

Human Papilloma Virus Vaccine



Introduction

- HPVs appear to infect **only humans**
- HPVs infect **epithelial surfaces**, each HPV type has a tropism for specific epithelia.
- The **HPV types** may be classified according to the type of epithelia they infect (**cutaneous or mucosal**).



Introduction

- The **common cutaneous HPV types** are found in various skin warts (e.g., palmar warts, plantar warts, flat warts) and are **uniformly benign**.
- The mucosal HPVs occur mainly in **the anogenital tract** but also infect and produce disease at mucosal sites in the **respiratory tract, the oropharyngeal cavity, and the conjunctiva**.



Introduction

- The mucosal HPV types are **subclassified** according to the **oncogenic potential** of each virus
- The mucosal HPVs are subgrouped into **low-, high-, and intermediate** or moderate-risk types, depending on the **frequency** with which they are found in invasive cancers.
- Certain mucosal types (**low risk**) are associated with **warts or papillomas of mucous membranes**, including the upper respiratory tract and anogenital, oral, nasal, and conjunctival areas.
- (**high risk**) mucosal types can cause precancers and cancers, including cervical, anogenital, and oropharyngeal cancers.



Cutaneous warts



Condition	Usual Location	Morphology	HPV Type
Cutaneous (Skin) Warts			
Common (verruca vulgaris)	Hands, lips, extremities	Multiple, dome shaped	2, 4
Plantar (verruca plantaris)	Bottom of feet	Single, painful	1
Flat (verruca plana)	Arms, face, knees	Multiple	3, 10, 28, 41
Filiform	Face, neck	Multiple, threadlike	2, 4
Mosaic	Feet, hands	Multiple, superficial	7
Butcher's	Hands	Multiple, dome shaped	7
Epidermodysplasia verruciformis	Face, trunk, extremities	Multiple flat warts or reddish-brown plaques	5, 8, 9, 12, 14, 15, 17, 19–25, 36–38, 47, 49
Immunosuppressed patients	Face, trunk, extremities	Dome-shaped or epidermodysplasia verruciformis–like plaques; may be persistent or progressive	1–5, 8, 10, 20, 23, 28, 49



Mucosal warts



Mucosal (Anogenital) Warts

Subclinical	Cervix	Asymptomatic	6, 11, 13, 16, 18, 30–35, 39, 40, 42–45, 51–59
Condylomata acuminata	Cervix, vulva, urethra, anus, penis, scrotum	Multiple exophytic, pink, gray	6, 11, 16
Flat condylomata	Cervix	Asymptomatic, flat plaques	6, 11, 16, 18, 31
Giant condylomata acuminata (Buschke-Löwenstein tumors)	Perirectal area	Large, tumorlike	6, 11
Bowenoid papulosis	Penis, vulva, perirectal area	Multiple, large	16
Cervical cancer	Cervix	Asymptomatic; pigmented papillomas; erythematous or white plaques; ulcerations; mass lesion	Strong association: 16, 18, 31, 45 Moderate association: 30, 33, 35, 39, 51, 52, 56, 58, 59, 68 Weak association: 6, 11, 26, 34, 40, 43, 44, 53–55, 57, 62, 66, 74
Vaginal cancer	Vagina	Asymptomatic; ulcerative mass lesions; vascular pattern with punctation and mosaicism	16
Vulvar cancer	Vulva	Asymptomatic; pigmented papillomas; erythematous or white plaques; ulcerations; mass lesion	16
Penile cancer	Penis	Painless, ulcerative mass lesion	16
Anal cancer	Perianal area, anal canal	Asymptomatic; pigmented papillomas; erythematous or white plaques; ulcerations; mass lesion	16, 18, 31
Ovarian cancer	Ovaries	Unknown	6?, 16?, 18?

Mucosal warts



Mucosal (Other) Warts			
Respiratory papillomatosis	Larynx, trachea, bronchi, lungs	Multiple papillomas	6, 11
Nasal and paranasal papillomas	Nose, paranasal sinuses	Single or multiple papillomas	6, 11, 57, 57b
Focal epithelial hyperplasia (Heck disease)	Oral cavity	Discrete, multiple nodules	13, 32
Oral cavity papillomas	Gums, buccal mucosa, soft palate, tonsils	Single or multiple papillomas	6, 11, 16
Conjunctival papillomas	Conjunctivae	Single or multiple papillomas	6, 11, 16
Giant cell hepatitis	Liver	Unknown	6?



HPV Vaccines

- Three HPV vaccines have been licensed by the FDA:
 - ✓ A **quadrivalent** vaccine (4vHPV [types 6, 11, 16, and 18], **Gardasil**) was licensed by the FDA in **2006**.
 - ✓ A **bivalent** vaccine (2vHPV [types 16 and 18], **Cervarix**) in **2009**.
 - ✓ A **9-valent** HPV vaccine (9vHPV [types 6, 11, 16, 18, 31, 33, 45, 52, and 58], **Gardasil 9**) in **2014**.



HPV Vaccines

- ✓ **Oncogenic HPV types**
 - 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68
- ✓ **9-valent HPV vaccine (Gardasil 9)**
 - types 6, 11, 16, 18, 31, 33, 45, 52, 58
- ✓ **quadrivalent vaccine (Gardasil 4)**
 - types 6, 11, 16, 18
- ✓ **bivalent vaccine (Cervarix)**
 - types 16 and 18
- HPV types 16 and 18 are found in 70% of cervical cancers



Vaccine name	Gardasil-4	Cervarix	Gardasil-9	Cecolin	Papilloguard-2	Cervavax	Walrinvax (Walvax)	Papilloguard-4
valency	Quadrivalent	Bivalent	Nonavalent	Bivalent	Bivalent	Quadrivalent	Bivalent	Quadrivalent
Manufacturer	Merck	GSK	Merck	Wantai BioPharm	Nivad pharmed	Serum Institute of India (SII)	Shanghai Zerun Biotechnology	Nivad pharmed
Country	USA	Belgium	USA	China	Iran	India	China	Iran
Approval date	2006(FDA)	2009(FDA)	2014(FDA)	2019	2020	2023	2023	2025

Immunogenicity

- **More** than **97%** of **healthy** vaccine recipients develop antibodies to HPV vaccine types after vaccination.
- Antibody titers are **higher** in adolescent females and males aged **9 through 15** years compared with females and males **16 through 26** years of age.



Efficacy

- HPV vaccines are **most effective** when administered **before exposure** to any of the HPV types included in the vaccine.
- HPV vaccines have not been proven to have a **therapeutic effect** on existing HPV infection or disease and do not offer protection against **progression of infection** to disease from HPV acquired before immunization.



Vaccine Recommendations

- The AAP and the ACIP recommend routine HPV vaccination for **females and males**.
- The **AAP** recommends starting the series between **9 and 12** years,
- The **Advisory Committee on Immunization Practices (ACIP)** recommends starting the series at age **11 or 12** years of age and can be administered starting at age 9.
- When HPV vaccine is begun at 9 or 10 years of age, other adolescent vaccines (eg, **MenACWY and Tdap**) still are recommended to be administered at 11 to 12 years of age.



Catch-up HPV vaccination

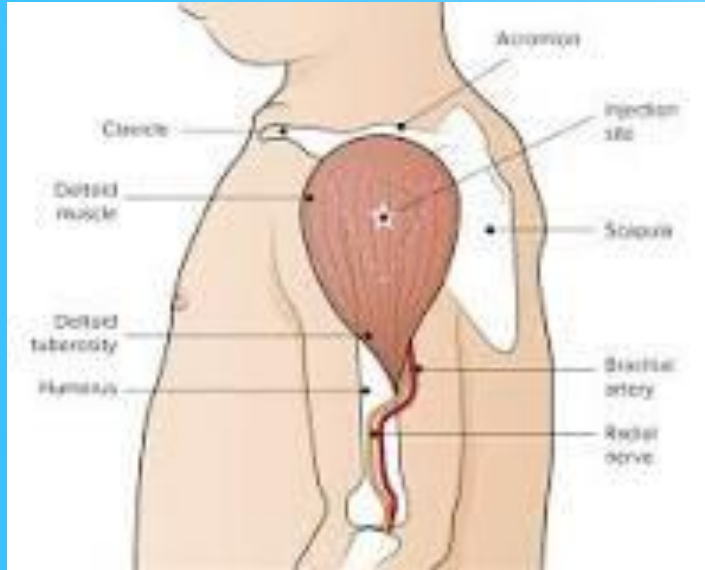
- Catch-up HPV vaccination is recommended for **all people through age 26 years** who are not adequately vaccinated.
- Catch-up HPV vaccination **is not recommended** for all **adults >26 years of age**.
- Instead, shared clinical decision-making regarding HPV vaccination is recommended for **some adults 27 through 45 years of age** who are not adequately vaccinated.



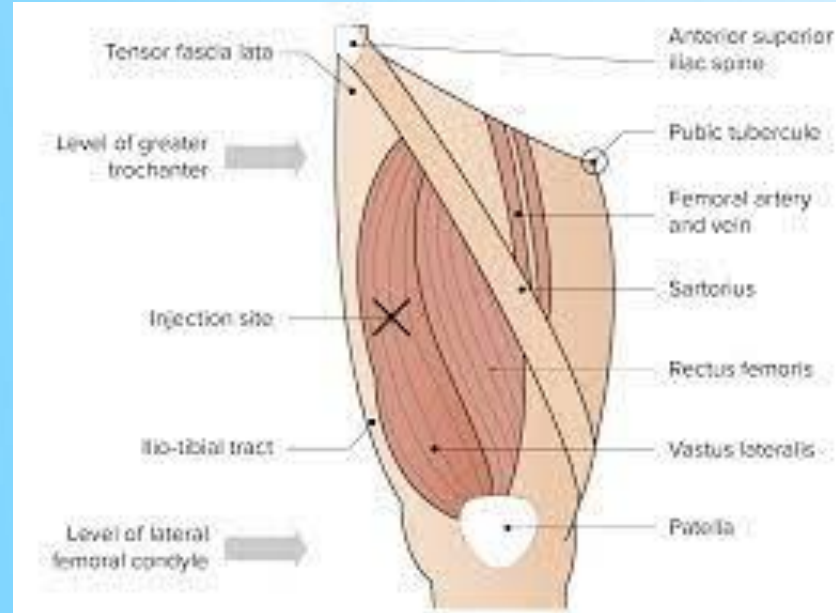
Dosage and Administration

- HPV vaccine is administered in either **2 or 3 doses** of **0.5 mL**, **IM**, preferably in a **deltoid muscle**.
- For people initiating vaccination **before their 15th birthday**, the recommended schedule is **2 doses** of HPV vaccine, with the second dose administered **6 to 12 months** after the first dose (**minimum interval 5 months**).





Deltoid region of the upper arm



Higher anterolateral thigh area



Dosage and Administration

- For people initiating vaccination **on or after their 15th birthday**, the recommended schedule is **3 doses** of HPV vaccine.
- In a **3-dose** schedule, the second dose should be administered at least **1 to 2 months** after the first dose (**minimum interval 4 weeks**), and the third dose should be administered 6 months after the first dose (**minimum interval 5 months after first dose, and 12 weeks after second dose**).



Administration

- If the vaccine schedule is **interrupted**, the vaccine series can be continued with the next recommended dose and does not need to be restarted.
- **9vHPV** may be used to **complete a series** started with 4vHPV or 2vHPV.
- There is **no recommendation** regarding additional vaccination with 9vHPV for people who previously **completed a 4vHPV or 2vHPV series**.



Co-administration

- HPV vaccines are **not live vaccines**.
- HPV vaccines can be **coadministered with any live or inactivated vaccine** indicated at the same visit.



Evidence of past HPV or current HPV infection or disease

- Evidence of **past HPV exposure or current HPV infection or disease**, such as **abnormal Pap test results, cervical lesions, anogenital warts**, or a positive HPV DNA test result, are not **contraindications** to HPV immunization to protect against any HPV types not already acquired.



Recommendations for Special Populations

- For people ages 9 through 26 years with **immunocompromising** conditions (including primary or secondary immunocompromising conditions that might reduce cell-mediated or humoral immunity), **a 3-dose** schedule of HPV vaccine is recommended **regardless of age** at initiation.
- **Immune response** and vaccine efficacy in immunocompromised people might be **less than** that in immunocompetent people.



primary or secondary immunocompromising conditions

- B-lymphocyte antibody deficiencies
- T-lymphocyte complete or partial defects
- HIV infection
- malignant neoplasms
- transplantation
- autoimmune disease
- immunosuppressive therapy



The recommendation for a 3-dose HPV schedule does not apply to children 9 through 14 years with:

- asplenia
- asthma
- CGD
- chronic liver disease
- CRF
- CNS anatomic barrier defects (such as a cochlear implant)
- complement deficiency
- diabetes
- heart disease
- sickle cell disease

unless the person is receiving immunosuppressive therapy for the condition.



WHO recommendation

- WHO has updated its recommendations for the HPV vaccine.
- a **single-dose schedule**, can provide a comparable **efficacy and durability** of protection to a two-dose regimen.
- The optimization of the HPV schedule is expected to improve **access to the vaccine**, offering countries the opportunity to expand the number of girls who can be vaccinated



WHO now recommends:

- A **one or two**-dose schedule for girls aged **9-14** years
- A **one or two**-dose schedule for girls and women aged **15-20** years
- **Two doses** with a **6-month interval** for women older than **21** years



WHO now recommends:

- The position paper underscores the importance of vaccinating as a **priority immunocompromised** people, or those living with HIV.
- Immunocompromised individuals should receive at a **minimum two doses** and where **possible three doses**.



WHO now recommends:

- The **primary target** of vaccination is **girls** aged **9-14**, prior to the start of sexual activity.
- The vaccination of **secondary targets** such as **boys** and **older females** is recommended where feasible and affordable.
- **Cervical cancer** is the **fourth most common** type of cancer in women, and more than **95% of cervical cancer** is caused by sexually transmitted HPV.



WHO

- more research is needed to determine the **efficacy and duration** of protection for this schedule, particularly in **males**.
- **Vaccine Choice:** The nonavalent (**9vHPV**) vaccine is recommended as it provides protection against the most HPV types



Vaccine Adverse Events, Precautions, and Contraindications

- shown **no serious safety** concerns.
- **local** adverse events of injection site discomfort or pain, redness, and swelling are the **most commonly** reported.
- **Systemic** symptoms after HPV vaccine can include headache, fever, nausea, dizziness, and fatigue/malaise.



Vaccine Adverse Events, Precautions, and Contraindications

- **Syncope (fainting)** has been reported in adolescents after receipt of any vaccination, including HPV vaccine.
- Vaccine providers, particularly when vaccinating adolescents, should observe patients (with patients **seated or lying down**) for **15 minutes** after vaccination to decrease the risk for injury should they faint.
- If syncope develops, patients should be observed until symptoms resolve.



Precautions and Contraindications

- HPV vaccines can be administered to people with **minor acute illnesses**.
- Immunization of people with **moderate or severe** acute illnesses should be deferred until after their condition improves.
- HPV vaccines are **produced in yeast(*Saccharomyces cerevisiae*)** and are **contraindicated** in people with a history of immediate hypersensitivity to any vaccine component, including yeast.



pregnancy and lactation

- HPV vaccines are **not recommended** for use during **pregnancy** because of **limited information** about safety but a **pregnancy test** is not required before starting the HPV vaccination
- If a vaccine recipient becomes pregnant, **subsequent doses** should be postponed until she is no longer pregnant.
- Data to date show no evidence of adverse effect of any HPV vaccine on **outcomes of pregnancy**.
- If a dose has been administered inadvertently during pregnancy, **no intervention** is needed.
- HPV vaccines can be **administered to lactating women**.



THANK
YOU

