Managing HPV: A New Era in Patient Care

Presented By:
• Association of Reproductive Health Professionals www.arhp.org
• Planned Parenthood Federation of America www.ppf.org

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HPV and the Adolescent
Learning Objectives

• Apply knowledge about HPV transmission to accurately counsel patients about prevention
• Accurately answer patient questions about adverse events associated with HPV vaccination

more…

Learning Objectives (Continued)

• Effectively explain to patients the need for ongoing Pap screening after HPV vaccination
• Practice evidence-based protocols for effective administration of the HPV vaccine
• State the recommended timing for initiation of cervical cancer screening in adolescents.

Learning Objectives (Continued)

• Explain the correct use of HPV testing in the management of ASC-US and LSIL in adolescents.
• Correctly apply the recommended management of HSIL in adolescents in your clinical practice.

What is HPV?

• Human papillomavirus (HPV) is the name of a group of viruses that infect:
  – Skin (eg, warts on the hands and feet)
  – Mucous membranes (eg, lining of the mouth, vagina)

• There are more than 100 different types of HPV.

Genital HPV and how it affects the female anatomy

The Female Reproductive Tract

- Body of uterus
- Cervix
- Ovary
- Vagina
About 30 types of HPV affect the genital area

"High-risk" types can cause abnormalities to develop in the lining of the cervix (the lower portion of the uterus or womb) that sometimes turn into cancer.

"Low-risk" types can cause genital warts and benign (abnormal but noncancerous) changes in the cervix.

All types of genital HPV can cause abnormal Pap tests.

HPV affects both women and men

• Anyone who has any kind of sexual activity involving genital contact with an infected person can get HPV. Intercourse isn’t necessary, and transmission can take place by oral-to-genital, hand-to-genital, and genital-to-genital contact.

• Most people do not know they have HPV, because most infections do not cause signs and symptoms.

HPV affects both women and men (cont)

• People can pass the virus on without even knowing it.

• It is estimated that most people get HPV within their first 2 to 3 years of becoming sexually active.

• By age 50, at least 80% of women will have acquired genital HPV infection.

HPV-Associated Disease

Anogenital cancers
– Cervical
– Anal
– Vulvar and vaginal

more...

HPV-Associated Disease (Continued)

• Other cancers
  • Oral cavity, pharynx, larynx
  • Skin
  • Conjunctiva

• External genital warts
• Laryngeal papillomatosis

Condom Use and HPV Prevention

Rate of HPV infection per 100 patient-years at risk

Frequency of condom use by partner

Munoz N. Vaccine 2006; Lacey C.J.N. Vaccine 2006.
Most new cases of HPV occur in adolescents and young adults

- Study results indicate that women are at risk of acquiring an HPV infection from as few as 1 sex partner; risky sexual behavior is not necessary.¹
- Of the approximately 6 million new cases of genital HPV in the United States every year, it is estimated that 74% occur in 15- to 24-year-olds.


HPV and Cervical Cancer

- Virtually all cervical cancers are associated with persistent infection with high-risk HPV types
- Data from a variety of studies have confirmed that certain HPV types are associated with cervical cancer:
  - 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59
- Others are probably associated:
  - 26, 53, 66, 68, 73, 82


HPV Impact: Cervical Cancer

- In the US in 2007:
  - 11,150 cases
  - 3,670 deaths
- Worldwide (2005 estimate):
  - 288,000 deaths per year
  - 80% of deaths occur in developing countries
- Cervical cancer screening: costs $3.4 billion annually


HPV and Non-Cervical Cancers

- HPV 16 and 18
  - Evidence of causal role in cancer of vagina, vulva, penis, anus
- HPV 16
  - Evidence of carcinogenicity in oral cavity, oropharynx, perirectal skin


HPV and Non-Cervical Cancers (Continued)

- HPV 18
  - Some evidence of carcinogenicity in oral cavity
- HPV 6, 11, 16, and 18
  - Limited evidence for carcinogenicity in larynx


HPV Associated Cancer - US

<table>
<thead>
<tr>
<th>Site</th>
<th>Total Cancers</th>
<th># Cases Attributable to HPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>11,150</td>
<td>11,150 (100)</td>
</tr>
<tr>
<td>Penis</td>
<td>1,280</td>
<td>512 (40)</td>
</tr>
<tr>
<td>Vulva/Vagina</td>
<td>5,630</td>
<td>2,252 (40)</td>
</tr>
<tr>
<td>Anus</td>
<td>4,650</td>
<td>4,185 (90)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>47,250</td>
<td>24,479 (12)</td>
</tr>
</tbody>
</table>

### HPV 16 and Abnormal Pap Tests

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
<th>Total per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paps</td>
<td>5.1%</td>
<td>399,000</td>
</tr>
<tr>
<td>ASC</td>
<td>13.3%</td>
<td></td>
</tr>
<tr>
<td>LSIL</td>
<td>2.6%</td>
<td>295,000</td>
</tr>
<tr>
<td>HSIL</td>
<td>60.7%</td>
<td>182,100</td>
</tr>
</tbody>
</table>


### 2007 estimated burden of HPV-related diagnoses in the United States

- 1.4 million new cases of mildly abnormal cells
- 1.1 million new cases of cervical cancer
- 330,000 new cases of highly abnormal cells
- 11,150 new cases of genital warts

### High Lifetime Risk of HPV Infection

- 6.2 million new infections
- NHANES 2003-2004 reports a prevalence rate of 26.8% in US females age 14-59
- Approximately 75% lifetime risk for sexually active individuals


### New HPV Infection is Common in Young Women

Study of 603 female college students
- About 20% were HPV positive at entry
- Almost 40% converted to positive within 24 months


### HPV Cumulative Incidence: Brown Study

Two-year study
- 60 female adolescents 14-17 years old
- 80% had high-risk HPV at some point
- Only 3 had all specimens test negative
- All 3 denied any sexual exposure

**HPV Cumulative Incidence: Ho Study**

Three-year study
- 608 college students in NJ
- Mean age 20 years
- Cumulative 36-month incidence of high-risk HPV in women negative at baseline: 43%
- By 12 months after infection, 70% had cleared the infection
- By 24 months, over 90% had cleared the infection


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**HPV Transmission**

- Virus primarily transmitted via genital contact
- Primarily through sexual intercourse, including receptive anal intercourse
- Can also be transmitted by:
  - Non-penetrating sexual activities
  - Oral-genital contact

Burchell AN. Vaccine. 2006.

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**Natural History of HPV & Cervical Cancer**

Persistence

Infection → Progression → Pre-cancer → Invasion → Regression → Clearance

Normal Cervix → HPV Infection → Pre-cancer → Invasion → Regression

Transformation Zones and HPV Infection

- Area where one type of epithelium contacts and gradually replaces another through process of metaplasia
- Present in cervix, anus, tonsils
- Areas of HPV-related carcinogenesis

Moscicki AB. Vaccine. 2006.

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**How are abnormal cells detected?**

- Abnormal cervical cells are detected through Pap tests (routine cervical cancer screening).
- Pap tests involve taking a small sample of cells from the cervix, usually during a routine pelvic exam.
- The cells are sent to a laboratory where they are prepared and evaluated under a microscope.

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**Cervical Transformation Zone**

Abnormal cells

- Cells in the lining of the cervix, vagina, or external genitals (vulva) that have changed in appearance are called abnormal cells.
- Often, the abnormal cells are caused by HPV.
- Low-risk types of HPV cause mild changes and clear on their own.
- High-risk types may not go away on their own, and abnormal cells may remain in the lining of the cervix.

Risk Factors for HPV Infection

Sexual Activity

Multiple Partners

Recommenations for Cervical Cancer Screening in Adolescents

ACOG, USPSTF, and ACS recommend Pap testing initiation:
- 3 years after vaginal intercourse
- By 21 years of age

Adolescents: Cervical Cancer in the US

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Incidence per 100,000 women</th>
<th># of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19 Years</td>
<td>0.3</td>
<td>22</td>
</tr>
<tr>
<td>20-24 Years</td>
<td>2.3</td>
<td>137</td>
</tr>
</tbody>
</table>

Screening Adolescents

<table>
<thead>
<tr>
<th>Age</th>
<th>HPV Testing Sensitivity</th>
<th>HPV Testing Referred for Colpo</th>
<th>Cytology Sensitivity</th>
<th>Cytology Referred for Colpo</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-22 Years</td>
<td>0.98</td>
<td>71%</td>
<td>0.80</td>
<td>66%</td>
</tr>
<tr>
<td>23-28 Years</td>
<td>0.96</td>
<td>65%</td>
<td>0.88</td>
<td>64%</td>
</tr>
<tr>
<td>≥ 29 Years</td>
<td>0.94</td>
<td>31%</td>
<td>0.91</td>
<td>50%</td>
</tr>
<tr>
<td>All</td>
<td>0.96</td>
<td>54%</td>
<td>0.86</td>
<td>59%</td>
</tr>
</tbody>
</table>

Screening Adolescents (Continued)

- Adolescents should not be screened unless they have been sexually active for 3 years.
- ASC-US rates are high in adolescents due to high prevalence of HPV.
- Cervical cancer is rare in adolescents in the U.S.
Management of LSIL in Adolescents

• Follow-up study of adolescents and young women with LSIL cytology results
• After 12 months of follow-up 60% showed regression to normal
• After an additional 24 months of follow-up, another 60% showed regression
• Cumulative regression at 36 months was 91%


Role of Persistent Infection

• Persistent infection with high-risk types of HPV is necessary for the progression of high grade lesions to invasive cancer
• Only persistent infection with high-risk types of HPV progresses to high-grade precancerous lesions and invasive cancer

Trottier H. Vaccine. 2006.

Infection &/or Neoplastic Progression

• Smoking
• HPV type
• Increasing age
• Lack of condom use
• Immunodeficiency (eg, HIV)
• Possibly OC use
• Possibly other STIs, such as chlamydia


Management of ASC-US or LSIL in Adolescents

<table>
<thead>
<tr>
<th>Repeat cytology in 12 months regardless of HPV status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pap @ 12 months</td>
</tr>
<tr>
<td>Pap @ 12 months</td>
</tr>
<tr>
<td>Pap @ 24 months</td>
</tr>
<tr>
<td>Pap @ 24 months</td>
</tr>
</tbody>
</table>

ASA and ASC-H not included in Consensus Guidelines; ARHP and PPFA adaptation.

Wright TC, Jr. ACOG. 2007. Adapted and printed with permission from ASCCP's Algorithms: 2006 Consensus Guidelines Speaker's Kit © 2006, 2007 ASCCP. All rights reserved.

Role of Persistent Infection (Continued)

• Average episode lasts 4-20 months
• <50% of women have same type 1 year later
• Type 16 has a greater risk of persistence

Trottier H. Vaccine. 2006.

Case Study: Cervical Screening in Adolescents

• 18-year-old female presents for annual exam: Pap done
• Patient History:
  • 1st intercourse at age 16
  • Came to clinic one month later requesting OCs
  • Pap and STD screening negative
  • Given OCs

Case Study: Cervical Screening in Adolescents (Continued)

–Exam at age 17
  • Pap negative
  • STD screen negative
  • OCs renewed
  • Result of current Pap test reported as ASC, HPV+


HPV Counseling

Learning Objectives

• Correct commonly held misperceptions about HPV infection

• Accurately counsel patients about management of HPV test results, especially women who are over 30 years of age, have a negative Pap test, and test positive for HPV

HPV Awareness: National Cancer Institute Survey

• NCI sponsored random telephone interview of adults
• All women (3,500) asked about HPV
• Only 38% had ever heard of human papillomavirus or HPV
• Of these, only 47% were aware that HPV causes cervical cancer

NCI Website. 2007.
### Counseling Women Age 30 or Older with HPV and a Negative Pap

- Diligent follow-up is important
- Need to return in 12 months for a Pap and HPV Test
- If HPV is still present at follow-up, colposcopy will be recommended even if the Pap is still negative


### Counseling Women with HPV

Remind your patient that:
- Most women will have HPV at some point
- There is no way of knowing how long HPV has been present
- Having HPV is not a sign of infidelity

### HPV Educational Messages

- HPV is sexually transmitted
- HPV is very common
- Most women with HPV will not get cancer
- HPV infection usually clears without treatment
- Pap tests are used to detect HPV-related pre-cancers


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### HPV Educational Messages (Continued)

- Many women initially positive for high-risk HPV will not have pre-cancer on further evaluation or be diagnosed with cancer
- 30% of cervical cancers caused by HPV types not covered by vaccine
- Women will continue to need cervical cancer screening even if vaccinated

CDC. HPV Information for Clinicians. 2006.

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### HPood Parenthood

Managing HPV

A New Era in Patient Care
Current Status of Prophylactic Vaccines

- June 2006: Merck quadrivalent HPV 6, 11, 16, 18 vaccine approved by FDA
- Recommendations for use by ACIP and included in VFC program
- GSK has filed with FDA for approval of bivalent HPV 16, 18 vaccine

HPV Vaccination

What age should be targeted?
- Vaccine is most effective when administered before HPV exposure
- Over 80% of sexually active adolescents become exposed to HPV within 3 years of sexual activity
- Best to administer prior to sexual activity

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Initiation of Sexual Activity Among Females in the United States

<table>
<thead>
<tr>
<th>Grade</th>
<th>Had Sex</th>
<th>≥ 3 Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>6th Grade</td>
<td>8.6%</td>
<td>4.3%</td>
</tr>
<tr>
<td>7th Grade</td>
<td>15.6%</td>
<td>8.5%</td>
</tr>
<tr>
<td>8th Grade</td>
<td>19.1%</td>
<td>9.7%</td>
</tr>
</tbody>
</table>

HPV Vaccine: Who Should Not Receive

- Moderate or severe acute illnesses
- History of immediate hypersensitivity to vaccine component or yeast

HPV Vaccine Issues: Previous HPV Exposure

- Most sexually active women will have been exposed to some type(s) of HPV
- Majority will not have evidence of exposure to vaccine types of HPV
- Almost none will have been exposed to all four vaccine types of HPV
HPV Vaccine Issues: Testing Before Vaccination

- Almost no women will have been exposed to all four vaccine HPV types
- Serology not accurate index of exposure
- Prevaccination screening is a waste of money and an unnecessary barrier

Wright TC, Jr. Vaccine. 2006.

HPV Vaccine Issues: Males

- Vaccine efficacy has not been proven in males – trials are underway
- Herd immunity is not important until a very high coverage rate in population – need to reach “high-risk transmitter”
- No recommendation for male vaccination

Wright TC, Jr. Vaccine. 2006.

HPV Vaccine: Outstanding Issues

- Target population?
- Which providers?
- Duration of protection? Need for booster?
- Management of missed doses?
- Patient adherence with three doses?

Wright TC, Jr. Vaccine. 2006; Bosch X. Gynecol Oncol. 2006.

HPV Vaccine: Outstanding Issues (Continued)

- Coverage provided for other high risk types?
- Optimal screening after widespread vaccination?
- Parental consent issues?

Wright TC, Jr. Vaccine. 2006; Bosch X. Gynecol Oncol. 2006.

Cervical Cancer Screening After Vaccination: Why Necessary?

- No national vaccine registry
- Poor recall of prior vaccination
- Exposure prior to vaccination
- Infection with other HPV types

Wright TC, Jr. Vaccine. 2006.
HPV Vaccine: Potential Barriers to Use

- Funding and cost
- Lack of provider awareness
- Lack of patient awareness
- Parental non-acceptance
- Myths about vaccination
- Adherence with 3-dose regimen

Wright TC, Jr. Vaccine. 2006.

HPV Vaccine: Cost

- Cost of vaccine alone: $360 for full series
- Some private insurance companies may not cover all costs
- Federal vaccine programs are available


HPV Vaccine: Other Provider Barriers

- Discomfort discussing STIs with parents, pre-teens
- Concern about parent reaction
- Stocking and administrating vaccine
- Administrative issues


Offer resources for patients

- www.arhp.org
- www.plannedparenthood.org
- www.familydoctor.org
- www.ashastd.org
- www.reproductiveaccess.org
- (section for consumers/patients)
- www.reproline.jhu.edu