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MICROBIOLOGY IN SCHOOLS ADVISORY COMMITTEE
50th Anniversary Articles

Herpesviruses – hidden viruses

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Herpesviruses infect many animal species. In humans they are responsible for a range of diseases, including cold sores, genital herpes, chickenpox, shingles and glandular fever; some are linked to cancers.

Viruses are not composed of cells, they are particles that are produced when a virus infects cells; these virus particles can then infect other cells. Herpesvirus particles are spherical with a membrane containing proteins at the surface. Inside the membrane is a protein structure called a capsid; this contains the virus genome (**Figure 1**). Some viruses have their genes encoded in RNA, while others have their genes encoded in DNA. The genes of herpesviruses are encoded in DNA.

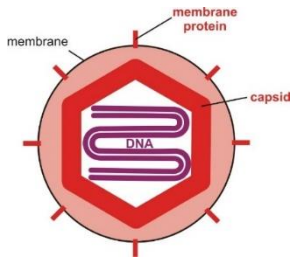

Figure 1. Herpesvirus structure. The red and pink structures are composed of proteins.

The virus membrane proteins play vital roles in the infection of a host cell; they can attach to receptors on the surface of a suitable cell enabling the virus membrane to fuse with the cell membrane. This process delivers the capsid containing the virus DNA into the cell. The capsid is then moved to the nuclear membrane and the virus DNA is released into the nucleus.

Most of us become infected with one or more herpesviruses during our lives. These infections may or may not result in disease. After initial infection the virus often persists in the body as a hidden (or latent) infection. When this happens the virus DNA persists in the nuclei of cells, with most of the virus genes switched off. The host's immune system does not recognise the virus DNA and cells carrying the hidden infections continue to function normally. The latent virus DNA can be reactivated by certain triggers, then the virus replicates and the cell releases new virus particles which can infect and kill other cells. This may result in disease.

One of the diseases that may result from reactivation of a latent infection is a cold sore. The virus involved here is herpes simplex virus 1 (HSV-1). Blisters appear on the face, commonly on a lip (**Figure 2A**); the blisters burst and form a scab. Infection with HSV-1 usually occurs in early childhood, often transmitted from an adult by kissing. Epithelial cells are infected, following which the virus can spread to a nerve cell, where the infection may become latent. The individual may suffer repeated cold sores if the infection is reactivated by triggers such as sunlight (ultra-violet radiation) and stress.

Herpes simplex virus 2 (HSV-2) is related to HSV-1, but prefers to infect the genitals. This virus is normally transmitted by sexual contact; it replicates in cells of the penis, vagina or anus, then it infects nerve cells in which it becomes latent. Triggers for reactivation include sexual activity and

hormonal changes. When the virus is reactivated it replicates again in the genitals, sometimes causing painful sores. Both HSV-1 and HSV-2 hidden infections can be re-activated without symptoms and the infected person may transmit the infection to others. These two viruses are not totally restricted to the sites in the body that they normally infect; HSV-2 can cause cold sores and HSV-1 can cause genital herpes.

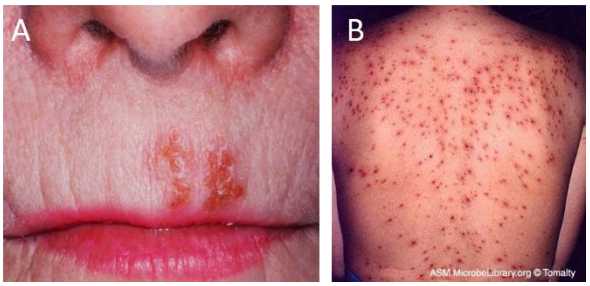

Figure 2 (A) Cold sore (cc Dr JW Eveson, Bristol University) and (B) Chicken pox (cc. Lewis L Tomalty)

Another herpesvirus causes both chickenpox and shingles. The medical terms for these diseases are varicella and zoster; the virus is called varicella-zoster virus (VZV). The virus enters the body through the nose or mouth and infection results in chickenpox, usually occurring in childhood. Spots appear which develop into blisters, and subsequently into scabs (**Figure 2B**). Like the herpes simplex viruses, VZV can remain hidden in a nerve cell. Later in life the virus may be reactivated, causing a rash (shingles), which can be very painful.

The herpesvirus responsible for glandular fever is called Epstein-Barr virus (EBV). It infects B cells, also known as B lymphocytes; these are important components of the immune system as they develop into antibody-producing cells. Most infections occur in early childhood, often as a result of a kiss from an adult with EBV in the saliva. These early infections are usually without symptoms, but if infection occurs later glandular fever can result, causing the patient to feel ill and tired for weeks or months. EBV is also thought to play a role in a number of cancers, including Hodgkin's Disease.

The main tools to prevent and treat virus infections are vaccines and anti-viral drugs. Chickenpox and shingles vaccines can protect people at high risk from VZV. Several anti-herpesvirus drugs have been developed; the one most commonly used to treat herpesvirus infections is aciclovir. These vaccines and drugs are not appropriate for dealing with all the risks posed by herpesviruses, so there are career opportunities to work on the development of more and better weapons to combat these viruses that so often remain hidden.

AUTHOR PROFILE

Dr John Carter graduated from the Universities of Birmingham and Glasgow and has been a lecturer at the West of Scotland Agricultural College, Newcastle University and Liverpool John Moores University. During his career he has taught virology and microbiology, carried out research into viral pathogens of insects and was the principal author of a virology textbook for universities (Carter J.B and Saunders V.A (2013) 'Virology: Principles and Applications', 2nd edition, Wiley).