Chapter

Introductory Chapter: Human Herpesvirus - A Short Introduction

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1. Introduction

The relationship between herpesviruses and humans probably proceeds from thousands of years. In the last decades, many aspects of herpesviral infections have been understood since infections with a severe outcome to mild or subclinical manifestations. Several conditions have been related to herpesviral reactivation since complications in transplant-organ recipients to immune regulatory modification in the elderly.

The manifestations caused by the herpesvirus simples in the oral region are classically known. Manifestations with labial lesions and sometimes stomatitis can occur in a considerable part of the population at some point in the individual's life. Usually, these lip lesions are self-limiting although they are often recurrent [1]. Other herpesviruses have been considered as emerging pathogens in the etiology of different diseases.

Human herpesviruses belong to the family *Herpesviridae*, they are ubiquitous viruses and once the first infection occurs, they remain in the body of the affected individual (latency) during the lifetime. These viruses cause a wide variety of diseases, and infections are often benign, but may in immunocompromised individuals cause clinical manifestations with different level of severity [2, 3].

The *Herpesviridae* family is divided into 3 subfamilies: Alphaherpesvirinae (*α-herpesvirinae*), Betaherpesvirinae (*β-herpesvirinae*) and Gammaherpesvirinae (*γ-herpesvirinae*). These are distinguished by their viral and structural characteristics, as well as by their pathogenic potential. All types of viruses classified into this

Virus	Synonymous	Subfamily	Abbreviation
Human herpesvirus 1	Herpes simplex-1	α	HSV-1/HHV-1
Human herpesvirus 2	Herpes simplex-2	α	HSV-2/HHV-2
Human herpesvirus 3	Varicella-zoster	α	VZV/HHV-3
Human herpesvirus 4	Epstein-Barr	γ	EBV/HSV-4
Human herpesvirus 5	Cytomegalovirus	β	CMV/HHV-5
Human herpesvirus 6	None	β	HHV-6
Human herpesvirus 7	None	β	HHV-7
Human herpesvirus 8	None	γ	KSHV/HHV-8

Table 1.
Members of the human herpesvirus family.

family are double-stranded DNA viruses and the different types of herpes viruses share similar structural characteristics. List of herpesviruses that infect humans are summarized in **Table 1** [2, 3].

Herpesvirus group can establish primary infections with nonsevere symptoms, which can result in an efficient immune response that prevents a new infection. However, the virus is not completely eliminated, its genome remains within cells without productive infection. Latent infections may become active (reactivation) due to factors related to the host and these manifestations allow the spread of herpesviruses, since a release of extracellular virions occurs which can infect other cells [4].

2. The human herpesviruses

2.1 Herpesvirus simplex 1 and 2

Human herpesviruses type 1 and 2 (HSV-1 and HSV-2) are usually associated with herpes and genital herpes, respectively. However, genital herpes may be a consequence of HSV-1 infection and cold sores may also be caused by HSV-2. Once the individual has been infected, reactivation is extremely common in both clinical forms: oral or genital. The lesions are bullous and painful although it tends to disappear in a few intervals of time [5, 6].

In some individual, especially in severely immunocompromised patients but not only but also in individuals with a moderate or mild reduction in immune response, in particular, cell-mediated, these viruses can cause more severe disease such central nervous system affections. The frequent labial and genital herpes recurrence show that severe immunosuppression is not a *sine qua non* condition to herpes simples reactivation.

2.2 Varicella-zoster virus

Human herpesvirus type 3 (Varicella-zoster) causes varicella (chickenpox) in a primary infection that occurs especially in children and reactivation can cause the onset of zoster that is more frequent in the elderly. Neurologic zoster is an important complication of this infection, especially in elderly and immunosuppressed patients [7, 8].

Varicella in children is often benign although rarely could cause hepatitis and encephalitis. In adults, varicella tends to cause more severe outcomes, and the fact is not completely understood. Zoster is related to decrease of the self-reported level of satisfaction with the life and depression in the elderly. Besides the zoster being frequently recurrent, the pain remains for several weeks after the lesions have disappeared. Fortunately, the vaccination is available for both children [9] and elderly [10] and it will probably lead to a decrease of incidence not only of varicella but also of zoster due to the consequence of reactivation of VZV which remained from a Varicella episode. However, in the elderly, the prescription of vaccination must be carefully made to avoid complications caused by a vaccine containing attenuated viruses.

2.3 Epstein-Barr virus

Human herpesvirus type 4 (Epstein-Barr virus; EBV) is associated with infectious mononucleosis, Burkitt's lymphoma, and nasopharyngeal carcinoma. The most important aspect of EBV is its oncogenic potential. A majority of cases of

EBV infection have a low impact on the individual; however, a complication such as hepatitis [11], lymphoproliferative syndrome [12], and encephalitis can rarely occur [13]. There is no vaccine to prevent EBV infection; however, concerning a progressive putative relation with the pathogenesis of several types of tumors, a possibility of the development of a vaccine must be considered.

2.4 Cytomegalovirus

Primary cytomegalovirus infection causes a "mononucleosis-like syndrome" known as cytomegaly or "cytomegalic inclusion disease." Cytomegalovirus is not well known by the general public because it causes often not severe clinical conditions. The impact of cytomegalovirus infection HIV-infected [14] and transplant patients [15] is well recognized. Most recently, the cytomegalovirus has been associated with immunosenescence and, perhaps, frailty syndrome in the elderly [16]. It is not clear whether is the virus that modulates the immune system as a mechanism of evasion or the immune system declines along with the aging and to allow the virus replication.

2.5 Human herpesviruses 6 and 7

Primary HHV-6 and HHV-7 infections cause a common early febrile infectious syndrome known as roseola infantum or exanthem subitum [17]. The HHV-6 has been related to transplant rejection and graft-versus-host disease in bone marrow transplantation [18]. In other types of transplantation, the HHV-6 effects are much less related. HHV-7 have been studied in several types of conditions but its influence remains still not clear.

2.6 Human herpesviruses 8

Human herpesvirus type 8 is associated with Kaposi's sarcoma and can lead to death in immunosuppressed patients, especially acquired immunodeficiency syndrome (HIV/AIDS) [19].

3. Conclusions

In the last decades, a large number of research regarding herpesviruses have been published. Although a considerable number of conditions are irrefutably linked to a specific type of herpesvirus, many others remain well less explained and with lack of cause-effect definitions. It is clear that further studies must be designed with the aim of better understanding each hypothesis. The *status quo* about the knowledge about the human herpesvirus simples, varicella-zoster virus, and cytomegalovirus was presented and discussed in this book.

Conflict of interest

The author declares that there is no conflict of interest.

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