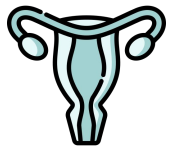


TEAM 443
MICROBIOLOGY

L5- Herpes simplex and genital warts

-Dr. Mona & Dr. Abdulkarim Al Hetheel





OBJECTIVES

1

The main structural components of HSV-2 and HPV.

2

Mode of transmission in HSV-2 and HPV infections.

3

Main clinical features of HSV-2 and HPV infections.

4

Diagnosis.

5

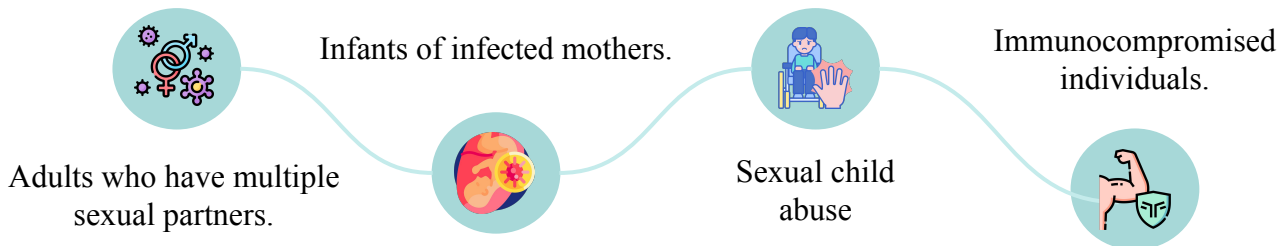
Management & treatment.



Herpes

Introduction: Genital herpes and genital warts are recognized as the **main sexual transmitted viral infections** that might be acquired by any types of sexual contact.

Risk Groups



Etiology

There are two species of herpes virus capable of causing genital herpes:

- Herpes simplex virus type 1 (HSV-1).
- **Herpes simplex virus type 2 (HSV-2).**

90% of genital herpes cases are due to HSV-2 infection, whereas 10% are due to HSV-1.

Both (HSV-1 & HSV-2) are **structurally** very **similar** and share about 70% sequence homology.

HSV-1 cause symptoms in upper part of body (oral), while HSV-2 cause symptoms in lower part (genital)

Characteristics of Herpes virus

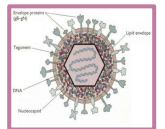
The Herpes viruses has the ability to induce **latent infection**

- HSV (1&2) → Nerve cells
- HSV-1 → Trigeminal ganglia
- HSV-2 → Sacral ganglia

Virion consist of:

- Glycoprotein envelope
- Icosahedral capsid Linear ds-DNA

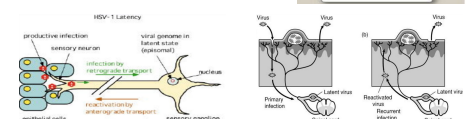
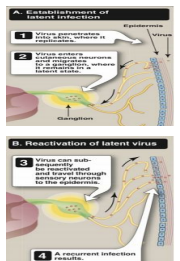
Family of herpesviridae



Pathogenesis of HSV-2 (Genital herpes infection)

-Primary infection occurs when HSV-2 infects **epithelial cells** covering the mucosa → Then the virus replicates and migrates to the nearest **ganglion (sacral ganglia)** via neurons **where it establishes latency** for life → Once its reactivated (**due to immunosuppression**) it travels back through neurons to the site of the **primary infection and causes recurrent infection.**

-Once the virus enters the human body, it remains for life (latency).





Herpes



Transmission of genital HSV infection

<p>1- Sexual transmission</p>	<ul style="list-style-type: none"> - The number of different sexual partners correlates directly with acquisition of HSV-2 in both male & female. - Homosexual men are more susceptible to HSV-2 infection. - Genital infection can be acquired by auto-inoculation from lesions elsewhere on the body by touching vesicular fluids from any herpetic lesions (HSV-1&2). - HSV-1 can cause genital herpes infection after oral sex, also can be seen in cases of child abuse.
<p>2- Perinatal transmission (during delivery)</p>	<ul style="list-style-type: none"> - The majority of maternal infection (85%) occurs during delivery, due to direct contact between the baby and infected maternal birth canal. - The risk of perinatal transmission is about 50% if the mother has primary genital herpes, while the risk is 8% if mother has recurrent infection. - In the baby: this infection can lead to either massive herpetic skin lesions or generalized infection affecting skin and internal organs e.g. lungs (inhale/drink secretions during delivery), liver or brain (neonatal herpes infections) - To avoid perinatal infection we do caesarean section (Any pregnant woman who is infected by HSV2 should have a caesarean section delivery it doesn't matter if it is a primary or a recurrent infection)
<p>3- Intrauterine (vertical) transmission (10%)</p>	<ul style="list-style-type: none"> - Maternal primary genital HSV (HSV-2) infection of the mother during first trimester can lead to spontaneous abortion. - Maternal primary genital HSV (HSV-2) infection which develops after 20 weeks of gestations may induce malformation such as microcephaly, jaundice, hepatosplenomegaly, chorioretinitis and herpetic vesicles on the skin Fatal



Clinical features of HSV-2 infection

Primary genital herpes	Recurrent genital herpes
<ul style="list-style-type: none"> • Vary from asymptomatic to mild or severe painful episode. • If symptoms are present (Incubation period: 2-12 days) they may include: <ol style="list-style-type: none"> 1. Fever, Malaise, dysuria 2. Inguinal lymphadenopathy 3. Vesicular herpetic lesion or ulcer localized to the cervix, vagina, vulva or perineum of the female or the shaft of the penis in the male. 4. Aseptic meningitis have been observed in about 10% of cases as extra genital presentation. 	<ul style="list-style-type: none"> • Occurs after reactivation by environmental or physiological factors such as stress, exposure to U.V. light, menstruation, pregnancy or any condition that decreased the immunity. • This can be as frequent as six or more episode a year, the attacks are milder and shorter than primary episode. • Accompanied with the appearance of herpetic vesicles on the external genitalia. • Symptoms may include pain and itching.



Neonatal herpes infection

- is not a common condition, but the **mortality is >70%** when it happens.
- It occurs **during labor and delivery through the vaginal canal** when a mother is having a **primary active herpetic lesion** (50% chance) and shedding the virus, also in small % as vertical transmission during pregnancy.
- It may spread to other organs such as lungs, liver, brain



Neonatal herpes infection (has three forms):



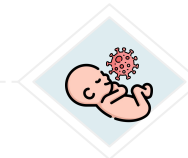
Localized Brain Infection

limited to **CNS invasion** causing encephalitis.
mortality is high



Localized Skin Infection

limited to massive **skin vesicular lesions**
mild infection



most feared form

Generalized Neonatal Herpes Infection

-severe **massive** infection of the **skin** (massive skin herpetic lesions) accompanied with **internal organs infection** including lungs (pneumonia), liver (hepatosplenomegaly), and brain (encephalitis). usually **fatal**.

Lab Diagnosis

1-ELISA Gold standard	Serum sample is analyzed for detection the IgM Ab. (For routine diagnosis)	The presence of: - Both IgM & IgG indicates previous exposure → recurrent infection - IgM only → primary infection. - IgG only → inactive (latent)
2- IF (Direct immunofluorescence)	Scraping of the base of the lesion sample or vesicle fluid sample is analyzed for detection the viral Ag.	
3- PCR	CSF sample in case of Meningitis or neonatal herpes.	
Tissue culture	vesicle fluid sample is cultured in cell line (Vero or Hep-2 cells) and then identified by the following: ○ Observe the viral CPE (cytopathic effect) ○ Direct immunofluorescence (IF)	



Treatment

- **Acyclovir** : The 1st choice therapy, and suitable for pregnant women. (to lessen severity of condition, not cure)
- Famciclovir
- Valacyclovir



Management

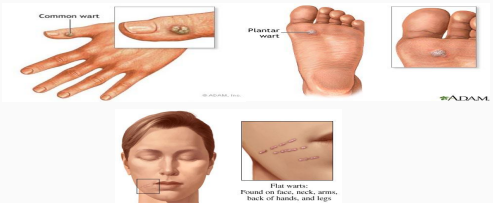
- **No vaccine is available** to prevent HSV-2 infection, and thus the best way to control the HSV infection is by:
- Avoid sexual contact with infected individuals.
- Abstain from making prohibited relations.
- Note: Condoms are not 100% protective against genital herpes infection
- Cesarean section is recommended for women who are having genital herpetic lesion.



Human Papillomavirus

Human Papillomavirus	<p>Family:</p> <ul style="list-style-type: none"> Family of Papillomaviridae
	<p>Characteristics:</p> <ul style="list-style-type: none"> Virion is small non-enveloped and consist of: <ul style="list-style-type: none"> Icosahedral capsid Circular ds-DNA They cause disease only in skin and mucous membrane Does not grow in tissue culture Resists detergent, heat, and can remain infectious in the environment for long time. (like hep B, strong virus)
	<p>Type of wart and HPV genotypes:</p> <ul style="list-style-type: none"> 1- Cutaneous warts 2- Genital/Anogenital and Mucosal warts

1- Cutaneous Warts

Transmission	<p>The virus is transmitted from infected skin, either by direct contact hand to hand (common warts) or through fomites and enter its new host through abrasions especially in swimming pools (plantar warts).</p>
Types	<ul style="list-style-type: none"> Common Warts:: (HPV genotype 2,4) Plantar Warts:: (HPV1,) Flat Wart:: (HPV 3,10) 

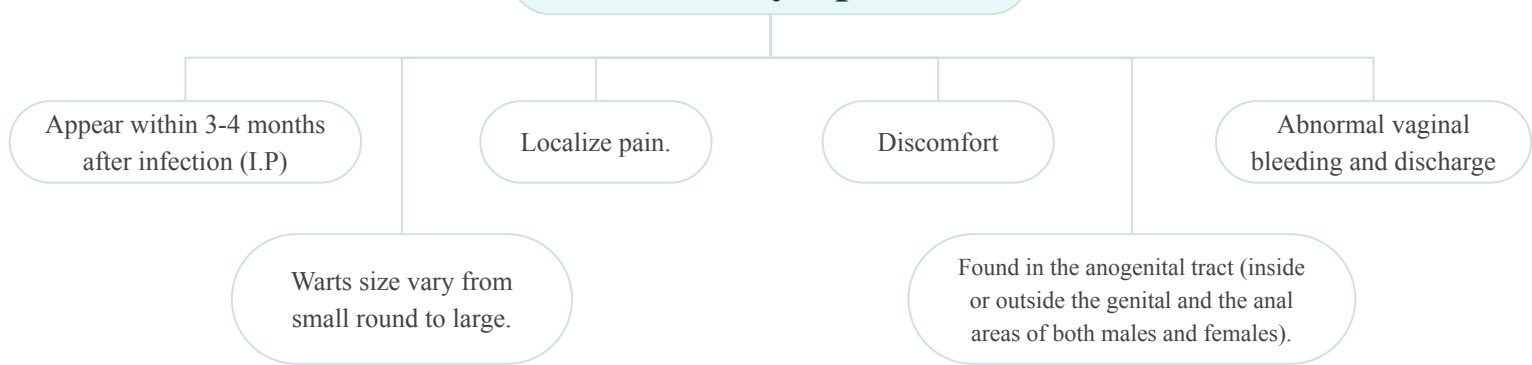
2- Genital / Anogenital or Mucosal Warts

Transmission	<p>Transmission of genital warts mainly occurs during sexual activity,</p> <ul style="list-style-type: none"> There is strong association between increasing numbers of sexual partners and prevalence of genital HPV infections. often occur in association with other sexual diseases as gonorrhea or chlamydial infection. Vertical transmission; from mother to infant or prenatal transmission lesions appear within the first 6 weeks of life have been demonstrated. <i>seen as laryngeal warts</i>
Types	<ul style="list-style-type: none"> -Condyloma acuminata (benign): (HPV 6,11) -Cervical carcinoma (malignant): (HPV 16, 18, 31,45) o Penile and anal carcinoma in men (malignant): (HPV 16,18) o Laryngeal Warts (benign): (HPV 6,11)



Human Papillomavirus

Clinical symptoms



Link between HPV and cervical cancer

- **Persistent HPV infection is considered the main cause of cervical cancer.**
- **HPV DNA** can be **detected in** most grades of **pre-malignant lesions** of the female and male genital tract.
- **Dr mona:** type 6 and 11 are benign but if it was left untreated for a long time it might become malignant.
- **HPV type 6 and 11** (Condylomata acuminata) are mostly found in **low-grade disease**, is unusual to become malignant, but they occasionally progress to squamous cell carcinoma.
- **HPV 16 and 18** are more commonly associated with lesions of greater severity and great dysplasia which involve all layers of stratified epithelium, and has **high chance of progression to metastasizing carcinoma and invasive cancer.**
- **> 90% of positive Pap-smear is due to HPV infection type 16 & 18.**
- **Pap-smear:** is a **screening test** for detection abnormal epithelial cells of the cervix.

Diagnosis

- **External genital warts** can be easily diagnosed by **medical examination.**
- **Internal genital warts** can be visualized by **colposcopy.**
- **Lab diagnosis:**
 - 1- **Polymerase chain reaction (PCR)** (**main test for diagnosis**) is used to detect HPV DNA.
 - 2 -In-situ DNA hybridization is used for HPV genotyping to **detect 16-18 or 6-12.**
 - 3- **Pap-smear** test is used to identify abnormal epithelial cells of the cervix (cervical dysplasia).
screening test only! not for diagnosis. first, lady will get pap-smear, & if +ve she will need to do **PCR** for **diagnosis.**

Dr mona: Pap smear is **NOT** diagnostic for HPV itself! It only tells us if the epithelium was abnormal.



Human Papillomavirus

Treatment

Topical Treatment	<p>Applied directly on external warts and Used for several weeks. Examples:</p> <ul style="list-style-type: none"> ○ Imiquimod, Podofilox. ○ Podophyllin is applied by a doctor and contraindicated in pregnancy. ○ Trichloroacetic acid (T.C.A) safe in pregnancy.
Injection	<ul style="list-style-type: none"> ○ Interferon alpha, 5-fluorouracil epinephrine gel. ○ Could be taken for several weeks (8-12).
Cryotherapy	freezing warts by liquid nitrogen.
Electrocautery Treatment	destroying warts by an electric current.
Laser Therapy	destroying warts by a focused light beam.
Surgical Excision	removing warts by surgical tools.

Prevention

There are **two vaccines available Gardasil and Cervarix** and both are:

- Recombinant viral-like particles with **no DNA**.
- Given in 3 doses at 0[1], 2, 6 months.
- **Recommended for young individuals ages 9-26 yrs old. (before marriage)**
- **Not given to pregnant women.**
- **Gardasil:** a **quadrivalent** vaccine, **provides protection against HPV genotypes 6,11,16,18** which causes genital warts and cervical cancer. **(better, protect against benign & malignant)**
- **Cervarix:** a **divalent** vaccine, **provides protection against HPV genotypes 16 and 18** which causes cervical cancer. **(malignant only)**





MCQs - SAQ

Q1 -How to diagnose genital herpes?			
A- ELISA to detect IgM Ab	B- tissue culture	C- IF	D- PCR
Q2 - Herpes simplex type 1 mainly affects :			
A- sacral ganglia	B- trigeminal ganglia	C- optic chiasm	D- Sympathetic trunk
Q3 - Regarding herpes choose the correct answer:			
A- 90% are caused by HSV-2	B- Herpes simplex 1 & 2 have some similarity in the structure	C- Herpes simplex 1 & 2 have some similarity in the structure	D- All of the above
Q4 - which of the following can't grow on tissue culture ?			
A- measles	B- HPV	C- HSV	D- Rabies
Q5 - how to mainly diagnose HPV ?			
A- PCR	B- pap smear	C- ELISA	D- immunofluorescence
Q6 - HPV-6 infection is considered :			
A- malignant	B- benign	:)	:)
Q7 - Gardasil vaccine protect against :			
A- HPV-6&11	B- HPV- 16&18	C- HPV-31	D- HPV 8,11,16,18
Q8 - A 21 year pregnant lady gets a primary HSV type 2 infection during her 38th week of pregnancy. What can you do to prevent the transmission of the infection to the baby?			
A- Caesarean section	B- Give acyclovir to the mother	C- Give immunoglobulins to the baby	D- Normal delivery
Q9 - Which one of the following sexually-transmitted viral infections can be treated by acyclovir?			
A- HBV infection	B- HIV infection	C- HPV infection	D- HSV infection



MCQs - SAQ

1

A 37 year old female presented to the OB/GYN clinic due to abnormal vaginal bleed and increased vaginal discharge. She reported a regular menstrual cycle every 4 weeks with no previous sexual transmitted diseases. Cervical sample for Pap smear showed high grade squamous intraepithelial lesion.

Q1: What is the most likely causative organism?

Human papillomavirus

Q2: How would you confirm the diagnosis?

PCR used to detect the HPV DNA

Q3: How can we prevent such infection?

Gardasil vaccine: quadrivalent HPV vaccine targets HPV types 6, 11, 16, & 18. Cervarix vaccine: bivalent vaccine targets HPV types 16 and 18.

2

A 28 year old female came to the hospital and had a natural delivery to a baby. during examination of the mother she had localized vesicles on her vulva & the baby it was found to have malformations : jaundice, microcephaly, hepatosplenomegaly ,and chorioretinitis.

Q1: what is the mothers most likely diagnosis?

primary HSV-2 (genital herpes infection)

Q2: What is the routine method for diagnosis?

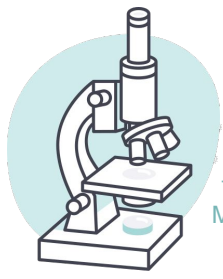
ELISA for detection of IgM antibodies in the serum sample.

Q3: Name two complications that could develop and how we can avoid them.

1- Perinatal infection

2- Spontaneous abortion if mother is primary infected during first trimester.

We can avoid perinatal infection by doing C- section to the mother. Also, advise the mother to avoid any sexual contact with infected individuals.



TEAM 443
MICROBIOLOGY



TEAM LEADERS

Nazmi M Alqutub

Reemas Aljeadi

Farah Abukhalaf

TEAM MEMBERS

Mohammed Alqutub

Aroub Almahmoud

Nazmi A Alqutub

 Aishah Boureggah

Danah Almuhausen

Sarah Aldossary

Luay Alhudaithy

Raghad Almuslih

Abdulrahman Almusallam

Reuf Alahmari

 Khalid Alanezi

Lama Alotaibi

 Mohammed Alarfaj

اللهم إني استودعك ما قرأت وما حفظت فرده إليّ عند حاجتي إليه انك على كل شيء قدير

Any future corrections will be in the editing file, so please check it
frequently

Special Thanks to Aishah Boureggah for the Amazing theme !