433 Teams

MEDICINE

30| Common viral infections {herpes virus infections}

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The objectives of this lecture:

- ✓ To know the clinically important HVs.
- ✓ To know the common characteristics of HVs.
- ✓ To know the common modes of transmission of different HVs.
- ✓ 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)

Characteristics:

- ✓ DNA viruses
- ✓ Encapsulated
- ✓ Latency after the initial infection
- ✓ Mostly require close contact for transmission
- ✓ Human beings are the only reservoir

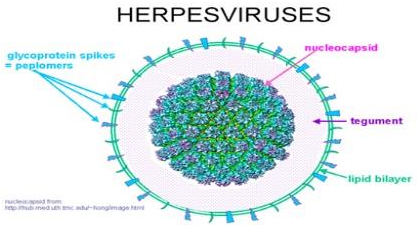
CLINICAL MANIFESTATIONS OF GENITAL ULCERS WITH REGIONAL LYMPHADENOPATHY

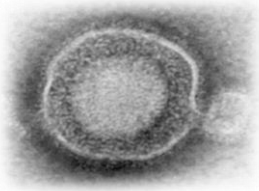
GENITAL LESIONS	Incubation (days)	Type	Pain	Number	Duration
PRIMARY HSV	1-26	Grouped papules, vesicles,pustules,ulcers	Yes	Often multiple	1–3 wks.
INGUINAL ADENOPATHY	Onset	Pain	Type	Frequency	Constitutional Symptoms

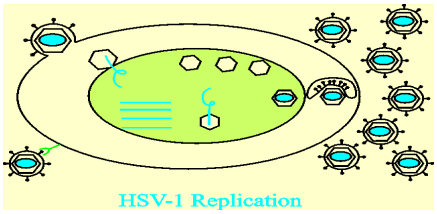
PRIMARY HSV	Same time	Yes	Firm	80%, usually bilateral	Common

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 Enteritis Mononucleosis-like generalized syndrome
Epstein-Barr virus (EBV)	Infectious mononucleosis Burkitt's lymphoma Nasopharyngeal carcinoma Oral hairy leukoplakia (AIDS patients)
Human herpes virus 6 (HHV-6) and 7 (HHV-7)	Exanthem subitum Disease in immunocompromised patients
Human herpes virus 8 (HHV-8)	Associated with Kaposi's sarcoma

Herpes viruses' structure:







Recurrences of HSV:
- Recurrences are associated
With the following: Stress, fever, infection, and Sun exposure.
- Recurrent episodes tend to become shorter in duration and less frequent over time.

HSV-1	HSV-2
Both are very prevalent in the general population	
Non-genital Typically associated with lesions of the oropharynx. (Gingivostomatitis and pharyngitis)	Genital Herpes infection
Clinical features	
Primary infection * { usually asymptomatic} *{When symptomatic}: Primary infection is associated with systemic manifestations (e.g. Fevers, malaise) as well as oral lesions involve groups of vesicles on patches of erythematous skin. Herpes labialis (cold sores) are most common on the lips (usually painful, heal in 2 to 6 weeks). *Bell's palsy	*Primary infection results in more severe and prolonged symptoms, lasting up to 3 weeks in duration. *Recurrent episodes are milder and of shorter duration, usually resolving within10 days. *painful genital vesicles or pustules. *tender inguinal lymphadenopathy and vaginal and/or urethral discharge.
Constitutional symptoms (e.g., fever, headache, malaise) often present in a primary infection.	
Neonatal HSV (vertical transmission at the time of delivery) is associated with congenital malformations, intrauterine growth retardation (IUGR), chorioamnionitis, and even neonatal death.	

Both viruses can cause either genital or oral lesions

- ✓ Transmission: by *close contact with body secretions*.
- ✓ Exposure to HSV: at mucosal surfaces or abraded skin sites permits entry of the virus and initiation of replication in epidermis and dermis.
- ✓ After initial infection, the virus infects the sensory and autonomic nerves and become dormant in the ganglion (trigeminal nerve for HSV1 and sacral root for HSV2).
- ✓ Disseminated HSV:

a. Usually limited to immunocompromised patients.

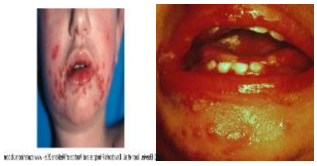
b. May result in encephalitis (mainly with HSV-1)**, meningitis (HSV-2)**, keratitis, chorioretinitis, pneumonitis, and esophagitis.

c. Rarely, pregnant women may develop disseminated HSV, which can be fatal to the mother and fetus.

** From Davidson

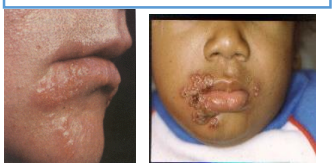
- ✓ Ocular disease—either form of herpes simplex can cause keratitis, blepharitis, and keratoconjunctivitis.

HSV Gingivostomatitis



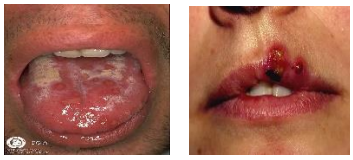
Gingivostomatitis and pharyngitis are the most frequent clinical manifestations of first-episode HSV-1 infection

Herpes Labialis

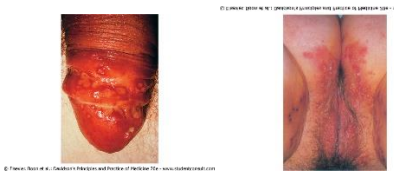


Recurrent herpes labialis is the most frequent clinical manifestation of reactivation HSV infection

NON-GENITAL HSV



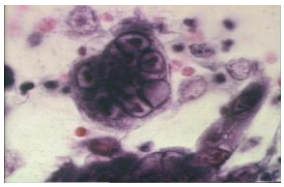
Genital HSV



Diagnosis of HSV:

Penile herpes simplex (HSV-2) infection

Herpetic ulceration of the vulva



- ✓ Clinical picture
- ✓ Viral culture
- ✓ Cytology
- ✓ PCR

If there is uncertainty, perform the following tests to confirm the diagnosis:

a. Tzanck smear—quickest test:

•Perform by swabbing the base of the ulcer and staining with Wright's stain.

• This shows multinucleated giant cells. It does not differentiate between HSV and VZV. Infectious Diseases

b. Culture of HSV is the gold standard of diagnosis:

• Perform by swabbing the base of the ulcer.

• Results are available within 2 to 3 days.

c. Direct fluorescent assay and ELISA:

• 80% sensitive

• Results available within minutes to hours

HSV TREATMENT:

In case of CNS infection we should give high dose though IV

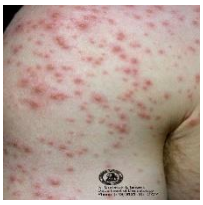
- ✓ Acyclovir 200 mg five times daily.
- ✓ Famciclovir 250 mg 8-hourly.
- ✓ Valaciclovir 500 mg 12-hourly.
- ✓ The treatment is usually for 5 days.
- ✓ Oral acyclovir may be given as prophylaxis for patients with frequent Recurrences.
- ✓ Foscarnet may be given for resistant disease in immunocompromised patients.
- ✓ Disseminated HSV warrants hospital admission. Treat with parenteral acyclovir.

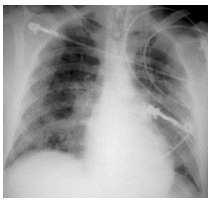
Varicella zoster virus:

- ✓ Primary infection :
  Chickenpox
- ✓ Recurrent infection :
  Herpes zoster (Shingles)

- ✓ The virus is spread by the respiratory route 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.
- ✓ The incubation period is 11–20 days
- ✓

Chickenpox



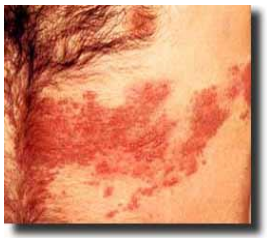


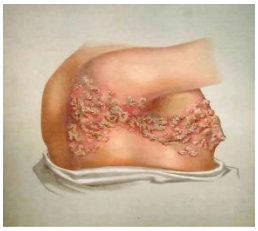
Overall, chickenpox is a disease of childhood, because 90% of cases occur in children younger than 13 years of age.

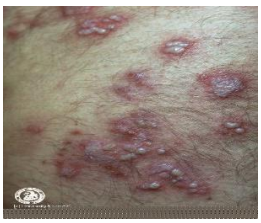
VZV: seen in immunocompromised patients

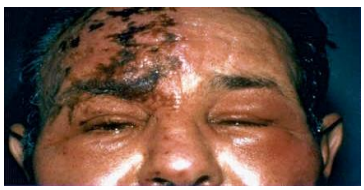
VZV

Reactivation of VZV leads to VZ









VZV treatment:

- ✓ Acyclovir (DOUPLE doses)
- ✓ Valacyclovir
- ✓ Famciclovir

Prevention:

- ✓ VZV vaccination
- ✓ VZV immunoglobulin (VZIG)

Cytomegalovirus (CMV):

- ✓ The largest virus that infects a human being.
- ✓ Worldwide distribution.
- ✓ Latency after primary infection.
- ✓ Infection ranges from asymptomatic to severe multisystem disease.

Sero-epidemiology:

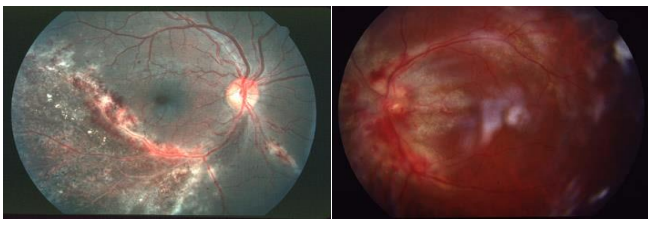
Primary > infection mononucleosis
Secondary > in immunocompromised patients (retinitis)

Primary infection:

- ✓ Asymptomatic
- ✓ Infectious mononucleosis

Secondary infections in immunocompromised patients:

- ✓ Pneumonitis
- ✓ Retinitis
- ✓ GI such as colitis
- ✓ Multisystem involvement



Diagnosis:

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

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

Treatment:

- ✓ Ganciclovir
- ✓ Foscarnet has side effect (cause severe leukopenia)
- ✓ cidofovir

Epstein-Barr Virus (EBV):

- ✓ 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
- ✓ Permanent emergence of antibodies to EBV

Diagnosis:

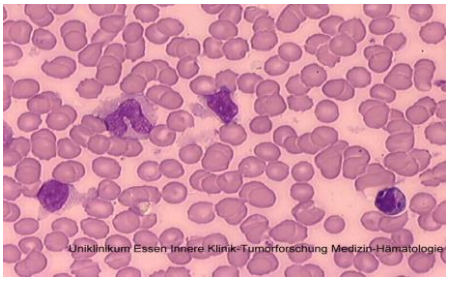
- ✓ Heterophile Antibodies are present in about 90%

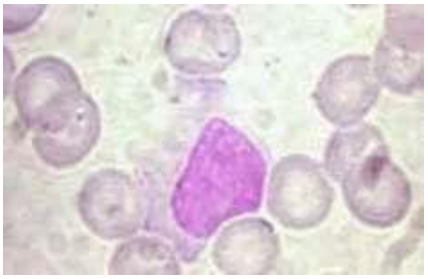
Hematologic Findings:

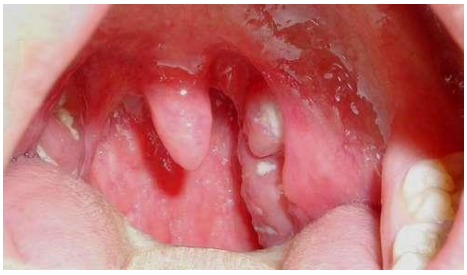
- ✓ Lymphocytosis, neutropenia , thrombocytopenia
- ✓ EBV-specific antibodies

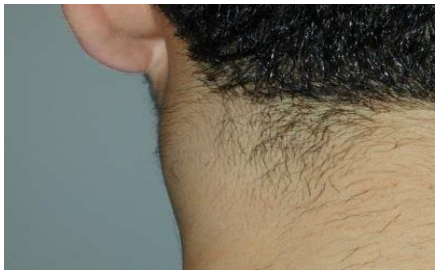
EBV Infection

Atypical Lymphocytes









Treatment:

Treatment of infectious mononucleosis is largely supportive because

More than 95% of the patients recover uneventfully without specific therapy.

- ✓ Corticosteroids

MCQs

Kaplan:

A woman comes to clinic with multiple painful genital vesicles.

What is the next step in management?

a. Acyclovir orally

b. Acyclovir topically

c. Tzanck prep

d. Viral culture

e. Serology

f. PCR

Answer: A. If the presentation is clear for herpes with multiple vesicles of the mouth or Genitals, diagnostic testing is not necessary. Acyclovir, famciclovir, and valacyclovir are All equal in efficacy, so any one of them could be the right choice. Topical acyclovir is Worthless. Viral culture is the most accurate test, but not necessary if the vesicles are clear. Serology is always worthless since it cannot distinguish an acute genital infection from an oral herpes infection in the past.

Female, 16 y came complaining of multiple painful blisters in her mouth, the doctor gave her an antiviral medication and told her the virus found dormant in the trigeminal root, what is the most likely organism ?

HSV-1

HSV 2

VZV

What is the drug of choice for the above patient?

Acyclovir – Valacyclovir - Famciclovir

The most common presentation of Cytomegalovirus infection is

Asymptomatic

Rash under chin

Fever

Which virus associated with Burkitt's lymphoma and Nasopharyngeal carcinoma ?

HSV 2 , CMV , EBV *note: both EBV and CMV can cause infectious mono…

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