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Microbiology Team

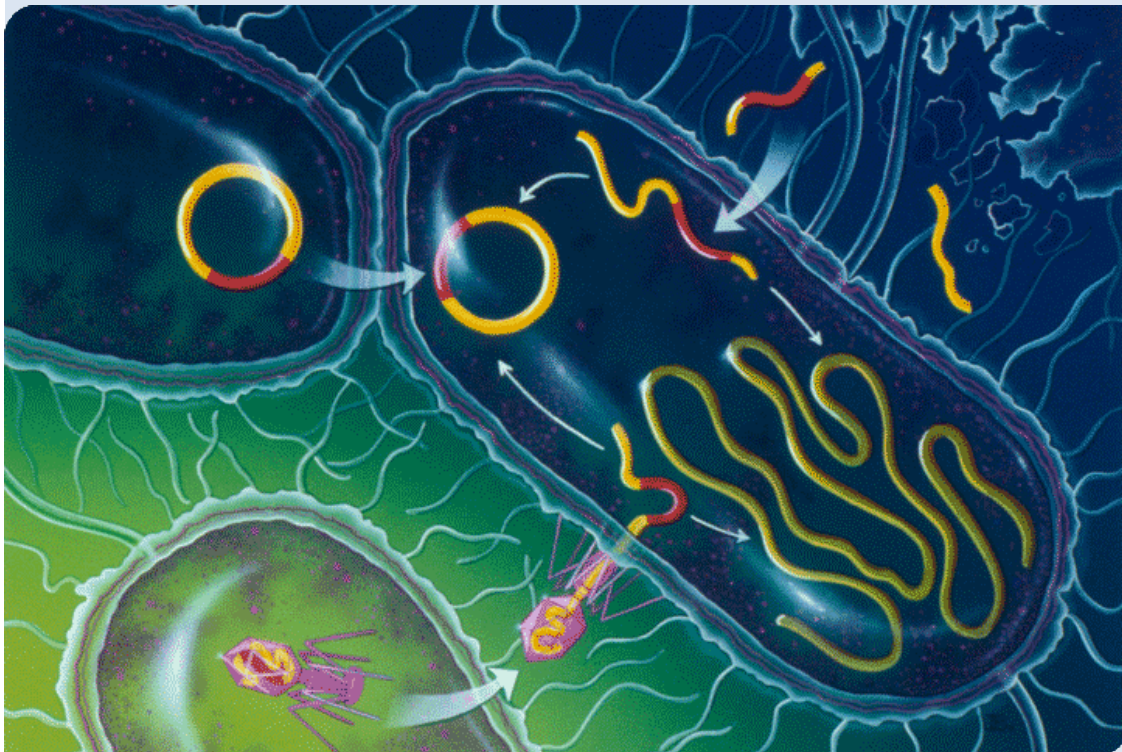
Genital Herpes & Genital Warts

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Red → important

Green → doctors
notes

Purple → teams notes

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:

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

Etiology of HSV

Genital herpes can be caused by two species of herpes virus:

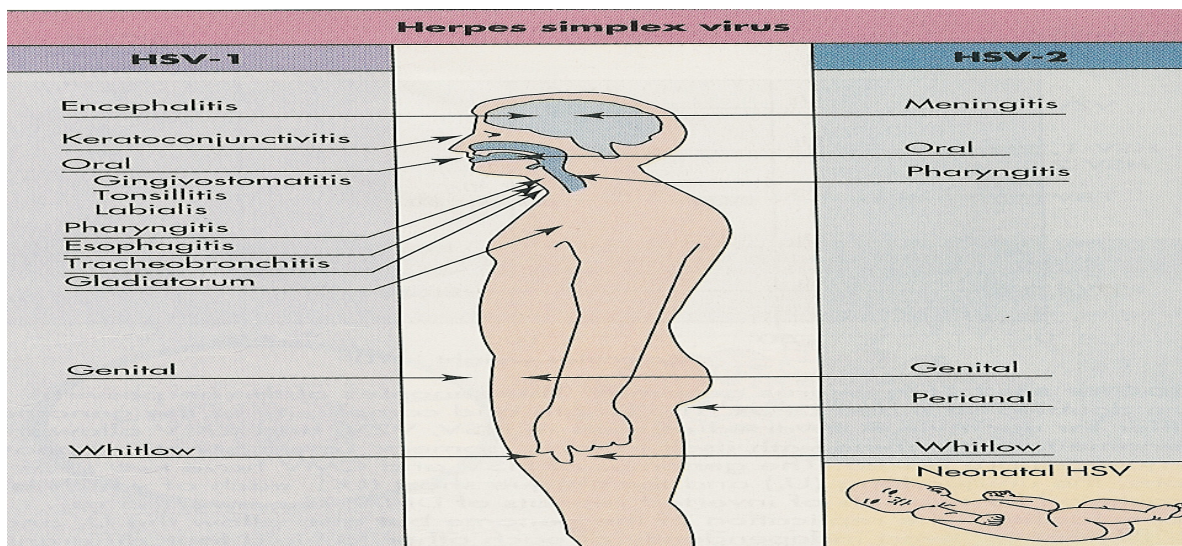
1- Herpes simplex virus type 1 (HSV-1)

- Causes **10%** of genital herpes cases
- Infection in the upper part of the body.
- Doesn't get transmitted via sexual contact but by direct contact.
- Can be transmitted to the genital area via touch
- Causes encephalitis, Keratoconjunctivitis or Gingivostomatitis

2- Herpes simplex 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

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



If a person got HSV-1 antibody from a previous infection → it may result in lowering the effect of HSV-2, because HSV-1 antibody is protecting against HSV-2

Characteristics Of Herpes Virus

Family of *herpesviridae*

Other examples of herpes virus:
cytomegalovirus, varicella zoster, Epstein-Barr

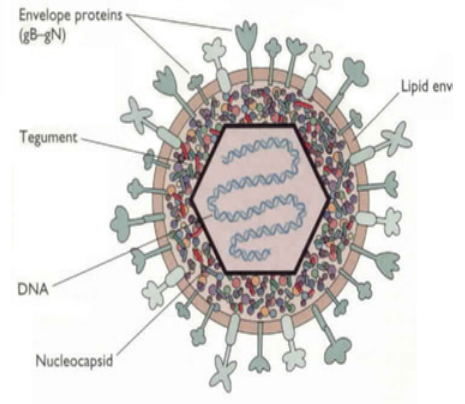
Virion consist of:

- Glycoprotein envelope
- Icosahedral capsid.
- Liner ds-DNA.

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

HSV (1&2) stays in NERVE CELLS:

- **HSV-1** → **Trigeminal ganglia**
 - * Upper part of body → occurs under stress
 - * Recurrence occurs in the same area
- **HSV-2** → **Sacral ganglia**
 - * In the genital area
 - * Recurrence in the sexual area



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 infection

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 **autoinoculation** 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.

Due to Sex through anal area → anal area is very bloody, and mucus is very transparent with blood vessels → easy transmission of virus

2. Perinatal transmission (during delivery):

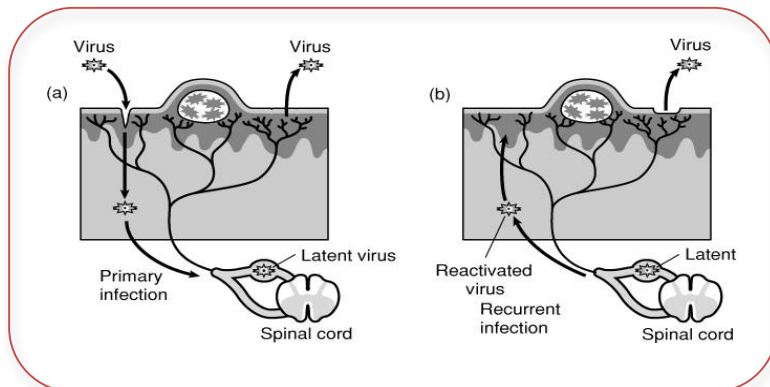
- * Majority of maternal infection (85%) occurs during delivery, due to direct contact between the baby and infected maternal birth canal. (Birth canal is filled with bacteria)
- * **Primary** genital herpes → risk of perinatal transmission usually occurs in about 50%
- * **Recurrent** infection → risk of perinatal transmission usually occurs in about 8% (Because the mother has the antibody and she gives it to the baby during pregnancy)
- * 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 (first 16 weeks) can lead 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



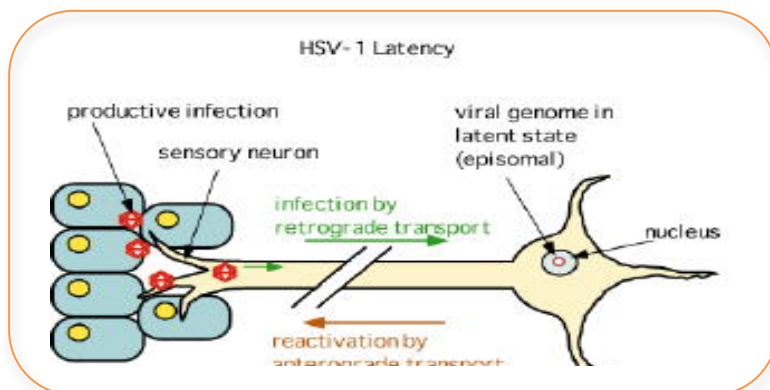
Primary infection:

- 1- Occurs when HSV-2 infects epithelial cells covering the mucosa.
- 2- The virus then migrates to the nearest ganglion (sacral ganglia) via neurons
- 3- There it replicates and establish latency for life.

Recurrent infection:

Once its reactivated, it travels back through neurons to the site of the primary infection inducing a recurrent infection.

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



Clinical features of HSV-2 infection

Primary genital infection with an incubation period of **2-12 days** (short incubation period unlike HPV).

- Symptoms (Vary from mild symptoms to severe painful episode)
 - 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 (seen in the anal area) can be seen in homosexuals.
 - **Aseptic meningitis** has been observed in about 10% of cases as extra genital presentation.

Neonatal herpes infection

- **Not common**
- 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, and brain.

It has three forms:

1- Localized skin infection.

- Limited to massive skin vesicular lesions
- Mild infection

HSV-1 causes encephalitis while HSV-2 causes meningitis

2- Localized brain infection.

- Limited to CNS invasion causing encephalitis. (Encephalitis or meningitis)
- 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

Diagnosed firstly by history then:

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 that decreases the immunity.
- Can be as **frequent as six or more episode a year**
- Attacks are milder and shorter than primary genital herpes episode.
- Accompanied with the appearance of herpetic vesicles on the external genitalia.
- Symptoms may include pain and itching.

Recurrence in HSV-2 s more than HSV-1

Lab diagnosis of HSV

Diagnosed by history first, followed by:-

- 1- **ELISA:** (done when ulcer is seen) 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. (To detect if it is HSV-1 or HSV-2)
- 3- **Polymerase chain reaction (PCR):** CSF sample in case of neonatal herpes.
 - Expensive
 - Done in neonatal HSV to detect meningitis and 100% determine whether it is HSV-1 or HSV-2

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)

- 1- Will give you a 100% accurate result
- 2- Not done routinely, done for research

Management of HSV

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

Drugs:

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

Human Papillomavirus (HPV)

Family of *Papillomaviridae*.

Virion is small non-enveloped, and consist of:

Icosahedral capsid. Circular ds-DNA, 55nm in diameter.

HPV infect epithelial tissues of skin and mucous membrane (**genital area**)

There are more than 150 distinct HPV subtypes.

HPV can not grow in tissue culture (**unlike HSV**)

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 of HPV

HPV cause disease only in skin and mucous membranes, 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
- The potential to cause malignant lesions (**HPV 16,18, 31,45**)

Types of warts and HPV genotype

1. Cutaneous warts (All three are benign and only cause a cosmetic problem more than anything else)

- The virus is transmitted from infected skin, either by direct contact or through fomites and enters its new host through **abrasions** (scraped area of skin).
- Swimming pools and changing rooms are fertile sources of infection; skin warts are most liable to affect young children.
 - * Common Warts (strain HPV 2,4) **Benign and never turns malignant but is cosmetically bad → contagious**
 - * Plantar Warts (strain HPV 1,2,4) **Mostly seen in changing rooms and swimming pools**
 - * Flat Warts (strain HPV 3,10)

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

Diagnosis of cutaneous warts: (doctor said its not important)

- 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 hybridization techniques e.g. Southern blot, PCR, and hybridization in situ.

2. Genital warts (Anogenital or mucosal Warts):

- These Warts are acquired by sexual contact
- One of the most common sexually transmitted diseases
- Often occur in association with other sexual diseases as gonorrhoea 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.

Clinical symptoms of genital warts:

- Appear after **3-4 months** after infection (I.P) (Long incubation period unlike HSV)
- Warts size varies 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.

Common sites for infection include:

- The penis, scrotum, perineum, anal canal,
- Perianal region, vagina, vulva and cervix.

The major manifestations of anogenital HPV include:

They may be transmitted to baby during delivery.

1. Genital warts (condyloma acuminatum) **Benign HPV 6,11**
 - * Low risk
 - * It could be benign but could block the genital area, causes cosmetic issues, or cause infertility
2. Squamous intraepithelial lesions **Malignant**
 - * **High-risk**
 - * Cervical carcinoma in females (**HPV 16,18, 31,45**)
 - * Penile and anal carcinoma in males (**HPV 16,18**)
3. Laryngeal Warts (**benign HPV 6,11**)
 - * It is transmitted to the baby with a mother infected with condyloma acuminata
 - * Can affect the babies voice, vocal cords or its breathing

Link between HPV and cervical cancer

- HPV type 6 and 11 (Condylomata acuminata):
 - is usually benign and unusual to become malignant
- HPV 16 and 18 (squamous intraepithelial lesion):
 - 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 HPV

- External genital warts → easily diagnosed by medical examination.
- Internal genital warts → visualized by colposcopy.

Lab diagnosis:

- **Polymerase chain reaction (PCR) is used to detect HPV DNA** (it's important to know the genotype to help determine whether it's benign or malignant)
- Pap-smear test is used to identify abnormal epithelial cells of the cervix (cervical dysplasia). (For follow up and protection against cervical cancer)
- In-situ DNA hybridization is used for HPV genotyping.

HPV treatment

1- Cryotherapy:

- freezing warts by liquid nitrogen
- suitable for small external warts

2- Electrocautery 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- Topical treatment:

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

6- Injection:

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

The Doctor said it's not that important to know all of this just read it

She only mentioned that in cutaneous warts the treatment is cutaneous

Laser and Cryotherapy are the most common

HPV Prevention

There are two vaccines available **Gardasil** and **Cervarix** and both are: (Both are given IM)

- 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 useful for older patients)
- Not given to pregnant women.

Gardasil:

A quadrivalent vaccine (Protects against benign and malignant) 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.

Herpes has no vaccine unlike HPV

Herpes has a treatment unlike HPV

Summary

Genital Herpes:

- Genital herpes can be caused by two species of herpes virus HSV-1 (10%) and HSV-2 (90%)
- Once the virus enters the human body it remains for life (latency)
- Transmitted : 1- Sexually 2- Perinatally 3- Intra-uterine (vertically)
- an incubation period of 2-12 days
- To avoid perinatal infection we do Caesarean section.
- Diagnosed by: 1- Elisa 2- Immunofluorescence (IF) 3- PCR 4- Tissue Culture
- Has no vaccine
- Treated by: Acyclovir (First choice + safe in pregnancy), Famciclovir, Valacyclovir

HPV:

- Icosahedral capsid. Circular ds-DNA,
- Types of warts: 1- Cutaneous warts 2- Genital warts (3-4 months incubation period)
- Important genotypes: Malignant (HPV 16,18, 31,45) Benign (HPV 6,11)
- Persistent HPV infection is considered the main cause of cervical cancer
- 90% of positive Pap-smear is due to HPV infection
- Trichloroacetic acid (T.C.A) safe in pregnancy (topical treatment)
- Has two available Vaccines: Gardasil, Cervarix (contraindicated in pregnancy)
- Diagnoses :
 - External genital warts → easily diagnosed by medical examination.
 - Internal genital warts → visualized by colposcopy
- Lab diagnosis:
 - PCR
 - Pap-smear
 - In-situ DNA hybridization is used for HPV genotyping

Herpes has no vaccine unlike HPV

Herpes has a treatment unlike HPV

Questions

Q1: 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

Q2: Which of the following HPV genotypes is malignant?

- A. 6
- B. 18
- C. 11
- D. 70

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

Q4: Primary cause of Cervical cancer is:

- A. HIV
- B. Gonorrhoe
- C. HPV
- D. HSV



Good luck on your
exams everyone!

Answers:

- A
- B
- A
- C