INTERNATIONAL COUNCIL of OPHTHALMOLOGY

Ocular HIV/AIDS Related Diseases (Initial and Follow-up Evaluation)

(Ratings: A: Most important, B: Moderately important, C: Relevant but not critical **Strength of Evidence:** I: Strong, II: Substantial but lacks some of I, III: consensus of expert opinion in absence of evidence for I & II)

General - Initial Exam History

- Age **(B:III)**
- Ocular symptoms including laterality **(A:III)**
- Systemic symptoms **(A:III)**
- Complete review of systems **(A:III)**
- Prior ocular history **(A:III)**
- Prior medical history **(A:III)**
- Prior surgical history **(B:III)**
- History of other sexually transmitted diseases **(A:III)**
- History of AIDS-defining illnesses or complications **(A:III)**
- Method of HIV acquisition **(B:III)**
- Duration of HIV infection **(A:III)**
- Past and current risk factors – sexual behavior, intravenous drug abuse, transfusion history **(A:III)**
- Current anti-HIV regimen – duration and compliance **(A:III)**
- Current medications **(A:II)**
- Current CD4 count **(A:II)**
- Current viral load **(A:II)**
- Medication allergies **(B:III)**

General - Initial Physical Exam

- General appearance **(A:III)**
- External examination – face, ocular adnexa **(A:III)**
- Lymphatics – preauricular and submandibular nodes **(A:III)**
- Visual acuity **(A:III)**
- Extraocular motility **(A:III)**
- Confrontation visual fields **(A:III)**
- Eyelids – lid closure, interpalpebral fissure height **(B:III)**
- Lacrimal gland **(B:III)**
- Evaluation of tear film – Schirmer, rose bengal and fluorescein staining **(A:III)**
- Nasolacrimal function **(B:III)**

- Slit-lamp examination
  - Eyelid margins **(A:III)**
  - Conjunctiva **(A:III)**
  - Sclera **(A:III)**
  - Cornea **(A:III)**
  - Anterior chamber **(A:III)**
  - Iris **(A:III)**
  - Lens **(A:III)**
  - Anterior vitreous **(A:III)**
- Dilated ophthalmoscopic examination
  - Vitreous – cell/flare, blood, condensations **(A:III)**
  - Optic disc **(A:III)**
  - Retinal vasculature **(A:III)**
  - Macula/fovea **(A:III)**
  - Peripheral retina with scleral depression **(A:III)**
  - Choroid **(A:III)**

General - Diagnostic Tests

- HIV infection – for increased risk populations and/or suspected infection
  - Anti-HIV ELISA to screen for infection, followed by confirmation with Western blot **(A:II)**
- AIDS
  - Presence of AIDS-defining illness(es) **(A:III)**
  - CD4 (< 200 cells/µl, per CDC criteria) **(A:II)**
- Known HIV/AIDS patient
  - CD4 count **(A:II)**
  - Viral load **(A:II)**

General - Care Management

- Management of HIV/AIDS should involve a multidisciplinary team, including an infectious disease specialist and an ophthalmologist **(A:III)**
- Anti-Retroviral Therapy (ART) or Highly Active Anti-Retroviral Therapy (HAART), where available **(A:II)**
- Emphasis on prevention of disease transmission **(A:III)**
- Identification and treatment of HIV/AIDS associated illnesses/infections (particularly tuberculosis and syphilis) **(A:II)**

HIV Retinopathy – Initial Exam History

- CD4 count **(A:II)**
- Ocular symptoms – usually asymptomatic **(B:III)**

HIV Retinopathy – Initial Physical Exam

- Visual acuity **(A:III)**
- Slit lamp examination **(B:III)**
- Dilated ophthalmoscopic examination **(A:II)**
- Screen for other HIV/AIDS related illnesses/infections **(B:III)**

HIV Retinopathy - Care Management

- Treat immune compromise with HAART **(A:II)**
- Consider corticosteroids **(B:III)** or focal laser **(A:II)** for macular edema

HIV Retinopathy – Follow-up Evaluation

- Lesions usually resolve over weeks to months **(A:II)**
- Dilated ophthalmoscopic examination every 3 months for CD4 counts persistently below 50 cells/µl **(A:II)**

Cytomegalovirus (CMV) Retinitis – Initial Exam History

- Interval since AIDS diagnosis **(A:II)**
- History of CMV related systemic complications **(A:II)**
- Ocular symptoms –blurred vision, floaters, photopsias, scotomata **(A:II)**

Cytomegalovirus (CMV) Retinitis – Initial Physical Exam

- Visual acuity **(A:II)**
- Cornea for small endothelial deposits **(B:III)**
- Anterior chamber for signs of inflammation **(A:II)**
- Dilated ophthalmoscopic examination of both eyes – including optic disc, macula, and retinal periphery. The choroid should be examined to rule out co-infection with other agents **(A:II)**

Cytomegalovirus Retinitis – Diagnostic Tests

- CD4 count – typically less than 50 cells/µl **(A:II)**

Cytomegalovirus Retinitis – Ancillary Testing

- Fundus photography may be useful to document disease progression or response to treatment and fluorescein angiography as indicated to evaluate for the presence of macular edema or ischemia **(A:III)**
- Test for syphilis and vitreous biopsy for other causes of necrotizing retinitis (varicella zoster virus, herpes simplex virus, toxoplasmosis) when diagnosis uncertain **(A:II)**

Cytomegalovirus – Care Management

- Main objectives include direct treatment of CMV retinitis with anti-CMV medications, and improvement of immune status with initiation/optimization of HAART if not already taking anti-retroviral therapy **(A:II)**
- To reduce the possibility of immune recovery uveitis, patients with newly diagnosed CMV retinitis who are not on HAART should be treated with anti-CMV medications until the retinitis is inactive, or at least less active. HAART should then be initiated **(A:II)**
- Also, in cases with expected persistent immune suppression, e.g. poor response to or unavailability of ART, immediate treatment is indicated **(A:II)**
- Local anti-CMV therapy, as might be achieved using intravitreal injection of ganciclovir or foscarnet, may be used immediately when active CMV retinitis either involves or threatens the optic disc or macula **(A:II)**
- Induction followed by indefinite maintenance therapy in cases of persistent immune suppression **(A:II)**
- Ganciclovir
    - Intravenous – 5 mg/kg every 12 hours for 2 to 3 weeks, then 5 mg/kg/day 5 to 7 times per week indefinitely. **(A:I)** Monitor for leukopenia, the risk of which may be lessened by administering leukocyte-stimulating factors such as granulocyte colony-stimulating factor **(A:II)**
    - Intraocular – 2 to 2.5 mg/0.1 ml intravitreal injection twice per week until inactive, then weekly **(A:I)**
    - Intravitreal sustained-release implant (Vitrasert) – 4.5 mg implant that releases 1 µg/hr for eight months. This should be combined with oral valganciclovir therapy for systemic coverage **(A:I)**
- Foscarnet
    - Intravenous – 60 mg/kg every 8 hours or 90 mg/kg every 12 hours for 14 days, then 90 to 120 mg/kg/day. Monitor for renal toxicity **(A:I)**
    - Intraocular – 1.2 mg/0.05 ml (or 2.4 mg/0.1 ml) **(A:I)**
- Valganciclovir
    - Oral – 900 mg twice daily for 2 weeks, **(A:I)** then 900 mg daily indefinitely. **(A:II)** Monitor for leukopenia **(A:II)**

Cytomegalovirus – Follow-up Evaluation

- Recurrence is very common, and patients being treated with anti-CMV medications should be evaluated monthly **(A:II)**
- Intervals may be extended when CD4 counts are elevated, anti-CMV medications are discontinued, and the disease remains inactive in the setting of immune recovery **(A:II)**
- Visual symptoms **(A:II)**
- CD4 count and HIV viral load **(A:II)**
- Review of systems for CMV related systemic complications or drug-induced side effects **(A:II)**

Cytomegalovirus – Follow-up Examination

- Visual acuity **(A:II)**
- Slit lamp examination **(B:II)**
- Ophthalmoscopic examination – including the macula and peripheral retina **(A:II)**
- Serial fundus photography **(B:II)**

Cytomegalovirus – Follow-up Management

- No treatment can eliminate CMV from the eye **(A:II)**
- Patient education about the symptoms of CMV retinitis is crucial **(A:III)**
- For recurrences, first line is re-induction with the same therapy in the absence of side effects or evidence of drug resistance **(A:II)**
- Persistent or progressive retinitis after 6 weeks of induction-level therapy implies resistance or incorrect diagnosis **(A:II)**
- UL97 and UL54 mutations in CMV DNA are associated with relative ganciclovir resistance **(A:II)**
- Anti-CMV drugs may be discontinued in patients on HAART with no signs of active CMV retinitis in whom CD4 counts are above 100 to 150 cells/µl for at least three to six months **(A:II)**

Tuberculosis – Initial Exam History

- CD4 count (typically < 200 cells/µl) **(A:II)**
- Visual and ocular symptoms **(A:II)**
- History *M. Tuberculosis* infection, systemic complications, or exposure **(A:II)**

Tuberculosis – Initial Physical Exam

- Visual acuity **(A:III)**
- External examination – including eyelids and adnexa **(B:III)**
- Slit lamp examination **(B:III)**
- Intraocular pressure **(B:III)**
- Dilated ophthalmoscopic examination - optic disc, macula, retinal periphery, and choroid **(A:II)**

Tuberculosis – Diagnostic Tests

- Presumptive diagnosis by clinical examination combined with PPD skin testing and chest x-ray **(A:II)**
- Requires a high index of clinical suspicion **(B:III)**
- Consider leukocyte stimulation based assays where available, particularly when PPD skin testing is unreliable (QuantiFERON® -TB Gold Test; T.SPOT-TB® test) **(A:II)**
- Definitive diagnosis requires biopsy with histopathologic examination **(A:III)**

Tuberculosis – Ancillary Testing

- Fluorescein angiography to evaluate suspected retinal vasculitis **(A:III)**
- Indocyanine green angiography may be helpful to detect subclinical choroidal involvement **(A:III)**
- Optical coherence tomography to diagnose and monitor for cystoid macular edema **(A:III)**

Tuberculosis – Care Management

- Systemic treatment is indicated with rifampin (500 mg/day for weight > 50 kg and 600 mg/day for weight < 50 kg), isoniazid (5 mg/kg/day), pyrimethamine (25 to 30 mg/kg/day, and ethambutol (15 mg/kg/day) for 2 months then rifampin and isoniazid for another 4 to 7 months **(A:II)**
- Oral prednisone (1 mg/kg/day), taper as directed by clinical response **(A:II)**
- Initiate/optimize HAART if not already taking anti-retroviral therapy **(A:II)**
- Coordinate care with an infectious disease specialist **(A:III)**

Tuberculosis – Follow-up Evaluation

- Monitor all patients for medication toxicity **(A:II)**
- Examine patients monthly until there is significant clinical improvement **(A:III)**

Toxoplasmosis (T. gondii) – Initial Exam History

- CD4 count (typically < 200 cells/µl) **(A:II)**
- Visual and ocular symptoms **(A:III)**
- History of *T. gondii* infection, systemic complications, or exposure **(A:III)**

Toxoplasmosis – Initial Physical Exam

- Visual acuity **(A:II)**
- Intraocular pressure **(B:II)**
- Slit lamp examination **(C:II)**
- Dilated ophthalmoscopic examination **(A:II)**

Toxoplasmosis – Diagnostic Tests

- Primarily a clinical diagnosis **(A:III)**
- Serologic testing for anti-*T. gondii* IgM/IgG antibodies **(A:II)**
- In unclear cases, can perform PCR on aqueous or vitreous for *T. gondii* DNA **(B:II)**

Toxoplasmosis – Care Management

- Initial treatment involves oral antimicrobials for 4 to 6 weeks. Options include:
    - Trimethoprim/sulfamethoxazole (800/160) 500 mg PO twice daily **(A:II)**
    - Pyrimethamine (100 mg loading dose given over 24 hours, followed by 25 to 50 mg daily) and sulfadiazine (1 g given four times daily) for 4 to 6 weeks. Should be given concurrently with folinic acid (3 to 5 mg twice weekly) to prevent leukopenia and thrombocytopenia **(B:II)**
    - Clindamycin (300 mg orally every 6 hours) for 3 or more weeks **(B:II)**

    - Atovaquone (750 mg orally four times daily) for 3 months **(B:II)**
    - Consider use of Azithromycin in patients with sulfa-related allergy **(B:III)**
- Maintenance therapy with at least one of the above medications is recommended for patients with ocular toxoplasmosis who remain severely immunodeficient **(A:III)**
- Oral corticosteroids may be considered when inflammation contributes to vision loss (vitritis, vasculitis, serous retinal detachment, lesion involving or threatening the optic disc or macula) - 0.5 mg/kg/day with taper, initiated and ended concurrent with antimicrobial therapy **(A:III)**
- Topical corticosteroids may be considered for significant anterior chamber inflammation **(A:III)**

Toxoplasmosis – Follow-up Evaluation

- Initial follow-up should be one week after initiation of treatment, then as indicated by examination and treatment response **(A:III)**
- Lesions typically take several months to resolve **(A:III)**

Syphilis – Initial Exam History

- CD4 count (often less than 200 cells/µl). However, ocular syphilis in the setting of HIV/AIDS may occur at any CD4 count. **(A:II)**
- Visual symptoms and rapidity of onset **(A:III)**
- Previous syphilis infection, related complications, or exposure **(A:III)**
- History of other sexually-transmitted diseases **(B:III)**

Syphilis – Initial Physical Exam

- Visual acuity **(A:II)**
- Intraocular pressure **(B:II)**
- Slit lamp examination **(B:III)**
- Dilated ophthalmoscopic examination **(A:II)**

Syphilis – Diagnostic Tests

- Both non-treponemal (RPR or VDRL) and treponemal (MHA-TP or FTA-ABS) testing should be obtained (up to one-third of patients with syphilitic uveitis have a negative non-treponemal test) **(A:II)**
- Patients with profound immune suppression may present with seronegative syphilis **(A:II)**
- CSF examination (RPR or VDRL) in all HIV/AIDS patients with ocular syphilis **(A:II)**

Syphilis – Care Management

- Treat as neurosyphilis **(A:II)**
- Involve an infectious disease specialist in coordinating systemic management **(A:III)**
- First-line treatment is with IV penicillin G, 18 to 24 million units for 14 days **(A:II)**
- Worsening ocular inflammation following the initiation of penicillin may be indicative of a Jarish-Herxheimer reaction **(A:II)**

Syphilis – Follow-up Evaluation

- Serial serum and CSF antibody levels every month for 3 months, then every 6 months until CSF cell count normalizes and CSF VDRL/RPR becomes non-reactive **(A:III)**
- Serum quantitative nontreponemal testing every 3 months for one year, then yearly **(A:III)**
- Maintenance therapy is not necessary or recommended **(B:II)**

Table 1. Adnexal Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity	CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
Herpes Zoster Ophthalmicus	< 200 cells/µl **(A:II)**	• Prior zoster infection **(A:II)** • Age	• Periorbita • Eyelids • SLE • Sclera • AC • DOE	• Vesiculobullous dermatitis in CN V1 distribution (**A:II)** • Complications include keratitis, uveitis, scleritis, retinitis, and optic neuritis **(A:II)** • Hemorrhagic hypopyon **(B:II)**	• Clinical examination • Can confirm diagnosis with viral culture, Tzanck smear, PCR **(A:II)**	• IV acyclovir 10 mg/kg every 8 hours for 7 days **(A:II)** • Alternatives: valacyclovir (1 gram PO 3 times daily) or oral acyclovir (800 mg PO 5 times daily); close follow-up for signs of disseminated infection including cerebritis **(A:II)** • Patient receiving high doses of valacyclovir should be monitored for TTP/HUS **(A:II)** • Maintain on oral acyclovir 800 mg, 3 to 5 times daily indefinitely **(A:II)** • Alternatively, can maintain on oral famciclovir or valacyclovir • Topical corticosteroids for iridocyclitis and/or stromal keratitis **(A:II)**	• Observe for post-herpetic neuralgia • Serial DOE
Kaposi's Sarcoma	< 200 cells/µl **(A:II)**	• Manner of HIV acquisition (sexual more common) **(B:II)** • Dry eye symptoms **(B:II)** • Pain (rare) **(B:II)** • Reduced vision (rare) **(C:II)**	• External examination • Lymphatics • Oral cavity • SLE • Eyelids • Lacrimal gland • Skin of face and upper body	• Highly vascularized tumor of the skin or mucous membranes (**A:II)** • May involve eyelids and/or conjunctiva (**A:II)** • Eyelid lesions may appear as a purplish nodule (**A:II)** • Conjunctival lesions can mimic SCH **(B:II)**	• Clinical examination • Biopsy with histopathology of suspicious lesions **(A:II)**	• Immune reconstitution **(A:II)** • Indications for treatment: 1) loss of normal lid function, 2) discomfort, 3) cosmesis • Treatment depends on the size and location of lesions **(A:II)** • Treatment options include intralesional vinblastine or interferon-alpha, local radiation therapy, excision, and cryotherapy **(A:II)** • Systemic chemotherapy if disseminated disease **(A:II)** • Reduce size of large lesions prior to excision	• Recurrences are common **(A:II)**
Molluscum Contagiosum	Any **(A:II)**	• History of molluscum exposure **(A:II)**	• Periorbita • SLE • Trunk and genitalia **(B:III)**	• Papulonodular dermatitis of the skin and mucous membranes (**A:II)** • Multiple small umbilicated lesions (**A:II)**	• Clinical examination	• Immune reconstitution **(A:II)** • Topical agents: liquid nitrogen, trichloracetic acid, cantharadin **(A:II)** • Incision with curettage, excision, or cryotherapy **(A:II)**	• Eyelid lesions commonly recur within 6 to 8 weeks **(A:II)**
Squamous Cell Carcinoma (SCC) and Conjunctival Intraepithelial Neoplasia (CIN)	Any **(A:II)**	• Geographic location – higher risk in Africa **(A:II)** • History of HPV infection **(B:II)**	• VA • External examination • SLE • Gonioscopy	• Papilliform, gelatinous, or leukoplakic lesion at the interpalpebral limbus (**A:II)** • SCC: lesion is more extensive, feeder vessels more common (**A:II)**	• Biopsy with histopathologic examination **(A:II)**	• Wide excision with cryotherapy for non-invasive lesions **(A:II)** • Frozen section pathologic examination **(A:II)** • Alternatives include MMC, 5-FU, and interferon **(A:II)**	• Routine pre- and post-operative examinations
Cutaneous or Conjunctival Lymphoma	Any **(A:II)**	• Presence/history of systemic lymphoma **(A:II)** • Ocular symptoms	• VA • External examination • SLE • DOE **(C:III)**	• Erythematous lesion of the eyelid or conjunctiva (**A:II)**	• Biopsy **(A:II)** • Systemic evaluation **(A:II)**	• Radiation **(A:II)** • Chemotherapy **(A:II)** • Involve an oncologist	• As directed by treatment in coordination with oncologist

SLE = slit lamp examination, AC = anterior chamber, DOE = dilated ophthalmoscopic examination, PCR = polymerase chain reaction, PO = per os (by mouth), IV = intravenous, TTP/HUS = thrombotic thrombocytopenic purpura/hemolytic uremic syndrome, HIV = human immunodeficiency virus, SCH = subconjunctival hemorrhage, HPV = human papilloma virus, VA = visual acuity, MMC = mitomycin C, 5-FU = 5-fluorouracil, FBS = foreign body sensation = visual acuity, MMC = mitomycin C, 5-FU = 5-fluorouracil, FBS = foreign body sensation

Table 1. (continued) Adnexal Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity	CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
Conjunctival Microvasculopathy	Any **(A:II)**	• Typically asymptomatic **(B:II)**	• SLE • DOE **(B:III)**	• Inferior perilimbus (**A:II)** • Segmental vascular dilation and narrowing (**A:II)** • Comma-shaped vascular fragments (**A:II)** • Microaneurysms (**A:II)** • Blood column granularity (**A:II)**	• Clinical examination	• Not indicated	• Unnecessary
Conjunctivitis	Any **(A:II)**	• Symptoms of irritation, discharge **(A:II)**	• VA • SLE	• Conjunctival erythema (**A:II)** • Watery, mucoid, or purulent discharge (**A:II)**	• Clinical examination • Culture and gram stain of discharge **(A:II)**	• Guided by results of gram stain and culture • Clinical examination should be used to initiate empiric treatment	• Every 5 to 7 days until resolution
Atopic dermatitis	Any **(A:II)**	• History of atopic triad: dermatitis, rhinitis, asthma • Typical symptomatology **(B:II)** • Triggers **(A:II)**	• External examination • Eyelids	• Pruritis and excematous changes of the periorbital skin (**A:II)**	• Clinical examination	• Topical corticosteroids (i.e. hydrocortisone 0.5% cream) **(A:II)** • Topical calcineurin inhibitors, Elidel (pimecrolimus) and Protopic (tacrolimus) are contraindicated in immunosuppressed patients **(B:II)**	• Serial examinations until resolution
Blepharitis	Any **(A:II)**	• Use of Indonavir **(B:II)** • Itching, FBS, redness	• External examination • Eyelids • SLE – including tear film and cornea	• Crusting and erythema of eyelid margins (**A:II)**	• Clinical examination	• Lid hygiene • Consider culture in high-risk patients	• Every 4 weeks

SLE = slit lamp examination, AC = anterior chamber, DOE = dilated ophthalmoscopic examination, PCR = polymerase chain reaction, PO = per os (by mouth), IV = intravenous, TTP/HUS = thrombotic thrombocytopenic purpura/hemolytic uremic syndrome, HIV = human immunodeficiency virus, SCH = subconjunctival hemorrhage, HPV = human papilloma virus, VA = visual acuity, MMC = mitomycin C, 5-FU = 5-fluorouracil, FBS = foreign body sensation = visual acuity, MMC = mitomycin C, 5-FU = 5-fluorouracil, FBS = foreign body sensation

Table 2. Corneal and Anterior Segment Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity		CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
Keratoconjunctivitis sicca		Any **(A:II)**	• Typical history • History of HIV encephalopathy **(B:III)** • Duration of infection with HIV **(B:III)**	• VA • Periorbita **(B:III)** • Lacrimal gland **(C:III)** • Eyelids **(A:II)** • SLE with fluorescein	• Lagophthalmos and reduced blink rate (**B:II)** • Diminished tear meniscus (**B:III)** • Rapid TBUT (**A:II)** • Interpalpebral staining with rose bengal or fluorescein (**A:II)**	• Clinical examination • Schirmer testing **(A:II)** • TBUT **(B:II)** • Rose bengal or fluorescein staining **(A:II)**	• Artificial tears • Long-acting lubricants • Consider punctual occlusion in resistant cases	• As dictated by examination
Viral keratitis	VZV	Any **(B:II)**	• Reduced vision • Ocular symptoms • Presence or recent history of zoster dermatitis **(A:II)** • Prior history of zoster or herpes infection **(A:II)**	• VA • IOP • Periorbita • Eyelids/lashes • Corneal sensation • SLE with fluorescein • DOE with scleral depression	• Dendritic epithelial keratitis **(A:II)** • Decreased corneal sensation **(A:II)** • Elevated IOP **(B:II)** • Iris atrophy **(B:II)** • May present with a mild conjunctivitis or anterior uveitis **(B:II)** • 1/3 develop stromal involvement **(B:II)**	• Clinical examination • Corneal sensation **(A:II)** • May confirm with viral culture, DFA, PCR **(B:II)**	• Acyclovir 800 mg PO 5 times daily or 10 mg/kg IV tid **(A:II)** • Foscarnet IV for resistant cases **(A:II)** • Consider maintenance dose of acyclovir (600 mg PO tid) **(A:II)** • Infectious dendrites can be treated with oral (as described above) or topical antiviral medications (trifluridine 1% 9 times daily) **(A:II)**	• Every 1 to 7 days until resolution, then every 6 months • Observe for stromal and/or neurotrophic keratitis and postherpetic neuralgia **(B:III)**
	HSV				• Dendritic epithelial keratitis, which may be larger in HIV+ patients (**A:II)** • Limbal involvement (**B:II)**		• Topical trifluridine 1% 9 times daily or Acyclovir ointment 5 times daily **(A:II)** • May treat with oral acyclovir (400-800 mg PO 5 times daily) alone **(A:II)** • Consider lesion debridement **(B:III)** • Long term suppression with acyclovir 400 mg PO bid for 1 year **(A:I)**	• Every 1 to 7 days until resolution • HSV appears to recur more frequently in HIV/AIDS patients **(A:II)**

HIV = human immunodeficiency virus, VA = visual acuity, SLE = slit lamp examination, TBUT = tear film breakup time, VZV = varicella zoster virus, HSV = herpes zoster virus, IOP = intraocular pressure, DOE = dilated ophthalmoscopic examination, DFA = direct fluorescent antibody, PCR = polymerase chain reaction, PO = per os (by mouth), IV = intravenous, AIDS = acquired immunodeficiency syndrome, FBS = foreign body sensation, AC = anterior chamber, HAART = highly active antiretroviral therapy, CMV = cytomegalovirus

Table 2. (continued) Corneal and Anterior Segment Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity		CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
Bacterial or fungal keratitis	Gonorrhea Syphilis Tuberculosis Cryptococcus	Any **(B:II)**	• Reduced vision • Discharge • Timing of symptom onset **(B:III)**	• VA • SLE with fluorescein • DOE **(C:III)**	• Epithelial defect with stromal infiltrate **(A:II)** • Tend to be more severe and bilateral in HIV+ patients **(A:II)**	• Clinical examination • Culture and gram stain **(A:II)**	• Guided by culture results **(B:II)** • Aggressive treatment with topical fortified antibiotics and/or antifungal agents **(A:II)**	• Daily follow-up until substantial improvement • High risk for corneal perforation **(A:II)**
Microsporidial keratitis		< 100 cells/µl **(A:II)**	• Reduced vision • Ocular symptoms – FBS, irritation, photophobia	• VA • SLE with fluorescein	• Punctate epithelial keratopathy (**A:II)** • Mild papillary conjunctivitis (**A:II)** • Mild AC inflammation (**A:II)**	• Scraping or biopsy of suspicious corneal and conjunctival lesions **(A:II)** • Giemsa stain **(A:II)**	• Immune reconstitution **(A:II)** • Directed treatment options include: topical propamidine isethionate, topical fumagillin, oral albendazole, oral itraconazole **(A:II)** • Consider debulking **(B:III)**	• Serial examinations until resolution
Vortex keratopathy (Phospholipidosis)		Any **(B:II)**	• FBS • Medication history (eg. amiodarone, chloroquine, chlorpromazine, ganciclovir, acyclovir) (**A:II)**	• VA • SLE	• Characteristic whorl-like pattern of gray-white subepithelial corneal deposits (**A:II)**	• History and clinical examination	• Reduce or discontinue offending medication, if possible **(A:II)**	• Lesions resolve slowly
Drug-associated uveitis • Cidofovir • Rifabutin • Terbinafine		Any **(A:II)**	• Reduced vision • Medication history, including daily doses **(A:II)** • Immune status **(B:III)** • Duration on HAART **(B:III)** • History of CMV retinitis **(A:II)**	• VA • SLE • IOP **(B:III)** • DOE **(B:III)**	• AC inflammation (**A:II)** • Rifabutin-associated hypopyon (**A:II)**	• History and clinical examination	• Topical corticosteroids with or without dose reduction of offending medication **(A:II)** • Usually unnecessary to discontinue offending medication **(B:III)** • Mydriatic agent	• Serial every 1 to 2 weeks examinations until resolution

HIV = human immunodeficiency virus, VA = visual acuity, SLE = slit lamp examination, TBUT = tear film breakup time, VZV = varicella zoster virus, HSV = herpes zoster virus, IOP = intraocular pressure, DOE = dilated ophthalmoscopic examination, DFA = direct fluorescent antibody, PCR = polymerase chain reaction, PO = per os (by mouth), IV = intravenous, AIDS = acquired immunodeficiency syndrome, FBS = foreign body sensation, AC = anterior chamber, HAART = highly active antiretroviral therapy, CMV = cytomegalovirus

Table 3. Posterior Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity	CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
HIV retinopathy	< 50 cells/µl **(A:II)**	• Visual and ocular symptoms (typically asymptomatic) **(B:III)**	• VA • SLE **(B:III)** • DOE **(A:II)**	• Conjunctival microvascular changes **(B:II)** • CWS (**A:II)** • IRH (**A:II)** • MAs (**A:II)** • Retinal ischemia (**A:II)** • CME (**A:II)**	• Clinical diagnosis	• Improve immune status with HAART **(A:II)** • Screen for other infections/illnesses • Consider corticosteroids **(B:III)** or focal laser **(A:II)** for macular edema	• Lesions spontaneously resolve over weeks to months (**A:II)** • DOE every 3 months for CD4 counts persistently < 50 cells/µl **(A:II)**
CMV retinitis	< 50 cells/µl **(A:II)**	• Duration of AIDS **(A:II)** • History of systemic CMV infection (**A:II)** • Ocular symptoms including blurred vision, gradual visual field loss, photopsia, and floaters **(A:II)**	• VA **(A:II)** • SLE **(B:II)** • DOE **(A:II)**	• Geographic thickening and opacification of the retina (**A:II)** • Mild anterior chamber and vitreous inflammation (**B:II)** • Characteristic linear or stellate KP **(B:II)** • 3 main types: granular retinitis with satellite lesions, hemorrhagic retinitis with prominent edema, or perivascular retinitis (**A:II)**	• Primarily a clinical diagnosis • CD4 count **(A:II)** • Rule out syphilis and other causes of retinitis **(A:II)** • Consider vitreous biopsy in challenging cases	• Improve immune status, although consider delay of HAART in HAART-naïve patients until retinitis is improved to reduce the risk of IRU **(A:II)** • Immediate treatment if persistent immune suppression is expected **(A:II)** • Induction followed by maintenance **(A:II)** • Ganciclovir: IV (5 mg/kg every 12 hours for 3 weeks, then 5 mg/kg/day) **(A:I);** IO (2-2.5mg/0.1ml twice weekly until inactive) **(A:I)**; intraocular implant **(A:I)**, combine with oral anti-CMV medications for systemic coverage **(A:II)** • Foscarnet: IV (60 mg/kg every 8 hours or 90 mg/kg every 12 hours for 14 days, then 90 to 120 mg/kg/day) **(A:I)**; IO (1.2 mg/0.05 ml) **(A:I)** • Valganciclovir: PO (900 mg bid for 2 weeks, then 900 mg daily). Monitor for leukopenia **(A:II)**	• CMV cannot be eliminated from the eye **(A:II)**; patient education for recurrences is crucial • Reevaluate patients monthly while treating with anti-CMV medications **(A:II)** • Extend visit intervals when CD4 counts are elevated, anti-CMV medications are discontinued, and the disease remains inactive in the setting of immune recovery **(A:II)** • Consider serial fundus photography **(B:II)** • Treat recurrences with re-induction of same therapy, unless contraindicated due to side effects or resistance **(A:II)** • May discontinue maintenance therapy in patients without active CMV retinitis and at least 6 months of CD4 cell counts above 150 cells/µl **(A:II)**

HIV = human immunodeficiency virus, VA = visual acuity, SLE = slit lamp examination, DOE = dilated ophthalmoscopic examination, CWS = cotton wool spots, IRH = intraretinal hemorrhages, MA = microaneurysms, CME = cystoid macular edema, HAART = highly active antiretroviral therapy, CMV = cytomegalovirus, AIDS = acquired immunodeficiency syndrome, KP = keratic precipitates, IRU = Immune recovery uveitis, IV = intravenous, IO = intraocular, PO = per os (by mouth), IOP = intraocular pressure, AC = anterior chamber, PCR = polymerase chain reaction, IOP = intraocular pressure, PPD = purified protein derivative, CXR = chest X-ray, IGRA = Interferon-gamma release assay, FA = fluorescein angiography, ICG = indocyanine green angiography, OCT = optical coherence tomography, RPR = rapid plasma reagin, VDRL = venereal disease research laboratory, FTA-ABS = fluorescent treponemal antibody absorption, MHA-TP = microhemagluttination-Treponema pallidum, CSF = cerebrospinal fluid, PORN = progressive outer retinal necrosis, ARN = acute retinal necrosis, HZO = herpes zoster ophthalmicus, TTP/HUS = thrombotic thrombocytopenic purpura/hemolytic uremic syndrome, TRD = tractional retinal detachment, RNV = retinal neovascularization, ERM = epiretinal membrane, CME = cystoid macular edema, FA = fluoroscein angiography, PPV = pars plana vitrectomy, VMTS = vitreomacular traction syndrome, PVR = proliferative vitreoretinopathy, OU = oculus uterque (both eyes), CXR = chest X-ray, ABG = arterial blood gas, CT = computed tomography, TMP-SMX = trimethoprim sulfamethoxazole, EOM = extraocular motility, CNS = central nervous system, MRI = magnetic resonance imaging, N/A = not applicable

Table 3. (continued) Posterior Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity	CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
Toxoplasmosis	< 200 cells/µl **(A:II)**	• Visual symptoms (**A:II)** • Exposure to undercooked meat or cats **(A:II)**	• VA **(A:II)** • IOP **(B:II)** • SLE **(C:II)** • DOE **(A:II)**	• Moderate-to-severe AC and vitreous inflammation (**B:II)** • Retinochoroiditis with a relative lack of retinal hemorrhage (**A:II)** • Smooth leading edge without satellite lesions (**B:II)** • A rare cause of isolated anterior uveitis(**C:II)**	• Clinical diagnosis • Anti-*Toxoplasma* IgM/IgG **(A:II)** • PCR of aqueous in unclear cases (**B:II)**	• Trimethoprim/sulfamethoxazole (800/160) 500 mg PO bid for 4 to 6 weeks **(A:II)** • Pyrimethamine and sulfamethoxazole for 4 to 6 weeks (option of combination with azithromycin) **(B:II)** • Clindamycin (300 mg PO every 6 hours) for 3 or more weeks **(B:II)** • Atovaquone (750 mg PO qid) for 3 months **(B:II)**	• Initially every 3 to 5 days, then as indicated by examination • Maintenance therapy with at least one medication is recommended for all patients with persistent severe immune deficiency
Tuberculosis	< 200 cells/µl **(A:II)**	• Visual symptoms (**A:II)** • History of *M. Tuberculosis* infection, systemic complications, or exposure **(A:II)**	• VA • External examination **(B:III)** • SLE **(B:III)** • IOP **(B:III)** • DOE **(A:II)**	• Vitritis (**A:II)** • Choroidal tubercles and tuberculomas (**A:II)** • Overlying exudative retinal detachment (**B:II)** • Retinal periphlebitis (**A:II)**	• Presumptive diagnosis combined with PPD skin testing and CXR **(A:II)** • Consider IGRAs (eg. QuantiFERON®-TB Gold; T.SPOT-TB®) (**B:II)** • FA, ICG, and OCT when indicated (see text) **(B:III)**	• Systemic treatment with rifampin (500 mg/day for weight > 50 kg and 600 mg/day for weight < 50 kg), isoniazid (5 mg/kg/day), pyrimethamine (25 to 30 mg/kg/day, and ethambutol (15 mg/kg/day) for 2 months then rifampin and isoniazid for another 4 to 7 months **(A:II)** • PO prednisone (1 mg/kg/day), taper as directed by clinical response **(A:II)** • Immune reconstitution **(A:II)** • Involve an infectious disease specialist	• Monitor all patients for drug toxicity **(A:II)** • Examine patients monthly until a significant improvement

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Table 3. (continued) Posterior Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity	CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
Syphilis	Often < 200 cells/µl, but can vary **(A:II)**	• Visual symptoms (**A:II)** • Sexual history (**B:II)**	• VA **(A:II)** • IOP **(B:II)** • SLE **(B:II)** • DOE **(A:II)**	• Iridocyclitis or diffuse inflammation (**A:II)** • Necrotizing retinitis (**A:II)** • Subretinal plaque (**B:II)** • Papillitis, optic neuritis, or neuroretinitis (**A:II)**	• RPR or VDRL **(A:II)** • FTA-ABS or MH-ATP **(A:II)** • Consider seronegative syphilis **(B:II)** • CSF examination **(A:II)**	• Treat as neurosyphilis **(A:II)** • Involve an infectious disease specialist • IV penicillin G, 18 to 24 million units for 14 days **(A:II)**	• Serial serum and CSF antibody levels – every month for 3 months, then every 6 months until CSF cell count normalizes and CSF VDRL becomes non-reactive **(A:III)** • Maintenance therapy not recommended **(B:II)** • Monitor patients for a Jarish-Herxheimer reaction **(A:II)**
Non-CMV necrotizing herpetic retinitis	PORN: < 50 cells/µl **(A:II)** ARN: > 50cells/µl **(A:II)**	• History of HZO or dermatitis (**A:II)** • History of herpes encephalitis (**B:II)** • Visual symptoms (pain, vision loss, new floaters or scotomata) (**A:II)**	• VA **(A:II)** • IOP **(B:III)** • SLE **(B:III)** • DOE **(A:II)**	• Retinal whitening with occasional hemorrhages (**A:II)** • Multiple large confluent areas of retinitis (**A:II)** • Rapid progression (**A:II)** • Prominent (ARN) or minimal (PORN) vitreal inflammation (**B:II)**	• Clinical diagnosis • Aqueous or vitreous biopsy for PCR-based analysis can aid in diagnosis **(B:II)** • Note location and extent of involved retina	• Induction with high-dose intravenous acyclovir (15 mg/kg q 8 hours) **(A:II)** • Intraocular ganciclovir (2 to 2.5mg/0.1ml twice weekly) or foscarnet (1.2 mg/0.05ml) as indicated **(A:II)** • Maintenance with long term oral valacyclovir or valganciclovir may be considered **(B:II)** • Patients receiving high doses of valacyclovir should be monitored for TTP/HUS (**A:II)** • Patients receiving valganciclovir should be monitored for leukopenia (**A:II)**	• Can progress rapidly **(A:II)** • Daily until significant improvement, then weekly

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Table 3. (continued) Posterior Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity	CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
Immune recovery uveitis	>100 cells/µl or 50 cell/µl increase **(A:II)**	• History/extent of CMV retinitis (**A:II)** • History of cidofovir use (**B:II)**	• VA **(A:II)** • IOP **(B:II)** • SLE **(A:II)** • DOE **(A:II)**	• Panuveitis with vitreous predominance (**A:II)** • May be complicated by TRD, RNV, ERM formation, or CME (**A:II)**	• Diagnosis based on history and clinical examination • Consider FA to rule out CME **(B:III)**	• Topical, periocular, or intraocular corticosteroids (**A:II)** • PPV for VMTS, ERM, cataract, PVR (**A:II)**	• Weekly until resolution
Pneumocystis choroiditis	< 200 cells/µl **(A:II)**	• History of aerosolized pentamidine use **(A:II)**	• VA **(A:II)** • SLE **(C:III)** • DOE OU **(A:II)**	• Multiple well-demarcated yellowish choroidal lesions in the posterior pole (**A:II)** • Lack of iritis, vitritis, or vasculitis (**A:II)**	• Clinical diagnosis • Consider workup for systemic disease, including CXR, ABG analysis, abdominal CT, and liver function testing	• TMP-SMX or pentamidine (4 mg/kg/day) **(A:II)**	• Monthly until resolution – usually 1 to 3 months • Following a 3 week IV induction regimen, maintain on oral prophylactic treatment until immune system recovers (CD4 count above 200 cells/µl) **(A:II)**
Cryptococcus	< 50 cells/µl **(A:II)**	• Visual symptoms including vision loss, diplopia, and new scotomata **(A:II)** • Headache/ meningismus **(A:II)**	• VA • SLE **(B:II)** • EOM **(A:II)** • DOE **(A:II)**	• Signs and symptoms of central nervous system infection (**A:II)** • Papilledema (**A:II)** • Retrobulbar optic neuritis (**B:II)** • Multifocal choroiditis (**A:II)** • Other findings may include iritis, iris mass, vitritis, necrotizing retinitis, and eyelid or conjunctival mass (**B:II)**	• Clinical diagnosis • CNS symptoms – think of cryptococcal meningitis **(A:II)** • Skin lesions – biopsy **(B:II)**	Isolated choroiditis: • IV fluconazole, 400 mg/day and IV flucytosine, 100 to 150 mg/kg/day for 10 weeks **(A:II)** Associated with meningitis: • IV amphotericin B, 0.7 to 1 mg/kg/day and IV flucytosine 100 mg/kg/day for 2 weeks followed by IV fluconazole for at least 10 weeks **(A:II)**	• Weekly until resolution

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Table 3. (continued) Posterior Manifestations of HIV/AIDS **(A:III** unless otherwise indicated)

Entity	CD4 count	History	Examination	Key Findings	Diagnostic workup	Management	Follow-up
HIV-associated retinitis	> 120 cells/µl **(A:II)**	• Visual symptoms (**A:II)**	• VA • IOP **(C:II)** • SLE **(C:III)** • DOE **(A:II)**	• Peripheral multifocal retinitis (**A:II)** • Retinal vasculitis (**A:II)** • Mild vitreous inflammation (**B:II)** • Lack of retinal hemorrhage (**B:II)** • Slow progression (**B:II)**	• Clinical diagnosis • Rule out other entities, particularly syphilis **(A:II)**	• Antiretroviral therapy should lead to regression (**A:II)**	• Weekly until resolution
Intraocular lymphoma	< 500 cells/µl **(A:II)**	• Floaters (**A:II)** • Vision loss (**A:II)**	• VA **(A:II)** • DOE **(A:II)**	• Necrotizing retinitis (**A:II)** • Retinal vasculitis (**B:II)** • Subretinal mass (**A:II)** • Vitritis (**A:II)** • Multifocal choroiditis (**A:II)** • Poor response to treatment (**A:II)** • CNS symptoms (**A:II)**	• Workup and treatment for infectious processes **(A:II)** • AC tap for IL-10 **(B:II)** • Vitreous biopsy with cytologic examination **(A:II)** • Consider retinal biopsy • MRI for CNS lymphoma **(A:II)**	• Radiation and chemotherapy **(A:II)** • Involve Oncology • Immune reconstitution (**B:II)**	• Monthly DOE • Poor prognosis **(A:II)**
Retinal detachment	N/A	• History/extent of necrotizing retinitis (**A:II)** • History of trauma **(B:II)** • History of myopia **(B:II)**	• VA **(A:II)** • SLE **(B:II)** • DOE **(A:II)**	• Rhegmatogenous retinal detachment **(A:II)** • Holes or microholes in areas of areas of atrophic retina or chronic retinitis **(A:II)** • Note extent of detachment, number, size, and location of retinal holes, and involvement of the macula **(A:II)**	• Clinical diagnosis • B-scan ultrasound if visualization is poor	• PPV with long-term silicone oil tamponade and scleral buckling (**A:II)**	• Routine post-operative follow-up • As directed by other disorders

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