Genital Warts –
CDC Recommendations

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Disclosure

Ad board and speakers bureau for
• Merck
• Pharmaderm

Learning Objectives

1. Counsel patients on lifestyle modifications and screening for HPV and EGWs.
2. Detect, diagnose, treat and monitor HPV and EGWs to avoid long-term health consequences, especially as they relate to patients.
3. Determine if the safety and efficacy of the HPV vaccine is appropriate for the patient.
4. Reference the 2010 CDC STD guidelines and current treatment modalities for HPV and EGWs.
U.S. Genital HPV Statistics

- By age 50, ~75-80% of men and women will acquire genital HPV
  - ~6.2 million new infections/year
  - ~20 million active infections
- Highest prevalence = 20-24 years old
- High physical and emotional burdens with HPV infections and HPV-related diseases


Common HPV Types

<table>
<thead>
<tr>
<th>HPV Types</th>
<th>Disease Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82</td>
</tr>
<tr>
<td>Low risk</td>
<td>6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81</td>
</tr>
</tbody>
</table>

- Low-grade cervical changes
- High-grade cervical changes
- Cervical cancer
- Other anogenital cancers
- Head and neck cancer
- Benign low-grade cervical changes
- Condylomata acuminata (genital warts)
- Recurrent respiratory papillomatosis

Genital Warts

- HPV 6 or 11 caused 90% GWs
  - HPV 16, 18, 31, 33, and 35 are found occasionally as coinfections
  - Also associated with conjunctival, nasal, oral, and laryngeal warts
- Usually asymptomatic
  - Can be painful or pruritic
Genital Warts

- Usually flat, papular, or pedunculated growths on the genital mucosa
- Commonly at certain anatomic sites
  - Introitus in women
  - Under foreskin of uncircumcised penis
  - Shaft of penis
- Also occur at multiple sites
- Intra-anal warts mainly with receptive anal intercourse


Courtesy of E.J. Mayeaux Jr., MD

HPV Risk Factors

Women

- Age\(^1,2\)
- Greater number of male partners\(^1,2\)
- Earlier age of first sexual intercourse\(^4\)
- Sexual behaviors of previous male sexual partners\(^1,2\)
- Immunological status\(^2\)

Men

- Lifetime number of sexual partners\(^5\)
- Number of recent sexual partners\(^5\)
- Uncircumcised\(^6\)
- Same-sex encounters\(^6\)

References:

Reduce HPV Transmission

- Abstinence from genital contact\(^1,2\)
- Lifetime mutual monogamy\(^2,3\)
- Condom use may help reduce risk, but is not fully protective\(^1,5\)
  - If HPV is present on uncovered skin, transmission is possible.\(^2\)


- HPV effective condoms….
- Condoms decrease transmission but do not prevent infection where they don’t cover
Recurrent Respiratory Papillomatosis

- 5977 new cases/year in U.S. (1993)
- 2354 peds
- 3623 adult
- >90% HPV 6/11
- HPV not an indication for C-section

Detect, diagnose, treat and monitor HPV and EGWs to avoid long-term health consequences

Diagnosis of EGW

- Majority diagnosed by visual inspection in bright light
  - Magnifying glass helpful
Genital Warts Diagnosis

- Can be confirmed by biopsy
  - If diagnosis is uncertain
  - Lesions do not respond to standard tx
  - Worsens during therapy
  - Atypical lesion
  - Patient has compromised immunity
  - GW pigmented, indurated, fixed, bleeding, or ulcerated

Genital Warts Diagnosis

- Use of HPV DNA testing is not recommended for genital warts
  - Does not alter clinical management
- Routine use of 3%–5% acetic acid for screening to detect mucosal changes attributed to HPV infection is not recommended
Differential Diagnosis of Genital Warts

- Normal anatomy
  - Pearly penile papules
  - Micropapillomatosis
- Other STDs
  - Condyloma latum
  - Molluscum contagiosum
- Benign skin lesions
- Neoplasms


DDx Pearly Penile Papules

Courtesy of Richard P. Usatine, MD

DDx Herpes

Courtesy of E.J. Mayeaux Jr., MD
DDx Condyloma latum

Reference the 2010 CDC STD guidelines and current treatment modalities for HPV and EGWs
Genital Warts Treatment

- Primary reason is symptoms (including relieving cosmetic concerns)
  - Can usually induce wart-free periods
  - Visible GWs can resolve on their own
- Tx likely reduces but not eradicates HPV infectivity
  - ? reduces future transmission unclear
- GW not associated with cervical Ca

Genital Warts Treatment

- Guided by
  - Preference of the patient
  - Available resources
  - Experience of the healthcare provider
- No treatment superior to any other
- No single tx is ideal
- Acceptable alternative to forgo tx

Genital Warts Treatment

- Warts on moist surfaces or in folds respond best to topical treatment
- Change modality if a patient has not improved after a complete course of tx
  - Or if side effects are severe
  - Most respond within 3 months

US Treatment Guidelines

**Patient-Applied**
- Podofilox 0.5% solution or gel
- Imiquimod 5% cream
- Sinecatechins 15% ointment

**Provider-Applied**
- Cryotherapy repeated every 1–2 weeks
- Podophyllum Resin 10%–25%
- TCA 70%–90%
- Surgical removal

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**Therapy Clearance Rates**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Clearance Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imiquimod</td>
<td>37-54%</td>
</tr>
<tr>
<td>Podofilox</td>
<td>45-77%</td>
</tr>
<tr>
<td>Sinecatechins</td>
<td>41-58%</td>
</tr>
<tr>
<td>Podophyllum</td>
<td>38-79%</td>
</tr>
<tr>
<td>Surgical Excision</td>
<td>89-93%</td>
</tr>
<tr>
<td>Electrodesication</td>
<td>94%</td>
</tr>
<tr>
<td>TCA</td>
<td>63-70%</td>
</tr>
<tr>
<td>Cryotherapy</td>
<td>71-79%</td>
</tr>
</tbody>
</table>

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**GWs and Pregnancy**

- Imiquimod, sinecatechins, podophyllum, and podofilox should not be used
- Can proliferate and become friable
- Rarely, HPV types 6 and 11 can cause respiratory papillomatosis
  - Route of transmission not understood
  - Unclear if C-section prevents
  - CDC – C-section not indicated
  - Only if pelvic outlet is obstructed

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Sinecatechin 15% Ointment

• Green-tea extract

• Stimulates immune response
• 0.5-cm strand of ointment in a thin layer to each wart 3x/day using a finger
  – Up to 16 weeks
  – Do not wash off
• Avoid genital, anal, or oral sexual contact while ointment on skin

Sinecatechin 15% Ointment

• SE = erythema, pruritus/burning, pain, ulceration, edema, induration, and vesicular rash
• May weaken condoms and diaphragms
• Not recommended for HIV-infected persons, immunocompromised persons, or persons with clinical genital herpes
• Pregnancy Class C
Imiquimod 5% Cream

- Immune enhancer
  - Stimulates production of interferon and other cytokines
  - Apply once at bedtime, 3x a week for up to 16 weeks
  - Wash area with soap and water 6-10 hours after the application

Imiquimod 5% Cream

- SE = Local inflammatory reactions
  - Redness, irritation, induration, ulceration/erosions, vesicles, and hypopigmentation
- Imiquimod might weaken condoms and vaginal diaphragms
- Pregnancy Class C

Podofilox 0.5% Solution or Gel

- Podophyllotoxin
- Purified extract of podophyllum plant
Podofilox 0.5% Solution or Gel

- Antimitotic drug
  - Relatively inexpensive
  - Easy to use, safe, and self-applied
- Applied with swab 2x/day for 3 days, followed by 4 days of no tx
  - Repeat up to four cycles
  - Total wart area treated <10 cm²
  - Volume of podofilox <0.5 mL per day


Podofilox 0.5% Solution or Gel

- Healthcare provider should apply the initial treatment
  - Demonstrate proper application technique
  - Identify which warts should be treated
- Mild to moderate pain
- Local irritation
- Safety in pregnancy not established


Cryotherapy Treatment

- Thermal-induced cytolysis
- Providers must be trained on the proper use of this therapy
  - Over- and under-treatment can result in complications or low efficacy
- Pain followed by blistering & necrosis
- Local anesthesia (topical or injected) might facilitate therapy if warts large
Cryotherapy

• Large cotton-tipped applicators
• Cryo units use CO₂ and NO₂
  – Water-soluble gel for thermal bond
  – Cryo unit is activated in 30-second bursts until an area 2 to 3 mm around the base of the lesion is frozen
• Repeat at 2-week intervals


Cryotherapy Treatment

Podophyllum Resin 10%–25%

• Apply to each wart and allow to air-dry before touching clothing
• Local irritation
• Repeat weekly as necessary
• Systemic absorption and toxicity
  – Application limited to <0.5 mL or an area of <10 cm² of warts per session
  – No open lesions or wounds

CDC. Sexually transmitted diseases treatment guidelines. MMWR. 2010 Dec 17;59 (RR-12):1-110.
Podophyllum Resin 10%–25%

- Wash off 1-4 hours after application
- Pregnancy Category X
- Podophyllum resin preparations differ in the concentration of active components
- Shelf life and stability of podophyllum preparations are unknown

TCA 70%-90%

- Caustic agent that destroys warts by chemical coagulation of proteins
- Widely used, but not investigated well
- Low viscosity – can spread rapidly if applied excessively
- A small amount should be applied only to the warts and allowed to dry
  - White frosting develops

TCA 70%-90%

- If pain is intense, acid can be neutralized with soap or HCO₃
- If an excess amount of acid applied, the treated area should be powdered with talc, or treated with HCO₃ or liquid soap preparations to remove unreacted acid
- Can be repeated weekly, if necessary
- Pregnancy Class C
**Electrocautery Treatment**

- Local anesthesia is applied
- Warts physically destroyed
- No additional hemostasis required
- Carefully control depth of electrocautery
  – To prevent scarring

**Surgical Treatment**

- Eliminating warts at a single visit
- Requires substantial clinical training, additional equipment, and longer visits

**Sharp Treatment**

- Local anesthesia is applied
- Tangential excision with fine scissors or a scalpel, by laser, or by curettage
- Wound extends into upper dermis
- Hemostasis by electrocautery unit or a chemical styptic
- Suturing unnecessary
Sharp Treatment

LEEP Therapy

5-Fluorouracil

- Once commonly used
- Cases of clear cell carcinoma arising in the vaginal adenosis after 5-FU treatment for condylomas
- These problems and side effects have eliminated this drug as a preferred treatment modality
Determine if the safety and efficacy of the HPV vaccine is appropriate for the patient

Genital Warts Counseling

- Quadrivalent HPV vaccine protects
  - Against the types that cause 90% of GWs (Types 6/11) in males and females
  - And against the types that cause 70% of Cx Ca
- Recommended for 11- and 12-year-old girls and boys age 13-26 years
  - Most effective when given before sexual contact
- Bivalent does not protect against GWs


HPV-4 Efficacy Against EGWs

**HPV-4 Prophylactic Efficacy EGWs**

**Per-Protocol Population (Protocols 007, 013, and 015)**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Mean Follow-Up</th>
<th>HPV-4 Cases (N = 9075)</th>
<th>Placebo Cases (N = 9075)</th>
<th>% Efficacy</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV 6/11/16/18-related Ext Gen Lesion</td>
<td>44 months</td>
<td>2</td>
<td>227</td>
<td>99</td>
<td>(97, 100)</td>
</tr>
<tr>
<td>By Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HPV 6-related</td>
<td></td>
<td>2</td>
<td>179</td>
<td>99</td>
<td>(96, 100)</td>
</tr>
<tr>
<td>HPV 11-related</td>
<td></td>
<td>0</td>
<td>36</td>
<td>100</td>
<td>(89, 100)</td>
</tr>
<tr>
<td>HPV 16-related</td>
<td></td>
<td>0</td>
<td>46</td>
<td>100</td>
<td>(92, 100)</td>
</tr>
<tr>
<td>HPV 18-related</td>
<td></td>
<td>0</td>
<td>13</td>
<td>100</td>
<td>(68, 100)</td>
</tr>
<tr>
<td>By Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genital Warts</td>
<td>2</td>
<td>193</td>
<td>99</td>
<td>(96, 100)</td>
<td></td>
</tr>
<tr>
<td>VIN 1 or VaIN 1</td>
<td>0</td>
<td>28</td>
<td>100</td>
<td>(86, 100)</td>
<td></td>
</tr>
</tbody>
</table>

**HPV-4 SAEs - Males**

**Injection-Site Adverse Reactions**

<table>
<thead>
<tr>
<th></th>
<th>HPV-4 (n = 3,093)</th>
<th>Adjuvant Only (n = 2,029)</th>
<th>Saline placebo (n = 274)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>61%</td>
<td>51%</td>
<td>42%</td>
</tr>
<tr>
<td>Erythema</td>
<td>17%</td>
<td>14%</td>
<td>15%</td>
</tr>
<tr>
<td>Swelling</td>
<td>14%</td>
<td>10%</td>
<td>8%</td>
</tr>
</tbody>
</table>

**Systemic Adverse Reactions**

<table>
<thead>
<tr>
<th></th>
<th>HPV-4 (n = 3,093)</th>
<th>Placebo (n = 2,303)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>12%</td>
<td>11%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>8%</td>
<td>7%</td>
</tr>
<tr>
<td>Oropharyngeal Pain</td>
<td>3%</td>
<td>2%</td>
</tr>
</tbody>
</table>

**Decline in Genital Warts after HPV-4**

![Graph showing decline in genital warts after HPV-4 vaccination](image)
Counsel patients on lifestyle modifications and screening for HPV and EGWs.

ACOG Pap Guidelines 2009

<table>
<thead>
<tr>
<th>First Screen</th>
<th>Women &lt;30 years</th>
<th>Women ≥30 Years</th>
</tr>
</thead>
</table>
| 21 years of age | Cervical cytology testing every 2 years | + Women who have had 3 consecutive negative cervical cytology test results may be screened every 3 years.
|               |               | + Women who have had negative test results on both cervical cytology and HPV DNA tests should be rescreened no sooner than 3 years.

Women who are immunosuppressed, are infected with HIV, were exposed in utero to DES, or were previously treated for CIN 2, CIN 3, or cancer may require more frequent cervical cytology screening.

Genital Warts Counseling

- HPV infection is very common
- Passed on through genital contact
- Most sexually active adults will get HPV at some point in their lives
  - Most will never know it
  - Usually has no signs or symptoms
- Clears spontaneously in most cases
Genital Warts Counseling

- HPV types that cause GWs different from the types that can cause cancer
- Both partners are usually infected
- Does not indicate sexual infidelity
- Does not affect a woman’s fertility
- Condom use decreases transmission but is not fully protective

Genital Warts Counseling

- Only definitive method to avoid HPV is to abstain from sexual activity
- HPV tests should not be used to screen:
  - men
  - partners of women with HPV
  - adolescent females, or
  - Any condition other than cervical cancer

Genital Warts Counseling

- Genital warts are not life-threatening
- If untreated, might go away
- It is difficult to determine how or when a person became infected with HPV
- Often recur after treatment
- Women with GWs do not need Pap tests more often than recommended
- Get screened for other STDs
Thank you for joining me today for Genital Warts – CDC Recommendations. Please click on the link to complete the Post-Assessment. https://nf.aafp.org/a/1811