IOSR Journal Of Pharmacy
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
www.iosrphr.org Volume 4, Issue 10 (October 2014), PP. 39-41

Herpes Viruses – An Overview

Dr. K. Badari Rao
Associate Professor, Department of Oral Pathology & Microbiology, NSVK Sri Venkateshwara Dental College & Hospital
Kariyappanahalli, Anekal Road, Bannerughatta, Bengaluru – 560 083

ABSTRACT: *Most human viruses known to cause oral diseases are deoxyribose nucleic acid (DNA) viruses that are contracted either in childhood or early adulthood through contact with blood, saliva, or other secretions. Herpes viruses seem to be the most important DNA viruses in oral pathology. Clinically, herpes viruses can cause a spectrum of diseases; the hallmark of their infections being immune impairment. Active herpes virus infections may have particularly severe consequences in human immunodeficiency virus (HIV) infected and other immunocompromised individuals. This review highlights the description of herpes viruses, organization of its genome and proteins, and the diseases affecting the mankind. It brings to fore the need for newer drugs to effectively manage the ever increasing diseases caused by herpes viruses.*

KEY WORDS: *DNA viruses, herpes viruses, HIV, immunocompromised humans*

I. INTRODUCTION

Viruses are obligate intracellular parasites that depend on the host cell's machinery for their survival and replication. They consist of a nucleic acid genome either deoxyribose nucleic acid (DNA) or ribose nucleic acid (RNA), surrounded by a capsid (protein coat), that is sometimes encased in a lipid membrane. Herpes viruses are DNA viruses and their genome contains information necessary for programming the infected host cell to synthesize specific macromolecules required for their replication.[1] They can persist within the host cells for years (non-replicating form) only to be reactivated later.[2]

II. GENERAL DESCRIPTION OF HERPES VIRUSES

The following are characteristics common to the herpes viruses:[1,2,3]

- Herpes viruses are large encapsulated viruses that contain four layers:

1. *Genome*: an inner core of double-stranded DNA molecule ranging in size from 124 to 235 kbp
2. *Capsid*: made up of proteins of 162 capsomeres
3. *Tegument*: an amorphous structure between the capsid and envelope
4. *Envelope*: derived from the nuclear membrane of the infected cell and containing viral glycoprotein spikes about 8 nm long. The enveloped form (icosahedral) measures 150-200 nm and the naked virion (spherical) about 100 nm in diameter.

- Herpes viruses cause primary infection (usually acute) followed by latent infection in which they persist in a non-infectious form with periodic reactivation and shedding of infectious virus. Latency is the inability to recover infectious particles from cells that harbor the virus thus ensuring survival of the viral genome throughout the lifetime of the infected individual. After reactivation, latent herpes viruses enter the productive phase and interestingly, the reactivated infection may be clinically quite different from the disease caused by the primary infection.
- Herpes viruses exhibit tissue tropism i.e. highly selective with regard to the surfaces or organs that they infect or invade.
- They are transmitted from host to host by direct contact with saliva or genital secretions. Some may even be transmitted by way of organ transplantation.
- They are shed in the saliva of asymptomatic hosts who act as constant reservoirs for new primary infections in previously uninfected individuals.

III. CLASSIFICATION OF HUMAN HERPES VIRUSES

There are eight types of human herpes viruses, belonging to three subgroups defined by the type of cell most frequently infected and the site of latency:[1,3,4] (*Table 1*)

1. *α-group viruses:* herpes simplex virus 1 (HSV-1), herpes simplex virus 2 (HSV-2), and varicella zoster virus (VZV); infect epithelial cells and produce latent infection in neurons
2. *β-group viruses:* cytomegalo virus (CMV), human herpes virus 6 (HHV-6), and human herpes virus 7 (HHV-7); infect and produce latent infection in a variety of cell types
3. *γ-group viruses:* Epstein-Barr virus (EBV) and human herpes virus 8 (HHV-8); produce latent infection mainly in lymphoid cells.

Table 1: Classification of Herpes Viruses

Subfamily	Biological Properties		Examples	
	Cytopathology	Site of Latency	Official Name	Common Name
Alpha (α)	Cytolytic	Neurons	HHV-1	HSV-1
			HHV-2	HSV-2
			HHV-3	VZV
Beta (β)	Cytomegalic	Glands, kidneys	HHV-5	CMV
	Lympho-proliferative	Lymphoid tissue	HHV-6	HHV-6
			HHV-7	HHV-7
Gamma (γ)	Lympho-proliferative	Lymphoid tissue	HHV-4	EBV
			HHV-8	KSHV

HHV: human herpes virus, HSV: herpes simplex virus, VZV: varicella zoster virus, CMV: cytomegalo virus, EBV: Epstein-Barr virus, KSHV: Kaposi's sarcoma-associated herpes virus

IV. STRUCTURE AND ORGANIZATION OF HERPES VIRUS GENOME

Human herpes viruses share homologous genes and blocks of conserved genes. These conserved genes grouped in blocks, called as the herpes virus core define the herpes viruses. Several genes in the conserved core regions encode proteins characteristic of them. In general, herpes virus species of the same subfamily share the greatest number and exhibit the closest alignment of homologous genes. Seven blocks of genes that are conserved among all herpes virus subfamilies are located in the center of most human herpes virus genomes. Although latency is a biologic characteristic of herpes viruses, the few known latency genes and transcripts are not located in the conserved core region and are hence not conserved among the herpes virus subfamilies.

Herpes virus species differ greatly in their genomic composition, sequence arrangement, and base composition. Human herpes virus genome sizes range from 125 kbp (VZV) to 230 kbp (CMV). A striking feature of herpes virus DNA is their sequence arrangement. Herpes virus genomes possess terminal and internal repeated sequences. Some such as the herpes simplex virus undergo genome rearrangements, giving rise to different genome 'isomers'. The nucleotide composition varies considerably too. For example, guanine-cytosine content in the α-herpes viruses, HSV (1&2) and VZV is 68% and 46% respectively. There is little DNA homology among different herpes viruses except for HSV types 1 and 2, which show 50% sequence homology, and HHV types 6 and 7, which display 30-50% sequence homology. Treatment with restricted endonucleases yields characteristically different cleavage patterns for herpes viruses and even for different strains of each type. This "fingerprinting" of strains allow epidemiologic tracing of a given strain. [1,3]

IV.I. Herpes Virus Proteins

The herpes virus genome is large and encodes at least 100 different proteins. Of these, more than 35 polypeptides are involved in the structure of the virus particle; some are part of the viral envelope. Herpes viruses encode many of the proteins necessary for viral DNA replication. Herpes virus genes essential for viral

origin-dependent DNA replication have been identified, including genes for DNA polymerase, genes for an origin-binding protein and genes for a helicase/primase complex. Herpes viruses also encode proteins involved in nucleotide metabolism and DNA repair. One example is thymidine kinase encoded by HSV, VZV, and EBV. CMV or HHV (6&7) do not possess thymidine kinase gene or homolog genes. However, CMV encodes another type of protein kinase (UL97), which is conserved among all the herpes viruses, including viruses possessing a thymidine kinase gene.

Herpes viruses express several genes in the mode of a cascade which can be divided into the following phases: immediate-early, early, and late phase. Immediate-early transcripts are mainly regulatory proteins that transactivate later phases.

Herpes virus genes encode numerous glycoproteins expressed on the surface of the infected cell and the viral envelope, some of which are conserved among all human herpes viruses. These glycoproteins mediate entry into susceptible cells, cell-to-cell viral spread, and serve as major determinants of tissue tropism and host range. Herpes viruses also encode the entire set of proteins necessary for assembly of the icosahedral capsid.

Genes conserved among the various herpes virus species, encode several of their basic biological characteristics and genes that are not conserved may be responsible for the biologic diversity of herpes viruses. [1,3]

V. HERPES VIRUS DISEASES

A wide variety of diseases in humans are associated with infection by herpes viruses (primary infection). They are also frequently reactivated in immunocompromised patients (e.g. transplant recipients, human immunodeficiency virus-infected individuals, cancer patients) and may cause severe disease, such as pneumonia or lymphoma. [3] Primary infection and reactivated disease may involve different cell types and present different clinical pictures depending on the type of herpes virus.

HSV-1 and HSV-2 infect epithelial cells and establish latent infections in neurons. HSV-1 is classically associated with oropharyngeal lesions and causes recurrent attacks of "fever blisters". HSV-2 primarily infects the genital mucosa and is responsible for genital herpes. They can cause neurologic disease. Both HSV-1 and HSV-2 can also cause neonatal infections which are often severe.

VZV causes chickenpox (varicella) on primary infection and establishes latency in neurons. Upon reactivation, it causes herpes zoster (shingles).

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

HHV-6 infects T-lymphocytes which is typically acquired in early infancy. It causes exanthem subitum (roseola infantum), and sixth disease, a benign rash of infants. Target cells for latent infection and the consequences of reactivation are not known. HHV-7, also a T-lymphotropic virus, has not yet been linked to any specific disease.

EBV replicates in epithelial cells of the oropharynx and parotid gland and establishes latent infection in lymphocytes. It causes infectious mononucleosis and is the cause of human cancers namely, lymphomas and nasopharyngeal carcinoma.

HHV-8 is associated with the development of Kaposi's sarcoma, a vascular tumor that is common in patients with acquired immunodeficiency syndrome.

VI. CONCLUSIONS

Despite the exponential growth in virology during the last 50 years, mankind still suffers from transmission and disease when humans serve as hosts to many viruses. Herpes viruses, a large group of DNA viruses, cause a wide spectrum of diseases in humans and treatment is often symptomatic. Of great importance is the fact that the oral cavity continues to be the source of transmission, the site of replication, and asymptomatic shedding of these viruses, and the site where persistent viral infection may exist albeit in a latent form. These facts highlight the need for newer drugs and management protocols to effectively counter the herpes viruses.

References

[1]. Contreras A, Slots J. Herpesviruses in human periodontal disease. J Periodont Res 2000; 35: 3-16.
[2]. Stoopler ET, Greenberg MS. Update on herpes virus infections. Dent Clin N Am 2003; 47: 517-32.
[3]. Brooks GF, Butel JS, Morse SA, editors. Medical microbiology. USA: McGraw-Hill 2001; p. 370-4.
[4]. McAdam AJ, Sharpe AH. Infectious diseases. In: Kumar V, Abbas AK, Fausto N, editors. Pathologic basis of disease. Pennsylvania: Saunders 2004; p. 343-414.