

Herpesviruses

*Herpesviruses:

A large group of viruses (100 strains), but we are concerned with only 8 strains as they are the only ones to infect human beings

*herpesviruses groups:

HSV-1

HSV-2

VZV

CMV

EBV

HHV-6

HHV-7

HHV-8.

***-Herpes Virus 9 (Herpes B virus) transmitted from monkeys to humans, and causes fatal encephalitis.

#characterized by:

- **latency**: a type of persistent infection in which the viral genome is present but the infectious virus is not produced except during intermittent episodes of reactivation.

- **Reactivation**: asymptomatic virus shedding (no symptoms). {the virus is replicating but the patient doesn't feel anything }.

- **Recurrence**: clinically obvious disease due to reactivation.

Reactivation and recurrence are used interchangeably.

- Latency makes them very successful viruses.
- Reactivation occurs after immunosuppression.

*Structure:

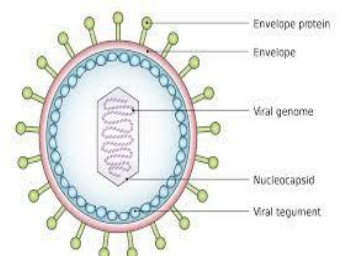
-Large circular double stranded DNA.

-Icosahedral capsid.

-They have a tegument (an amorphous proteinaceous layer that is important in replication and virulence, and it's very unique for herpesvirus).

Envelope: acquired from the cell membrane.

-They have spikes (glycoproteins) on the surface , which are



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highly variable (there are many types and used in fusion for entry into the cell) .
--herpesvirus Diameter can reach up to 200nm (the largest is CMV) .

***Subgroups {according to their genetic sequence}**

- A) Alpha-herpes virus (HSV-1, HSV-2, VZV): rapid growth in few hours.
- B) Beta-herpes virus (CMV, HHV-6, HHV-7): slow growth (need days)
- C) Gamma-herpes virus (EBV and HHV-8).

-herpesviruses can also be divided into:

Neurotropic: affect neurons , {HSV-1 , HSV-2 & VZV}

Lymphotropic: affect lymphocytes, {EBV , HHV-6 & HHV-7.}



Remember that HHV-8 causes kaposi's sarcoma .

***Pathogenesis:**

Modes of transmission:

-Direct contact (auto-inoculation): VZV and HSV.

They travel along the nerve endings to the ganglia assuming a lytic phase, or they enter a latent phase and in this phase we call them (episome), then at certain points when the immunity is decreased the virus becomes apparent as a lesion.

*proteins of the herpes are produced in the cytoplasm, then they go to the nucleus forming the viral capsid ,then they go back to the cytoplasm to form other important proteins and so on .

-Each cell produces 100 herpes viruses.

***Epidemiology:**

-Children are the most affected group.

-70% of the adult population has already been infected with HSV-1.

-HSV-2 is acquired during adulthood.

-VZV affects 95% of the population.

***HSV Clinical Syndromes:**

Mucosal:

-Gingivostomatitis: very bad lesions with crusting vesicles, ulcers, fever, difficulty in eating, hospitalization may sometimes be needed.

-Pharyngitis.

-Genital lesions especially in old people.

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Eye:

- Keratitis may end up with blindness.
- Blepharitis/Conjunctivitis.

Skin:

- Painful vesicles.
- Erythema multiforme.

CNS:

- Encephalitis.
- Bell's palsy.

In general HSV-1 mainly affects: CNS, Mouth, Eye
HSV-2: Genital



HSV:

Herpes labialis:

- Acquired mostly in childhood.
- Vesicle → ulcerates especially in the mucosa → scab → healing.
- Herpes usually occurs at the junction between the skin and lips!!

Biopsy:

Tzank Smear (bizarre looking giant cells acquired from the fluid in the vesicles) (however it's not specific for HSV, it can appear in CMV, VZV, and pemphigus).

Immunity:

T-cells combat infected cells and activate B-cells to produce antibodies ((SO T and B cells are needed)) .

The antibodies can provide cross protection against HSV1 and HSV2. People that have antibodies have less severe diseases.

Latency:

occurs in the ganglia (1 neuron out of a 100 neurons might house a latent virus).

Primary infection of herpes labialis:

Gingivostomatitis.

Asymptomatic.

Pharyngitis.

*Recurrence: can occur in the form of cold sores, fever blisters.

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*viremia might happen but it rarely forms a significance except in immunocompromised patients ,and through it (viremia) the virus reaches the kidneys and liver.

Recurrence in herpes labialis: due to subjection to stimuli (sunlight – UV light, stress, trauma, fever),in most of the patients that have recurrent herpes the cause is unknown

*Shedding of the virus in asymptomatic people can occur.



Herpetic Witlow:

- Herpes virus is found in the fingers mainly .
- Occurs in people who are exposed to secretions of patients as in anesthetists, barbers, nurses and people working in kindergartens, so you can inoculate the virus easily and before reaching the hand the virus becomes latent and hard to get rid of.
- Recurrent attacks of herpes and blisters.
- Very annoying and painful disease.



Eczema Herpeticum:

In patients with eczema and especially children who have eczema, the virus spreads and can cause a very bad disease and the patients might die .



Keratoconjunctivitis(keratitis):

- Affects the eye.
- Detected by fluorescent dyes and by observing dendritic shaped cells like a tree that is diagnostic for herpes
- Patients shouldn't take steroids because they cause flare up of the disease and loss of cornea (steroid eye drops should only be given by an ophthalmologist) .

HSV of CNS (Encephalitis):

Reaches the brain by these ways:

- 1) Viremia
- 2) Olfactory tract: primary infections (most common mode of primary infection) enter through the olfactory tract.
- 3) Trigeminal ganglia: usually caused by reactivation of HSV (most common mode of reactivation) .

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-It's a rare disease.

-The most common cause of **sporadic** encephalitis is HSV (epidemic or encephalitis after outbreaks is caused by West Nile virus -WNV-).

-High mortality (70%).

-Morbidity: low IQ (occurs in patients with meningitis or encephalitis), paralysis, confusion, paresis, seizures, etc.

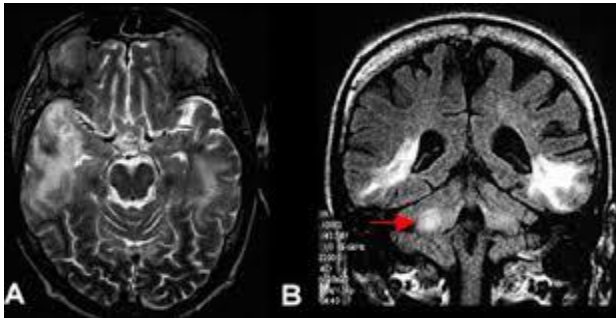
-how does this disease present?

Affects males & females and all ages, but mainly elderly people (50-70 years old because elderly people have been exposed to the virus before and then it reached the trigeminal ganglia and having some sort of immunodeficiency).

Presentation: fever, malaise, headache, behavioral changes (the patient doesn't know people around him), focal seizures (the hallmark of the disease), coma, and death if not treated.

*Encephalitis patients due to HSV rarely have blisters.

*The earlier the treatment, the better chances of recovery.



- This picture shows temporal lobe involvement that is almost **pathognomonic** for herpes encephalitis.

-Hemorrhagic lesions also are almost diagnostic for herpes encephalitis.

Treatment: IV Acyclovir .

-The only encephalitis that has a successful treatment is the herpes encephalitis, because other viruses that cause encephalitis their treatment is either unsuccessful or it's still under research or there is no treatment for them.

-Treatment is more successful than other viruses.

Diagnosis:

-PCR of CSF : not highly sensitive but it is highly specific (if PCR is positive then you got the diagnosis and if it was negative that doesn't exclude the disease) .

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*If PCR was negative in the first time then the test must be repeated within 2 days, and if you got 2 negative PCRs then it's not the disease .

-Tzank smear from a lesion .

-Biopsy: biopsies are no more done for encephalitis because it's an invasive procedure, and nowadays we have much better methods like PCR.

Note:

HSV1 is the major cause of encephalitis .

HSV Meningitis:

-Fever, neck stiffness, photophobia

Note: Patient with fever, and confusion, this is encephalitis while patient with fever ,neck stiffness ,photophobia ,confusion ,this is meningio-encephalitis

-Cause: HSV-2.

-Less severe disease (patients might be cured without knowing)

-Common disease.

-Axis: from genital herpes through the nerves that supply the genital area that reaches the meninges

-Recurrent episodes of meningitis (Mollaret's Meningitis): abnormal giant cells similar to the Tzank smear cells.

Genital Herpes:

-HSV-2 causes 90% of genital herpes(HSV2>HSV1)

-Transmission: inoculation (a child touched a blister then touched the genital area) and sexual contact (most common).

-Very distressing disease.

-Can be recurrent.

-causes dysurea ,fever ,abdominal pain .

-First attack can be a nightmare for the patient , it's very painful and might continue up to 2 weeks .

-Later attacks are less severe due to the antibodies and immunity(this immunity lowers the chances for reactivation but it doesn't completely eradicate the virus).

-Can later cause urinary retention because nerve roots can be affected .

-90% of people infected with HSV2(people that have antibodies and the virus in their body) don't know that they're infected (called Asymptomatic shedding) .

-patients might have recurrent attacks

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-Primary/secondary prevention with acyclovir (has a prophylactic role) is effective and lowers the number of attacks, but the disease occurs again when acyclovir is discontinued.

Good luck ☺

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Sorry for any mistake ☺