I. INTRODUCTION

RECOMMENDATIONS:

Patients with CD4 counts <50 cells/mm³ should be examined by an ophthalmologist every 6 months.¹,²

Patients with visual disturbances or unremitting ocular symptoms, regardless of CD4 cell count, should be evaluated by an ophthalmologist. The severity of signs and symptoms should guide the clinician in choosing whether to request emergency consultation.

Retinal examination in HIV-infected patients should include indirect ophthalmoscopy through a dilated pupil so the entire peripheral fundus can be evaluated.

The primary care clinician and the ophthalmologist should work in conjunction to manage ocular opportunistic infections in HIV-infected patients.

All areas of the visual system can potentially be affected in patients with HIV infection or AIDS. Cytomegalovirus (CMV) retinitis, which can lead to blindness, is the most common infectious ocular complication and may affect 30% of severely immunocompromised individuals.³ Since the advent of HAART, the incidence of CMV retinitis has decreased significantly. However, in HAART-naïve patients or in those who are immunocompromised while receiving ARV treatment, CMV infections can still occur.

There is a significant incidence of asymptomatic CMV retinitis in patients with CD4 counts <50 cells/mm³; therefore, a screening program is advisable. Although some lesions can be seen with a direct ophthalmoscope, direct ophthalmoscopy will only allow visualization of the central portion of the retina, and peripheral lesions will not be seen. There has not been a large study regarding optimal screening intervals. The frequency of these examinations depends on immune function and the resources available to the ophthalmologist and primary care physician. It is the consensus of the Committee that patients with CD4 counts <50 cells/mm³ should be evaluated every 6 months by an ophthalmologist even in the absence of visual symptoms. HIV-infected patients who develop visual disturbances or unremitting ocular symptoms should be evaluated by an ophthalmologist.

II. ANTERIOR SEGMENT COMPLICATIONS OF HIV

A. Herpes Zoster Ophthalmicus

RECOMMENDATIONS:

The clinician should refer patients with herpes zoster ophthalmicus for evaluation by an ophthalmologist because uveitis, corneal opacities, or secondary glaucoma may develop. The retina should also be examined because the infection can involve the posterior segment as well, which is a medical emergency. See Section IV, B: Infectious Retinitis and Choroiditis for information on zoster retinitis (progressive outer retinal necrosis).
1. **Presentation**
   Patients with herpes zoster ophthalmicus (HZO) present with the classic rash of herpes zoster on the face in the distribution of the first branch of the trigeminal nerve. Although patients with HZO are usually symptomatic, they may have ocular involvement without any symptoms. Therefore, all patients with HZO should be evaluated by an ophthalmologist. Ocular complications may occur after the skin lesions have resolved.

2. **Diagnosis**
   The diagnosis of herpes zoster ophthalmicus is usually based on history and physical examination.

3. **Treatment**
   **RECOMMENDATION:**
   Clinicians should treat HIV-infected patients with herpes zoster ophthalmicus with intravenous acyclovir (10 mg/kg) every 8 hours for 10 to 14 days. It should be administered at a constant rate for 1 hour to prevent renal tubular damage. The course of intravenous acyclovir should be followed by oral therapy with valganciclovir (1 g tid) until lesions have healed.

  Use of oral anti-varicella zoster virus therapy can be considered in mild cases.

B. **Kaposi's Sarcoma of the Lids and/or Conjunctiva**

   1. **Presentation**
      Kaposi's sarcoma (KS) lesions on the lid skin or the conjunctiva rarely have visual consequences. The lesions are similar in appearance to classic cutaneous KS. See Appendix A for a photographic example.

   2. **Diagnosis**
      The diagnosis of KS on the lid skin or the conjunctiva is usually made by clinical inspection of the lesions. The clinical impression can be confirmed by histopathologic examination of a biopsy.

   3. **Treatment**
      Ocular KS lesions will respond to systemic chemotherapy in the same fashion as KS lesions presenting in other locations. Cryosurgery, alpha interferon, local radiation, or surgical excision may be used. In many situations, treatment is not required, and lid lesions can be camouflaged with cosmetics. Immune reconstitution with the use of HAART, particularly PI based, may result in regression or resolution of KS lesions.4

C. **Microsporidia**

   1. **Presentation**
      Microsporidial keratoconjunctivitis is thought to be rare. Patients may complain of a sandy feeling in the eyes and, although the eye is usually not red, the cornea often has multiple tiny lesions.

   2. **Diagnosis**
      Punctate epithelial keratitis is diagnosed by an ophthalmologist on slit lamp examination and can be caused by *Encephalitozoon hellem*. Definitive diagnosis of microsporidial infection depends on examination of conjunctival scrapings or biopsy specimens.

   3. **Treatment**
      Topical fumagillin may be used if vision is disturbed. Fumagillin can be made by hospital pharmacists. Microsporidial infection may resolve with immune reconstitution.
D. Molluscum contagiosum

1. Presentation

Molluscum is caused by poxvirus and presents as classic dome-shaped papular lesions. HIV-infected patients may develop multiple molluscum lesions on the eyelids. These lesions may cause conjunctivitis, as seen in immunocompetent patients, or they may be asymptomatic.

2. Diagnosis

The diagnosis of molluscum is usually made by clinical inspection of the lesions.

3. Treatment

In symptomatic patients, surgical excision, curettage, cryotherapy, or cautery may be used to ablate the lesions. HAART-related immune reconstitution may lead to spontaneous resolution of lesions.

E. Anterior uveitis

1. Presentation

Although uveitis can be associated with infectious ocular diseases, many presentations occur without an infectious etiology. A severe anterior uveitis has been described secondary to rifabutin therapy. Patients may present with red eye, pain, and photophobia.

2. Diagnosis

Anterior uveitis is diagnosed by an ophthalmologist on slit lamp examination.

3. Treatment

A uveitis associated with HIV infection alone and possibly responsive to ARV therapy has been described. A severe immune recovery uveitis is seen in some patients with CMV retinitis who have responded to HAART. Topical cycloplegics and topical steroids are often used to treat anterior uveitis; however, the treatment will depend on the etiology.

III. Neuro-Ophthalmic Complications of HIV

Recommendation:

Patients with orbital and central nervous system opportunistic infections and malignancies should undergo neurologic evaluation, neuroimaging studies, and further evaluation by specialists.

Table 1 lists the ocular disturbances associated with orbital and central nervous system opportunistic infections and malignancies, as well as which chapter to refer to for recommendations concerning diagnosis and treatment.
IV. RETINAL AND CHOROIDAL MANIFESTATIONS OF HIV INFECTION

A. HIV-Related Retinal Microangiopathy

1. Presentation

Retinal microvascular changes identical to those seen in patients with diabetes and hypertension have been observed in patients with HIV/AIDS. Retinal cotton wool spots, intraretinal hemorrhages, and microaneurysms can be seen. These findings are not associated with any particular ocular opportunistic infection and do not typically have lasting visual consequences. Changes are more common when patients are more severely immunocompromised. Anemia can produce retinal microangiopathy, which disappears upon normalization of the hemoglobin. See Appendix A for a photographic example.

2. Diagnosis

**RECOMMENDATION:**

Patients who are suspected of having retinal microangiopathy but have visual complaints should be re-evaluated serially to exclude an alternative diagnosis.

3. Treatment

AIDS-related retinal microangiopathy does not require treatment. HAART that leads to immune reconstitution may reverse these findings.

---

### Table 1

<table>
<thead>
<tr>
<th>Malignancy/OI</th>
<th>Ocular Symptoms</th>
<th>For Diagnosis and Treatment Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orbital lymphoma</td>
<td>- Proptosis&lt;br&gt;- Visual loss through a mass effect&lt;br&gt;- When the tumor is more indolent, pain and diplopia may be the first signs of lymphoma</td>
<td>See Chapter 12: Neoplastic Complications of HIV Infection</td>
</tr>
<tr>
<td>CNS lymphoma</td>
<td>Depending on its location, may produce a variety of abnormalities, including visual field defects, ocular motility disturbances, or uveitis</td>
<td>See Chapter 12: Neoplastic Complications of HIV Infection</td>
</tr>
<tr>
<td>Orbital infection with <em>Aspergillus</em> organisms</td>
<td>- Proptosis&lt;br&gt;- May involve the adjacent sinuses in an aggressive manner</td>
<td>See Chapter 7: Infectious Diseases Associated With HIV Infection</td>
</tr>
<tr>
<td>Progressive multifocal leukoencephalopathy (PML)</td>
<td>- Visual field defects&lt;br&gt;- Cortical blindness</td>
<td>See Chapter 7: Infectious Diseases Associated With HIV Infection</td>
</tr>
<tr>
<td>CNS toxoplasmosis</td>
<td>Depending on its location, may produce visual field abnormalities or ocular motility disturbances</td>
<td>See Chapter 7: Infectious Diseases Associated With HIV Infection</td>
</tr>
<tr>
<td>Cryptococcal meningitis</td>
<td>- Papilledema may be seen in patients who have increased intracranial pressure associated with cryptococcal meningitis&lt;br&gt;- Sudden visual loss is thought to be secondary to optic neuropathy or occipital cerebral involvement&lt;br&gt;- Motility disturbances with diplopia</td>
<td>See Chapter 7: Infectious Diseases Associated With HIV Infection</td>
</tr>
</tbody>
</table>
B. Infectious Retinitis and Choroiditis

RECOMMENDATION:

The primary care clinician and the ophthalmologist should work in conjunction to manage infectious retinitis and choroiditis in HIV-infected patients.

Unlike opportunistic infections in other areas of the body where biopsy is often required to make the diagnosis, retinal and choroidal lesions are usually diagnosed clinically. At times, when the diagnosis is in doubt, fluid or ocular tissue may be analyzed, but this is rarely necessary.

1. Cytomegalovirus Retinitis

CMV retinitis is the most common ocular opportunistic infection in patients with HIV/AIDS, developing in approximately 30% of patients with CD4 counts <50 cells/mm³. In ACTG 360, which examined the risk of developing CMV end-organ disease in 403 patients who were CMV IgG positive and had a CD4 <50 cells/mm³, 5.2% developed disease during a mean follow-up of 2.9 years. Twenty-one patients developed CMV end-organ disease (18 cases confirmed and 3 cases probable); half of these cases were diagnosed during the first year of the study. Other patients developed CMV retinitis (n = 17), CMV colitis (n = 2), CMV pneumonitis (n = 1), and CMV esophagitis (n = 1). All but one of the patients had a CD4 <50 cells/mm³, and all had a viral load >10,000 copies/mL.

a. Presentation

CMV infection classically produces a hemorrhagic, necrotic retinitis that can destroy the entire retina if left untreated. Frequency of bilateral presentation of newly diagnosed CMV retinitis varies among studies but seems to be between 35% and 45%.

The main symptoms of CMV retinitis include floaters, blurred vision, visual field defects, and flashing lights/sparks. Even subtle changes, such as a minor loss of peripheral vision, can indicate the development of CMV retinitis. There is usually no pain involved. It is important for patients to report any and all visual abnormalities to a primary care physician so that a referral to an ophthalmologist can be made. Some patients can have progressive CMV retinitis and still be asymptomatic.

Clinical manifestations of progressive CMV retinitis include a dry-appearing, granular border with little vitreous inflammation. Edema and necrosis are also known to cause irregular patches of retinal whitening. A “brushfire” pattern emerges when a photograph of the lesion is enlarged. See Appendix A for a photographic example of CMV retinitis.

b. Diagnosis

An experienced observer can diagnose CMV retinitis ophthalmoscopically.

c. Treatment

RECOMMENDATIONS:

Clinicians should initiate HAART in ARV-naïve patients who present with CMV retinitis (see Chapter 4A: Antiretroviral Treatment for HIV Infection, Section IV: Initiating Therapy).

When patients who are receiving HAART present with CMV retinitis, clinicians should re-evaluate the ARV regimen in an attempt to maximize the effect of HAART on the immune system. However, CMV retinitis should be treated with both HAART and specific antiviral treatment, which varies depending on the immune status of the patient (see Figure 1).

Because the ganciclovir implant does not start consistent delivery of medication to the retina until the second week after placement, patients should receive 2 weeks of an anti-CMV agent, such as intravenous ganciclovir or oral valganciclovir, immediately following implant placement.
When systemic therapy alone is indicated:

A 2- to 3-week induction period with one of the following should be used to stabilize CMV retinitis:

Typical first-line therapy options:
- Intravenous ganciclovir (5 mg/kg bid for 14 to 21 days, then 5 mg/kg qd for 21 days), or
- Oral valganciclovir (900 mg PO bid for 21 days, then 900 mg PO qd).

Acceptable first-line therapy options in select cases (e.g., long-standing previous prophylaxis with ganciclovir):
- Foscarnet (60 mg/kg IV every 8 hours or 90 mg/kg IV every 12 hours for 14 to 21 days, then 90-120 mg/kg IV every 12 hours), or
- Cidofovir (5 mg/kg IV once weekly for 2 weeks, then 5 mg/kg every 2 weeks; with probenecid, 2 g PO 3 hours before each cidofovir dose, 1 g PO at 2 hours and again at 8 hours post cidofovir dose

The clinician should base the need for all maintenance regimens on the patient’s immune status. If patients have achieved immune reconstitution with a CD4 count >100 cells/mm³ for more than 6 months, discontinuation of maintenance therapy should be considered.

**Figure 1**

Initiation of Treatment for CMV Retinitis

- Determine HIV viral load and optimize/initiate HAART

  Determine whether retinitis is sight-threatening and requires aggressive therapy

- If retinitis is sight-threatening, initiate therapy based on the potential for immune reconstitution
- If retinitis is not sight-threatening, valganciclovir induction and maintenance is usually the initial choice

  When immune reconstitution is unlikely, prompt initiation of a combination of local and parenteral therapy + implant + valganciclovir is often first-line therapy

  When immune reconstitution is likely, intravitreous injections (ganciclovir or foscarnet) + valganciclovir may be used to obviate implant placement (although some prefer using an implant) while awaiting HAART response
Evaluation of the patient’s anti-HIV regimen should be the initial step in developing a treatment plan. Maximal suppression of HIV RNA with a subsequent increase in CD4 count will improve the response to anti-CMV therapy.

As in the pre-HAART era, recommendations concerning the treatment of CMV retinitis should include both ocular and systemic considerations. Table 2 lists considerations that will help the clinician decide on the most suitable modality of treatment for each individual patient.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>CHOOSING THE TREATMENT MODALITY FOR CMV RETINITIS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Consideration</strong></td>
<td><strong>Effect on Treatment Choice</strong></td>
</tr>
<tr>
<td>The location and extent of CMV retinitis (i.e., sight threatening or peripheral) and the status of the fellow eye</td>
<td>If the patient has sight-threatening CMV retinitis or bilateral disease, parenteral therapy should be used.</td>
</tr>
<tr>
<td>Whether the disease is newly diagnosed or relapsed</td>
<td>If the patient is experiencing a relapse, combination therapy with two parenteral agents has produced the best results.</td>
</tr>
<tr>
<td>The immune status of the patient</td>
<td>The immune status of the patient will determine whether an implant is required (see Figure 1).</td>
</tr>
<tr>
<td>Whether the patient is HAART naïve or whether HAART has failed</td>
<td>HAART should be initiated in naïve patients, and the regimen should be optimized in patients with failing HAART.</td>
</tr>
<tr>
<td>The presence of other conditions that can affect medication choice</td>
<td>For example, for patients actively using drugs, the implant may facilitate treatment.</td>
</tr>
<tr>
<td>Other medications with overlapping toxicities</td>
<td>Overlapping toxicities may help decide between ganciclovir vs foscarnet. For example, if a patient has neutropenia that is unlikely to resolve, ganciclovir should be avoided.</td>
</tr>
<tr>
<td>Adherence to follow-up</td>
<td>For patients with poor adherence, the implant may facilitate treatment.</td>
</tr>
<tr>
<td>Patient’s preference and quality-of-life concerns</td>
<td>Quality-of-life issues may sway a patient away from parenteral therapy.</td>
</tr>
</tbody>
</table>

Currently approved treatments for CMV retinitis include ganciclovir, cidofovir, foscarnet, valganciclovir, and fomivirsen (see Table 3).

Ganciclovir is available in intravenous and oral forms and as an implant that can be placed in the vitreous. The ganciclovir implant releases ganciclovir into the eye for about 6 to 8 months before it needs to be replaced. It should be used with systemic therapy whenever possible. Neutropenia is the most common side effect.

Valganciclovir is a monovalyl ester of ganciclovir and acts as a prodrug; it is given orally and has higher bioavailability than oral ganciclovir. Neutropenia is the most common side effect.

Cidofovir and foscarnet, both intravenous medications, should be avoided in patients with renal insufficiency (creatinine clearance <55; creatinine >1.5) and should not be used concomitantly with other nephrotoxic agents. Dose adjustments should take hematologic and serum chemistry values into consideration.

Cidofovir must be administered with probenecid (2 g 3 hours before and 1 g 2 and 8 hours after cidofovir dose) and adequate hydration. Cidofovir requires strict adherence to an infusion regimen.
Foscarnet therapy may have been associated with longer survival in the pre-HAART era; however, fewer patients are able to tolerate foscarnet because of toxicities. This medication requires an infusion pump, long infusion time, and saline hydration.

Fomivirsen, an anti-sense molecule, is approved for intravitreous injection in patients with relapsed CMV retinitis but has been associated with pigmentary retinopathy.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Available Form</th>
<th>Disadvantages</th>
<th>Possible Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ganciclovir</td>
<td>Induction</td>
<td>5 mg/kg IV q12h for 14-21 days</td>
<td>Requires permanent IV access</td>
<td>Neutropenia, thrombocytopenia, GI symptoms, diarrhea, nausea, anemia</td>
</tr>
<tr>
<td></td>
<td>Maintenance</td>
<td>5 mg/kg IV qd</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valganciclovir</td>
<td>Induction</td>
<td>900 mg PO bid for 21 days</td>
<td>—</td>
<td>GI symptoms, neutropenia, anemia, thrombocytopenia</td>
</tr>
<tr>
<td></td>
<td>Maintenance</td>
<td>900 mg PO daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foscarnet*</td>
<td>Induction</td>
<td>90 mg/kg IV q12h for 14-21 days, given as IV infusion over 2 hours</td>
<td>Patients should have serum creatinine, calcium, ionized Ca+, potassium, magnesium, and phosphorus levels monitored closely.</td>
<td>Nephrotoxicity, hypomagnesemia, hypocalcemia, hypokalemia, penile and genital ulcers in uncircumcised men receiving high doses with poor hydration prior to treatment</td>
</tr>
<tr>
<td></td>
<td>Maintenance</td>
<td>90-120 mg/kg IV qd, given as IV infusion over 2 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cidofovir†</td>
<td>Induction</td>
<td>5 mg/kg IV once weekly for 2 weeks§, given as IV infusion at a consistent rate over 1 hour</td>
<td>Highly toxic to the kidneys. Requires supervised administration, including co-administration of probenecid and IV saline.</td>
<td>Vomiting, nausea, rash, headache, anorexia, anemia, severe uveitis, irreversible hypotony, neutropenia</td>
</tr>
<tr>
<td></td>
<td>Maintenance</td>
<td>3-5 mg/kg IV every other week§</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral ganciclovir‡</td>
<td>Maintenance</td>
<td>1 g PO tid</td>
<td>Poor bioavailability. The risk of early relapse should be weighed against the need for an indwelling catheter.</td>
<td>Neutropenia, diarrhea, anemia, thrombocytopenia</td>
</tr>
<tr>
<td>Intraocular ganciclovir implant</td>
<td>FDA-approved as local treatment for both induction and maintenance</td>
<td></td>
<td>Ineffective in protecting the unimplanted eye or in preventing systemic disseminated CMV disease.</td>
<td>Temporary loss of functional visual acuity after surgery, risk of early retinal detachment, endophthalmitis</td>
</tr>
<tr>
<td>Drug</td>
<td>Indication</td>
<td>Available Form</td>
<td>Disadvantages</td>
<td>Possible Side Effects</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>--------------------------------------</td>
<td>---------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>---------------------------------------</td>
</tr>
<tr>
<td>Intravitreal injections</td>
<td>Local treatments not FDA-approved</td>
<td>Injection</td>
<td>Ineffective in protecting the uninfected eye or in preventing systemic disseminated CMV disease. Must be given at least weekly.</td>
<td>Endophthalmitis, vitreous hemorrhage</td>
</tr>
<tr>
<td>(ganciclovir, foscarnet)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination ganciclovir and foscarnet</td>
<td>Relapse or disease progression</td>
<td>Full standard parenteral doses of each agent as listed above</td>
<td>Prolonged infusion times and diminished quality of life.</td>
<td>See Side Effects listed above for ganciclovir and foscarnet</td>
</tr>
<tr>
<td>Fomivirsen</td>
<td>Relapse</td>
<td>Injection, 330 mcg/dose</td>
<td>Ineffective in protecting the uninfected eye or in preventing systemic dissemination of CMV disease.</td>
<td>Ocular inflammation (uveitis, vitritis), increased intraocular pressure, pigmentary retinopathy</td>
</tr>
<tr>
<td></td>
<td>Induction</td>
<td>One injection every 2 weeks for two doses</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maintenance</td>
<td>One injection every 4 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination local and systemic therapy</td>
<td>Relapse, induction, maintenance</td>
<td>Can tailor choices to unique conditions</td>
<td>Other problems relate to the individual toxicities of the medications used.</td>
<td>See Side Effects listed under each individual agent</td>
</tr>
<tr>
<td></td>
<td>Adding parenteral therapy to local treatment protects the uninfected eye and prevents systemic dissemination.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Requires an infusion pump, long infusion time, and saline hydration.
† Probenecid must be administered orally with each dose of cidofovir. Administer 2 g 3 hours prior to the cidofovir dose, 1 g at 2 hours, and again at 8 hours after the completion of the 1-hour cidofovir infusion (for a total of 4 g).
‡ Oral ganciclovir should only be used when valganciclovir cannot be tolerated.
§ If the 5-mg dose is not well tolerated due to renal toxicity, 3 mg/kg should be used.
|| Some experts administer parenteral therapy as well.

Choice of initial anti-CMV therapy should take into account the patient’s overall medical condition as well as the location of the retinitis. A logical approach is outlined in Figure 1.

d. Reactivation or Progression of CMV Retinitis

**RECOMMENDATION:**

**During therapy, the ophthalmologist should monitor for progression or reactivation of retinitis by examination and serial retinal photography.**

Nearly all patients eventually relapse if they do not achieve immune reconstitution. The development of resistance to ganciclovir is rare during relapses in the first 3 to 6 months but becomes more common thereafter. However, this is often relative resistance; therefore, an implant may still be effective because it provides high local level of drug.
Careful monitoring of patients with retinitis is best achieved by a combination of clinical evaluation by the ophthalmologist and serial retinal photography. These are necessary to detect early progression or reactivation of disease as well as complications of both retinitis and its treatments.

Treatment for reactivation or progression may include reinduction with the same drug, reinduction with another drug, or use of combination therapy. Combination therapy can include a combination of systemic therapies or a combination of systemic and local treatments. Combination therapy with intravenously administered ganciclovir and intravenously administered foscarnet has been shown to be significantly more effective than monotherapy in delaying progression of relapsed CMV retinitis. However, combination therapy is associated with a diminished quality of life in some patients.

Direct intraocular injection with ganciclovir, foscarnet, or fomivirsen has been used with success in patients who need supplemental treatment or in situations in which systemic therapy is contraindicated or needs to be temporarily discontinued. Although the use of intravitreous cidofovir has been reported, the risks of toxicity are high because the drug has a narrow therapeutic index. Intravitreous cidofovir is not recommended under ordinary circumstances.

Retinal detachments may develop, particularly in patients with large peripheral CMV lesions. A repair with vitrectomy and silicone oil tamponade is usually required. At 6 months, silicone oil toxicity has been reported; however, removal of silicone oil increases the risk of retinal detachments. Cataracts are a frequent late complication of this kind of retinal detachment repair. There is no significant difference in the retinal detachment rate between patients treated with only systemic therapy and those treated with the ganciclovir implant. Successful HAART reduces the overall rate of retinal detachments. HIV infection is not a contraindication to cataract surgery; however, in patients who have undergone retinal detachment repair with silicone oil, intraocular lens calculations and final vision will be affected.

c. CMV Retinitis in Patients Who Have Undergone Immune Reconstitution

Immune recovery uveitis (IRU) is an inflammatory condition that can be seen in patients with CMV retinitis who have undergone immune reconstitution. This condition typically occurs in combination with quiescent CMV retinitis and can cause visual loss from macular edema, epiretinal membranes, or severe vitritis. There have been some reports of improvement in patients with visual loss who were treated with sub-Tenon’s injections of methylprednisolone; however, there is no consensus on the optimal therapy for this condition.

There is growing experience with withdrawal of anti-CMV therapy or non-replacement of ganciclovir implant in patients with CMV retinitis who have undergone immune reconstitution. The level of CD4 count or HIV viral load at which it is safe to do this is unknown. However, most clinicians believe that evidence of a sustained response to HAART should be demonstrated. Discontinuation of anti-CMV therapy may be considered in patients who have a sustained (>6 months) increase in CD4 cells to 100 to 150 cells/mm³ in response to HAART. Careful monitoring by the ophthalmologist should be continued, especially when immune status changes or when a small progression of retinitis would cause significant visual loss. There have been a few cases of reactivation of CMV after discontinuation of secondary prophylaxis despite high CD4 cell counts, which seem to reflect deficits in the CMV-specific immune response.
f. **Prophylaxis for CMV Retinitis**

**RECOMMENDATION:**

Patients receiving oral ganciclovir prophylaxis or therapy for extraocular CMV should be evaluated every 3 months by an ophthalmologist because treatment may mask the development of symptoms of retinitis.

Oral ganciclovir (1000 mg tid) has been approved as prophylaxis for CMV retinitis in severely immunocompromised patients (CD4 counts <50 cells/mm³), although it is rarely used. It is not clear which patients will derive maximum benefit from oral ganciclovir prophylaxis, and there is interest in developing a rational strategy of targeted prophylaxis to decrease the chance of development of resistance to ganciclovir. The decision should be individualized and based on risk/benefit analysis. Presumably, oral valganciclovir with improved bioavailability will also offer effective prophylaxis.

There have been a few cases of reactivation of CMV after discontinuation of secondary prophylaxis despite high CD4 cell counts, which seem to reflect deficits in the CMV-specific immune response. These cases seem to reflect deficits in the CMV-specific response and reinforce the need for continued monitoring.

2. **Progressive Outer Retinal Necrosis**

   a. **Presentation**

   Progressive outer retinal necrosis (PORN) is a rapidly progressive, necrotic retinitis caused by varicella zoster virus. The retinal lesions are often multiple punctate white spots that quickly coalesce. The presentation can be deceptive because there is typically an absence of dense vitritis. Hemorrhage and inflammation are rarely seen; however, the disease can result in permanent bilateral blindness within a few days. See Appendix A for a photographic example.

   b. **Diagnosis**

   PORN is usually diagnosed by clinical presentation of lesions.

   c. **Treatment**

   The optimal treatment has not been established and prognosis is poor even with high doses of combinations of ganciclovir, foscarnet (both intravenously and intravitreally), and acyclovir. Patients often develop retinal detachments.

3. **Ocular Toxoplasmosis**

   a. **Presentation**

   Ocular toxoplasmosis may present with single or multiple lesions that are white to cream in color. Lesions are thicker and lack the granular border that is seen in CMV lesions. There may be significant vitritis, which can partially obscure the view of the fundus. Retinal hemorrhage is rare. In contrast to ocular toxoplasmosis in immunocompetent individuals, patients with AIDS do not usually have pigmented lesions suggestive of previous retinal infection. See Appendix A for a photographic example.

   b. **Diagnosis**

   Ocular toxoplasmosis is usually diagnosed by clinical presentation of lesions.

   c. **Treatment**

   **RECOMMENDATIONS:**

   Clinicians should perform a central nervous system evaluation in patients with ocular toxoplasmosis.
Therapy for ocular toxoplasmosis should be the same as that for central nervous system toxoplasmosis (see Chapter 7: Infectious Diseases Associated With HIV Infection). Atovaquone and/or azithromycin can be considered for patients in whom standard therapy fails or may not be used (e.g., allergies to sulfa or clindamycin).

Clinicians should continue maintenance therapy to prevent relapse of toxoplasmosis lesions.

4. *Pneumocystis carinii* Choroidopathy

a. Presentation

*Pneumocystis carinii* choroidopathy is rare because aerosolized pentamidine use has declined, and systemic prophylaxis for *Pneumocystis carinii* pneumonia infection is now routine. *Pneumocystis carinii* choroidopathy implies disseminated pneumocystis infection. Lesions are yellow to orange in color and involve the posterior pole of the retina. Hemorrhage and inflammation are not seen. Even when the ocular disease is extensive, it is not symptomatic. See Appendix A for a photographic example.

b. Diagnosis

*Pneumocystis carinii* choroidopathy is usually diagnosed by clinical presentation of lesions.

c. Treatment

RECOMMENDATION:

Because ocular *Pneumocystis carinii* is a manifestation of disseminated pneumocystosis, clinicians should initiate standard anti-pneumocystis therapy (see Chapter 7: Infectious Diseases Associated With HIV Infection).

5. Syphilis

a. Presentation

The presence of unexplained uveitis or papillitis can be the result of syphilis.

b. Diagnosis and Treatment

RECOMMENDATION:

Clinicians should treat patients with syphilitic uveitis, chorioretinitis, or optic nerve disease for neurosyphilis. The treatment of ocular syphilis optimally will include 2 weeks of intravenous penicillin G.
REFERENCES


APPENDIX A
OPHTHALMOLOGIC COMPLICATIONS OF HIV

Cytomegalovirus (CMV) retinitis

Kaposi’s sarcoma of the eyelid

Kaposi’s sarcoma of the conjunctiva

HIV-related retinal microangiopathy

Pneumocystis carinii choroidopathy

Progressive outer retinal necrosis

Ocular toxoplasmosis