Human Papillomavirus

September 2018

Chapter 11

Human Papillomavirus

HPV Yoga

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

**Mucosal** ("High-risk"
- Low-grade cervical abnormalities
- High grade abnormalities/
  - Cervical precursors
  - Anogenital cancers

"Common"
- Warts (hands/feet)

Mucosal (other types)
- Common
  - Warts (hands/feet)

"Low-risk"
- Types (6, 11, others)
- Low-grade cervical abnormalities
- Genital warts
- Respiratory papillomas

Natural History of HPV Infection

**Within 1 Year**
- Initial HPV Infection
- Persistent Infection
- CIN 1
- CIN 2/3
- Cervical Cancer

**1-5 Years**
- CIN 2/3
- Cervical Cancer

**Up to Decades**
- Cervical Cancer

"CIN = cervical intraepithelial neoplasia"

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

Cumulative Incidence of any HPV Infection Months after Sexual Initiation

- 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

HPV Disease Burden in the U.S.
**Human Papillomavirus Vaccine**

- HPV L1 major capsid protein of the virus is antigen used for immunization
- L1 protein produced using recombinant DNA technology
- L1 proteins self-assemble into virus-like particles (VLP)
- VLPs are noninfectious and nononcogenic

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**9-valent HPV (Gardasil9)**

<table>
<thead>
<tr>
<th>L1 VLP types</th>
<th>6, 11, 16, 18, 31, 33, 45, 52, 58</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route</td>
<td>IM injection</td>
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<tr>
<td>Age Indications</td>
<td>9 through 26 years of age</td>
</tr>
<tr>
<td>FDA Indications</td>
<td>Females: Prevents anal, cervical, vaginal, and vulvar precancer and cancer; genital warts</td>
</tr>
<tr>
<td></td>
<td>Males: Prevents anal precancer and cancer; genital warts</td>
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Only 9-valent vaccine is currently available in the U.S.

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**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

Recommended Schedule for Children and Adolescents Aged 18 Years and Younger 2018

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- Routinely vaccinate boys and girls at 11–12 years of age*
- Catch-up those previously unvaccinated or are missing doses including:
  - Females age 13 through 26 years
  - Males age 13 through 21 years

Human Papillomavirus Vaccine
Routine Recommendations

- Routinely vaccinate boys and girls at 11–12 years of age*
- Catch-up those previously unvaccinated or are missing doses including:
  - Females age 13 through 26 years
  - Males age 13 through 21 years

Human Papillomavirus Vaccine
ACIP Recommendations

- 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
HPV Vaccination Schedules

- FDA has approved a 2-dose schedule for 9vHPV (Gardasil9)
- ACIP reviewed data on 2-dose schedules including data and studies of immune response, vaccine effectiveness, and duration of protection. Specifically:
  - Data from clinical trials showed two doses of HPV vaccine given in younger adolescents (aged 9-14 years) produced an immune response that was similar or higher than the response in young adults (aged 16-26 years) who received three doses
  - Data available to date show that a 3-dose schedule in older adolescents and young adults provides long-lasting protection.
  - Study data suggest that a 2-dose schedule given to younger adolescents will also provide long-lasting protection

ACIP HPV Immunization Recommendations
Previously Unvaccinated Adolescents

- Administer 2 doses of HPV vaccine to adolescents starting the series at 9 through 14 years of age
- Follow the routine 2-dose schedule
  - Administer dose 2 6-12 months after the 1st dose
  - If a 2nd dose is inadvertently administered prior to 6 months default to a 3-dose series

ACIP Immunization Recommendations
Previously Unvaccinated Adolescents

- Administer 3 doses of HPV vaccine to adolescents starting the series on or after the 15th birthday
- 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
ACIP Immunization Recommendations
Persons 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 be 9vHPV
- No additional doses are recommended, regardless of their current age

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

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
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

• Prevaccination assessments not recommended
  • HPV
  • Pregnancy testing

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:
    o Have equivocal or abnormal Pap test
    o Have positive HPV DNA test
    o Are breast-feeding
  • Males and females who:
    o Have genital warts
    o Are immunosuppressed
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

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*

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>2vHPV</th>
<th>4vHPV</th>
<th>9vHPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>92%</td>
<td>84%</td>
<td>89%</td>
</tr>
<tr>
<td>Swelling</td>
<td>44%</td>
<td>29%</td>
<td>40%</td>
</tr>
<tr>
<td>Erythema</td>
<td>48%</td>
<td>25%</td>
<td>34%</td>
</tr>
<tr>
<td>Fever</td>
<td>13%</td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>7%</td>
<td>GI 28%†*</td>
<td>4%</td>
</tr>
<tr>
<td>Headache</td>
<td>12%</td>
<td>55%</td>
<td>11%</td>
</tr>
</tbody>
</table>

FDA product approval data
†*Recommended treatment, including nausea, vomiting, diarrhea, and abdominal pain

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
Case Study: Olivia

- Olivia is 16 years old today with no significant medical history
- During basketball practice, she injured her ankle and diagnosis is a bad sprain. Prescribed treatment is rest, ice, and elevate for 1 week
- Her immunization history includes:
  - 4vHPV at 12 years of age
  - 9vHPV at 15 years of age

What Do You Think?

- When is Olivia's next dose of HPV due?
  - In 3 months
  - In 5 months
  - No additional doses are needed—her HPV series is complete

ACIP HPV Immunization Recommendations
Persons with an Incomplete Series

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- No additional doses are recommended, regardless of current age