

Human papillomavirusinfection epidemiology and disease associations

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HPV

- It's double-stranded DNA viruses and infect only humans
- There are more than 200 types of HPV
- (cutaneous or mucosal)
- 40 type infect anogenital organ
- HPVs are small, nonenveloped, capsid viruses with an 8 kilobase circular genome that encodes eight genes (2 encapsulating structural proteins, L1 and L2)

- The L1 protein expressed recombinantly in a cell-culture system self-assembles in the absence of the viral genome to form a virus-like particle (VLP)
- The L1 VLP is the immunogen used in the HPV vaccines
- L2 is the minor capsid protein

- Initial infection of the basal stem cell occurs as the result of microscopic breaks in the epithelium
- The infecting HPV virions attach to the basal stem cell via tissue-specific heparan sulfate proteoglycans
- Specific gene products are transcribed at every level of differentiation of the squamous keratinocyte

Natural history

- Most HPV infections, typically resolve within **12 months**
- During productive cervical HPV infection, low-grade cytological abnormalities may be detectable in screening, but are usually **transient**
- carcinogenic HPV infections that persist beyond 12 months increase the likelihood of precancerous or cancerous lesions
- the median age of cytologically detected precancerous cervical lesions occurs approximately **10 years** after the median age of sexual debut

- HPV can enter a **latent** state
- Incubation period is 3 weeks to 8 months
- there is evidence of cervical viral **reactivation** in some populations, including females with HIV and older females

Genotypes and tissue tropism

- **Cutaneous**
- plantar warts, common warts (types 1, 2, and 4.)
- flat warts (types 3 and 10),
- butcher's warts(types 7 and 2)
- **Anogenital epithelium**
- penis, scrotum, perineum, anal canal, perianal region, vaginal introitus, vulva, and cervix
- **40 mucosal** HPV genotypes can infect the genital tract

Anogenital disease

- Genital warts (condyloma acuminatum)
- These are benign anogenital warts, caused most often by HPV types 6 and 11
- Squamous intraepithelial lesions and/or carcinoma of the vagina, vulva, cervix, anus, or penis
- **15 HPV types** are associated with cancer and are known as high risk, carcinogenic, or cancer associated
- **HPV 16** is the most common and is associated with the highest risk of progression to cancer

- The presence of a cervical T-zone **is not necessary** for oncogenic HPV to infect the female genital tract
- the prevalence of oncogenic HPV subtypes in the vagina is similar in females who have and have not undergone hysterectomy
- **Other mucosal surfaces**
- HPV type 16 can infect the oral mucosa and has been associated with SCC of the oral cavity
- Recurrent respiratory papillomatosis

DISEASE ASSOCIATIONS

- **Cervical cancer**
- IT is the 4th most common cancer among females
- **All** cases of cervical cancer are attributable to HPV infection, with HPV **16** accounting for 50 % of cases and HPV **18** for 20 %
- 31,33,45,52,58(19%)
- **Vulvar and vaginal cancer**
- they are uncommon
- HPV infection has been estimated to be 29 to 43 % for vulvar cancer, 87 % for VIN, 70 % for vaginal cancer, and 69 to 100 % VaIN

- **Genital warts**
- Sexuality active (1 - 10%)
- Peak 17-33y
- HPV types 6 and 11 cause approximately 90 percent of genital warts
- In children, anogenital warts are associated with HPV types typically isolated from common warts (types 1 and 2)

- It may increase the number and size
- 1/3 regress with out treatment in 4 months
- HPV infection may persist despite resolution of visible warts and recurrence later
- Malignant transformation of warts is rare
- Biopsy refractory or atypical

- **Anal cancer**
- It is uncommon (90% HPV types 16 and 18)
- female > male
- Men who have sex with men and HIV
- **Oropharyngeal cancer**
- HPV-related oropharyngeal cancers occur in a younger population than the non-HPV-associated cancers and are associated with sexual risk factors (high-risk sexual behaviors, oropharyngeal HPV infection, and HPV 16)
- Non HPV-associated (alcohol and tobacco)

- **Recurrent respiratory papillomatosis**
- it is the most common benign laryngeal tumor in children and is thought to be caused by HPV acquired during passage through the birth canal of an infected mother (HPV 6 and 11)
- The incidence has been estimated at 4.5 per 100,000 children
- Morbidity obstruction of larynx by warts

Other cutaneous diseases

- Bowen's disease
- a form of high-grade intraepithelial neoplasia, has both genital and extragenital forms
- (fingers, toes, palms, feet, and on the genital mucosa)
- Epidermodysplasia verruciformis
- is a rare AR condition characterized by the appearance of HPV-induced wart-like lesions in childhood, with malignant transformation in half of patients during adulthood, often in skin surfaces with sun exposure
- Hpv 5 and 8

- **Penile cancer and precursor lesions**
- Penile cancer is uncommon and accounts for up to 10 % of male cancers
- not all cancers of the external genitalia are associated with HPV infection
- Hpv 16 ,18 40%
- Younger age

EPIDEMIOLOGY OF ANOGENITAL INFECTION

- anogenital HPV is the most common sexually transmitted infection
- 5.5 million infection annually in US
- peak prevalence of HPV infection occurs within the first decade after sexual debut, (between the ages of 15 to 25 years)
- Secondary minor peak after menopause (reactivation)
- at least 80 % of sexually active individuals are exposed to HPV once in their lifetime

- Most common worldwide hpv16
- But most of female are infected with at least one non-hpv 16 , 18 typ
- Geographic variation in the distribution of HPV genotype

Risk factor for infection

- Genital infection are transmitted by genital-genital or anal-genital contact (sexuality activity)
- Number of sex partener
- New sex partener
- Both vaginal and anal intercourse
- Prior STDs
- HIV and immunsupression

- Smoking
- Male circumcision

- Female to male transmission occur at higher rate than male to female
- Correct and consistent condom use reduce the risk of HPV infection
- But don't completely prevent