

VIRAL DISEASES

Introduction: Viruses are the smallest known infective agents. All viruses depend on host cell metabolism for their replication, that is, are obligate intracellular parasites. Viruses vary greatly in size from 20-300 nm. Viruses are either spherical or cylindrical in shape. A single virus particle, called virion is made up of a core consisting of a single molecule of nucleic acid either DNA or RNA and a surrounding protein shell called a capsid.

Diseases caused by viruses are either:

(1) Acute illness: e.g. common cold and influenza. (2) Lifelong latency and long-term reactivation: e.g. herpes viruses. (3) Chronic disease: e.g. HBV, HCV and HIV. (4) Neoplasia.

Mode of Infection:

- (1) Inhalation: e.g. Influenza and measles.
- (2) Ingestion: e.g. poliomyelitis and viral hepatitis.
- (3) Inoculation: e.g. trachoma.
- (4) Bite of a vector: e.g. yellow fever.

Disease spectrum and pathological changes associated with viral infections:

There are several possible consequences to a cell that is infected by a virus, and ultimately this may determine the pathology of a disease caused by the virus.

1. Lytic infections result in the destruction of the host cell.
2. Abortive infection: in which the virus couldn't complete its replication, due to lack of essential factors needed for replication or due to action of host immune mechanisms.
3. Persistent infections: Symptoms and signs remain over relatively long periods of time due to slow viral release.
4. Latent infections: there is a delay between the infection by the virus and the appearance of symptoms. Fever blisters (cold sores) caused by herpes simplex type 1 result from a latent infection; they appear sporadically as the virus emerges from latency, usually triggered by some sort of stress in the host.
5. Transformation: Some viruses have the potential to change a cell from a normal cell into a tumor cell. These viruses are referred to as oncogenic viruses.

Pathological Changes:

- (1) Cellular changes: include:
 - (a) Cellular proliferation as in warts.
 - (b) Cellular degeneration and necrosis as in poliomyelitis and viral hepatitis.

(c) Appearance of inclusion bodies as in rabies and smallpox.

(2) Inflammatory cellular exudate: Mainly perivascular and consists lymphocytes and macrophages.

Cytomegalic Inclusion Disease (CID)

The modes of transmission of the cytomegalovirus include

A. Intra-uterine transplacental transmission :_from newly infected or asymptomatic mother to her fetus leading to

- Abortion, stillbirth or premature baby.

- Severe multisystem disease in the form of anemia, purpura, thrombocytopenia jaundice, hepato-splenomegaly, pneumonia, hepatitis, encephalitis and mental retardation. Most of these patients die.

- Mild multisystem disease in the form of pneumonitis, hepatitis and encephalitis. Most of these patients recover but many may develop mental retardation

- Asymptomatic infection, but few patients may develop hearing defects or mental retardation.

B. Acquired transmission

- _Respiratory droplet transmission.

- Blood transfusions and organ transplantations. - Venereal transmission.

- Transmission through mother's milk to her baby.

The clinical picture ranged from an asymptomatic illness to serious multisystem affection in immunosuppressed persons. The manifestations include pneumonitis, hepatitis, enterocolitis, and retinochoroiditis. CNS involvement in adults is rare.

Acquired Immuno-Deficiency Syndrome: AIDS

The causative organism is the human immunodeficiency virus (HIV) which is a retrovirus (RNA virus containing the enzyme reverse transcriptase), 2 types are known : HIV-1 & HIV-2.

Transmission of the virus occurs through

1. Sexual contact.
2. Parenteral inoculation
3. From infected mothers to their newborns.

The persons at high risk for developing AIDS are

Promiscuous homosexuals, intravenous drug abusers, hemophiliacs, blood recipients and sexual partners or children of any individual with the disease. Only small numbers of cases have been free from all risk factors.

N.B. The virus may produce asymptomatic infection for many years.

Mechanism

1. Lymphopenia: mainly due to selective loss of CD4 + helper T-cell together with impairment in the function of the surviving helper T cells.

The total leucocytic count is low (less than 2000) and the CD4 + T cell count is below 200. The CD4/CD8 ratio is inverted, normally it is 2 while in AIDS it is 0.5.

2. Decreased and altered T cell functions: increased susceptibility to opportunistic infections and malignant neoplasms.

3. Decreased delayed type hypersensitivity, decreased proliferative response to antigens, decreased specific cytotoxicity & decreased production of IL-2 & IL-8.

4. Polyclonal B cell activation: hypergammaglobulinemia and inability to mount de novo antibody response to new antigens.

5. Altered Monocyte/Macrophage functions: decreased chemotaxis and phagocytosis.

Summary of the effects of the T4 helper lymphocytes:

- 1- Decreased response to antigens & ↓ lymphokines
- 2- Decreased specific cytotoxic action
- 3- Natural killer cells (NK) are less capable of killing tumor cells
- 4- B cell/plasma cells with decreased Ig production (poor helper T4 cell action)
- 5- disordered function of macrophage (no lymphokine release)
 - a) Decreased phagocytosis
 - b) Decreased chemotaxis
 - c) Decreased IL-1 secretion
 - d) Defective antigen processing & presentation

• The phases of HIV infection and their corresponding clinical features

- Early acute (Initial) phase (group I) Self limiting acute illness (acute infection) consisting of non-specific symptoms such as: sore throat, muscle pain, fever and skin rash. There is high level of virus replication with antiviral response.

- Middle (Latent or prodromal) chronic phase (group II): There is low level of HIV replication which may last for several years. Patients may be asymptomatic (group II) or develop persistent generalized lymphadenopathy (group III). Most if not all patients with HIV infection will progress to AIDS after a chronic phase lasting from 7 to 10 years

- final crisis (opportunistic infection & tumours) phase (group III) : There is breakdown of host defense with recrudescence of viral replication, this phase comprises

*Subgroup A : constitutional disease : fever, fatigue, diarrhea & weight loss .

* Subgroup B: neurologic disease : CNS affection, neuronal damage & dementia (AIDS dementia complex).

* Subgroup C. secondary and opportunistic infections such as Protozoal and Helminthic infections: toxoplasmosis, - strongyloidosis, pneumocystosis (Pneumocystis carimi pneumonia associated with alveolitis, alveolar damage and edema.

-Fungal infections: candidiasis, histoplasmosis and cryptococcosis.

-Bacterial infections: tuberculosis, atypical mycobacteriosis, salmonella and shigella infections.

-Viral infections: cytomegalovirus, herpes simplex virus and Varicella - Zooster virus.

*Subgroup D: secondary malignant neoplasms, such as non Hodgkin's lymphoma, Burkitt's lymphoma and Kaposi's sarcoma. -.

Several methods have been used to detect anti -HIV antibodies such as the ELISA technique, which when positive, it must be confirmed by Western blot analysis, or PCR. Prevention by passive or active immunization may be attempted in the future. The antiviral drug that is of some value in the treatment of AIDS is 3-azidoxy-3-deoxy-thymidine (AZT). It is an inhibitor of the reverse transcriptase enzyme.

Epstein-Barr virus

Definition: Epstein- Barr Virus (EBV) is herpes virus and is the causative agent of **Burkitt's lymphoma** in Africa, **nasopharyngeal cancer** in the orient and **infectious mononucleosis**.

Epidemiology: A large proportion of the population (90-95%) is infected with Epstein-Barr virus, and these people, although usually asymptomatic, will shed the virus from time to time throughout life.

Mode of transmission: The virus is spread by close contact (kissing). The virus can also be spread by blood transfusion.

Pathogenesis: EBV only infects a small number of cell types that express the receptor for complement C3d component (CR2 or CD21). These are certain epithelial cells (**oro & naso-pharynx**) and **B lymphocytes**. This explains the cellular tropism of the virus. The virus is replicated in pharyngeal epithelial cells, shed into the saliva and is taken up by B lymphocytes. As a result of EBV infection, these lymphocytes become stimulated

to divide and are protected from undergoing apoptosis (cell death). They become transformed cells and they begin to appear in high levels in the bloodstream.

Diseases caused by EBV:

1. **Infectious mononucleosis:** This disease is characterized by non specific symptoms and signs, including malaise, generalized lymphadenopathy, tonsillitis, enlarged spleen and liver, and fever. The disease usually runs a benign course.
2. **Burkitt's lymphoma:** A type of malignant tumor of B lymphocytes, affecting jaw and face of young children. Tumor cells show evidence of EBV DNA.
3. **Nasopharyngeal cancer:** The disease is a malignant tumor of the epithelium of the upper respiratory tract and the tumor cells contain EBV DNA.
4. The association between EBV and a number of **other tumors** has only come to light in more recent years, indicating that the oncogenic effects of the viruses may be evident when infecting other cell types. The best known of these examples is Hodgkin's disease, which another type of malignant lymphoma.

Human papillomavirus

Definition: Human papillomavirus (HPV) is a family of over 100 viruses including those which cause warts and are transmitted by contact. Some types of HPV are associated with tumors of the genital tract including cancer of the cervix.

Types of HPVs: The strains of HPV may be divided into two major groups

1. **Low-risk groups:** these are the strains which produce raised warts, namely HPV-6 & HPV-11.
2. **High-risk groups** are more likely to lead to the development of cancer. These high-risk types cause growths that are usually flat and nearly invisible. Examples include HPV-16 & HPV-18

Diseases caused by HPV:

1. **Common warts:** The majority of HPVs produce warts on the hands, fingers, and even the face. Most of these viruses are thus innocuous, causing nothing more than cosmetic concerns.

2. **Genital warts (Condylomata acuminatum),** sexually transmitted, and most commonly caused by two HPV strains, HPV-6 and HPV-11.

Gross: Genital wart appears as a 5 mm papule to large fleshy tumor mass involving anogenital region.

Microscopic: The epithelium of the genital wart showed hyperkeratosis, acanthosis, papillomatosis together with superficial koilocytosis.