Microbiology
Team 432

Lecture (4)
Genital Herpes &Genital Warts

Objectives:

- Not given.

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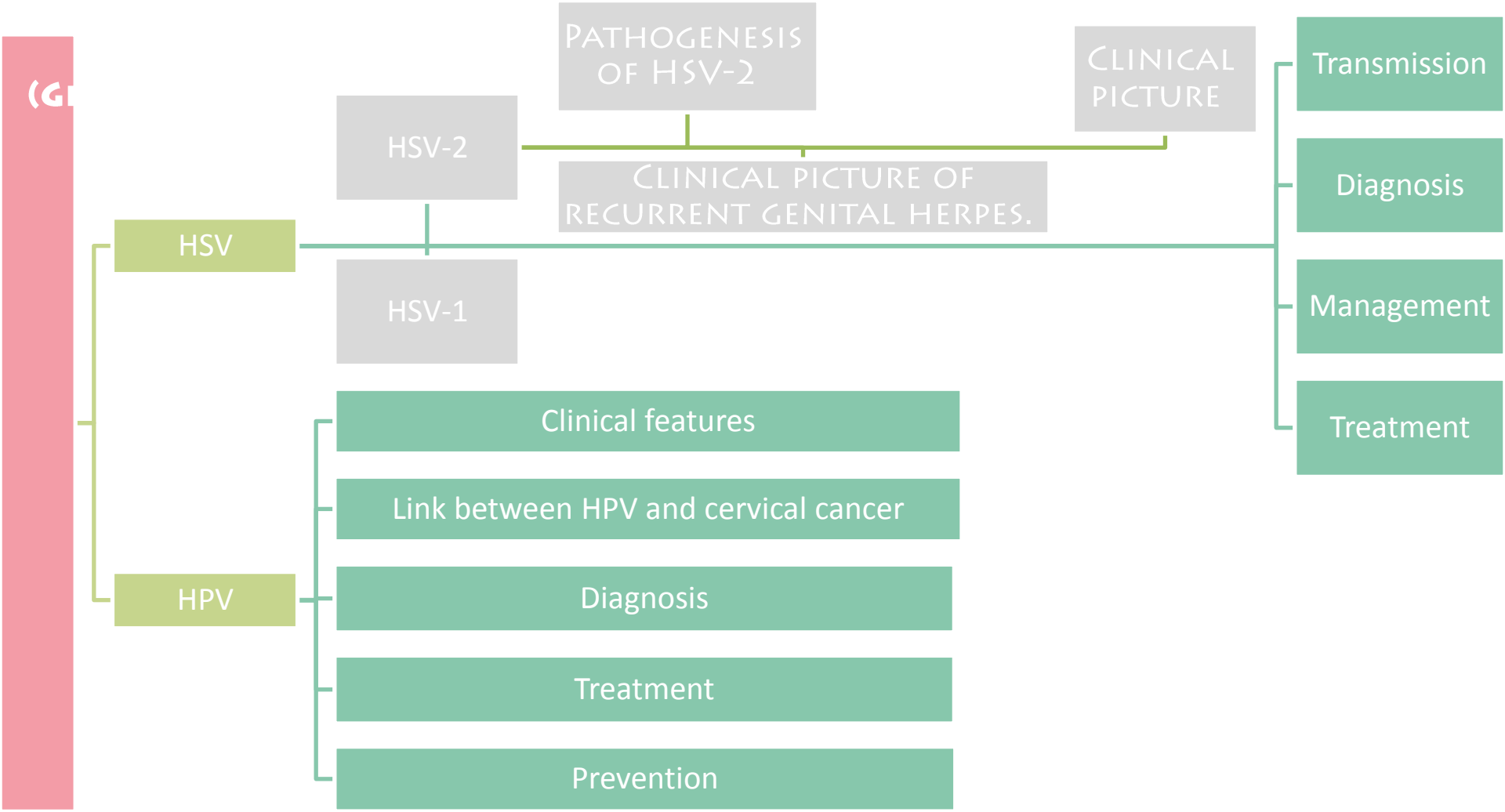
MIND MAP
(GENITAL HERPES &GENITAL WARTS)

MICROBIOLOGY
SEAM 432



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:

1- Adults who have multiple sexual partners.
2- Immune compromised individuals.
4- Infants who have infected mothers.
3- Sexual child abuse.

Genital herpes

Etiology:

•There are two species of herpes virus capable of causing genial herpes:
Herpes simplex virus type 2 (HSV-2) and **Herpes simplex virus type 1 (HSV-1).**

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

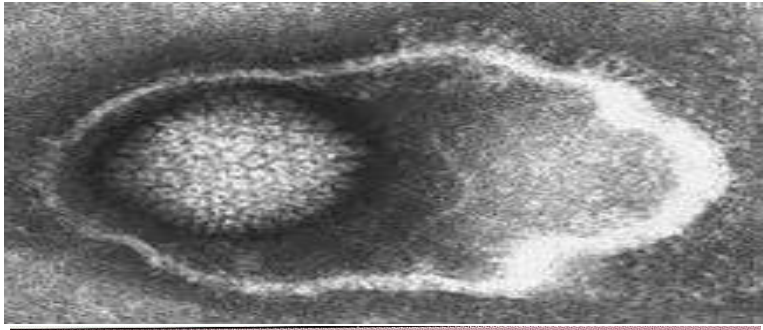
1- Herpessimplex virus type 1 (HSV-1)

- Causes 10% of genital herpes cases
- Infection in the upper partof the body.
- 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.**
- Causes encephalitis, Keratoconjunctivitis or Gingivostomatitis

2- Herpessimplex virus type 2 (HSV-2)

- Causes 90% of genital herpes cases
- Infection in the lower part of the body, the genital area
- Called genital herpes → sexually transmitted disease or vaginally, also intraplacental
- Causes meningitis

Characteristics Of Herpes Virus :



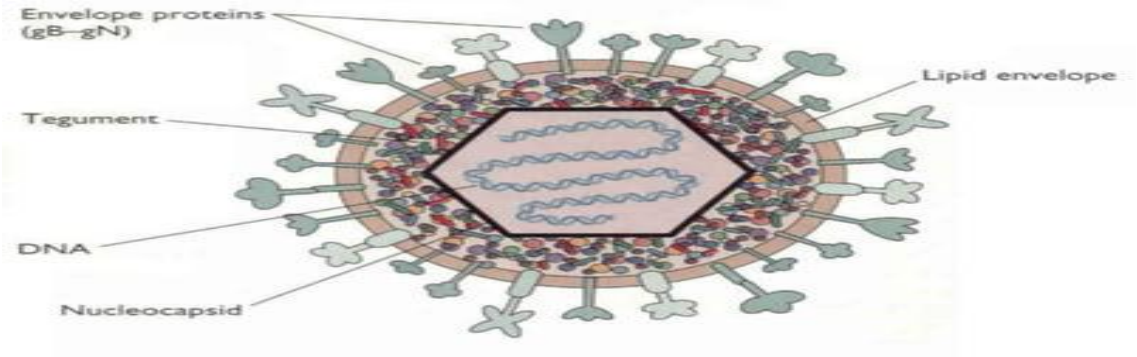
- Family of **herpesviridae**.
- Virion consist of:
  - Glycoprotein envelope
  - Icosahedral capsid
  - Liner **ds-DNA.**
- The Herpes viruses has the ability to induce **latent** infection,

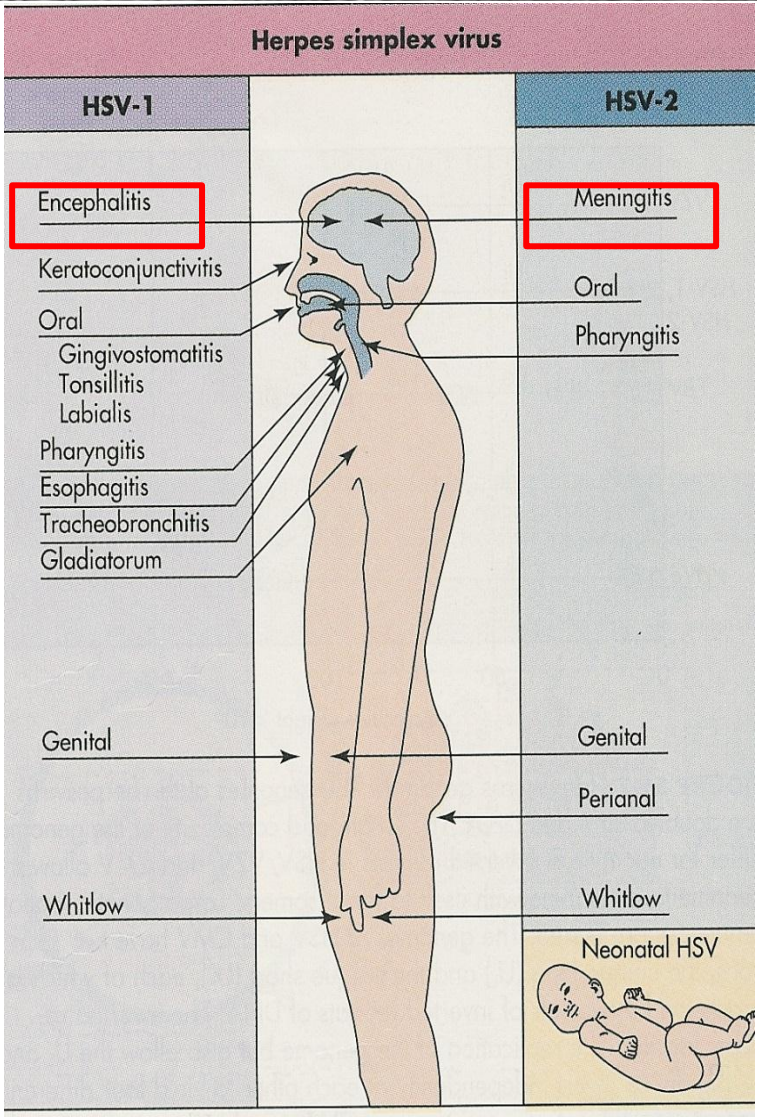
HSV (1&2) → NERVE CELLS.

HSV-1 → Trigeminal ganglia

HSV-2 → Sacral ganglia

Latent means it has the ability to stay in the body for a long time and never leave (hides in the body). Can stay in the body for 30-40 years without being activated





Transmission of Genital HSV infections

1- Sexual transmission:

- 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**.

2- Perinatal transmission (during delivery):

- 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 usually occurred in about 50% of mothers have **primary genital herpes**, while the risk is 8% if mother have **recurrent infection** (secondary)
- This infection can lead to either massive herpetic **skin lesions or generalized infection** affecting skin and internal organs e.g; lungs , liver or brain .
- To avoid perinatal infection we do **Caesarean section**.

3-Intrauterine (vertical) transmission (10%):

- Maternal **primary** genital HSV infection of the mother during first trimester (13 weeks) can leads to spontaneous abortion.
- Maternal **primary** genital HSV infection which develops after 20 weeks of gestations may induce malformation as; microcephally, jaundice, hepatosplenomegally, Chorioretinitis and herpetic vesicles on the skin.

Pathogenesis of HSV-2

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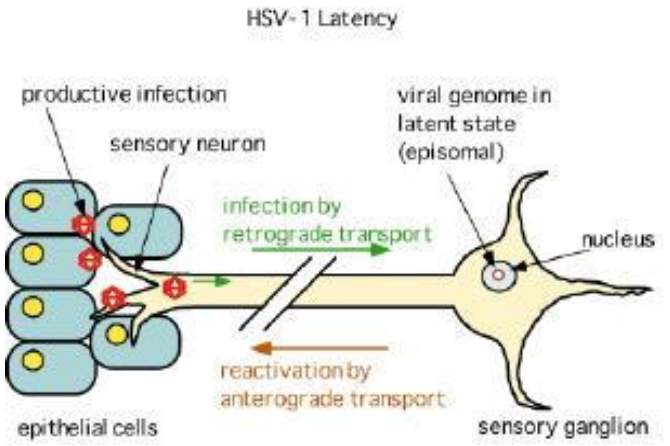
Genital herpes infection

- **Primary infection** occurs when HSV-2 infects **epithelial cells covering the mucosa.**
- The virus then migrates to the nearest ganglion (sacral ganglia) via neurons where it replicates and establish latency for life.
- Once its reactivated (in stress or ↓ immunity), it travels back through neurons to the site of the primary infection and causes **recurrent infection.**

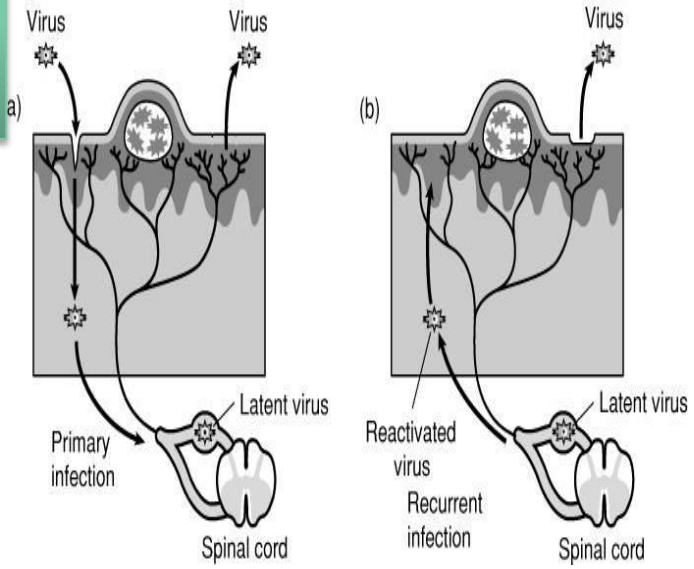
Once the virus enters the human body it remains for life **(latency) .**



Clinical picture of recurrent genital herpes.

Occurs after reactivation by environmental or physiological factors such as stress, exposure to U.V. light, menstruation, pregnancy or any condition 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.



Clinical features of HSV-2 infection

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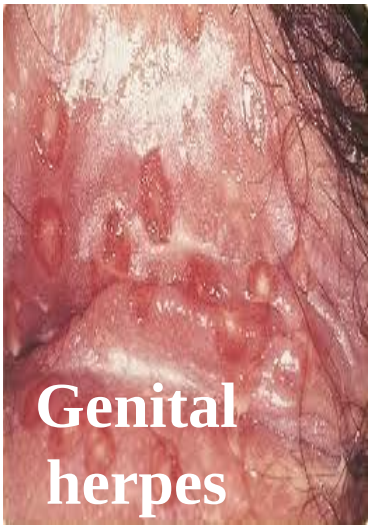
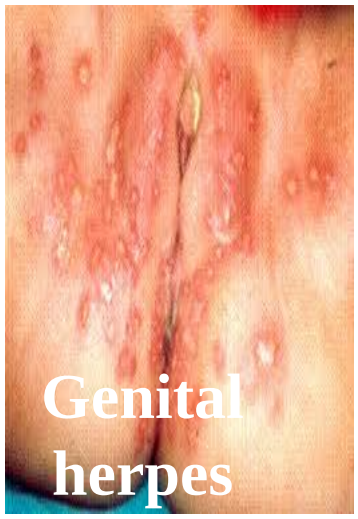
Primary genital infection:

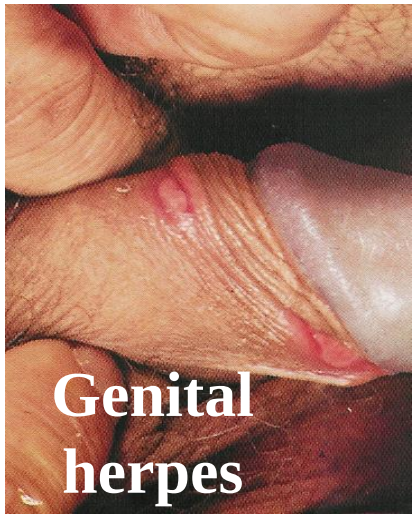
Vary from asymptomatic to mild or sever painful episode.

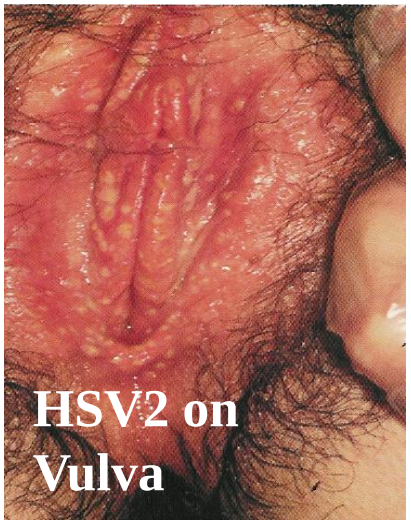
If symptoms are present(I.P 2-12 days) they may include;

- fever , malaise, dysuria,
- Inguinal lymphadenopathy
- 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 ,Herpetic proctitis can be seen in homosexuals.
- **Aseptic meningitis** have been observed in about 10% of cases as extra genital presentation.









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 and shedding the virus, also in small % as vertical transmission during pregnancy.

It may spread to other organs such as lungs, liver, brain.

It has three forms:

1- Localized skin infection.

limited to massive skin vesicular lesions

mild infection

2- Localized brain infection.

limited to CNS invasion causing encephalitis.

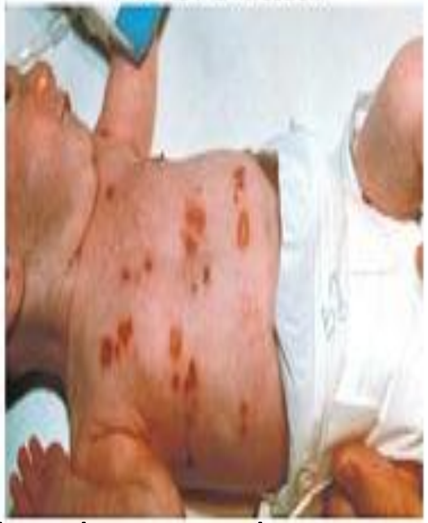
mortality is high

3- Generalized neonatal herpes infection.

Severe massive infection of the skin accompanied with internal organs infection as lungs (pneumonia), liver (hepatosplenomegally), and brain (encephalitis) with massive skin herpetic lesions.

usually fatal

Skin lesions of a newborn with HSV-2 infection



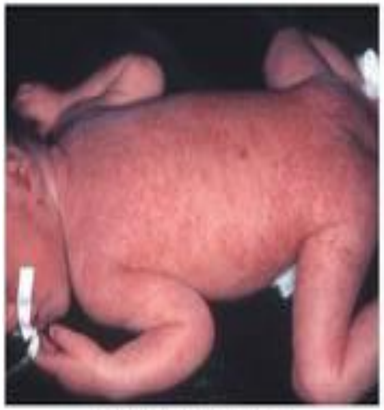
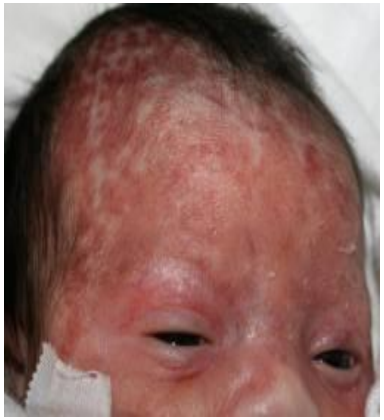


Figure 4: Congenital candidiasis



Lab diagnosis

1- ELISA:

serum sample is analyzed for detection the IgM Ab. (IgM means acute attack (either primary or recurrent).

2- Immunofluorescence (IF):

lesion scraping or vesicle fluid sample is analyzed for detection the Ag.

3- Polymerase chain reaction (PCR):

CSF sample in case of neonatal herpes.

4- 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
- Direct immunofluorescence (IF)

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.

Treatment

- Acyclovir:
  - The 1st choice therapy.
  - Suitable for pregnant women.
- Famciclovir.
- Valacyclovir.

The virus will never be eradicated even with treatment

Human Papillomavirus

Family of *Papillomaviridae*. **Virion is small non-enveloped,**

consist of:

- **Icosahedral capsid. Circular ds-DNA, 55nm in diameter.**
- **HPV infect epithelial tissues of skin and mucous membrane.**
- **There are more than 150 distinct HPV subtypes.**
- **HPV can not grow in tissue culture.**
- **The HPV early proteins (E6 and E7) are transforming proteins and associated with initiating cancer by the oncogenic HPV genotype.**
- **HPV resists detergent, and heat and can remain infectious in the environment for long time**

Clinical features:

HPV cause disease only in skin and mucous membranes (in cervix, mouth and jaw) , where they give rise to **WARTY LESIONS**.

They are usually benign, but some may become malignant depending on the type of HPV , the anatomical site involved ,and the potential to cause malignant lesions

1- Cutaneous warts:

The virus is transmitted from infected skin ,either by direct contact or through fomites and enter its new host through **abrasions** .Swimming pools and changing rooms are fertile sources of infection ,skin warts are most liable to affect children and young adult the incubation period following exposure is approximately **2 to 6 months** .

Spontaneous remission of warts occurs in up to 2/3 of the patients with normal cellular immunity within 2 years without treatment but recurrence is common.

A-Verruca Vulgaris "common warts " (2 ,4).	b-Plantar &Palmar Warts (1,2,4)	c-Flat Warts (verrucae planae 3,10)
The common warts has characteristically roughened surface ,occur in quite large numbers anywhere on the skin, but especially on the hands ,knees and feet ,occur most commonly in children and young adult. Butchers Warts (7) common among certain occupation such as handlers of meat ,poultry and fish.	On the soles of the feet ,they may be painful and need treatment not as other sites	They are flatter and smoother than common warts and present in different sites in the body.

Genital ,Anogenital or mucosal Warts:

These Warts are **acquired by sexual contact** ,they are in fact one of the most common sexually transmitted diseases, and often occur in association with other sexual diseases as gonorrhea or chlamydial infection.

There is strong association between increasing numbers of sexual partners and prevalence of genital HPV infections.

There are over 40 HPV types that infect the anogenital area.

Vertical transmission; from mother to infant or preinatal transmission lesions appear within the first 6 weeks of life have been demonstrated.

Clinical symptoms of genital warts:

Appear after **3-4** months after infection(I.P).

Warts size vary from small round to large complex mass.

Found in the anogenital tract (inside or outside the genital and the anal areas of both males and females).

Localized pain

Discomfort

Abnormal vaginal bleeding and discharge.

2- Ano-genital or mucosal

Very important

- Condyloma acuminata (**low-risk**)(**benign** HPV 6,11)
- Cervical carcinoma (**high-risk**) (**HPV 16,18, 31,45**)
- Penile and anal carcinoma (**HPV 16,18**) in men
- Laryngeal Warts (benign HPV 6,11) (HPV 6,11) They may be transmitted to baby during delivery.

Link between HPV and cervical cancer

HPV type 6 and 11(Condylomata acuminata) is unusual to become malignant ,but they occasionally progress to squamous cell carcinoma ,***while HPV 16 and 18*** are more commonly associated with lesions of great dysplasia which involves all layers of stratified epithelium , and has high chance of progression to metastasizing carcinoma & invasive cancer.

Persistent HPV infection is considered the main cause of cervical cancer, **HPV DNA** can be detected in most grades of premalignant lesions of the female and male genital tract.

> 90% of positive Pap-smear is due to HPV infection.

Pap-smear: is a screening test for detection abnormal epithelial cells of the cervix

DIAGNOSIS OF WARTS

CUTANEOUS WARTS

Routine laboratory diagnosis is not available for cutaneous warts and diagnosis is on basis of clinical history and appearance of the lesions on examination.

HPV can be detected from lesion biopsy by one of DNA hybridaization techniques e.g. Southern blot, PCR, and hybridaization in situ.

GENITAL WARTS

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) is used to detect HPV DNA.**

2- Pap-smear test is used to identify abnormal epithelial cells of the cervix (cervical dysplasia).

3- In-situ DNA hybridization is used for HPV genotyping.

HPV TREATMENT

1- Cryotherapy:

freezing warts by liquid nitrogen | suitable for small external warts

2- Elctrocautery treatment:

destroying warts by an electric current | suitable for small warts

3- Laser therapy:

destroying warts by a focused light beam | suitable for small and large warts

4- Surgical excision:

removing warts by surgical tools | suitable for all warts

5-Injection:

Interferon alpha, 5-flurouracil epinephrine gel. | Could be taken for several weeks (8-12).

6-Topical treatment:

a_)Applied directly on external warts.	**Examples: Imiquimod, Podofilox.**	. Podophyllin is applied by a doctor and contraindicated in pregnancy.
b)Used for several weeks		Trichloroacitic acid (T.C.A) safe in pregnancy.

HPV prevention

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There are two vaccines available Gardasil and Cervarix and both are:
- Recombinant viral-like particles with no DNA.
- Given in 3 doses at 0, 2, 6 months.
- Recommended for young individuals ages 9-26 yrs old.
- Not given to pregnant women.

GARDASIL,

- a quadrivalent vaccine, provides protection against HPV genotypes **6,11,16,18** which causes genital warts.

CERVARIX,

- a divalent vaccine, provides protection against HPV genotypes **16, and 18** which causes cervical cancer.

summary	Herpes Virus	HPV genital warts	HPV cutaneous warts
Transmission	1- Sexual transmission: 2- Perinatal transmission (during delivery): 3-Intrauterine (vertical) transmission (10%):	sexual contact Appear **after 3-4 months** after infection	from infected skin , by direct contact or through fomites and enter its new host through abrasions .Swimming pools and changing rooms are fertile sources of infection
Clinical symptoms	-fever , malaise, dysuria, - Inguinal - lymphadenopathy - Vesicular herpetic lesion or ulcer .	-Found in the anogenital tract -Localized pain -Discomfort -Abnormal vaginal bleeding and discharge.	incubation period following exposure is approximately **2 to 6 months**
Lab diagnosis	1- ELISA: 2- Immunofluorescence (IF): 3- Polymerase chain reaction (PCR): 4- Tissue culture:	1- Polymerase chain reaction (PCR) is used to detect HPV DNA. 2- Pap-smear test is used to identify abnormal epithelial cells of the cervix (cervical dysplasia). 3- In-situ DNA hybridization is used for HPV genotyping.	HPV can be detected from lesion biopsy by one of DNA hybridaization techniques e.g. Southern blot, PCR, and hybridaization in situ.
		HPV can not grow in tissue culture.	
management	Acyclovir:"The 1st choice therapy." Famciclovir. ,Valacyclovir. -To avoid perinatal infection we do Caesarean section.	1- Cryotherapy:2- Elctrocautery treatment: 3- Laser therapy:4- Surgical excision: 5-Injection:6-Topical treatment:	

Summary
Very important notes

1- Herpessimplex virus type 1 (HSV-1) Causes 10% of genital herpes cases

2- Herpessimplex virus type 2 (HSV-2) Causes 90% of genital herpes cases

3- To avoid HSV perinatal infection we do Caesarean section.

4-HPV can not grow in tissue culture.

5-The HPV early proteins (E6 and E7) are transforming proteins and associated with initiating cancer by the oncogenic HPV genotype

6-**Polymerase chain reaction (PCR) is** The **gold** standard method to **diagnose HPV in genital warts**

7- Gardasil, a quadrivalent vaccine, provides protection against HPV genotypes **6,11,16,18** which causes genital warts.

8-Cervarix, a divalent vaccine, provides protection against HPV genotypes **16, and 18** which causes cervical cancer.

Q1: HSV-2 lies dormant in:

A. trigeminal ganglia
B. sacral ganglia
C. ciliary ganglion
D. lumbar ganglion

Q2: A 27 year old pregnant female with HSV-2 will give birth in a few months, which of the following drugs is most suitable for her case?:

A. Acyclovir
B. Famcyclovir
C. Valacyclovir
D. None of the above

Q3: Incubation Period in HSV induced Genital warts is:

A. 2-12 days
B. 7-8 weeks
C. 1-2 years
D. 3-4 months

Questions

Q4: patient came to the clinic with genital warts what is the gold standard method to confirm your diagnosis

A. Tissue culture
B. ELISA
C. (PCR)

Q5: which one of the following vaccines provides protection against HPV genotypes 6,11,16,18 ?

A. Gardasil
B. Cervarix

For any suggestions or problems please contact
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Thank you