

MEDICINE

432 Team

62 Herpes Viral Infections



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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

1. Herpes Viruses
2. The common characteristics of Herpes Viruses
3. Mode of Transmission
4. Clinical Features, Diagnostics Methods, and Treatment

Herpes Viruses

1. Herpes Simplex Virus type 1 (HSV-1)
2. Herpes Simplex Virus type 2 (HSV-2)
3. Varicella Zoster Virus (VZV)
4. Cytomegalovirus (CMV)
5. Epstein-Barr Virus (EBV)
6. Human Herpes Virus 6 (HHV-6)
7. Human Herpes Virus 7 (HHV-7)
8. Human Herpes Virus 8 (HHV-8)

Common characteristics of herpes viruses:

They are DNA viruses, encapsulated, latency after the initial infection, mostly require close contact for transmission, and human beings are the only reservoir.

Human Herpes Virus 6 and 7:

cause **Exanthem Subitum**; disease in immunocompromised patients.

Human Herpes Virus 8:

associated with **Kaposi's sarcoma**.

Herpes simplex virus type 1 and 2:

Herpes simplex viruses (HSV) cause recurrent mucocutaneous infection; HSV-1 typically involves the **mucocutaneous surfaces of the head and neck**, whilst HSV-2 predominantly involves **the genital mucosa** ⁽¹⁾.

Pathogenesis of HSV-1: HSV-1 doesn't get transmitted via sexual contact but by direct contact. Can be transmitted to the genital area via touch, oral sex, and child abuse ⁽²⁾. HSV-1 could cause **herpes labialis "the most common"**, **keratoconjunctivitis**, **finger infections**, **encephalitis**, and **primary stomatitis**. **Trigeminal ganglia** generally become infected within 24 hours of exposure "latent infection" ⁽²⁾ ⁽³⁾.

Pathogenesis of HSV-2: transmitted sexually, vaginally, or intraplacental ⁽²⁾. So exposure at mucosal surfaces is necessary. HSV-2 could cause **genital infection** or neonatal infection (acquired during vaginal delivery), in addition to latent **sacral ganglia infection** ⁽²⁾.

Clinical manifestations ⁽¹⁾⁽²⁾⁽⁴⁾:

| HSV-1 | HSV-2 |
|--|-----------------------------|
| Primary HSV-1 or 2 infections cause gingivostomatitis and pharyngitis . | |
| Herpes labialis "recurrent infection" | Aseptic meningitis |
| Local lymphadenopathy "recurrent" | Fever, malaise, and dysuria |
| Pruritus and pain | Genital herpetic lesions |

Diagnosis:

1. Clinical picture
2. Viral culture
3. Cytology
4. **PCR (the main step of diagnosis)**
5. Serology is of limited value, it only confirms whether an individual has had previous infection (to determine the latency) ⁽¹⁾

Treatment:

1. **Acyclovir** 200 mg five times daily
2. **Famciclovir** 250 mg 8-hourly
3. **Valaciclovir** 500 mg 12-hourly

Varicella Zoster Virus:

Varicella Zoster virus (VZV) is a dermatropic and neurotropic virus that produces **primary infection results in varicella “chickenpox”** characterized by **vesicular lesions in different stages of development on the face, trunk, and extremities**. Herpes zoster, also known as **shingles** results from reactivation of endogenous latent VZV infection within the sensory ganglia ⁽¹⁾⁽⁵⁾. 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. The virus establishes latency within the **dorsal root ganglia**.

Clinical manifestations ⁽¹⁾⁽⁶⁾⁽⁷⁾: incubation period: 11-20 days

| <i>Chickenpox</i> | <i>Shingles</i> |
|--|---|
| Fever and flu-like symptoms | Follows previous infection |
| Rash on the trunk and limbs | Blistering rash with band like distribution |
| Malaise, pharyngitis, loss of appetite | Sever pain |

Diagnosis:

Primarily clinical by recognition of rash, could be confirmed by direct immunofluorescence or PCR of aspirated vesicular fluid. Serology is used to identify seronegative individuals at risk of infection ⁽¹⁾.

Treatment:

Treatment is not required for the primary infection. Antivirals are required for uncomplicated chickenpox when the patient presents within 24-48 hours of onset of vesicles, patients with complications, and the immunocompromised ⁽¹⁾.

Antivirals available:

1. Acyclovir
2. Valaciclovir
3. Famciclovir

Vaccines (1):

1. **Human VZ immunoglobulin (VZIG):** used to attenuate infection in people who have had significant contact with VZV, susceptible to infection and have no history of previous infection “seronegative for VZV IgG”.
2. **Live attenuated VZV vaccine:** children receive one dose after 1 year of age, and second dose at 4-6 years of age. Seronegative adults receive 2 doses at least one month apart.

Cytomegalovirus:

Cytomegalovirus has worldwide distribution and infects a large number of human beings. Infection ranges from asymptomatic to severe multisystem disease with a latency period. CMV infection is characterized by subclinical cycles of active virus replication and by persistent low-level virus shedding (1).

Mode of transmission: saliva, urine, semen and genital secretions, and oral.

1. Primary infection:

- ✓ Asymptomatic
- ✓ Infectious mononucleosis

2. Secondary infection in immunocompromised patients:

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

Clinical manifestations ⁽¹⁾⁽⁸⁾:

1. Fever of unknown origin
2. Pharyngitis
3. Fine crackles
4. The lymph nodes and spleen may be enlarged
5. Hepatomegaly

Diagnosis:

The diagnosis depends on **laboratory confirmation**, cannot be made on clinical grounds alone.

1. Viral cultures from blood, urine, or tissue.
2. Serologic tests (antigen detection).
3. PCR

Treatment:

1. Ganciclovir
2. Foscarnet
3. Cidofovir

Epstein-Barr Virus:

Ubiquitous human herpes viruses, 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. It creates a strong association with **African's Burkitt's lymphoma** and **nasopharyngeal carcinoma**.

Infectious mononucleosis "IM" is an acute viral illness characterized by pharyngitis, cervical lymphadenopathy, fever, and lymphocytosis. It is mostly caused by EBV infection. The virus is usually acquired from asymptomatic excretors via saliva, either by droplet infection or environmental contamination in childhood, or by kissing among adolescents and adults. The virus is not highly contagious ⁽¹⁾.

Clinical manifestations ⁽⁹⁾⁽¹⁰⁾:

1. Begins with malaise, headache, sore throat, and low-grade fever.
2. Tonsillitis and/or pharyngitis.
3. Cervical lymph node enlargement and tenderness with moderate to high fever.
4. Peripheral blood lymphocytosis.
5. Nausea and anorexia without vomiting.

Diagnosis:

1. Heterophile antibodies are present in about 90% of cases.
2. **Hematologic findings**:
 - ✓ **Lymphocytosis**
 - ✓ **Neutropenia**
 - ✓ **Thrombocytopenia**
3. **EBV specific antibodies** ⁽¹¹⁾: are not necessary since the vast majority of patients are heterophile positive, it might be needed for patients with suspected MI who have negative heterophile test.
4. **Viral capsid antigen** ⁽¹¹⁾: IgG and IgM antibodies against the Epstein-Barr viral capsid antigen (VCA) are usually present at the onset of clinical illness because of the long viral incubation period, they are a good marker of acute infection.

Treatment:

1. Treatment of infectious mononucleosis is largely **supportive** because more than 95% of the patients recover uneventfully without specific therapy.
2. Corticosteroids

SUMMARY

1. Herpes simplex viruses (HSV) cause recurrent mucocutaneous infection , Primary HSV-1 or 2 infections cause gingivostomatitis and pharyngitis
 - A- HSV-1: doesn't get transmitted via sexual contact but by direct contact , could cause herpes labialis
 - B- HSV-2 : transmitted sexually ,could cause genital infection or neonatal infection in addition to latent sacral ganglia infection
2. Herpes simplex viruses diagnosed by PCR and treat is with: Acyclovir,Famciclovir Valaciclovir.
3. Varicella Zoster virus produces primary infection results in **varicella "chickenpox"**. **Herpes zoster known as shingles**. The virus is spread by the respiratory route virus establishes latency within the dorsal root ganglia. And the treatment same as HSV
4. Cytomegalovirus transmitted through saliva, urine, semen and genital secretions, and oral. Have to type of infection either: primary (Asymptomatic) or Secondary infection in immnuocompremsed patients
5. Epstein-Barr Virus Spread by intimate contact between susceptible individuals and creates a strong association with African's Burkitt's lymphoma and nasopharyngeal carcinoma
6. Infectious mononucleosis "IM" is an acute viral illness characterized by pharyngitis, cervical lymphadenopathy, fever, and lymphocytosis. It is mostly caused by EBV infection

IMPORTANT NOTES FROM EXTERNAL RESOURCES

Notes

- | | |
|------|---|
| (1) | Davidson's Principles and Practice of Medicine, 22 nd Edition, Infectious Disease chapter |
| (2) | 432-microbiology teamwork. |
| (3) | http://www.uptodate.com/contents/pathogenesis-of-herpes-simplex-virus-type-1-infection#H8 |
| (4) | http://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-herpes-simplex-virus-type-1-infection#H14 |
| (5) | http://www.uptodate.com/contents/clinical-manifestations-of-varicella-zoster-virus-infection-herpes-zoster |
| (6) | http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/health+topics/health+conditions+prevention+and+treatment/infectious+diseases/chickenpox+and+shingles |
| (7) | http://www.uptodate.com/contents/clinical-features-of-varicella-zoster-virus-infection-chickenpox#H7 |
| (8) | http://emedicine.medscape.com/article/215702-clinical#a0217 |
| (9) | http://www.uptodate.com/contents/clinical-manifestations-and-treatment-of-epstein-barr-virus-infection |
| (10) | http://emedicine.medscape.com/article/222040-clinical |
| (11) | http://www.uptodate.com/contents/infectious-mononucleosis-in-adults-and-adolescents?source=see_link&sectionName=DIAGNOSIS&anchor=H18#H18 |

Questions

- 1) Which one of the following is the most common clinical manifestation of HSV-1?
- Pruritus and pain
 - Herpes labialis
 - Aseptic meningitis
 - Fever of unknown origin
- 2) An 18 year old freshman college student presents to the health center complaining of sore throat and fever for 3 days. She also states that she has been feeling tired for the past week. On physical exam, she is tired and subdued but not toxic in appearance with a temperature of 38 degrees C. Her tonsils are enlarged and erythematous. She has enlarged posterior cervical lymph nodes bilaterally, which are mildly tender to palpation the hematologic finding were : Lymphocytosis, Neutropenia and Thrombocytopenia
- What is most likely is the organism?
- Varicella Zoster Virus
 - Cytomegalovirus
 - Epstein-Barr Virus
 - HSV-2

432 Medicine Team Leaders

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Answers:

1st Questions: **B**

2nd Questions: **C**