Mycobacterium-selective media are usually positive. Treatment usually results in resolution of fever and weight gain. Aggressive non-Hodgkin's lymphoma may cause unexplained fever and weight loss, a rapidly enlarging spleen, or asymmetrical lymph node enlargement.

Wasting and Changes in Body Morphology

Cachexia may be prominent in advanced HIV disease. In some instances, the wasting is caused by an intercurrent infectious process. Heightened production of tumor necrosis factor may contribute to fever, cachexia, and hypertriglyceridemia in advanced HIV disease. If orthostatic hypotension occurs, especially if it is associated with hyperkalemia, the possibility of adrenal insufficiency, which rarely can result from CMV adrenalitis, should be investigated. Most patients with AIDS-associated cachexia gain weight and achieve a sense of well-being after initiation of effective ART. If the cachexia is refractory, weight gain may be enhanced by administration of recombinant growth hormone, nonmethylated androgens, or megestrol, but definitive indications for these therapies have not been established.

Older antiviral agents, particularly nucleoside/nucleotide reverse transcriptase inhibitors (e.g., didanosine, stavudine) and the early protease inhibitors, were associated with alterations in fat distribution known as lipodystrophy and lipoatrophy. Patients with long-term exposure to these medications may develop a loss of fat in the face and on the extremities. At the same time, they develop prominent central obesity including a buffalo hump and marked abdominal obesity. These changes typically persist even after the medication is discontinued and are associated with increased risk of cardiovascular disease.

Cutaneous Disease

Cutaneous infections ultimately occur in most patients with untreated HIV infection. Persons with HIV experience both higher rates of more typical skin infections (e.g., folliculitis, cellulitis) and OIs such as disseminated herpes zoster or HSV, bacillary angiomatosis, and fungal infections. Most of these diseases respond to specific therapy. Noninfectious skin manifestations include exacerbation of underlying psoriasis, seborrhea dermatitis, and eosinophilic folliculitis. Skin lesions can equally be associated with some disseminated infectious complications or malignancies. If a patient has unexplained constitutional symptoms, a thorough skin examination may provide important findings to support a diagnosis.

For a deeper discussion of these topics, please see Chapter 392, "Skin Manifestations in Patients with Human Immunodeficiency Virus Infection," in Goldman-Cecil Medicine, *25th Edition.*

Oral Disease

Oral *Candida* stomatitis (thrush) is often the earliest recognized OI. Early thrush may be entirely asymptomatic; as the infection becomes more extensive, it causes pain on eating. The characteristic cheesy white exudate on the mucous membranes can easily be scraped off, and the underlying mucosa may be normal or inflamed.

Xerostomia is common among patients with HIV and is often underappreciated. It can be a significant contributor to poor dentition and gingivitis, which can contribute to other adverse health consequences for the patient.

Severe gingivitis can be a significant problem in patients with AIDS, leading to local and systemic infection as well as loss of teeth.

Oral ulcers may be caused by HSV, but often they represent aphthous lesions of uncertain cause. Small oral aphthous ulcers may respond to topical corticosteroids, whereas large oral or esophageal ulcers require oral administration of thalidomide or corticosteroids. It is important to obtain cultures for HSV and CMV to exclude a viral origin before initiating corticosteroid or thalidomide therapy. Thalidomide should not be used in women of childbearing age because of its teratogenic effect.

Oral hairy leukoplakia is a white, lichenified, plaque-like lesion most commonly seen on the lateral surfaces of the tongue that is probably caused by Epstein-Barr virus (EBV). It is painless, may remit and relapse spontaneously, and almost always responds to effective ART.

Kaposi's sarcoma has a predilection for the oral cavity and skin. Oral lesions may be purple, red, or blue and may be raised or flat. Usually painless, these lesions cause symptoms when they enlarge, bleed, or ulcerate (see later discussion).

Esophageal Disease

Symptomatic esophageal disease seldom occurs with CD4 counts greater than 100 cells/mm^3. Pain on swallowing and substernal burning are common and most often indicate *Candida* esophagitis, particularly when oral thrush is present. Diagnostic esophagoscopy with biopsy, cytology, and culture should be performed if symptoms do not rapidly respond (within 3 to 5 days) to antifungal therapy.

If esophagoscopy shows ulcerative lesions, they are usually caused by CMV (50%), aphthae (45%), or HSV (5%). Because each of these lesions is responsive to appropriate therapy, definitive etiologic diagnosis is essential. CMV esophageal ulcers respond well to intravenous ganciclovir or foscarnet therapy for 2 to 3 weeks or until resolution is confirmed endoscopically. Esophageal ulcerations caused by HSV usually respond well to intravenous acyclovir.

For a deeper discussion of these topics, please see Chapter 390, "Gastrointestinal Manifestations of HIV and AIDS," in Goldman-Cecil Medicine, *25th Edition.*

Pulmonary Diseases

Pulmonary infections are common in persons living with HIV and range from nonspecific interstitial pneumonitis to life-threatening pneumonias (Table 101-6). HIV-infected persons have a threefold to fourfold increased risk of bacterial pneumonia, usually caused by encapsulated bacteria, including *S. pneumoniae* and *H. influenzae*. The increased risk begins with modest degrees of immunodeficiency (CD4 counts of 200 to 500 cells/mm^3). The onset is often abrupt, and the response to prompt initiation of therapy is usually good; however, delay in appropriate antimicrobial therapy may result in a fulminant downhill course. For those with CD4 counts greater than 200 cells/mm^3,