Programme: Bachelor of Science (Third Year)

Subject: Microbiology

Course Code: MIC 105

Course Title: Medical Microbiology

Unit 4: Viral diseases

Module Name: AIDS

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Notes

❖ ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)
Causative agent: HIV

- Acquired immunodeficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV).
- HIV is a retrovirus that belongs to the **lentivirus** subgroup.
- HIV is a spherical enveloped virus.
- The nucleocapsid has an outer icosahedral shell and an inner cone-shaped core, enclosing the ribonucleoproteins.
- The genome is composed of two identical single-stranded, positive sense RNA copies, with a reverse transcriptase enzyme.
- HIV is a highly mutable virus.
- Based on molecular and antigenic differences, HIV is of two types; HIV-1 and HIV-2.
- AIDS is the **end-stage disease** of HIV infection.
- This represents the irreversible breakdown of immune defence mechanisms, leaving the patient open to progressive opportunistic infections and malignancies.

↳ Mode of Transmission:

- HIV is acquired and may be passed from one person to another when infected blood, semen, or vaginal secretions come in contact with an uninfected person's broken skin or mucous membranes.
- Hence, HIV is spread only by three modes:

i. Sexual contact with infected persons (heterosexual or homosexual)

ii. By blood and blood products
Contaminated needles can transmit the infection. Prevalent in drug addicts who share syringes and needles.

iii. Infected mother to babies (intrapartum, perinatal, postnatal)

HIV may be present in breast milk and may be transmitted through breastfeeding.

- Risk Groups include:
  Men or women whose spouses have multiple sex partners, homosexual men, intravenous drug users, heterosexuals who have sex with drug users and prostitutes, children born of infected mothers, as well as their breast-fed infants, transfusion patients. and transplant recipients.

↳ **Pathogenesis and Symptoms**

- Once inside the body, HIV infects cells that have the CD4 cell surface protein such as $CD4^+$ T cells, macrophages, dendritic cells, and monocytes.
- Infection normally occurs first in macrophages. At the macrophage cell surface, the CD4 molecule binds to the gp120/gp41 capsid protein of HIV as the virus interacts with the macrophage receptor CCR5.
- CCR5 is a coreceptor for HIV and, together with CD4, forms the docking site where the HIV envelope fuses with the host cytoplasmic membrane
- After fusion of the virus with the host cell membrane, the virus releases its nucleocapsid containing two RNA strands into the cytoplasm.
- Viral reverse transcriptase mediates the reverse transcription of its RNA into dsDNA (provirus), which is integrated into the genome of the infected cell through the action of the viral enzyme integrase, causing a latent infection.
- At this point the cell may show no outward sign of infection.
- The provirus can force the cell to synthesize viral mRNA.
- Some of the RNA is translated to produce viral proteins by the cell's ribosomes.
- Some of the proteins affect host cell function.
- Viral proteins and the complete HIV-1 RNA genome are then assembled into new virions that bud from the infected host cell.
- Eventually the host cell lyses.

- The stages of HIV-related conditions: acute, asymptomatic, chronic symptomatic, and AIDS.
- The acute infection stage occurs 2 to 8 weeks after HIV infection.
- In this stage, infected individuals experience a brief illness referred to as acute retroviral syndrome, with symptoms that may include fever, malaise, headache, macular rash, weight loss, lymph node enlargement (lymphadenopathy), and oral candidiasis.

- During this stage the virus multiplies rapidly and disseminates to lymphoid tissues throughout the body, until an acquired immune response (antibodies and cytotoxic T cells, can be generated to bring virus replication under control.
- During the acute infection stage, levels of HIV may reach10^5 to10^6 copies of viral RNA per mL of plasma.

- The asymptomatic stage of HIV infection may last from 6 months to 10 years or more in some individuals.
- During this stage the levels of detectable HIV in the blood decrease, but the virus continues to replicate, particularly in lymphoid tissues.
- Even before any changes in $CD4^+$ T cells can be detected, the virus may affect certain immune functions, such as memory cell responses to common antigens like tetanus toxoid or *Candida albicans*.

- During the chronic symptomatic stage, which can last for months to years, virus replication continues and the number of $CD4^+$ T cells in the blood begins to significantly decrease.
- T-helper cells are critically important in the generation of acquired immunity, individuals, hence at this stage individuals develop symptoms including fever, weight loss, malaise, fatigue, anorexia, abdominal pain, diarrhea, headaches, and lymphadenopathy (enlarged lymph nodes).
- Some patients develop increased serum antibody production during this stage, as a result of generalized immune dysfunction.
- As $CD4^+$ T cell numbers continue to decline, some patients develop opportunistic infections.

- HIV may also inhibit or destroy dendritic (antigen-presenting) cells.
- HIV may disrupt the balance between the various types of T cells also altering immune system integrity.
- Viral replication eventually outpaces the host's attempts to control it, resulting in clinical AIDS.
- Some individuals would suffer from Kaposi sarcoma.
- The individual is susceptible to many opportunistic infections and this most commonly results in death of the individual in months or years.

- Mechanisms for depletion of $CD4^+$ T cells include:

1. Direct cytopathic effects of HIV on T cells.
   The cytopathic effect may be due to the disruption of plasma membrane integrity and function by excessive budding of virus.

2. Formation of syncytia.
   Insertion of HIV proviral DNA into the host cell's DNA can disrupt cell function, destroying the host T cells.
   gp120 on virally infected host cells may interact withT-cell CD4 receptors, causing them to fuse and form multinucleated syncytia that eventually die.
3. Effects of viral products (such as gp120) on uninfected cells.
   Free gp120 proteins released from infected cells may bind to CD4 on uninfected cells and induce those cells to undergo apoptosis (programmed cell death).
4. Immune-mediated destruction of HIV-infected cells.
   Multiple components of the immune system (cytotoxic or $CD8^+$ T cells, NK cells, complement, and antibody-dependent cellular cytotoxicity) may contribute to the continuing destruction of virus-infected $CD4^+$ T cells, resulting in acquired immune deficiency.

↳ **Lab Diagnosis:**

- The window period for detecting the virus is 7–21 days, as HIV multiplies in the mucosa and draining lymphoreticular tissues.
- The laboratory diagnosis of HIV infection can be by viral isolation and culture or by using assays for viral reverse transcriptase activity or viral antigens.
- HIV infection can be diagnosed by identifying antibodies to the pathogen in a patient blood sample.
- For routine screening purposes, an ELISAis commonly used because it is sensitive and relatively inexpensive.
- To rule out the possibility of a false positive test, a more specific method, Western Blot technique, can also be used.
- RT-PCR estimates the number of HIV virions present in the blood, i.e., the viral load.

↳ **Chemotherapy**

- At present there is no cure for AIDS.
- Primary treatment is directed at reducing the viral load and disease symptoms, and at treating opportunistic infections and malignancies.
- The strategy to accomplish this is called *highly active anti-retroviral therapy* (HAART).
- Effective anti-HIV drugs include nucleoside analogues like zidovudine (azidothmidine, AZT), didanosine, zalcitabine, lamivudine and protease

inhibitors like saquinavir, ritonavir, indinavir, which has been used as monotherapy, or in various combinations.

↳ **Prophylaxis:**

- Prevention of AIDS depends on general measures such as health education, identification of sources and decrease in high-risk behaviour.
- Barrier protection from blood and body fluids greatly limits risk of HIV infection.
- Prevention includes the continued screening of blood and blood products.
- No vaccine is available.
  This is because of its High mutability, Frequent antigenic variation, Long latency and Persistence as provirus in infected cells.