Human Herpes Viruses (HHV)

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HERPES VIRUS INFECTIONS

• objectives:

- ≻To know the clinically important HHVs.
- ➤To know the common characteristics of HHVs.
- ➤To know the common modes of transmission of different HHVs
- ➢To know the clinical features of these infections, diagnostic methods and treatment.

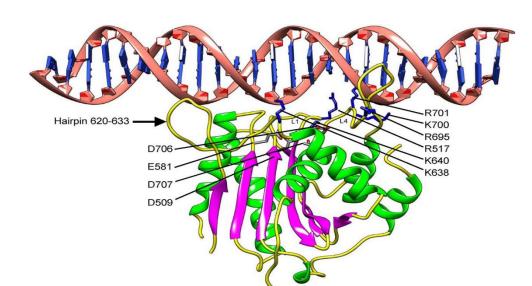
HERPES VIRUSES

- Herpes Simplex Virus type1 (HSV-1)
- Herpes Simplex Virus type2 (HSV-2)
- Varicella Zoster Virus (VZV)
- Cytomegalovirus (CMV)
- Epstein-Barr Virus (EBV)
- Human Herpes Virus 6 (HHS-6)
- Human Herpes Virus 7 (HHS-7)
- Human Herpes Virus 8 (HHS-8)

HERPES VIRUSES

Characteristics:

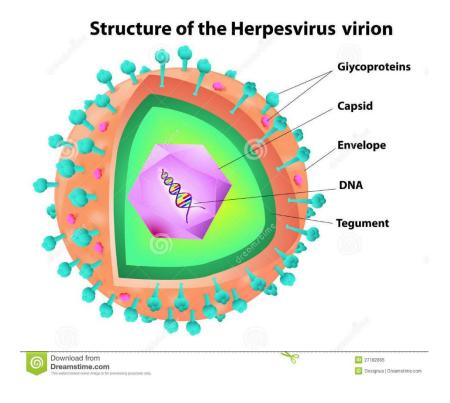
- All DNA viruses
- All encapsulated
- All have latency after the initial infection
- Mostly require close contact for transmission
- Human is the only reservoir



Virus	Infection
HSV Type 1	Herpes labialis ('cold sores') Keratoconjunctivitis Finger infections ('whitlows') Encephalitis Primary stomatitis Genital infections
HSV Type 2	Genital infections Neonatal infection (acquired during vaginal delivery)
Varicella zoster virus (VZV)	Chickenpox Shingles (herpes zoster)
Cytomegalovirus (CMV)	Congenital infection Disease in immunocompromised patients Pneumonitis Retinitis Colitis systemic infection
Epstein-Barr virus (EBV)	Infectious mononucleosis Burkitt's lymphoma Nasopharyngeal carcinoma Oral hairy Cell leucoplakia (AIDS patients)
Human herpes virus 6 (HHV-6) and 7 (HHV-7) Roseolovirus	Exanthem subitum (Roseola): three day fever ? Disease in immunocompromised patients
Human herpes virus 8 (HHV-8)	Associated with Kaposi's sarcoma

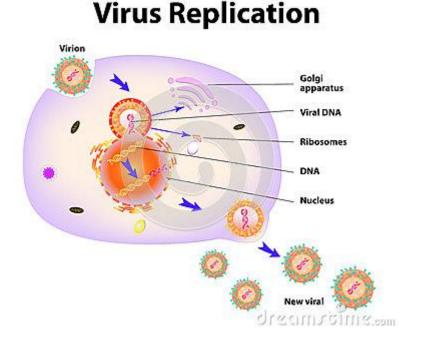
HERPES VIRUSES Structure

- Herpesviruses have a unique four-layered structure:
 - A core containing the large double-stranded DNA genome
 - Genome is enclosed by an icosapentahedral capsid which is composed of capsomers
 - The capsid is surrounded by an amorphous protein coat called the tegument
 - It is encased in a glycoproteinbearing lipid bilayer envelope



Viral Replication

- Upon entry into the host cell nucleus, three distinct phases of gene transcription and protein synthesis are initiated producing the immediate-early, early, and late proteins
- Viral nucleocapsid assembly occurs within the host cell nucleus.
- The virus acquires its final envelope by budding into cytoplasmic vesicles



HERPES VIRUSES

• HSV-1 vs HSV-2

Non-genital vs Genital Herpes infection Primary vs Recurrent infections Neonatal infection

HERPES VIRUSES

- Transmission is by close contact with body secretions
- Exposure to HSV at mucosal surfaces or abraded skin sites permits entry of the virus and initiation of its replication in cells of the epidermis and dermis
- After initial infection the virus infect the sensory and autonomic nerves and become dormant in the ganglion (trigeminal nerve for HSV1 and sacral rout for HSV2)

HSV Gingivostomatitis

Gingivostomatitis and pharyngitis are the most frequent clinical manifestations of firstepisode HSV-1 infection



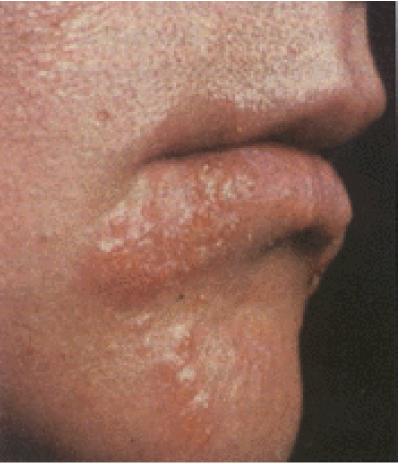
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Herpes Labialis

Recurrent herpes labialis is the most frequent clinical manifestation of reactivation HSV infection





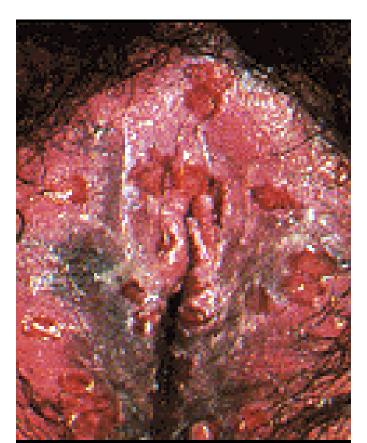
NON-GENITAL HSV





GENITAL HSV

Fever, headache, malaise, and myalgias. Pain, itching, dysuria, vaginal and urethral discharge, and tender inguinal lymphadenopathy





Genital HSV



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Herpetic ulceration of the vulva

Penile herpes simplex (HSV-2) infection

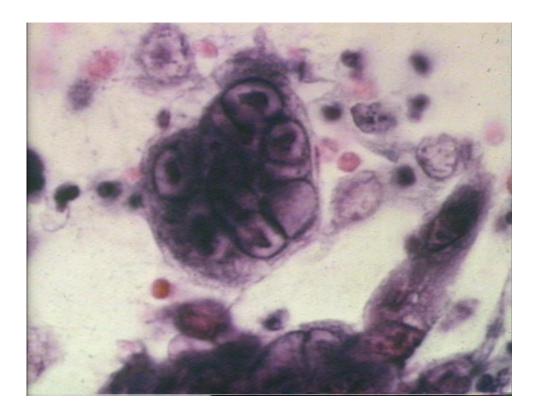
GENITAL HSV





Diagnosis of HSV

- Clinical picture
- Viral culture
- Cytology
- Serology
- PCR



HSV TREATMENT

- Acyclovir, PO, IV, topical
- Penciclovir topical
- Famciclovir PO
- Valacyclovir PO
- Route, dose, duration depends on clinical picture and whether immunocompromised or competent

Case 1

- 36 YO Indian professor presents to ID clinic with recurrent oral vesicular lesions that lasts for 10 to 14 days
- 4 to 5 lesion around his lip, slightly painful, interferes with his lecturing
- No fever, no oral cavity lesions
- Gets these episodes almost on a monthly basis,
- Previously diagnosed with HSV-1, took acyclovir on occasion with good results
- Brought on occasionally with stress
- You recommend ?
 - Chronic suppressive therapy with acyclovir

Case 2

- 32 YO 40 weeks pregnant lady who is in labour
- OB found her to have genital vesicular lesions suspected to be HSV-2
- She had similar genital lesions twice in the past 4 years
- You recommend:
 - C-Section if possible
 - IV acyclovir till delivery
 - Refer baby to neonatal ID once born

VARICILLA ZOSTER VIRUS (VZV)

- Primary infection
 - Chickenpox
- Recurrent infection

Herpes zoster (shingles)

VARICILLA ZOSTER VIRUS

- The virus is spread by the respiratory route (airborne and contact) and replicates in the nasopharynx or upper respiratory tract.
- Followed by localized replication at an undefined site, which leads to seeding of the reticuloendothelial system and, ultimately, viremia.
- The virus establishes latency within the dorsal root ganglia.

CHICKENPOX

Overall, chickenpox is a disease of childhood, because 90% of cases occur in children younger than 13 years of age.

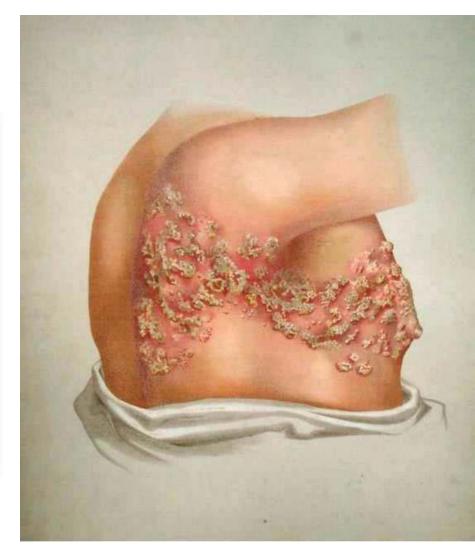




VARICILLA ZOSTER

Reactivation of VZV leads to VZ





VARICILLA ZOTER





VARICILLA ZOSTER



VARICILLA ZOTER



VARICILLA ZOTER





VZV Diagnosis

- Clinical picture
- Viral culture
- PCR
- Serology





VZV treatment

- Acyclovir
- Valacyclovir
- Famciclovir

Prevention

VZV vaccination

VZV immunoglobulin (VZIG)

If admitted need airborne infection isolation and contact precautions (HCW with VZV Ab IgG positive or history of chickenpox do not need PPE)

Cytomegalovirus (CMV)

- The largest virus that infects human beings
- World wide distribution
- Latency after primary infection
- Infection ranges from asymptomatic to severe multisystemic disease

CMV Seroepidemiology

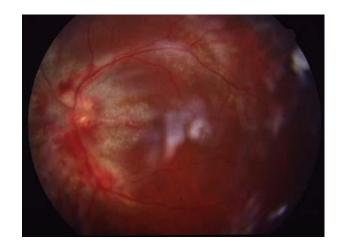


Cytomegalovirus (CMV)

Primary infection

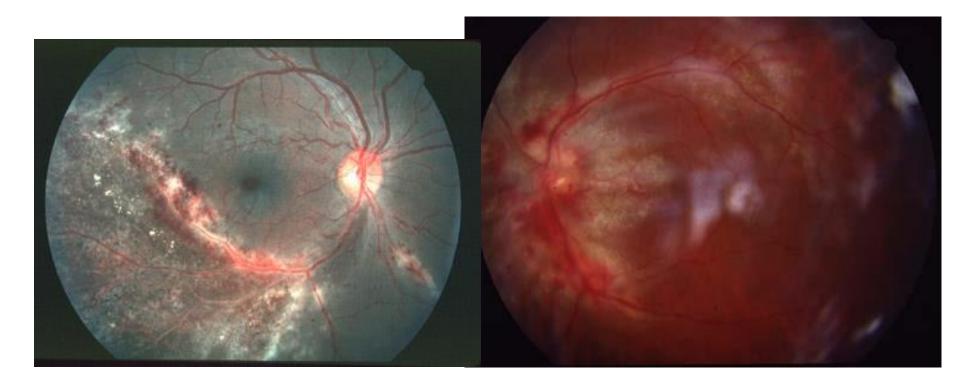
Asymptomatic Infectious mononucleosis Secondary infections in Immunocompromised patients:

> Pneomonitis Retinitis Colitis Multisystem





CMV Retinitis



Cytomegalovirus (CMV)

Diagnosis

Diagnosis almost always depends on laboratory confirmation and cannot be made on clinical grounds alone.

- ♦Viral cultures from blood ,urine ,tissue.
- ◆Serologic tests (antigen detection)
- ♦ PCR

Cytomegalovirus (CMV)

TREATMENT ganciclovir foscarnet cidofovir

- Ubiquitous human herpes virus.
- By adulthood 90 to 95% of most populations are positive.
- Spread occurs by intimate contact between susceptible individuals and asymptomatic shedders of EBV.
- Mostly causes asymptomatic infections.
- Strong association with African Burkitt's lymphoma and Nasopharyngeal carcinoma.

Infectious mononucleosis

Clinical

Fever, Sore throat ,Lymphadenopathy

Hematologic >50% mononuclear cells >10% atypical lymphocytes

Serologic

Transient appearance of heterophile antibodies (weak antibodies)

Permanent emergence of antibodies to EBV

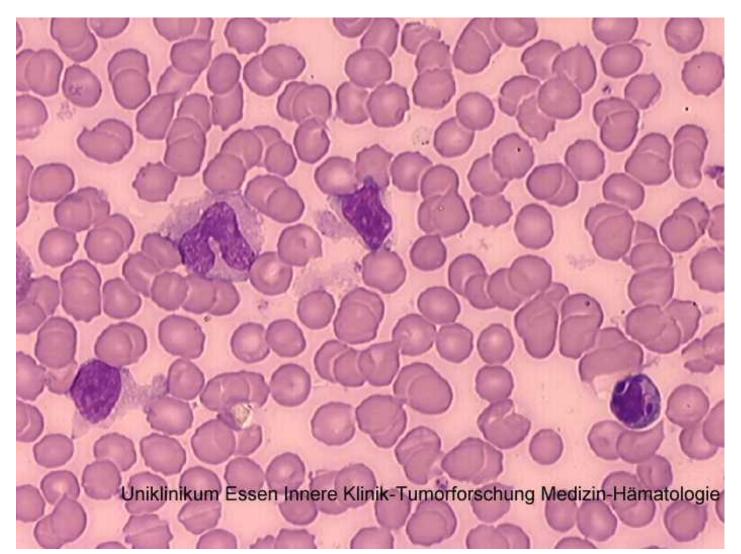
Diagnosis:

Heterophile Antibodies (monospot test) 70–92% sensitivty and 96– 100% specificity

Hematologic Findings

Lymphocytosis, neutropenia , thrombocytopenia EBV specific antibodies

EBV Infection Atypical Lymphocytes



EBV Infection Atypical Lymphocytes



EBV Infection



Treatment:

Treatment of infectious mononucleosis is largely supportive because more than 95% of the patients recover uneventfully without specific therapy

Corticosteroids

