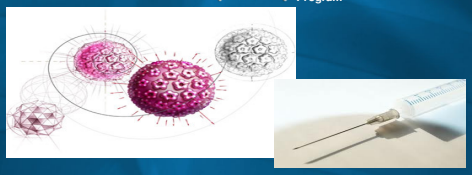
Adolescent Reproductive & Sexual Health Education Program



Human Papillomavirus (HPV) and HPV Vaccine

Allison Eliscu, MD, FAAP
Assistant Professor of Pediatrics
Head of Adolescent Medicine Division
Stony Brook Children's Hospital

Stony Brook Children's

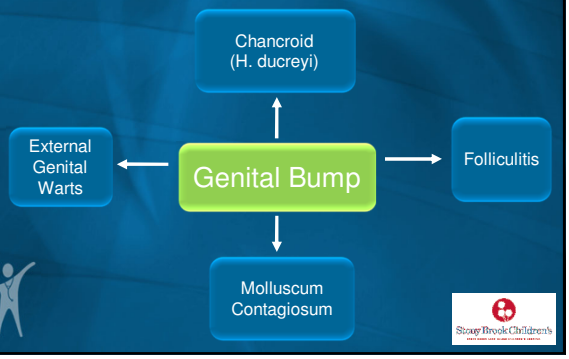
Objectives

- 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

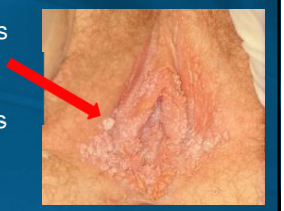
- Jenna is 15-year-old female who presents with a bump on her vagina.
- She has been sexually active for six months and has only had one partner.
- What is your differential diagnosis?

Differential Diagnosis

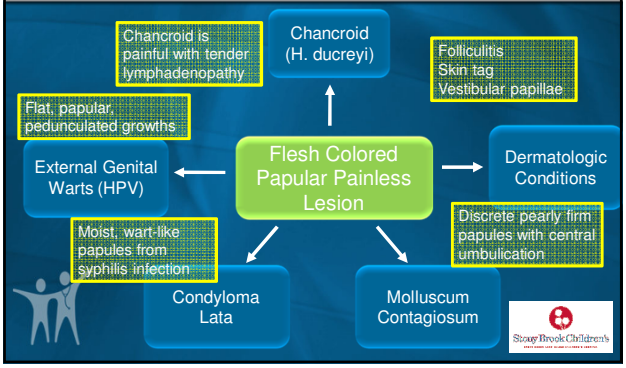


Physical Examination

- 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



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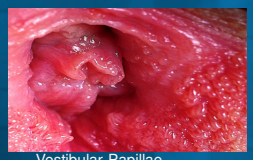
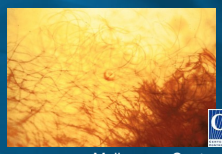
Differential Diagnosis

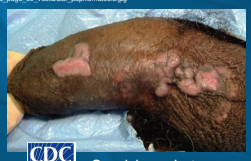


Vestibular Papillae

http://hymen.pro/Sallie_Neill_Fiona_Lewis_Ridleys_The_Vulva_page_39_vestibular_papillomatosis.jpg



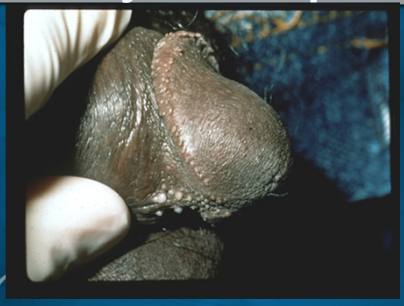
Molluscum Contagiosum



Condyloma Lata

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Differential Diagnosis: Pearly Penile Papules



Handsfield HH. Color atlas and synopsis of sexually transmitted diseases, 2nd ed. New York: McGraw-Hill, 2000:206.

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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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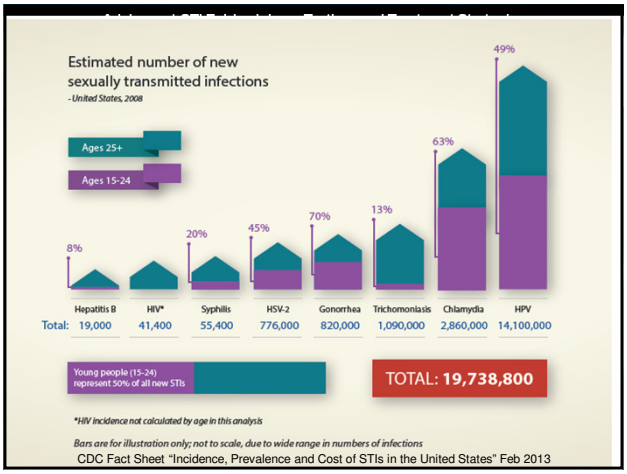
HPV Incidence and Prevalence

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



CDC Fact Sheet "Incidence, Prevalence and Cost of STIs in the United States" Feb 2013

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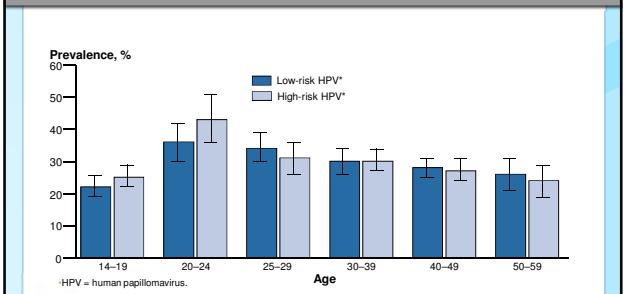
HPV Prevalence : Females Aged 14–59 Years



*HPV = human papillomavirus.

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) 2003–2006

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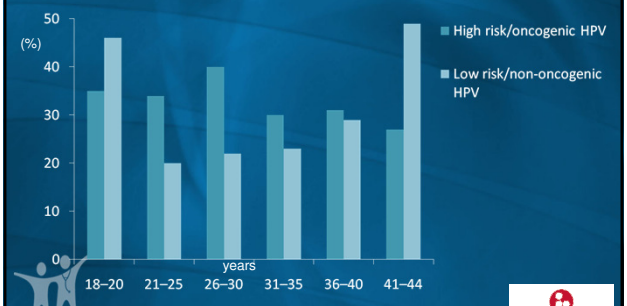
Genital HPV Prevalence Rates in Males



Giuliano AR et al. *J Infect Dis.* 2008;198:827–835.

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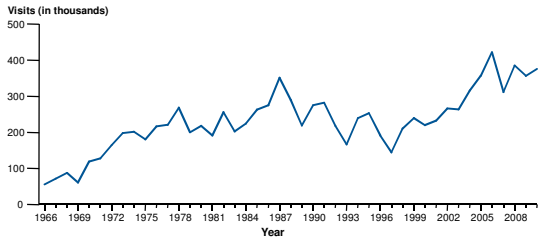
How often is genital warts diagnosed at the Doctor's Office?



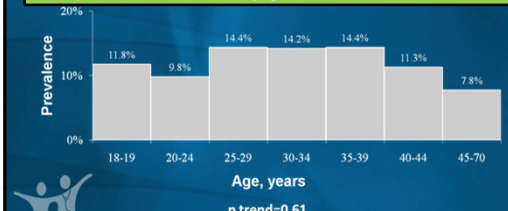
NOTE: The relative standard errors for genital warts estimates of more than 100,000 range from 18% to 30%.

SOURCE: IMS Health, Integrated Promotional Services™. IMS Health Report, 1966–2010.

Adolescent STI Epidemiology, Testing, and Treatment Strategies

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

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



Nyitray AG, et al. J Infect Dis. 2010;201:1498-1508

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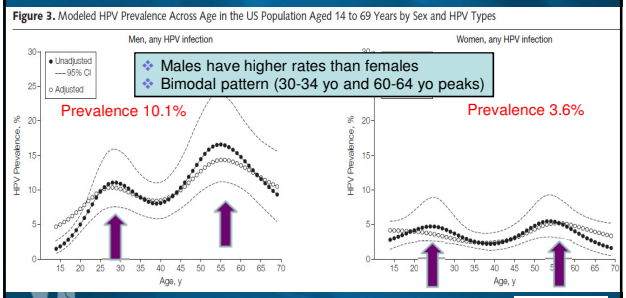
Prevalence of Oral HPV Infection: NHANES Data



Gillison ML, et al. *JAMA. 2012;307(7):doi:10.1001/jama.2012.101*

Adolescent STI Epidemiology, Testing, and Treatment Strategies

HPV Clinical Manifestations

Manifestations depend on oncogenic potential

- Majority are subclinical → Genital Warts
- Low Risk Types → Low grade squamous and glandular intraepithelial lesions
- High Risk Types → High grade squamous and glandular intraepithelial lesions

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts Appearance

Condyloma acuminata:	• Cauliflower-shaped, flesh colored, pink or hyperpigmented
Smooth papules:	• Usually dome-shaped and skin colored
Keratotic warts:	• Thick, horny layer which can resemble common warts
Flat papules:	• Macular to slightly raised, flesh colored, with smooth surface

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts Sites of Infection

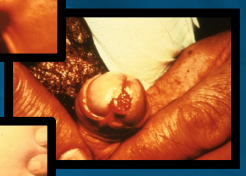
Genital Warts Commonly Occur in Areas of Coital Friction

Adolescent STI Epidemiology, Testing, and Treatment Strategies

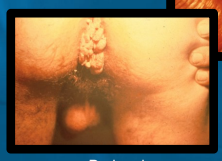
Genital Warts Sites of Infection

- Penis
- Scrotum
- Urethral Meatus
- Perianal

Glans



Meatus



Perianal

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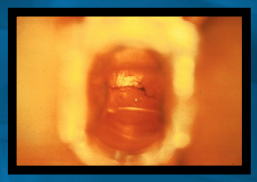
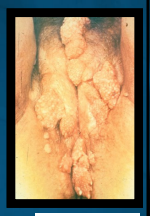
Genital Warts Sites of Infection

- Introitus
- Vulva
- Perineum
- Anus



Vaginal wall

Labia



(Vaginal and cervical lesions are less common)

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Genital Warts Symptoms

Genital Warts are Usually Asymptomatic

Symptoms may develop depending on size and location of warts

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts Symptoms

Vulvar:	• Dyspareunia, pruritus, burning
Penile:	• Occasional itching
Urethral meatal:	• Hematuria or difficulty urinating
Vaginal:	• Discharge, bleeding
Perianal:	• Pain, bleeding, itching
Cervical:	Irregular or postcoital bleeding

Adolescent STI Epidemiology, Testing, and Treatment Strategies

- You think that Jenna has external genital warts. Is there a confirmatory test to make the diagnosis?

Adolescent STI Epidemiology, Testing, and Treatment Strategies

External Genital Warts: Diagnosis

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

Adolescent STI Epidemiology, Testing, and Treatment Strategies

External Genital Warts: Diagnosis

- 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?

	<21 YEARS OLD	21-29 YEARS OLD	30-65 YEARS OLD	>65 YEARS OLD	PRIOR HPV VACCINE
USPSTF	Not Recommended	Pap every 3 years	Pap 3 yrs OR Pap + HPV 5 yrs	Not Recommended if low risk	Continue Regular Screening
ACS, ASCCP, ASCP	Not Recommended	Pap every 3 years	5 yrs OR Pap 3 yrs	Not Recommended	No Change
ACOG	Not Recommended	Pap every 2 years	Pap 3 yrs, cotest w/ HPV acceptable	Stop Paps at 65-70 yo	No Change

No need for more frequent or earlier screening if external genital warts are present

Adolescent STI Epidemiology, Testing, and Treatment Strategies

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

Adolescent STI Epidemiology, Testing, and Treatment Strategies

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

Adolescent STI Epidemiology, Testing, and Treatment Strategies

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

Initial Steps for Follow- Up of Abnormal Pap Smears in Adolescents

ASCUS, LGSIL, or CIN 1	ASC-H	HGSIL	Atypical Glandular Cells (rare in adolescents)	CIN 2	CIN 3
Repeat pap in 12 and 24 months	Colposcopy	Colposcopy with Endocervical Evaluation	Colposcopy with Endocervical Evaluation	Colposcopy with cytology every 6 mos for 2 yrs OR treatment	Treatment
Colpo if HGSIL develops or LGSIL/CIN persist for 2 years					

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

ACOG Committee Opinion. Vol 116, No 2, Part 1, Aug 2010

Adolescent STI Epidemiology, Testing, and Treatment Strategies

How would you treat Jenna's external genital warts?

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts: Treatment

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

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts: Treatment

- Patient applied modalities
- Provider administered treatments
- Alternative methods

No evidence that any method is superior to others

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts: Patient Applied Treatments

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

Redness, irritation, induration, ulcerations and vesicles common;
*May weaken condoms!

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

Mild to moderate pain or local irritation possible

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.

Erythema, itching, burning, ulceration, edema and rash;
*May weaken condoms!

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts: Costs of Patient Applied Treatments

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

•Usage dependant on total wart area
•Data from April 2008
www.pbm.va.gov

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts: Provider Applied Treatments

Cryotherapy
with liquid nitrogen or cryoprobe
Must be trained in use
Repeat every 1–2 weeks

Pain, necrosis, ulceration, blistering

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

Local irritation, burning pain
Low viscosity, can easily spread to adjacent tissue

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

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

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

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Genital Warts: Treatment of Internal Warts

Cervical Warts
-Biopsy to rule out high grade squamous intraepithelial lesion

Involve specialist for cervical lesions

Vaginal Warts
-Cryotherapy with liquid nitrogen (no cryoprobe use)
-TCA/BCA 80-90%

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

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

Involve specialist for Intra-anal lesions

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Should Jenna's partner receive any treatment?

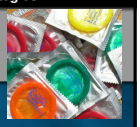
Adolescent STI Epidemiology, Testing, and Treatment Strategies

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

Adolescent STI Epidemiology, Testing, and Treatment Strategies

A Little Note on Condoms…

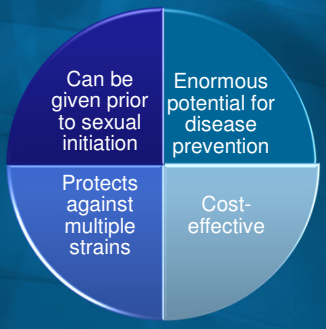


Regular and consistent condom use achieves about 60% protection against HPV

Adolescent STI Epidemiology, Testing, and Treatment Strategies

Should you give Jenna the HPV vaccine?

HPV Vaccine



HPV Vaccines: FDA Approved

- **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 6,11 cause 90% of genital warts

HPV 16,18 cause 70% of cervical cancer

ACIP HPV Vaccine Recommendations 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 13-26yo ♀

Vaccination recommended even if patient has genital warts or abnormal pap smear

Efficacy of HPV2 and HPV4 Vaccine in Females

TABLE 2. Efficacy of bivalent human papillomavirus vaccine (HPV2) and quadrivalent human papillomavirus vaccine (HPV4) in females

Vaccine/Endpoint/HPV type	Vaccine No.	Vaccine Cases	Control No.	Control Cases	Vaccine efficacy %	Vaccine efficacy (CI*)
Bivalent vaccine (HPV2)†						(96.1% CI)
CIN2/3 or AIS§						
HPV 16 and/or 18	7,344	4	7,312	56	92.9	(79.9–98.3)
HPV 16	6,303	2	6,165	46	95.7	(82.9–99.6)
HPV 18	6,794	2	6,746	15	86.7	(39.7–98.7)
Quadrivalent vaccine (HPV4)¶						(95% CI)
CIN2/3 or AIS**						
HPV 6, 11, 16, and/or 18	7,864	2	7,865	110	98.2	(93.3–99.8)
HPV 16	6,647	2	6,455	81	97.6	(91.1–99.7)
HPV 18	7,382	0	7,316	29	100.0	(86.6–100.0)
VIN2/3 or VaIN2/3 ††						
HPV 6, 11, 16, and/or 18	7,900	0	7,902	23	100.0	(82.6–100.0)
HPV 16	6,654	0	6,467	17	100.0	(76.5–100.0)
HPV 18	7,414	0	7,343	2	100.0	(<0–100.0)
Genital warts§§						
HPV 6 and/or 11	6,932	2	6,856	189	99.0	(96.2–99.9)

CDC. *MMWR* **2010;** Vol. 59 / No. 20

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 13-21yo ♂
- Recommended for all MSM and immunocompromised ♂
- Permissive recommendation for 22-26 yo ♂ without risk factors

CDC. Recommendations on the Use of Quadrivalent Human Papillomavirus Vaccine in Males — Advisory Committee on Immunization Practices (ACIP), 2011. MMWR 60(50);1705-1708

Is HPV vaccination cost-effective for boys?

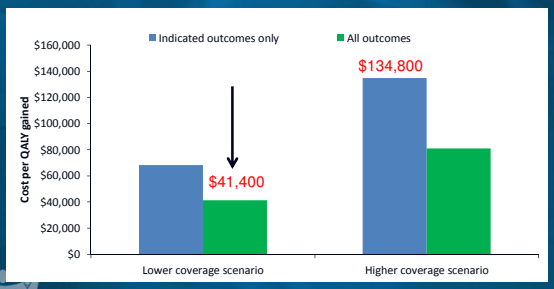
YES

- 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
    - **FDA indications** (CIN, genital warts; cervical, vaginal, vulvar & anal cancers)
    - **Non FDA indications** (oropharyngeal & penile cancers, Recurrent Respiratory Papillomatosis)

Chesson HW, et al. Vaccine 2011;29:8443–50.

Cost-Effectiveness of Male Vaccination*

Cost per QALY gained by vaccinating 12 year-old boys



*Includes transmission effects to females

*Chesson HW, et al. Vaccine 2011

For Comparison…

Cost per QALY gained by adolescent vaccines in the US

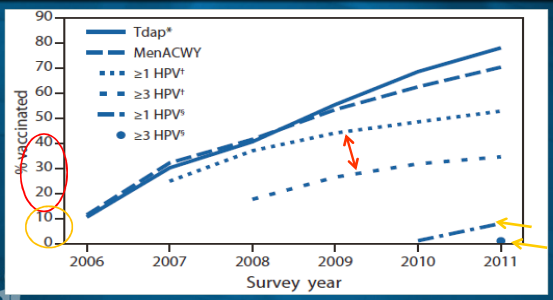
Vaccine	Target group	Cost per QALY gained (compared to no vaccination)
Hepatitis B	College freshmen	<$0 (cost-saving) to ≈ $10,000
Hepatitis A	College freshmen	<$0 (cost-saving) to ≈ $15,000
HPV	**12-year-old girls**	**≈ $3,000 to $45,000**
Influenza	12- to 17-year-olds, high risk	≈ $10,000
Tdap	All 11-year-olds	≈ $25,000
Influenza	12- to 17-year-olds, healthy	≈ $140,000
Meningococcal	2-dose, all 11 & 16-year-olds	≈ $160,000

HPV 12 yo boys $41,400 - $134,800

Source: Ortega-Sanchez et al. *Pediatrics* (2008), except HPV and Meningococcal (see notes).

How are we doing with HPV immunization rates?

Vaccination Coverage among 13-17 yr olds, Males & Females, 2006-20011



HPV; Females HPV; **Males**

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
  - ♀ living below poverty line more likely fully protected w/ 3 doses vs ♀ 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.

Pediatrics 2012; 130:798-805.

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:

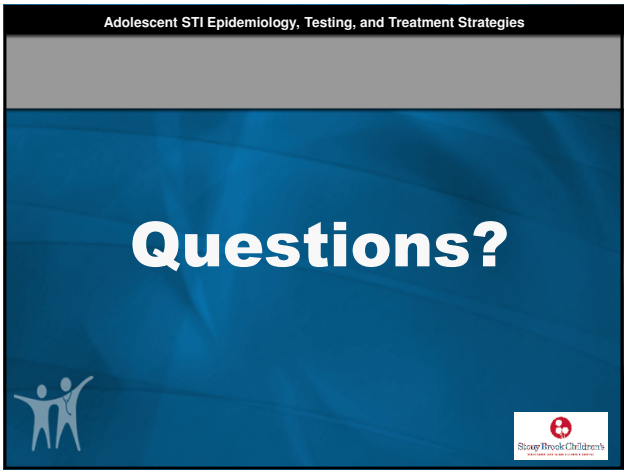
- Describe the extent of HPV infection in adolescents
- Describe clinical presentations of HPV
- Describe how to diagnose and manage HPV infection in adolescents
- Understand how to prevent HPV infections

HPV-specific Resources

- U.S. Centers for Disease Control and Prevention
  - Statistics and Surveillance Reports: http://www.cdc.gov/std/stats/default.htm
  - Treatment Guidelines: http://www.cdc.gov/STD/treatment/default.htm
  - American Social Health Association: http://www.ashastd.org/std-sti/hpv.html
  - U.S. Department of Health and Human Services http://womenshealth.gov/faq/stdhpv.htm

Provider Resources

- http://www.nycptc.org/ —New York City STD/HIV Prevention Training Center (PTC)
- 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
- www.adolescenthealth.org—The Society for Adolescent Health and Medicine
- http://www.aclu.org/reproductiverights—The Reproductive Freedom Project of the American Civil Liberties Union
- www.advocatesforyouth.org—Advocates for Youth
- www.guttmacher.org—Guttmacher Institute
- www.cahl.org—Center for Adolescent Health and the Law
- http://janefondacenter.emory.edu/—The Jane Fonda Center of Emory University
- www.siecus.org—The Sexuality Information and Education Council of the United States
- www.arhp.org—The Association of Reproductive Health Professionals
- www.rhtp.org—Reproductive Health Technologies Project


Adolescent STI Epidemiology, Testing, and Treatment Strategies
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