REVIEW ARTICLE

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Eye Infections

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EYE INFECTIONS ARE AN IMPORTANT CAUSE OF VISION LOSS WORLDWIDE. Patients with these infections are commonly seen by primary care providers, internists, emergency medicine specialists, hospitalists, and ophthalmologists. Each year in the United States alone, conjunctivitis accounts for more than 550,000 visits to emergency departments[1] and many more visits to outpatient offices, keratitis is diagnosed at more than 1 million office and emergency department visits,[2] exogenous endophthalmitis complicates up to 0.1% of the more than 7 million cataract surgeries and intravitreal injections performed,[3-5] and thousands of patients are admitted to general hospitals to treat vision-threatening eye infections such as endogenous endophthalmitis and infectious uveitis. This review summarizes the epidemiology, diagnosis, and treatment of eye infections. Figure 1 illustrates eye anatomy as it relates to eye infections. Table S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org, summarizes the microbiologic features, clinical characteristics, and treatment of these infections.

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INFECTIOUS CONJUNCTIVITIS

The conjunctiva is a translucent membrane that covers the visible part of the sclera and lines the eyelids. Acute infectious conjunctivitis is the most common eye infection seen by primary care providers[6] and accounts for one third of eye-related emergency department visits in the United States.[7]

VIRAL CONJUNCTIVITIS

Viruses cause approximately 80% of cases of acute infectious conjunctivitis in adults but less than 20% of pediatric cases.[6] Watery discharge is typical of viral conjunctivitis but may also be seen in one quarter of bacterial cases.[6] The findings of pharyngitis, preauricular lymphadenopathy, and contact with another person with a red eye suggest a viral cause.[6] Adenoviruses cause 65 to 90% of cases of viral conjunctivitis, and treatment is supportive.[8] Certain types of adenoviruses (e.g., types 8, 37, and 64) can cause epidemic keratoconjunctivitis, a severe and highly contagious conjunctivitis in which the cornea is often involved. Corneal involvement causes eye pain and may lead to corneal opacities that can persist for months. Infection-control measures are essential to prevent epidemic keratoconjunctivitis outbreaks. Virus can be recovered from the hands of nearly half of patients and can survive for more than 1 month on plastic and metal objects.[9] Herpes simplex virus (HSV), varicella zoster virus (VZV), enterovirus, measles virus, mumps virus, rubella virus, severe acute respiratory syndrome coronavirus 2, Ebola virus, mpox (formerly known as monkeypox) virus, and other viruses can also cause conjunctivitis.[8]

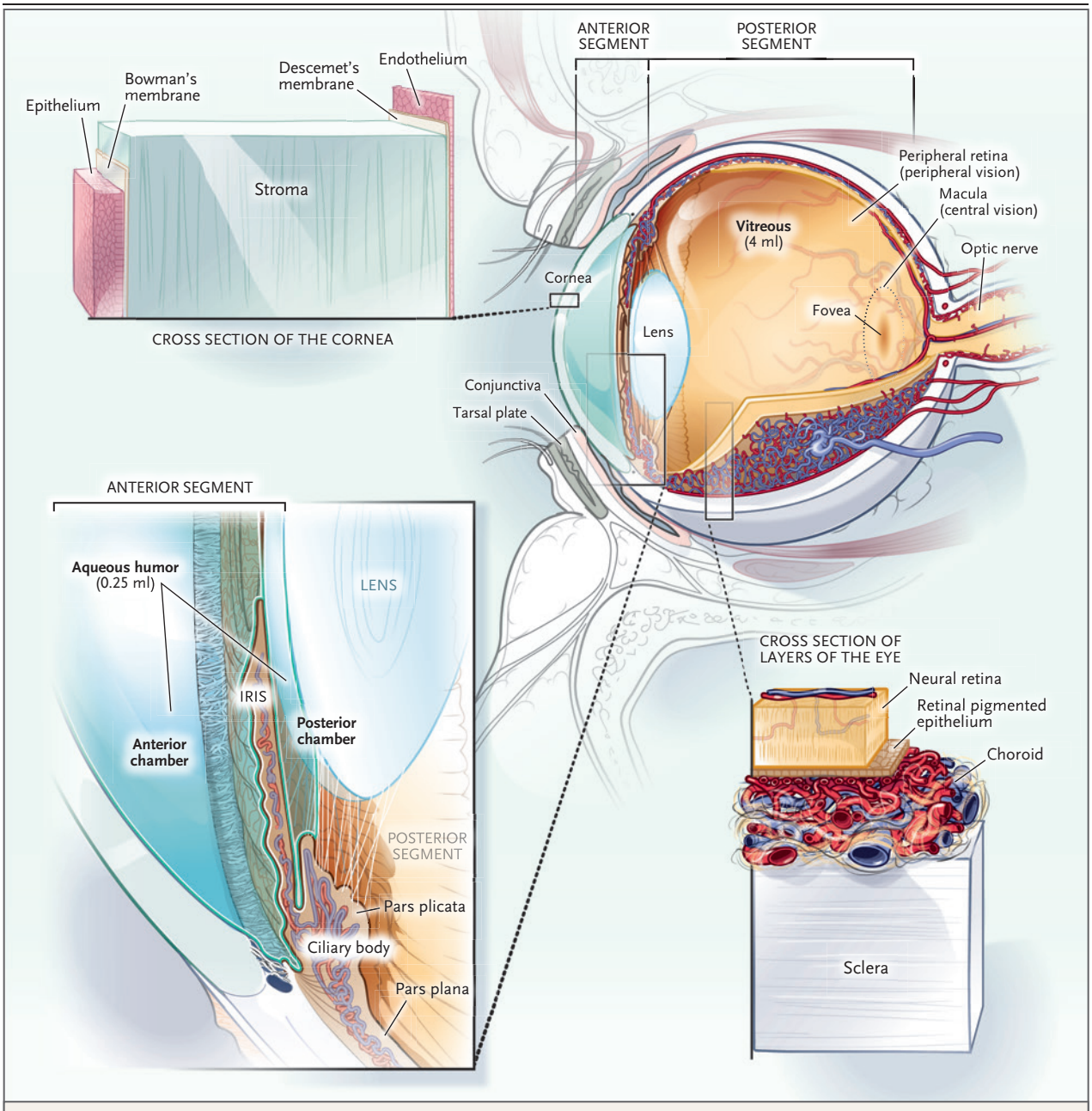

Figure 1. Eye Anatomy.

The eye has three coats (sclera–cornea, uvea, and retina) and two humors (aqueous and vitreous). The conjunctiva covers the visible portion of the sclera (bulbar conjunctiva) and lines the eyelids (tarsal conjunctiva). The cornea has a six-cell-thick epithelium, stroma, and a one-cell-thick endothelium. The eye is divided by the lens into anterior and posterior segments. The anterior segment is further divided (by the iris) into the anterior chamber (AC) and posterior chamber (PC). The anterior segment is filled with aqueous humor (approximately 0.25 ml), which is produced by the ciliary body and reabsorbed into the systemic circulation; the turnover time is approximately 100 minutes. The posterior segment is filled with gel-like vitreous (approximately 4 ml), which does not regenerate but may be surgically removed (vitrectomy). The uvea (iris, ciliary body, and choroid), which forms the middle coat of the eye, is pigmented and highly vascular. Microbes that reach the eye through the bloodstream often seed the uvea first. The choroid underlies the retina, so both layers may be affected by infection. The retina is part of the central nervous system and has a blood–eye barrier that is similar to the blood–brain barrier and affects antibiotic penetration into the eye. The retina can be divided into the macula, which provides the sharpest vision, as well as central vision, and the peripheral retina (the remainder of the retina), which provides low-light, peripheral vision. Infection involving the peripheral retina may be asymptomatic initially.

BACTERIAL CONJUNCTIVITIS

Bacteria cause less than 20% of acute cases of infectious conjunctivitis in adults but more than 70% of pediatric cases.[6] Purulent conjunctival discharge and morning eyelash crusting suggest a bacterial cause but do not rule out a viral cause.[6] *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Hemophilus influenzae*, and *Moraxella catarrhalis* are the most common causes of bacterial conjunctivitis. The infection is treated with topical antibiotics (e.g., trimethoprim–polymyxin).

Rare causes of bacterial conjunctivitis include neisseria and chlamydia. *Neisseria meningitidis* or *N. gonorrhoeae* typically cause hyperacute conjunctivitis, characterized by copious, purulent conjunctival discharge. Primary meningococcal conjunctivitis occurs mainly in children and carries the risk of subsequent invasive meningococcal disease. Treatment with systemic antibiotics is recommended to reduce this risk.[10] *N. gonorrhoeae* and *Chlamydia trachomatis* serotypes D through K are sexually transmitted infections that may cause conjunctivitis. Gonococcal conjunctivitis involves the cornea in one third of cases and can cause corneal perforation.[11] Inclusion conjunctivitis caused by *C. trachomatis* is usually subacute, with follicles seen on the everted lower eyelid. Genital tract involvement is often present but asymptomatic. Gonococcal conjunctivitis and chlamydial conjunctivitis are treated with systemic antibiotics (e.g., intramuscular ceftriaxone and oral doxycycline, respectively).[12]

C. trachomatis serotypes A, B, and C cause trachoma, the leading infectious cause of blindness worldwide, although it is rare in developed countries.[13] Infection is spread by flies or by direct or indirect contact with ocular or nasal discharge from an infected person. The active infection may be asymptomatic or cause a follicular conjunctivitis. Repeated infections can cause conjunctival scarring, entropion, trichiasis, and corneal scarring. The World Health Organization recommends eliminating trachoma through a strategy that includes mass azithromycin administration in regions where the infection is endemic.[13]

INFECTIOUS KERATITIS

Corneal infections, or infectious keratitis, can rapidly affect vision. A clear cornea is necessary for image transmission and focus; the cornea accounts for two thirds of the refractive power of the eye. Infectious keratitis is divided into viral infections and microbial (bacterial, fungal, or parasitic) infections (Fig. 2). The major viral causes of keratitis are HSV and VZV. HSV keratitis affects approximately 1.7 million people annually worldwide.[15,17] Microbial keratitis (corneal ulcer) is the primary cause of nontrachomatous corneal opacification, the fifth leading cause of blindness worldwide.[18] Risk factors include contact lens wear, eye trauma, underlying corneal disease, and ocular surface disease (e.g., severe dry eye). In rare cases, infectious keratitis complicates corneal procedures (e.g., 0.0005% of the approximately 2 million keratorefractive procedures performed annually worldwide).[19] Patients with keratitis usually present with eye pain, conjunctival injection, photophobia, and decreased vision. The site of the infection may be in the corneal epithelium, stroma, or both. There may be corneal edema and a hypopyon (a layer of white cells in the anterior chamber).

MICROBIAL KERATITIS

Contact lens wear is the most important risk factor for microbial keratitis in the United States. There are approximately 45 million contact lens wearers in the United States, and 1 million seek health care for contact lens–related complications annually.[2] Poor lens care practices are often responsible for contact lens–related keratitis. These practices include bathing or sleeping in contact lenses, rinsing or storing them in water, topping off rather than replacing the disinfecting solution in lens cases, and replacing contact lenses or lens cases less frequently than recommended.[20] Lens cases develop a biofilm of bacteria (e.g., from tap water), so they must be replacedregularly. Many cases of contact lens–related keratitis are preventable. Studies have shown that 99% of surveyed contact lens wearers practiced poor contact lens hygiene at least once, and one third recalled never receiving any lens wear or care instructions.[20,21] Bacteria cause approximately 90% of cases of contact lens–related keratitis in the United States, most commonly *Pseudomonas aeruginosa* (>40%), *S. aureus*, or streptococci; other pathogens include fungi and acanthamoeba (Fig. 2A, 2B, and 2C).[14] Acanthamoeba can contaminate contact lens cases through tap water exposure.

Corneal trauma is the primary risk factor for microbial keratitis in many agricultural regions

of the world. Molds (e.g., aspergillus and fusarium) are major keratitis pathogens in these regions. More than 1 million cases of fungal keratitis occur annually, with the highest rates in Asia and Africa; fungi cause more than 45% of microbial keratitis cases in some countries.[22]

Microbial keratitis is diagnosed by examination (e.g., with a slit lamp); in vivo confocal microscopy may be helpful in fungal or acanthamoeba cases.[23] Cultures of corneal scrapings are obtained for pathogen identification. Polymicrobial infections may occur (e.g., mold plus bacterial infection). Microbial keratitis is treated with frequent administration of topical antibiotics (e.g., a fluoroquinolone alone or vancomycin plus tobramycin for bacterial keratitis, natamycin for fungal keratitis, and chlorhexidine and polyhexamethylene biguanide for acanthamoeba keratitis).[14] Systemic antibiotics are sometimes added (e.g., if acanthamoeba keratitis does not respond to topical therapy).[14,24,25] Corneal transplantation during acute keratitis may be necessary, but the 5-year graft-survival rate is less than 60%.[26] Acanthamoeba keratitis and mold keratitis are especially difficult to treat and often have poor outcomes.[22,25]

VIRAL KERATITIS

Herpes simplex keratitis is usually caused by reactivation of latent HSV in the trigeminal ganglion. A branching (dendritic) infiltrate in the corneal epithelium is a classic finding (Fig. 2D). The infection often recurs as an epithelial keratitis, stromal keratitis, or anterior uveitis; recurrences can lead to corneal hypoesthesia and opacity.[16] Acyclovir prophylaxis reduces the recurrence rate (19% with acyclovir vs. 32% with placebo during a 1-year study).[27] Topical ganciclovir or an oral antiviral agent (e.g., acyclovir, valacyclovir, or

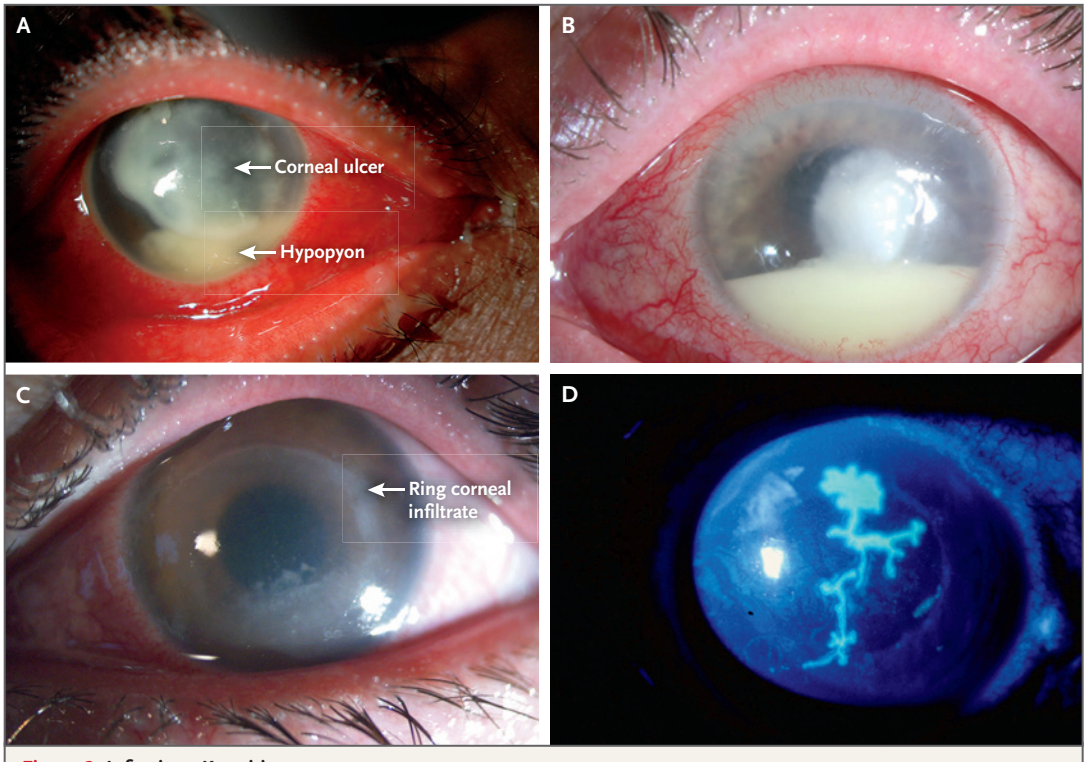

Figure 2. Infectious Keratitis.

Panel A shows pseudomonas keratitis related to contact lens wear. A large hypopyon (layer of white cells in the aqueous humor) is present. A different photograph of the same eye is shown in Durand et al.[14] Panel B shows fungal keratitis due to a mold (*Purpureocillium lilacinum*), related to contact lens wear. A large hypopyon is evident. Acanthamoeba keratitis related to contact lens wear is shown in Panel C. The ring corneal infiltrate seen here is typical of this infection. Panel D shows epithelial keratitis due to herpes simplex virus. Only the corneal epithelium is involved in this case, and the typical dendritic pattern is clearly seen with the use of fluorescein dye under cobalt blue light. Different stains and images of this eye are shown in Chodosh and Ung[15] and Guess et al.[16]

famciclovir) is used to treat epithelial keratitis. Other forms of HSV keratitis are treated with topical corticosteroids plus oral antiviral agents.[14] An important cause of VZV keratitis is herpes zoster ophthalmicus. Acute keratitis develops in 13 to 76% of herpes zoster ophthalmicus cases, usually within 1 month after the onset.[14] Herpes zoster ophthalmicus complicates approximately 8% of herpes zoster cases, and there are 1 million cases of herpes zoster annually in the United States.[14] Herpes zoster ophthalmicus–related keratitis is usually a dendritic epithelial keratitis initially, but stromal infiltrates subsequently develop in approximately half of patients, and some have corneal scarring.[28] Loss of corneal sensation may occur and can lead to further ulcerations. Herpes zoster ophthalmicus is treated with oral acyclovir, valacyclovir, or famciclovir. The recombinant zoster vaccine is highly effective in preventing zoster, including herpes zoster ophthalmicus.[14,29]

ENDOPHTHALMITIS

Endophthalmitis is a potentially blinding intraocular infection of the vitreous, aqueous humor, or both. Nearly all cases are caused by bacteria or fungi. Endophthalmitis results in severe vision loss (less than 20/200) in at least 20% of affected eyes.[3,30] The infection may be exogenous, developing after eye surgery, intravitreal injections, penetrating trauma, or keratitis, or it may be endogenous, resulting from bacteremia or fungemia. Whereas exogenous endophthalmitis affects only the at-risk eye (e.g., the eye affected by recent surgery), endogenous endophthalmitis affects both eyes in 8 to 20% of patients.[31-33]

The most common symptoms of endophthalmitis are vision loss and eye pain. Examination shows white cells in the vitreous, aqueous humor, or both (Figs. 1 and 3). Eye pain, a sudden onset of symptoms, hypopyon, and diffuse (rather than clumped) intraocular inflammation are more common in bacterial endophthalmitis than in fungal endophthalmitis. Systemic symptoms are absent in exogenous endophthalmitis but may be present in endogenous endophthalmitis.

The diagnosis of endophthalmitis is clinical and usually based on the finding of intraocular inflammation in a patient at risk for endophthalmitis, with confirmation of the diagnosis based on intraocular cultures in exogenous cases and on intraocular or blood cultures in endogenous cases. Negative intraocular cultures do not rule out endophthalmitis; 30% of postoperative cases are culture-negative.[34] Intraocular cultures from vitrectomy samples are most likely to be positive, followed by cultures from vitreous aspirate samples and then cultures from aqueous aspirate samples. Testing intraocular samples by means of a polymerase chain reaction (PCR) assay is not yet standard practice but has been used to identify pathogens.

The key component of treatment is injection of intravitreal antibiotics. Intravitreal antibiotics alone fail to sterilize some eyes, and the addition of vitrectomy can improve outcomes in severe cases (Fig. 3A and 3B).[34] Systemic antibiotics are given for all cases of endogenous endophthalmitis and as adjunctive therapy in some exogenous cases.[35]

EXOGENOUS ENDOPHTHALMITIS

Exogenous infection complicates 0.04 to 0.1% of the millions of cataract surgeries and intravitreal injections performed annually.[3-5,36,37] The most common intravitreally injected medications are anti–vascular endothelial growth factor (anti-VEGF) agents used to treat neovascular age-related macular degeneration and diabetic macular edema, among other conditions. Cataract surgery is one of the most common surgical procedures worldwide, with a median annual global rate of 1750 procedures per 1 million population (8300 per 1 million in high-income countries).[38] Gram-positive cocci, primarily coagulase-negative staphylococci (in approximately 70% of cases), *S. aureus*, and streptococci, cause more than 90% of postoperative and postinjection endophthalmitis in the United States.[34] Streptococcal endophthalmitis is more common after intravitreal injection than after cataract surgery and often has a poor outcome. Gram-negative bacilli and fungi are uncommon in the United States but cause 10 to 20% of cases in some tropical countries such as India.[39]

Endophthalmitis complicates penetrating eye trauma in 0.9 to 10% of cases.[40] Risk factors include injury with a metal object, lens disruption, retained intraocular foreign bodies, and delay (>24 hours) in primary closure. Coagulase-negative staphylococci and *Bacillus cereus* are major pathogens, the latter typically causing a fulminant endophthalmitis with rapid loss of vision.

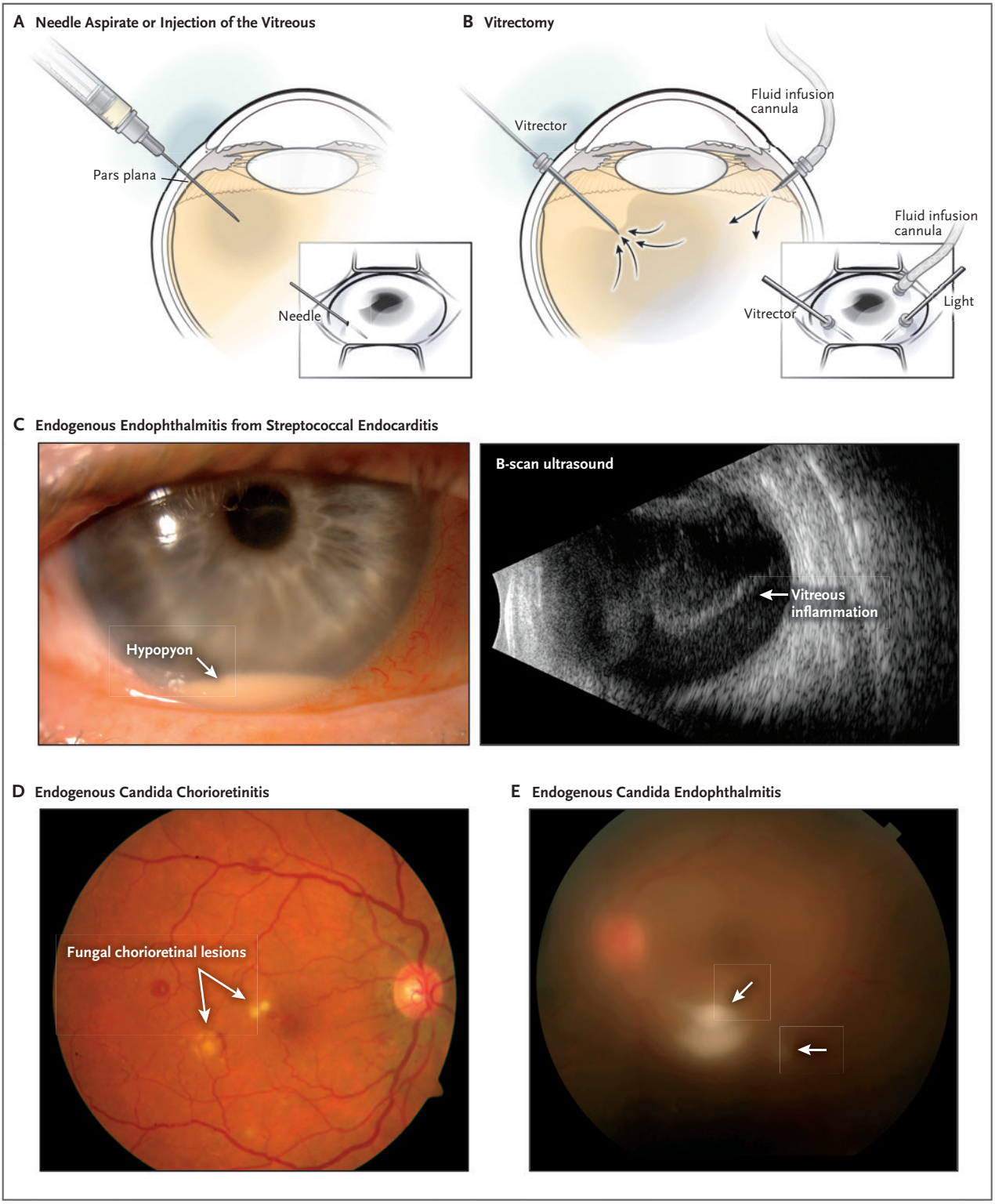

Figure 3 (facing page). Endophthalmitis.

Panel A shows a needle aspirate or injection of the vitreous. In a case of clinically suspected endophthalmitis, a sample of vitreous is obtained by needle aspirate (typically an office procedure) or during vitrectomy surgery. Then empirical antibiotics are injected into the vitreous. Panel B shows vitrectomy surgery; this is performed in the operating room. A vitrectomy is used to débride the vitreous, which may be especially helpful in severe cases of endophthalmitis. The vitrector cuts and aspirates the gel-like vitreous, while another cannula infuses balanced salt solution to maintain eye turgor. A light pipe provides intraocular illumination. Vitreous samples collected during vitrectomy are sent for culture, and intravitreal antibiotics are injected at the end of the surgery. Panel C shows endogenous endophthalmitis from streptococcal endocarditis. Whereas a hypopyon in keratitis usually represents a sterile inflammatory response, the hypopyon in endophthalmitis signifies intraocular infection. The ultrasound image (B-scan) of this eye shows echoes (arrow) in the vitreous, indicating vitreous inflammation. A B-scan is especially helpful when the view of the posterior segment is obscured (e.g., by anterior segment inflammation or an advanced cataract). Panel D shows endogenous candida chorioretinitis with fungal chorioretinal lesions. A different photograph of the same eye is shown in Javaheri et al.[47] Endogenous candida endophthalmitis, shown in Panel E, has the clumped pattern of inflammation that is characteristic of fungal endophthalmitis (arrows), as well as a hazy view of the retina due to vitreous inflammation.

Prophylactic antibiotics (e.g., intravenous vancomycin plus ceftazidime), administered for 48 hours after penetrating eye trauma, have reduced the incidence of endophthalmitis to 0.9%.[40,41]

ENDOGENOUS ENDOPHTHALMITIS

Endogenous infection accounts for 2 to 15% of endophthalmitis cases.[32] Sources of infection include endocarditis, urinary tract infections, abdominal (e.g., liver) abscesses, pneumonia, gastrointestinal procedures (e.g., endoscopy), central venous catheters, and injection-drug use. Up to 40% of patients present to a general medical provider, and many patients (30 to 60%) are afebrile.[30-33,42] Blood cultures are positive in 30 to 55% of patients overall but in only 6% of patients with candida endophthalmitis associated with injection-drug use.[30,31,33,43] The most common bacterial pathogens in endogenous endophthalmitis depend on the source of infection (e.g., *S. aureus* and streptococci in endocarditis [Fig. 3C], *Klebsiella pneumoniae* in liver abscess, and *Escherichia coli* in urinary tract infection). The most common fungal pathogen is *Candida albicans*. Endogenous endophthalmitis due to mold is rare and usually occurs in immunocompromised patients.

Patients with current or recently removed central venous catheters are at particular risk for candida endophthalmitis, which may be indolent and initially mistaken for uveitis. Injection-drug use is a risk factor for fungal endophthalmitis, primarily caused by *C. albicans* but also by other species of candida or molds (e.g., aspergillus). The diagnosis may be suspected on the basis of a history of gradual vision loss in one or both eyes. Eye pain is usually absent until late in the infection. The finding of fluffy vitreous infiltrates is consistent with the diagnosis. Endogenous fungal endophthalmitis is often diagnosed on the basis of vitreous cultures, because blood cultures are frequently negative. The incidence of drug use–associated endophthalmitis cases quadrupled in the United States from 2003 to 2016, from 0.08 to 0.32 per 100,000 population,[44] and in some U.S. centers, more than 40% of patients with endogenous endophthalmitis have a history of drug use.[31]

In a large prospective trial involving inpatients, candidemia was associated with chorioretinitis in 9.2% of patients and with endophthalmitis in 1.6%.[45] A recent meta-analysis showed a pooled prevalence of 1.8% for candida endophthalmitis in patients with candidemia, with a higher prevalence in Asian studies (3.6%) than in European or U.S. studies (1.4%).[46] Seeding of the highly vascular choroid causes chorioretinitis, which is usually the first manifestation of ocular candidiasis. Fluffy white chorioretinal lesions are seen on examination, and endophthalmitis ensues as the infection extends into the vitreous[47] (Fig. 3D and 3E). Patients with chorioretinitis usually have no eye symptoms unless the macula is involved or there is endophthalmitis. More than 80% of patients with candidemia report no ocular symptoms at the time that ocular candidiasis is diagnosed.[45,48]

A diagnosis of ocular candidiasis influences the choice of systemic antibiotics and the duration of treatment as recommended by the Infectious Diseases Society of America (IDSA) guide-

lines. Treatment with an echinocandin is not recommended because of poor intraocular penetration, and prolonged treatment is indicated for ocular involvement.[49] Close ophthalmologic follow-up is also necessary, even for chorioretinitis alone. In addition to systemic therapy, intravitreal injection of amphotericin B or voriconazole is indicated for macula-threatening chorioretinitis or for endophthalmitis.[49] Vitrectomy is also helpful in some cases of endophthalmitis. The IDSA recommends screening eye examinations in asymptomatic patients with candidemia, but the American Academy of Ophthalmology does not.[49,50] Both societies agree on the need for an eye examination in patients with signs or symptoms of eye infection.

Visual outcomes in patients with endophthalmitis depend on several factors, including the virulence of the pathogen. Endophthalmitis due to coagulase-negative staphylococci, for example, is associated with a good visual outcome (i.e., 20/100 or better) in approximately 80% of patients, whereas streptococcal endophthalmitis has a very poor visual outcome (i.e., 20/400 or worse) in the majority of infected eyes.[34]

INFECTIOUS UVEITIS

Uveitis refers to inflammation of the uvea (composed of the iris, ciliary body, and choroid), but inflammation may also involve adjacent structures (e.g., the vitreous humor and retina). Uveitis is an important cause of blindness worldwide. Most cases are idiopathic or immune-mediated, but the cause is infectious in 10 to 20% of cases in developed countries and in 30 to 50% in developing countries.[51]

Uveitis is divided into categories on the basis of the anatomical site of greatest inflammation (Fig. 4). Anterior uveitis is most common, but posterior and panuveitis are generally more vision-threatening. In anterior uveitis, the greatest (or only) inflammation is in the anterior segment, and there are frequently keratic precipitates, which are clusters of white cells that have coalesced on the corneal endothelium (Fig. 5A). These keratic clusters may be large (granulomatous) or small (fine). Despite the name, there are no granulomas in granulomatous keratic precipitates, but the precipitates are associated with granulomatous conditions (e.g., sarcoidosis and tuberculosis). In intermediate uveitis, the greatest inflammation is in the vitreous, primarily in proximity to the pars plana. In posterior uveitis, the greatest inflammation is in the posterior segment. In panuveitis, inflammation is present in both the anterior and posterior segments.

Knowledge of the anatomical category of uveitis provides information about the likelihood of infection and the likely infectious agents. In many large series, infections (most often due to HSV) cause 10 to 15% of anterior uveitis cases, whereas more than 50% of posterior uveitis cases are due to infection, most often toxoplasmosis (Fig. 4).[52-58] The frequency of some pathogens varies geographically. Tuberculosis, for example, causes only approximately 0.5% of uveitis cases in the United States but 5 to 20% of cases in India.[52,54,59]

Most patients with uveitis present with decreased vision. Eye pain is more common in anterior uveitis than in posterior uveitis. Four types of infectious uveitis are described below. Other types of uveitis are listed in Table S1.

OCULAR TOXOPLASMOSIS

Toxoplasma gondii is acquired congenitally or postnatally. Ocular toxoplasmosis is the leading infectious cause of posterior uveitis in most studies worldwide and typically causes a chorioretinitis that is self-limited but that heals with scarring. Patients often report decreased vision, but ocular toxoplasmosis may be asymptomatic, especially if the lesions affect the peripheral retina. Antibiotic treatment does not kill toxoplasma cysts. Frequent recurrences of ocular toxoplasmosis are common[60] and may lead to permanent vision loss, especially if the macula is involved. The classic finding in symptomatic ocular toxoplasmosis is a creamy chorioretinal lesion adjacent to a pigmented scar (Fig. 5B). Vitritis is common and may result in a hazy view of the fundus. The diagnosis is made through funduscopic examination and is supported by positive serologic testing; PCR testing of the vitreous is occasionally helpful. Most patients are treated for acute flares of ocular toxoplasmosis. Antibiotic treatment is systemic (e.g., pyrimethamine plus sulfadiazine or trimethoprim–sulfamethoxazole), intravitreal (clindamycin), or both. Long-term trimethoprim–sulfamethoxazole prophylaxis is very effective in preventing recurrences.[60,61]

ACUTE RETINAL NECROSIS

Acute retinal necrosis refers to a pattern of rapidly necrotizing retinitis primarily due to VZV or HSV, with the former accounting for two thirds of cases. Most patients (>70%) are immunocompetent. Rare cases of acute retinal necrosis are due to CMV and occur almost exclusively in immunocompromised patients. Most patients have no evidence of other herpetic infection and report only eye symptoms when they present with acute retinal necrosis. Some patients have a history of herpes zoster ophthalmicus, herpes meningitis, or herpes encephalitis. Patients usually present with mild eye pain, photophobia, and decreased vision; vision rapidly worsens. Most cases of acute retinal necrosis are unilateral, but without treatment, the disease can rapidly progress to involve the other eye. Some patients present with bilateral disease. The general physical examination is usually normal. Eye examination reveals focal areas of necrosis in the peripheral retina (i.e., the area outside the macula), occlusive retinal vasculopathy, and white cells in the vitreous and aqueous humor (Fig. 5C). The areas of retinal necrosis rapidly progress circumferentially if untreated and can lead to blindness within a few days. The diagnosis is clinical, but PCR of an aqueous or vitreous sample is highly sensitive (>80%) for detecting the virus.[62] Prompt treatment with antiviral agents is important for halting the destructive retinitis and for reducing the risk of bilateral disease from 70 to 13%.[63] Treatment consists of

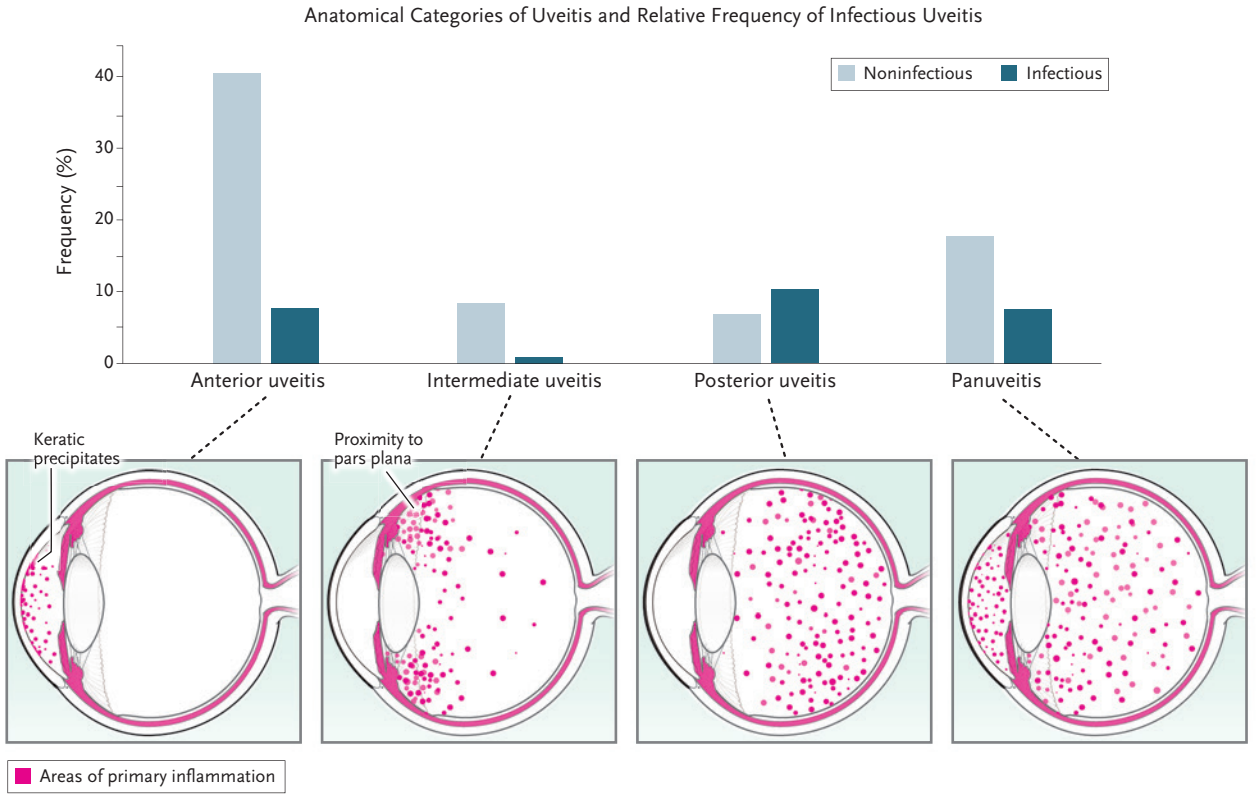

Figure 4. Uveitis.

This figure shows the anatomical categories of uveitis according to the location of maximum inflammation: anterior uveitis, intermediate uveitis, posterior uveitis, and panuveitis. The bar graph shows the relative frequency of infectious uveitis in each category. This graph was derived by averaging the frequencies of infectious and noninfectious uveitis in seven large series of uveitis cases from around the world, including India,[52] the Philippines,[53] the United States,[54] Colombia,[55] Italy,[56] South Africa,[57] and Iran.[58]In the eye diagrams, the dots in the vitreous and aqueous humor represent inflammation (white cells). Vitreous inflammation in posterior uveitis, shown here as pronounced, may be minimal in some cases.

high-dose valacyclovir or intravenous acyclovir for acute retinal necrosis due to VZV or HSV and intravenous ganciclovir for disease due to CMV; intravitreal foscarnet is often added.[62] If acute retinal necrosis due to VZV or HSV progresses despite intravenous acyclovir plus intravitreal foscarnet injections, a switch to intravenous foscarnet should be considered.[64]

OCULAR SYPHILIS

Ocular syphilis occurs in approximately 1% of U.S. syphilis cases, usually in secondary or late-stage syphilis or in syphilis of unknown duration.[65] The manifestations are protean, but uveitis is most common, occurring in approximately 65% of cases.[66] Both eyes are affected in half of patients.[66] Patients often have only eye symptoms (e.g., decreased vision), with no rash to suggest secondary syphilis or neurologic findings to suggest neurosyphilis. However, cerebrospinal fluid analysis is abnormal in up to 70% of patients in whom lumbar punctures are performed.[66,67] The diagnosis of ocular syphilis is made in patients with compatible eye findings and positive trepo-

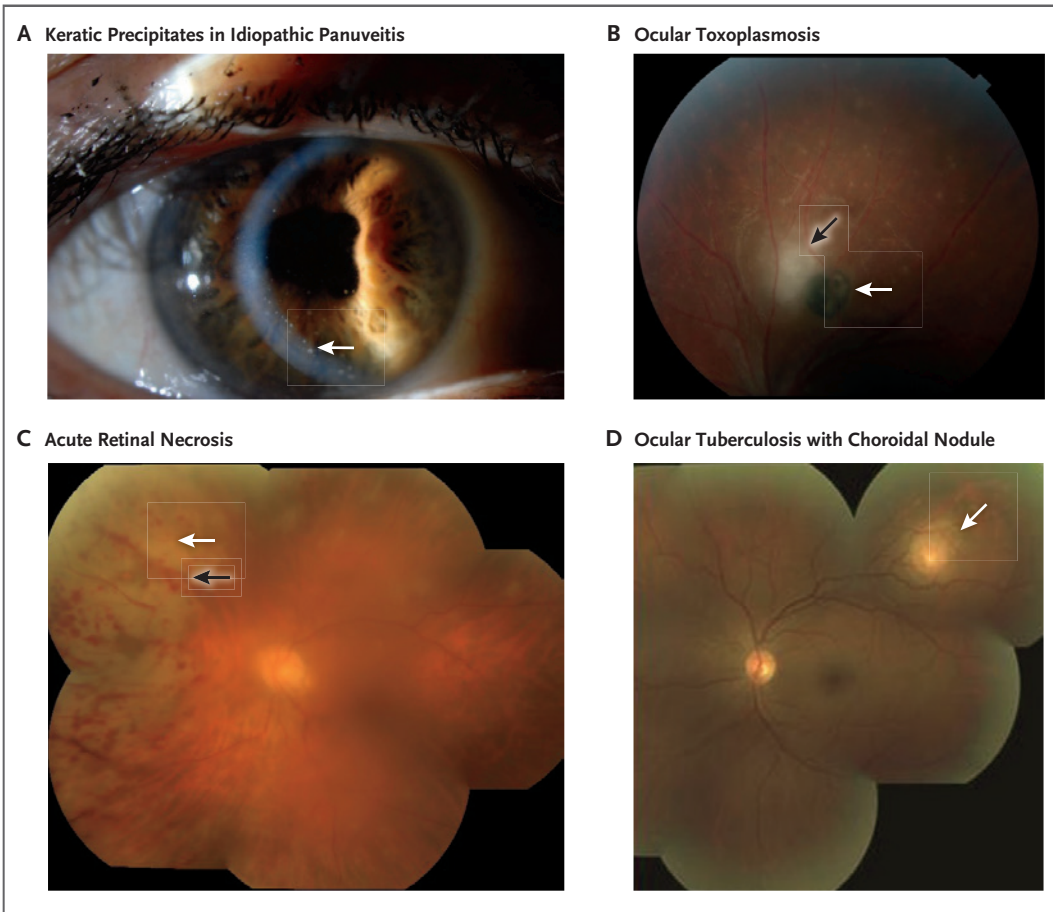

Figure 5. Clinical Features of Infectious Uveitis.

Panel A shows keratic precipitates (arrow), clusters of white cells that have adhered to the corneal endothelium. They are visible here as white dots in the slit lamp beam of light (center of photo). The iris is irregular because of synechiae (adhesions between the iris and cornea or lens) in this case of idiopathic panuveitis. Panel B shows ocular toxoplasmosis. The active lesion (black arrow) is adjacent to an old scar (white arrow), a classic finding in ocular toxoplasmosis. Often there is marked vitreous inflammation and the view of the fundus is obscured. Panel C shows acute retinal necrosis, in this case due to varicella zoster virus, with areas of retinal necrosis (whitening, white arrow) and hemorrhage (black arrow). The optic disk is in the center of the photograph. A composite image of the fundus is shown. Panel D shows ocular tuberculosis with a choroidal lesion (arrow) in a patient with disseminated tuberculosis. A composite image of the fundus is shown.

nemal serologic testing; a nontreponemal test is usually but not always positive.[66] Treatment is the same as for neurosyphilis, with high-dose intravenous penicillin administered for 10 to 14 days.[12] As of 2021, the Centers for Disease Control and Prevention no longer recommends a lumbar puncture before treatment in patients with isolated ocular syphilis and no neurologic abnormalities.[12]

OCULAR TUBERCULOSIS

Tuberculosis involves the eye in approximately 1.5% of patients with confirmed systemic tuberculosis,[68,69] and in these patients, the most common eye findings are multifocal choroiditis, a solitary choroidal nodule, anterior granulomatous uveitis, and retinal vasculitis. Scleritis, interstitial keratitis, and optic neuritis are less common manifestations of ocular tuberculosis. Choroiditis is the most common finding (Fig. 5D), and patients usually have fewer than 5 choroidal tubercles (range, 1 to 60).[70] Other diseases, such as sarcoidosis, syphilis, and metastatic cancer, can cause a similar appearance of the choroid. Serpiginous-like choroiditis is a pattern of choroiditis thought to be highly suggestive of tuberculosis, but it must be distinguished from idiopathic serpiginous choroiditis. In idiopathic serpiginous choroiditis, the lesions classically extend from around the optic nerve into the macula, whereas in more than 85% of cases of serpiginous-like choroiditis, the lesions are noncontiguous with the optic disk.[71,72] Vitreous cultures in cases of presumed ocular tuberculosis are nearly always negative. Molecular diagnostic studies of intraocular fluids offer promise, although their sensitivity and specificity are not well established.[73,74] Ocular tuberculosis is treated with a multidrug regimen of antitubercular antibiotics.

CONCLUSIONS

Eye infections are important to recognize and treat, and many cases can be prevented. Preventive measures include infection-control practices to prevent the spread of viral conjunctivitis, contact lens care to prevent microbial keratitis, use of safety glasses to prevent eye injuries and related infections, prophylactic antibiotics to prevent endophthalmitis after penetrating eye trauma, and vaccination against herpes zoster to prevent herpes zoster ophthalmicus.

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