Challenging Cases References

CAC Medical Provider Conference

November 2024

Jacqueline Sugarman, MD

HPV: The evaluation of children with anogenital warts

- Detailed medical history (i.e., history of HPV cutaneous and mucocal infections in mother, caregivers and child)
- Forensic interview of verbal children
- Examination
- Testing for other STIs
- Reporting to child protection agencies should be considered when abuse remains a possibility.
- It should be noted that a negative history of known HPV infection in a household contact does not imply sexual abuse by a non-family member. Likewise, a history of HPV in a household contact does not exclude the possibility of sexual abuse of the child.

HPV infections

- Mucosal HPV subtypes have been identified in vaginal samples of prepubertal and postpubertal children without a history of sexual contact and the mode of transmission or transference of the virus is unknown in these situations.

Genital HPV in Children and Adolescents: Does Sexual Activity Make a Difference?

Flora Bacopoulou MD, IFEPAG, PhD [1,*], Petros Karakitsos MD, PhD [2], Christine Kottaridi PhD [2], Charikleia Stefanaki MD [1], Efthymios Deligeoroglou MD, PhD [1], Kalliopi Theodoridou MD, PhD [1], George P. Chrousos MD, MACP, MACE, FRCP (London) [1], Athanasios Michos MD, PhD [3]

[1] *Center for Adolescent Medicine and United Nations Educational, Scientific and Cultural Organization (UNESCO) Chair on Adolescent Health Care, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece*
[2] *Department of Cytopathology, Attikon University Hospital, Athens, Greece*
[3] *Division of Infectious Diseases, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece*

A B S T R A C T

Study Objective: To compare the prevalence of human papillomavirus (HPV) genital infection among prepubertal children, sexually active and not sexually active adolescents, and assess potential risk factors for transmission.
Design: Prospective study.
Setting: Outpatient adolescent health clinic.
Participants: Ninety-five girls aged 2-21 years; 38 sexually active adolescents (group A), 28 not sexually active adolescents (group B), and 29 prepubertal children (group C).
Interventions: Participants' vaginal or cervical specimens were tested for HPV with the CLART HPV 2 assay (Clinical Array Technology, Genomica, Madrid, Spain) and for cytological abnormalities with liquid-based cytology.
Main Outcome Measures: Differences in prevalence of low- and high-risk HPV infections among the 3 groups.
Results: Genital HPV was detected in 37.9% (36/95) of all participants; 47.4% (18/38) of group A, 28.6% (8/28) of group B, and 34.5% (10/29)of group C ($P = .27$). Multiple HPV infection was detected in 26.3% (10/38), 10.7% (3/28), and 13.8% (4/29) of groups A, B, and C, respectively ($P = .21$). High-risk genotypes were detected in 47.4% (18/38), 28.6% (8/28), and 24.1% (7/29) of groups A, B, and C, respectively ($P = .10$). Main high-risk genotypes were HPV 16 (27%, 10/37), HPV 31 (21.6%, 8/37), HPV 35 (13.5%, 5/37), HPV 53 (13.5%, 5/37), and low-risk HPV 6 (18.9%, 7/37). Sexual activity was associated with increased risk for genital high-risk HPV infection (odds ratio = 3.41; 95% confidence interval, 1.19-9.78); specifically with HPV 33 and HPV 51. Forty percent of sexually active adolescents with normal cervical cytology were infected with high-risk HPV types. Family history of skin HPV was positively associated with genital HPV in the sexually active group (odds ratio = 2.01; 95% confidence interval, 1.17-3.46).
Conclusion: Timeline and target population for HPV vaccination might need to be reappraised, in view of significant nonsexual transmission of genital HPV so early in childhood.
Key Words: HPV, Prepubertal girls, Children, Adolescents, Sexual activity, Epidemiology, Greece

Original Study

Genital HPV in Children and Adolescents: Does Sexual Activity Make a Difference?

Flora Bacopoulou MD, IFEPAG, PhD [1,*], Petros Karakitsos MD, PhD [2], Christine Kottaridi PhD [2], Charikleia Stefanaki MD [1], Efthymios Deligeoroglou MD, PhD [1], Kalliopi Theodoridou MD, PhD [1], George P. Chrousos MD, MACP, MACE, FRCP (London) [1], Athanasios Michos MD, PhD [3]

[1] *Center for Adolescent Medicine and United Nations Educational, Scientific and Cultural Organization (UNESCO) Chair on Adolescent Health Care, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece*
[2] *Department of Cytopathology, Attikon University Hospital, Athens, Greece*
[3] *Division of Infectious Diseases, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece*

- Female children who presented to an outpatient GYN clinic were recruited
- Detailed social, family and medical history including risk factors, person and family history of HPV genital or skin infections
- Anogenital exam and vaginal smears
- 103 girls were recruited
- Eight excluded because of “lack of cooperation” – no vaginal swab could be obtained

Original Study

Genital HPV in Children and Adolescents: Does Sexual Activity Make a Difference?

Flora Bacopoulou MD, IFEPAG, PhD [1,*], Petros Karakitsos MD, PhD [2], Christine Kottaridi PhD [2], Charikleia Stefanaki MD [1], Efthymios Deligeoroglou MD, PhD [1], Kalliopi Theodoridou MD, PhD [1], George P. Chrousos MD, MACP, MACE, FRCP (London) [1], Athanasios Michos MD, PhD [3]

[1] *Center for Adolescent Medicine and United Nations Educational, Scientific and Cultural Organization (UNESCO) Chair on Adolescent Health Care, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece*
[2] *Department of Cytopathology, Attikon University Hospital, Athens, Greece*
[3] *Division of Infectious Diseases, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece*

- There are no longitudinal studies available to clarify whether children exposed to genital HPV are at risk for developing carcinoma in adulthood.
- Does HPV carriage lessen with age?
- Does infection in early childhood offer protection against infection in adulthood?
- Almost a third of all participants were infected with oncogenic types represented in HPV vaccine.
- Do not delay HPV vaccination because a child is not sexually active.

Original Study

Genital HPV in Children and Adolescents: Does Sexual Activity Make a Difference?

Flora Bacopoulou MD, IFEPAG, PhD [1,*], Petros Karakitsos MD, PhD [2], Christine Kottaridi PhD [2], Charikleia Stefanaki MD [1], Efthymios Deligeoroglou MD, PhD [1], Kalliopi Theodoridou MD, PhD [1], George P. Chrousos MD, MACP, MACE, FRCP (London) [1], Athanasios Michos MD, PhD [3]

[1] *Center for Adolescent Medicine and United Nations Educational, Scientific and Cultural Organization (UNESCO) Chair on Adolescent Health Care, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece*
[2] *Department of Cytopathology, Attikon University Hospital, Athens, Greece*
[3] *Division of Infectious Diseases, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece*

- High risk HPV identified in all subgroups.
- Although, high risk types 33 and 51 were only identified in sexually active girls.
- Family history of skin, but not genital warts was associated with HPV cervicovaginal infection risk.
- A significant number of high risk HPV genotypes was found in children and adolescents with cutaneous warts (that could possibly be inoculated into the anogenital area)

Original Study

Genital HPV in Children and Adolescents: Does Sexual Activity Make a Difference?

Flora Bacopoulou MD, IFEPAG, PhD [1,*], Petros Karakitsos MD, PhD [2], Christine Kottaridi PhD [2], Charikleia Stefanaki MD [1], Efthymios Deligeoroglou MD, PhD [1], Kalliopi Theodoridou MD, PhD [1], George P. Chrousos MD, MACP, MACE, FRCP (London) [1], Athanasios Michos MD, PhD [3]

[1] Center for Adolescent Medicine and United Nations Educational, Scientific and Cultural Organization (UNESCO) Chair on Adolescent Health Care, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece
[2] Department of Cytopathology, Attikon University Hospital, Athens, Greece
[3] Division of Infectious Diseases, First Department of Pediatrics, University of Athens, Aghia Sophia Children's Hospital, Athens, Greece

Ages	Genital Warts	Skin Warts	Family history genital or skin warts	Molecular analysis % infected with HPV (37.9% of all participants)	Number of children in group	Vulvovaginitis symptoms %
Sexually active 16.4 +/- 2.4 years	10.5%	15.8%	10.6%	47.4 %	38	8 %
Not sexually active pubertal girls 13.4 +/- 2.2 years	3.6%	17.9%	7.1 %	28.6 %	28	71 %
Prepubertal girls, mean age 8.2 +/- 2.4 years	10.3%	10.3%	27.6 %	34.5 %	29	93 %

HPV vaccination

- Because HPV infections can occur as a result of sexual assault, the Center for Disease Control and prevention has recommended the HPV vaccine for sexually abused children who are age 9 years and older (Workowski et al., 2015) due to an increased risk for unhealthy or premature sexual behavior.
- An HPV vaccine can also be provided for unvaccinated or partially vaccinated adolescents presenting acutely following a sexual assault; some evidence suggests a preventative or prophylactic role for the vaccine in this clinical setting.

When to consider STI testing in prepubertal children

- Child has experienced penetration of the genitals, anus, or oropharynx
- Child has been abused by a stranger
- Child has been abused by a perpetrator known to be infected with an STI or is at high risk for being infected (intravenous drug users, men who have sex with men, or people with multiple sexual encounters)
- Child has a sibling or other relative in the household with an STI
- Child discloses sexual abuse and lives in an area with a high rate of STI in the community
- Child has signs or symptoms of an STI
- Child has already been diagnosed with one STI
- The abused child or their parent requests STI testing
- The child is unable to verbalize details of the assault
- The sexual abuse has been witnessed or documented with photos or video, given that child subjects typically do not fully disclose details of their abuse

https://www.cdc.gov/std/treatment-guidelines/default.htm

Infections that can be spread by nonsexual as well as sexual transmission

- Molluscum contagiosum in the genital or anal area. In young children, transmission is most likely non-sexual. Transmission from intimate skin-to-skin contact in the adolescent population has been described.
- Condyloma acuminatum (HPV) in the genital or anal area.
- Herpes Simplex Type 1 or 2 infections in the oral, genital or anal area diagnosed by culture or nucleic acid amplification test. ** serology has limited value
- Urogenital Gardnerella vaginalis (associated with sexual contact but also found in prepubertal and adolescent vaginal flora).
- Urogenital Mycoplasma genitalium or ureaplasma urealyticum; while sexually transmitted in adolescents, prevalence and transmission of these infections in children not well understood.

Nancy D. Kellogg, Karen J. Farst, Joyce A. Adams, Interpretation of medical findings in suspected child sexual abuse: An update for 2023, Child Abuse & Neglect, Volume 145, 2023, 106283, ISSN 0145-2134, https://doi.org/10.1016/j.chiabu.2023.106283.

Infections that can be spread by nonsexual as well as sexual transmission

- Interpretation of these findings regarding the likelihood of sexual abuse might require additional information, such as
  - mother's gynecologic history (HPV)
  - child's history of oral lesions (HSV),
  - presence of lesions elsewhere on the body (Molluscum)
- After complete assessment, a report to Child Protective Services might be indicated in some cases.

Nancy D. Kellogg, Karen J. Farst, Joyce A. Adams, Interpretation of medical findings in suspected child sexual abuse: An update for 2023, Child Abuse & Neglect, Volume 145, 2023, 106283, ISSN 0145-2134, https://doi.org/10.1016/j.chiabu.2023.106283.

Interpreting Sexual Behavior in Children

- Differentiate normal behaviors from those that are persistent, abusive, and/or intrusive and don't respond to redirection
- Was there exposure to inappropriate material? Behavior may become problematic if material was particularly disturbing or exposure was persistent
- Consider environment: life stresses, domestic violence, and physical abuse exposure have been linked to sexual behavior problems in children
- Children from homes where there is physical/sexual abuse or neglect are more likely to manifest sexual behavior problems

Kellogg N and the Committee on Child Abuse and Neglect. Clinical Report – The Evaluation of Sexual Behaviors in Children. Pediatrics 2009; 124:992-998

Interpreting Sexual Behavior in Children

TABLE 1 Examples of Sexual Behaviors in Children 2 to 6 Years of Age

Normal, Common Behaviors	Less Common Normal Behaviors[a]	Uncommon Behaviors in Normal Children[b]	Rarely Normal[c]
• Touching/masturbating genitals in public/private	• Rubbing body against others	• Asking peer/adult to engage in specific sexual act(s)	• Any sexual behaviors that involve children who are 4 or more years apart
• Viewing/touching peer or new sibling genitals	• Trying to insert tongue in mouth while kissing	• Inserting objects into genitals	• A variety of sexual behaviors displayed on a daily basis
• Showing genitals to peers	• Touching peer/adult genitals	• Explicitly imitating intercourse	• Sexual behavior that results in emotional distress or physical pain
• Standing/sitting too close	• Crude mimicking of movements associated with sexual acts	• Touching animal genitals	• Sexual behaviors associated with other physically aggressive behavior
• Trying to view peer/adult nudity	• Sexual behaviors that are occasionally, but persistently, disruptive to others	• Sexual behaviors that are frequently disruptive to others	• Sexual behaviors that involve coercion
• Behaviors are transient, few, and distractable	• Behaviors are transient and moderately responsive to distraction	• Behaviors are persistent and resistant to parental distraction	• Behaviors are persistent and child becomes angry if distracted

[a] Assessment of situational factors (family nudity, child care, new sibling, etc) contributing to behavior is recommended.
[b] Assessment of situational factors and family characteristics (violence, abuse, neglect) is recommended.
[c] Assessment of all family and environmental factors and report to child protective services is recommended.

Kellogg N and the Committee on Child Abuse and Neglect. Clinical Report – The Evaluation of Sexual Behaviors in Children. Pediatrics 2009; 124:992-998

McCann J, Miyamoto S, Boyle C, Rogers K. Healing of hymenal injuries in prepubertal and adolescent girls: a descriptive study. Pediatrics. 2007 May;119(5):e1094-106. doi: 10.1542/peds.2006-0964. Epub 2007 Apr 9. PMID: 17420260.

- **This article studied 113 prepubertal and 126 pubertal girls who sustained hymenal injuries. In the prepubertal population, 21 hymenal injuries were deemed the result of accidental trauma, 73 were the result of abuse and 19 were of unknown etiology. All of the pubertal girls reported sexual assault. Injuries included abrasions, petechiae, lacerations, blood blisters, submucosal hemorrhages and hematomas. Injuries were evaluated over time and the dates the lesions' earliest disappearance, last detection, and resolution were recorded. Findings included the following:**
- Hymenal injuries healed rapidly. Frequently, there was little or no evidence of previous trauma.
- Hymenal lacerations were identified at all locations on the hymenal rim.
- The majority of hymenal lacerations smoothed off over time.
- The age of the injury could not be determined based on the injury's evolving appearance.
- Petechiae, however, resolved quickly (by 48-72 hours).
- Blood blisters could take a long time to resolve. Their presence indicated that an injury had occurred in the past month.
- While most signs of acute injury were gone by 7-10 days, changes in the depth and configuration of a laceration continued for 3-4 weeks post injury.

Purpose of Follow Up

- Clarify exam findings
- To complete STI testing
- Assess/monitor treatment
- Assess and complete HPV vaccination

A follow up exam can yield valuable additional information

- Patient cooperation may be limited by pain or acute stress.
- Tissue swelling/edema and/or bleeding can obscure findings (mask a hymenal tear).
- You may be able to confirm a finding using a swab, foley catheter(if pubertal), or prone knee chest position at the follow up exam.
- Conversely, erythema or other findings can mimic injury. Seeing how a finding resolves or changes can aid in the interpretation of a finding's significance.

Gavril A, Kellogg N, and Nair P. (2012). Value of follow-up examinations of children and adolescents evaluated for sexual abuse and assault. Pediatrics, 129:282-289.

Genital Examination, Prepubertal Child		Anal Examination, Prepubertal Child	
Examination Positions	Supine Frog-leg or Lithotomy Prone Knee-chest (PKC)	Examination Positions (In Order of Preference)	Supine Knee-chest PKC Lateral Decubitus
Examination technique	Labial separation and traction PKC with gluteal lift Speculum examinations not indicated unless child sedated	Examination technique	Buttock separation PKC with gluteal lift
Confirmatory technique	Floating hymen with water or saline PKC with gluteal lift	Confirmatory technique	Reassess after bowel movement, ambulating, or alternate position
Genital Examination, Pubertal Child		**Anal Examination, Pubertal Child**	
Examination positions	Supine lithotomy PKC with gluteal lift	Examination positions	Supine knee-chest PKC Lateral decubitus
Examination technique	Labial separation and traction Speculum examination can be done if Tanner 3 or greater	Examination technique	Lateral buttock separation Gluteal lift in PKC
Confirmatory technique	Trace hymenal rim with cotton tip swab Foley catheter[58] PKC with gluteal lift	Confirmatory technique	Reassess after bowel movement, ambulating, or alternate position

D. No expert consensus regarding degree of significance

These physical findings have been associated with a history of sexual abuse in some studies, but at present, there is no expert consensus as to how much weight they should be given with respect to abuse. Findings 28 and 29 should be confirmed using additional examination positions and/or techniques, to ensure they are not normal variants (findings 1. i. 1.j) or a finding of residual traumatic injury (finding 38)

27. Complete and immediate anal dilation with relaxation of the internal as well as external anal sphincters, in the absence of other predisposing factors such as constipation, encopresis, sedation, anesthesia, and neuromuscular conditions
28. Notch or cleft in the hymen rim, at or below the 3 o'clock or 9 o'clock location, which extends nearly to the base of the hymen, but is not a complete transection. This is a very rare finding that should be interpreted with caution unless an acute injury was documented at the same location.
29. Complete cleft/suspected transection to the base of the hymen at the 3 or 9 o'clock location

Nancy D. Kellogg, Karen J. Farst, Joyce A. Adams, Interpretation of medical findings in suspected child sexual abuse: An update for 2023, Child Abuse & Neglect, Volume 145, 2023, 106283, ISSN 0145-2134, https://doi.org/10.1016/j.chiabu.2023.106283.

Landberg, A., Kaldal, A., & Eriksson, M. (2023). Paths of disclosure – The process of sharing experiences of child sexual abuse. *Children & Society*, 37, 1535–1554. https://doi.org/10.1111/chso.12710

- In this small study, investigators interviewed fourteen Swedish teens/young adults aged 15-28 years about sexual abuse that they experienced when they were preschool to age 12, attempting to identify facilitators, rather than barriers to disclosure.
- They discuss four main recurring themes identified within all the interviews, “silence, voice, interaction and managing dissemination” [of the information regarding the abuse].
- One conclusion made was that since some of the interviewees reported telling peers before adults about their abuse, there is a need not only to educate all children about sexual abuse, but also about where they can seek help if they are, or their friends report to them, being abused.