Herpesviridae

Herpesviridae is a family of **large viruses** with enveloped **DNA**. The nucleocapsid spherical **icosahedral** core surrounded by a lipoprotein **envelope**. The **genome** is linear, double-stranded DNA (**dsDNA**).

The herpesviruses derive their name from the Greek word *herpein* (to creep), describing the spreading nature of skin lesions caused by these viruses.

The outstanding property of herpesviruses is their ability to establish lifelong persistent infections in their hosts and to undergo periodic reactivation. Their frequent reactivation in immunosuppressed patients causes serious health complications. These infections are often **latent infections***, which can be reactivated from time to time, especially if the host becomes immunecompromised. Curiously, the reactivated infection may be clinically quite different from the disease caused by the primary infection.

*** latent infection or Virus latency** is the ability of a pathogenic virus to lie dormant (latent) within a cell, denoted as the lysogenic part of the viral life cycle.

Virion: Spherical, (icosahedral)

Genome: Double-stranded DNA, linear.

Envelope: enveloped , contains viral glycoprotein spikes.

Replication: Nucleus, bud from nuclear membrane.

Outstanding characteristics:

- Encode many enzymes
- Establish latent infections
- Persist indefinitely in infected hosts
- Frequently reactivated in immunosuppressed hosts
- Some cause cancer

Classification of Human Herpesviruses

Herpesviruses are divided into three subfamilies:

1. **α-herpesviruses** include:
   - **Herpes simplex virus types 1 (HSV1)**
   - **Herpes simplex virus types 2 (HSV2)**
   - **Varicella-zoster virus (VZV)**
2. **β- herpesviruses** include:
   - **Cytomegalovirus (CMV)**
   - **Human herpes viruses 6 (HHV6)**
   - **Human herpes viruses 7 (HHV7)**
3. **γ- herpesviruses** include:
   - **Epstein-Barr virus (EBV)**
   - **Human herpes virus 8 (HHV8) or (Kaposi sarcoma-associated herpesvirus_ KSHV)**

Herpes simplex virus 1 and 2 (HSV-1 and HSV-2): infect epithelial cells and establish latent infections in neurons.

1. **HSV-1**: initially infect epithelial cells of the oral via the lips or the nose, HSV-1 infections are associated with oropharyngeal lesions and causes recurrent attacks of "fever blisters." Mode of transmission of HSV-1 is spread by contact, usually involving infected saliva or respiratory droplets.

Disease: cold sore on lips may be complicated to encephalitis, especially in immune-compromised hosts.

Site of latent infection: neurons and may be transported to their nuclei.

2. **HSV-2**: initially infect epithelial cells of the genital mucosa, the skin or the cornea, mainly responsible for genital herpes. Transmitted by HSV-2 is transmitted sexually or from a maternal genital infection to a newborn.

Disease: genital herpes, which is a sexually transmitted disease. In new born babies infection can result in serious disease, with a mortality rate of about 54 per cent.

Site of latent infection: neurons and may be transported to their nuclei.

Both viruses in general causes:

1. Oropharyngeal Disease
2. Keratoconjunctivitis
3. Skin infections
4. Encephalitis
5. Neonatal Herpes
6. infections in immunocompromised Hosts

3. **Varicella-zoster virus (VZV):** causes chickenpox (varicella) on primary infection and establishes latent infection in neurons. Upon reactivation, the virus causes zoster (shingles). Adults who are infected for the first time with varicella-zoster virus are apt to develop serious viral pneumonia.

Disease: **varicella (chickenpox),** a mild, highly contagious disease, chiefly of children, characterized by vesicular eruption of the skin and mucous membranes. The disease may be severe in adults and in immunocompromised individuals, when the virus spreads through the blood to the skin, causing a rash. When a latent infection is reactivated the nerves most often affected are those in the face or the trunk, and these are the area most commonly affected in **zoster (shingles)**. Zoster

(shingles) is a sporadic, incapacitating disease of elderly or immunocompromised individuals that is characterized by pain and a rash limited in distribution to the skin innervated by a single sensory ganglion. The lesions are similar to those of varicella.

Both diseases are caused by the same virus. Whereas varicella is the acute disease that follows primary contact with the virus, zoster is the response of the partially immune host to reactivation of varicella virus present in latent form in neurons in sensory ganglia.

Site of latent infection: the virus lies dormant in the nerve cells.

4. Cytomegalovirus (CMV) or (HHV-5)

CMV replicates in epithelial cells of the respiratory tract, salivary glands, and kidneys and persists in lymphocytes. It causes an infectious mononucleosis. In newborns, cytomegalic inclusion disease may occur. CMV is an important cause of congenital defects and mental retardation.

Disease: Human cytomegalovirus can cause severe disease (e.g. pneumonitis, hepatitis) in immune-compromised patients such as those with AIDS, those who have received treatment for cancer and those who are immunosuppressed because they have received an organ transplant.

Site of latent infection: monocyte, lymphocyte. The virus remain dormant in the body, can cause complications during pregnancy, the virus can infect the placenta and then the fetus.

5. Human herpesvirus-6 (HHV- 6)

Disease: exanthem subitum (roseola infantum, or "sixth disease**")**: the mild common childhood disease characterized by a high fever and skin rash. The mode of transmission of HHV-6 via oral secretions. The fact

that it is a ubiquitous agent suggests that it must be shed into the environment from an infected carrier.

The virus grows well in CD4 T lymphocytes. Other cell types also support viral replication, including B cells and cells of glial, fibroblastoid, and megakaryocyte origin. Cells in the oropharynx must become infected because virus is present in saliva.

Site of latent infection: lymphoid tissues, reactivation appears to be common in transplant patients and during pregnancy.

6. Human herpesvirus-7 (HHV-7)

A T-lymphotropic human herpesvirus, most infections occurring in childhood. Persistent infections are established in salivary glands, and the virus can be isolated from saliva of most individuals. Similar to HHV-6, primary infection with HHV-7 has been linked with roseola infantum in infants and young children.

7. Epstein-Barr Virus (EBV)

Also called Human gamma herpesvirus 4.

Disease: infectious mononucleosis (glandular fever), commonly called 'the kissing disease' by doctors. Most people are infected by the virus as children. In young adults, the disease often results in fever, sore throat, enlarged lymph nodes in the neck, and tiredness.

There is **few or no symptoms** for the disease. **Spread** of the disease occur through **saliva**, **semen** or **blood**. Spread may occur by **objects** such as **drinking glasses** or **toothbrushes** or through a **cough** or **sneeze**. EBV is associated with a number of tumours in man.

8. Human herpesvirus-8 (HHV-8)

A new herpesvirus, designated HHV-8 and also called KSHV (Kaposi sarcoma-associated herpesvirus),

Disease: KSHV is the cause of Kaposi sarcomas, vascular tumors of mixed cellular composition, and is involved in the pathogenesis of body cavity-based lymphomas occurring in AIDS patients and of multicentric Castleman disease.

KSHV is not as ubiquitous as other herpesviruses, Contact with oral secretions is likely the most common route of transmission. The virus can also be transmitted sexually, vertically, by blood, and through organ transplants.

Diagnosis

Diagnosis of all other herpes virus infection relies on:

1. isolation of the virus through culturing
2. detection of viral genes or gene products, particularly using polymerase chain reaction (PCR) technology.
3. Serological tests by using immunofluorescence tests for serum antibodies.

Control of Herpes viruses Infections

Prevention:

A vaccine to prevent varicella-zoster virus infections was recently licensed in the United States. Vaccines against herpes simplex virus 2, and cytomegalovirus are undergoing extensive evaluations in field trials**.**

Treatment:

Infections with herpes simplex virus 1 and 2 and varicella-zoster virus are the most amenable to therapy; acyclovir, valaciclovir and famciclovir are all licensed therapeutics. Ganciclovir is used to treat cytomegalovirus retinitis. There is as yet no treatment for Epstein-Barr virus or human herpesvirus 6,7 or 8 infections.