



January 2009

International Council of Ophthalmology

ICO International Clinical Guidelines 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**)

International Council of Ophthalmology
945 Green Street, San Francisco, CA 94133 USA
Fax: +1 (415) 409-8403 E-mail: info@icoph.org Web: www.icoph.org

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/ μ l, 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/ μ l (**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/ μ l (**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 μ g/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/ μ l for at least three to six months (A:II)

Tuberculosis - Initial Exam History

- CD4 count (typically < 200 cells/ μ l) (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/ μ l) (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/ μ l). 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)**

Preface to the Guidelines:

International Clinical Guidelines are prepared and distributed by the International Council of Ophthalmology.

These Guidelines are to serve a supportive and educational role for ophthalmologists worldwide. These guidelines are intended to improve the quality of eye care for patients. They have been adapted in many cases from similar documents (Benchmarks of Care) created by the American Academy of Ophthalmology based on their Preferred Practice Patterns.

While it is tempting to equate these to Standards, it is impossible and inappropriate to do so. The multiple circumstances of geography, equipment availability, patient variation and practice settings preclude a single standard.

Guidelines on the other hand are a clear statement of expectations. These include comments of the preferred level of performance assuming conditions that allow the use of optimum equipment, pharmaceuticals and/or surgical circumstances.

Thus, a basic expectation is created and if the situation is optimum, the optimum facets of diagnosis, treatment and follow up may be employed. Excellent, appropriate and successful care can also be provided where optimum conditions do not exist.

Simply following the Guidelines does not guarantee a successful outcome. It is understood that, given the uniqueness of a patient and his or her particular circumstance, physician judgment must be employed. This can result in a modification in application of a guideline in individual situations.

Medical experience has been relied upon in the preparation of these guidelines, and they are whenever possible, evidence-based. This means these Guidelines are based on the latest available scientific information. The ICO is committed to provide updates of these guidelines on a regular basis (approximately every two to three years).

(Also see the Introduction to the ICO International Clinical Guidelines at www.icoph.org/guide/guideintro.html and the list of other Guidelines at www.icoph.org/guide/guidelist.html.)

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/ μ l (A:II)	<ul style="list-style-type: none"> Prior zoster infection (A:II) Age 	<ul style="list-style-type: none"> Periorbita Eyelids SLE Sclera AC DOE 	<ul style="list-style-type: none"> Vesiculobullous dermatitis in CN V1 distribution (A:II) Complications include keratitis, uveitis, scleritis, retinitis, and optic neuritis (A:II) Hemorrhagic hypopyon (B:II) 	<ul style="list-style-type: none"> Clinical examination Can confirm diagnosis with viral culture, Tzanck smear, PCR (A:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Observe for post-herpetic neuralgia Serial DOE
Kaposi's Sarcoma	< 200 cells/ μ l (A:II)	<ul style="list-style-type: none"> Manner of HIV acquisition (sexual more common) (B:II) Dry eye symptoms (B:II) Pain (rare) (B:II) Reduced vision (rare) (C:II) 	<ul style="list-style-type: none"> External examination Lymphatics Oral cavity SLE Eyelids Lacrimal gland Skin of face and upper body 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Clinical examination Biopsy with histopathology of suspicious lesions (A:II) 	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> Recurrences are common (A:II)
Molluscum Contagiosum	Any (A:II)	<ul style="list-style-type: none"> History of molluscum exposure (A:II) 	<ul style="list-style-type: none"> Periorbita SLE Trunk and genitalia (B:III) 	<ul style="list-style-type: none"> Papulonodular dermatitis of the skin and mucous membranes (A:II) Multiple small umbilicated lesions (A:II) 	<ul style="list-style-type: none"> Clinical examination 	<ul style="list-style-type: none"> Immune reconstitution (A:II) Topical agents: liquid nitrogen, trichloroacetic acid, cantharadin (A:II) Incision with curettage, excision, or cryotherapy (A:II) 	<ul style="list-style-type: none"> Eyelid lesions commonly recur within 6 to 8 weeks (A:II)
Squamous Cell Carcinoma (SCC) and Conjunctival Intraepithelial Neoplasia (CIN)	Any (A:II)	<ul style="list-style-type: none"> Geographic location – higher risk in Africa (A:II) History of HPV infection (B:II) 	<ul style="list-style-type: none"> VA External examination SLE Gonioscopy 	<ul style="list-style-type: none"> Papilliform, gelatinous, or leukoplakic lesion at the interpalpebral limbus (A:II) SCC: lesion is more extensive, feeder vessels more common (A:II) 	<ul style="list-style-type: none"> Biopsy with histopathologic examination (A:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Routine pre- and post-operative examinations
Cutaneous or Conjunctival Lymphoma	Any (A:II)	<ul style="list-style-type: none"> Presence/history of systemic lymphoma (A:II) Ocular symptoms 	<ul style="list-style-type: none"> VA External examination SLE DOE (C:III) 	<ul style="list-style-type: none"> Erythematous lesion of the eyelid or conjunctiva (A:II) 	<ul style="list-style-type: none"> Biopsy (A:II) Systemic evaluation (A:II) 	<ul style="list-style-type: none"> Radiation (A:II) Chemotherapy (A:II) Involve an oncologist 	<ul style="list-style-type: none"> As directed by treatment in coordination with oncologist
Conjunctival Microvasculopathy	Any (A:II)	<ul style="list-style-type: none"> Typically asymptomatic (B:II) 	<ul style="list-style-type: none"> SLE DOE (B:III) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Clinical examination 	<ul style="list-style-type: none"> Not indicated 	<ul style="list-style-type: none"> Unnecessary
Conjunctivitis	Any (A:II)	<ul style="list-style-type: none"> Symptoms of irritation, discharge (A:II) 	<ul style="list-style-type: none"> VA SLE 	<ul style="list-style-type: none"> Conjunctival erythema (A:II) Watery, mucoid, or purulent discharge (A:II) 	<ul style="list-style-type: none"> Clinical examination Culture and gram stain of discharge (A:II) 	<ul style="list-style-type: none"> Guided by results of gram stain and culture Clinical examination should be used to initiate empiric treatment 	<ul style="list-style-type: none"> Every 5 to 7 days until resolution
Atopic dermatitis	Any (A:II)	<ul style="list-style-type: none"> History of atopic triad: dermatitis, rhinitis, asthma Typical symptomatology (B:II) Triggers (A:II) 	<ul style="list-style-type: none"> External examination Eyelids 	<ul style="list-style-type: none"> Pruritis and excematous changes of the periorbital skin (A:II) 	<ul style="list-style-type: none"> Clinical examination 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Serial examinations until resolution
Blepharitis	Any (A:II)	<ul style="list-style-type: none"> Use of Indonavir (B:II) Itching, FBS, redness 	<ul style="list-style-type: none"> External examination Eyelids SLE – including tear film and cornea 	<ul style="list-style-type: none"> Crusting and erythema of eyelid margins (A:II) 	<ul style="list-style-type: none"> Clinical examination 	<ul style="list-style-type: none"> Lid hygiene Consider culture in high-risk patients 	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> • Typical history • History of HIV encephalopathy (B:III) • Duration of infection with HIV (B:III) 	<ul style="list-style-type: none"> • VA • Periorbita (B:III) • Lacrimal gland (C:III) • Eyelids (A:II) • SLE with fluorescein 	<ul style="list-style-type: none"> • 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) 	<ul style="list-style-type: none"> • Clinical examination • Schirmer testing (A:II) • TBUT (B:II) • Rose bengal or fluorescein staining (A:II) 	<ul style="list-style-type: none"> • Artificial tears • Long-acting lubricants • Consider punctual occlusion in resistant cases 	<ul style="list-style-type: none"> • As dictated by examination
Viral keratitis	VZV	Any (B:II)	<ul style="list-style-type: none"> • Reduced vision • Ocular symptoms • Presence or recent history of zoster dermatitis (A:II) • Prior history of zoster or herpes infection (A:II) 	<ul style="list-style-type: none"> • VA • IOP • Periorbita • Eyelids/lashes • Corneal sensation • SLE with fluorescein • DOE with scleral depression 	<ul style="list-style-type: none"> • 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) 	<ul style="list-style-type: none"> • Clinical examination • Corneal sensation (A:II) • May confirm with viral culture, DFA, PCR (B:II) 	<ul style="list-style-type: none"> • 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) 	<ul style="list-style-type: none"> • Every 1 to 7 days until resolution, then every 6 months • Observe for stromal and/or neurotrophic keratitis and postherpetic neuralgia (B:III)
	HSV				<ul style="list-style-type: none"> • Dendritic epithelial keratitis, which may be larger in HIV+ patients (A:II) • Limbal involvement (B:II) 		<ul style="list-style-type: none"> • 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) 	<ul style="list-style-type: none"> • Every 1 to 7 days until resolution • HSV appears to recur more frequently in HIV/AIDS patients (A:II)
Bacterial or fungal keratitis	Gonorrhea	Any (B:II)	<ul style="list-style-type: none"> • Reduced vision • Discharge • Timing of symptom onset (B:III) 	<ul style="list-style-type: none"> • VA • SLE with fluorescein • DOE (C:III) 	<ul style="list-style-type: none"> • Epithelial defect with stromal infiltrate (A:II) • Tend to be more severe and bilateral in HIV+ patients (A:II) 	<ul style="list-style-type: none"> • Clinical examination • Culture and gram stain (A:II) 	<ul style="list-style-type: none"> • Guided by culture results (B:II) • Aggressive treatment with topical fortified antibiotics and/or antifungal agents (A:II) 	<ul style="list-style-type: none"> • Daily follow-up until substantial improvement • High risk for corneal perforation (A:II)
	Syphilis							
	Tuberculosis							
	Cryptococcus							
Microsporidial keratitis	< 100 cells/μl (A:II)	<ul style="list-style-type: none"> • Reduced vision • Ocular symptoms – FBS, irritation, photophobia 	<ul style="list-style-type: none"> • VA • SLE with fluorescein 	<ul style="list-style-type: none"> • Punctate epithelial keratopathy (A:II) • Mild papillary conjunctivitis (A:II) • Mild AC inflammation (A:II) 	<ul style="list-style-type: none"> • Scraping or biopsy of suspicious corneal and conjunctival lesions (A:II) • Giemsa stain (A:II) 	<ul style="list-style-type: none"> • Immune reconstitution (A:II) • Directed treatment options include: topical propamide isethionate, topical fumagillin, oral albendazole, oral itraconazole (A:II) • Consider debulking (B:III) 	<ul style="list-style-type: none"> • Serial examinations until resolution 	
Vortex keratopathy (Phospholipidosis)	Any (B:II)	<ul style="list-style-type: none"> • FBS • Medication history (eg. amiodarone, chloroquine, chlorpromazine, ganciclovir, acyclovir) (A:II) 	<ul style="list-style-type: none"> • VA • SLE 	<ul style="list-style-type: none"> • Characteristic whorl-like pattern of gray-white subepithelial corneal deposits (A:II) 	<ul style="list-style-type: none"> • History and clinical examination 	<ul style="list-style-type: none"> • Reduce or discontinue offending medication, if possible (A:II) 	<ul style="list-style-type: none"> • Lesions resolve slowly 	
Drug-associated uveitis	Any (A:II)	<ul style="list-style-type: none"> • Reduced vision • Medication history, including daily doses (A:II) • Immune status (B:III) • Duration on HAART (B:III) • History of CMV retinitis (A:II) 	<ul style="list-style-type: none"> • VA • SLE • IOP (B:III) • DOE (B:III) 	<ul style="list-style-type: none"> • AC inflammation (A:II) • Rifabutin-associated hypopyon (A:II) 	<ul style="list-style-type: none"> • History and clinical examination 	<ul style="list-style-type: none"> • Topical corticosteroids with or without dose reduction of offending medication (A:II) • Usually unnecessary to discontinue offending medication (B:III) • Mydriatic agent 	<ul style="list-style-type: none"> • 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/ μ l (A:II)	<ul style="list-style-type: none"> Visual and ocular symptoms (typically asymptomatic) (B:III) 	<ul style="list-style-type: none"> VA SLE (B:III) DOE (A:II) 	<ul style="list-style-type: none"> Conjunctival microvascular changes (B:II) CWS (A:II) IRH (A:II) MAs (A:II) Retinal ischemia (A:II) CME (A:II) 	<ul style="list-style-type: none"> Clinical diagnosis 	<ul style="list-style-type: none"> Improve immune status with HAART (A:II) Screen for other infections/illnesses Consider corticosteroids (B:III) or focal laser (A:II) for macular edema 	<ul style="list-style-type: none"> 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/ μ l (A:II)	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> VA (A:II) SLE (B:II) DOE (A:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Primarily a clinical diagnosis CD4 count (A:II) Rule out syphilis and other causes of retinitis (A:II) Consider vitreous biopsy in challenging cases 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> 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)
Toxoplasmosis	< 200 cells/ μ l (A:II)	<ul style="list-style-type: none"> Visual symptoms (A:II) Exposure to undercooked meat or cats (A:II) 	<ul style="list-style-type: none"> VA (A:II) IOP (B:II) SLE (C:II) DOE (A:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Clinical diagnosis Anti-<i>Toxoplasma</i> IgM/IgG (A:II) PCR of aqueous in unclear cases (B:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> 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/ μ l (A:II)	<ul style="list-style-type: none"> Visual symptoms (A:II) History of <i>M. Tuberculosis</i> infection, systemic complications, or exposure (A:II) 	<ul style="list-style-type: none"> VA External examination (B:III) SLE (B:III) IOP (B:III) DOE (A:II) 	<ul style="list-style-type: none"> Vitritis (A:II) Choroidal tubercles and tuberculomas (A:II) Overlying exudative retinal detachment (B:II) Retinal periphlebitis (A:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> Monitor all patients for drug toxicity (A:II) Examine patients monthly until a significant improvement

Syphilis	Often < 200 cells/μl, but can vary (A:II)	<ul style="list-style-type: none"> Visual symptoms (A:II) Sexual history (B:II) 	<ul style="list-style-type: none"> VA (A:II) IOP (B:II) SLE (B:II) DOE (A:II) 	<ul style="list-style-type: none"> Iridocyclitis or diffuse inflammation (A:II) Necrotizing retinitis (A:II) Subretinal plaque (B:II) Papillitis, optic neuritis, or neuroretinitis (A:II) 	<ul style="list-style-type: none"> RPR or VDRL (A:II) FTA-ABS or MH-ATP (A:II) Consider seronegative syphilis (B:II) CSF examination (A:II) 	<ul style="list-style-type: none"> Treat as neurosyphilis (A:II) Involve an infectious disease specialist IV penicillin G, 18 to 24 million units for 14 days (A:II) 	<ul style="list-style-type: none"> 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)	<ul style="list-style-type: none"> History of HZO or dermatitis (A:II) History of herpes encephalitis (B:II) Visual symptoms (pain, vision loss, new floaters or scotomata) (A:II) 	<ul style="list-style-type: none"> VA (A:II) IOP (B:III) SLE (B:III) DOE (A:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Clinical diagnosis Aqueous or vitreous biopsy for PCR-based analysis can aid in diagnosis (B:II) Note location and extent of involved retina 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Can progress rapidly (A:II) Daily until significant improvement, then weekly
Immune recovery uveitis	>100 cells/μl or 50 cell/μl increase (A:II)	<ul style="list-style-type: none"> History/extent of CMV retinitis (A:II) History of cidofovir use (B:II) 	<ul style="list-style-type: none"> VA (A:II) IOP (B:II) SLE (A:II) DOE (A:II) 	<ul style="list-style-type: none"> Panuveitis with vitreous predominance (A:II) May be complicated by TRD, RNV, ERM formation, or CME (A:II) 	<ul style="list-style-type: none"> Diagnosis based on history and clinical examination Consider FA to rule out CME (B:III) 	<ul style="list-style-type: none"> Topical, periocular, or intraocular corticosteroids (A:II) PPV for VMTS, ERM, cataract, PVR (A:II) 	<ul style="list-style-type: none"> Weekly until resolution
<i>Pneumocystis</i> choroiditis	< 200 cells/μl (A:II)	<ul style="list-style-type: none"> History of aerosolized pentamidine use (A:II) 	<ul style="list-style-type: none"> VA (A:II) SLE (C:III) DOE OU (A:II) 	<ul style="list-style-type: none"> Multiple well-demarcated yellowish choroidal lesions in the posterior pole (A:II) Lack of iritis, vitritis, or vasculitis (A:II) 	<ul style="list-style-type: none"> Clinical diagnosis Consider workup for systemic disease, including CXR, ABG analysis, abdominal CT, and liver function testing 	<ul style="list-style-type: none"> TMP-SMX or pentamidine (4 mg/kg/day) (A:II) 	<ul style="list-style-type: none"> 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)
<i>Cryptococcus</i>	< 50 cells/μl (A:II)	<ul style="list-style-type: none"> Visual symptoms including vision loss, diplopia, and new scotomata (A:II) Headache/meningismus (A:II) 	<ul style="list-style-type: none"> VA SLE (B:II) EOM (A:II) DOE (A:II) 	<ul style="list-style-type: none"> Signs and symptoms of central nervous system infection (A:II) Papilledema (A:II) Retrolbulbar 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) 	<ul style="list-style-type: none"> Clinical diagnosis CNS symptoms – think of cryptococcal meningitis (A:II) Skin lesions – biopsy (B:II) 	<p>Isolated choroiditis:</p> <ul style="list-style-type: none"> IV fluconazole, 400 mg/day and IV flucytosine, 100 to 150 mg/kg/day for 10 weeks (A:II) <p>Associated with meningitis:</p> <ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Weekly until resolution
HIV-associated retinitis	> 120 cells/μl (A:II)	<ul style="list-style-type: none"> Visual symptoms (A:II) 	<ul style="list-style-type: none"> VA IOP (C:II) SLE (C:III) DOE (A:II) 	<ul style="list-style-type: none"> Peripheral multifocal retinitis (A:II) Retinal vasculitis (A:II) Mild vitreous inflammation (B:II) Lack of retinal hemorrhage (B:II) Slow progression (B:II) 	<ul style="list-style-type: none"> Clinical diagnosis Rule out other entities, particularly syphilis (A:II) 	<ul style="list-style-type: none"> Antiretroviral therapy should lead to regression (A:II) 	<ul style="list-style-type: none"> Weekly until resolution

Intraocular lymphoma	< 500 cells/ μ l (A:II)	<ul style="list-style-type: none"> Floaters (A:II) Vision loss (A:II) 	<ul style="list-style-type: none"> VA (A:II) DOE (A:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Radiation and chemotherapy (A:II) Involve Oncology Immune reconstitution (B:II) 	<ul style="list-style-type: none"> Monthly DOE Poor prognosis (A:II)
Retinal detachment	N/A	<ul style="list-style-type: none"> History/extent of necrotizing retinitis (A:II) History of trauma (B:II) History of myopia (B:II) 	<ul style="list-style-type: none"> VA (A:II) SLE (B:II) DOE (A:II) 	<ul style="list-style-type: none"> 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) 	<ul style="list-style-type: none"> Clinical diagnosis B-scan ultrasound if visualization is poor 	<ul style="list-style-type: none"> PPV with long-term silicone oil tamponade and scleral buckling (A:II) 	<ul style="list-style-type: none"> Routine post-operative follow-up As directed by other disorders
<p>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 = microhemagglutination-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 = fluorescein 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</p>							