Human Papilloma Viruses
HPV

Testing and Treatment of STDs

<table>
<thead>
<tr>
<th>Medical Care</th>
<th>Hours</th>
<th>Weeks</th>
<th>Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute &amp; Follow-up Examinations</td>
<td></td>
<td></td>
<td>Follow-up Exam 1 to 2 weeks</td>
</tr>
<tr>
<td>Forensic Specimen Collection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV Post-Exposure Prophylaxis &amp; Testing</td>
<td>36 hours</td>
<td></td>
<td>Re-test 6-8 weeks</td>
</tr>
<tr>
<td>Pregnancy Testing &amp; Prevention</td>
<td>72 hours</td>
<td>Follow-up 1 to 2 weeks</td>
<td>SaraminilHS 3 months</td>
</tr>
<tr>
<td>STI Testing</td>
<td></td>
<td>Follow-up cultures 1 to 2 weeks</td>
<td>RPR, HSV 4-6 weeks</td>
</tr>
<tr>
<td>STI Treatment</td>
<td></td>
<td></td>
<td>Treatment may be offered in the acute post-assault setting.</td>
</tr>
</tbody>
</table>

TABLE 6. Implications of commonly encountered sexually transmitted (ST) or sexually associated (SA) infections for diagnosis and reporting of sexual abuse among infants and prepubertal children

<table>
<thead>
<tr>
<th>ST/SA Confirmed</th>
<th>Evidence for sexual abuse</th>
<th>Suggested action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea*</td>
<td>Diagnostic†</td>
<td>Report§</td>
</tr>
<tr>
<td>Syphilis*</td>
<td>Diagnostic</td>
<td>Report§</td>
</tr>
<tr>
<td>Human immunodeficiency virus†</td>
<td>Diagnostic</td>
<td>Report§</td>
</tr>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td>Diagnostic†</td>
<td>Report§</td>
</tr>
<tr>
<td>Trichomonas vaginalis</td>
<td>Highly suspicious</td>
<td>Report§</td>
</tr>
<tr>
<td>Condylomata acuminata (anogenital warts)*</td>
<td>Suspicious</td>
<td>Report§</td>
</tr>
<tr>
<td>Genital herpes*</td>
<td>Suspicious</td>
<td>Report§**</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>Inconclusive</td>
<td>Medical follow-up</td>
</tr>
</tbody>
</table>


* If not likely to be perinatally acquired and rare nonsexual vertical transmission is excluded.
† Although culture is the gold standard, current studies are investigating the use of nucleic acid amplification tests as an alternative diagnostic method.
§ Report to the agency mandated to receive reports of suspected child abuse.
‖ If not likely to be acquired perinatally or through transfusion.
** Unless a clear history of autoinoculation is evident.
**HPV**

Wart-like lesions in the genital or anal area

- Indeterminate findings: insufficient or conflicting data from research studies (may require additional studies/evaluation to determine significance)
  

**Which STDs are commonly transmitted?**

- HPV is the most common STD (more than 40% of sexually active teens)
- Anogenital infections are usually subclinical, transmitted by sexual contact. Most are transient and have no clinical consequences.
- More than 40 types can infect the anogenital tract

**HPV Epidemiology**

- It is estimated that at least 50% of sexually active men and women acquire genital HPV at some point in their lives.
- The incidence of reported anogenital warts in children has increased dramatically since 1990.

**HPV Risk Factors: Adolescents**

*Females:*

- Sexual behavior
  - Risk increases with increasing lifetime number of male sex partners
  - Early age of first sexual intercourse
- Sexual behavior of male sex partners—risk increases for women whose sex partners had multiple sex partners
- Immune status—HPV more likely to be detected in immune-suppressed women

*Males:*

- Greater lifetime number of sex partners
- Greater number of recent sex partners
- Being uncircumcised

**HPV Risk Factors: Infants and Children**

- Sexual abuse
- Maternal HPV, abnormal PAP
- Subclinical oral HPV (maternal or other)
- Diaper changes with transmission of non-genital HPV types to genital surface
- Possibly fomite transmission in household with HPV
- Immunosuppressed state
- Skin abnormalities
2 year old with growth on his penis and no rectal warts
What is the work-up? What is the question?

Questions about warts
- Are these warts?
- How did he get them?
- Will he get cancer or other problems from this? What type are they?
- How do we treat this?

Are these really warts?

HPV Clinical Presentation
- Be able to recognize HPV on clinical presentation
- Develop a differential diagnosis for lesions that look like HPV
- Interpret cervical cytological changes that result from HPV
- Genital HPV infection is usually transient, has no clinical manifestations or sequelae.
- Clinical manifestations of genital HPV infection may include:
  - Genital warts
  - Cervical cell abnormalities
  - Anogenital squamous cell cancers
  - Recurrent respiratory papillomatosis

HPV Clinical Appearance
- Condylomata acuminata
- Smooth papules
  - Usually dome-shaped and skin-colored
- Flat papules
  - Macular to slightly raised
  - Flesh-colored, with smooth surface
  - More commonly found on internal structures (i.e., cervix), but also occur on external genitalia
- Keratotic warts
  - Thick horny layer that can resemble common warts or seborrheic keratosis
- HPV infections in infants and children may present as laryngeal papillomatosis—juvenile onset recurrent respiratory papillomatosis (JORRP).
- Respiratory papillomatosis is a rare condition, associated with HPV types 6 and 11.
HPV Differential Diagnosis

- Normal anatomic variants
  - “Pink pearly penile papules”
  - Vestibular papillae (micropapillomatosis labialis)
  - Skin tags (acrochordons)
    - A protrusion of the anal verge which interrupts the symmetry of the perianal skin folds.
- Acquired dermatologic conditions
  - Seborrheic keratosis
  - Lichen planus
  - Fibroepithelial polyp, adenoma
  - Melanocytic nevus
  - Neoplastic lesions
- Molluscum contagiosum
  - Papules with central dimple, caused by a pox virus
  - Rarely involves mucosal surfaces
- Condylomata lata
  - Tend to be smoother, moist, more rounded
  - Darkfield-positive for Treponema pallidum

How did he get them?

- What is the pathogenesis of HPV, including vertical transmission, non-sexual transmission, sexual transmission?
- What is currently known about the latency period of HPV?

HPV Pathogenesis

- HPV infects stratified squamous epithelium and stimulates cellular proliferation.
- Affected cells display a broad spectrum of changes ranging from benign hyperplasia to dysplasia to invasive carcinoma.
  (Adapted from CDC Slide Set for Educators on HPV.)
- HPV DNA in infants born to infected mothers ranges from 1%-77% and in uninfected mothers ranges from 1%-50%!
- Vertical transmission via placenta, birth canal and post-neonatal caregiving are possible modes of transmission.
- Sexual transmission occurs on areas of increased friction.
- The incubation period varies depending on host immune response, virus type and clinical appearance of the lesions.
- Most infections are latent (subclinical infections).
- Perinatal transmission has been theorized to be an average of 8 months, but could be as long as several years.
**HPV Forensic Interpretation**

- The absence of warts in perpetrators does not preclude sexual transmission to a child.
- Age in years 0-2-3-? Probably perinatally transmitted
- Older children- sexual transmission more likely, but not definitive
- Typing HPV is usually not helpful
- Recurrences may occur, they are not reinfection
- Considered suspicious if “not likely to be perinatally acquired and rare nonsexual vertical transmission is excluded”

**What type is it? Will he get cancer?**

**HPV Epidemiology**

- More than 130 types of DNA viruses, members of the Papillomaviridae family
  - Cutaneous types: flat warts, plantar warts, filiform warts (Types 1 and 2 most common..3,4,7,10)
  - Mucosal types: respiratory papillomatosis, anogenital warts, dysplasias, cancers
    - Low risk: most common are 6 and 11
    - High risk (more than 18 types, most common are 16,18,31,35)
  - Types 16 and 18 may be associated with external genital intraepithelial neoplasia = Vulval Intraepithelial Neoplasia (VIN)

**HPV Genotyping**

- Ano-genital warts in children are associated with both mucosotropic types HPV 6 and 11 and cutaneotropic types HPV 1 and 2 (Myhre et al.).
- Low-risk types
  - Most visible warts caused by HPV types 6 and 11
  - Recurrent respiratory papillomatosis associated with HPV types 6 and 11
- High-risk types
  - HPV types 16 and 18 found in more than half of anogenital cancers
  - Most women with high-risk HPV infection have normal Pap test results and never develop precancerous cell changes or cervical cancer.

**HPV Cervical Cytology**

- Low-grade squamous intraepithelial lesion (LSIL)--generally a transient infection with a high-risk HPV type
- High-grade squamous intraepithelial lesion (HSIL)--generally a persistent infection with a high-risk HPV type with a higher risk for progression to cervical cancer
HPV Diagnosis

- Diagnosis is usually made by visual inspection with bright light.
- Diagnosis can be confirmed by biopsy when:
  - Diagnosis is uncertain
  - Patient is immunocompromised
  - Warts are pigmented, indurated, or fixed
  - Lesions do not respond or worsen with standard treatment
  - There is persistent ulceration or bleeding
- Use of type-specific HPV DNA tests for routine diagnosis and management of genital warts is not recommended.
- Acetic acid evaluation (acetowhitening) of external genitalia is not recommended.
- External genital warts are not an indication for cervical colposcopy or increased frequency of Pap test screening (assuming patient is receiving screening at intervals recommended by her health care provider).
  (Adapted from CDC Educator Slides)
- Nucleic acid testing
  - FDA-approved for two optional uses:
    - To triage women with atypical cells of undetermined significance (ASC-US) Pap test results
    - As an adjunct to the Pap test to screen for cervical cancer in women 30 years or older.
  - Use of HPV DNA testing for women with SIL Pap test results is unnecessary because the vast majority of women with SIL are infected with HPV.
  (Adapted from CDC Slide Set)

HPV Pros and Cons of Subtyping

- Multiple HPV subtypes may co-exist in the same individual
- HPV may be subclinical in the perpetrator
- High prevalence of HPV in the community
- Cutaneous warts may appear in the genital area and vice versa in children

HPV Pathogenesis

- May regress spontaneously or persist with or without proliferation.
  - Frequency of spontaneous regression is unknown.
  - Persistence of infection occurs, but frequency and duration are unknown.
  - Recurrences after treatment are common.
**How do we treat this?**

**HPV Treatment Modalities**
- Treatment goal is removal of symptomatic warts.
- Provider administered:
  - Cryotherapy with liquid nitrogen or cryoprobe
  - Podophyllin resin 10%-25% in compound tincture of benzoin
  - Trichloroacetic acid (TCA) or bichloroacetic acid (BCA) 80%-90%
  - Surgical removal
- Patient applied regimens:
  - Podofilox 0.5% solution or gel
  - Imiquimod 5% cream

**HPV Treatment Limitations**
- Recurrences frequently occur within 3 months
- If left untreated, visible genital warts regress spontaneously or persist with or without proliferation.
- Currently available therapies may reduce infectivity, but probably do not eradicate it.
- There is no evidence that presence of genital warts or their treatment is associated with development of cervical cancer.

**HPV Vaccination (for girls)**
- Apply the recommended guidelines for administration of HPV vaccine:
  - Recommended for girls 11 and 12 years of age and is given in a series of three injections over a six-month period. The second and third doses should be given two and six months (respectively) after the first dose.
  - Recommended for girls and women 13 through 26 years of age who did not receive it when they were younger.
  - HPV vaccine may be given at the same time as other vaccines.
Documentation

Key points for documentation of HPV infection in order to facilitate review of the case by an expert

- Maternal history
- Exposure within family
- Hand warts on caregivers
- Sexual abuse risk factors
- Other symptoms of STDs
- Age of child
- Descriptors of warts, locations and size
- Generally NOT type

Summary

- The finding of genital warts in children should prompt a medical evaluation for other STDs and possible sexual transmission.
- Based on the age of the child, transmission factors and low risk of sexual abuse, reporting may not be necessary.
- Treatment is rarely complete and disease often recurs.