

Reproductive Block **Pathology of Aids**

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Objectives

At the end of this lecture, the medical student should be able to:

- a. Understand the aetiology and pathogenesis of the aids syndrome.
- b. Become aware of the meaning of the word: opportunistic infections” and its significance in relation to the aids syndrome.
- c. Know the clinicopathologic features of the major systemic manifestations of the aids syndrome with special emphasis on pneumocystis carinii pneumoniae, fungal and other viral infections and some tumours like Kaposi sarcoma and lymphomas.

Acquired immunodeficiency syndrome (AIDS)

1. **Cause:** AIDS is caused by **human immunodeficiency virus (HIV)** infection and has become a worldwide epidemic since the first clinical description in 1981. The vast majority of AIDS cases in the U.S. and Europe are caused by infection with the retrovirus **HIV-1**.
2. **Mechanisms of HIV infection**
 - a. The HIV virion expresses a cell surface protein, **gp120**, with binding sites for the CD4 molecule on the surface of **CD4+T cells**. The interaction of viral gp120 with cellular CD4 explains the affinity of HIV for CD4+T cells. In addition, two recognition sites on gp120 for the coreceptors CCR5 and CXCR4 are involved in the entry of HIV into the cell.
 - b. **Other CD4+cell types** that are targets for HIV infection include monocytes, macrophages, dendritic cells, Langerhans cells, and microglial cells of the central nervous system (CNS).
 1. **Monocytes and macrophages** may function as reservoirs for HIV and possibly as vehicles for viral entry into the CNS.
 2. HIV may infect **neural cells** directly by way of CD4 receptors or may compete (through the gp120 protein) for neural receptor sites for neuroleukin, a neural tissue growth factor.
 - c. After cellular binding of gp120 to CD4 and internalization of HIV into the cell, proviral DNA is synthesized by reverse transcription from genomic viral RNA.
 - d. The HIV virus is found in blood, semen, vaginal secretions, breast milk, and saliva.
 - e. Diagnosis by the ELISA test is presumptive; follow-up tests include molecular techniques like: Western blot and direct assessment of viral RNA.

3. High-risk populations: AIDS

- a. **Homosexual or bisexual men** (75% of cases)
 1. The risk is apparently greater with anal receptive intercourse.
 2. In Central Africa, the incidence in both sexes is about equal and is no higher in homosexual or bisexual men than in the general population.
- b. **Intravenous drug abusers** (15% of cases). The virus is spread by sharing needles used by infected drug users.
- c. **Heterosexual partners of persons in high-risk groups** (4% of cases). Sexual transmission from intravenous drug abusers is the major mode of entry of HIV into the heterosexual population.
- d. **Patients receiving multiple blood transfusions** (2% of cases). Risk has been greatly diminished by screening donor blood for anti-HIV antibodies, HIV p24 antigen and HIV-1 RNA.
- e. **Hemophiliacs** (1% of cases). Most likely, the entire cohort of hemophiliac who received factor VIII concentrates between 1981 and 1985 became infected with HIV. Since 1985, HIV screening and heat inactivation of HIV in factor VIII concentrates have become universal.
- f. **Infants of high-risk parents.** Infection can be transplacental or can occur at the time of delivery.

4. Pathogenesis of AIDS

- a. Infection with HIV results in the **depletion of CD4+ T cells**. The number of circulating lymphocytes is greatly decreased, and this decrease is accounted for by a loss of CD4+ T cells. The CD4+:CD8+ ratio is also greatly reduced, often to less than 1.0.

- b. ***Pneumocystis carinii* pneumonia** is the most common opportunistic infection in patients with acquired immunodeficiency syndrome (AIDS); it also occurs in other forms of immunodeficiency.
 - 1. It is caused by *P. carinii* (recently renamed *Pneumocystis jiroveci*), which is now classified as a fungus.
 - 2. Diagnosis is by morphologic demonstration of the organism in biopsy or bronchial washing specimens.
- c. Increased incidence of malignancy, particularly multifocal **Kaposi sarcoma**, an otherwise rare lesion that in AIDS is almost entirely confined to the homosexual male population, and B-cell **non-Hodgkin lymphoma**; an increased incidence of Hodgkin disease and hepatocellular carcinoma also occurs.
- d. **Central and peripheral nervous system manifestations** occur due to opportunistic infections, CNS tumors, or direct neural infection with HIV.

6. Stages of HIV Infection

HIV disease may be asymptomatic for many years. Before fully developed AIDS occurs, there is acute illness resembling infectious mononucleosis; a long latent phase followed by generalized lymphadenopathy; and a stage marked by chronic fever, weight loss, and diarrhea.

- a. **HIV seropositivity** begins soon after initial HIV infection. Antibodies to the proteins coded by the genes of retroviral *gag*, *env*, and *pol* regions can be demonstrated, especially antibodies to the gp120 and p24 proteins. HIV infection can also be demonstrated by amplification of viral genetic sequences by polymerase chain reaction or by viral culture.
- b. The last stage, defined as **AIDS**, is marked by HIV infection complicated by specified secondary opportunistic infection or malignant neoplasms.