Everything you and your patients should know about HPV vaccination

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Off Label Use of Vaccines	Will be discussed, but in accordance with current ACIP recommendations	



Questions for you (1)

- 1. Do you routinely see pre-teens and young adolescents (ages 10-14) in your clinical practice?
 - a. Yes
 - b. No
 - c. Sometimes



Questions for you (2)

- 2. Do you routinely see middle/late adolescents and young adults (15-26) in your clinical practice?
 - a. Yes
 - **b**. No
 - c. Sometimes



Objectives

Overview of HPV-related disease

HPV vaccine and recommendations

Vaccine safety, impact, and vaccination rates

Discuss common barriers in vaccine discussions with parents and evidence-based ways to overcome them



What is the morbidity from HPV?

- 3 million Americans seek medical care for HPV each year
- 33,000 develop HPV-related cancers
- HPV currently causes more illness and death than all other vaccine-preventable diseases combined (except influenza)



Why do we vaccinate?

To prevent HPV-associated cancer

Current screening is NOT enough



Pap history in women diagnosed with cervical cancer

Pap smear within 3 years of cancer diagnosis	% women diagnosed with cervical cancer
None	53%
Normal	28%
Abnormal with f/u	9%
Abnormal, no f/u	4%

Sung et al, Cancer 2000; 88: 2283-9



Average Number of New HPV-Associated Cancers by Sex, in the United States, 2005-2009 Women (N=20,413) Men (N=12,002)



Jemal A et al. J Natl Cancer Inst 2013;105:175-201

Incidence of oropharyngeal cancer 1988-2<u>004</u>



Risk factors for HPV+ and HPVoropharyngeal cancers differ:

•HPV+: sexual behavior, tobacco •HPV-: tobacco, alcohol

- Overall: 28% increase
- HPV-positive: 225% increase
- HPV-negative: 50% decline

Survival from HPV+ and HPVoropharyngeal cancers differs: •HPV+: 69% reduction in risk of death (after adjustment for age, when dxed, etc.)

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16

Why do we want to protect boys from HPV?

Oropharyngeal cancers more common in men No screening test for oropharyngeal cancers Estimated to surpass annual cervical cancers by 2020



Without vaccination, annual burden of genital HPV in U.S. females: 3 million cases, \$7 billion



American Cancer Society. 2008;. Schiffman *Arch Pathol Lab Med*. 2003; Koshiol *Sex Transm Dis*. 2004; Insinga, Pharmacoeconomics, 2005



HPV infection causes preterm delivery

- 330,000 women undergo cone/
- **LEEP procedures every year**
- LEEP/HPV infection associated
- with obstetric morbidity
 - Preterm delivery
 - Preterm rupture of membranes
 - Low birth weight
 - Long term developmental outcomes, neonatal intensive care costs

HPV vaccination can prevent preterm deliveries!





Recommendations, Safety, Impact, & Coverage Rates HPV VACCINE



HPV Prophylactic Vaccines

- Recombinant L1 capsid proteins that form "virus like" particles (VLP)
- Non-infectious and non-oncogenic
- Produce higher levels of neutralizing antibody than natural infection



HPV VLP



ACIP HPV Vaccine Recommendations

Population		Recommendation
Females	11-12 (as young as 9)	Routine vaccination with either HPV4 or HPV2
	13-26	Routine catch-up vaccination either HPV4 or HPV2*
Males	11-12 (as young as 9)	Routine vaccination with HPV4
	13-21	Catch-up vaccination HPV4
	22-26	Permissive recommendation HPV4
MSM & HIV+ Males	22-26	Catch-up vaccination HPV4

* Irrespective of history of abnormal Pap, HPV, genital warts

MMWR, May 28 2010; 59(20):626-629 , 630-632 MMWR , December 23 2011; 60(50);1705-1708



Parents and adolescents want to know...

IS IT SAFE? DOES IT WORK? WILL IT CHANGE MY CHILD'S BEHAVIOR?



HPV Vaccine Safety

- Most common adverse events reported were considered mild
- For serious adverse events reported, no unusual pattern or clustering that would suggest that the events were caused by the HPV vaccine
- These findings are similar to the safety reviews of MCV4 and Tdap vaccines
- 57 million doses of HPV vaccine distributed in US since 2006
- 100 million doses worldwide (Europe, Australia)



HPV vaccine long-term safety data

- ► Kaiser-Permanente: 190,000 females who received ≥ 1 dose of HPV vaccine August 2006 and March 2008
- No increase in emergency room visits, hospitalizations, or any of 200 categories of illnesses
- Karolinska Institute: Register based cohort study, Denmark and Sweden, October 2006 to December 2010.
- 997,585 girls aged 10-17, among whom 296,826 received a total of 696,420 qHPV vaccine doses
- No increase in auto-immune disease, thromboembolic disease, neurologic disease

Arnheim-Dahlström, BMJ, Oct 2013 Klein NP, Archives of Pediatrics and Adolescent Medicine Oct 2012



HPV Vaccine Impact: US

33% of teens are fully vaccinated

- 56% decline in HPV 6/11/16/18 in girls age 14-19
- 20% decrease in all CIN2/3 among 21-24 year olds
- Substantial decrease in genital warts among female military under age 26 between 2007 to 2010





Ali H et al. BMJ 2013;346:bmj.f2032 ©2013 by British Medical Journal Publishing Group

Percentage (%)

Year





BMJ 2014;348:g1458 doi: 10.1136/bmj.g1458 (Published 4 March 2014)



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RESEARCH

Effectiveness of quadrivalent human papillomavirus vaccine for the prevention of cervical abnormalities: case-control study nested within a population based screening programme in Australia

46% effectiveness against high-grade cervical lesions

Efficacy exceeds trial data

Crowe E et al. BMJ 2014;348:bmj.g1458 ©2013 by British Medical Journal Publishing Group



Extrapolating the prior pyramid with projections of vaccine efficacy based on Australian data





35% reduction in CIN1

Having sex gives you HPV, but getting an HPV vaccine does not make you have sex!



HPV Transmission

80% of people will be infected with HPV

- Most common route is sexual intercourse
 - genital-genital, anal-genital, oral-genital, manualgenital
- Nearly 50% of high school students have already engaged in sexual (vaginal-penile) intercourse
 - 1/3 of 9th graders and 2/3 of 12th graders have engaged in sexual intercourse
 - 24% of high school seniors have had sexual intercourse with 4 or more partners



HPV is found in virgins

- Study examined the frequency of vaginal HPV and the association with non-coital sexual behavior in longitudinally followed cohort of adolescent women without prior vaginal intercourse
- HPV was detected in 46% of women prior to first vaginal sex
- 70% of these women reported non-coital behaviors that may in part explain genital transmission



Rapid acquisition of HPV in following sexual debut

Study of 18-23 year-old males (n=240)
Study of female college students (N=603)



Months Since First Intercourse

From Winer RL, Lee S-K, Hughes JP, Adam DE, Kiviat NB, Koutsky LA. Genital human papillomavirus infection: incidence and risk factors in a cohort of female university students. *Am J Epidemiol.* 2003;157:218–226. Reprinted with the permission of Oxford University Press. Partridge, JID 2007

HPV may never go away

Infection remains dormant for decades, then reactivates later in life as immune system declines

- Risk of HPV infection among women 50+ was associated with total lifetime partners but not new partners.
- Conclusion: "Reactivation risk may increase around age 50 years and contribute to a larger fraction of HPV detection at older ages, compared with new acquisition."
- 85% of incident infections occurred during periods of abstinence of monogamy, and were associated with lifetime number of sexual partners

Gravitt, JID 2013; Rostich Cancer Res 2012



Receiving HPV Vaccine Does Not Increase Promiscuity

- National Survey of Family Growth n=1243 15-24 yo females
 - HPV vaccination NOT associated with:
 - Being sexually active
 - Number of sexual partners
 - HPV vaccination was associated with:
 - More consistent condom use among 15-19 year olds (AOR=3.0, "always" wearing condom)
- Kaiser Permanente Center for Health Research n=1398 11-12 yo girls in 2006, 30% of whom were vaccinated, followed thru 2010
 - No difference in markers of sexual activity including pregnancies, counseling on contraceptives, and testing for or diagnoses of sexually transmitted diseases

Liddon NC, *Am J Prev Med* 2012;42:44 Bednarczyk RA, *Pediatrics* 2012;130:798





WHY AREN'T WE VACCINATING MORE?

Understanding missed opportunities

Questions for you (3)

- 3. What proportion of high school students have had one dose of the <u>meningitis vaccine</u>?
 - **a. 25%**
 - **b**. 50%
 - **c. 75%**



Questions for you (4)

- 4. What proportion of <u>female</u> high school students have had at least one dose of <u>HPV vaccine</u>?
 - **a. 25%**
 - **b**. 50%
 - **c**. 75%



US behind other nations in uptake of 3 doses HPV vaccine





National Estimated Vaccination Coverage Levels among Adolescents 13-17 Years, National Immunization Survey-Teen, 2006-2012



HPV: human papillomavirus vaccine

Actual and Achievable Vaccination Coverage if Missed Opportunities Were Eliminated: Adolescents 13-17 Years, NIS-Teen 2012



Missed opportunity: Encounter when some, but not all ACIP-recommended vaccines are given. HPV-1: Receipt of at least one dose of HPV.



Strength of HPV Vaccine Recommendation for Female Patients, Pediatricians and Family Physicians (N=609)



Allison et al. https://cdc.confex.com/cdc/nic2011/webprogram/Paper25181.html



Delay more common than refusal

Providers introduce HPV vaccination at 11 but do not recommend it strongly

"I'd honestly say it's rare that I spend more than 20 seconds on it at 11... So few 11 year olds are physically mature to be sexually active that it's, I find it's almost sort of an awkward conversation."

Parents do not understand the reason to vaccinate at early

"I thought that it didn't really make any difference as long as they had the three vaccines before their 20's."



Uptake of 3 doses HPV vaccine by age





Prevalence of sexual activity by age



Markowitz MMWR 2007; Holl Henry J Kaiser Found 2003; Mosher Adv Data 2006



The younger the better, but better late than never

Vaccine 50% more effective when vaccination occurs age 15-17 compared with over age 18

46% vs. 35% reduction in HSIL

35% vs. 0% reduction in LSIL

No protection if evidence of infection prior to vaccination (i.e. abnormal pap)

Mahmud et al, J Clin Onc, Jan 2014



HPV vaccine effectiveness for cervical abnormalities in Australia



Gertig DM, BMC Med 2013



HPV vaccination for ages 18-26

<20% of eligible females vaccinated</p>

- National Longitudinal Study of Adolescent Health (n=3276)
 - 9% of women positive for HPV 6,11,16 or 18
 - •0% of women positive for all 4 types
- Provider recommendation most influential factor in this age group

Price Cancer 2011; Dempsey Vaccine 2008 and 2011; Rosenthal, Vaccine, 2010



Top 5 reasons for not vaccinating daughter, among parents with no intention to vaccinate in the next 12 months, NIS-Teen 2012



* Not mutually exclusive.

** Did not know much about HPV or HPV vaccine.



Framing makes a difference

BAD

Provider: Meghan and Mark are due for some shots today: Tdap and the meningococcal vaccine. There is also the HPV vaccine...

- Vaccine perceived as different, optional, unimportant

GOOD

Provider: Meghan and Mark are due for some shots today: HPV, meningococcal vaccine, and Tdap.

- Presumption of vaccine uptake
- Vaccination percieved as normative, important

CATCH UP

Provider: I see that Meghan and Mark haven't gotten their HPV vaccines yet. We should definitely start that today!

- Presumption of vaccine uptake, conveys message of importance



Opel et al 2014

Addressing all concerns in 45 seconds

Provider: Meghan and Mark are due for their HPV vaccine.

Parent: Why do they need an HPV vaccine?

Provider: The HPV vaccine will help protect them from cancer caused by HPV infection. We know that HPV infection is dangerous– 33,000 people in the US get cancer from HPV every year. And we know that the HPV vaccine is safe– over 100 million doses have been given and there haven't been any serious side effects.

Parent: I don't think they need that yet...

Provider: Vaccines only work if they're given before exposure we never wait until a child is at risk to give any recommended vaccines. HPV vaccine is also given as early as possible because it produces a better immune response in younger adolescents. That's why it is so important to start the shots now and finish all 3 of them in the next 6 months.



Parents weigh risks and benefits

Parents who declined vaccine and those who accepted had similar concerns

Both had concerns related to safety and sexuality but accepters weighed cancer prevention more heavily

Most parents also believed their daughters would at some point be at risk for STIs

Perkins et al, Clin Peds 2013; Perkins et al J of Peds 2010; Perkins et al J Healthcare Poor Underserved 2013



Providers overestimate parent's concerns

"From what I understand the vaccine is safe, efficacious and I'd be a fool and also have amnesia to believe that high schoolers do not engage in unwise sexual practices at times." —Father of a 12 year-old

55-90% of parents and adolescents will follow provider recommendations

Many adolescents seeking contraception will be unvaccinated– family planners are very important vaccinators

Perkins et al, published abstract JAH, Brewer 2007, Prev Med



Discuss HPV vaccination when you screen moms for cervical cancer

One doctor says:

"In your experience with your health right now, you may be screened for cervical cancer by means of a pap smear... because cervical cancer can obviously be something that can be lifethreatening but if caught soon, it can be taken care of, and this is how your health is impacted by this virus right now. Well, children now have the option of getting the HPV vaccine which is actually very effective at reducing the risk for contracting that same virus."



HPV is common and dangerous

- 3 million Americans seek medical treatment for HPV-related disease every year
- 11,000 women every year get cervical cancer— 30% of them were screened on time
- 21,000 men and women every year get HPV-related cancers for which there are no screening tests

We can do better



HPV vaccination IS high quality care

75% reduction in cervical pre-cancer BEFORE AGE 14

35% reduction after age 14

- 85% reduction in genital warts
- 100 million doses have been given worldwide with no evidence of serious side effects
- A strong recommendation is critical



Conclusions

Vaccinating all your patients with HPV vaccines will save lives and improve health

For more information, including free resources for providers and patients: cdc.gov/vaccines/teens



