Human Papillomavirus (HPV): Current Status & Controversies

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Human Papillomavirus (HPV): Current Status & Controversies

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Sunday, January 8th, 2017
Objectives

1. Discuss the epidemiology of HPV infections in the United States.
2. Describe the pathophysiology, risk factors, signs and symptoms, and modes of HPV transmission.
3. Identify the negative health consequences associated with HPV.
Objectives

4. Summarize the current recommendations for preventing HPV infections.

5. Identify the different HPV vaccinations available and describe the latest recommendations for their use.

6. Discuss controversies related to HPV infections and vaccinations.
Pre-Test

- **Question 1:** The most common sexually transmitted infections in the United States are HPV infections.

- **Question 2:** An individual can become infected with only one strain of HPV at a time.

- **Question 3:** The only type of cancer linked to HPV is cervical cancer.
Epidemiology

Estimated number of new sexually transmitted infections
- United States, 2008

<table>
<thead>
<tr>
<th>Disease</th>
<th>Age Group</th>
<th>Estimated Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ages 25+</td>
<td>19,000</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>Ages 15-24</td>
<td>41,400</td>
</tr>
<tr>
<td>HIV*</td>
<td>Ages 15-24</td>
<td>55,400</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Ages 15-24</td>
<td>776,000</td>
</tr>
<tr>
<td>HSV-2</td>
<td>Ages 15-24</td>
<td>820,000</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>Ages 15-24</td>
<td>1,090,000</td>
</tr>
<tr>
<td>Trichomonias</td>
<td>Ages 15-24</td>
<td>2,860,000</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>Ages 15-24</td>
<td>14,100,000</td>
</tr>
<tr>
<td>HPV</td>
<td>Ages 15-24</td>
<td>49%</td>
</tr>
</tbody>
</table>

Young people (15-24) represent 50% of all new STIs

*HIV incidence not calculated by age in this analysis

Bars are for illustration only; not to scale, due to wide range in numbers of infections

TOTAL: 19,738,800
Epidemiology

Estimated number of new and existing (total) sexually transmitted infections
- United States, 2008

<table>
<thead>
<tr>
<th>Infection</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis</td>
<td>117,000</td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>270,000</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>422,000</td>
</tr>
<tr>
<td>HIV</td>
<td>908,000</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>1,570,000</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>3,710,000</td>
</tr>
<tr>
<td>HSV-2</td>
<td>24,100,000</td>
</tr>
<tr>
<td>HPV</td>
<td>79,100,000</td>
</tr>
</tbody>
</table>

Gender totals do not equal overall total, due to rounding

Bars are for illustration only; not to scale, due to wide range in numbers of infections

TOTAL: 110,197,000
Epidemiology

- Cervicovaginal Prevalence of Types 6, 11, 16 and 18 Among Women Aged 14–59 Years by Age Group and Time Period
HPV

- Family of >200 non-enveloped, double-stranded DNA viruses that target human epithelial cells
  - >40 types are sexually transmitted
  - >13 types may cause cancer

- Numbered in order of discovery

- Classified into groups based on anatomic areas they affect
HPV

- Individuals may be infected with more than one type at a time

- The most common viral infection of the reproductive tract

- The most common sexually transmitted infection (STI) in the United States
Risk Factors

- Early first sexual intercourse
- Multiple sexual partners
- Tobacco use
- Immunosuppression
Signs and Symptoms

- Most HPV infections are asymptomatic and resolve spontaneously.

- Persistent, untreated high risk infections may result in precancerous lesions.
Modes of Transmission

- Spreads from one person to another by skin-to-skin contact
  - Sexual intercourse
  - Intimate, non-penetrative encounters
Sexually Transmitted HPV

Two categories:

1. **Low risk:** Cause skin warts around the mouth, throat, genitals/anus as well as respiratory papillomatosis
   - HPV 6, 11

2. **High risk:** Cause cancer
   - HPV 16, 18
Sexually Transmitted HPV

- Affects 6.2 million 14-44 year olds every year
  - 74% between the ages of 15 and 24

- Up to 70% of young women will be infected with at least 1 type of HPV within the first 5 years of starting sexual activity
Complications

- Precancerous lesions may progress to different types of cancer
  - Cervical
  - Anal
  - Oropharyngeal
  - Vaginal
  - Vulvar
  - Penile
Complications: HPV-Associated Cancers

Based on data from 2008-2012, 38,793 HPV-associated cancers occur in the U.S. each year

- ~23,000 among women
- ~16,000 in men

Cervical cancer is the most common among women

Oropharyngeal cancers are the most common among men
### Complications:

**HPV-Associated Cancers**

![Image of table]

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Average number of cancers per year in sites where HPV is often found (HPV-associated cancers)</th>
<th>Percentage probably caused by any HPV type(^a)</th>
<th>Number probably caused by any HPV type(^b)</th>
<th>Percentage probably caused by HPV types 16/18(^c)</th>
<th>Number probably caused by HPV types 31/33/45/52/58(^d)</th>
<th>Percentage probably caused by HPV types 31/33/45/52/58(^d)</th>
<th>Number probably caused by HPV types 31/33/45/52/58(^d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>11,771</td>
<td>91%</td>
<td>10,700</td>
<td>66%</td>
<td>7,800</td>
<td>15%</td>
<td>1,700</td>
</tr>
<tr>
<td>Vagina</td>
<td>802</td>
<td>75%</td>
<td>600</td>
<td>55%</td>
<td>400</td>
<td>18%</td>
<td>100</td>
</tr>
<tr>
<td>Vulva</td>
<td>3,554</td>
<td>69%</td>
<td>2,400</td>
<td>49%</td>
<td>1,700</td>
<td>14%</td>
<td>500</td>
</tr>
<tr>
<td>Penis</td>
<td>1,168</td>
<td>63%</td>
<td>700</td>
<td>48%</td>
<td>600</td>
<td>9%</td>
<td>100</td>
</tr>
<tr>
<td>Anus</td>
<td>5,010</td>
<td>91%</td>
<td>4,600</td>
<td>79%</td>
<td>4,000</td>
<td>8%</td>
<td>400</td>
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<tr>
<td>Female</td>
<td>3,260</td>
<td>93%</td>
<td>3,000</td>
<td>80%</td>
<td>2,600</td>
<td>11%</td>
<td>400</td>
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<tr>
<td>Male</td>
<td>1,750</td>
<td>89%</td>
<td>1,600</td>
<td>79%</td>
<td>1,400</td>
<td>4%</td>
<td>100</td>
</tr>
<tr>
<td>Rectum</td>
<td>750</td>
<td>91%</td>
<td>700</td>
<td>79%</td>
<td>600</td>
<td>8%</td>
<td>100</td>
</tr>
<tr>
<td>Female</td>
<td>513</td>
<td>93%</td>
<td>500</td>
<td>80%</td>
<td>400</td>
<td>11%</td>
<td>100</td>
</tr>
<tr>
<td>Male</td>
<td>237</td>
<td>89%</td>
<td>200</td>
<td>79%</td>
<td>200</td>
<td>4%</td>
<td>&lt;100</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>15,738</td>
<td>70%</td>
<td>11,000</td>
<td>60%</td>
<td>9,500</td>
<td>6%</td>
<td>900</td>
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<tr>
<td>Female</td>
<td>3,100</td>
<td>63%</td>
<td>2,000</td>
<td>51%</td>
<td>1,600</td>
<td>10%</td>
<td>300</td>
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<tr>
<td>Male</td>
<td>12,638</td>
<td>72%</td>
<td>9,100</td>
<td>63%</td>
<td>8,000</td>
<td>4%</td>
<td>600</td>
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<tr>
<td>TOTAL</td>
<td>38,793</td>
<td>30,700</td>
<td>24,600</td>
<td>3,800</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Complications: Cervical Cancer

- HPV 16 & 18 cause 70% of all cases

Symptoms

- Fatigue
- Weight loss, loss of appetite
- Back, leg, or pelvic pain
- Single swollen leg
- Vaginal discomfort or odorous discharge
- Irregular, intermenstrual, or abnormal vaginal bleeding after sexual intercourse
Treatment

- Aimed at genital warts and precancerous lesions
  - Cryotherapy
  - Electrocautery
  - Surgical excision
  - Topical therapies
Prevention

- Abstinence
- Safe sex practices
- Cervical cancer screening
- HPV testing for oncogenic types
- Immunizations
Prevention: Cervical Cancer Screening

- Females 21-65 years old
  - Conventional or liquid-based cytologic testing (Papanicolaou test) every 3 years

- Females 30-65 years old
  - Co-testing with oncogenic HPV tests every 5 years
American Cancer Society Guidelines for the Early Detection of Cervical Cancer

Ages 21 to 29 years
Get a Pap test every 3 years.

Ages 30 to 65 years
Get a Pap test and an HPV test every 5 years (this is best) or get just a Pap test every 3 years.

If you are at high risk for cervical cancer, talk with your doctor or nurse to make a testing plan that’s right for you.

Women over 65 years
Stop testing if you’ve had regular testing for the past 10 years and have not had any bad pre-cancers in the past 20 years.

Women who have had cervical pre-cancer
Get tested for at least 20 years after the cell changes were found and treated.

Women who had a hysterectomy and their cervix was removed
Stop testing unless the surgery was done to treat cervical cancer or pre-cancer.

Women who got the HPV vaccine
Follow the same screening plan as above.

These guidelines are not for women who have cervical cancer.
Prevention: Cervical Cancer Screening

- Positive HPV test
  - Second HPV test in 1 year and/or
  - Test to identify HPV type
Prevention: HPV Testing for Oncogenic Types

- Detect viral DNA or messenger RNA (mRNA)

- Indications
  - In conjunction with conventional cervical screening in females 30-65 years old
  - To triage abnormal results of conventional cervical screening
  - As follow-up after treatment of cervical precancers
Prevention: Screening in Men

- No Food and Drug Administration (FDA)-approved tests to detect HPV in men
- No recommended screening methods to detect HPV-related cell changes in men
Prevention: Immunizations

Healthy People 2020

- **Goal:** Increase immunization rates and reduce preventable infectious diseases
- **Objectives:**

<table>
<thead>
<tr>
<th>IID-11</th>
<th>Increase routine vaccination coverage levels for adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>IID-11.1</td>
<td>Increase the vaccination coverage level of 1 dose of tetanus-diphtheria-acellular pertussis (Tdap) booster vaccine for adolescents by age 13 to 15 years</td>
</tr>
<tr>
<td>IID-11.2</td>
<td>Increase the vaccination coverage level of 2 doses of varicella vaccine for adolescents by age 13 to 15 years (excluding children who have had varicella)</td>
</tr>
<tr>
<td>IID-11.3</td>
<td>Increase the vaccination coverage level of 1 dose meningococcal conjugate vaccine for adolescents by age 13 to 15 years</td>
</tr>
<tr>
<td>IID-11.4</td>
<td>Increase the vaccination coverage level of 3 doses of human papillomavirus (HPV) vaccine for females by age 13 to 15 years</td>
</tr>
<tr>
<td>IID-11.5</td>
<td>Increase the vaccination coverage level of 3 doses of human papillomavirus (HPV) vaccine for males by age 13 to 15 years</td>
</tr>
</tbody>
</table>
### Prevention: Immunizations

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th></th>
<th>Males</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1 Tdap</td>
<td>80%</td>
<td>80%</td>
<td>80%</td>
<td>80%</td>
<td>90%</td>
<td>80%</td>
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<tr>
<td>≥ 1 MenACWY</td>
<td>88.3±1.1</td>
<td>79.4±1.4</td>
<td>34.4±2.3</td>
<td>20.6±2.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3 HPV†</td>
<td></td>
<td></td>
<td>80%</td>
<td>80%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3 HPV†</td>
<td></td>
<td></td>
<td>36.8±12.1</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 2 doses varicella</td>
<td></td>
<td></td>
<td>22.8±8.3</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>vaccine if had no</td>
<td></td>
<td></td>
<td>23.7±10.6</td>
<td>12.4±7.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>history of disease</td>
<td></td>
<td></td>
<td></td>
<td>71.2±8.7</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>State</th>
<th>Females</th>
<th></th>
<th>Males</th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Healthy People 2020</td>
<td>80%</td>
<td>80%</td>
<td>80%</td>
<td>80%</td>
<td>90%</td>
<td>80%</td>
<td></td>
</tr>
<tr>
<td>Target</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>US National</td>
<td>88.3±1.1</td>
<td>79.4±1.4</td>
<td>34.4±2.3</td>
<td>20.6±2.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alabama</td>
<td>87.0±5.8</td>
<td>69.8±7.8</td>
<td>36.8±12.1</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alaska</td>
<td>71.9±6.8</td>
<td>56.8±7.9</td>
<td>22.8±8.3</td>
<td>NA</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Arizona</td>
<td>84.1±6.1</td>
<td>86.3±5.9</td>
<td>24.3±9.6</td>
<td>16.8±7.3</td>
<td>73.9±7.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arkansas</td>
<td>87.9±5.8</td>
<td>65.4±7.9</td>
<td>23.7±10.6</td>
<td>12.4±7.1</td>
<td>71.2±8.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>California</td>
<td>88.1±5.6</td>
<td>78.1±7.5</td>
<td>43.2±13.0</td>
<td>29.5±11.1</td>
<td>82.1±6.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colorado</td>
<td>89.3±4.6</td>
<td>76.7±6.4</td>
<td>41.1±11.0</td>
<td>23.7±9.6</td>
<td>86.2±6.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connecticut</td>
<td>96.2±3.1</td>
<td>97.3±2.1</td>
<td>36.9±11.4</td>
<td>19.9±8.4</td>
<td>97.1±2.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delaware</td>
<td>91.4±4.8</td>
<td>86.5±6.2</td>
<td>40.3±12.5</td>
<td>26.3±11.9</td>
<td>91.7±5.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dist. of Columbia</td>
<td>80.9±7.7</td>
<td>92.3±4.2</td>
<td>55.9±13.8</td>
<td>37.6±15.3</td>
<td>92.1±5.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Florida</td>
<td>89.4±6.0</td>
<td>72.9±8.2</td>
<td>21.4±10.7</td>
<td>21.5±12.0</td>
<td>79.3±8.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prevention: Immunizations

Table 67. Vaccination coverage for selected diseases among adolescents aged 13–17, by selected characteristics: United States, 2008–2014

Updated data when available, Excel, and PDF: http://www.cdc.gov/nchs/hus/contents2015.htm#067.

[Data are based on telephone interviews of a sample of the civilian noninstitutionalized population, supplemented by a survey of interview participants’ immunization providers]

<table>
<thead>
<tr>
<th>Vaccination coverage</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013¹</th>
<th>2014¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles, mumps, rubella (2 doses or more)</td>
<td>89.3</td>
<td>89.1</td>
<td>90.5</td>
<td>91.1</td>
<td>91.4</td>
<td>89.6</td>
<td>90.7</td>
</tr>
<tr>
<td>Hepatitis B (3 doses or more)</td>
<td>87.9</td>
<td>89.9</td>
<td>91.6</td>
<td>92.3</td>
<td>92.8</td>
<td>91.3</td>
<td>91.4</td>
</tr>
<tr>
<td>History of varicella or received varicella vaccine (2 doses or more)²</td>
<td>73.5</td>
<td>75.7</td>
<td>76.8</td>
<td>79.9</td>
<td>82.6</td>
<td>82.7</td>
<td>85.0</td>
</tr>
<tr>
<td>Tdap (1 dose or more)³</td>
<td>40.8</td>
<td>55.6</td>
<td>68.7</td>
<td>78.2</td>
<td>84.6</td>
<td>84.7</td>
<td>87.6</td>
</tr>
<tr>
<td>Meningococcal conjugate vaccine (MenACWY) (1 dose or more)⁴</td>
<td>41.8</td>
<td>53.6</td>
<td>62.7</td>
<td>70.5</td>
<td>74.0</td>
<td>76.6</td>
<td>79.3</td>
</tr>
<tr>
<td>Human papillomavirus (HPV) (3 doses or more among males)⁵</td>
<td>17.9</td>
<td>26.7</td>
<td>32.0</td>
<td>34.8</td>
<td>33.4</td>
<td>36.8</td>
<td>39.7</td>
</tr>
<tr>
<td>Human papillomavirus (HPV) (3 doses or more among females)⁵</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>1.3</td>
<td>6.8</td>
<td>13.4</td>
</tr>
</tbody>
</table>

¹ Denotes preliminary data
² Includes varicella vaccine series started at any age
³ Tetanus, diphtheria, and pertussis
⁴ Includes conjugate meningococcal C
⁵ Includes 3 doses of HPV Vaccine for females and males

---

Table credits and sources:

- CDC National Center for Health Statistics (NCHS)
- Data from the National Health Interview Survey (NHIS)
# Prevention: Immunizations

<table>
<thead>
<tr>
<th>Vaccine type</th>
<th>Brand name</th>
<th>HPV types covered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivalent (2vHPV)</td>
<td>Cervarix®</td>
<td>16, 18</td>
</tr>
<tr>
<td>Quadrivalent (4vHPV)</td>
<td>Gardasil®</td>
<td>6, 11 16, 18</td>
</tr>
<tr>
<td>9-valent (9vHPV)</td>
<td>Gardasil®9</td>
<td>6, 11 16, 18 31, 33, 45, 52, 58</td>
</tr>
</tbody>
</table>

- Gardasil®9 replaced the bivalent and quadrivalent HPV vaccines by the end of 2016
Prevention: Immunizations

Cancer probably caused by HPV type

- HPV types 16/18 targeted by bivalent and quadrivalent vaccines
- HPV types 31/33/45/52/58 targeted by 9-valent vaccine
- Other HPV types
- HPV-negative*

Sex / Cancer Site

- Women:
  - Cervix
  - Vagina
  - Vulva
  - Anus
  - Rectum
  - Oropharynx

- Men:
  - Penis
  - Anus
  - Rectum
  - Oropharynx

Average number of cases per year

0 1,000 2,000 3,000 4,000 5,000 6,000 7,000 8,000 9,000 10,000 11,000 12,000 13,000
Cervarix®

- Initial U.S. approval: 2009
- Manufacturer: GlaxoSmithKline
- FDA indication: Females 9-25 years old
- Dosage & administration:
  - Three 0.5 mL intramuscular (IM) injections at 0, 1, and 6 months
Gardasil®

- **Initial U.S. approval:** 2006
- **Manufacturer:** Merck Sharp & Dohme Corp.

**FDA indications:**
- Females 9-26 years old
- Males 9-26 years old

**Dosage & administration:**
- Three 0.5 mL IM injections at 0, 2, and 6 months
Gardasil®9

- **Initial U.S. approval:** 2014

- **Manufacturer:** Merck Sharp & Dohme Corp.

- **FDA indications:**
  - Females 9-26 years old
  - Males 9-26 years old

- **Dosage & administration:**
  - Three 0.5 mL IM injections at 0, 2, and 6 months
If the 3-dose HPV vaccination series is initiated with the bivalent or quadrivalent vaccines, it may be continued or completed with Gardasil®9.

If the 3-dose HPV vaccination series has been completed with the bivalent or quadrivalent vaccines, Gardasil®9 is not recommended.
Gardasil®9

- Safety assessed across 7 Phase III trials involving >15,000 patients aged 9-26 years

- Common side effects
  - Injection site reactions [pain, swelling, erythema] (84.8%)
  - Headache (13.2%)
  - Fever (6.1%)
# Prevention: Immunizations

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bivalent (2vHPV) *</th>
<th>Quadrivalent (4vHPV) †</th>
<th>9-valent (9vHPV) §</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand name</td>
<td>Cervarix</td>
<td>Gardasil</td>
<td>Gardasil 9</td>
</tr>
<tr>
<td>VLPs</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>GlaxoSmithKline</td>
<td>Merck and Co., Inc.</td>
<td>Merck and Co., Inc.</td>
</tr>
<tr>
<td>Manufacturing</td>
<td><em>Trichoplusia ni</em> insect cell line infected with L1 encoding recombinant baculovirus</td>
<td><em>Saccharomyces cerevisiae</em> (Baker’s yeast), expressing L1</td>
<td><em>Saccharomyces cerevisiae</em> (Baker’s yeast), expressing L1</td>
</tr>
<tr>
<td>Adjuvant</td>
<td>500 µg aluminum hydroxide, 50 µg 3-O-desacyl-4' monophosphoryl lipid A</td>
<td>225 µg amorphous aluminum hydroxyphosphate sulfate</td>
<td>500 µg amorphous aluminum hydroxyphosphate sulfate</td>
</tr>
<tr>
<td>Volume per dose</td>
<td>0.5 ml</td>
<td>0.5 ml</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>Administration</td>
<td>Intramuscular</td>
<td>Intramuscular</td>
<td>Intramuscular</td>
</tr>
</tbody>
</table>

**Abbreviation:** L1 = the HPV major capsid protein; VLPs = virus-like particles.


<table>
<thead>
<tr>
<th>Vaccines</th>
<th>18 mos</th>
<th>19-23 mos</th>
<th>2-3 yrs</th>
<th>4-6 yrs</th>
<th>7-10 yrs</th>
<th>11-12 yrs</th>
<th>13-15 yrs</th>
<th>16-18 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B</strong> (? HepB)</td>
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<tr>
<td><strong>Rotavirus</strong> (? RV)</td>
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<tr>
<td>RV1 (2-dose series): RV5 (3-dose series)</td>
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<tr>
<td><strong>Diphtheria, tetanus, &amp; acellular pertussis</strong> (? DTaP: &lt; 7 yrs)</td>
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<tr>
<td><strong>Haemophilus influenzae type b</strong> (? Hib)</td>
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<tr>
<td><strong>Pneumococcal conjugate</strong> (? PCV13)</td>
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<tr>
<td><strong>Inactivated poliovirus</strong> (? IPV) (&lt; 18 yrs)</td>
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</tr>
<tr>
<td><strong>Influenza</strong> (? IIV; LAIV)</td>
<td>Annual vaccination (IIV only) 1 or 2 doses</td>
<td>Annual vaccination (LAIV or IIV) 1 or 2 doses</td>
<td>Annual vaccination (LAIV or IIV) 1 dose only</td>
<td></td>
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<tr>
<td><strong>Measles, mumps, rubella</strong> (? MMR)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Varicella</strong> (? VAR)</td>
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<tr>
<td><strong>Hepatitis A</strong> (? HepA)</td>
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</tr>
<tr>
<td><strong>Meningococcal</strong> (? Hib-MenCY ≥ 6 weeks; MenACWY-D ≥ 9 mos; MenACWY-CRM ≥ 2 mos)</td>
<td>See footnote 11</td>
<td></td>
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</tr>
<tr>
<td><strong>Tetanus, diphtheria, &amp; acellular pertussis</strong> (? Tdap: ≥ 7 yrs)</td>
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<tr>
<td><strong>Human papillomavirus</strong> (? (2vHPV: females only; 4vHPV, 9vHPV: males and females)</td>
<td>3 dose series</td>
<td></td>
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<tr>
<td>Vaccine</td>
<td>19-21 years</td>
<td>22-26 years</td>
<td>27-49 years</td>
<td>50-59 years</td>
<td>60-64 years</td>
<td>≥ 65 years</td>
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<tr>
<td>Influenza</td>
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<td></td>
<td>1 dose annually</td>
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<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Substitute Tdap for Td once, then Td booster every 10 yrs</td>
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<tr>
<td>Varicella</td>
<td></td>
<td></td>
<td></td>
<td>2 doses</td>
<td></td>
<td>2 doses</td>
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<tr>
<td>Human papillomavirus (HPV) Female</td>
<td>3 doses</td>
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<td></td>
<td></td>
<td>3 doses</td>
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<tr>
<td>Human papillomavirus (HPV) Male</td>
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<td></td>
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<td>3 doses</td>
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<tr>
<td>Zoster</td>
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<td></td>
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<td>1 dose</td>
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<tr>
<td>Measles, mumps, rubella (MMR)</td>
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<td>1 or 2 doses depending on indication</td>
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<tr>
<td>Pneumococcal 13-valent conjugate (PCV13)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 dose</td>
<td>1 dose</td>
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<tr>
<td>Pneumococcal 23-valent polysaccharide (PPSV23)</td>
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<td>1 or 2 doses depending on indication</td>
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<tr>
<td>Hepatitis A</td>
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<td></td>
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<td></td>
<td>2 or 3 doses depending on vaccine</td>
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<tr>
<td>Hepatitis B</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>3 doses</td>
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<td></td>
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<tr>
<td>Meningococcal 4-valent conjugate (MenACWY)</td>
<td></td>
<td></td>
<td></td>
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<td>1 or more doses depending on indication</td>
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<tr>
<td>Meningococcal B (MenB)</td>
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<td></td>
<td>2 or 3 doses depending on vaccine</td>
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<tr>
<td>Haemophilus influenza type b (Hib)</td>
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<td></td>
<td></td>
<td></td>
<td>1 or 3 doses depending on indication</td>
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</tr>
</tbody>
</table>
Prevention: Immunizations

- Routine vaccination:
  - Administer a 3-dose series of HPV vaccine on a schedule of 0, 1-2, and 6 months to all adolescents aged 11-12 years.
  - Administer the second dose 1-2 months after the first dose (minimum interval of 4 weeks), administer the third dose 16 weeks after the second dose (minimum interval of 12 weeks) and 24 weeks after the first dose.
  - Administer HPV vaccine beginning at age 9 years to children and youth with any history of sexual abuse or assault who have not initiated or completed the 3-dose series.
Prevention: Immunizations

Catch-up vaccination:

- Administer the vaccine series to females (2vHPV, 4vHPV, or 9vHPV) and males (4vHPV or 9vHPV) at age 13-18 years if not previously vaccinated.

- Use recommended routine dosing intervals (see previous slide) for vaccine series catch-up.
For men who have sex with men and immunocompromised individuals, use:

- Gardasil®, or
- Gardasil®9
Prevention: Immunizations

- Not recommended during pregnancy
- Pregnancy testing is not needed before vaccination
- If a woman is found to be pregnant after initiating the vaccination series, no intervention is needed
  - The remainder of the 3-dose series should be delayed until completion or termination of pregnancy
- Ongoing pregnancy registry
October 20th, 2016:

- CDC and ACIP state that children 9-14 years old may receive just 2 doses of the vaccine, 6 months apart.

- The first HPV vaccine dose is routinely recommended at 11-12 years old. The second dose of the vaccine should be given 6-12 months after the first dose.

- Teens and young adults who start getting the vaccination at ages 15-26 years will continue to need 3 doses.

- Children and teens ages 9-14 who already received 2 doses of the HPV vaccine less than 6 months apart will require a third dose.

- Three doses are recommended for people with weakened immune systems aged 9-26 years.
Prevention: Immunizations

ACIP recommendations

Who should get the HPV vaccine?

- **Girls 11 to 12 years old** as early as age 9
- **Girls and Women 13 to 26 years old** not previously vaccinated
- **Boys 11 to 12 years old** as early as age 9
- **Boys and Men 13 to 21 years old** not previously vaccinated; men 22-26 may also be vaccinated
- **Men who have sex with men up to 26 years old** not previously vaccinated

For girls and women, recommend either Cervarix®: prevents cervical cancer
   Gardasil®: prevents cervical, vulvar, vaginal, anal cancers and genital warts

For boys and men, recommend Gardasil® only: prevents anal cancers and genital warts

Note: The vaccinations are administered as 3 injections over a 6-month period, irrespective of sexual history.
For optimal effectiveness, HPV vaccines should be administered prior to engaging in sexual activity.
Controversies: Age-related Concerns

- Parents, pro-abstinence activists, and social conservatives have expressed concern about the recommended age for vaccination.

- They argue that it should be up to the parents to decide when their child gets vaccinated and when to discuss the topic of sex.
Controversies: Age-related Concerns

Many believe that the added protection from the vaccine will prompt adolescents to start engaging in sexual activity.

Others maintain that it will increase the rate of teenage promiscuity.
Controversies: Misconceptions About HPV

- Surveys of parents have found several misconceptions that hinder vaccine acceptability:
  - Failure to recognize HPV as an STI
  - Low concern about child’s risk of acquiring HPV
  - Lack of knowledge about disease features and sequelae
Controversies: Cost of Vaccination

- Each dose of the HPV vaccine costs approximately $120-$200
- The total cost for the 3-dose series ranges from ~$360-$600
- Administration fees may apply
Controversies: Cost of Vaccination

- Many insurance plans cover the cost for all 3 doses

- Vaccines for Children (VFC) Program covers HPV vaccination
  - Males and females up to 18 years old
Controversies: Side Effects vs. Adverse Events

- **Side effects**: Health problems that have been shown to be linked to a vaccine by scientific studies.

- **Adverse events**: Health problems that occur after vaccination that may or may not be caused by a vaccine.
An adverse event is defined by law as serious if it is:

- Life threatening, or
- Results in death, a persistent or significant disability or incapacity, congenital anomaly or birth defect, hospitalization, or prolongation of existing hospitalization
Controversies: Serious Adverse Events

~90 million doses of HPV vaccines have been distributed in the U.S. from June 2006-March 2016

<table>
<thead>
<tr>
<th>HPV vaccine</th>
<th>Number of doses distributed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervarix®</td>
<td>720,000</td>
</tr>
<tr>
<td>Gardasil®</td>
<td>79 million</td>
</tr>
<tr>
<td>Gardasil®9</td>
<td>10 million</td>
</tr>
</tbody>
</table>
Controversies: Serious Adverse Events

In this same time period, the most commonly reported symptoms to the Vaccine Adverse Event Reporting System (VAERS) database were non-serious:

- Fainting
- Dizziness
- Headache
- Nausea
- Fever
- Pain, redness, swelling in the arm where the vaccine was given
Controversies: Serious Adverse Events

- **2011**: Safety assessment of Gardasil® in 9-26 year old female vaccine recipients between August 2006-October 2009
  - 600,558 doses analyzed
  - **No statistically significant increased risk for Guillain-Barré syndrome, stroke, venous thromboembolism, appendicitis, seizures, syncope, allergic reactions, or anaphylaxis**
Controversies: Damage to Ovaries

After over a decade of experience, neither the CDC nor the FDA have noted patterns between HPV vaccination and reproductive problems, including:

- Premature ovarian failure
- Premature menopause
- Amenorrhea
Controversies: Vaccine Safety in Pregnancy

- 2015: Analysis of VAERS data for pregnant women who received Gardasil® from June 2006-December 2013
  - No unexpected patterns in maternal or fetal outcomes
  - No safety concerns for pregnant women or their babies

- Gardasil® Pregnancy Registry
  - No evidence that the vaccine affects fertility, pregnancy, or the baby’s health
Controversies: Venous Thromboembolism (VTE)

- 2014: Analysis of Denmark data from October 2006-July 2013
  - 1,613,798 females aged 10-44 years
  - Found no association between Gardasil® and VTE during 42 days following vaccination
  - Subgroup analyses by age, anticoagulant treatment, and oral contraceptive use also found no association
Controversies: Complex Regional Pain Syndrome (CRPS)

- A chronic, painful condition that typically affects a single limb following an episode of trauma or immobilization

- Occurs in the general population, including adolescents
Controversies:
Postural Orthostatic Tachycardia Syndrome (POTS)

- An abnormally large and sustained increase in heart rate when changing from a lying down to an upright position
- Relatively common in young adolescents
- Difficult to distinguish from normal physiologic responses in this age group
Controversies: CRPS & POTS

- Review of >80 million females who received the vaccine worldwide

- Rates of syndromes in vaccinated females were no different from expected rates in their age groups

- Review of data provides no evidence of association with HPV vaccination

- No evidence justifies leaving individuals vulnerable to HPV-related cancers
Controversies: Guillain-Barré Syndrome (GBS)

- A rare disorder in which a person’s own immune system damages nerve cells, causing muscle weakness and sometimes paralysis.
- Most individuals fully recover.
- CDC’s Vaccine Safety Datalink was monitored for GBS following administration of >1.4 million doses of Gardasil® from August 2006-February 2012.
  - No cases of GBS were identified.
Controversies: Autoimmune Diseases

- 2012: Kaiser Permanente Vaccine Study Center
- 2013: Department of Medical Epidemiology and Biostatistics at the Karolinska Institute in Sweden and the Statens Serum Institute in Denmark
- 2014: Institute Pasteur and 113 medical centers in Europe
- 2015: HPV vaccine safety data from the United States and Europe
- 2015: Cohort study from 2006-2013 in Denmark and Sweden

  - *No* statistically significant differences in the incidence of immune thrombocytopenia, autoimmune hemolytic anemia, systemic lupus erythematosus, rheumatoid arthritis, juvenile rheumatoid arthritis, type 1 diabetes, Hashimoto’s disease, Graves’ disease, multiple sclerosis, acute disseminated encephalomyelitis, GBS, neuromyelitis optica, optic neuritis, or uveitis
Controversies: Deaths

- CDC reviews all available information on reports of death following vaccines

- It has concluded that there is **no** evidence suggesting that HPV vaccination has resulted in death
  - There is **no** pattern of death occurring with respect to time after vaccination
  - There is **no** consistent vaccine dose number or combination of vaccines given among the reports
Post-Test

- **Question 1:** The most common sexually transmitted infections in the United States are HPV infections.
  
  **Answer:** True

- **Question 2:** An individual can become infected with only one strain of HPV at a time.
  
  **Answer:** False

- **Question 3:** The only type of cancer linked to HPV is cervical cancer.
  
  **Answer:** False
Thank you.
References


- Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines. MMWR 2010;59(No. RR-12):69-78.
References