# Study Questions

Please note that these questions are not part of your CME reporting process. They are provided here for your own educational use and for identification of any professional practice gaps. The required CME posttest is available online (see "Requesting Continuing Medical Education Credit"). Following the questions are answers with discussions. Although a concerted effort has been made to avoid ambiguity and redundancy in these questions, the authors recognize that differences of opinion may occur regarding the "best" answer. The discussions are provided to demonstrate the rationale used to derive the answer. They may also be helpful in confirming that your approach to the problem was correct or, if necessary, in fixing the principle in your memory. The Section 9 faculty thanks the Resident Self-Assessment Committee for developing these self-assessment questions and the discussions that follow.

1. What are the main effector cells of the innate immune system?
   a. $CD4^+$ T cells and $CD8^+$ T cells
   b. macrophages and neutrophils
   c. mast cells and dendritic cells
   d. plasma cells and B lymphocytes

2. What type of macrophage produces the full spectrum of inflammatory and cytotoxic cytokines?
   a. resting macrophage
   b. primed macrophage
   c. activated macrophage
   d. stimulated macrophage

3. Which type of white blood cell can become an antigen-presenting cell?
   a. basophil
   b. eosinophil
   c. monocyte
   d. neutrophil

4. What is the term for antigenic sites on antibodies?
   a. allotopes
   b. epitopes
   c. idiotopes
   d. isotopes

5. What agent used in therapy for uveitis may induce anti-idiotypic antibodies?
   a. infliximab
   b. interferon alfa-2a/2b
   c. methotrexate
   d. tacrolimus

6. What feature allows the ocular surface to mount an antibody-mediated effector response to influenza viral antigens after a patient is administered an intranasal influenza vaccine?
   a. abundance of antigen-presenting cells in the conjunctiva
   b. predominance of immunoglobulin (Ig) A within the tear film
   c. presence of conjunctiva-associated lymphoid tissue
   d. high density of mast cells within the conjunctiva

7. What is a major component that affords immune privilege to the cornea?
   a. complement
   b. conjunctival-associated lymphoid tissue
   c. cytokines (eg, interleukin 1)
   d. limbal physiology

8. What immune cells are present in the choroid under normal physiologic conditions?
   a. B lymphocytes
   b. eosinophils
   c. macrophages
   d. neutrophils

9. What ocular inflammatory disease has the strongest human leukocyte antigen (HLA) association?
   a. birdshot chorioretinopathy and HLA-A29
   b. acute anterior uveitis and HLA-B27
   c. Behçet disease and HLA-B51
   d. intermediate uveitis and HLA-DR15

10. HLA-DR4 is weakly associated with what ophthalmic disease?
    a. acute anterior uveitis
    b. Behçet disease
    c. birdshot chorioretinopathy
    d. sympathetic ophthalmia

11. A patient is treated with topical corticosteroids for anterior uveitis in the right eye. At the 1-month visit, the eye is quiet without medication. Four months later, the patient returns

and is again found to have anterior uveitis in the right eye. According to the Standardization of Uveitis Nomenclature (SUN) Working Group classification, what is the best description of this patient's uveitis?

a. acute
b. chronic
c. limited
d. recurrent

12. What medication used to treat uveitis may exacerbate multiple sclerosis?
    a. adalimumab
    b. interferon alfa-2a/2b
    c. methylprednisolone
    d. rituximab

13. A patient is being treated for first-time presentation of undifferentiated granulomatous iridocyclitis. She responds very well to hourly topical corticosteroid, but in the past 3 months, the intraocular inflammation recurred every time the ophthalmologist tried to taper the corticosteroid frequency to less than 4 times per day. A posterior subcapsular cataract is beginning to develop, and the intraocular pressure is now 23 mm Hg despite the patient's use of 3 types of antiglaucoma eyedrops. What is the most appropriate next step in management of this case?
    a. Continue topical corticosteroids and schedule the patient for glaucoma drainage implant surgery.
    b. Continue topical corticosteroids and initiate therapy with methotrexate.
    c. Increase topical corticosteroids and initiate therapy with oral acetazolamide.
    d. Increase topical corticosteroids and initiate therapy with an oral nonsteroidal anti-inflammatory drug (NSAID).

14. What type of scleritis is most likely to be associated with life-threatening systemic disease?
    a. nodular scleritis
    b. posterior scleritis
    c. diffuse scleritis
    d. necrotizing scleritis

15. What finding is associated with an increased risk of uveitis in patients with juvenile idiopathic arthritis (JIA)?
    a. antinuclear antibody positivity
    b. polyarticular involvement
    c. rheumatoid factor positivity
    d. systemic involvement

16. Abnormal urinalysis findings, with increased $\beta_2$-microglobulin level, in a patient with uveitis should prompt initiation of what systemic treatment?
    a. antibiotics
    b. anticoagulants
    c. corticosteroids
    d. xanthine oxidase inhibitor

17. A 23-year-old man purchases a genetic testing kit and learns that he is positive for HLA-B27. He becomes worried about developing acute anterior uveitis after reading stories on the Internet and presents for an eye examination. What is the most likely finding on this patient's slit-lamp examination?
    a. hypopyon
    b. posterior synechiae
    c. posterior subcapsular cataract
    d. quiet anterior chamber

18. How often should a 6-year-old girl with a 2-year history of antinuclear antibody–positive oligoarticular JIA be screened for uveitis?
    a. every 3 months
    b. every 6 months
    c. every 9 months
    d. every 12 months

19. A patient is referred for evaluation of anterior uveitis in the right eye. On examination, there is conjunctival injection, 1+ cell, and granulomatous keratic precipitates (KPs). The patient is on topical therapy (dorzolamide, timolol, and brimonidine) for glaucoma and is also undergoing treatment for latent tuberculosis with oral rifampin. What medication is most likely to be responsible for this patient's presentation?
    a. brimonidine
    b. dorzolamide
    c. rifampin
    d. timolol

20. What is the typical onset and disease course for birdshot chorioretinopathy?
    a. acute onset with progressive course
    b. acute onset with self-limiting course
    c. insidious onset with progressive course
    d. insidious onset with self-limiting course

21. Peripheral necrotizing retinochoroiditis resembling acute retinal necrosis can be seen in patients infected with what pathogen?
    a. *Mycobacterium tuberculosis*
    b. *Nocardia asteroides*

c. *Pneumocystis jirovecii*
d. *Treponema pallidum*

22. When stellate KPs are present in intraocular infections caused by herpes simplex virus type 1 (HSV-1), what description best characterizes their appearance on the corneal endothelium?
    a. They are distributed diffusely, often extending above the corneal equator.
    b. They are distributed inferiorly, specifically only in the Arlt triangle.
    c. They manifest as ring-shaped clusters.
    d. KPs are not found in HSV-1 intraocular infections.

23. What is an appropriate induction treatment option for a patient with varicella-zoster virus–associated acute retinal necrosis?
    a. oral acyclovir 800 mg 5 times/day
    b. oral valacyclovir 1 g 3 times/day
    c. oral valacyclovir 2 g 3 times/day
    d. oral valganciclovir 900 mg twice/day

24. A patient is referred with a history of disseminated coccidioidomycosis. Which form of inflammation is the most common ocular manifestation of the disease?
    a. phlyctenular and granulomatous conjunctivitis
    b. hypertensive anterior uveitis
    c. intermediate uveitis
    d. multifocal choroidal granulomas

25. What pathogen is associated with the development of Kaposi sarcoma?
    a. cytomegalovirus
    b. Epstein-Barr virus
    c. HSV-1
    d. human herpesvirus 8

26. A patient with a history of AIDS (last $CD4^+$ T-lymphocyte count 89 cells/μL) presents for evaluation of decreased vision and is diagnosed with ocular toxoplasmosis. What test should be ordered promptly for this patient?
    a. serologic tests for syphilis (rapid plasma reagin/fluorescent treponemal antibody absorption test)
    b. serologic tests for *Toxoplasma gondii* (IgG and IgM)
    c. computed tomography of the chest
    d. magnetic resonance imaging of the brain

27. A patient with AIDS presents with bilateral pale-yellow, placoid retinal lesions. What testing and treatment should be ordered?
    a. Check $CD4^+$ helper T-lymphocyte count and start antiretroviral therapy.
    b. Check $CD4^+$ helper T-lymphocyte count and start systemic corticosteroids.
    c. Check syphilis antibodies and rapid plasmin reagin and start intramuscular benzathine penicillin G, 2.4 million units.
    d. Check syphilis antibodies and rapid plasmin reagin and start intravenous penicillin G, 18–24 million units.

28. An immunosuppressed patient presents with features consistent with unilateral endophthalmitis. A pars plana vitrectomy is performed, and analysis of vitreous fluid specimens reveals septate hyphae with dichotomous branching on silver stain. What is the most likely organism?
    a. *Aspergillus fumigatus*
    b. *Candida albicans*
    c. *Coccidioides immitis*
    d. *Cryptococcus neoformans*

29. A patient with candidemia is found to have yellow-white chorioretinal lesions without vitritis. What is the most appropriate initial treatment option?
    a. intravitreal vancomycin
    b. oral voriconazole
    c. pars plana vitrectomy
    d. posterior sub-Tenon injection of triamcinolone

30. Four months after cataract surgery in the right eye, a patient had recurrent 1–2+ anterior chamber cell and flare each time topical corticosteroids were tapered. Now, a hypopyon, an iris mass, necrotizing scleritis, and vitreous snowballs have developed. Infection with what organism most likely caused this condition?
    a. *Candida* species
    b. *Histoplasma* species
    c. *Pseudomonas* species
    d. *Streptococcus* species

31. A 78-year-old man presents for a routine eye examination. His ocular history is notable only for uncomplicated bilateral cataract surgery 5 years earlier. On examination, intraocular pressure is 6 mm Hg in the right eye and 13 mm Hg in the left eye. The right-eye examination is notable for 1+ cell and 2+ flare in the anterior chamber. Findings from the left-eye examination are unremarkable. The fundus examination shows clear vitreous in both eyes and dilated retinal venules and narrowed arterioles, worse in the right eye. What is the most appropriate next step in the care of this patient?
    a. Start topical corticosteroid drops.
    b. Perform a vitreous biopsy to obtain a specimen for flow cytometry.

c. Order carotid Doppler ultrasonography.
d. Reassure the patient that these are normal findings after cataract surgery.

32. A 65-year-old woman with vitritis and negative results on the treponemal antibody test and interferon-gamma release assay responds well initially to systemic corticosteroids; however, as the corticosteroids are tapered, the vitritis recurs. A vitreous biopsy is performed, and cytologic analysis shows pleomorphic lymphoid cells with a high nuclear-to-cytoplasm ratio. Approximately what proportion of patients with this condition will develop intracranial lesions characterized by the same cells?
    a. less than 1 in 10
    b. 1 in 3
    c. 1 in 2
    d. more than 2 in 3

33. A child with a history of reddish-yellow skin lesions presents with unilateral recurrent hyphema and anterior chamber cells. A few iris lesions are noted. What is the best test to identify the etiology of this patient's intraocular inflammation and hyphema?
    a. anterior chamber paracentesis with directed polymerase chain reaction (PCR) for cytomegalovirus
    b. skin or iris biopsy to evaluate for foamy macrophages
    c. anterior chamber paracentesis with directed PCR for rubella virus
    d. skin or iris biopsy to evaluate for caseating granulomas

34. A patient who is being treated with mycophenolate mofetil for bilateral pars planitis has persistent macular edema in the right eye. Examination of the anterior chamber and vitreous shows no evidence of active inflammation. What is the most appropriate next step to manage the macular edema in this patient?
    a. Switch to cyclophosphamide.
    b. Administer intravenous methylprednisolone 1 g daily for 3 days.
    c. Administer periocular or intravitreal triamcinolone acetonide injection.
    d. Perform pars plana vitrectomy with membrane peeling.

35. A 12-year-old patient with a 7-year history of JIA-associated chronic anterior uveitis (CAU) presents for her regular follow-up appointment. She uses prednisolone drops once daily and is asymptomatic. What finding can be observed on examination?
    a. band keratopathy
    b. fibrinous anterior chamber reaction
    c. hypopyon
    d. vitritis

36. A child with JIA-associated chronic bilateral nongranulomatous uveitis has developed band keratopathy. What pathologic finding can be observed in this patient's cornea?
    a. subepithelial urate deposition
    b. subepithelial calcium deposition
    c. pre-Descemet urate deposition
    d. pre-Descemet calcium deposition

# Answers

1. **b.** The innate immune system is a relatively broad-acting rapid reaction force that recognizes "nonself" (foreign) substances, proteins, or lipopolysaccharides. The innate response can be thought of as a preprogrammed reaction that is immediate, requires no prior exposure to the foreign substance, and is similar for all encountered triggers. The result is the generation of biochemical mediators and cytokines that recruit innate effector cells, especially macrophages and neutrophils, to remove the offending stimulus through phagocytosis or enzymatic degradation.
2. **c.** Activated macrophages are classically defined as macrophages that produce the full spectrum of inflammatory and cytotoxic cytokines; thus, they mediate and amplify acute inflammation, tumor killing, and major antibacterial activity. Epithelioid cells and giant cells represent different terminal differentiations of the activated macrophage.

   Resting macrophages are the classic scavenging cell, capable of phagocytosis and uptake of dead cell membranes, chemically modified extracellular protein (ie, acetylated or oxidized lipoproteins), sugar ligands, naked nucleic acids, and bacterial pathogens. Resting monocytes express at least 3 types of scavenging receptors but synthesize very low levels of proinflammatory cytokines. Scavenging can occur in the absence of inflammation. Primed macrophages are derived from resting macrophages that become primed by exposure to certain cytokines. Upon priming, these cells become positive for human leukocyte antigen (HLA) class II molecules and capable of functioning as antigen-presenting cells (APCs) to T lymphocytes. Primed macrophages thus resemble dendritic cells. They can exit tissue sites by afferent lymphatic vessels to reenter the lymph node. Stimulated (or reparative) macrophages are partially activated and produce some inflammatory cytokines that contribute to fibrosis and wound healing.
3. **c.** Monocytes can be primed and induced to become APCs. Basophils, eosinophils, and neutrophils generally do not have the ability to act as APCs.
4. **c.** Because they are proteins, antibodies themselves can be antigenic. Their antigenic sites are called *idiotopes,* as distinguished from *epitopes*, which are the antigenic sites on foreign molecules. An allotope is a site on the constant or nonvarying part of an antibody molecule that is recognizable by a combining site of other antibodies. Isotopes are 2 or more atoms whose nuclei have the same number of protons but different numbers of neutrons.
5. **a.** Infliximab is a mouse/human-chimeric monoclonal antibody directed against tumor necrosis factor α (TNF-α). One study showed that as many as 75% of patients receiving more than 3 infusions develop antinuclear antibodies, causing drug-induced lupus syndrome and the formation of human anti-idiotypic (anti-chimeric) antibodies, which can lead to reduced efficacy of infliximab.

   Methotrexate, interferon alfa-2a/2b, and tacrolimus are not associated with formation of anti-idiotypic antibodies. Methotrexate is an antimetabolite drug that is often coadministered with biologics for synergistic effect and to *reduce* the risk of developing antidrug antibodies. Interferon alfa-2a/2b, administered subcutaneously, has been beneficial in some patients with uveitis. Interferon alfa-2a has antiviral, immunomodulatory, and antiangiogenic effects. Tacrolimus, a product of *Streptomyces tsukubaensis,* is a calcineurin inhibitor that eliminates T-cell receptor signal transduction and downregulates interleukin-2 gene transcription and receptor expression of $CD4^+$ T lymphocytes.

6. **c.** Conjunctiva-associated lymphoid tissue (CALT) is part of the mucosal immune system, which utilizes innate and adaptive immune responses to maintain the homeostasis of mucosal surfaces. Although there is an abundance of APCs (macrophages, dendritic cells) in CALT, their role is to convey antigen to local lymph nodes for processing. They do not create a population of memory B cells. While immunoglobulin A (IgA) is present abundantly in tears, IgA does not provide for a secondary adaptive immune response. One defining feature of the mucosal immune system is that it is an interconnected system of lymphatic function, such that prior exposure at any mucosal immune system site will allow for a secondary adaptive immune response (eg, via a population of memory B cells) at every mucosal immune system site. Prior exposure at a non-mucosal location in the body (eg, abrasion of the skin or vaccination within a muscle) does not sensitize and prime the mucosal immune system for future exposure. Although there is a high density of mast cells within the conjunctiva, these cells do not explain the ability of an intranasal vaccine to facilitate an antibody-mediated effector response on the ocular surface.
7. **d.** Normal limbal physiology is a major component of corneal immune privilege, especially the maintenance of avascularity and the scarcity of APCs in the paracentral and central cornea. The lack of APCs and lymphatic channels partially inhibits the afferent response in the central cornea. The absence of postcapillary venules centrally can limit the efficiency of effector recruitment, although effector cells and molecules can infiltrate even avascular cornea.

   Cytokines and complement help recruit immune mediators to the central cornea, which is otherwise relatively devoid of immune effectors. CALT is responsible for antigen processing, but the effector limb of this system can extend to the corneal surface, resulting in recruitment of immune effectors to the cornea.
8. **c.** Both the choroid and the retina have abundant potential APCs, including macrophages and dendritic cells in the choroid and choriocapillaris and microglia in the retina. Effector cells such as B lymphocytes typically are very rare in normal retina and choroid. Eosinophils and neutrophils are also absent but may be induced to infiltrate the retina and choroid by various stimuli.
9. **a.** The ocular inflammatory disease with the strongest HLA association is birdshot chorioretinopathy (BCR); nearly all patients with BCR are HLA-A29 positive (relative risk up to 224 for North American and European populations). HLA-B27, HLA-B51, and HLA-DR15 are associated with low relative risks (between 2 and 10) for acute anterior uveitis, Behçet disease, and intermediate uveitis, respectively. It is important to remember that the HLA association identifies individuals at risk, but it is not a diagnostic marker. The associated haplotype is not necessarily present in all people with the disease, nor does its presence ensure the associated diagnosis.
10. **d.** HLA-DR4 has been weakly associated with both Vogt-Koyanagi-Harada syndrome and sympathetic ophthalmia.
11. **d.** This patient has *recurrent uveitis,* a term used to describe repeated episodes of uveitis separated by periods of quiescence lasting 3 months or more without therapy. *Acute uveitis* refers to episodes characterized by sudden onset and limited (eg, <3 months') duration. *Chronic uveitis* refers to episodes of uveitis that recur less than 3 months after treatment has been discontinued. *Limited* refers to episodes lasting 3 months or less.
12. **a.** TNF-α is believed to play a major role in the pathogenesis of juvenile idiopathic arthritis, ankylosing spondylitis, and other forms of spondyloarthritis. Adalimumab, infliximab, certolizumab, golimumab, and etanercept are TNF-α inhibitors. TNF inhibitors have been

associated with central nervous system demyelination (promoting or unmasking multiple sclerosis [MS]), hepatitis B reactivation, and deep fungal and other serious atypical infections. This class of medication is not recommended in patients with demyelinating disease. Screening for tuberculosis and viral hepatitis is performed before starting these medications.

A number of immunomodulatory agents, including interferon β preparations, alemtuzumab, dimethyl fumarate, ocrelizumab, rituximab, and teriflunomide, have important beneficial effects for patients with MS. Acute attacks of MS are typically treated with glucocorticoids. Systemic corticosteroids such as methylprednisolone can safely be used in uveitis associated with MS.

13. **b.** The increasing intraocular pressure (IOP) is a concern; however, if additional anti-inflammatory treatment is not added, it is very likely that the cataract will become visually significant and the uveitis will not be sufficiently controlled to safely perform cataract extraction. A systemic immunomodulatory medication should be added to attain control of inflammation and allow the eventual taper of topical corticosteroids. Glaucoma surgery is likely to worsen the uveitis, which already requires topical corticosteroids at least 4 times per day. While oral acetazolamide may improve IOP control, the increase in topical corticosteroids will likely result in cataract progression, and cataract surgery will be contraindicated as long as very frequent topical treatment is necessary to control the uveitis. Although an oral nonsteroidal anti-inflammatory drug (NSAID) may decrease the amount of topical corticosteroids necessary to control chronic anterior uveitis, it is unlikely that this class of medication will adequately control the patient's uveitis and allow the discontinuation of topical corticosteroids.

14. **d.** Necrotizing scleritis is the most severe and destructive type of scleritis. Approximately 50%–60% of cases are associated with systemic disease, including life-threatening systemic vasculitides. Necrotizing scleritis is more likely than the other forms of anterior scleritis to lead to vision loss. In the past, mortality rates of patients with necrotizing scleritis associated with systemic inflammatory diseases were as high as 30%; prompt diagnosis as well as the use of biologic therapies can improve prognosis.

15. **a.** Juvenile idiopathic arthritis (JIA; formerly referred to as *juvenile chronic arthritis* and *juvenile rheumatoid arthritis*) is the most common systemic disorder associated with anterior uveitis in the pediatric age group. It is characterized by arthritis beginning before age 16 years and lasting for at least 6 weeks. Girls younger than 5 years who are positive for antinuclear antibody (ANA) have an increased risk of developing chronic anterior uveitis. Ocular involvement is rare in children with systemic arthritis (Still disease) or polyarticular involvement and in those with positive rheumatoid factor. In JIA-associated uveitis, affected eyes are frequently white and asymptomatic. Children with JIA, especially those who are ANA positive or who have oligoarticular disease, should undergo regular slit-lamp examinations to screen for uveitis.

16. **c.** Tubulointerstitial nephritis and uveitis (TINU) syndrome occurs predominantly in adolescent girls and women. The median age at onset is 15 years. The uveitis is typically a bilateral nongranulomatous anterior uveitis. Posterior segment involvement may include vitritis, multifocal chorioretinal lesions or scars, and retinal vascular leakage, as well as optic disc and macular edema. Patients may present with systemic symptoms before the development of uveitis. Abnormal laboratory findings include elevated serum creatinine level or decreased creatinine clearance, increased *urinary* $\beta_2$-microglobulin level, proteinuria, presence of urine eosinophils, pyuria or hematuria, urinary white cell casts, and normoglycemic

glycosuria. TINU syndrome is responsive to high-dose oral corticosteroids, but patients with a prolonged inflammatory course may require systemic immunomodulatory therapy.

17. **d.** The prevalence of HLA-B27 varies by population. Although approximately 8% of the US population is positive for HLA-B27, only 0.012% of them (or 1 in 667) will develop acute anterior uveitis (AAU). Therefore, the most likely finding on this patient's slit-lamp examination is a quiet anterior chamber; eye examination results would be normal. Hypopyon, posterior synechiae, and posterior subcapsular cataract can occur in patients with AAU; however, these findings are unlikely in this patient, who is asymptomatic and who has a very low risk of developing AAU.
18. **a.** This patient demonstrates all the high-risk characteristics for developing uveitis and should be screened for uveitis every 3 months. High-risk children are those with antinuclear antibodies and oligoarticular arthritis, polyarticular arthritis (rheumatoid factor negative), psoriatic arthritis, or undifferentiated arthritis; those who were younger than 7 years at the time of JIA onset; and those with JIA duration of 4 years or less. All other children with JIA should be screened every 6–12 months.
19. **a.** A common presentation of brimonidine-associated uveitis is a red and irritated eye with extensive (often granulomatous) keratic precipitates (KPs) and low-grade anterior uveitis in a patient receiving long-term brimonidine therapy. Corneal edema and vitreous inflammation may also be present. Dorzolamide and timolol are not associated with drug-induced uveitis. While rifabutin is associated with drug-induced uveitis, rifampin is not.
20. **c.** Birdshot chorioretinopathy typically has an insidious onset. While a small subset of patients may have self-limited disease, the clinical course of BCR is characteristically chronic and progressive.
21. **d.** Syphilis should be considered in the differential diagnosis of any intraocular inflammatory disease. It is caused by the spirochete *Treponema pallidum* and is associated with numerous ocular manifestations. Posterior segment findings of acquired syphilis include vitritis, chorioretinitis, focal or multifocal retinitis, necrotizing retinochoroiditis, retinal vasculitis, exudative retinal detachment, isolated papillitis, and neuroretinitis. Syphilis may present as a focal retinitis or as a peripheral necrotizing retinochoroiditis that may resemble acute retinal necrosis or progressive outer retinal necrosis.
22. **a.** Stellate KPs are very suggestive of a viral intraocular infection and are a frequent finding in these cases. However, larger nongranulomatous or granulomatous KPs can also occur in herpetic intraocular infections, including herpes simplex virus (HSV) types 1 and 2 and varicella-zoster virus (VZV). When stellate KPs are present, they are often distributed diffusely. The KPs localizing only to the Arlt triangle may be granulomatous or nongranulomatous and classically occur in noninfectious intraocular inflammation. Ring-shaped clusters of corneal endothelial lesions or small, white-domed KPs have been observed in cytomegalovirus (CMV) anterior uveitis.
23. **c.** Induction therapy for VZV-associated acute retinal necrosis may consist of intravenous (IV) acyclovir 10 mg/kg every 8 hours for 10–14 days or oral valacyclovir 2 g 3 times/day. Valacyclovir 1 g 3 times/day is the dosage used for HSV-associated acute retinal necrosis or active herpetic keratitis. Oral valganciclovir is appropriate for CMV-associated intraocular infections.
24. **a.** Ocular manifestations of coccidioidomycosis (caused by *Coccidioides immitis*) such as phlyctenular and granulomatous conjunctivitis are more common than uveal involvement.

Uveal manifestations can include granulomatous KPs and iris nodules, which are granulomas on histologic examination. Hypertensive anterior uveitis does not occur, however. Choroidal involvement manifests as multifocal choroidal granulomas most frequently located in the postequatorial fundus.

25. **d.** The pathogen associated with the development of Kaposi sarcoma is human herpesvirus (HHV)-8. Epstein-Barr virus (HHV-4) is associated with the development of primary central nervous system lymphomas and vitreoretinal lymphomas in HIV-infected individuals. HSV-1 (HHV-1) and CMV (HHV-5) are not associated with any specific neoplasias in persons with HIV infection.

26. **d.** Ocular toxoplasmosis in immunocompromised patients may be associated with cerebral or disseminated toxoplasmosis. For patients with AIDS who have active ocular toxoplasmosis, neuroimaging (preferably magnetic resonance imaging) should be performed to evaluate for central nervous system involvement. Although syphilis is reemerging globally, particularly in association with HIV coinfection, there is no indication for urgent syphilis testing in this patient. Since the patient has already been diagnosed with ocular toxoplasmosis, serologic testing is not immediately useful. Computed tomography of the chest might be indicated if there is concern for pulmonary infection or inflammation, but in this case, expeditious investigation for toxoplasmic encephalitis is necessary.

27. **d.** Suspicion for syphilis should be high in this patient. Syphilis is a common coinfection in HIV-infected individuals. A classic manifestation of syphilis in patients with AIDS is unilateral or bilateral pale-yellow, placoid retinal lesions that preferentially involve the macula. Checking syphilis antibodies (treponemal test) and the rapid plasmin reagin (RPR, nontreponemal test) will help confirm the diagnosis and assess response to treatment. Ocular cases of syphilis should be treated in the same manner as neurosyphilis, and 18–24 million units of IV penicillin G administered daily for 10–14 days is indicated. Syphilis without neurologic or ocular involvement may be treated intramuscularly as a single dose.

    Checking $CD4^+$ helper T-lymphocyte count and starting antiretroviral therapy (ART) would be appropriate if the patient exhibited features of HIV retinopathy (cotton-wool spots, microaneurysms, and retinal hemorrhages) only. Systemic corticosteroids may be used in treating immune recovery uveitis, an inflammatory process that affects patients with a history of CMV retinitis and AIDS whose immune status improves with ART. Systemic corticosteroids may also be used if there is a prominent inflammatory reaction in syphilis, but this medication should not be started until after treatment with IV penicillin has commenced.

28. **a.** Histologically, *Aspergillus* species is characterized by septate hyphae with dichotomous branching. *Candida* species are recognized as budding yeast with a characteristic pseudohyphate appearance. Histologically, *C immitis* appears as spherules with multiple endospores. *Cryptococcus neoformans* does not appear as hyphae but rather as round capsules with a halo on India ink; periodic acid–Schiff (PAS) and Gomori methenamine silver (GMS) stain the organism and leave the capsule unstained.

29. **b.** In this case, the hematogenous dissemination of *Candida* organisms involves only the choroid, so appropriate initial treatment includes systemic antifungal medication and close monitoring. Oral voriconazole has excellent intraocular penetration. If there is vitreal involvement, pars plana vitrectomy in conjunction with systemic and intravitreal antifungals may be necessary. Monotherapy with periocular or intraocular depot corticosteroids will worsen the infectious endophthalmitis. Intravitreal injection of the antibiotic vancomycin will not treat the *Candida* infection.

30. **a.** Recurrent inflammation in an eye that has previously undergone surgery is concerning for chronic postoperative endophthalmitis. While the presentation of chronic postoperative fungal endophthalmitis may be similar to that of a bacterial infection, certain clinical signs make a fungal etiology more likely, including a corneal infiltrate or edema, a mass in the iris or ciliary body, necrotizing scleritis, vitreous snowballs, or a "string-of-pearls" appearance in the vitreous. Chronic postoperative bacterial endophthalmitis is most commonly caused by *Cutibacterium acnes* (formerly *Propionibacterium acnes*), a gram-positive anaerobe. Other gram-positive bacteria, gram-negative bacteria, *Mycobacterium* species, and fungi (such as *Candida parapsilosis, Aspergillus flavus,* and *Torulopsis candida*) can also cause chronic postoperative endophthalmitis.

31. **c.** The most likely diagnosis is ocular ischemic syndrome, which can masquerade as uveitis. Carotid Doppler ultrasonography should be ordered to assess for ipsilateral stenosis of the carotid artery. Given the lack of symptoms and lack of previous uveitic episodes, this presentation in an older man is unlikely to be caused by uveitis; therefore, empiric topical corticosteroid therapy is not indicated. Given this patient's age, it is appropriate to consider lymphoma in the differential diagnosis. however, the patient's vitreous cavity is clear, and the diagnosis of vitreoretinal lymphoma (formerly called *primary intraocular lymphoma*) is unlikely. While extensive intraocular surgery can result in breakdown of the blood–aqueous barrier, this breakdown does not typically result from uncomplicated cataract surgery (nor would it explain the hypotony and absence of cells in the left eye).

32. **d.** The case described clinically is consistent with vitreoretinal lymphoma (VRL), and the cytopathologic findings confirm the diagnosis. In more than two-thirds of cases of VRL, patients will have or will go on to develop intracranial disease. In fact, VRL is a subset of primary central nervous system lymphoma (PCNSL). Approximately 25% of patients with PCNSL (who do not yet have intraocular involvement) will go on to develop VRL.

33. **b.** The case described is consistent with juvenile xanthogranuloma, which may feature reddish-yellow skin lesions. Intraocular features may include recurrent hyphema. Histologically, skin or iris biopsy specimens would be expected to show large histiocytes with foamy cytoplasm and Touton giant cells. Caseating granulomas are a feature of tuberculous granulomas, but tuberculosis-associated uveitis does not feature recurrent hyphemas. CMV and rubella virus have been associated with forms of hypertensive anterior uveitis, but they are not associated with the skin lesions described in this case.

34. **c.** Uveitic macular edema is a frequent complication of uveitis and may occur or persist even when inflammation seems otherwise controlled. The use of periocular or intravitreal corticosteroids is the most appropriate next step to resolve this patient's uveitic macular edema. The PeriOcular vs. INTravitreal Corticosteroids for Uveitic Macular Edema (POINT) trial demonstrated superior visual outcomes with intravitreal triamcinolone and intravitreal dexamethasone implant compared with sub-Tenon triamcinolone injection.

    Macular optical coherence tomography can help identify factors contributing to the macular edema, such as vitreomacular traction. Since there is no evidence of prominent vitreomacular traction in this case, a pars plana vitrectomy with membrane peeling is not indicated. Although macular edema can result in irreversible vision loss, an alkylating agent such as cyclophosphamide would be reserved for more aggressive, sight-threatening ocular inflammation. Similarly, pulses of IV methylprednisolone are more typically used to rapidly control acute, high-grade inflammation.

35. **a.** Chronic anterior uveitis (CAU) associated with JIA is an indolent, relatively asymptomatic anterior uveitis in children. After years of low-grade inflammation, these eyes may develop signs of chronic inflammation, which include band keratopathy, cataracts, and/or synechiae. Fibrinous anterior chamber reaction and hypopyon are characteristic of acute anterior uveitis, which is usually symptomatic. Although patients with JIA-associated CAU may have anterior vitreous cells, the vitreous is not the predominant site of inflammation and therefore vitritis is usually not present.

36. **b.** Band keratopathy results from the deposition of calcium hydroxyapatite at the level of the Bowman membrane. Aside from chronic inflammation associated with uveitis, other etiologies of calcific band keratopathy include systemic disorders that cause hypercalcemia or elevated serum phosphorus levels, as well as silicone oil (particularly in an aphakic eye), exposure to mercurial vapors or preservative, and primary hereditary band keratopathy.