

# MODULE 4

## VIRAL INFECTIONS

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- Herpes simplex virus infections
- Varicella zoster virus infections
- Cytomegalovirus infections
- Human papilloma virus infections
- Epstein Barr virus
- Human herpes virus type 8

### Learning Objectives

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When you have completed this module you should:

- Know the common clinical manifestations of herpes simplex virus infection
  - Understand that some viral infections are associated the development of cancers
  - Understand that some viral infections respond to antiviral therapy
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#### 4.1 HERPES SIMPLEX VIRUS INFECTIONS

Herpes simplex virus infection (HSV), which causes sores around the mouth and genitals, can become disseminated in immunosuppressed subjects. Dissemination may lead to infection of the lungs, the oesophagus, and the brain. Herpes simplex virus may also cause meningoencephalitis.

##### Diagnosis

It is often difficult to make a diagnosis of disseminated herpes and special laboratory tests, such as viral culture, radioimmunoblot assay and fluorescent and monoclonal antibody tests, may be necessary. Herpes simplex encephalitis leads to the development of multiple lesions in different parts of the brain and typical changes may be seen on CT scan studies of the brain.

**Treatment**

Specific antiviral treatment is summarized below:

**FIRST LINE TREATMENT**

**Herpes virus mild infection**

Antiviral agent	Dose	Frequency	Route	Duration
Aciclovir	400mg	TID	PO	7-10 days
<b>OR</b>				
Famciclovir	250mg	TID	PO	7-10 days
<b>OR</b>				
Valaciclovir	500mg	BID	PO	7-10 days

**FIRST LINE TREATMENT**

**Herpes virus recurrences**

Antiviral agent	Dose	Frequency	Route	Duration
Aciclovir	800mg	BID	PO	7-10 days
<b>OR</b>				
Famciclovir	500mg	BID	PO	7-10 days
<b>OR</b>				
Valaciclovir	1g	BID	PO	7-10 days

**FIRST LINE TREATMENT**

**Herpes virus severe infection**

Antiviral agent	Dose	Frequency	Route	Duration
Aciclovir	15-30mg/kg	OD	IV	7-10 days
<b>OR</b>				
Valaciclovir	1g	BID	PO	7-10 days

**FIRST LINE TREATMENT**

**Herpes virus visceral infection**

Antiviral agent	Dose	Frequency	Route	Duration
Aciclovir	30mg/kg	OD	IV	14-21 days

**SECOND LINE**

**TREATMENT**

**Herpes virus severe and visceral infection**

Antiviral agent	Dose	Frequency	Route	Duration
Foscarnet	60mg/kg	BID	IV	14 days
<b>OR</b>				
Valaciclovir	1g	TID	PO	14 days

**Activity 4.1**

**This is a group exercise**

What are the important aspects in the management of a patient with recurrent genital herpes?

**There will be a discussion when this exercise has been completed**

**4.2 VARICELLA ZOSTER VIRUS INFECTIONS**

Herpes virus varicella zoster often causes disseminated infection after initial exposure. In children initial infection results in the development of chicken pox, though most persons that become infected develop no symptoms and signs of infection. The virus lays dormant in the paraspinal ganglia for years and with immune suppression, from whatever cause, the virus replicates and produces lesions along the length of a cutaneous nerve in a dermatomal distribution. Dissemination can also occur at this time with involvement of skin, nervous system, lungs and mucous membranes. In immune suppressed persons zoster is often multidermatomal in distribution and is persistent and extensive. It is associated with severe pain and debility.

Diagnosis

The diagnosis is usually made on clinical grounds.

Treatment

**No treatment is necessary unless zoster is persistent.** Treatment is summarized in the tables below:

<b>FIRST LINE TREATMENT</b>				
<b>Dermatomal zoster</b>				
<b>Antiviral agent</b>	<b>Dose</b>	<b>Frequency</b>	<b>Route</b>	<b>Duration</b>
Aciclovir	800mg	QID	PO	7-10 days
<b>OR</b>				
Famciclovir	500mg	TID	PO	7-10 days

<b>FIRST LINE TREATMENT</b>				
<b>Disseminated, visceral, ophthalmic zoster</b>				
<b>Antiviral agent</b>	<b>Dose</b>	<b>Frequency</b>	<b>Route</b>	<b>Duration</b>
Aciclovir	30-35mg/kg	OD	IV	7-10 days
<b>OR</b>				
Famciclovir	500mg	TID	PO	7-10 days

<b>SECOND LINE TREATMENT</b>				
<b>Dermatomal, disseminated, visceral, ophthalmic</b>				
<b>Antiviral agent</b>	<b>Dose</b>	<b>Frequency</b>	<b>Route</b>	<b>Duration</b>
Aciclovir	30-35mg/kg	OD	IV	7-10 days
<b>OR</b>				
Foscarnet	60mg/kg	OD	IV	7-10 days

See EDLIZ for role of steroids.

**Activity 4.2**

**This is an individual exercise**

Why is it said that a person can get chickenpox after contact with a person with herpes zoster and not herpes zoster after contact with a person with chickenpox when the same virus causes both conditions?

**There will be a discussion when this exercise has been completed**

**4.3 CYTOMEGALOVIRUS INFECTIONS**

Cytomegalovirus may affect multiple systems and organs in the body in immunosuppressed individuals. The incidence of CMV disease varies between geographical locations, but CMV causes significant suffering in HIV-infected persons worldwide. Symptoms include fever and diarrhoea from CMV colitis, dyspnoea from CMV pneumonitis, and blindness caused by CMV retinitis.

Diagnosis

The making of a diagnosis requires costly tests, such as, tissue biopsies and DNA hybridization studies and sophisticated equipment.

Treatment

1. CMV gastrointestinal disease, neurologic disease and retinitis:

**CMV GI disease, neurologic disease and retinitis**  
**First line treatment**

Antiviral agent	Dose	Frequency	Route	Duration
Ganciclovir	5mg/kg	BID	IV	2-3 weeks

Long-term treatment with ganciclovir 5mg/kg given IV daily may be needed after successful treatment.

**CMV GI disease and neurologic**

**disease**

**Second line treatment**

Antiviral agent	Dose	Frequency	Route	Duration
Foscarnet	90mg/kg	BID	IV	3 weeks

Long-term treatment with foscarnet 90mg/kg given IV daily may be needed after successful treatment.

2. CMV retinitis, second line treatment:

**CMV retinitis**

**Second line treatment**

Antiviral agent	Dose	Frequency	Route	Duration
<b>Ganciclovir intraocular implant</b>				
<b>PLUS</b>				
Valganciclovir	900mg	BID	PO	21 days

**4.4 Human papilloma virus infections**

The human papilloma virus (HPV) causes genital warts, flat warts and skin warts. Both overt and subclinical infection occurs. PV is also associated with cervical cancer and intraepithelial neoplasia of the cervix, vagina, vulva, penis and anus. The strains of the human papilloma virus that cause genital warts are known as the "genital strains", while the strains that cause warts in sites other than the genital region are commonly referred to as the "non-genital" strains. It is known that the "genital strains" can infect non-genital sites such as the anus and perianal areas. Anal and genital warts are commonly found in men and women who have genital warts. Infants born to mothers with genital warts can develop warts.

Over 75 different strains of the human papilloma virus are known to cause infection in humans. Each viral strain appears to have an affinity for a particular anatomical site and each produces a defined spectrum of pathological features. Some strains cause oral lesions, others cause genital warts, while others cause cervical cancer. The genital tract is the reservoir for

all except two of the viral strains. The two exceptions being HPV 13 and HPV 32 which are restricted to the oral cavity.

The large exophytic genital warts are caused by HPV types 6 and 11 and occasionally by type 16. HPV types 16 and 18 are associated with flat warts and types 16, 18, 31, 33 and 35 are associated with cancer of the cervix, cancer of the penis and anal and other cancers. The following table summarizes the virus strain types and the associated conditions.

HPV Strain	Associated condition
HPV-1, HPV-2, HPV-4	Common skin warts
HPV-13, HPV-32	Oral warts
HPV-6, HPV-11, HPV-16, HPV-18	Anogenital warts
HPV-16, HPV-18, HPV-31, HPV-33, HPV-35	Cervical cancer, anogenital cancer, other cancers

#### 4.5 EPSTEIN BARR VIRUS INFECTION

Infection with Epstein Barr Virus (EBV), a herpes virus, occurs commonly in persons with HIV infection as well as in persons without HIV infection. Patients with HIV have increased amounts of EBV in their oropharyngeal secretions and have higher EBV antibody titers than HIV-seronegative persons.

EBV is thought to cause a number of conditions including,

- **Oral hairy leukoplakia**
- **Lymphocytic interstitial pneumonitis (LIP)**
- **Non-Hodgkins lymphoma**
- **Burkitts lymphoma**
- **Nasopharyngeal carcinoma**

### **1. Oral Hairy Leukoplakia**

Oral hairy leukoplakia occurs in HIV-infected patients as well as in some immunosuppressed transplant recipients. It presents as raised, white, corrugated lesions of the oral mucosa, especially on the lateral aspect of the tongue. It is a nonmalignant lesion of epithelial cells.

### **2. Lymphocytic Interstitial pneumonitis (LIP)**

Lymphocytic interstitial pneumonitis (LIP) occurs primarily in children, but it also occurs in adults infected with HIV. It is characterized by diffuse interstitial pulmonary infiltrates.

### **3. Non-Hodgkin's Lymphoma**

Non-Hodgkins lymphoma occurs fairly commonly in persons with immunosuppression from HIV. It is thought that EBV plays a role in the causation of the tumour. EBV has been found in biopsy specimens of lymph nodes obtained from persons with non-Hodgkins lymphoma.

### **4. Burkitt-type lymphoma in HIV infected persons**

Burkitt-type lymphomas are associated with HIV infection and may occur before advanced immunosuppression sets in. This tumour is associated with EBV. The diagnosis of Burkitt-type lymphoma is made on careful examination of lymph node biopsies.

#### **4.6 HUMAN HERPES VIRUS TYPE 8 (HHV8, KSHV)**

The human herpes virus type 8, also known as HHV8 or Kaposi's sarcoma herpes virus (KSHV) has been shown to be the cause of Kaposi's sarcoma. This cancer of the lymphatics system leads to generalised lymphadenopathy and lymphoedema of affected areas. Kaposi's sarcoma is the commonest AIDS-related malignancy seen in Zimbabwe. The cancer also occurs in persons without HIV infection (endemic Kaposi's sarcoma). In HIV infected persons the cancer (epidemic Kaposi's sarcoma) is more generalised and more rapidly progressive than in the endemic variety and it often affects the viscera. Though any viscus in the body may be affected, the effects of the cancer are most severe on the lungs. Pulmonary Kaposi's sarcoma carries a poor prognosis.

### Important points to remember

- Infection with the herpes viruses, herpes simplex virus, varicella-zoster virus, cytomegalovirus, human herpes virus type 8, occur commonly in immunosuppressed persons with HIV infection
- Human papilloma virus infection and molluscum contagiosum virus infections are commonly seen in persons with HIV infection
- Antiviral agents are available for the treatment of some herpes virus infections
- Recurrences occur commonly and infections are commonly persistent
- A strong association exists between human papilloma virus infection and cervical and anogenital cancer