Overview of Opportunistic Infections

Patients with AIDS are susceptible to many infections that rarely afflict individuals who have a normal immune system. They contract **opportunistic infections** because HIV has severely weakened or destroyed their immune system.

The Immune System in HIV Infection

As you have learned, the immune response to viruses, fungi, parasites, and **mycobacteria** (the group of pathogens that includes MAC) is accomplished by various T lymphocytes; therefore, it is called **cell-mediated immunity**.

HIV infection destroys monocytes, macrophages, and CD4/T4 lymphocytes, seriously impairing the body's ability to fight infectious organisms. The loss of monocytes and macrophages decreases:

- Phagocytosis
- The release of **cytokines** that promote lymphocyte growth and replication

At first, CD4/T4 destruction impairs cell-mediated immunity; B-cell response remains intact. Over time, the host loses the ability to mount a cellular response. The absolute decrease in CD4/T4 lymphocytes minimizes cell-mediated and B-cell responses. With the reduced release of cytokines by CD4/T4 lymphocytes, there is less:

- Activation of T8 (also known as CD8) and suppressor T lymphocytes
- Activation of macrophages
- Enhancement of B and T lymphocyte activity

The decrease in the ratio of CD4/T4 to T8 lymphocytes and immune system regulation enables cytotoxic activity to flourish. T8 lymphocytes may then attack and destroy normal blood, tissue, and nerve cells, producing **thrombocytopenia**, **neutropenia**, and **peripheral neuropathy**.

HIV infection has a long-term impact on B-cell-mediated immunity. Initially, B lymphocytes may overreact to HIV, producing antibodies to each viral protein. Such hyperactivity diminishes the number of dormant B lymphocytes available to produce antibodies for new pathogens. Eventually, the host may be unable to respond with antibodies to newly encountered antigens.

Mechanism of Opportunistic Infection

The development of opportunistic infections and cancers reflects the persistent decline in immune function. Opportunistic infections occur *because* the immune system has broken down. They generally appear once the body has lost its ability to mount a cell-mediated immune response (Figure 1).[1,2] Initial infections are generally not life-threatening and may affect only one organ; as immune function continues to decline, however, infections become more severe and may affect multiple organs.

[INSERT FIGURE 1]

Fungal and viral **mucocutaneous** infections, such as thrush and herpes simplex, are often the initial indications of diminished cell-mediated immunity. These infections generally herald the onset of early symptomatic HIV infection. Certain cancers — such as early **lymphomas** and **Kaposi's sarcoma** — may occur with the further decline of cell-mediated immune activity. Early lymphomas may result from previous B-cell hyperactivity.[1] Kaposi's sarcoma and later lymphomas may be due to compromised T lymphocyte function, such as:

- Alterations in cytokine production by CD4/T4 lymphocytes[1]
- Inability of T8 lymphocytes to recognize and destroy cancer-causing viruses and malignant cells[1]

Advanced HIV disease is generally characterized by severe systemic or **disseminated** infections. These infections reflect the patient's profound immune deficit and general debility. Pathogens that can be eradicated only through vigorous cell-mediated immunity cause serious disease in individuals with advanced HIV infection and AIDS.

Current Issues: The Changing Nature of Opportunistic Infections

Recently, several new drugs have become available for treating advanced HIV infection and AIDS (some of the more common drugs used in treating HIV infection, AIDS, and associated infections are listed in Table 1). These include:

- Reverse transcriptase inhibitors: interfere with synthesis of viral nucleic acid (didanosine, zidovudine, salcitabine, stavudine, lamivudine, nevirapine, delavirdine)

- Protease inhibitors: interfere with the action of certain enzymes that are vital to the replication of HIV (indinavir, ritonavir, saquinavir, nelfinavir)

[INSERT TABLE 1]

These drugs are being used in various combinations. The changing trend in treatment strategy is shown in Figure 2.

[INSERT FIGURE 2]

The new treatments involve several potent drugs given simultaneously. They must also be administered continuously to prevent the virus from replicating. Some patients may have drug interactions, especially if they are taking antiretroviral medications in conjunction with other drugs to prevent or treat opportunistic infections. This situation has created new and rapidly changing considerations in the overall management of HIV infection and AIDS, many of which have yet to be resolved.

The CD4/T4-lymphocyte counts increase in many AIDS patients receiving the new treatments. The full or partial recovery of their immune system helps protect these patients from opportunistic infections. They become healthier and live longer.[3] Because of their longer life, they have prolonged exposure to organisms that cause opportunistic infections, partly offsetting the protection from their recovering immune system.

The virus is probably not totally eradicated, however, so that patients may not be "cured" of their HIV. Intense, well monitored treatment must continue, or the HIV may begin again to replicate.

The new treatment protocols are changing the outlook for patients with AIDS. The risk of certain opportunistic infections might increase, while the risk of most opportunistic infections probably will decrease; most will have a delayed onset. Management of the disease is changing to a program typical of that for a chronic disease, such as diabetes. Patients with AIDS often resume work and lead an essentially normal life, although they are committed to continual consumption of a great variety of medications.

Opportunistic Infections other than MAC

This section describes common opportunistic infections of the skin and mucous membranes, lower gastrointestinal tract, central nervous system, and respiratory system. The *Mycobacterium avium* complex is discussed later.

Mucocutaneous Opportunistic Infections

Fungal and viral infections of the skin and mucous membranes are frequently the first signs of early symptomatic HIV infection. These problems persist as the disease evolves. Common mucocutaneous problems are:

- Localized and disseminated candidiasis
- Reactivated viral infections
- Kaposi's sarcoma
- Cutaneous bacterial infections