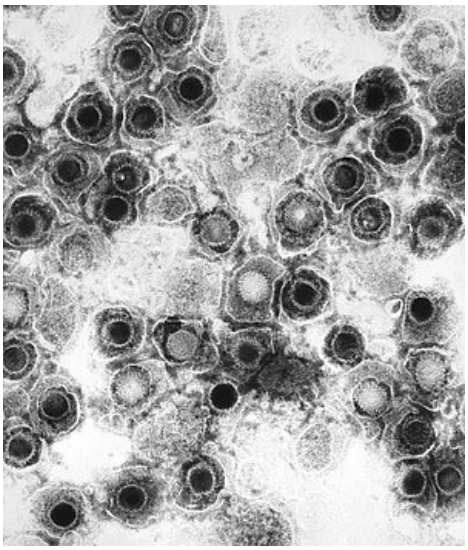
Herpesviridae

It is a large group of DNA viruses that cause predominantly latent infections in animals and humans. The most important for a person are:

- **herpes simplex virus type 1 and 2** (HSV 1, 2)
- **varicella zoster virus** (VZV)
- **cytomegalovirus** (CMV)
- **Epstein-Barr virus** (EBV, HHV 4)
- **human herpesviruses** (HHV 6, 7, 8)



Herpes simplex virions, TEM

Virion

The capsid is coated with a lipid membrane. The virus is about 100-180 nm in size and is highly sensitive to external conditions (mainly fatty solvents and oxidizing agents). There is a tegument (protein layer) between the cover and the capsid. The cover predetermines some properties - viruses are sensitive to acidic pH and drying, as well as to non-polar solvents and detergents. Thus, the infection is transmitted only by direct contact with the infected person.

Herpes simplex virus type 1 (HSV 1)

Diseases

clinical manifestation:

- gingivostomatitis with fever, local lymphadenopathy – in early childhood
- tonsillitis
- keratoconjunctivitis
- meningoencephalitis – it can manifest itself throughout life, has a difficult course, high lethality and leaves severe consequences after healing.
- **herpes labialis** – manifestation in adults

Complications of primary infection - Kaposi's varicelliform eruption (Eczema herpeticatum; vesicular-pustular)

Herpes Virus

Herpes simplex virus type 2 (HSV2)

Diseases

- it most often affects the mucous membranes of the **genital tract** (glans penis, cervix, vagina), especially in puberty. Fever and blisters are characteristic.
- the virus may be excreted by cervical secretion.
- development of severe generalized disease in neonatal infection

Pathogenesis

- Gate of entry: the mucous membranes most often of the oral cavity
- Multiplication of the virus
- Spread through neurons to the sensory part of the trigeminal ganglia (ggl. Gasseri), where it persists.
- During immunosuppression, endogenous infection is activated and herpes (herpes) develops.
- the gateway for HSV 2 is the mucosa of the genital tract and the site of persistence = nerve ganglia in the small pelvis

Diagnostics

- virus isolation from saliva, blister, cerebrospinal fluid
- PCR
- serological test for antibodies – ELISA

Epidemiology

- The source of the virus is the person who excretes the virus through **saliva, cervical secretion** (symptoms of the disease may not be present).

Varicella zoster virus (VZV)

Diseases

Clinically, the virus manifests as chickenpox. The course is usually light with a slightly elevated temperature. If primary infection occurs in adulthood, complications can occur. Reactivation of the endogenous virus manifests itself clinically as shingles.

Pathogenesis

- entrance gate - respiratory tract
- multiplication
- hematogenous to the skin and mucous membranes, where they form blisters
- persistence in the spinal ganglia of the intercostal nerves - when the immunity is weakened, it spreads anterogradely into the sensitive area of the given nerve and shingles is formed.

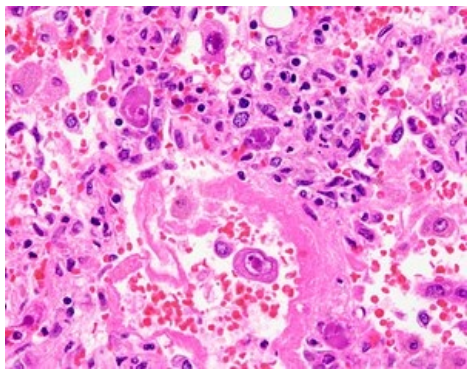
Diagnostics

- PCR
- ELISA

Cytomegalovirus

It infects 90% of the adult population.

Primary infection


HE CMV lungs1

Primary infection is usually mild or asymptomatic. It manifests as:

- **infectious mononucleosis syndrome**,
- febrile illness with lymphadenitis,
- hepatitis (especially in infants),
- **severe congenital infections** (microcephaly, blindness, hepatomegaly, purpura),
- congenital or postnatal infection - usually asymptomatic,
- rarely pneumonia, colitis, meningitis.

Reactivation in **immunosuppressed** manifests as:

- febrile illness with lymphadenitis,
- pneumonia,
- septic disease,
- colitis, oesophagitis,
- retinitis (especially in HIV positive),
- encephalitis.

Following a kidney transplant, a virus infection can cause transplant rejection.

Pathogenesis

The gateway is the respiratory tract or upper gastrointestinal tract. Then there is multiplication and subsequent hematogenous spread. It is associated with atherosclerosis and restenosis after heart surgery. The virus persists in salivary gland cells, renal tubules and leukocytes. An infected individual occasionally excretes viruses through saliva, urine, cervical secretion, and breast milk.

Diagnostics

Cultivation

Cultivation is easy. CMV grows with a typical cytopathic effect in 5-25 days on human diploid cells. Identification can be accelerated by evidence of nuclear inclusions with a mononuclear antibody (24-48 hours). We can use urine, saliva, vaginal secretion, breast milk (difficult), leukocytes (difficult) for cultivation.

Quick diagnostics

Antigen detection and microscopy are insensitive. Nucleic acid detection (PCR) is used, it is fast and reliable. Most sample types can be used. It is also possible to perform quantitative determinations. PCR is more sensitive than cultivation.

Evidence of antibodies

IgG, IgM or IgA are determined. IgG is anamnestic, they are of little importance for the diagnosis of reactivation, it is possible to determine the avidity of IgG. Both IgM and IgA are important in acute infections and reactivations. Non-specific reactions are described. Serology is only an orientation method. Antibodies do not indicate immunity.

Therapy

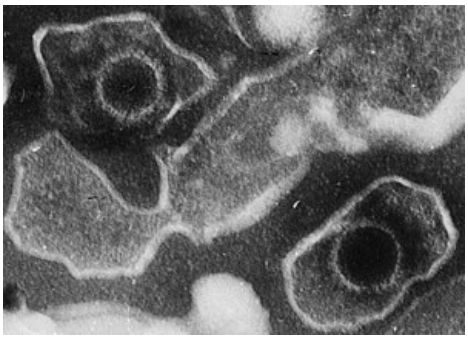
- Hyperimmune gamma globulin
- Antiviral therapy: ganciclovir; foscarnet; special new antivirals (cidofovir).
- Prophylaxis in high-risk patients; aciclovir (not suitable for the treatment of advanced infection).

Prevention

Vaccine attempts have so far failed. There are epidemiological measures in organ recipients (CMV negative recipients should not receive organs from a CMV positive donor) - due to the high population density, this is difficult to follow.

Epstein-Barr virus (EBV)

The widespread virus, from 10 years of age, is infected almost the entire population A small proportion is clinically manifest. It has been linked to Burkitt's lymphoma in Africa and nasopharyngeal carcinoma in Asia.



Epstein Barr Virus virions EM 10.1371 journal.pbio.0030430.g001-L

Diseases

- clinical manifestations such as angina pectoris with lymphadenitis, fever and hepatic impairment.
- relativně dlouh rekonvalescence

Pathogenesis

- entrance gate - respiratory tract
- proliferation and persistence in B-cells
- the persistent presence of antibodies and immunity to reinfection.

Diagnostics

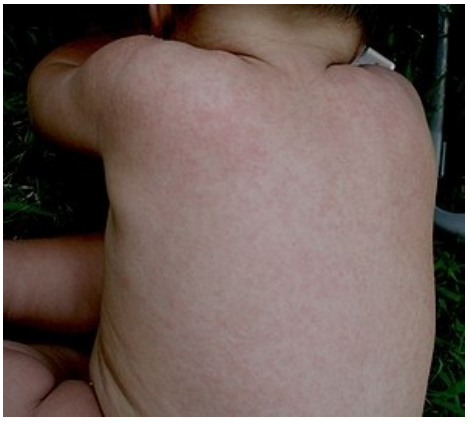
- isolation is complicated and practically impossible.
- **serological diagnostics**: evidence of non-specific antibodies (Paul-Bunnell reaction), evidence of specific antibodies - indirect immunofluorescence, ELISA

Epidemiology

The virus spreads by droplets and is widespread worldwide.

HHV-6 and HHV-7

HHV-6 and HHV-7 belong to the family Herpesviridae. HHV-6 is divided into two subspecies - HHV-6A and HHV-6B. They are the **enveloped viruses** that contain **double-stranded DNA**. The size of the virion is 120-150 nm. They replicate in the nucleus, mature in the cytoplasm. They are lymphotropic viruses similar to CMV, they persist in the body for life.



Sixth disease - exanthema subitum

Diagnostics

- Based on clinical signs;
- serology - IgG and IgM antibodies by immunofluorescence or ELISA methods;
- cultivation - demanding, on special lymphocyte soils;
- PCR - from different tissues, the most sensitive method.

Manifestations of infection

Primary infection usually takes place in childhood, often without symptoms. **HHV-6** causes one of the most well-known manifestations of these viruses - a minor **febrile condition in infants and young children** with either exanthema - **exanthema subitum** (sixth childhood disease) or without skin manifestations. The severity increases with the occurrence of **febrile convulsions**. **HHV-7** also produces similar symptoms. The infection spreads through the air. After an incubation period of 5-12 days, a high temperature *without catarrhal manifestations* lasting about 3 days, which is typical for the disease, begins. At a time of temperature drop, a small rash is sown, which must be distinguished from toxoalergic rash (after antibiotics, which are often given).

Rare clinical manifestations are **encephalitis**, **hepatitis**, eventually **infectious mononucleosis syndrome**.

In immunosuppressed (lymphoproliferative diseases, after transplantation ...) there is a possibility of reactivation of the infection.

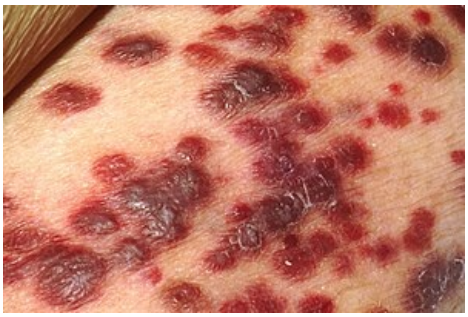
HHV-6A is more neurotropic, often detectable in patients with inflammatory CNS (multiple sclerosis).

Therapy

Therapy is only asymptomatic.

HHV-8

- HHV-8 (Human Herpesvirus 8), also known as KSHV (Kaposi's sarcoma-associated herpesvirus), is a dsDNA virus of the Herpesviridae family.
- Described in patients with immune defects (HIV).
- In immunodeficiency, it causes Kaposi's sarcoma (mesenchymal malignant vascular tumor).
- Other diseases caused by the virus include primarily exudative lymphoma (when malignant B-lymphoma develops) or Castleman's disease.
- It also occurs in immunocompetent individuals, causing only latent infection.


Kaposi's Sarcoma Lesions

- Diagnostics of the current state only by PCR.
- Serological diagnostics: IgG antibodies - anamnestic

Links

Related articles

- Herpetic encefalitis
- Infection caused by HHV-6 and HHV-7

Literature

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References

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