


Centers for Disease Control and Prevention
National Center for Immunization and Respiratory Diseases



Human Papillomavirus

September 2018
Chapter 11

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Human Papillomavirus (HPV) Disease

- Most common sexually transmitted infection in the U.S.
- Small DNA virus
- More than 150 types
- First vaccine was licensed in 2006

Human Papillomavirus Type and Disease Association

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graph TD; Mucosal["Mucosal (~40 types)"] --> HighRisk["High-risk Types (16, 18, others)"]; Mucosal --> LowRisk["Low-risk Types (6, 11, others)"]; HighRisk --> HR["Low-grade cervical abnormalities<br/>High grade abnormalities/<br/>Cancer precursors<br/>Anogenital cancers"]; LowRisk --> LR["Low-grade cervical abnormalities<br/>Genital warts<br/>Respiratory papillomas"]; Cutaneous["Cutaneous (other types) 'Common' Warts (hands/feet)"]
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HPV Clinical Features

- Most HPV infections are asymptomatic and result in no clinical disease
- Clinical manifestations of HPV infection include:
 - Anogenital warts
 - Recurrent respiratory papillomatosis
 - Cervical cancer precursors (cervical intraepithelial neoplasia)
 - Cancer (cervical, anal, vaginal, vulvar, penile, and some oropharyngeal cancers)

HPV Epidemiology

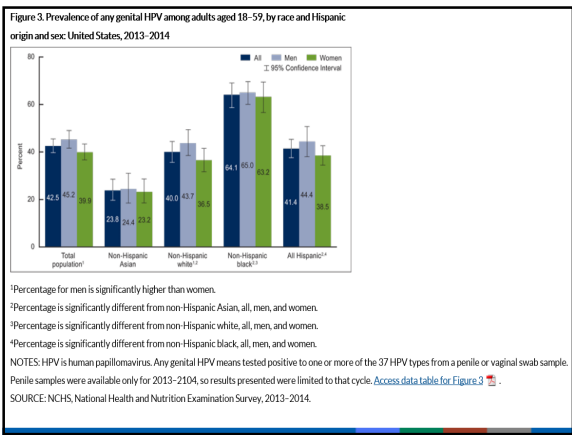
- Reservoir Human
- Transmission Direct contact (usually sexual)
- Temporal pattern None
- Communicability Presumed to be high

HPV Disease Burden in the U.S.

- HPV is so common that nearly all sexually active men and women get the virus at some point in their lives
- Estimated 79 million persons are infected
 - ~ 14 million new infections annually
- Common among adolescents and young adults
 - 50% of new infections occur in persons 15–24 years of age
- About \$8 billion spent annually on management of sequelae of HPV infections

Cancers Caused by HPV, United States				
Cancer site	Average number of cancers per year probably caused by any HPV type ¹			Percentage per year by any HPV type
	Male	Female	Both Sexes	
Anus	1,600	3,200	4,800	91%
Cervix	0	10,600	10,600	91%
Oropharynx	9,600	2,000	11,600	70%
Penis	700	0	700	63%
Vagina	0	600	600	75%
Vulva	0	2,500	2,400	69%

¹HPV types detected in genotyping study; most were high-risk HPV types known to cause cancer (Saraiya M et al. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. Journal of the National Cancer Institute 2015;107:djv086). CDC, United States Cancer Statistics (USCS), 2006-2010 www.cdc.gov/cancer/hpv/statistics/cases.htm



HPV Adult Vaccination Rates 2016

- Females 19-26 years: 48.5% reported receipt of at least one dose of HPV vaccine**
 - 6.9 percentage point increase compared with the estimate reported for 2015
- Females 19-21 years, HPV vaccination coverage was 51.6%**
 - a 9.6 percentage point increase compared with the estimate for 2015
- Females 22-26 years, HPV vaccination coverage was 46.6%,**
 - Similar to the 2015 estimate

Vaccination Coverage Among Adults in the United States, National Health Interview Survey, 2016
https://www.cdc.gov/nchs/data/behaviors/HPV_vaccination_coverage_data_updates/HPV_vaccination_coverage_2015-2016.html

HPV Adult Vaccination Rates 2016

- **Males 19-26 years: 13.5% reported receipt at least 1 dose of HPV vaccine**
 - 3.4 percentage point increase compared with the estimate reported for 2015
- **Males 19-21 years: 21.2%, HPV reported receipt at least 1 dose of HPV vaccine**
 - 5.5 percentage point increase compared with the estimate reported for 2015
- **HPV vaccination (at least one dose) among females and males 19-26 years who had not received HPV vaccination prior to 19 years was 8.6% and 2.7%, similar to estimates for 2015**

Vaccination Coverage Among Adults in the United States, National Health Interview Survey, 2016
<https://www.cdc.gov/od/oc/media/press-releases/r091616a.htm>

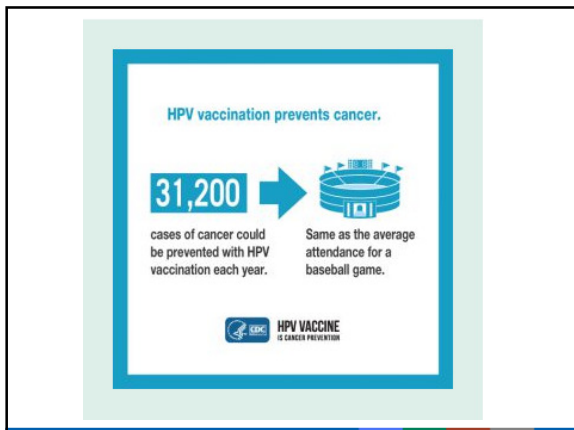
Human Papillomavirus Vaccine

	9-valent HPV (Gardasil9)
L1 VLP types	6, 11, 16, 18, 31, 33, 45, 52, 58
Route	IM injection
Age Indications	9 through 26 years of age
FDA Indications	Females: Prevents anal, cervical, vaginal, and vulvar precancer and cancer; genital warts
	Males: Prevents anal precancer and cancer; genital warts

Only 9-valent vaccine is currently available in the U.S.

Human Papillomavirus Vaccine Efficacy

- High efficacy among females without evidence of infection with vaccine HPV types (>95%)
- No evidence of efficacy against disease caused by vaccine types participants were infected with at the time of vaccination
- Prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types



9vHPV (Gardasil9)
Efficacy and Safety

- **Efficacy**
 - ~97% protection against 31-,33-,45-,52-,58-related outcomes
 - Similar protection against 6-,11-,16-,18-related disease
- **Noninferior immunogenicity to 4vHPV**
- **5 additional types account for 11% of invasive cancers**
 - Differences by gender: 14% for females; 5% for males
- **9vHPV can be administered at the same medical visit with MenACWY and Tdap**
- **Safety profile similar to 4vHPV across age, gender, race, ethnicity groups**

Human Papillomavirus Vaccine
Routine Adult Recommendations

- **Vaccinate women through 26 years of age who are:**
 - Previously unvaccinated or
 - Missing doses
- **Vaccinate men 19 through 21 years of age who are:**
 - Previously unvaccinated or
 - Missing doses
- **Vaccinate men 22 through 26 years of age who are previously unvaccinated or are missing doses including:**
 - Men who have sex with men
 - Immunocompromised (including those with HIV infection)
- **Other men 22 through 26 years of age vaccinated**

*Vaccination series can be started at 9 years of age
MMWR 2015;64:300-4

ACIP HPV Immunization Recommendations Previously Unvaccinated Adults

- **Routine 3-dose schedule*:** 0, 1-2, 6 months
 - Dose #2: Administer at least 1 to 2 months after dose 1
 - Dose #3: Administer at least:
 - 12 weeks after dose 2 AND
 - 6 months (24 weeks) after dose 1
- **An accelerated schedule using minimum intervals is not recommended**
- **Schedule begun before 26 years of age may be completed at 27 years of age and older**

*ACIP off-label recommendation, MMWR 2015;64(2):302-4

ACIP HPV Immunization Recommendations Adults with an Incomplete Series

- **Adolescents who initiated vaccination with 9vHPV, 4vHPV, or 2vHPV**
 - Before their 15th birthday, are fully vaccinated if they received
 - 2 doses at the recommended dosing schedule (0, 6-12 month), OR
 - 3 doses at the recommended dosing schedule (0, 1-2, 6 month)
 - On or after the 15th birthday are fully vaccinated if they received,
 - 3 doses at the recommended dosing schedule (0, 1-2, 6 month)
- **All doses do not have to 9vHPV**
- **No additional doses are recommended, regardless of their current age**

MMWR 2016;65(48):1405-08

ACIP HPV Immunization Recommendations Medical Condition Considerations

- **ACIP recommends HPV vaccination for immunocompromised females and males aged 9 through 26 years with 3 doses of HPV vaccine (0, 1-2, 6 months)**
- **Administer a 3-dose series to immunocompromised persons including those with:**
 - Primary or secondary immunocompromising conditions that might reduce cell-mediated or humoral immunity, such as B lymphocyte antibody deficiencies, T lymphocyte complete or partial defects, HIV infection, malignant neoplasm, transplantation, autoimmune disease or immunosuppressive therapy

MMWR 2016;65(48):1405-08

**ACIP HPV Immunization Recommendations
Schedule Considerations**

- Number of recommended doses is based on:
 - Age at administration of the first dose OR
 - Health status – immunosuppression

- Series does not need to be restarted if interrupted
 - There is NO maximum interval between HPV vaccine doses

- HPV vaccine can be administered during the same clinical visit other vaccines

- 9vHPV may be used to continue or complete a series started with 4vHPV or 2vHPV regardless of the dosing schedule

MMWR 2016;65(24):545-58

**ACIP HPV Immunization Recommendations
Additional Considerations**

- For persons who have completed a series of 4vHPV or 2vHPV, there is no ACIP recommendation for additional vaccination with 9vHPV

- No therapeutic effect on HPV infection, genital warts, cervical lesions

- Prevacination assessments not recommended
 - HPV
 - Pregnancy testing

HPV Vaccination and Pap Smears

- Vaccinated women still need to see their healthcare provider for periodic cervical cancer screening

- The vaccine does not provide protection against all types of HPV that cause cervical cancer, so even vaccinated women will still be at risk for some cancers from HPV

Cervical Cancer Screening

- Revised in 2012
- Screening should begin at age 21 years
- Screen women 21 to 65 years of age with Pap test every 3 years
- Co-testing (Pap and HPV testing) every 5 years in women 30 to 65 years of age

HPV FAQs

- If a patient has been sexually active for a number of years, is it still recommended to give HPV vaccine or to complete the HPV vaccine series?
- Yes. HPV vaccine should be administered to people who are already sexually active. Ideally, patients should be vaccinated before onset of sexual activity; however, patients who have already been infected with one or more HPV types still be protected from other HPV types in the vaccine that have not been acquired.

HPV FAQs

- If a 40-year-old female patient insists that she wants to receive HPV vaccine, can I give it to her?
- HPV vaccine is not approved for use in women older than age 26 years. Studies have shown that the vaccine is safe in women age 27 years and older. ACIP does not recommend the use of this vaccine outside the FDA licensing guidelines unless the series was started but not completed by age 26 years. Clinicians may choose to administer HPV vaccine off-label to men and women age 27 years or older and should decide if the benefit of the vaccine outweighs the hypothetical risk.

Human Papillomavirus Vaccine Product Interchangeability

- No data on schedules that include 2vHPV and 4vHPV and/or 9vHPV
- Response to types 16 and 18 likely to be similar when 2vHPV, 4vHPV, or 9vHPV used in the same series
- Protection against types that are not 16 or 18 is probably reduced if fewer than 3 doses of 4vHPV or 9vHPV received

Human Papillomavirus Vaccine Special Situations

- Administer vaccine to:
 - Females who:
 - Have equivocal or abnormal Pap test
 - Have positive HPV DNA test
 - Are breast-feeding
 - Males and females who:
 - Have genital warts
 - Are immunosuppressed

MMWR 2014;63(Nn): 51-3-30
MMWR 2015;64(20):300-4

Human Papillomavirus Vaccine and Pregnancy

- Initiation of the vaccine series should be delayed until after completion of pregnancy
- If a woman is found to be pregnant after initiating the vaccination series, remaining doses should be delayed until after the pregnancy
- If a vaccine dose has been administered during pregnancy, there is no indication for intervention
- Women vaccinated during pregnancy should be reported to the respective manufacturer
 - Active pregnancy registry for 9vHPV established; others are closed
 - Contact information is in the package insert

MMWR 2014;63(Nn): 51-3-30
MMWR 2015;64(20):300-4

Human Papillomavirus Vaccine Administration

- Administer HPV vaccines via intramuscular (IM) injection
 - Needle size: 1- to 1½- inch, 22- to 25-gauge
 - Site: Deltoid muscle in the upper arm
- Follow proper injection practices
 - Use aseptic technique
 - Use a new needle and syringe for each injection
- Administer at the same medical visit as other vaccines

Human Papillomavirus Vaccine Contraindications and Precautions

- Contraindication
 - Severe allergic reaction to a vaccine component or following a prior dose
- Precaution
 - Moderate or severe acute illnesses (defer until symptoms improve)

Adverse Events Following Any Dose of HPV Vaccine Among Females*

Adverse Event	2vHPV	4vHPV	9vHPV
Pain	92%	84%	89%
Swelling	44%	29%	40%
Erythema	48%	25%	34%
Fever	13%	13%	5%
Nausea	7%	GI 28%**	4%
Headache	12%	55%	11%

**GI = gastrointestinal symptoms, including nausea, vomiting, diarrhea, and/or abdominal pain

Syncope Following Vaccination

- An increase in the number of reports of syncope has been detected by the Vaccine Adverse Event Reporting System (VAERS)
 - Most of the increase among females 11-18 years
- Serious injuries have resulted
- ACIP recommends providers strongly consider observing patients for 15 minutes after they are vaccinated

Vaccine Storage and Handling

- Store HPV vaccine in a refrigerator between 2°C - 8°C (36°F - 46°F)
- Store HPV vaccines:
 - In the original packaging with the lids closed
 - In a clearly labeled bin and/or area of the storage unit
- Do not freeze the vaccine

9vHPV (Gardasil 9)
Administer to females and males

Use for: 9 years through 26 years
Recommended ages: 11 years or 12 years
Catch-up ages: 13 years through 26 years
Route: Intramuscular (IM) injection

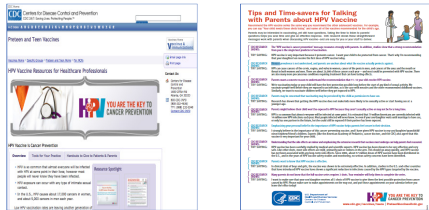
Vaccine storage label example
Available at www.cdc.gov/vaccines/imz/downloads/9vhpv/vaccine-storage-label.pdf

Clinician & Health Systems Action Guides

System Guides

HPV Roundtable <http://www.roundtable.org/action-guides/>

HPV Vaccination Resources for HCP



www.cdc.gov/vaccines/youarethekey

Questions?