Virology

Lec (8)
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Varicella - Zoster Virus (VZV) Or Human herpesvirus-3(HHV-3)

Varicella (chickenpox) is a mild highly contagious disease, chiefly of children, characterized clinically by a generalized vesicular eruption of the skin and mucous membrane. More than 90% of people in the United States have antibody by age 10 years. The disease may be severe in adults and immunocompromised patients.

Zoster (shingles) is a sporadic incapacitating disease of adults or immunocompromised individuals that is characterized by a rash limited in distribution to the skin innervated by a single sensory ganglion.

Both diseases are caused by the same virus. Varicella is the acute primary infection, while zoster s the reactivation of varicella virus present in latent form in neurons in sensory ganglia.

Important Properties of VZV

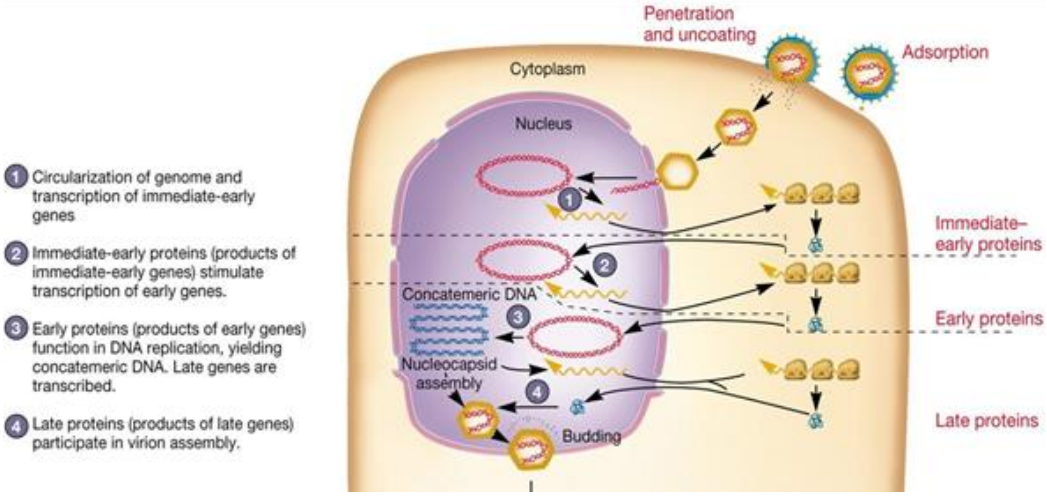
VZV is structurally and morphologically identical to other herpisviruses but is antigenically different. It has a single serotype. The same virus cause both varicella and zoster, human are the natural hosts.

Transmission

- The virus is transmitted by respiratory droplets
- Direct contact with the lesions

Summary of replicative cycle:

The cycle is similar to that of HSV.



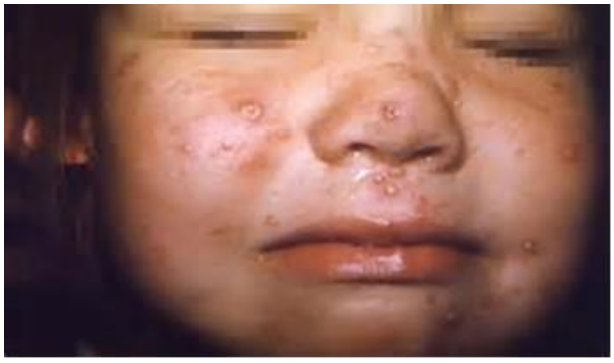
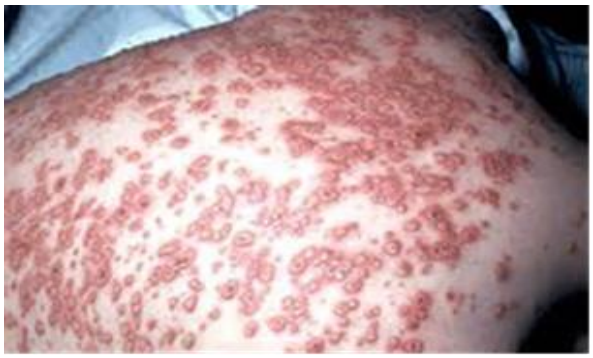
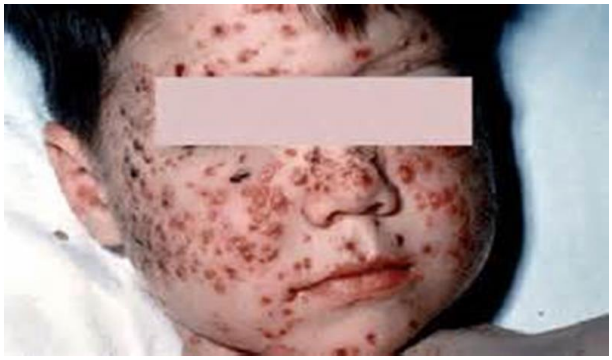
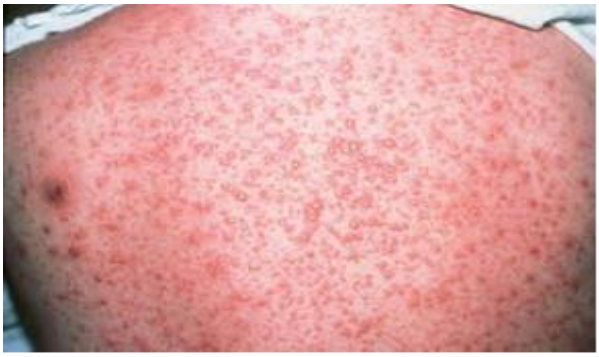
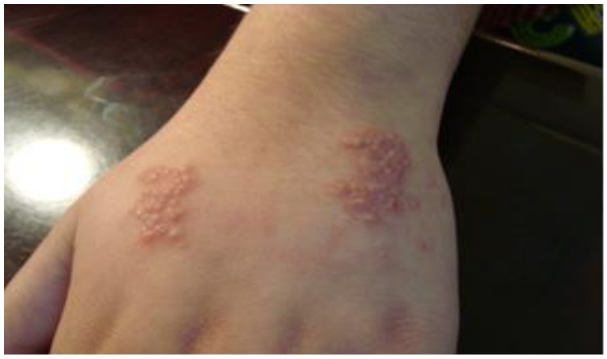
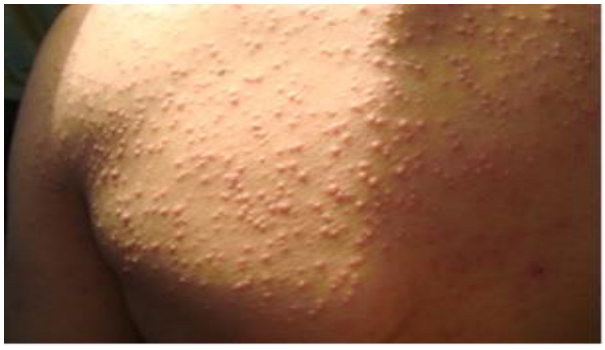
Pathogenesis

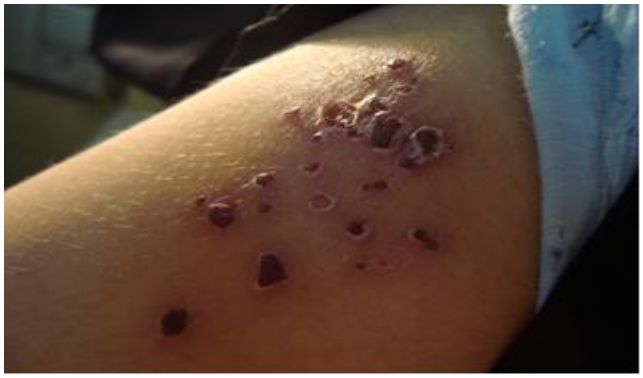
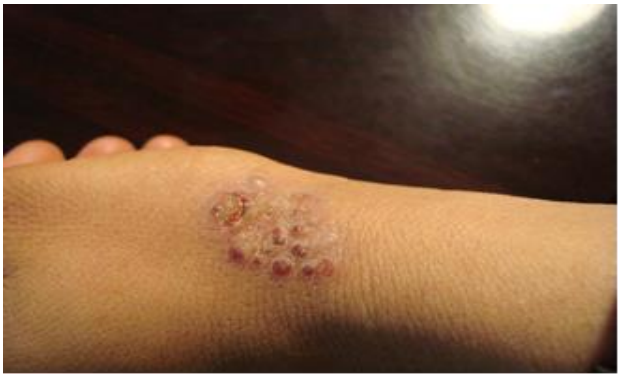
The virus infected the mucosa of upper respiratory tract or the conjunctiva. Initial replication in regional lymph nodes. Then spread via the blood to the skin, where the typical vesicular rash. Swelling of epithelial cell, ballooning degeneration, and the accumulation of tissue fluids result in vesicle formation, multinucleated giant cells with intranuclear inclusion are seen in the base of the lesion, after the host has recovered, the virus becomes latent, probable in the dorsal root ganglia. During latency most if not all DNA is located in the cytoplasm rater than integrated into nuclear DNA. Latent in life at time of reduced cell-mediated immunity or local trauma, the virus is activated and cause vesicular skin lesion and nerve pain of zoster.

Clinical Findings

A- Varicella

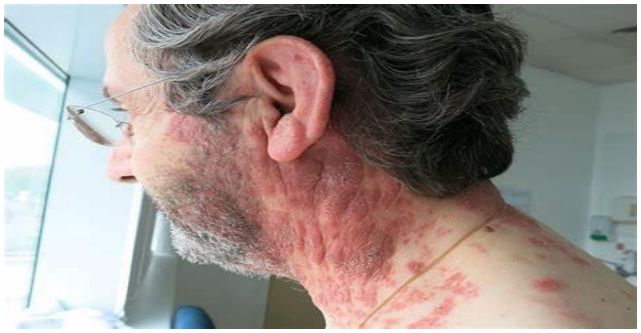
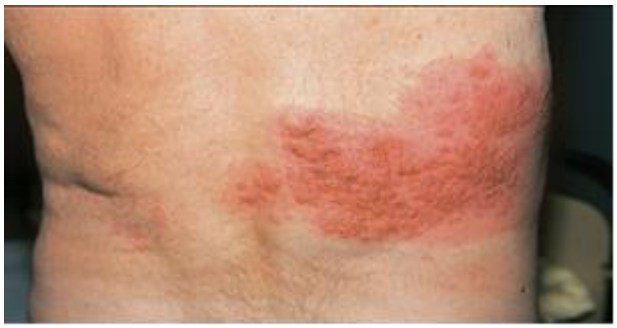
The incubation period of typical disease is 14-21 days. Malaise and fever are the earliest symptoms, soon followed by the rash, first on the trunk and then on the face, the limbs and the buccal and pharyngeal mucosa in the mouth, successive fresh vesicles appear in crops. So that all stage of macules, papules, vesicles, and crusts may be seen at one time. Varicella is mild in children but more severe in adults, and leading to varicell pneumonia, encephalitis and Reye's syndrome.

B- Zoster

There is an acute inflammation of the sensory nerve and ganglia, the skin lesion are histologically identical to those of varicella but more sever and more painful.(the pain can last for weeks).

Diagnosis

Most cases diagnosed clinically also can be use the laboratory diagnosis as the followings.

1 - Isolation of virus in cell culture and then identification with specific antiserum.

2- A raise the titer of antibody can be used to diagnose varicella but is less useful in the diagnosis of zoster, since antibody is already present.

3- Tzanek smears to detect of viral antigens in scrapings.

4- Histological examination, multinucleated giant cells are seen in skin

Treatment and Prevention:

- No antiviral therapy
- Acyclovir used to treat immunocompromised patients to reduce the duration and severity of symptoms.
- Live, attenuated vaccine containing the live virus strain, one dose recommended for children 1-12 years of age, adult and teenagers who have no had the disease should receive two doses.
- VZIG, which contains a high titer of immunoglobulin used as prophylaxis in person travel to endemic area.

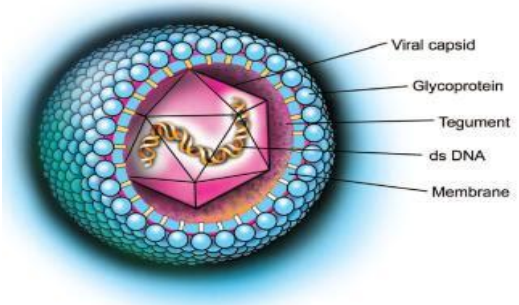
Human cytomegalovirus (HCMV)

Human cytomegalovirus cause cytomegalic inclusion disease (especially congenital abnormalities) in neonatal.

Important Properties of CMV

Cytomegalovirus is structurally and morphologically identical to other herpisviruses but is antigenically different. It has a single serotype. Human are the natural hosts.

Cytomegalovirus has the largest genetic content of herpesviruses. One of the virally encoded protein act as Fc receptor which is non-specifically binds to Fc portion of immunoglobulin, CMV-infected cells assembly of MHC class I-viral peptide complex is unstable, so viral antigens are not displayed on the cell surface and killing by cytotoxic T cells does not occur, thus enable the virus infected cells to evade elimination by immune system.



HCMV Human Cytomegalovirus

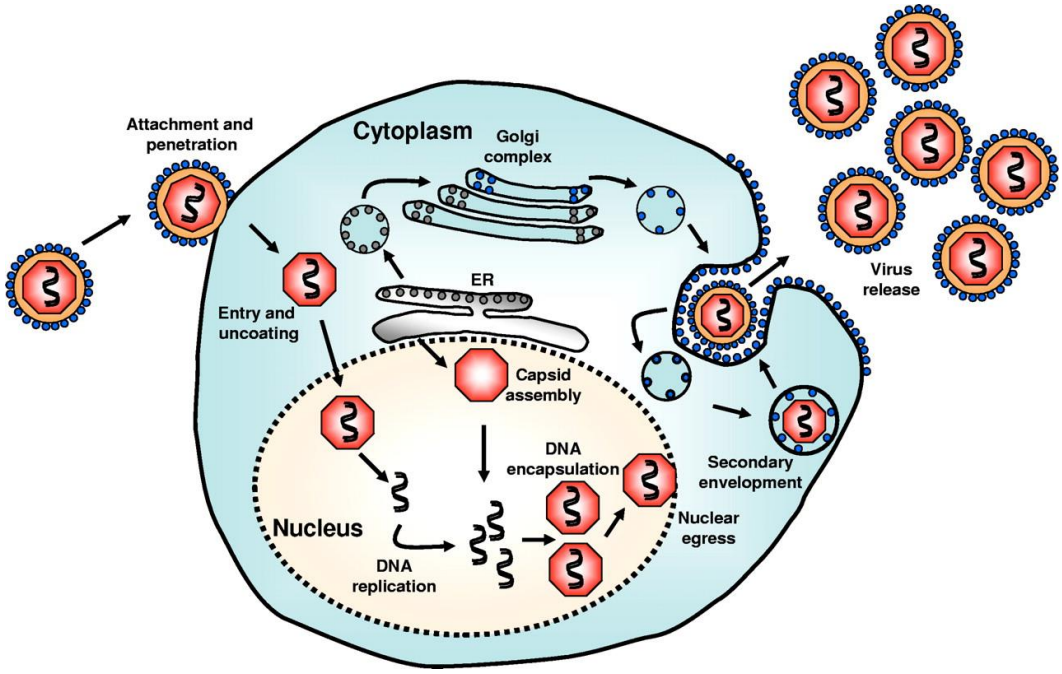
Mode of Transmission

Cytomegalovirus is transmitted via saliva and sexual contact, or from infected donated blood and organs.

- In fetuses: The virus is transmitted through placenta
- In infant: Through birth canal or feed breast
- In young children: Respiratory rout through saliva.
-In adult: sexual intercourse which the virus present in both semen and cervical secretion.

Summary of replicative cycle:

The cycle is similar to that of HSV but found some differences.



Pathogenesis and pathology:

Human cytomegalovirus is transmitted from person-to-person contact. The incubation period is 4-8 weeks, HCMV is very species specific and cell type specific. Human cytomegalovirus produces a characteristic cytopathic effect, perinuclear cytoplasmic inclusion form in addition to the intranuclear inclusion typical of herpesviruses

Clinical findings:

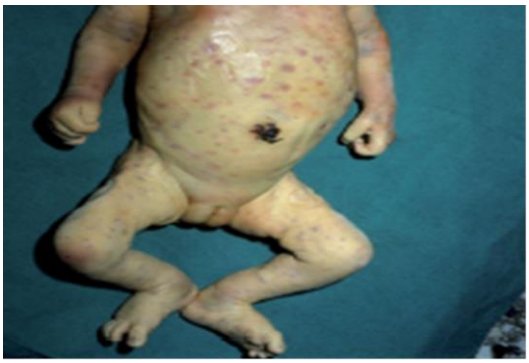
1- **Primary HCMV infection** in older children and adults are usually asymptomatic and the virus latent in the leukocyte cell then reactivation occurs under certain condition.

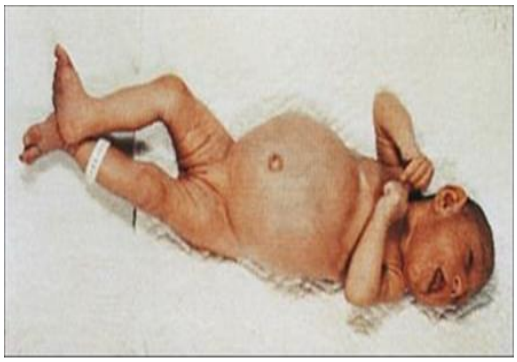
2- **Immunocompromised patients**. Human cytomegalovirus symptoms vary in different groups of immunocompromised patients. In patients with HIV/AIDS, HCMV disease is frequently more sever and associated with heterophil-negative mononucleosis, which is characterized by malaise, fever, lethargy and the presence of abnormal lymphocyte in peripheral blood smears. Hepatitis and pneumonia also occurs in this group also associated with retinitis, colitis, encephalitis and falling white blood cell counts.

- **Pregnant women:** Human cytomegalovirus infection at any stage of pregnancy can give rise to congenital infection even in women who have no symptoms. **Primary** infection is associated with a higher risk of congenital infection than reactivation. Symptoms in newborn babies include chorioretinitis, deafness, brain damage, hepatosplenomegaly, petechial rash, and inter-uterine and neonatal death. Because the mother has not antibody to neutralize the virus before infect the fetus. The fetus acquired the virus **during delivery** by birth canal or by maternal breast milk, in this cases subclinical infection occur.

Approximately 90% will be asymptomatic at birth, although they may develop signs and symptoms of congenital HCMV disease (retinitis, deafness) early in life.

3- In patients who have received solid organ transplants, the highest risk of severe or fatal HCMV disease occurs with primary infection, when HCMV infection is acquired with the donated organ. In general, patients receiving kidney, liver and heart transplants will have less severe disease than those receiving bowel, heart-lung and lung transplants.





Laboratory Diagnosis

1 - Samples collected from patients are throat swab, bronchial wash, urine and tissue. Isolation the virus in human fibroblast and identification with specific antiserum.

2- Serological test for IgM and IgG by used IFA, ELIZA.

3- PCR testing for HCMV genome is available

Treatment and Prevention

1- Ganciclovir: [dihydroxypropoxymethyl guanine (DHPG)] It is structurally similar to acyclovir but is more active against HCMV. The ganciclovir is activated by a HCMV-encoded phosphokinase in a process similar to that by which HSV activates.

2- No vaccine available.

3- High titer of immunoglobulin used to prevent disseminated infection in organ transplant patients.