Consultation with the Specialist: Genital Warts
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Genital Warts

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Objectives After completing this article, readers should be able to:

1. Recognize the clinical syndrome of anogenital warts.
2. Describe how human papillomavirus (HPV) is transmitted in children.
3. Identify the risks associated with HPV infection in adolescents.

EDITOR’S NOTE. Readers are used to the term “sexually transmitted disease” (STD). This article uses the term “sexually transmitted infection” (STI), which is becoming accepted more widely as appropriate usage. Not all sexually transmitted infections result in disease. –LFN

Case Study
A 22-month-old girl is brought to her pediatrician by her parents for “bumps” in her diaper area. They initially noted the lesions during a diaper change earlier in the week. The patient has not complained about the lesions, and her parents do not believe that they bother her. Physical examination reveals three perianal flesh-colored, hyperkeratotic papules, 3 to 6 mm in diameter, with the largest lesion being pedunculated. The patient attends a local accredited child care center and otherwise is cared for by her parents.

Clinical Syndrome
Anogenital warts (also called venereal warts or condyloma acuminatum [plural: condylomata acuminata]) can be solitary or multiple and are exophytic, flesh- to gray-brown-colored papillomatous lesions that are hyperkeratotic on keratinized epithelia. They may be sessile or pedunculated and can range in size from several millimeters to many centimeters. In girls, they occur most often in the perianal area and the labia minora, but can occur anywhere on the perineum. In boys, perianal warts are most common, but lesions may involve the penis. In adolescent women, the posterior introitus is the most common site; adolescent men typically have involvement of the penile shaft and preputial cavity (in uncircumcised patients). Occasionally, anogenital warts on keratinized skin may be pigmented. The likelihood of perianal lesions in sexually active adolescents varies with sexual practice.

Anogenital warts usually are asymptomatic, although itching, discomfort, tenderness, and bleeding can occur. Immunodeficiency, including that from human immunodeficiency virus (HIV) or chemotherapy, may lead to the development of large or numerous anogenital warts. Unusually large lesions may disrupt physiologic functions, necessitating surgical debulking.

Pathogenesis
Anogenital warts are caused by human papillomaviruses (HPVs), which are small, nonenveloped, icosahedral viruses that have a double-stranded circular DNA genome. About 100 genotypes have been characterized, but the total number likely is much

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larger. The incubation period is usually 3 to 4 months, with a range of 6 weeks to more than 2 years. HPV infection can be asymptomatic.

Specific viral genotypes are associated with infection site, with types 6, 11, 16, 18, 31, and 45 associated with genital infections. DNA from genital HPV types also has been identified in the oral cavity and the nasopharynx. Some of the genital HPV types carry an increased oncogenic risk. Infection with HPV types 16, 18, 31, or 45 is regarded as a necessary condition for the development of squamous cell carcinoma of the cervix and anus and some squamous cell carcinomas of the vulva, vagina, penis, and oropharynx. It is not known whether young children infected with high-risk HPV types have similar risks of developing cancer as adults.

Anogenital warts typically are caused by HPV6 or HPV11; association with invasive cancer for these two types is exceedingly rare. In young children, anogenital warts also can be caused by HPV types typically associated with cutaneous warts (common, plantar, and flat warts).

Epidemiology
Genital HPV infection is very common: Estimates indicate that as many as 75% of people in the United States are infected sometime during their life. HPV probably is the most common sexually transmitted infection (STI) in sexually active adolescent women. In one urban adolescent clinic, 64% of adolescent females had HPV DNA detected from cervical samples; 50% of the HPV-positive patients had two or more different types of HPV, and 77% had at least one high-risk type. (1) The prevalence of anogenital warts in the general population is about 1%, but the incidence is increasing rapidly in some populations. Most infections in young persons are transient, but persistent infection increases the risk of anogenital cancers. Nevertheless, the epidemiology and natural history of HPV infections are not well understood.

A major difficulty in the study of HPV is the ability to identify infected individuals accurately. HPV cannot be grown by using traditional virologic methods, and serology is not an effective or sensitive method for tracking infection. Recently, many studies have been performed using newer technologies, such as polymerase chain reaction (PCR) and other nucleic acid detection methods. Although these techniques are very sensitive, the PCR methods used often are not standardized. Furthermore, the sensitivity and specificity vary significantly with the type of sample, laboratory processing, and types of reagents used. (2)

In adolescents and adults, transmission of genital HPV infection is almost exclusively through sexual contact. Approximately two thirds of sexual contacts of an individual who has anogenital warts develop anogenital warts. Although sexual abuse always should be considered as a source of transmission of HPV to young children, it now is clear that there are other routes of transmission in children.

Vertical transmission of HPV infection, including ascending infection during pregnancy and perinatal acquisition, has been well documented, (3)(4) but its frequency is a subject of ongoing controversy. In one study, oral HPV DNA was identified in approximately one third of children born to HPV-infected mothers. However, only 50% of these children had the same HPV type as their mothers. (5) In contrast, another study identified anogenital HPV DNA in 4% of infants born to mothers whose genital HPV DNA tests were positive and 8% of infants born to mothers whose HPV DNA tests were negative. Additional routes of transmission include autoinoculation, heteroinoculation, and possibly transmission through fomites. In autoinoculation, children who have cutaneous HPV or oral infection with genital HPV types introduce the virus to their anogenital area through self contact. In children, cutaneous HPV types cause a significant minority of anogenital infections—more than 31% in one study. (6) In heteroinoculation, cutaneous or genital HPV types can be transmitted from the hands of caretakers during care of the anogenital area of the child. Transmission through auto- and heteroinoculation is difficult to demonstrate, leading to the speculation that transmission may occur through fomites. Most likely, most transmission occurs through direct contact.

Diagnosis
The mainstay of diagnosing anogenital warts is recognizing the clinical appearance of the lesion. HPV DNA detection tests are available for cervical samples; detection of HPV DNA in oral, genital, or anal samples remains a tool used only in research settings. The differential diagnosis of anogenital warts includes: molluscum contagiosum, which can be differentiated from anogenital warts based on the smooth surface and domed or umbilicated shape; pearly penile papules, which are a normal anatomic variant found on the rim of the corona; enlarged sebaceous glands or cysts; seborrheic keratosis; pigmented nevi; skin tags; and intraepithelial neoplasias or invasive carcinomas.

Sexually active adolescent females who have vulvar warts have a 50% to
Anogenital Warts and Sexual Abuse

Given the long latency period and potential for vertical and “innocent” horizontal transmission, the presence of anogenital warts in children cannot be used as the sole evidence of sexual abuse. Anogenital warts in children younger than 2 to 3 years of age are particularly unlikely to be acquired by sexual transmission. (8) Because cutaneous HPV types may cause anogenital warts in children, a child presenting with anogenital warts should be examined for the presence of coexisting cutaneous warts. Cutaneous warts also can be found among caretakers of children who have anogenital warts. Such findings do not rule out abuse, however, because abusive fondling can result in the transmission of HPV.

The presence of anogenital warts in children should prompt the consideration of sexual abuse. A careful history pertaining to abuse should be obtained for every child who has anogenital warts. If there are any risk factors for abuse found on history or if a corroborating physical finding is identified, the child should be referred to a specialist for a full forensic history and examination, including colposcopy. If there are no risk factors found on the history or physical examination, an “innocent” route of transmission is more likely.

Management

As with many viral infections, the focus of therapy for anogenital warts is amelioration of symptoms rather than eradication of the virus. As with cutaneous warts, anogenital warts have a significant rate of spontaneous resolution. In adults, 10% to 20% of patients have spontaneous resolution within 3 to 4 months of presentation. (7) In a recent study of anogenital warts in children, 75% of untreated children experienced spontaneous regression. (9) Of treated children, 27% experienced a treatment-associated resolution and 49% experienced spontaneous resolution 1 month or more after stopping therapy. The high spontaneous resolution rate suggests that observation without medical therapy for up to 1 to 2 years is a reasonable option.

Young children who require treatment for anogenital warts usually are managed in conjunction with a pediatric dermatologist or gynecologist. Therapeutic options currently include topical medications and surgical excision. Among the topical therapies are podofilox or podophyllin, which are mitotic poisons, and imiquimod, which induces local cytokine production. Podofilox is applied as a 0.5% solution or gel twice a day for 3 consecutive days each week for up to 4 weeks. Podophyllin, which is applied in the doctor’s office weekly or biweekly, is less expensive than podofilox, but is used less often because of its less reliable activity and potentially greater toxicity. Imiquimod is applied as a 5% cream on 3 alternate days per week for up to 8 to 16 weeks. Adverse effects with any of these regimens include pain, a burning sensation, and local inflammation, with erosions or ulcerations.

A young child treated with any of these agents might transfer the medication digitally to a vulnerable area such as the eye. Surgical therapies for anogenital warts include scissors excision, cryotherapy, and laser therapy. All usually are performed under general anesthesia when treating young children; older children may tolerate such procedures with the help of local anesthetic agents such as EMLA (lidocaine and prilocaine) or LMX (lidocaine) creams. Large or giant anogenital warts may require surgical intervention to restore normal physiologic functions. Adverse effects of cryotherapy include pain, a burning sensation, and ulceration, but lesions usually heal almost completely within 2 weeks, typically without long-term scarring.

Prognosis

Because HPV usually is not eradicated, recurrence of lesions is common. Vulvar or perianal warts that recur may warrant vaginoscopy or anoscopy for evaluation of an internal source of reinfection. Sexually active adolescents are at risk for infection with oncogenic HPV types and other STIs. Identification of high-risk HPV infection in adolescents is particularly important because it is a major risk factor for cervical cancer. All sexually active adolescent females should undergo regular cervical cancer screening. A bivalent (HPV16, HPV18) and a quadrivalent (HPV6, HPV11, HPV16, HPV18) vaccine are in clinical development. Phase II studies have shown protection of 90% or more against infection with the vaccine HPV type and 100% against the development of incipient cervical cancer. (7) Phase III studies are ongoing, and a vaccine may be available commercially by the end of 2006. It is likely that an HPV vaccine...
would be recommended for the adolescent age group at 11 to 12 years of age.

**Summary**

Anogenital warts in children usually can be diagnosed clinically. Biopsy is not necessary for typical lesions, but should be considered if the diagnosis is in question or if the lesions are large or pigmented. A history and physical examination focused on potential sexual abuse should be conducted. If any “red flags” are identified, the child should be referred to a specialist capable of conducting a forensic history and examination. Otherwise, reassurance and education about possible transmission modes should be provided to the family.

Sexually active adolescents who have HPV should receive a thorough evaluation for other sites of HPV infection and other STIs. They also should receive education and counseling about the prognosis of HPV, the associated risks of cancer, and effective methods of preventing acquisition of STI.

If the lesions are not causing significant physical or emotional distress, a period of observation without therapy can be suggested. If the lesions do not begin to improve within 12 months, if they progress, or if the patient or parents desire therapy, the patient should be referred to a pediatric dermatologist or gynecologist familiar with the management of anogenital warts in children.

The patient described in the case study did not have any findings suggestive of abuse. The parents were reassured to learn that HPV can be transmitted nonsexually. After a discussion of the benefits and risks of therapy, the parents elected a period of observation, during which the lesions resolved spontaneously.

**References**


**Suggested Reading**


Moresi JM, Herbert CR, Cohen BA. Treatment of anogenital warts in children with topical 0.05% podofilox gel and 5% imiquimod cream. *Pediatr Dermatol.* 2001;18:448–450
14. Which of the following statements regarding human papillomavirus (HPV) is true?
   A. All HPV types are associated with an increased risk of malignancy.
   B. Common cutaneous warts are not caused by HPV.
   C. Cutaneous HPV types can be found in the anogenital region.
   D. Genital HPV infections in infants almost always are caused by sexual abuse.
   E. Genital HPV infections rarely are associated with other sexually transmitted infections.

15. A 9-year-old girl is brought to your clinic because of “sores” around the anus for 2 weeks. Physical examination reveals several 2- to 3-mm pedunculated, light brown lesions around her anus. The remainder of the genital examination and skin examination is normal. You suspect HPV infection. Of the following, the most appropriate next step in the evaluation of this girl is:
   A. A history regarding the possibility of sexual abuse.
   B. Biopsy of one of the perianal lesions.
   C. Colposcopy with Papanicolaou smear testing.
   D. Observation only.
   E. Treatment with topical podofilox.

16. A 4-year-old boy presents to the emergency department with a complaint of genital itching for 3 days. Physical examination reveals several common warts on his hands and four flesh-colored papillomatous lesions on his penis. Which of the following statements regarding this child’s management and prognosis is true?
   A. He should be referred to a surgeon for anoscopy to evaluate for rectal lesions.
   B. His penile lesions should be biopsied.
   C. His risk of developing penile cancer is greatly increased.
   D. Sexual abuse is the most likely cause of his infection.
   E. The chance of spontaneous regression of both types of lesions is high.

17. Which of the following statements regarding HPV infection in adolescents is true?
   A. All adolescents who have genital HPV should undergo anoscopy.
   B. Genital HPV disease in adolescent females carries an increased risk of cervical cancer.
   C. Genital HPV in adolescents typically is acquired via nonsexual transmission.
   D. Recurrence is rare if the HPV lesions are treated promptly.
   E. Spontaneous resolution of lesions is rare in adolescence.