



# ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

#### Definition :

AIDS actually refers to the clinically evident late and end stage of HIV disease, but in lay terms is often used as an equivalent of HIV infection.

#### Cause:

Caused by Human Immunodeficiency Virus (H.I.V) which is a Lentivirus, a subgroup of retroviruses. These have the ability to transcribe their RNA genome to DNA one.

- There are 2 types of HIV
- HIV-1: found in America and Europe and is more aggressive.
- HIV-2: found in central Africa.
- Modes of transmission :
- 1-Sexual intercourse: homosexual or heterosexual intercourse (anal, vaginal)
- 2- Contaminated blood and blood products:
  - Blood transfusion.
  - Blood products e.g. factor VIII.

# 3- Contaminated needles and syringes.

#### 4- Mother to Child:

- In utero.
- During childbirth.
- Breast milk.

# 5- Organ and tissue donation:

- Semen.
- Kidney, skin, and corneas.
- Bone marrow.

- Sweat, urine, saliva and tears are noninfectious under ordinary circumstances because the virus is hardly detected in these fluids.
- There is no evidence that HIV is spread by social or household contact nor by blood-sucking insects such as mosquitoes and bed bugs.

# Pathogenesis:

- The manifestations of HIV disease are related to progressive destruction of the immune system (mainly T-helper cell or CD4) or direct viral effect (CNS).
- Once the virus enters a cell, HIV can replicate & cause cell fusion or death by unknown mechanism.
- In many cases, a latent state is established with integration of the HIV genome into the host cell genome.
- With increasing duration of infection, The number of CD4 Lymphocytes fall. Other defects in the immune system includes infection of B-lymphocytes & macrophages.

CCR5 Receptor

**CXCR4 Receptor** 

#### **HIV LIFE CYCLE**

2 Binding and Fusion: Virus binds to a CD4 molecule and one of two "coreceptors" (either CCR5 or CXCR4). Receptor molecules are common on 1 Free Virus the cell surface. Then the virus fuses with the cell.

3 Infection: Virus penetrates cell. Contents emptied into cell.

4 Reverse Transcription: Single strands of viral RNA are converted into double-stranded DNA by the reverse transcriptase enzyme.

5 Integration: Viral DNA is combined with the cell's own DNA by the integrase enzyme.

6 Transcription: When the infected cell divides, the viral DNA is "read" and long chains of proteins are made.

7 Assembly: Sets of viral protein chains come together.

HIV RNA HIV DNA

> DNA Human

CD4

Human

Receptor

8 Budding: Immature √irus pushes out of the cell, taking some cell membrane with it. The protease enzyme starts processing the proteins in the newly forming virus.

9 Immature virus breaks free of the infected cell.

10 Maturation: The protease enzyme finishes cutting HIV protein chains into individual proteins that combine to make a new working virus.

Revised April 30, 2005



The mature virus

### **Clinical picture**

#### **Early stage infection**

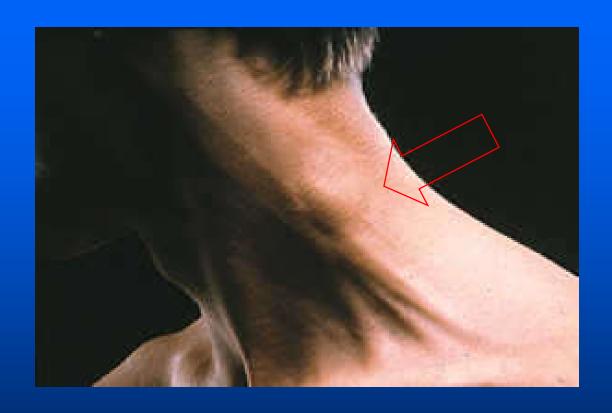
- 1) (Group I): Acute infection after 3-6 weeks incubation period. usually transient.
- The earliest clinical presentation may be symptoms are of a glandular fever or flu-like illness with a sore throat, malaise, fever, maculo-papular rash.
- Lymph node enlargement, diarrhoea, arthralgia
- Occasionally encephalopathy, neuropathy or meningitis.

# 2- Group II: Asymptomatic infection.

Symptoms and signs usually resolve, and patients enter a prolonged phase in which they may remain asymptomatic but are potentially infectious.

3- Group III: Persistent generalized lymphadenopathy; after 3 to 10 years.

There is an insidious and variable progression, in which there is lymph node enlargement, tonsillar enlargement, episodes of unexplained fever.



Painless lymph node enlargement in HIV infection.

#### Advanced HIV diseases

- 4- Group IV: Other diseases, usually after 11 years.
- Conistitutional:
  - Major constitutional symptom complexes
  - These include malaise, fever, night sweats, arthralgia, diarrhoea and weight loss
- Neurological involvement:
  - Myelopathy and peripheral neuropathy, for which the only explanation is HIV infection.
- Opportunistic infections

# Opportunistic infections

- Pneumocystis carinii pneumonia
- Chronic cryptosporidiosis
- Toxoplasmosis
- Extra-intestinal strongyloidiasis
- Isosporiasis
- Cryptococcosis

- Candidiasis

   (oesophageal,
   bronchial, pulmonary)
- Histoplasmosis
- Mycobacterium avium intracellulare or M kansasii
- Cytomegalovirus
- Herpes simplex

- Secondary cancers:
- Kaposi's sarcoma.
- Non-Hodjkin's lymphoma.
- Primary cerebral lymphoma.

# HIV-Related Malignancy

Kaposi's Sarcoma

Non-Hodgkin's lymphomas

Primary cerebral lymphoma

Hairy Leukoplakia Caused by E.B.V

# Clinical picture:

# 1- GIT manifestations of AIDS:

- Oral:
  - Oral candidiasis.
  - Hairy leukoplakia
  - Oral ulcers (due to Herpes simplex virus).
  - Papilloma and condylomata (due to Human paiplloma virus).
  - Kaposi's sarcoma.
  - Lymphoma.



Extensive oral infection with Candida albican in a patient with HIV infection.

# -Oesophageal:

- Candidiasis.
- Leukoplakia.
- Ulceration.
- Herpes infection.
- CMV infection.
- Kaposi's sarcoma.
- Lymphoma.

#### -Gastric:

- Reduced acid secretion.
- Reduced gastric juice volume.
- Reduced pepsin output.

The cause of gastric lesions may be infections as cytomegalovirus, campylobacter pylorides, cryptosporidium or neoplasms as Kaposi;s sarcoma.

#### Intestinal manifestations:

# AIDS enteropathy:

- Direct HIV infection to intestinal immune system leading to secretory diarrhea.
- Partial villous atrophy.
- Autonomic neuropathy.
- Bacterial colonisation
- Parasitic infestation (cryptosporidium, Giardia lamblia, Isospora belli, E. Histolytica).

### **2- Chest manifestaions:**

- -Pneomcystis carinii pneumonia.
  - It is a protozoan widely distributed in animals.
  - The diagnosis is by transbronchial biopsy or lavage and examination using silver staining technique.
- Bacterial pneumonia
  - Caused by streptococcus, staphyococcus aureus, Mycobacterium tuberculosis, Mycobacterium avium intracellulare.
- Others: as cytomegalovirus, candida, Kaposi's sarcoma, and lymphoma.

# 3- Neurological manifestations:

- -Encephalopathy
- Myelopathy and acute transverse myelitis.
- Neuropathy: mostly peripheral sensory neuropathy.
- Encephalitis
- Meningitis: most commonly caused by cryptococcus neophormans.
- Toxoplasosis.
- CNS lymphoma.

# Kaposi's sarcoma

Kaposi's sarcoma: Common tumor in AIDS patients. It develops as multiple, small dusky purple-red or purple nodular, painless lesions of the skin or buccal mucosa, but may also be found anywhere in the gastrointestinal tract or bronchial mucosa.



Kaposi's sarcoma is a common complication in patients with AIDS.

Main symptoms of AIDS

#### Neurologic<del>al</del>

- Encephalitis
- Meningitis

#### Eyes-

- Retinitis

#### Lungs

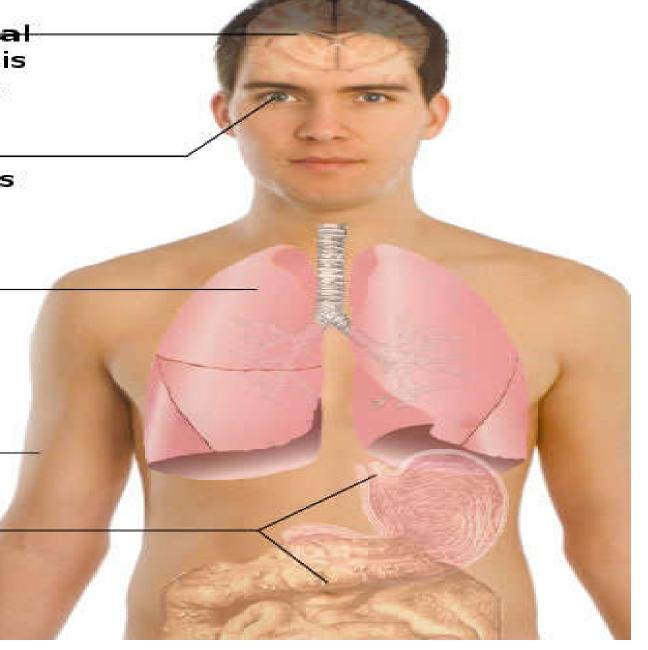
- Pneumocystis pneumonia
- Tuberculosis (multiple organs)
- Tumors

#### Skin

- Tumors

#### Gastrointestin<del>al</del>

- Esophagitis
- Chronic diarrhea
- Tumors



# Diagnosis:

# A) Clinical suspicion:

- The presence of at least 2 major symptoms and at least 1 minor symptom
- Major symptoms include:
- 1- Unexplained fever for more than 1 month.
- 2- Unexplained diarrhea for more than 1 month.
- 3- Unexplained weight loss greater than 10% of previous weight.

- Minor symptoms include:
- 1- Presence of maculopapular rash.
- 2- Oral candidiasis.
- 3- Herpes zoster.
- 4- Aggressive uncontrolled herpes simplex.
- 5- Unexplained cough for more than 1 month
- 6- Enlarged lymph nodes in more than one extrainguinal site.

#### **B)** Laboratory

- CBC which shows anaemia, neutropenia, thrombocytopenia are common with advanced HIV infection, lymphopenia especially T cells, \CD4 /CD8 ratio.
- HIV ELISA: a screening test for HIV

  Sensitivity > 99.9%. To avoid false positive results repeatedly reactive results must be confirmed by Western blot technique
- Polymerase chain reaction: is very specific for DNA replication.

# **Treatment:**

# -Anti retro viral drugs:

- reverse transcriptase inhibitors
- Nucleoside analogues as →Zidovudine (AZT), Lamivudine.
- Nonnucleoside analogues as nevirapine
- Protease inhibitors as saquinavir, indinavir.
- Ganciclovir: is the drug of choice for CMV infection.

- -Acyclovir: for herpes simplex virus infection topically, orally or intravenously.
- Desciclovir for therapy of hairy leukoplakia.
- -Anti protozoal.
- -Anti fungal.
- -Anti TB.

# **Prevention:**

Prevention of the spread of HIV infection involves:

- 1- Screening of blood donors,
- 2- Advice on safer sexual practices,
- 3- Measures to curtail intravenous drug abuse and the provision of sterile syringe and needle

