HPV: A New Era in the Prevention of Cervical Cancer

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Human Papillomavirus (HPV)

- Genital HPV is the most prevalent sexually transmitted infection in the US
  - ~20 million currently infected
  - 6 million new infections/year
  - Estimated 80% of sexually active persons will have been infected by age 50
- Vast majority of infections are transient and asymptomatic
- Persistent infection may lead to anogenital cancer decades after initial infection

Cumulative Incidence of Any HPV Infection

Months after sexual initiation

4 years, > 50%

Winer: Am J Epidemiol, 2003;157
Cervical Cancer Disease Burden in the United States

• The National Cancer Institute estimates that in 2007
  – 11,150 new cervical cancer cases
  – 3,670 cervical cancer deaths

• Almost 100% of these cervical cancer cases will be caused by one of the 40 HPV types that infect the mucosa
Human Papillomavirus Types and Disease Association

mucosal/genital
(~40 types)

high-risk types
16, 18, 31, 45

low-risk types
6, 11

• low grade cervical abnormalities
• cancer precursors
• genital cancers

nonmucosal/cutaneous
(~60 types)

skin warts
(hands and feet)

• low grade cervical abnormalities
• genital warts
• laryngeal papillomas
# HPV-Associated Disease

<table>
<thead>
<tr>
<th>Type</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>16/18</td>
<td>70% of Cervical Cancer</td>
<td>70% of Anal Cancer</td>
</tr>
<tr>
<td></td>
<td>70% of Anal/genital Cancer</td>
<td>Transmission to women</td>
</tr>
<tr>
<td>6/11</td>
<td>90% of Genital Warts</td>
<td>90% of Genital Warts</td>
</tr>
<tr>
<td></td>
<td>90% of RRP lesions</td>
<td>90% of RRP lesions</td>
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<tr>
<td></td>
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<td>Transmission to women</td>
</tr>
</tbody>
</table>
Correct and consistent condom use may have a protective effect on HPV acquisition, reduce the risk for HPV-associated diseases, and mitigate the adverse consequences of infection with HPV.

This statement is required by section 317 of the Public Health Service Act, 42 U.S.C., 243
Human Papillomavirus Vaccine

- HPV L1 major capsid protein of the virus is antigen used for immunization
- Expression of L1 protein uses recombinant technology similar to that used to produce hepatitis B vaccine
- L1 proteins self-assemble into virus-like particles (VLP)
- Noninfectious, nononcogenic, and very effective
Efficacy for Prevention of Clinical HPV Disease Due to HPV 6/11/16/18 Among 16-26 year-old Females*

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Vaccine</th>
<th>Placebo</th>
<th>Efficacy</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 16/18-related CIN2/3 or AIS</td>
<td>8487 0</td>
<td>8460 53</td>
<td>100</td>
<td>(93,100)</td>
</tr>
<tr>
<td>HPV 6/11/16/18 related CIN</td>
<td>7858 4</td>
<td>7861 83</td>
<td>95</td>
<td>(87, 99)</td>
</tr>
<tr>
<td>HPV 6/11/16/18 related genital warts</td>
<td>7897 1</td>
<td>7899 91</td>
<td>99</td>
<td>(94,100)</td>
</tr>
</tbody>
</table>

*Package insert: Gardasil®. Integrated dataset; results in the per-protocol populations
CIN – cervical intraepithelial neoplasia; AIS – adenocarcinoma in situ
Serologic “Bridging” Studies of HPV Vaccine

• Clinical trials among women 16-26 years defined serologic response and clinical efficacy against CIN and AIS

• Girls 9-15 years were evaluated with serologic testing only
  – Younger girls developed higher level of antibodies than older girls and women
  – Clinical efficacy assumed based on serology studies of older females
Quadrivalent HPV Vaccine

• High efficacy among females without evidence of infection with vaccine HPV types

• No evidence that the vaccine had efficacy against existing disease or infection (i.e., the vaccine is not therapeutic)

• Prior infection with one HPV type did not diminish efficacy of the vaccine against other vaccine HPV types
Routine HPV Vaccination Recommendations

• ACIP recommends routine vaccination of females 11-12 years of age with three doses of quadrivalent HPV vaccine

• The vaccination series can be started as young as 9 years of age at the clinician’s discretion

• “Catch-up” vaccination through age 26 years

Percentage of Adolescents Who Have Had Vaginal Sex, By Gender and Age

HPV Vaccination Schedule

• Routine schedule is 0, 2, 6 months
• Intramuscular injection in the deltoid
• Minimum intervals
  – 4 weeks between doses 1 and 2
  – 12 weeks between doses 2 and 3
• Minimum age is 9 years
• Maximum age is 26 years

Incomplete Schedules and Duration of Immunity

• The efficacy of less than three doses of HPV vaccine is not known

• The duration of immunity after a complete 3-dose schedule is not known
  – Available evidence indicates protection for at least 5 years
  – Multiple studies are in progress to monitor the duration of immunity
Quadrivalent HPV Vaccine

• HPV vaccine should not be administered to males and women older than 26 years
  – Limited safety and immunogenicity data available
  – No clinical efficacy data
  – Off-label use not recommended

• Studies of clinical efficacy in progress now
Special Situations - HPV Vaccine May Be Administered

- Equivocal or abnormal Pap test
- Positive HPV test
- Genital warts
- Immunosuppression
- Lactating women

HPV 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)
HPV Vaccination During 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

• Woman vaccinated during pregnancy should be reported to Merck registry (800.986.8999)

Cervical Cancer Screening

• Cervical cancer screening – no change
  – 30% of cervical cancers caused by HPV types not prevented by the quadrivalent HPV vaccine
  – Vaccinated females could subsequently be infected with non-vaccine HPV types
  – Sexually active females could have been infected prior to vaccination

• Providers should educate women about the importance of cervical cancer screening
National Immunization Program
Contact Information

• Telephone       800.CDC.INFO
• Email            nipinfo@cdc.gov
• Website          www.cdc.gov/nip

• Vaccine Safety   http://www.cdc.gov/od/science/iso/