




population. Up to 40% of AIDS-related systemic lymphomas, and almost all of those in a primary CNS location, are related to EBV. Extranodal presentation of these tumors is the rule, and there is a high frequency of gastrointestinal or intracranial presentation. Chemotherapy for systemic disease or radiation therapy for CNS disease usually provides a clinical response, which may be maintained if it is accompanied by effective ART.

Other malignancies, including Hodgkin's disease, have an increased incidence in patients with untreated HIV infection. Now that more treated persons are surviving, an increasing incidence of a variety of non-AIDS-defining malignancies is being observed. Among these, increased rates of anal cancer, non-small cell lung cancer, Hodgkin's disease, and liver cancer (related to hepatitis viruses) have been associated with HIV.

 For a deeper discussion of these topics, please see Chapter 394, "Neurologic Complications of Human Immunodeficiency Virus Infection," in Goldman-Cecil Medicine, 25th Edition.

### Renal Disorders

Renal insufficiency in patients with HIV may be a consequence of nephrotoxic drug administration, long-term use of certain antiviral agents (particularly tenofovir), substance use (e.g., heroin), or HIV-associated nephropathy (HIVAN). HIVAN typically improves with ART. In some cases, renal biopsy is indicated to establish a diagnosis, particularly if rapid decline in glomerular function is observed. In the United States, HIVAN is seen almost exclusively in African Americans and usually manifests as heavy proteinuria and progressive renal insufficiency. Without treatment, most patients develop end-stage renal disease within several months. Treatment is primarily with combination antiretroviral drugs.

### Musculoskeletal and Rheumatologic Disorders

Musculoskeletal complaints are common among patients with HIV, and distinguishing acute complications of HIV from more indolent degenerative joint disease or recurrent muscle strain is important. Septic arthritis is a particular concern in persons who use injection drugs or have hemophilia.

Reiter's syndrome has been associated with HIV, and patients with HIV may experience a more severe or more prolonged course. Flares related to immune reconstitution have been described; they frequently respond quickly to doxycycline.

Declining CD4 counts in persons with psoriasis is associated with flares of both cutaneous disease and psoriatic arthritis. Standard therapy for both can now be supplemented if necessary with disease-modifying antirheumatic drugs.


Both lupus and rheumatoid arthritis, when present, may be relatively quiescent in persons with low CD4 counts. When treatment for HIV is initiated and the CD4 count rises, these persons may experience flares of their underlying connective tissue disease.

Avascular necrosis of the hip has been well described in persons with HIV, including those on ART. MRI may be necessary to confirm the diagnosis, and surgery is the mainstay of treatment.

Muscle weakness, if localized, may be indicative of myelopathy-neuropathy. If weakness is proximal or is associated with myalgia and tenderness, myopathy should be suspected. ART is the primary treatment for HIV-associated myopathy. Myopathy may rarely be caused by zidovudine toxicity.

### Immune Reconstitution Inflammatory Syndrome

Persons with low CD4 counts at the start of treatment who experience a rapid rise in CD4 count on treatment may be at risk for development of what is termed the immune reconstitution inflammatory syndrome (IRIS). The syndrome results from the development of a pronounced immune response to a previously tolerated antigen, usually an infection. The specific symptoms depend on the pathogen or antigen and the involved area of the body. Entities commonly associated with IRIS include *M. tuberculosis* and other mycobacteria, *Pneumocystis pneumonia*, cryptococcal infections, herpesviruses, and hepatitis B or C virus. Treatment is supportive, although in severe cases, for example IRIS associated with meningitis or inflammation of the lungs leading to respiratory compromise, corticosteroids may be used to reduce inflammation and alleviate the symptoms.

 For a deeper discussion of these topics, please see Chapter 395, "Immune Reconstitution Inflammatory Syndrome in HIV/AIDS," in Goldman-Cecil Medicine, 25th Edition.

### PREVENTION OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION

Three approaches—behavioral modification, treatment of sexually transmitted diseases, and ART—have had a major impact on HIV transmission. All of these activities are supported by expanded testing and improved linkage to care.

In several communities at increased risk for HIV (e.g., homosexually active men in the United States and western Europe, young adults in Uganda and Thailand), adoption of safer sexual practices, specifically the use of condoms during sexual activity, has been associated with a decrease in incidence of HIV infection. Sustaining these behavioral changes over long periods is challenging and requires behavioral reinforcement. Several recent controlled trials have demonstrated that male circumcision can decrease the risk of acquiring HIV infection by more than half.

Increasingly, ART is becoming a key goal of prevention programs. Antiretroviral treatment of HIV-infected pregnant women and their infants in the peripartum period has decreased maternal-child transmission from 25% to less than 5% in North America. If a pregnant woman maintains viral suppression during pregnancy and during breast-feeding, the risk of transmission to her infant is less than 1%.

Prophylactic use of ART has been shown to be effective for postexposure prophylaxis after occupational exposures to HIV and after unprotected sexual exposures. Recently, studies have shown the benefit of preexposure prophylaxis in preventing transmission of HIV among high-risk MSM, and the fixed-dose combination of tenofovir and emtricitabine has received an FDA indication for this use. The most compelling reinforcement of the importance of ART for prevention was a large multisite clinical