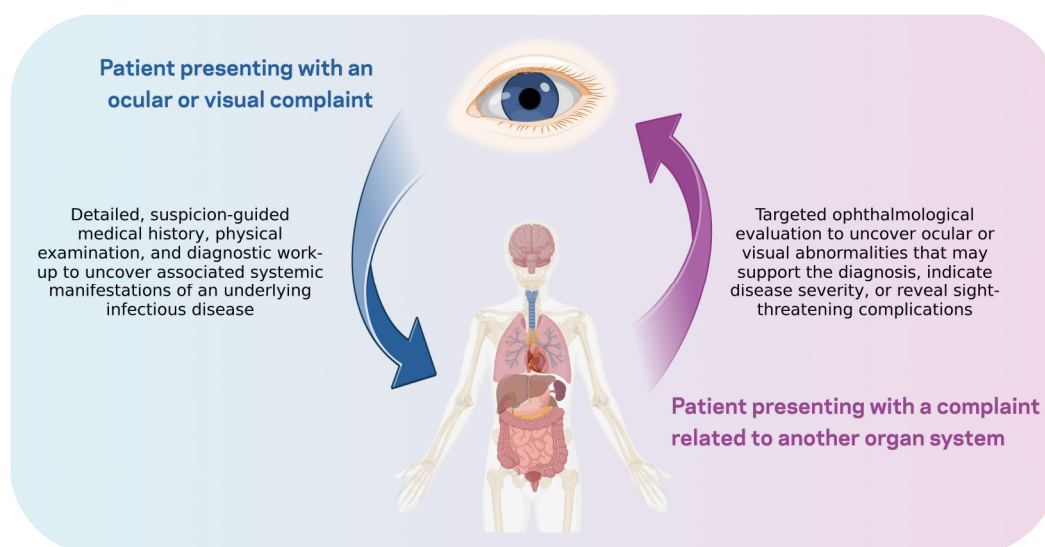


Figure 2. Bidirectional clinical reasoning in suspected systemic infections with potential ocular involvement. Ophthalmological findings may serve as clues to an underlying systemic infection, while, conversely, systemic manifestations may help interpret ocular presentations. A multidisciplinary approach is essential for timely diagnosis and optimal management of patients with systemic infectious diseases.

plinary approach involving ophthalmologists and other specialists is central to both directions of this clinical reasoning process. Created in BioRender. Kanavos, T. (2026). <https://BioRender.com/zmgntf6>.

The eye's response against, and susceptibility to, invading pathogens is shaped by its status as an immune-privileged site. Ocular immune privilege, an evolutionary adaptation that limits local immune responses to protect the delicate ocular tissues from collateral inflammatory damage and preserve vision, is mediated by several anatomical, physiological, and immunological mechanisms: blood–ocular barriers, absence of direct lymphatic drainage pathways, anti-inflammatory ocular microenvironment formed by soluble and cell-bound immunomodulatory factors, and the presence of indigenous tolerogenic antigen-presenting cells [11,12]. While this immune-privileged state is beneficial in preserving the integrity of the visual axis, it also carries an inherent biological cost, as immune responses occurring inside the eye are materially blunted [11]. Furthermore, ocular immune privilege may be permissive for latent infection, allowing the eye to act as a pathogen reservoir [13].

Systemic infectious diseases with potential ocular involvement can be caused by bacterial, viral, fungal, and parasitic pathogens. Notable examples include tuberculosis (TB); the spirochetal illnesses syphilis, Lyme disease, and leptospirosis; brucellosis; cat-scratch disease; leprosy; infective endocarditis; HIV, cytomegalovirus (CMV), West Nile virus, and adenovirus infections; rubeola; dengue fever; candidiasis; cryptococcosis; aspergillosis; mucormycosis; toxoplasmosis; malaria; onchocerciasis; and cysticercosis. Table 1 summarizes selected systemic infections with potential ocular involvement and details their characteristic ocular and systemic manifestations, providing an overview of clinical features that may guide the diagnostic approach. Each of these infections is described individually below.

Table 1. Summary of the manifestations of systemic infections that may involve the eye.

Systemic Infection	Ocular Manifestations	Other Manifestations
<i>Bacterial</i>		
Tuberculosis	Palpebral abscess, mucopurulent conjunctivitis, scleritis, phlyctenulosis, interstitial keratitis, uveitis, retinal tubercles, subretinal abscesses, focal or diffuse retinitis, retinal vasculitis, optic nerve tubercles, optic neuritis, neuroretinitis, papillitis, papilledema, and drug-induced toxic optic neuropathy	Fever, night sweats, weight loss; pulmonary, skeletal, genitourinary, gastrointestinal, and miliary tuberculosis; and tuberculous lymphadenitis, meningitis, pleuritis, pericarditis, and peritonitis
Syphilis	Keratitis, uveitis, retinitis, retinal vasculitis, optic neuropathy, and Argyll Robertson pupil	Chancres, lymphadenopathy, maculopapular rash, condylomata lata, mucous patches, alopecia, aortitis, aortic aneurysm, aortic regurgitation, coronary ostial occlusion, gummas, meningitis, stroke, tabes dorsalis, and general paresis
Lyme disease	Conjunctivitis, keratitis, episcleritis, scleritis, uveitis, neuroretinitis, optic neuritis and perineuritis, papilledema, orbital myositis, involvement of cranial nerves III, IV, V, VI, VII, and VIII, Horner syndrome, and Argyll Robertson pupil	Erythema migrans, borrelial lymphocytoma, acrodermatitis chronica atrophicans, lymphadenopathy, meningitis, radiculoneuritis, arthritis, atrioventricular conduction disturbances, acute myopericarditis, and cardiomyopathy
Leptospirosis	Conjunctival suffusion and uveitis	High remittent fever, intense headache, muscle pain and tenderness predominantly in the calves and lower back, rash, lymphadenopathy, cough, hepatosplenomegaly, abdominal pain, nausea/vomiting, diarrhea, aseptic meningitis, acute kidney injury, alveolar hemorrhage, acute acalculous cholecystitis, jaundice, bleeding diathesis, hypotension, and arrhythmias

Brucellosis	Uveitis, conjunctivitis, scleritis, episcleritis, and dacryoadenitis	Undulant fever, profuse night sweats occasionally with a characteristic odor that resembles mold or wet hay, weight loss, osteomyelitis, septic arthritis, lymphadenopathy, hepatosplenomegaly, granulomatous hepatitis, orchiepididymitis, meningoencephalitis, and endocarditis
Infective endocarditis	Roth spots, conjunctival hemorrhages, retinal artery occlusion, chorioretinitis, endophthalmitis, and cortical blindness	Fever, Osler nodes, Janeway lesions, splinter hemorrhages, murmurs, conduction abnormalities, heart failure, glomerulonephritis, septic infarcts, abscesses, and mycotic aneurysms
<i>Viral</i>		
HIV infection	HIV retinal microvasculopathy, opportunistic ocular infections, ocular tumors, neuro-ophthalmologic disorders, immune recovery uveitis, and drug-induced uveitis	Mononucleosis syndrome; numerous non-ocular opportunistic infections, including <i>Pneumocystis jirovecii</i> pneumonia, candidiasis, cryptococcosis, histoplasmosis, coccidioidomycosis, toxoplasmosis, CMV infection, <i>Mycobacterium avium</i> complex infection, and tuberculosis; and non-ocular malignancies, such as Kaposi sarcoma, PCNSL, and cervical cancer
CMV infection	Retinitis, involvement of the macula and optic nerve, and rhegmatogenous retinal detachment	Mononucleosis syndrome, encephalitis, pneumonitis, hepatitis, esophagitis, and colitis
<i>Fungal</i>		
Candidiasis	Retinochoroiditis and endophthalmitis	Candidemia, meningitis, endocarditis, osteomyelitis, septic arthritis, and hepatosplenic candidiasis
Cryptococcosis	Papilledema, optic atrophy, cranial nerve II, III, and VI palsies, chorioretinitis, vitritis, endophthalmitis, and granulomatous conjunctivitis	Pneumonia, meningoencephalitis, cutaneous lesions, osteomyelitis, septic arthritis, prostatitis, and peritonitis
<i>Parasitic</i>		
Toxoplasmosis	Retinochoroiditis commonly accompanied by vitritis or anterior uveitis, scleritis, glaucoma, cataract, band keratopathy, cystoid macular edema, choroidal neovascularization, retinal vascular occlusion, epiretinal membrane formation, retinal detachment, and optic nerve atrophy	Mononucleosis syndrome, encephalitis, pneumonitis, myocarditis, hepatitis, and myositis
Onchocerciasis	Punctate or sclerosing keratitis, torpid iritis with pear-shaped iris deformity, optic neuropathy, and chorioretinitis	Papular and lichenified onchodermatitis, skin atrophy, depigmentation, subcutaneous onchocercomata over bony prominences, epilepsy, and nodding syndrome

Abbreviations: CMV, cytomegalovirus; HIV, human immunodeficiency virus; PCNSL, primary central nervous system lymphoma.

3.1. Bacterial Infections

3.1.1. Tuberculosis

TB is a multisystemic infectious disease caused by a group of closely related mycobacteria collectively known as the *Mycobacterium tuberculosis* complex [14]. The disease constitutes a significant public health concern in many low- and middle-income countries and represents the leading cause of death from a single infectious agent as well as the most common cause of death among patients with HIV [15,16]. Transmission occurs mainly via aerosols released by affected individuals [17]. Although the lungs are most frequently involved, TB can affect virtually any organ in the body, including the eye [17,18]. Owing to its protean clinical features and capacity to involve any organ system, TB has been referred to as a “great masquerader” [19], although this term has historically and most famously been applied to syphilis [20], which is presented next in this article.

Ocular TB can involve any part of the eye and may occur with or without evidence of pulmonary or other extrapulmonary disease [21]. Therefore, it should be included in the differential diagnosis of any form of intraocular inflammation, particularly in the presence of risk factors for TB, such as immunosuppression, poor living conditions, and con-

tact with infected individuals [4,22]. This rare condition can manifest in numerous different ways and constitutes a major diagnostic challenge due to its diverse clinical features, the mixed ocular tissue involvement, the lack of universally accepted diagnostic criteria, and the absence of a single gold-standard diagnostic test [23,24]. Based on the mechanism of infection, ocular TB can be classified as primary, where the eye serves as the initial port of entry of the mycobacteria into the body, or secondary, which results from hematogenous spread from a distant site of infection. Primary disease can affect the eyelid, conjunctiva, sclera, and cornea. It may present as palpebral abscess, mucopurulent conjunctivitis, scleritis, phlyctenulosis, and interstitial keratitis. In contrast, secondary disease can involve the uveal tract, retina, and optic nerve. The uvea, particularly the choroid, is most commonly affected, likely due to its rich blood supply and the preference of *M. tuberculosis* for highly oxygenated tissues [4,25,26]. The proportion of TB as the etiology of uveitis ranges from 0.5% in the United States [27] to more than 10% in endemic regions [28,29]. Tuberculous uveitis can be anterior, intermediate, posterior, which is the predominant form, or panuveitis [4,25,26]. Retinal lesions almost always arise from the extension of choroidal involvement and may include tubercles, subretinal abscesses, focal or diffuse retinitis, and retinal vasculitis [4,21,25,26]. Optic nerve manifestations comprise tubercles, optic neuritis, neuroretinitis, papillitis, and papilledema [4,21,25]. In addition, toxic optic neuropathy can be observed as an adverse effect of antitubercular medications [30].

Microbiological confirmation of ocular TB relies on the direct demonstration of the culprit organism through aqueous or vitreous sampling. Available diagnostic techniques include nucleic acid amplification testing, microscopic visualization of acid-fast bacilli using Ziehl–Neelsen staining, and culture. However, the definitive identification of *M. tuberculosis* is challenging due to its low yield and the small size of the obtained ocular specimens [23,24]. Therefore, diagnosis is often presumed on the basis of suggestive ocular findings in combination with a positive tuberculin skin test or interferon- γ release assay, chest radiograph findings consistent with pulmonary TB, and/or evidence compatible with systemic TB in the absence of an alternative underlying disease [31].

Albeit rare, ocular TB should not be underestimated, given its potential vision-threatening nature without proper diagnosis and treatment [4,23]. It can lead to moderate to severe visual impairment in affected individuals, especially in cases with posterior uveitis or panuveitis, while proper management can result in significant visual recovery [32]. Timely recognition and prompt initiation of antitubercular therapy may be sight-saving for patients with ocular TB [25]. However, clinicians should be aware that, even after clinical inactivity is achieved following treatment, relapse occurs in roughly one-third of patients, most often manifesting as anterior uveitis. Poor response to treatment for the initial uveitis episode, defined as persistent ocular inflammation beyond six months of therapy, has been identified as a significant predictor of relapse. These findings underscore the importance of long-term follow-up after the resolution of ocular TB, particularly for poor responders to therapy [33].

3.1.2. Syphilis

Syphilis is a sexually and vertically transmitted systemic disease caused by the spirochete *Treponema pallidum*. The natural history of the untreated disease includes four distinct stages, namely, primary, secondary, latent, and tertiary syphilis [34,35]. Ocular involvement can be observed at any stage of the disease and any structure of the eye can be affected [36]. Frequent ocular manifestations include interstitial keratitis, anterior, intermediate, and posterior uveitis as well as panuveitis, retinitis, retinal vasculitis, and optic neuropathy [37]. In addition, patients with neurosyphilis may present with Argyll Robertson pupil, which refers to an irregular and small pupil with light-near dissociation. In other words, Argyll Robertson pupil constricts poorly to light but briskly to accommoda-

tion [38]. The pathophysiologic mechanism responsible for Argyll Robertson pupil remains unclear although it is believed that the condition is primarily associated with damage to the olivary pretectal nucleus of the midbrain (Figure 3) [39]. Although Argyll Robertson pupil is strongly indicative of neurosyphilis, it is not pathognomonic as it can also be attributed to diabetes mellitus, multiple sclerosis, Wernicke encephalopathy, neurosarcoidosis, and Lyme disease [40]. It has been demonstrated that ocular syphilis can result in poor outcomes if detected late and may lead to blindness if left untreated, while early recognition and treatment initiation are vital to prevent permanent visual loss [41]. Therefore, ocular syphilis should always be considered in the differential diagnosis of most inflammatory eye conditions [36]. According to current Centers for Disease Control and Prevention guidelines, suspected ocular syphilis warrants immediate referral to and management in collaboration with an ophthalmologist. All patients with ocular symptoms and reactive syphilis serology require a complete ophthalmological examination, including cranial nerve assessment. In the presence of cranial nerve dysfunction, a cerebrospinal fluid (CSF) analysis is needed. CSF evaluation may also be helpful in patients with ocular symptoms and reactive syphilis serology without ocular findings on examination. Ocular syphilis should be treated similarly to neurosyphilis (aqueous crystalline penicillin G administered intravenously), even if a CSF analysis is normal [42].

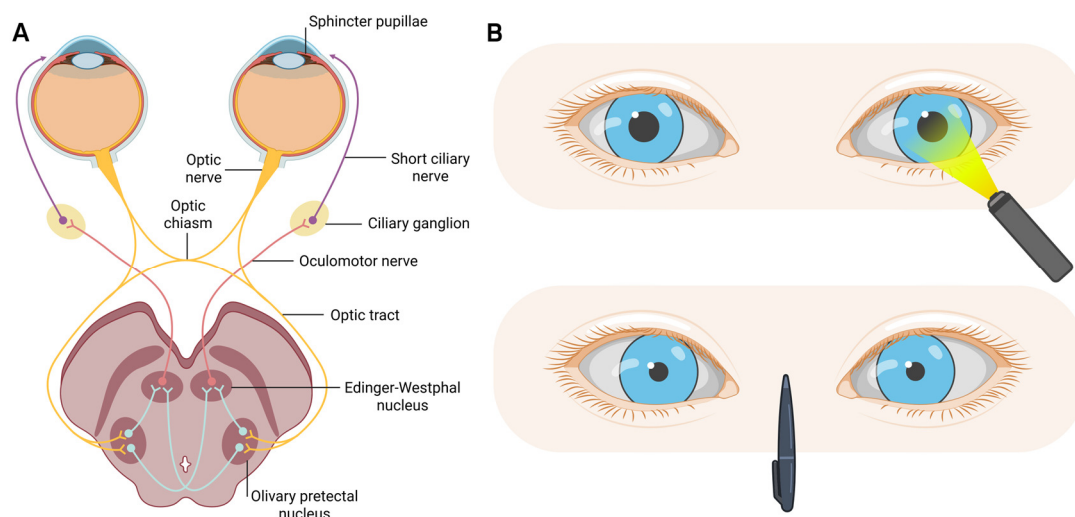


Figure 3. Schematic illustration of the pupillary light reflex pathway alongside clinical findings in Argyll Robertson pupil. The olivary pretectal nucleus of the midbrain is a key component of the pupillary light reflex pathway, where it receives light signals directly from retinal ganglion cells and relays them to the Edinger–Westphal nuclei. Argyll Robertson pupil is presumably caused by damage to the olivary pretectal nucleus, which interrupts the pupillary light reflex pathway while sparing the accommodation reflex pathway (A). As a result, Argyll Robertson pupil responds poorly to light but constricts briskly during accommodation, a condition described as light–near dissociation (B). Created in BioRender. Kanavos, T. (2026). <https://BioRender.com/upaqu74>.

3.1.3. Lyme Disease

Lyme disease constitutes a systemic illness predominantly caused by the spirochete *Borrelia burgdorferi* in North America and *Borrelia afzelii* or *Borrelia garinii* in Europe and Asia [43]. It is transmitted by the bite of ticks of the genus *Ixodes* and represents the most frequent vector-borne disease in the northern hemisphere [44]. However, it is usual for affected individuals to not recall the preceding tick bite [45].

Lyme disease manifests with various symptoms and signs and displays a variable and complex clinical course [10]. Ocular manifestations include follicular conjunctivitis, keratitis, episcleritis, scleritis, anterior, intermediate, and posterior uveitis as well as

panuveitis, neuroretinitis, optic neuritis and perineuritis, papilledema, and orbital myositis [46–48]. In addition, ophthalmologic symptoms and signs may also arise from the involvement of the oculomotor, trochlear, trigeminal, abducent, facial, and vestibulocochlear nerves as well as from Horner syndrome and Argyll Robertson pupil [40,45,49]. In fact, peripheral facial palsy is the most frequent manifestation of Lyme neuroborreliosis in the United States [50]. Although ocular involvement is uncommon in Lyme disease, clinicians need to remain aware of this possibility [48]. The criteria for attributing the above ophthalmologic problems to Lyme disease include the presence of other manifestations associated with the illness, such as fever, erythema migrans, borrelial lymphocytoma, acrodermatitis chronica atrophicans, meningitis, radiculoneuritis, arthritis, and carditis, occurrence in individuals who live in, or have recently traveled to, endemic areas, positive serology, and absence of other conditions that could explain the findings [44,48]. It is suggested that physicians who encounter patients with peripheral facial palsy of acute onset, particularly bilateral, should actively seek a history of a rash consistent with erythema migrans or a febrile illness in the preceding weeks, which are useful clues pointing toward Lyme disease [50].

3.1.4. Leptospirosis

Leptospirosis is a zoonotic systemic disease typically caused by the spirochete *Leptospira interrogans*, which is transmitted to humans through either direct contact with infected animals or indirect contact via urine-contaminated soil or water [51]. A wide range of domestic and wild mammals serve as reservoir hosts, with rodents, particularly rats, being the most important, although dogs and livestock can also maintain and shed the microorganism [51,52]. The spectrum of human disease is extremely broad, ranging from subclinical cases to severe life-threatening infections [52]. The disease can manifest in two distinct forms, namely, anicteric leptospirosis, which is a mild and self-limited condition that constitutes approximately 90% of cases, and icteric leptospirosis or Weil's disease, which is potentially lethal and accounts for roughly 10% of cases [53]. Leptospirosis has been classically described as a biphasic illness and its clinical course is divided into an acute or leptospiremic phase and an immune or leptospiruric phase [54]. Ocular involvement can occur in both phases [55]. Conjunctival suffusion, which refers to the dilation of conjunctival blood vessels causing erythema without purulent discharge, occurs in approximately 50% of cases and is considered a hallmark of the acute phase, which is also characterized by high remittent fever, intense headache, and muscle pain and tenderness predominantly in the calves and lower back [54,56]. In addition, uveitis can frequently be observed during the immune phase of the disease. Its most common presentation is either anterior uveitis or panuveitis and its prognosis is generally favorable, even in cases with severe inflammation [55]. It is worth mentioning that aseptic meningitis is the principal feature of the immune phase [57]. Based on the above, when encountering patients with conjunctival suffusion or uveitis, clinicians should consider the likelihood of leptospirosis and search for other characteristic symptoms and signs of the disease as well as a history of occupational or recreational exposure to potentially infected animals or an environment that could be contaminated with their urine.

3.1.5. Brucellosis

Brucellosis is a zoonotic systemic disease caused by bacteria of the genus *Brucella*, most commonly *B. melitensis*, which is typically transmitted to humans through either direct contact with infected animals or consumption of unpasteurized dairy products. It exhibits a wide range of clinical manifestations and can affect multiple organ systems throughout the body [58]. Ocular involvement is observed in approximately 25% of patients with brucellosis [59–61]. The most common ocular manifestations are uveitis and

conjunctivitis, while scleritis, episcleritis, and dacryoadenitis occur less frequently [59–62]. It has been demonstrated that patients with brucellosis and ocular involvement tend to be older than those without ophthalmic manifestations, are more likely to experience weight loss and spondylodiscitis, and present higher erythrocyte sedimentation rates and serum lactate dehydrogenase levels [59]. The suspicion of brucellosis in a patient with ocular inflammation is heightened by the presence of other symptoms and signs closely associated with the disease, such as undulant fever, profuse night sweats occasionally with a characteristic odor that resembles mold or wet hay, weight loss, low back pain, and arthralgia [63]. An overlooked or late diagnosis of brucellosis with ophthalmic involvement may lead to the development of severe sequelae and even vision loss [62,64]. Therefore, brucellosis should always be part of the differential diagnosis of eye inflammations, especially in endemic regions [60]. Furthermore, it is recommended that all patients diagnosed with brucellosis should undergo a routine ophthalmologic examination [62].

3.1.6. Infective Endocarditis

Infective endocarditis refers to an infection of the endocardial surface of the heart, typically involving the cardiac valves or a cardiac implantable electronic device [65]. The prompt identification of the disease is essential for improving outcomes, and fundoscopy is considered a standard component of the initial workup of patients suspected of infective endocarditis [66]. Classical ocular manifestations of this infection include Roth spots, conjunctival hemorrhages, retinal artery occlusion, chorioretinitis, and endophthalmitis [67–69]. Roth spots constitute an immunological phenomenon caused by immune complex deposition and appear as retinal hemorrhages with a pale center [67,70]. They are unspecific and present in only 2–9% of the patients [66,71]. Conjunctival hemorrhages represent a vascular phenomenon attributed to septic microemboli and are observed in roughly 5% of cases [70,71]. Another potential manifestation of infective endocarditis is cortical blindness caused by bilateral occipital lobe infarctions due to septic embolization from endocardial vegetations. Cortical blindness is characterized by intact pupillary light reflexes, normal fundoscopy, and, infrequently, denial of visual loss, which is referred to as Anton syndrome [72]. When infective endocarditis is suspected based on the observation of the above ophthalmic problems, clinicians should perform a thorough physical examination and investigate for other signs associated with the disease, such as fever, murmurs, Osler nodes, Janeway lesions, and splinter hemorrhages [65,70].

Endogenous endophthalmitis, which develops following hematogenous spread of microorganisms from a distant primary focus of infection to the eye, is not confined to infective endocarditis. More broadly, it can complicate purulent infections at other extra-ocular sites through hematogenous seeding of the eye. A noteworthy example is pyogenic liver abscess caused by *Klebsiella pneumoniae*, which has been increasingly recognized as a source of endogenous endophthalmitis, particularly in patients with diabetes mellitus and in East and Southeast Asian populations [73].

3.1.7. Miscellaneous Bacterial Infections

Other notable systemic bacterial infections with potential ocular involvement include cat-scratch disease caused by *Bartonella henselae*, which may manifest with Parinaud oculoglandular syndrome, neuroretinitis, multifocal retinitis, uveitis, and retinal artery occlusion [74]; and leprosy caused by *Mycobacterium leprae*, which can lead to madarosis, trichiasis, lagophthalmos, and corneal anesthesia [75].

3.2. Viral Infections

3.2.1. Human Immunodeficiency Virus Infection

HIV infection is a progressive disease that gradually depletes CD4⁺ T cells and eventually results in immunosuppression [76]. The clinical course of the infection includes three stages, namely, the acute stage, which is also named primary HIV infection or acute retroviral syndrome, the chronic stage, which is also known as asymptomatic HIV infection or clinical latency stage, and finally acquired immunodeficiency syndrome (AIDS) [77,78]. Ophthalmic manifestations are common in individuals infected by HIV, affecting 50–75% of the patients [79], while most of them occur in the stage of AIDS [5]. Ocular and visual abnormalities associated with HIV infection can be classified as retinal microvasculopathy, opportunistic infections, related neoplasms, neuro-ophthalmologic disorders, immune recovery uveitis, and adverse effects of medications (Figure 4).

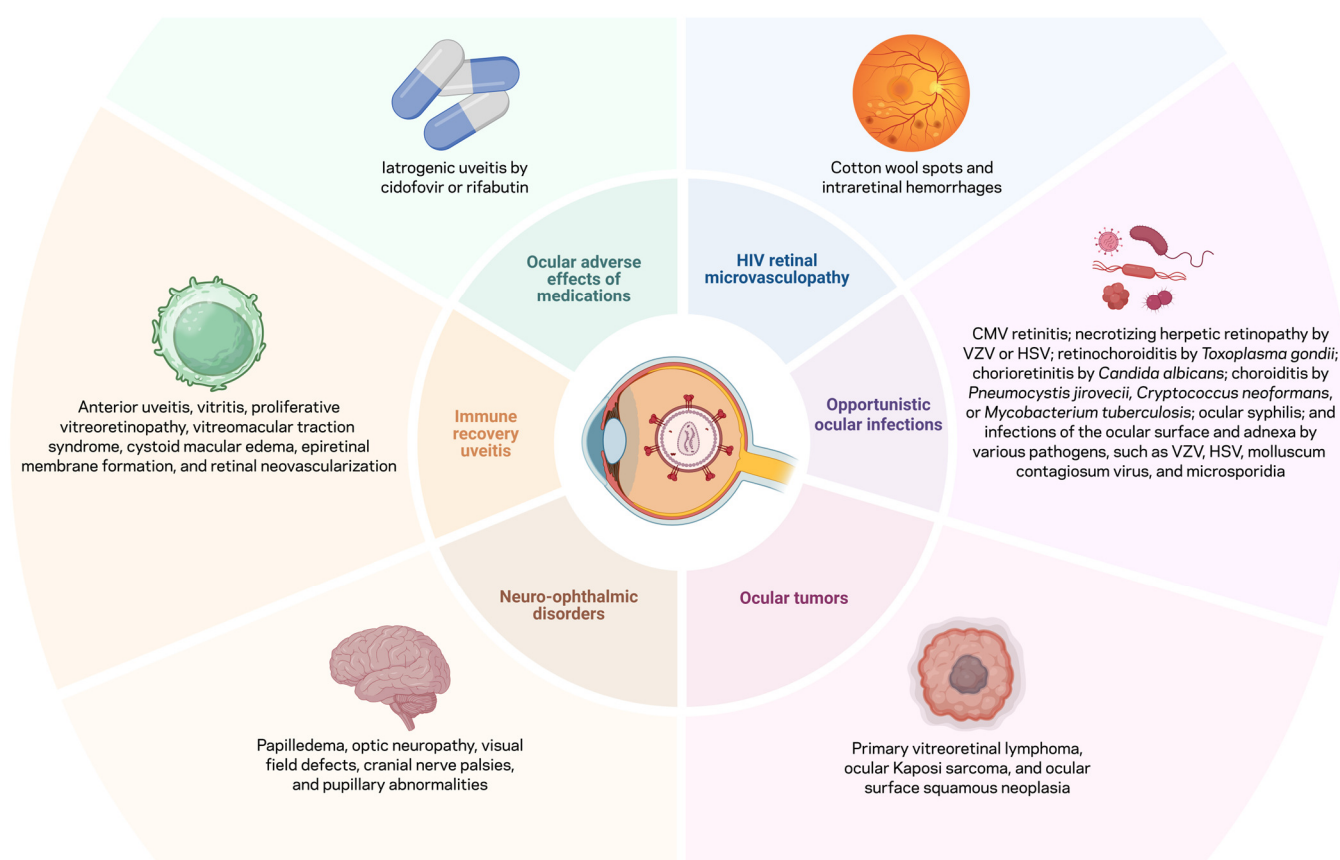


Figure 4. Ocular and visual manifestations that can occur in the context of human immunodeficiency virus infection. Created in BioRender. Kanavos, T. (2026). <https://BioRender.com/j0u9gvd>.

The most frequent HIV-related ocular disorder is HIV retinal microvasculopathy or HIV retinopathy [80], which mainly presents with cotton-wool spots although intraretinal hemorrhages, microaneurysms, and ischemic maculopathy may also be observed less frequently. The latter, which occurs in roughly 3% of patients with HIV retinopathy, can cause sudden vision loss and is characterized by dot and blot hemorrhages and perifoveal cotton-wool spots. The pathogenesis of HIV retinal microvasculopathy remains unclear; however, it is speculated to be multifactorial, and hypotheses include direct infection of the retinal vascular endothelium by the virus, immune complex deposition, increased plasma viscosity caused by the virus, and augmented rigidity of circulating neutrophils [5].

Ocular opportunistic infections have been a significant concern in individuals with HIV since the onset of the epidemic. However, improvements in modern antiretroviral therapy have resulted in a notable decline in their incidence [81,82]. CMV retinitis affected approximately one-third of patients with AIDS in the preantiretroviral era. Although its infection rate has decreased by 75% since then, CMV retinitis remains the most common ocular opportunistic infection associated with AIDS [5]. Other opportunistic infections that affect the eye and may occur in patients with HIV include necrotizing herpetic retinopathy by varicella-zoster virus (VZV) or herpes simplex virus (HSV), retinochoroiditis by *Toxoplasma gondii*, chorioretinitis by *Candida albicans*, choroiditis by *Pneumocystis jirovecii*, *Cryptococcus neoformans*, or *Mycobacterium tuberculosis*, ocular syphilis, and infections of the ocular surface and adnexa by various pathogens, such as VZV, HSV, molluscum contagiosum virus, and microsporidia [5,81,83,84]. Interestingly, ocular syphilis represents a strong predictor of HIV coinfection, with over 50% of cases leading to initial HIV diagnosis [5].

Patients with HIV face an increased risk of certain ocular malignancies, including lymphoma, Kaposi sarcoma, and squamous cell carcinoma (Table 2) [85]. Primary vitreoretinal lymphoma (PVRL) represents an intraocular subset of primary central nervous system (CNS) lymphoma (PCNSL), which usually masquerades as an intermediate or posterior uveitis. Floaters and blurred vision constitute the most common symptoms, while eye redness and pain are reported less frequently. HIV-related cases occur in patients who are relatively young and typically severely immunocompromised [86]. Kaposi sarcoma is a low-grade vascular malignancy that is caused by the oncogenic human herpesvirus 8 (HHV8) and occurs in the skin and mucous membranes. When the eye is affected, it can develop on either the conjunctiva, most commonly in the inferior fornix, or the eyelid. Lesions typically appear as flat or elevated, fleshy, mobile masses of bright red, dark brown, or violaceous color with or without hemorrhage [87]. Conjunctival lesions may mimic benign subconjunctival hemorrhage, while palpebral masses may resemble chalazia [83]. Patients with ocular Kaposi sarcoma frequently present with foreign body sensation, irritation, or epiphora [87]. Patients with HIV are additionally predisposed to ocular surface squamous neoplasia (OSSN). Specifically, HIV increases the risk for its development by nearly eight times, while infection from cutaneous subtypes of human papillomavirus (HPV) is also considered a risk factor for this tumor [88]. OSSN typically manifests as a nodular, noduloulcerative, papillary, gelatinous, leukoplakic, or placoid mass on the nasal limbus and can be mistaken for a pterygium, while patients usually complain of eye irritation or pain and occasionally visual impairment [89,90].

Table 2. Overview of the clinical characteristics of ocular tumors associated with human immunodeficiency virus infection.

Ocular Tumor	Location	Symptoms & Signs	Clinical Mimic
Primary vitreoretinal lymphoma	Vitreous body and/or retina	Floaters, blurred vision, eye redness and pain	Intermediate or posterior uveitis
Kaposi sarcoma	Inferior conjunctival fornix or eyelid	Foreign body sensation, irritation, epiphora; flat or elevated, fleshy, mobile mass of bright red, dark brown, or violaceous color with or without hemorrhage	Benign subconjunctival hemorrhage and chalazion for conjunctival and palpebral lesions, respectively
Ocular surface squamous neoplasia	Nasal limbus	Eye irritation or pain, visual impairment; nodular, noduloulcerative, papillary, gelatinous, leukoplakic, or placoid mass	Pterygium

Neuro-ophthalmologic manifestations have been reported to occur in individuals infected by HIV with or without AIDS. They are estimated to affect 2–8% of patients with

AIDS and 60% of neurologically symptomatic patients with HIV. CNS opportunistic infections, including toxoplasmosis and cryptococcosis, and malignancies, such as PCNSL, as well as the direct effects of the virus itself on the CNS are considered responsible for these abnormalities. Neuro-ophthalmologic disorders in patients with HIV include papilledema, optic neuropathy, visual-field defects, cranial nerve palsies, and pupillary abnormalities [91]. It is essential for clinicians to be able to recognize these disturbances as their identification may lead to the discovery of underlying infectious or neoplastic diseases amenable to treatment [92].

Immune reconstitution inflammatory syndrome (IRIS) is a collection of disorders that can occur in patients with HIV after the initiation of antiretroviral treatment, characterized by exaggerated inflammatory responses to various pathogens as a result of restored immunity [5]. It is estimated that 10–25% of patients under antiretroviral treatment experience this phenomenon [93]. Immune recovery uveitis (IRU) is the ocular manifestation of IRIS, most frequently observed after the restoration of immunity to CMV [5]. It has been reported to occur in approximately 17% of patients with HIV 4 to 30 months after the initiation of antiretroviral therapy [94]. A rapid rise in CD4⁺ T-cell count following antiretroviral treatment and prior use of cidofovir are recognized as significant risk factors for IRU [95]. Consistent with this, Dalessandro et al. [96] described an HIV-positive patient who developed IRU in close temporal association with a CD4⁺ T-cell rebound from 177 to 561 cells/mm³ after 5 weeks of highly active antiretroviral therapy. Patients with this disorder typically present with floaters and a decline in visual acuity. Potential clinical findings of IRU include anterior uveitis, vitritis, proliferative vitreoretinopathy, vitreomacular traction syndrome, cystoid macular edema, epiretinal membrane formation, and retinal neovascularization [97].

Medications used for the management of opportunistic infections in individuals with HIV are considered established causes of drug-induced uveitis in these patients. Cidofovir, an antiviral agent recommended for the treatment of CMV retinitis in patients with HIV, has been reported to cause anterior uveitis in 14–26% of patients when injected intravitreally and in 26–59% of them when administered intravenously. Cidofovir-induced uveitis is usually an anterior granulomatous uveitis that can be either unilateral or bilateral and is often accompanied by posterior synechiae and ocular hypotony. Furthermore, rifabutin, a commonly used antibiotic in HIV patients for the prevention and treatment of *Mycobacterium avium* complex infections and the management of TB, can also rarely cause uveitis as a side effect. The risk of uveitis due to the administration of rifabutin appears to be higher in cases of increased dosage, prolonged treatment, low body weight, cachexia, and concurrent therapy with fluconazole or macrolides, which can lead to the accumulation of rifabutin in the serum by inhibiting cytochrome P-450 enzymes. Rifabutin-induced uveitis is typically an anterior nongranulomatous uveitis that can be either unilateral or bilateral and is frequently associated with hypopyon. Physicians should be aware of the above two entities and educate patients receiving cidofovir or rifabutin to promptly report any symptoms associated with uveitis [98].

3.2.2. Cytomegalovirus Infection

CMV infection is a common disease across all age groups and presents with diverse manifestations depending on the immune status of the host [99,100]. The illness in immunocompetent individuals is usually subclinical or manifests with a mononucleosis syndrome [99]. In neonates and immunocompromised patients, however, it can lead to devastating effects [101].

CMV infection in immunocompromised patients can lead to a broad range of severe manifestations, including retinitis, encephalitis, pneumonitis, hepatitis, esophagitis, and colitis [100]. CMV retinitis primarily occurs in individuals with AIDS, recipients of bone

marrow and solid organ transplants, patients with cancer, people with primary immunodeficiencies, and those receiving systemic immunosuppressive therapy or intravitreal corticosteroid injections [101]. Patients may be asymptomatic or experience blurred vision, visual-field defects, and floaters [102]. Three main forms of CMV retinitis have been described, namely, the hemorrhagic or fulminant, the granular or indolent, and the perivascular variant. The hemorrhagic form manifests with dense white necrotic areas along with retinal hemorrhages, which give rise to a distinctive “pizza-pie” or “cottage-cheese-and-ketchup” appearance, and exhibits a rapid progression. The granular type is characterized by small white granular lesions in the peripheral fundus, which are rarely accompanied by hemorrhage or vasculitis and progress slowly via fusion and enlargement. The perivascular form is uncommon and presents with frosted branch angiitis, in which retinal vessels become dendritic and sheathed with perivascular exudation [103,104]. Major vision-threatening complications of CMV retinitis include involvement of the macula and optic nerve, rhegmatogenous retinal detachment, and IRU [104,105]. Extensive retinal surface involvement and bilateralism, both of which indicate advanced disease, have been found to be risk factors for the development of retinal detachment, emphasizing the importance of early diagnosis and treatment [106,107]. According to current international consensus guidelines, the clinical diagnosis of CMV retinitis relies on the identification of characteristic fundus findings in a patient with a compatible immunocompromised background, while intraocular fluid testing for viral DNA through polymerase chain reaction is indicated when confirmation is necessary. Importantly, in immunosuppressed individuals in whom CMV retinitis is highly suspected, particularly when the macula is involved, more aggressive management should be considered, potentially including the initiation of empirical anti-CMV therapy [108].

Congenital CMV infection represents the most frequent intrauterine infection and the leading cause of nongenetic sensorineural hearing loss in children [109]. It may lead to fetal or neonatal death, intrauterine growth restriction, and preterm birth [110]. Roughly 10% of congenitally infected neonates present with clinically obvious abnormalities at birth, such as jaundice, petechiae, microcephaly, hepatosplenomegaly, seizures, hearing loss, and several ophthalmologic manifestations. The latter include chorioretinitis, retinal scars, optic nerve atrophy, strabismus, nystagmus, and cortical visual impairment [111]. Approximately 40–60% of symptomatic congenital CMV infection survivors experience permanent sequelae as a result of the disease, most commonly sensorineural hearing loss [112]. In addition, about 15% of neonates who are initially asymptomatic develop long-term neurological sequelae before reaching five years of age [110]. A study has shown that symptomatic patients with congenital CMV infection face more ocular sequelae and worse visual outcomes compared to asymptomatic ones [113].

3.2.3. Miscellaneous Viral Infections

Other noteworthy systemic viral illnesses with ocular clinical features include rubella, which can cause conjunctivitis and xerophthalmia [114]; West Nile virus infection, which may lead to multifocal chorioretinitis with a typical linear clustering of lesions [115]; dengue fever, which can manifest with maculopathy, retinal hemorrhage, and conjunctival petechiae [116]; and adenovirus infection, which is associated with ocular surface (the most common cause of viral conjunctivitis [117]), respiratory, gastrointestinal, genitourinary, and neurological involvement [118].

3.3. Fungal Infections

3.3.1. Candidiasis

Candidiasis constitutes a fungal infection caused by yeasts of the genus *Candida*. The clinical manifestations of *Candida* species range from superficial mucocutaneous processes

to invasive candidiasis, which encompasses both candidemia and deep-seated infections [119,120]. Risk factors for candidemia include immunocompromised status, prolonged broad-spectrum antibiotic use, total parenteral nutrition, indwelling central venous catheters, recent abdominal surgery, diabetes mellitus, and malignancy [121,122]. Ocular candidiasis is a major, potentially sight-threatening complication of candidemia that arises through hematogenous dissemination to the eye in approximately 10.7% of candidemic patients [123–125]. The condition is most commonly caused by *C. albicans*, followed by *C. glabrata*, *C. tropicalis*, and *C. parapsilosis* in descending frequency order (Table 3) [124,126–130]. Isolation of *C. albicans* as the etiological agent, higher serum β -D-glucan values, longer fungemia duration, unremoved central venous catheters, female sex, and presence of, or inability to articulate, visual symptoms have been identified as risk factors for ocular involvement in patients with candidemia [126–131]. The stronger propensity of *C. albicans* to cause ocular candidiasis could be attributable to its enhanced invasive capacity, the induction of inflammatory mediators, and the recruitment of neutrophils and inflammatory monocytes [126].

Table 3. Distribution of *Candida* species as etiologic agents in ocular candidiasis based on pooled data derived from six clinical series [124,126–130].

Etiologic Agent	Pooled Relative Frequency ¹
<i>C. albicans</i>	68.7%
<i>C. glabrata</i>	8.1%
<i>C. tropicalis</i>	7.6%
<i>C. parapsilosis</i>	6.6%
Other or mixed	9.1%

¹ Calculated by summing the number of cases attributed to each *Candida* species across the six clinical series and dividing by the total number of cases reported across the series.

Ocular candidiasis can manifest as chorioretinitis, which only involves the choroid and retina, or endophthalmitis, which is characterized by fungal infiltration of the vitreous chamber [125,132]. The hallmark of candidal chorioretinitis is the presence of white, creamy, fluffy lesions at the level of the choroid and retina. In contrast, candidal endophthalmitis exhibits more extensive ocular involvement with seeding of the vitreous body, producing the clinical appearance of “intravitreal fluff balls” or a “string of pearls” [133,134]. Both candidal chorioretinitis and endophthalmitis carry substantial risks of vision loss and morbidity. Effective management hinges on timely recognition and targeted therapy, which remain challenging in clinical practice [132]. Notably, ocular candidiasis is frequently asymptomatic, while, in many patients, symptoms cannot be elicited, and visual acuity cannot be assessed, particularly in the setting of critical illness [135]. It is estimated that roughly 33–55% of all candidemia cases occur in the intensive care unit [136], where patients may be unable to self-report ocular or visual symptoms due to mechanical ventilation or delirium.

The utility of ophthalmologic consultation to rule out ocular involvement in patients with candidemia remains controversial, largely owing to differing views on its necessity and cost-effectiveness [137]. The Infectious Diseases Society of America recommends dilated fundoscopic examinations, preferably performed by ophthalmologists, for all patients diagnosed with candidemia, arguing that the potential benefit of early detection of candidal endophthalmitis and preventing visual loss far surpasses the expense of predominantly negative ophthalmoscopies [138]. The American Academy of Ophthalmology, by contrast, advises against routine ocular screening in patients with candidemia, instead considering ophthalmologic consultation a reasonable practice for patients with symptoms and signs suggestive of ophthalmic infection regardless of candidal fungemia

[139]. Further investigations are needed to establish alignment between the guidelines of the above societies in order to optimize care while ensuring appropriate utilization of resources [137]. Future studies could also explore the role of digital fundus photography and teleophthalmology as an alternative to fundoscopic examinations performed by ophthalmologists in candidemic patients without ocular or visual symptoms, potentially reducing reliance on bedside ophthalmologic consultations while maintaining high-quality retinal assessments [135].

3.3.2. Cryptococcosis

Cryptococcosis is an opportunistic mycosis caused by yeasts of the genus *Cryptococcus*, primarily *C. neoformans* and *C. gattii*, which are found in soil, decaying wood, and avian excreta [140,141]. Infection is typically acquired through inhalation of environmental spores that are deposited in the pulmonary alveoli [140]. Cryptococcosis is historically associated with AIDS, while other risk factors include solid organ transplantation, GATA2 deficiency, chronic granulomatous disease, decompensated liver disease, sarcoidosis, and receipt of glucocorticoids or other immunosuppressive medications. Notably, the disease can also occur in immunocompetent individuals, underscoring the ability of *Cryptococcus* species to impact a variety of hosts [141]. Cryptococcosis most commonly affects the lower respiratory tract and the CNS, consistent with the primary route of inoculation and the neurotropic nature of the culprit microorganism; however, infection can disseminate widely and involve multiple sites, including the eye, particularly in immunocompromised patients [141].

Ocular sequelae may arise through two main mechanisms: neuro-ophthalmic manifestations secondary to intracranial hypertension from underlying meningoencephalitis and direct intraocular invasion via hematogenous dissemination or contiguous spread along the leptomeningeal sheaths [142]. The former category includes papilledema as well as cranial nerve II, III, and VI palsies, while the latter encompasses chorioretinitis, vitritis, endophthalmitis, and granulomatous conjunctivitis [140–142]. Patients may complain of visual impairment, floaters, and pain, either unilateral or bilateral, which can occur concurrently with symptoms and signs of meningitis or in isolation [140]. In a cohort of 44 previously healthy adults with cryptococcal meningitis, the most frequent ophthalmological abnormalities were visual-field defects in 66%, decreased visual acuity in 38%, and papilledema in 26% of the patients [143]. Importantly, ocular involvement may occasionally precede symptomatic meningitis [144]. Clinicians should also be mindful that ocular symptoms may worsen after commencing therapy for the fungal infection and the underlying immunocompromising condition due to IRIS [140].

With respect to the pattern of visual loss in the context of cryptococcosis, two distinct presentations have been described. Rapid visual loss develops over hours, is severe and bilateral, carries a poor prognosis, and is likely attributed to optic neuritis. By contrast, slow visual loss progresses gradually over days, exhibits a more favorable prognosis, is thought to occur secondary to intracranial hypertension and subarachnoid adhesions, and is more frequently observed in immunocompetent patients [145].

3.3.3. Miscellaneous Fungal Infections

Aspergillosis, most commonly caused by *Aspergillus fumigatus*, can lead to a variety of ocular manifestations in immunocompromised individuals, including endophthalmitis. In fact, *Aspergillus* represents the second most common cause of endogenous fungal endophthalmitis after *Candida* [146]. In addition, mucormycosis, commonly caused by fungi of the genus *Rhizopus* or *Mucor* in patients with diabetic ketoacidosis or immunosuppression, can manifest with rhino-orbito-cerebral disease with periorbital edema, chemosis, ptosis, ophthalmoplegia, proptosis, and central retinal artery occlusion [147].

3.4. Parasitic Infections

3.4.1. Toxoplasmosis

Toxoplasmosis is caused by *Toxoplasma gondii*, a parasite capable of infecting any warm-blooded vertebrate, including humans [148,149]. It can be transmitted to humans by ingesting water, soil, or crops contaminated with the feces of definitive feline hosts (domestic cats and wild felids) or by consuming intracellular cysts present in improperly cooked meat from intermediate hosts (sheep, goats, pigs, cattle, and chickens) [148,150]. The disease can also be transmitted vertically, resulting in congenital toxoplasmosis, and via transplantation [151,152]. Congenital infection may cause fetal or neonatal death, intrauterine growth restriction, preterm birth, and other severe complications, such as neurologic and ocular disorders, which can potentially manifest years later in life [152–154]. The combination of retinochoroiditis, intracranial calcifications, and hydrocephalus constitutes the classic triad of congenital toxoplasmosis [155]. In contrast, acquired toxoplasmosis in immunocompetent individuals is usually asymptomatic or presents with mononucleosis syndrome although it may also cause ocular disease [148,156,157]. In immunocompromised patients, toxoplasmosis frequently results in more severe and disseminated disease and most often manifests as encephalitis, which may be life-threatening [158,159].

Ocular toxoplasmosis is one of the most frequent causes of posterior uveitis worldwide and usually presents with retinochoroiditis commonly accompanied by vitritis or anterior uveitis [159–161]. At a molecular level, the immune response against *T. gondii* involves the activation of the purinergic P2X7 receptor, which enhances lysosome and inflammasome activity; polymorphisms in the encoding *P2RX7* gene can affect susceptibility to ocular toxoplasmosis [162]. Retinochoroiditis is typically characterized by whitish fluffy foci often close to a variably pigmented or atrophic chorioretinal scar. Severe vitritis results in the classic “headlight in the fog” sign during indirect ophthalmoscopy [159,161]. Optic nerve involvement occurs in roughly 5% of patients with ocular toxoplasmosis and can manifest as Jensen’s juxtapapillary retinochoroiditis, pure papillitis, neuroretinitis, optic disc edema in the presence of a concurrent distant active lesion, or a mixed picture, as categorized by Eckert et al. [163]. Patients may complain of decreased vision associated with floaters [164]. Unilateral lesions are more frequent in acquired toxoplasmosis, while bilateral involvement is more common in congenital cases [165,166]. Additionally, congenital disease tends to affect the macula more frequently, leading to an increased risk of legal blindness [159]. Despite perinatal treatment, congenital toxoplasmosis can lead to new ocular lesions even in adulthood, with peak incidences at the ages of 7 and 12 years, highlighting the need for prolonged follow-up into adulthood [167]. Special attention should be paid to patients with HIV suspected of toxoplasmic retinochoroiditis as up to 30% of individuals with HIV with ocular toxoplasmosis exhibit concurrent CNS involvement and should therefore undergo brain magnetic resonance imaging [5,168]. Ocular toxoplasmosis can lead to a broad spectrum of complications, including secondary glaucoma, cataract formation, scleritis, band keratopathy, cystoid macular edema, choroidal neovascularization, retinal vascular occlusion, epiretinal membrane formation, retinal detachment, and optic nerve atrophy [158,161].

3.4.2. Onchocerciasis

Onchocerciasis, also known as river blindness, is a parasitic infection caused by the nematode *Onchocerca volvulus*, which is transmitted through repeated bites of blackflies of the genus *Simulium* that breed in fast-flowing rivers and streams [169,170]. Despite decades of control interventions, the infection remains endemic across 28 countries in Sub-Saharan Africa, where 99% of disease burden is concentrated [171]. Onchocerciasis is the second leading cause of infectious blindness after trachoma in the developing world and

carries a profound psychosocial and economic burden, historically driving the depopulation of fertile river valley lands in affected communities [170].

Pathology arises mainly from the host immune response against dying microfilariae and their endosymbiotic *Wolbachia* bacteria rather than from the organisms themselves [171,172]. Patients may develop ocular, cutaneous, subcutaneous, and neurological manifestations. Ocular involvement encompasses a broad spectrum of anterior and posterior segment lesions although the cornea is most commonly affected. Corneal involvement begins with punctate keratitis, characterized by reversible snowflake opacities forming in the corneal stroma, which can later coalesce and progress into sclerosing keratitis, a chronic condition marked by full-thickness fibrovascular changes. Torpid iritis with a characteristic pear-shaped deformity of the iris, optic neuropathy, and chorioretinitis may also be observed. Cutaneous manifestations include papular and lichenified onchodermatitis, skin atrophy, and depigmentation resembling leopard skin, while palpable subcutaneous onchocercomas harboring adult worms may develop over bony prominences [169,170,173]. Growing epidemiological evidence suggests an association of onchocerciasis with epilepsy and nodding syndrome, an unexplained neurologic disorder predominantly affecting children in Sub-Saharan Africa and characterized by paroxysmal head nodding, seizures, and cognitive decline [170].

Clinicians should maintain a high index of suspicion for onchocerciasis in patients living in, migrating from, or traveling to endemic regions who present with characteristic keratitis or uveitis of unclear etiology, especially if accompanied by an intensely pruritic papular rash. Of note, although eosinophilia may facilitate diagnosis, it can occasionally be absent, and skin snip biopsies may yield false-negative results, as demonstrated in a recently reported case in which anterior chamber paracentesis guided the diagnosis by revealing unsheathed microfilariae [174].

3.4.3. Miscellaneous Parasitic Infections

Malaria from *Plasmodium falciparum* can lead to malarial retinopathy, characterized by patchy retinal whitening, focal vessel discoloration, retinal hemorrhages, and papilledema. Importantly, the discovery of these fundoscopic findings in a patient with encephalopathy can help distinguish between true cerebral malaria and coma due to another cause with incidental *Plasmodium* parasitemia [6]. Furthermore, cysticercosis, caused by *Taenia solium* larvae, may lead to helminthic cysts in intraocular structures, such as the vitreous body and subretinal space, and extraocular tissues, such as the extrinsic eye muscles and subconjunctival space [175]. B-scan ultrasonography, which may demonstrate a cyst containing a hyperechoic scolex, plays an important role in guiding the diagnosis of ocular and extraocular cysticercosis, particularly when ocular media are opacified [176,177]. Moreover, neuro-ophthalmologic signs, such as papilledema, pupillary abnormalities, and nystagmus, can be observed in the context of neurocysticercosis [178].

4. Conclusions

Infectious diseases remain a major contributor to morbidity and mortality worldwide. The eye, by virtue of its rich vascularity and unique immunological microenvironment, is susceptible to involvement by a wide spectrum of bacterial, viral, fungal, and parasitic pathogens, which may give rise to diverse ocular and visual manifestations through direct pathogen invasion, immune-mediated mechanisms, or complications of therapy. Ocular manifestations can provide early, sometimes crucial, clues to underlying systemic infections, while, conversely, systemic features can help interpret ophthalmic findings. The management of patients with systemic infectious diseases requires a multidisciplinary approach, in which ophthalmologists can contribute substantially to optimizing both visual and overall health outcomes.

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Abbreviations

The following abbreviations are used in this manuscript:

AIDS	Acquired immunodeficiency syndrome
CMV	Cytomegalovirus
CNS	Central nervous system
CSF	Cerebrospinal fluid
HIV	Human immunodeficiency virus
HSV	Herpes simplex virus
IRIS	Immune reconstitution inflammatory syndrome
IRU	Immune recovery uveitis
OSSN	Ocular surface squamous neoplasia
PCNSL	Primary central nervous system lymphoma
TB	Tuberculosis
VZV	Varicella-zoster virus

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