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HUMAN PAPILLOMA VIRUS VACCINE – A REVIEW

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ABSTRACT

Cervical and other anogenital malignancies are mostly caused by the human papilloma virus, or HPV. The prevalence of HPV-related illnesses has dramatically decreased globally as a result of preventative vaccination. This paper provides an in-depth overview of the HPV vaccine, including its mechanism of action, indications, dosing, safety profile, global availability, manufacturers, and cost-effectiveness.

Keywords: Cervical intraepithelial neoplasia, Gardasil, Cervarix, Cervavac ,Cecolin

INTRODUCTION

As a major contributor to the prevalence of cervical and other anogenital and oropharyngeal malignancies, the Human Papillomavirus (HPV) continues to be a widespread global health concern in 2025. Approximately 70% of cervical cancer occurrences worldwide are caused by high-risk HPV strains, particularly 16 and 18. While the majority of HPV infections are temporary and immune system-cleared, high-risk infections might cause cancer if they continue.

Epidemiology:

Current Epidemiology of HPV (2025)

Global Prevalence

1. Over 80% of sexually active people are predicted to get infected with HPV at some point, making it the most prevalent STI in the world.
2. The Approximately 70% of instances of cervical cancer are caused by high-risk HPV strains, particularly 16 and 18 **[1]**.

3. Increasing rates of oropharyngeal, anal, penile and vaginal cancers.

Burden by Region

High prevalence in sub-Saharan Africa, Southeast Asia and parts of Latin America where screening and vaccination are limited. In developed countries, HPV vaccination and screening programs have reduced cervical cancer incidence, particularly in women under 30.

Vaccination Coverage (as of 2025)

Global HPV vaccine coverage: ~60–65% in females, ~40–45% in males

Countries with school-based vaccination programs (e.g., UK, Australia, and Canada) show marked decline in genital warts and CIN lesions.

Trends

Decline in HPV 6, 11, 16, and 18 in countries using the 9-valent vaccine (Gardasil 9).

Increase in HPV-related oropharyngeal cancers, particularly in males, due to changes in sexual practices.

WHO goal (by 2030): 90% of girls fully vaccinated by age 15, 70% of women screened, 90% of positive cases treated **[2]**.

Infographic-style Breakdown: Key HPV Risk Factors

Risk FactorEx planation

1. Multiple Sexual Partners Increases exposure to different HPV strains.
2. Early Sexual Debut More years of exposure to potential infection.
3. Unprotected Sex Lack of condom use raises transmission risk
4. Immunosuppression (e.g., HIV) Reduces ability to clear infection.
5. Smoking Alters immune response and epithelial cell.
6. Oral Sex (unprotected) Associated with oropharyngeal HPV infections.

Pathogenesis:

- HPV typically occurs during sexual contact and infects basal epithelial cells through microabrasions in the skin or mucosa.
- After entering the host cell, the virus multiplies by taking advantage of the cellular apparatus.
- In high-risk HPV strains, the early viral genes E6 and E7 are especially significant because they disrupt the tumor suppressor proteins p53 and retinoblastoma protein (pRb), respectively **[3]**. Unchecked cell division, genetic instability, and the possibility of developing dysplasia and cancer are the results of this.
- HPV remains episomal (non-integrated) in benign lesions but may integrate into the host genome in high-grade lesions and cancers, further enhancing oncogene expression and malignant transformation **[4]**.

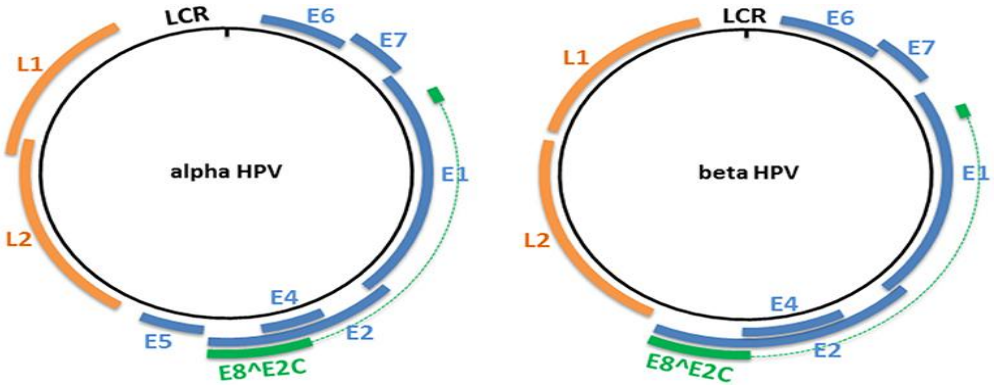

Figure 1:
(Adapted from: https://images.app.goo.gl/APThaX55KBhAKBJg8)

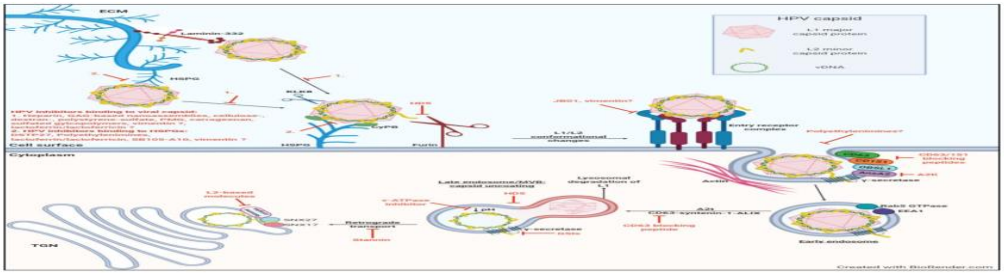

Figure 2:
(Adapted from: https://images.app.goo.gl/dXwquqwqHdYD7VA78)

Signs & symptoms:

HPV infections are often asymptomatic, especially in the early stages. Most individuals clear the virus spontaneously within 1–2 years. However, persistent infection—especially with high-risk types—can lead to clinical manifestations ranging from benign warts to precancerous lesions and cancers.

1. Cutaneous HPV (Low-Risk Types)

- Affects skin, especially hands and feet.
- Common in children and young adults.

Symptoms:

- Verruca vulgaris, or common warts, are elevated, rough-surfaced lesions that typically appear on the hands, knees, or fingers. Hard, uncomfortable nodules on the soles of the feet are called plantar warts.**[5]**
- Flat warts (verruca plana): Smooth, flat-topped lesions often found on the face or legs.

2. Anogenital Warts (*Condylomata Acuminata*)

- Caused mainly by HPV types 6 and 11 (low-risk).
- Highly contagious and transmitted via sexual contact.

Symptoms:

- Soft, fleshy growths in the genital or anal region.
- May be single or multiple, small or large, flat or cauliflower-like.

- Usually painless but may cause: ○ Itching ○ Burning ○ Bleeding ○
- Discomfort during intercourse or urination Locations: ● Males: penis, scrotum, anus.
- Females: vulva, vagina, cervix, anus.
- May also appear in the mouth and throat (oral-genital contact). **[6]**

3. High-Risk HPV Symptoms and Complications - High-Risk HPV and Associated Lesions Most commonly types 16, 18, 31, 33, 45, etc. **[7]**

Often asymptomatic in early stages.

Cervical Intraepithelial Neoplasia (CIN)

- Detected via Pap smear or HPV DNA test.
- Asymptomatic in early stages (CIN 1–3). **[8]**
- Progression may lead to cervical cancer if untreated.

Symptoms of advanced cervical cancer:**[9]**

a. Irregular vaginal bleeding (post-coital or intermenstrual)
b. Odorous vaginal discharge
c. Back or pelvic pain
d. Pain during intercourse

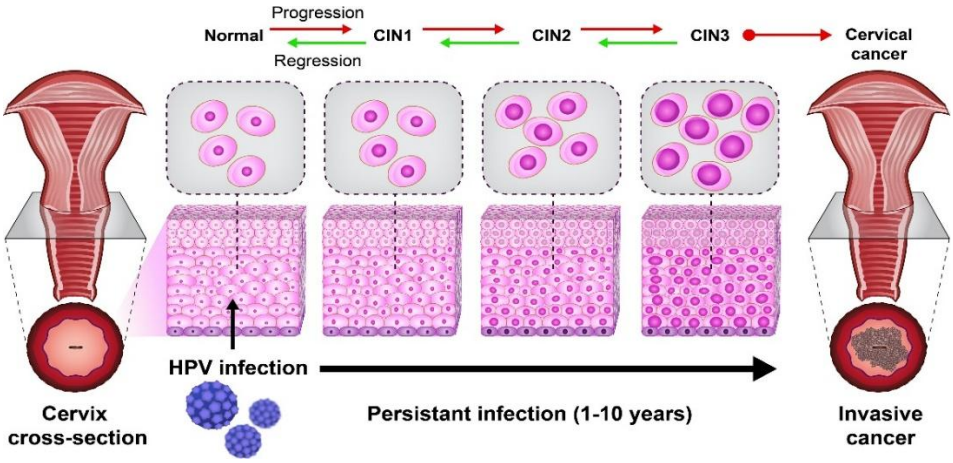

Figure 3
(Adapted from: https://images.app.goo.gl/Ahb6DRgtHyBPeWCa7)

PATHOLOGY:

1. Skin/Mucosa Layers ○ Show the stratified epithelium: basal layer → spinous → granular → superficial layer.**[10]**
2. HPV Entry ○ Arrows indicating entry through a micro-abrasion to basal cells.
3. Viral Life Cycle ○ Infection in basal cells → replication in mid-layer → assembly and release in superficial layers.
4. Molecular Targets ○ Highlight E6 → p53 degradation. ○ Highlight E7 → pRb inactivation.

5. Outcomes ○ Normal infection: transient lesions. ○ Persistent infection: genomic integration → dysplasia → cancer **[11]**.

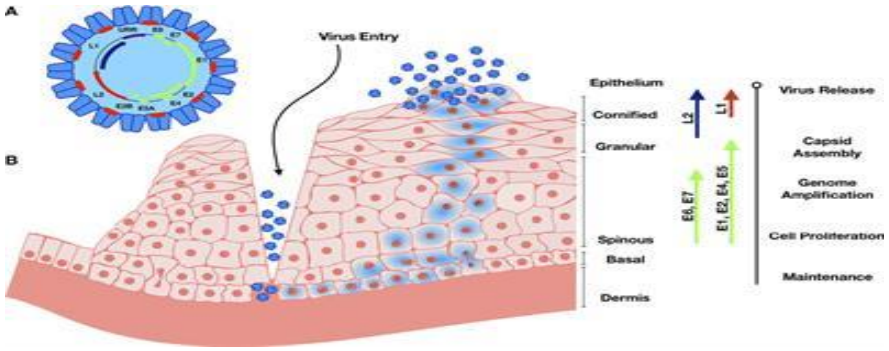

Figure 4
(Adapted from :https://images.app.goo.gl/SiHfbq5thWPDWhsT7)

Types of HPV:

Low-Risk HPV Types:

- These kinds are not linked to cancer and typically result in benign lesions like warts.
- HPV 6 – Commonly causes genital warts and respiratory papillomatosis.
- HPV 11 – Also causes genital warts and respiratory papillomatosis.
- Other low-risk types (not mentioned explicitly): HPV 42, 43, 44.**[12]**

High-Risk HPV Types

These types are associated with precancerous lesions and various cancers, especially cervical cancer.

- HPV 16 – Most oncogenic; linked to cervical, anal, oropharyngeal, and penile cancers.**[13]**
- HPV 18 – Second most common high-risk type for cervical cancer.
- HPV 31, 33, 45 – Also significantly associated with high-grade cervical lesions and other anogenital cancers. **[14]**

Note: High-risk HPV types can be asymptomatic for years but still pose a risk for progression to cancer if persistent.

Current and Emerging Treatments for HPV

No Cure for HPV Infection Itself: Treatment is targeted at HPV-induced lesions or cancers. Warts: Cryotherapy, topical agents (imiquimod, podophyllotoxin), laser therapy.

Cervical Precancer: Loop Electrosurgical Excision Procedure (LEEP), cryosurgery, conization.

Cancers:

1. Surgery, chemotherapy, and radiation depending on the cancer type and stage.

2. Immunotherapy and Targeted Therapies (2025 Updates):

Therapeutic Vaccines (Emerging): ○ Vaccines under trial to treat existing HPV infections by stimulating cytotoxic T-cell responses (e.g., VGX-3100, ISA101b).

Combining vaccines with immune checkpoint inhibitors (like PD-1 blockers) has shown promise.

Gene Editing Approaches: ○ CRISPR-Cas systems are being explored to target and disable HPV oncogenes (E6/E7).

Adoptive T-cell Therapy: ○ Autologous T-cells engineered to target HPV-infected cells are in early clinical trials.

3. Antiviral Research:

Cidofovir derivatives and new nucleoside analogs under evaluation for direct antiviral activity against HPV.

HUMAN PAPILLOMA VIRUS VACCINE

Vaccine Composition and Types HPV vaccines are based on virus-like particles (VLPs) composed of the L1 major capsid protein of HPV.**[15]**

These VLPs elicit a strong neutralizing antibody response without containing viral DNA, ensuring they are non-infectious.

The three major vaccines approved globally include:

a) Cervarix (bivalent; targets HPV types 16, 18) – GlaxoSmithKline
b) Gardasil (quadrivalent; targets HPV types 6, 11, 16, 18) – Merck & Co.
c) Gardasil 9 (nonavalent; targets types 6, 11, 16, 18, 31, 33, 45, 52, 58) – Merck & Co. Recent developments include Cervavac by the Serum Institute of India, a low-cost quadrivalent vaccine aimed at improving accessibility in low- and middle-income countries. **[16]**

Mechanism of Action:

The vaccine stimulates the host immune system by inducing the production of type-specific neutralizing antibodies against the HPV L1 protein.These antibodies prevent initial infection by neutralizing the virus at the site of entry. Since HPV infection is usually localized to epithelial tissues, circulating antibodies can effectively prevent viral attachment and entry into host basal epithelial cells.

Dosing Schedule and Administration

HPV vaccines are administered intramuscularly (usually in the deltoid region) based on age and immune status:

Ages 9–14 years : Two-dose schedule at 0 and 6–12 months **[17]**

Ages 15–26 years (and immunocompromised individuals): Three-dose schedule at 0, 1–2 months, and 6 months **[18]**. Catch-up vaccination is recommended up to age 26 ; vaccination between 27–45 years may be considered

based on individual risk and shared clinical decision-making.

Indications and Target Population

Both males and females should get vaccinated against HPV, preferably prior to engaging in sexual activity. Routine immunization is typically initiated at 11–12 years of age , though it can begin as early as age 9. The vaccine is approved for individuals up to 45 years in many countries, though the preventive benefit diminishes with age and prior exposure.

Safety and Adverse Effects

Vaccines are generally safe and well-tolerated.

Clinical trials and post-marketing surveillance have shown a strong safety profile. **[19]**

Common adverse effects include:

Local responses include injection site discomfort, edema, and redness. Systemic effects: headache, fever, fatigue, and myalgia Rare adverse effects: Syncope (especially in adolescents; observation recommended post-vaccination. Anaphylaxis (very rare; contraindication to further doses if occurred) No causal association has been established between HPV vaccination and autoimmune or neurological disorders.

Contraindications and Precautions

Hypersensitivity to any component of the vaccine (e.g., yeast proteins in Gardasil)

Pregnancy (vaccination should be postponed; no teratogenicity observed) Acute febrile illness (delay vaccination until recovery)

Cost and Accessibility

HPV vaccine pricing varies significantly by region and manufacturer:

Gardasil 9: USD 150–200 per dose (high-income countries)

Cervarix: USD 100–150 per dose

Cervavac (India): ~INR 250–400 per dose (~USD 3–5), making it the most affordable option globally National immunization programs in several countries, including Australia, the UK, and Rwanda, provide HPV vaccines free of cost to eligible populations.

Public Health Impact

Widespread HPV vaccination has led to:

>85% reduction in HPV types 6, 11, 16, and 18 infections

Significant decline in high-grade cervical intraepithelial neoplasia (CIN 2/3) **[20-22]**.

Early evidence of decreased cervical cancer incidence in vaccinated cohorts Herd immunity benefits have been observed in unvaccinated individuals, particularly males in communities with high female vaccination rates.

CONCLUSION

The HPV vaccine represents a landmark in cancer prevention, offering safe, effective, and long-term protection against multiple cancers and genital warts. Achieving the

World Health Organization's objective of eradicating cervical cancer as a public health issue requires expanding worldwide coverage, particularly in low-income areas.

REFERENCES

[1] Gultekin M., Ramirez P.T., Broutet N., Hutubessy R. World Health Organization call for action to eliminate cervical cancer globally. Int. J. Gynecol. Cancer. 2020;30:426–427. doi: 10.1136/ijgc-2020-001285. [DOI] [PubMed] [Google Scholar]

[2] Toh Z.Q., Russell F.M., Garland S.M., Mulholland E.K., Patton G., Licciardi P.V. Human Papillomavirus Vaccination After COVID-19. JNCI Cancer Spectr. 2021;5:pkab011. doi: 10.1093/jncics/pkab011. [DOI] [PMC free article] [PubMed] [Google Scholar]

[3] IARC Monographs On the Evaluation of Carcinogenic Risks to humans, Human Papillomaviruses, 90, International Agency for Research on Cancer, Lyon (FR) (2007) Google Scholar

[4] Straight, S. W., P. M. Hinkle, R. J. Jewers, and D. J. McCance. 1993. The E5 oncoprotein of human papillomavirus type 16 transforms fibroblasts and effects the downregulation of the epidermal growth factor receptor in keratinocytes. J. Virol. 67:4521-4532. [DOI] [PMC free article] [PubMed] [Google Scholar]

[5] Lin C, Franceschi S, Clifford GM. Human papilloma virus types from infection to cancer in the anus, according to sex and HIV status: a systematic review and meta-analysis. Lancet Infect Dis. 2018 Feb; 18(2): 198-206.

[6] H. Geng, Y. Xing, J. Zhang, K. Cao, M. Ye, G. Wang, et al.Association between viral infection other than human papillomavirus and risk of esophageal carcinoma: a comprehensive meta-analysis of epidemiological studies Arch Virol, 1 2022, 1, 1-20

[7] Satterwhite CL, Torrone E, Meites E, Dunne EF, Mahajan R, Ocfemia MCB. et al. Sexually transmitted infections among US women and men: prevalence and incidence estimates, 2008. Sex Transm Dis. 2013;40(3):187–93. doi: 10.1097/OLQ.0b013e318286bb53. [DOI] [PubMed] [Google Scholar]

[8] S. Lagström, A.H. Løvestad, S.U. U mu, *et al.* HPV16 and HPV18 type-specific APOBEC3 and integration profiles in different diagnostic categories of cervical samples

Tumour Virus Res., 12 (2021), Article 200221, 10.1016/j.tvr.2021.200221

[9] Massad LS, Einstein MH, Huh WK, Katki HA, Kinney WK, Schiffman M, Solomon D, Wentzensen N, Lawson HW., 2012 ASCCP Consensus Guidelines Conference. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis. 2013 Apr;17(5 Suppl 1):Suresh. [PubMed] [Reference list]

[10] Hummel, M., J. B. Hudson, and L. A. Laimins. 1992. Differentiation-induced and constitutive transcription of human papillomavirus type 31b in cell lines containing viral episomes. J. Virol. 66:6070-6080. [DOI] [PMC free article] [PubMed] [Google Scholar]

[11] Graham SV. The human papillomavirus replication cycle, and its links to cancer progression: a comprehensive review. Clin Sci (Lond). 2017;131(17):2201–21.

[12] Bouvard V., Baan R., Straif K., Grosse Y., Secretan B., El Ghissassi F., Benbrahim-Tallaa L., Guha N., Freeman C., Galichet L., et al. A review of human carcinogens—Part B: Biological agents. Lancet. Oncol. 2009;10:321–322. doi: 10.1016/S1470-2045(09)70096-8. [DOI] [PubMed] [Google Scholar]

[13] Pimenta J.M., Galindo C., Jenkins D., Taylor S.M. Estimate of the global burden of cervical adenocarcinoma and potential impact of prophylactic human papillomavirus vaccination. BMC Cancer. 2013;13:553. doi: 10.1186/1471-2407-13-553. [DOI] [PMC free article] [PubMed] [Google Scholar]

[14] Lin C., Franceschi S., Clifford G.M. Human papillomavirus types from infection to cancer in the anus, according to sex and HIV status: A systematic review and meta-analysis. Lancet Infect. Dis. 2018;18:198–206. doi: 10.1016/S1473-3099(17)30653-9. [DOI] [PMC free article] [PubMed] [Google Scholar]

[15] Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human papillomavirus vaccination for adults: updated recommendations of the Advisory Committee on Immunization Practices. MMWR

Morb Mortal Wkly Rep 2019; 68: 698– 702.

[16] World Health Organization Human papillomavirus vaccines: WHO position paper, May 2017. Wkly. Epidemiol. Rec. 2017;92:241–268. [PubMed] [Google Scholar]

[17] World Health Organization. Evidence based recommendations on human papilloma virus (HPV) vaccines schedules. Background paper for SAGE discussions. Geneva: WHO; 2014.

[18] Munoz N, Kjaer SK, Sigurdsson K, Iversen OE, Hernandez-Avila M, Wheeler CM, et al. Impact of human papillomavirus (HPV)-6/11/16/18 vaccine on all HPV-associated genital diseases in young women. J Natl Cancer Inst 2010; 102: 325– 39.

[19] American Cancer Society. HPV vaccine facts. Atlanta, GA: ACS; 2018. Available at: https://www.cancer.org/cancer/cancer-causes/infectious-agents/hpv/hpv-vaccine-facts-and-fears.html.

[20] Zimet GD, Mays RM, Winston Y, Kee R, Dickes J, Su L. Acceptability of human papillomavirus immunization. J Womens Health Gend Based Med 2000; 9: 47– 50.

[21] Vasantha G, Ravi Kiran D, Sirisha K. A Review on virus outbreak affecting human era during. 2000-2022. 2024, 13(3): 1091-1114.

[22] Vasantha G, Sirisha K, Ravikiran D. Overview of Viruses and their Pandemic Impact during 20th Century.2023,14(18): 63080-63100.