
“Up Close & Personal: HPV Vaccine in a Clinical Setting”

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Outline

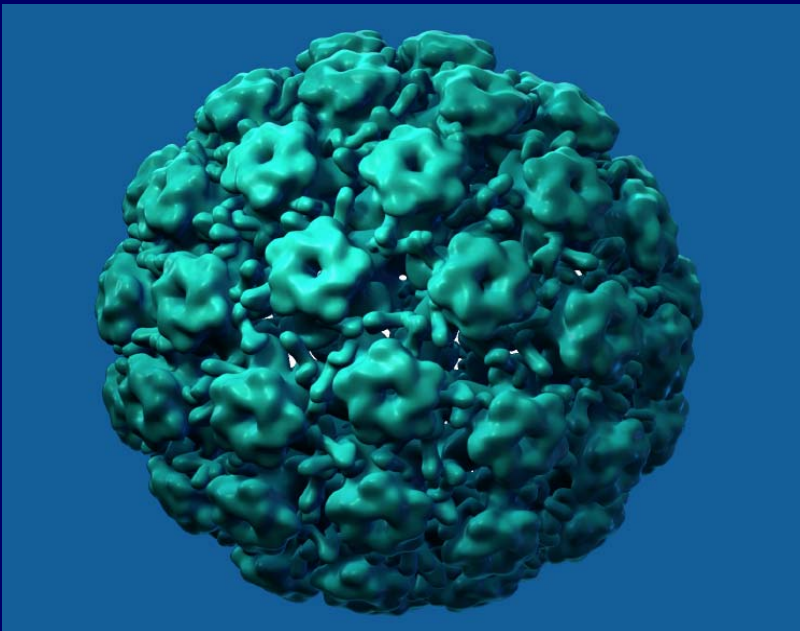
- Definition of Genital HPV Infection
- HPV Types
- Prevalence
- Classification of Histological Findings
- Clinical Manifestations of HPV
- Clinical Diagnosis of HPV
- Natural History of HPV Infection and Potential Progression to Cervical Cancer
- Prevention of Cervical Cancer: GARDASIL Vaccine
- Common Questions By Parents
- Concluding Statements

What is genital HPV infection?

- Genital HPV infection is a sexually transmitted disease/infection (STD/STI) that is caused by human papillomavirus (HPV).
- Human papillomavirus is the name of a group of viruses that includes more than 100 different strains or types.
- More than 30 of these viruses are sexually transmitted.
- HPV is transmitted primarily through genital contact.
- Most infected persons are unaware they are infected, yet they can transmit the virus to a sex partner.
- Rarely, a pregnant woman can pass HPV to her baby during vaginal delivery.
- **Infections with high-risk HPV types may ultimately lead to cervical cancer**

Human Papillomavirus (HPV)

Nonenveloped double-stranded
DNA virus¹



- >100 types identified²
- 30–40 anogenital^{2,3}
 - 15–20 oncogenic^{*,2,3} types, including 16, 18, 31, 33, 35, 39, 45, 51, 52, 58⁴
 - ✓ HPV 16 (54%) and HPV 18 (13%) account for the majority of worldwide cervical cancers.⁵
 - Nononcogenic[†] types include: 6, 11, 40, 42, 43, 44, 54⁴
 - ✓ HPV 6 and 11 are most often associated with external anogenital warts.³

*High risk; †Low risk

1. Howley PM. In: Fields BN, Knipe DM, Howley PM, eds. *Fields Virology*. 4th ed. Philadelphia, Pa: Lippincott-Raven; 2001:2197–2229. Reprinted with the permission of Lippincott-Raven. 2. Schiffman M, Castle PE. *Arch Pathol Lab Med*. 2003;127:930–934. 3. Wiley DJ, Douglas J, Beutner K, et al. *Clin Infect Dis*. 2002;35(suppl 2):S210–S224. 4. Muñoz N, Bosch FX, de Sanjosé S, et al. *N Engl J Med*. 2003;348:518–527. 5. Clifford GM, Smith JS, Aguado T, Franceschi S. *Br J Cancer*. 2003;89:101–105.

US HPV Anogenital Infection Statistics

- By 50 years of age, at least 80% of women will have acquired genital HPV infection.¹
- Estimated new infections per year: 6.2 million¹
- Estimated active infections (prevalence): 20 million²
- In sexually active individuals 15–24 years of age, ~9.2 million are currently infected.³
 - An estimated 74% of new HPV infections occur in this age group.³
 - In studies of women <25 years of age, prevalence rates ranged from 28% to 46%.^{4,5}

1. Centers for Disease Control and Prevention. Rockville, Md: CDC National Prevention Information Network; 2004. 2. Cates W Jr, and the American Social Health Association Panel. *Sex Transm Dis*. 1999;26(suppl):S2–S7. 3. Weinstock H, Berman S, Cates W Jr. *Perspect Sex Reprod Health*. 2004;36:6–10. 4. Burk RD, Ho GYF, Beardsley L, Lempa M, Peters M, Bierman R. *J Infect Dis*. 1996;174:679–689. 5. Bauer HM, Ting Y, Greer CE, et al. *JAMA*. 1991;265:472–477.

Estimated Annual Burden of HPV-Related Diagnoses in the United States

9,710 new cases of cervical cancer¹

3,700 deaths estimated in 2006¹

330,000 new cases of high-grade cervical dysplasia (CIN 2/3)²

CIN = cervical intraepithelial neoplasia.

1.4 million new cases of low-grade cervical dysplasia (CIN 1)²

1 million new cases of genital warts³

CIN = cervical intraepithelial neoplasia.

1. American Cancer Society. *Cancer Facts and Figures 2006*. Atlanta, Ga: American Cancer Society; 2006:4.
2. Schiffman M, Solomon D. Findings to date from the ASCUS-LSIL Triage Study (ALTS). *Arch Pathol Lab Med*. 2003;127:946–949.
3. Fleischer AB, Parrish CA, Glenn R, Feldman SR. Condylomata acuminata (genital warts): Patient demographics and treating physicians. *Sex Transm Dis*. 2001;28:643–647.

Classification of Histological Findings: CIN

- Cervical Intraepithelial Neoplasia (CIN)¹
 - CIN 1: Mild dysplasia; includes condyloma (anogenital warts)
 - CIN 2: Moderate dysplasia
 - CIN 3: Severe dysplasia; includes carcinoma *in situ* (CIS)

| CIN ¹ | Normal | CIN 1 (condyloma) | CIN 1 (mild dysplasia) | CIN 2 (moderate dysplasia) | CIN 3 (severe dysplasia/CIS) | | Invasive Cancer |
|--|--------|----------------------|------------------------------|----------------------------------|---------------------------------|--|--------------------|
| Histology of squamous cervical epithelium¹ | | | | | | | |
| Basal cell → Basal membrane → | | | | | | | |

- CIN caused by HPV can clear without treatment; however, rates of regression are dependent on grade of CIN.²

1. Bonnez W. In: Richman DD, Whitley RJ, Hayden FJ, eds. Washington, DC: American Society for Microbiology Press; 2002:557–596. Reprinted with the permission of the American Society for Microbiology Press. 2. Östör AG. *Int J Gynecol Pathol.* 1993;12:186–192.

Clinical Manifestations of HPV

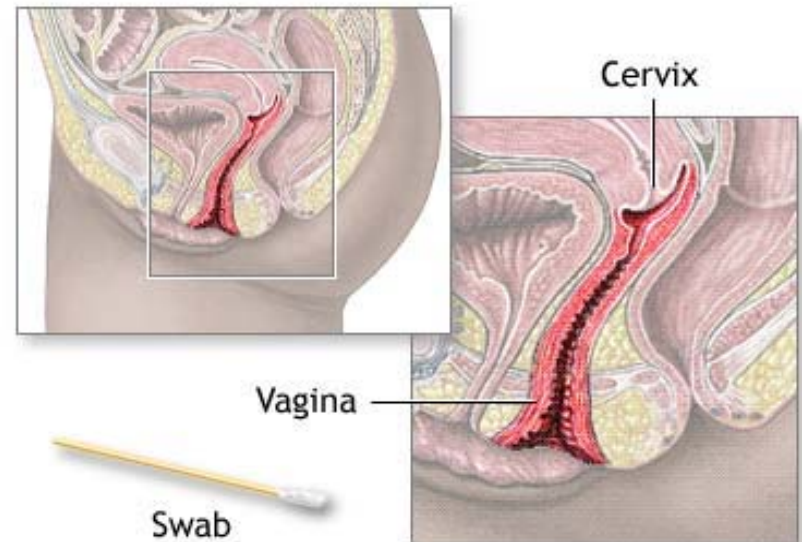
- Most people who have a genital HPV infection do not know they are infected.
- The virus lives in the skin or mucous membranes and usually causes no symptoms.
- Some people get visible genital warts, or have pre-cancerous changes in the cervix, vulva, anus, or penis.

HPV and Anogenital Warts

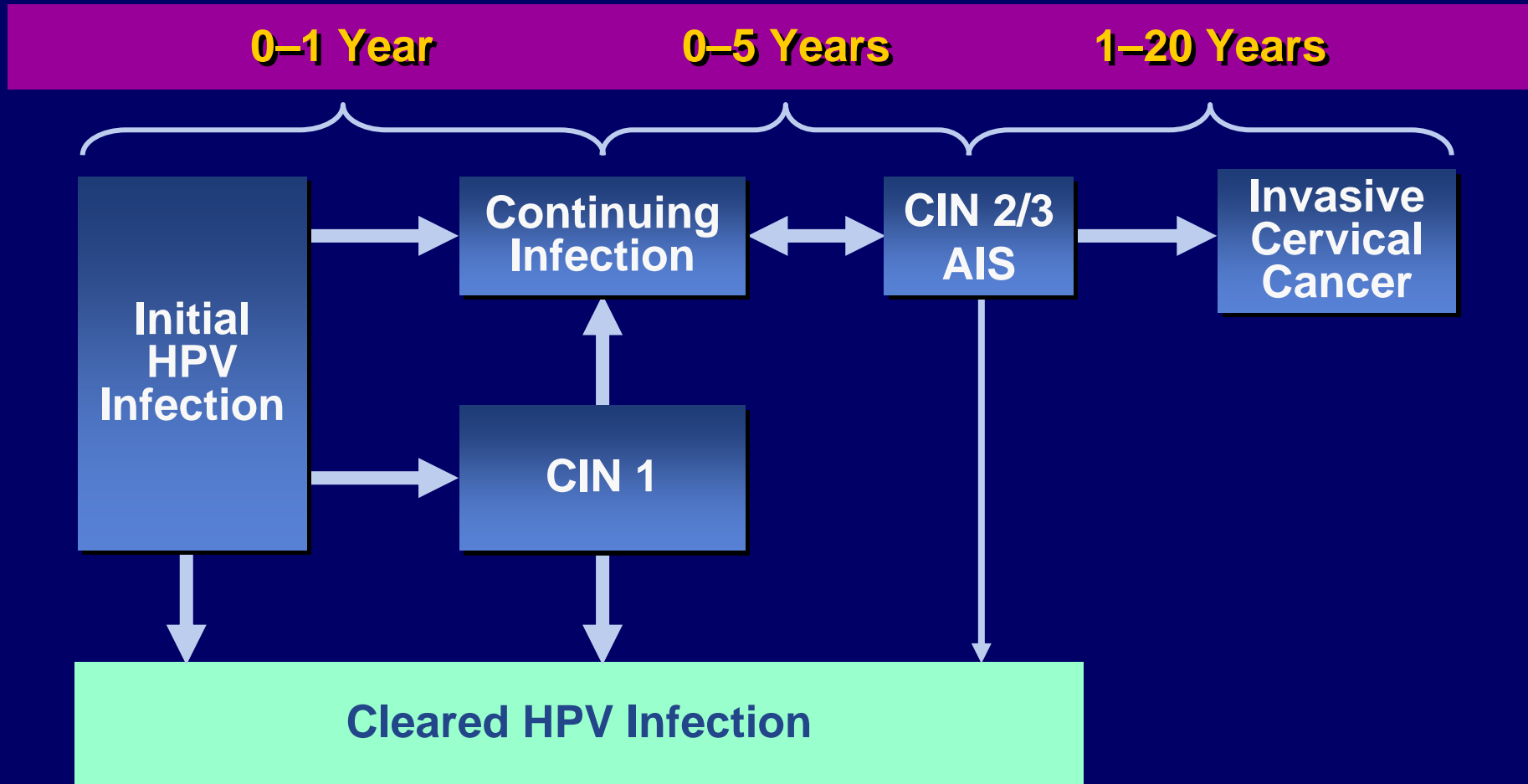
- HPV 6 and 11 responsible for >90% of anogenital warts¹
- Infectivity >75%²
- Up to 30% spontaneously regress within 4 months in women.³
- Treatment can be painful and embarrassing.⁴
- Topical and surgical therapies are available for genital warts.⁵
- Recurrence rates vary greatly.⁵
 - As low as 5% with podofilox or laser treatment
 - As high as 65% with other treatments

Clinical Diagnosis of HPV

- Most women are diagnosed with HPV on the basis of abnormal Pap tests.
- A Pap test is the primary cancer-screening tool for cervical cancer or pre-cancerous changes in the cervix.



Natural History of HPV Infection and Potential Progression to Cervical Cancer¹



AIS = adenocarcinoma *in situ*.

CIN = cervical intraepithelial neoplasia.

1. Pinto AP, Crum CP. *Clin Obstet Gynecol.* 2000;43:352-362.

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Prevention of Cervical Cancer: GARDASIL Vaccine

- GARDASIL is a vaccine that helps protect against the following diseases caused by HPV types 6/11/16/18
 - Cervical cancer (cancer of the lower end of the uterus)
 - Abnormal and precancerous cervical, vaginal and vulvar lesions
 - Genital warts



GARDASIL Vaccine (Con't)

- WHO SHOULD GET GARDASIL?
 - It is indicated for girls and women as young as 9 years (but typically given at 11 years) to 26 years
- PURPOSE OF GARDASIL VACCINATION:
 - To prevent cervical cancer, precancerous or dysplastic lesions, and genital warts caused by HPV Types 6, 11, 16, and 18.
- HOW IS GARDASIL GIVEN?
- GARDASIL is given as an intramuscular injection
- You or your child will receive 3 doses of the vaccine
 - First dose: at a date you and the health provider decide
 - Second dose: 2 months after the first dose
 - Third dose: 6 months after the first dose

Vaccine-Related Adverse Experiences

- At the Site of Injection
 - Pain
 - Swelling
 - Erythema
 - Pruritis (Itching)
- General Side Effects
 - Fever, Nausea , Dizziness



Common Questions By Parents

- Will GARDASIL help if you already have HPV?
- Does my child still have to get PAP Tests?
- Do I have to pay for the vaccine and if so, how much does it cost?
- What are the benefits of the vaccine?
- What is the vaccines duration?



Common Questions By Parents (Cont'd)

- How can HPV infection be prevented?
- Does the vaccine send a message that it's okay to have sex and therefore encourage or lead to increased sexual activity?
- Why should my daughter be vaccinated at age 11 or 12? She's not sexually active. Can't we wait?



Conclusion: Important Facts About GARDASIL

- GARDASIL is contraindicated in individuals who are hypersensitive or allergic to any of the ingredients in the vaccine.
- Vaccination with GARDASIL does not substitute for routine cervical cancer screening, and people who receive GARDASIL should continue to undergo screening per standard of care.
- Vaccination with GARDASIL may not result in protection in all vaccine recipients.
- GARDASIL is not intended to be used for treatment of active genital warts; cervical cancer; CIN, VIN, or VaIN.
- GARDASIL has not been shown to protect against diseases due to non-vaccine HPV types.

For More Information

- CDC National Prevention Information Network: <http://www.cdcnpin.org>
- Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines 2002:
<http://www.cdc.gov/STD/treatment>
- Cervical Cancer Awareness: <http://www.cdc.gov/cancer/cervical>
- American Cancer Society: <http://www.cancer.org>