Human Papilloma Virus.

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- HPV is the most common sexually transmitted infection (STI).
- HPV is so common that nearly all sexually active men and women get it at some point in their lives.
- There are many different types of HPV, some types can cause health problems including genital warts and cancers.

How is HPV spread?

- It spreads by having vaginal, anal, or oral sex with someone who has the virus.
- It is most commonly spread during vaginal or anal sex.
- HPV can be passed even when infected person has no signs or symptoms.

- The person can can develop symptoms years after having sex with someone who is infected making it hard to know when the person first became infected.

Does HPV cause health problems?

- In most cases, HPV goes away on its own and does not cause any health problems.
- But when HPV does not go away, it can cause health problems like genital warts and cancer.

1. Genital warts (condyloma acuminata)

2. Vulvar intraepithelial neoplasia (VIN)(dysplasia) low grade and high grades
3. Vaginal intraepithelial neoplasia (VaIN) low and high grades
4. Cervical intraepithelial neoplasia (CIN)(SIL) low and high grades

5. Cervical adenocarcinoma in situ
6. Anal intrapeithelial neoplasia
7. Vaginal and vulvar carcinomas
8. Cervical squamous cell carcinoma
9. Cancer of anus
10. Cancer of penis

- Cancer often takes years, even decades, to develop after a person gets HPV.
- The types of HPV that can cause genital warts are not the same as the types of HPV that can cause dysplasia and cancers

- There is no way to know which people who have HPV will develop cancer
- People with weak immune systems (including individuals with HIV/AIDS) may be less able to fight off HPV and more likely to develop health problems from it.

- At least 70 genetically distinct types of HPV have been identified.
- Some types (e.g., 1, 2, 4, and 7) cause benign skin squamous papillomas (warts) in humans.

Lesions in genital tract

1. Genital warts(condyloma acuminaum):

- Are associated with low-risk HPVs, predominantly HPV-6 and HPV-11.

2. Vulvar , vaginal and cervical intraepithelial neoplasia

- Are caused mainly by high risk HPV 16, 18

3. Baseloid and warty vulvar carcinoma

- Caused mainly by HPV 16

4. Vaginal squamous cell carcinoma

- Caused mainly by HPV 16,18

5. Cervical squamous cell carcinoma

- Caused by HPV 16,18

6. Cervical adenocarcinoma insitu

- Caused by HPV 16, 18

pathogenesis

- In benign genital warts , the HPV genome is maintained in a nonintegrated form
- In cancers the HPV genome is integrated into the host genome, suggesting that integration of viral DNA is important for malignant transformation,

- Integration interrupts the viral DNA within the E1/E2 open reading frame, leading to loss of the E2 viral repressor and overexpression of the oncoproteins E6 and E7.

- The oncogenic potential of HPV can largely be explained by the activities of the two viral genes encoding E6 and E7

Oncogenic activities of E6.

- The E6 protein binds to and mediates the degradation of p53,

- E6 from high-risk HPV types has a higher affinity for p53 than E6 from low-risk HPV types.

- Interestingly the E6-p53 interaction may offer some clues regarding polymorphisms and risk factors for development of cervical cancer.
- *TP53* is polymorphic at codon 72, encoding either a proline or arginine residue at that position.

- The p53 Arg72 variant is much more susceptible to degradation by E6.
- Not surprisingly, infected individuals with the Arg72 polymorphism are more likely to develop cervical carcinomas.

Oncogenic activities of E7.

- The E7 protein has effects that complement those of E6, all of which are centered on speeding cells through the G_1-S cell cycle checkpoint.

- It binds to the RB protein and displaces the E2F transcription factors that are normally sequestered by RB, promoting progression through the cell cycle.
- As with E6 proteins and p53 ,E7 proteins from high-risk

HPV types have a higher affinity for RB than do E7 proteins from low-risk HPV types.

- E7 also inactivates the CDK inhibitors p21 and p27.
- Finally, E7 proteins from high-risk HPVs (types 16, 18, and 31) also bind and presumably activate cyclins E and A.

- Co-transfection with a mutated *RAS* gene results in full malignant transformation.
- In addition to such genetic co-factors, HPV in all likelihood also acts in concert with environmental factors.

- These include

a. Cigarette smoking,

b. Coexisting microbial infections,

c. Dietary deficiencies, and hormonal changes, all of which have been implicated in the pathogenesis of cervical cancers.

- A high proportion of women infected with HPV clear the infection by immunologic mechanisms, but others do not, some for unknown reasons, some because of acquired immune abnormalities, such as those that result from HIV infection.

- As might be expected, women who are coinfected with high-risk HPV types and HIV have an elevated risk of cervical cancer.

- The peak risk for HPV infection is within the first five to ten years of the first sexual experience.
- A second peak in HPV infection prevalence occurs in women ≥45 years of age in all regions with the exception of Asia, where rates continue to decline beyond 45 years of age.(

- Possible explanations for the second peak of HPV infection include

a. Reactivation of latent infection,

b. or new infections because of age-related social or behavioral change

- The extent to which infections occurring in later life are associated with subsequent risk of cancer and pre-cancer is not yet known.

HPV in men

- The HPV in Men (HIM) study is an ongoing study
- Multiple types were detected
- while HPV type 16 is the most common oncogenic type detected , followed by HPV type 51 and HPV type 59)

- The overall seroprevalence of HPV was significantly higher among women
- Among males, type-specific seropositivity varied by age with peaks observed at ages 40 to 49 years for types 6 and 11 respectively) and 50 to 59 years for types 16 and 18

- The peaks occurred approximately ten years later among males than among females.
- overall HPV seroprevalence is lower than for females and is likely due to differences in the immune response induced by HPV infection among males, rather than lower infection rates.