

Human Papillomavirus (HPV)

Clinical Manifestation & Diagnosis

Eshaghi H. MD

Associated professor in pediatric infectious disease

Tehran university of medical sciences

Children medical center

Routes of HPV Transmission in Children

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graph LR; A[Routes of HPV Transmission in Children] --> B[Vertical (Perinatal) Transmission]; A --> C[Horizontal (NonSexual) Transmission]; A --> D[Sexual Transmission]; B --> B1[Exposure during passage through infected birth canal]; B --> B2[Detection of HPV DNA in neonates shortly after delivery]; B --> B3[Most infections are transient and cleared within months]; C --> C1[Direct skin-to-skin contact (common warts)]; C --> C2[Fomites: shared objects, towels, toys (less common)]; C --> C3[Autoinoculation from existing lesions]; D --> D1[Relevant mainly in adolescents and Not in younger children]; D --> D2[In prepubertal children, requires careful evaluation for possible abuse]; D --> D3[Genital-to-genital ,Oral-genital ,Hand-genital contact];
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Vertical (Perinatal) Transmission

- Exposure during passage through infected birth canal
- Detection of HPV DNA in neonates shortly after delivery
- Most infections are transient and cleared within months

Horizontal (NonSexual) Transmission

- Direct skin-to-skin contact (common warts)
- Fomites: shared objects, towels, toys (less common)
- Autoinoculation from existing lesions

Sexual Transmission

- Relevant mainly in adolescents and Not in younger children
- In prepubertal children, requires careful evaluation for possible abuse
- Genital-to-genital ,Oral-genital ,Hand-genital contact

NonSexual Transmission

- ❑ Human papillomavirus (HPV) is a non-enveloped virus, making it relatively resistant to desiccation, mild heat, and common detergents.
- ❑ HPV is more resistant to 70% ethanol than enveloped viruses.
- ❑ Effective virucidal agents include:
 - Sodium hypochlorite (0.5–1%)
 - Glutaraldehyde (2%)
 - Hydrogen peroxide (>1%)
 - Steam autoclaving (121 °C, moist heat)

NonSexual Transmission

- ❑ In vitro studies have demonstrated that HPV virions can persist for several days to even weeks on *moist or semi-moist* surfaces such as doorknobs, towels, examination tables, or medical instruments.
- ❑ Under *dry conditions* at room temperature, viral DNA may remain detectable for up to 3 days, with limited infectivity.

NonSexual Transmission

- ❑ HPV may remain viable on environmental surfaces for several days up to one week, but fomite-borne transmission is unproven and extremely unlikely.
- ❑ Therefore, in nonsexual exposures among children (e.g., shared towels, toilets, or swimming facilities), the risk of transmission is very low but not zero.

Vertical transmission

- Vertical transmission through mother-to-child is critical as the transmitted infection could persist asymptomatically for a long time
- Perinatal transmission has been is the most possible cause of HPV presence in newborns.
- Furthermore, the risk of infection in infants increases if they are born to HPV-positive mothers

Notic

- Mucosal HPVs are generally sexually transmitted.
- Nonetheless, these lesions have been detected in infants and children either in oral or anogenital mucosa, indicating a nonsexual pattern of transmission.

Clinical Manifestation

Clinical Manifestation

- ❑ HPV: DNA virus with >100 types in children.
- ❑ Most infections are benign and self-limited
- ❑ Clinical spectrum:
 - Cutaneous
 - Mucosal
 - Respiratory lesions

☐ Cutaneous Manifestation

Cutaneous Manifestation

❑ Common warts (verruca vulgaris)

- Common warts are small, grainy skin growths that occur most often on the fingers or hands.
- They're rough to the touch and often have tiny black dots. These dots are clotted blood vessels
- Can appear as a single wart or in clusters
- Exposure to HPV within family and school environments significantly contributes to wart development in children, with higher transmission risks in these settings



Cutaneous Manifestation

❑ Plantar warts

- Plantar warts are small, rough growths on the feet.
- They usually show up on the balls and heels of the feet, the areas that bear the most pressure
- Painful, may impair walking



Cutaneous Manifestation

❑ Flat warts

- Face, Dorsal hands,
- Often multiple
- Typically resolve spontaneously within months to years



□ Mucosal Manifestations

Mucosal Manifestations

❑ Oral papillomas

- Small, Exophytic lesions on Tongue, Palate, Buccal mucosa
- Of the classified HPV genotypes, approximately 25 types are associated with oral lesions, including high-risk ones such as HPV 16, HPV 18, and low-risk HPVs like types 6 and 11 as the most commonly detected ones.



Mucosal Manifestations

❑ Anogenital warts

- Condyloma acuminata
- Rare in prepubertal children
- Require careful evaluation for possible sexual abuse
- Usually caused by HPV types 6 and 11
- Spread through skin-to-skin contact during sexual activity
- May be asymptomatic in some cases, Itching, burning, or pain
- Diagnosed by visual examination by a healthcare professional however biopsy may be performed to confirm the diagnosis

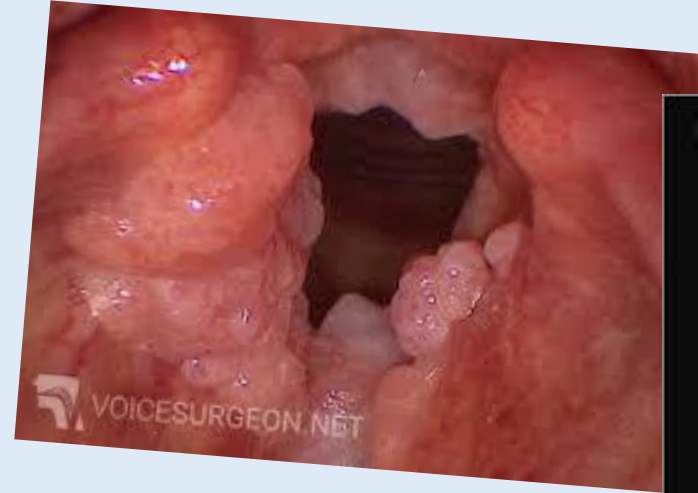


□ Respiratory Manifestations

Mucosal Manifestations

□ Respiratory Manifestations

- Recurrent Respiratory Papillomatosis (RRP)
 - Caused mainly by HPV 6 and 11
 - Hoarseness, stridor, airway obstruction
 - May require repeated surgical interventions
 - Strongly linked to vertical transmission during birth



Juvenile-onset recurrent respiratory papillomatosis (JORRP)

- The most common benign proliferative disease of the respiratory epithelium in children, caused by chronic infection with the human papillomavirus (HPV) 6/11.
- Typically, JORRP manifests first between ages 2 and 3_{yrs}, with a roughly equal distribution between males and females.

Juvenile-onset recurrent respiratory papillomatosis (JORRP)

- ❑ For children with JORRP lasting more than one year, it is recommended to distinguish between invasive and non-invasive JORRP based on clinical features.
- ❑ The criteria for invasive JORRP are as follows:
 - Total number of surgeries ≥ 10
 - Average number of surgeries per year ≥ 4
 - Distant spread to the lower airway
 - Children who need or have undergone tracheostomy (GPS)

□ What are the high-risk factors for JORRP recurrence?

- Children with early-onset disease and HPV11 positivity are at higher risk of recurrence and warrant special attention.
- Children from low socioeconomic backgrounds and those with a history of maternal condyloma acuminatum during pregnancy are more likely to relapse, and surveillance is recommended for such patients.

Diagnosis

Diagnosis

Clinical Diagnosis

- Careful inspection of cutaneous, mucosal, and anogenital lesions
- Although most HPV infections are asymptomatic, the typical appearance of verrucae vulgaris on the skin and condyloma acuminata in the anogenital area in otherwise healthy individuals usually is sufficient to establish the clinical diagnosis of HPV infection.
- Clinical morphology often sufficient for warts

➤ What clinical signs and symptoms should be considered in diagnosing JORRP?

❑ Concerning symptoms:

- Emphasis should be placed on hoarseness, particularly if lasting more than 2 months or showing progressive deterioration.
- Attention is advised for inspiratory dyspnea and wheezing.

❑ Signs:

- Focus should be placed on cyanosis, chest retraction, and abnormal breath sounds, especially in severe cases and patients with lower airway lesions

➤ Should all children with hoarseness combined with wheezing, laryngeal obstruction, or difficulty in breathing undergo flexible laryngoscopy?

❑ It is recommended that all children with hoarseness combined with wheezing, laryngeal obstruction, or difficulty in breathing undergo flexible laryngopharyngoscopy once their vital signs are assessed and deemed stable

laboratory Diagnosis

- Laboratory confirmation of HPV-associated lesions may be necessary for unusual manifestations in healthy individuals, for immunocompromised patients, and for patients with suspected malignant lesions.
- Because HPVs cannot be grown in cell culture monolayers, a variety of *molecular methods*, used alone or in combination, are used in research and clinical settings.
- *Cytologic and histologic* approaches also are helpful in diagnosing HPV-associated cancers

Electron Microscopy

- Although not used clinically, electron microscopy can be used to detect virions with typical papillomavirus morphology in cutaneous warts.
- Such virions are difficult to detect in tissue from patients with RRP, JORRP, genital warts, or in histologically diagnosed cancers.

laboratory Diagnosis

Cell Culture

- HPV's have not been propagated in cell culture monolayer.
- Therefore the *routine viral cultures* available in most diagnostic virology laboratories will not detect the presence of HPV's

laboratory Diagnosis

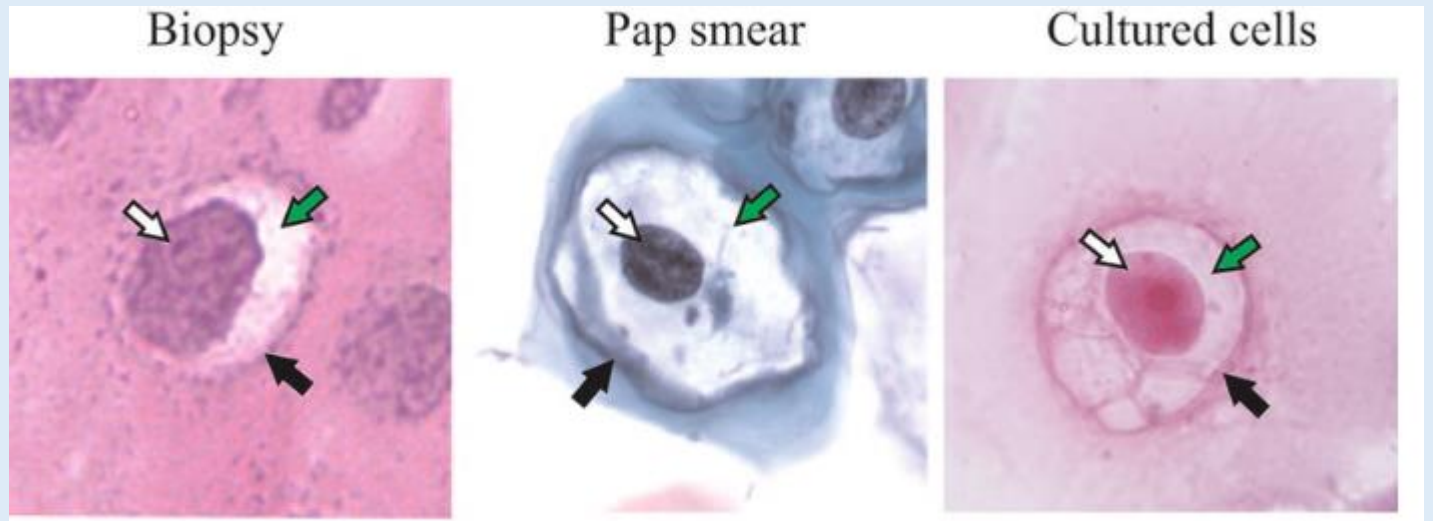
Serology

- HPV serologies are not used clinically and are not available in most diagnostic laboratories.
- Serologic methods have been used extensively in *recent clinical trials of HPV vaccines*.
- However, in natural infection, only 60% of women with proven genital HPV infections mount a detectable type-specific immunoglobulin G (IgG) response

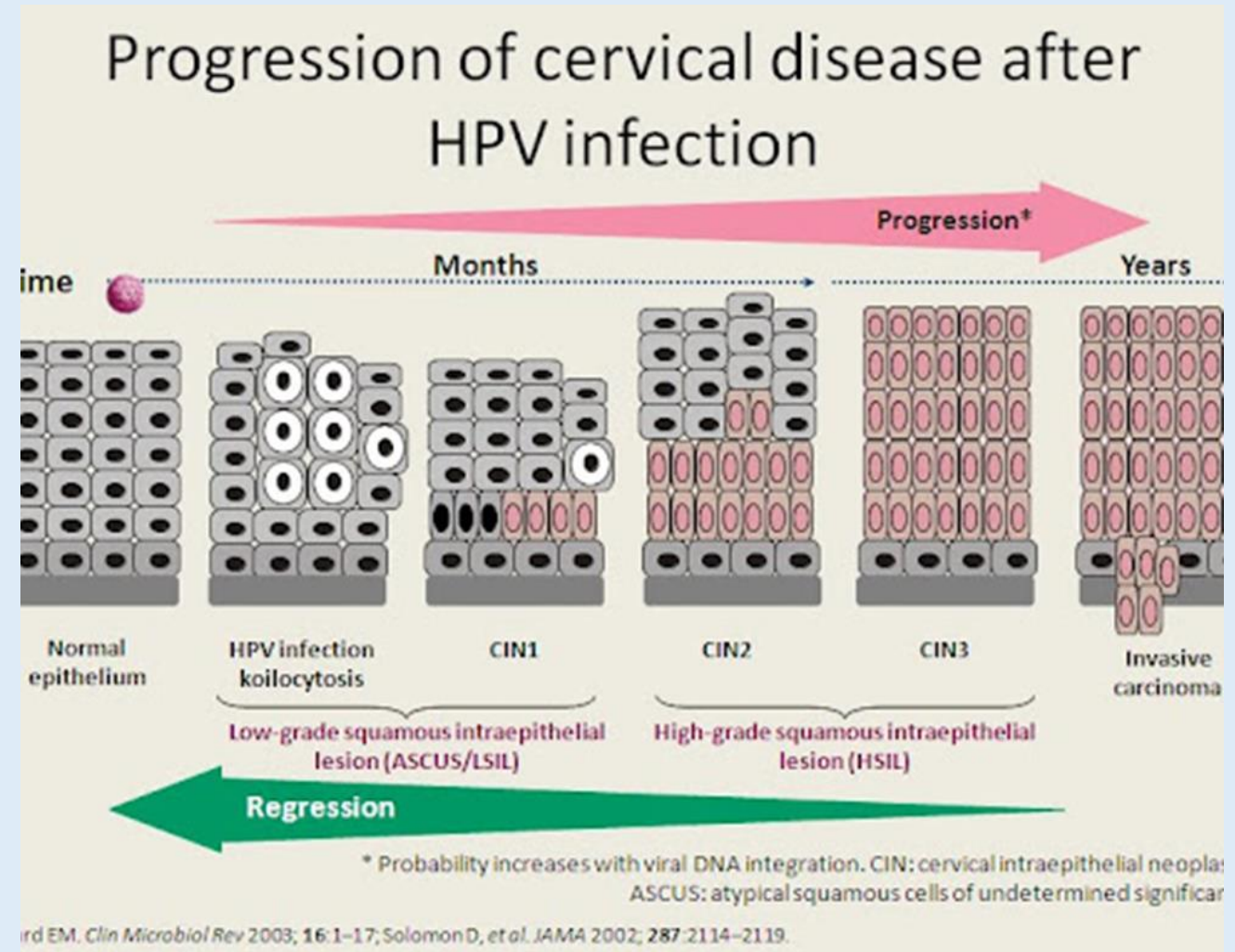
Cytology

- Since the 1960s the Papanicolaou technique for obtaining and staining exfoliated cervical cells (i.e., the Pap smear) has been a procedure used widely as a screening method for detection of dysplastic and malignant cervical epithelial cells.
- The cytologic abnormalities identified on Pap smears reflect the cytopathic effects of HPV infection in cervical epithelial cells.
- The cytologic abnormality characteristic of HPV infection is **koilocytosis**

- Koilocytotic cells display fat, swollen, wrinkled, or raisin-like nuclei surrounded by a halo, giving infected cells an owl's eye-like appearance.



- Cytologic abnormalities evolve in some patients, reflecting progression from infection through dysplasia to cervical squamous cell carcinoma.
- As HPV infection progresses to disease, the *koilocytosis* typically diminishes and the cervical epithelial cells begin to display dysplastic changes and nuclear abnormalities.



- Reflecting the spontaneous resolution rate of HPV infections, most cytologic abnormalities detected on Pap smears resolve spontaneously in 3 to 6 months.

- Despite its relative insensitivity, the widespread and consistent use of the Pap smear has reduced dramatically the incidence of invasive squamous cell carcinoma of the cervix in nations with robust screening programs.
- WHO recommends starting regular cervical cancer screening at the age of 30 years among the general population of women.
- Although screening guidelines vary by country and evolve constantly, cervical cytology *screening* is generally recommended at 1- to 3-year intervals for *sexually active women*

Molecular Methods for Detection of Human Papillomavirus DNA

- In many countries, molecular detection of high-risk HPVs has replaced cytology as the preferred screening method for cervical disease.
- Molecular (typically DNA PCR) HPV testing is based on the observations that HPV genomes are generally present in women with HPV-associated dysplasias. (HPV testing)
- Studies of the sensitivity and specificity of **HPV testing** compared with **HPV cytology** have found that *HPV testing* is more sensitive in detecting HSIL/CIN grade 2 and above (HSIL/CIN2+) in all ages, but *cytology* has a higher specificity.

Colposcopy

- Evaluation by cervical colposcopy typically follows for women with *abnormal Pap* smears or *external anogenital warts*.
- The cervix, vulva, and anus in females or the urethral meatus, penis, scrotum, and anus in males are visualized under magnification with a colposcope to identify lesions, with special attention paid to their topography, the presence of abnormal whitening, and their vascular architecture.
- Biopsy is required for definitive diagnosis. Tissue biopsy specimens are sent for histologic examination and for detection of HPV DNA by molecular techniques.

Histology

- HPV infection most often occurs in histologically normal tissue and is detectable only by molecular methods that detect viral DNA.
- koilocytosis and other histopathologic characteristics of active HPV infection, such as hyperkeratosis, parakeratosis, acanthosis, and lengthening of the rete pegs.
- Atypical features, including mitotic figures above the basal layer, dysplastic cells, and single-cell keratinization, indicate higher grades of dysplasia.
- Grading ,according to cellular atypia and invasion

Cervical Cancer Screening

- Primary high-risk HPV testing should be performed with molecular HPV testing alone (no cytology) with a test that detects high-risk HPV types and is approved by the US Food and Drug Administration (FDA) for stand-alone screening.
- Consistent with prior guidance, screening should begin at age 21 years. Sexually active adolescents should be counseled and tested for sexually transmitted infections and counseled about safe sexual practices and contraception.
- The expertise of the physician who obtains the specimen and of the cytologist who performs the cytologic analysis.
- Care must be taken to obtain cells from at the junction of the squamous and columnar epithelium of the cervix (transformation zone).

Endoscopy & Imaging

- ❑ Flexible laryngoscopy / bronchoscopy:
 - Gold standard for diagnosing RRP
 - Direct visualization of papillomas in airway
- ❑ Imaging (CT/MRI): rarely needed, reserved for extensive airway or atypical cases

Frequently Asked Questions

□ When do antibodies become positive?

- Target antigens: HPV capsid proteins (mainly L1, sometimes L2).
- Antibodies usually appear months after infection, not immediately.
- Seroconversion is more likely after persistent infection or after clinical lesions (e.g., warts, RRP).

□ How long do antibodies remain positive?

- Antibodies can remain detectable for years, especially after persistent mucosal infection or vaccination.
- However, titers may wane over time if infection is cleared.
- Maternal antibodies may be present at birth but decline within the first months.

❑ Should serology be checked clinically?

- Not recommended for routine diagnosis in children.
- Serology cannot distinguish past vs. current infection.
- Many infected children remain seronegative, so a negative test does not exclude infection.

□ When is serology valuable?

- Research & epidemiology:
 - To study exposure rates in populations.
 - To assess maternal–child transmission dynamics.
 - Vaccine monitoring

□ Asymptomatic child exposed to high-risk contact:

- The majority of infected individuals develop transient infections with no visible lesions or symptoms leading to viral clearance within 12–24 months and molecular or serologic tests have no significant clinical value in this context.
- Routine HPV testing is not recommended.
- Periodic clinical examination is sufficient unless a lesion appears.

❑ Asymptomatic neonate born to a high-risk mother:

- Routine HPV testing is not indicated.
- Many neonates who test HPV DNA–positive at birth clear the virus spontaneously within a few months.
- Clinical follow-up only; testing should be performed only if symptoms develop (such as respiratory papillomatosis or mucosal lesions).

□ Child with clinical symptoms or lesions:

- If cutaneous, mucosal, or respiratory lesions are present: clinical diagnosis is the first step.
- In atypical or doubtful cases: perform PCR or biopsy for confirmation.
- For respiratory lesions (e.g., hoarseness, stridor): laryngoscopy or bronchoscopy is mandatory.

□ Asymptomatic child with an HPV-positive parent

- No routine screening is recommended.
- Household contact can lead to transmission, but most infections are transient.
- Educate parents to monitor for cutaneous or mucosal lesions in the child and seek medical evaluation if symptoms appear.

Thank you

For your attention