Human Papillomavirus (HPV) and HPV Vaccine

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Adolescent STI Epidemiology, Testing, and Treatment Strategies

Objectives
- Describe the extent of HPV infection in adolescents
- Describe clinical presentations of HPV
- Describe how to diagnose and manage HPV infection in adolescents
- Understand how to prevent HPV infections

Case: Jenna

- Jenna is 15-year-old female who presents with a bump on her vagina.
- She has been sexually active for six months and has only had one partner.
- What is your differential diagnosis?

Physical Examination
- You perform an exam of the external genitalia and find small, firm, painless bumps
- No other abnormal findings found during pelvic and speculum exam and discharge is not present

Differential Diagnosis

- Chancroid (H. ducreyi)
- Genital Bump
- Molluscum Contagiosum
- Folliculitis
- External Genital Warts
- Molluscum Contagiosum
- Condyloma Lata
- Dermatologic Conditions
- Lentil papular, pedunculated growths
- Wet papules, papules with central umbilication
- Moist, verrucous papules from syphilis infection
- Condyloma Lata
- Molluscum Contagiosum
- Dermatologic Conditions

Discrete pearly firm papules with central umbilication
Flesh Colored Papular Painless Lesion
- Chancroid (H. ducreyi)
- Condyoma Lata
- Molluscum Contagiosum
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Genital Bump
- Folliculitis
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Differential Diagnosis

- Vestibular Papillae
- Condyloma Lata
- Molluscum Contagiosum

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Differential Diagnosis: Pearly Penile Papules

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Human Papillomavirus (HPV)

A member of a group of viruses in the genus Papillomavirus

Of the 100 strains, more than 40 are sexually transmitted and infect the genital area of males and females

Strains are classified as:
- **High-risk (oncogenic)**
  - (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68)
- **Low-risk (non-oncogenic)**
  - (6, 11, 40, 42, 43, 44, 53, 54, 61, 72, 73, and 81)

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HPV Incidence and Prevalence

Highest incident STI in the U.S.

Approximate prevalence in adolescents and young adults is 9.2 million

By age 50, at least 80% of females will have acquired genital HPV infection

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HPV Prevalence:

Females Aged 14–59 Years

<table>
<thead>
<tr>
<th>Age</th>
<th>Low-risk HPV*</th>
<th>High-risk HPV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>14–19</td>
<td>13%</td>
<td>6%</td>
</tr>
<tr>
<td>20–24</td>
<td>26%</td>
<td>8%</td>
</tr>
<tr>
<td>25–29</td>
<td>36%</td>
<td>9%</td>
</tr>
<tr>
<td>30–39</td>
<td>40%</td>
<td>10%</td>
</tr>
<tr>
<td>40–49</td>
<td>43%</td>
<td>12%</td>
</tr>
<tr>
<td>50–59</td>
<td>45%</td>
<td>13%</td>
</tr>
</tbody>
</table>

NOTE: Error bars indicate 95% confidence intervals. Both high-risk and low-risk HPV types were detected in some females.

From the National Health and Nutrition Examination Survey (NHANES) 2005–2006
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Genital HPV Prevalence Rates in Males

How often is genital warts diagnosed at the Doctor’s Office?


Perianal and possibly anal HPV may be caused by:
- Autoinoculation
- Sexual activity other than insertive anal sex
- Spread from a nearby genital infection site

Prevalence of Oral HPV Infection: NHANES Data

Majority are subclinical
- High grade squamous and glandular intraepithelial lesions

Genital Warts Appearance
- Cauliflower-shaped, flesh colored, pink or hyperpigmented
- Usually dome-shaped and skin colored
- Thick, horny layer which can resemble common warts
- Macular to slightly raised, flesh colored, with smooth surface

HPV Clinical Manifestations

Manfestations depend on oncogenic potential
- Majority are subclinical
- Low Risk Types
- High Risk Types

Prevalence 10.1%
Prevalence 3.6%


How often is genital warts diagnosed at the Doctor’s Office?

NOTE: The relative standard errors for genital warts estimates of more than 100,000 range from 18% to 30%.

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Prevalence 10.1%
Prevalence 3.6%


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Age-Specific Anal Canal HPV Prevalence Among Men Having Sex with Women

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HPV Clinical Manifestations

Manifestations depend on oncogenic potential
- Majority are subclinical
- Low Risk Types
- High Risk Types

Genital Warts
- Low grade squamous and glandular intraepithelial lesions
- High grade squamous and glandular intraepithelial lesions

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Prevalence 10.1%
Prevalence 3.6%


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Genital Warts Sites of Infection

Genital Warts Commonly Occur in Areas of Coital Friction

Genital Warts Sites of Infection

- Penis
- Scrotum
- Urethral Meatus
- Perianal

Genital Warts Sites of Infection

- Introitus
- Vulva
- Perineum
- Anus

(Vaginal and cervical lesions are less common)

Genital Warts Symptoms

Genital Warts are Usually Asymptomatic

Symptoms may develop depending on size and location of warts

You think that Jenna has external genital warts. Is there a confirmatory test to make the diagnosis?
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External Genital Warts: Diagnosis

- Clinical diagnosis by visual inspection
- Acetic acid application NOT recommended (low specificity)
- Type-specific HPV DNA tests NOT recommended

Consider biopsy for warts if:
- Atypical appearance
- Unresponsive or worsen with standard therapy
- Persistent ulceration or bleeding
- Irregular pigmentation

Should you Perform a Pap Smear?

<table>
<thead>
<tr>
<th>Age Group</th>
<th>USPSTF</th>
<th>ASCCP, ASCP</th>
<th>ACOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;21 YEARS OLD</td>
<td>Not Recommended</td>
<td>Pap every 3 yrs</td>
<td>Not Recommended</td>
</tr>
<tr>
<td>21-29 YEARS OLD</td>
<td>Pap every 3 yrs, 5 yrs OR Pap 3 yrs</td>
<td>Recommended</td>
<td>No Change</td>
</tr>
<tr>
<td>30-65 YEARS OLD</td>
<td>Pap 3 yrs OR Pap + HPV acceptable</td>
<td>Recommended</td>
<td>No Change</td>
</tr>
<tr>
<td>&gt;65 YEARS OLD</td>
<td>Not Recommended</td>
<td>Pap every 2 yrs</td>
<td>Stop Paps at 65-70 yrs</td>
</tr>
</tbody>
</table>

Natural History of HPV Infection

- Most infections subclinical with no clinical consequences
- Incubation period is variable
  - Weeks to months for genital warts
  - Months to years for cellular changes
- Most infections are transient and self-resolve
  - Median duration is 8 months

Why the Change in Screening for Adolescents?

- Invasive cervical cancer is very rare in ♀ under age 21
- Immune system clears HPV infection within 1-2 years in most adolescent ♀
- Large majority of cervical dysplasia (HPV-related precancerous lesions) resolve on their own with no treatment

New Pap Smear Recommendations: Why The Change?

- Abnormal pap smears lead to:
  - Increased procedures
  - Patient anxiety
  - Stigma of having an STD
  - Side effects of procedures
  - Pregnancy complications
  - Increased cost
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Initial Steps for Follow-Up of Abnormal Pap Smears in Adolescents

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Initial Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASC-US, LGSIL, or CIN 1</td>
<td>Repeat pap in 12 and 24 months</td>
</tr>
<tr>
<td>ASC-H</td>
<td>Colposcopy</td>
</tr>
<tr>
<td>LGSIL</td>
<td>Colposcopy with Endocervical Evaluation</td>
</tr>
<tr>
<td>Atypical Glandular Cells (rare in adolescents)</td>
<td>Colposcopy with Endocervical Evaluation</td>
</tr>
<tr>
<td>CIN 2</td>
<td>No therapy</td>
</tr>
<tr>
<td>CIN 3</td>
<td>Treatment</td>
</tr>
</tbody>
</table>

- HPV testing not recommended at all
- Emphasize minimal to no intervention


How would you treat Jenna’s external genital warts?

Genital Warts: Treatment

- Goal: Removal of symptomatic or cosmetically concerning warts
- Does not eradicate underlying infection
- Recurrence is common

Genital Warts: Patient Applied Treatments

- Podofilox 0.5% solution/gel
  - Apply to visible genital warts twice a day for three days, followed by four days of no therapy
  - Repeat if necessary

- Imiquimod 5% cream (Aldara™)
  - Apply once daily at bedtime, wash off in AM, use three times a week for up to 16 weeks

- Sinecatechins (Veregen™) 15% ointment
  - Apply 3 times daily (0.5cm strand of ointment to each wart) using finger to ensure coverage. Use no longer than 16 wks. Do not wash after use.

Genital Warts: Costs of Patient Applied Treatments

<table>
<thead>
<tr>
<th>Drug and Strength</th>
<th>Estimated Cost/Month Supply ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinecatechins ointment 15% (Veregen™)</td>
<td>Estimated 1 month supply: (1-2 15mg tubes) $150-$300</td>
</tr>
<tr>
<td>Podofilox 0.5% topical solution</td>
<td>Estimated 1 month supply: $24</td>
</tr>
<tr>
<td>Imiquimod 5% topical cream (Aldara™)</td>
<td>1 month supply: $95</td>
</tr>
</tbody>
</table>

- Usage dependent on total wart area
- Data from April 2008
- www.pbm.va.gov
Cryotherapy
- with liquid nitrogen or cryoprobe
- Must be trained in use
- Repeat every 1–2 weeks

Podophyllin resin 10%–25% in compound tincture of benzoin
- Apply small amount, allow to dry, wash off in 1–4 hours
- May repeat weekly

Trichloroacetic acid (TCA) or Bichloroacetic acid (BCA) 80-90%
- Apply small amount, allow to dry
- May repeat weekly

Genital Warts: Provider Applied Treatments

Local irritation
- Limit to <0.5mL or <10cm² of warts
- No open wounds in treated area

Pain, necrosis, ulceration, blistering

Surgical removal
- scissor excision, shave excision, curettage, or electrosurgery
- *Single Visit Elimination of Warts*

Best option for large number of warts or large affected area

Should Jenna’s partner receive any treatment?

Should you give Jenna the HPV vaccine?

Regular and consistent condom use achieves about 60% protection against HPV

Genital Warts: Treatment of Internal Warts

Cervical Warts
- Biopsy to rule out high grade squamous intraepithelial lesion
- Cryotherapy with liquid nitrogen (no cryoprobe use)
- TCA/BCA 80-90%

Involves specialist for cervical lesions

Vaginal Warts
- Cryotherapy with liquid nitrogen
- TCA/BCA 80-90%

Involves specialist for vulvar lesions

Urethral Meatal Warts
- Cryotherapy with liquid nitrogen
- Podophyllin 10-25%

Involves specialist for intra-anal lesions

Perianal Warts
- Cryotherapy with liquid nitrogen
- TCA/BCA 80-90%
- Surgical excision

Involves specialist for intra-anal lesions

Genital Warts: Partner Implications

- Counsel patients and partners about risk of transmission
- Recommend routine STD testing
- Recommend condom use
- No HPV DNA test recommended
- Treatment for subclinical warts or to prevent formation of warts NOT recommended

A Little Note on Condoms...

Counsel patients and partners about risk of transmission

Recommend routine STD testing

Recommend condom use

No HPV DNA test recommended

Treatment for subclinical warts or to prevent formation of warts NOT recommended

Regular and consistent condom use achieves about 60% protection against HPV

Should you give Jenna the HPV vaccine?
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HPV Vaccine

- Can be given prior to sexual initiation
- Enormous potential for disease prevention
- Protects against multiple strains
- Cost-effective

Gardasil
- Quadrivalent HPV vaccine
- Prevents HPV types 16/18 & 6/11
- FDA approved for females (2006) and males (2009)

Cervarix
- Bivalent HPV vaccine
- Prevents HPV types 16/18
- FDA approved for females (2009)

HPV Vaccines: FDA Approved

- HPV 6,11 cause 90% of genital warts
- HPV 16,18 cause 70% of cervical cancer

ACIP HPV Vaccine

Recommendation for FEMALES

- Recommend vaccination for all 11 and 12 yo
  - Can begin as young as age 9 yrs
  - Either HPV 4 or HPV 2 can be used
- Catch-up vaccination recommended for all 13-26 yo

Efficacy of HPV2 and HPV4 Vaccine in Females

<table>
<thead>
<tr>
<th>Vaccine/EndPoint HPV type</th>
<th>Vaccine</th>
<th>Control</th>
<th>Vaccine efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadrivalent vaccine (HPV1, 2, 4, 6)</td>
<td>6.8%</td>
<td>7.3%</td>
<td>63.9% (95.9-98.8)</td>
</tr>
<tr>
<td>HPV 16</td>
<td>2.1</td>
<td>2.1</td>
<td>95.7% (92.8-98.6)</td>
</tr>
<tr>
<td>HPV 18</td>
<td>2.1</td>
<td>2.1</td>
<td>95.7% (92.8-98.6)</td>
</tr>
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ACIP HPV Vaccine

Recommendations for MALES

- Recommend vaccination for all 11 and 12 yo
  - Can begin as young as age 9 yrs
  - Only HPV 4 approved for
  - Catch-up vaccination recommended for all 13-21 yo
  - Recommended for all MSM and immunocompromised
  - Permissive recommendation for 22-26 yo without risk factors

Is HPV vaccination cost-effective for boys?

- YES
- Adding the HPV immunization of 12 yr old to U.S. female only vaccination programs is cost-effective, particularly if:
  - HPV4 coverage is low
  - All potential HPV vaccine health benefits included in analysis

For Comparison...

Cost per QALY gained by adolescent vaccines in the US

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Target group</th>
<th>Cost per QALY gained (compared to no vaccination)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>College freshmen</td>
<td>&lt;$5 (cost-saving) to $10,000</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>College freshmen</td>
<td>&lt;$5 (cost-saving) to $15,000</td>
</tr>
<tr>
<td>HPV</td>
<td>12 year-old girls</td>
<td>&gt; $3,000 to $65,000</td>
</tr>
<tr>
<td>Influenza</td>
<td>12- to 17-year-olds, high risk</td>
<td>&gt; $10,000</td>
</tr>
<tr>
<td>Tdap</td>
<td>All 11-year-olds</td>
<td>&gt; $55,000</td>
</tr>
<tr>
<td>Influenza</td>
<td>12- to 17-year-olds, healthy</td>
<td>&gt; $140,000</td>
</tr>
<tr>
<td>Hemiploccal</td>
<td>2-dose at 11 &amp; 15 year-olds</td>
<td>&gt; $105,000</td>
</tr>
</tbody>
</table>

Cost per QALY gained by vaccinating 12 year-old boys

- Lower coverage scenario: $41,400
- Higher coverage scenario: $134,800

*Includes transmission effects to females

Why are HPV vaccination rates so low?

- Parental delay of HPV vaccination
- Fewer & weaker health-care provider recommendations
- Providers using risk-based approaches
  - Higher HPV initiation rates among blacks and Hispanics vs whites
  - Females living below poverty line more likely fully protected w/ 3 doses vs females living at or above poverty line

Communicating with Parents

- Jenna’s mom is hesitant about the HPV vaccine
  - How would you address her concerns that the vaccine would increase Jenna’s sexual activity?
Counseling Tips

- Remind parents that their behavior, messages and expectations play a key role in their children’s decisions regarding sex and relationships (NOT the HPV vaccine)
- Keep communication lines open
- Give positive feedback to parents who are vaccinating their children
- Provide accurate information

What does the Evidence say?

- Recent study published in Pediatrics (October 2012) evaluated sexual activity-related clinical outcomes after adolescent vaccination
- HPV Vaccination in the recommended ages (11-12) was not associated with increased sexual activity-related outcome rates.

Jenna: Case Synopsis

- Differential diagnosis for genital bumps:
  - HPV
  - Condyloma Lata
  - Molluscum contagiosum
  - Dermatological Conditions
- Majority of HPV infections will clear the system
- The HPV vaccine provides tremendous prevention opportunity

Review of Objectives

Can you:

- Describe the extent of HPV infection in adolescents
- Describe clinical presentations of HPV
- Describe how to diagnose and manage HPV infection in adolescents
- Understand how to prevent HPV infections

HPV-specific Resources

- U.S. Centers for Disease Control and Prevention
  - Treatment Guidelines: http://www.cdc.gov/STD/treatment/default.htm
- American Social Health Association: http://www.ashastd.org/std-sti/hpv.html

Provider Resources

- http://www.nycptc.org — New York City STD/HIV Prevention Training Center (PTC)
- www.acog.org — The American College of Obstetricians and Gynecologists
- www.adolescenthealth.org — The Society for Adolescent Health and Medicine
- http://www.cahl.org — The Center for Adolescent Health and the Law
- http://www.rhtp.org — The Reproductive Health Technologies Project
- http://www.ri.org — The Reproductive Freedom Project of the American Civil Liberties Union
- www.advocatesforyouth.org — Advocates for Youth
- www.ahrp.org — Physicians for Reproductive Choice and Health
- www.prch.org — Physicians for Reproductive Choice and Health
- www.aap.org — The American Academy of Pediatrics
- www.acog.org — The American College of Obstetricians and Gynecologists
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Questions?