به نام خدا

HUMAN PAPILLOMAVIRUS VACCINE

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KEY POINTS:

Cancers attributable to human papillomavirus (hpv) are on the rise

Vaccine against the ٧ HPV types that cause ٧٣ % of HPV associated cansers is available, safe, and very effective.

Vaccine also protects against the ٢ HPV types that cause ٩٠% of genital warts.

HPV vaccine should be recommended at the ١١- or ١٢ – year – old well-child visit and the series should be completed by the ١٣th birthday.

INTRODUCTION :

There are more than ١٢٠ different types of human papillomavirus (hpv) .most are responsible for warts found on the skin . Approximately ٤٠ HPV types infect mucosal surfaces and the genital tract . And ١٣of these are oncogenic .

EPIDEMIOLOGY

Approximately ٧٩ million people in the united states are infected with HPV , and ١٤ million acquire new infection each year . In ١ study measuring HPV prevalence just before introduction of a quadrivalent HPV vaccine in ٢٠٠٦ , ٣٣% of ١٤- to ١٩- year – old female patients and ٥٤% of ٢٠ – to ٢٤ – year – old female patients were infected with genital HPV.

- A systematic review published in ٢٠٠٦ included numerous Hpv prevalence studies among men but most studies did not stratify by age .
- Th difference in race and ethnicity among those who develop HPV-related cancers :

PATHOPHYSIOLOGY AND NATURAL HISTORY

Most HPV infections have no symptoms and are cleared by the host immune system, usually within ١ to ٢ years.

About prevention:

HPV ٦ and ١١ are the types that account for approximately ٩٠% of cases of genital warts.

Are HPV related genital warts oncogenic ?

ABOUT CANCER

When any of the ١٣ sexually transmitted oncogenic HPV types persist , precancer and cancer cancer can develop .

The time between infection and development of cancer :

About HPV ١٦ :

Which group of people are at the risk of HPV infection ?

BURDEN OF DISEASE

Sexually transmitted HPV-associated cancers include cancers of cervix , vulva , vagina , penis , oropharynx , anus and rectum .

About oropharyngeal cancers :

Analysis of ٢٠٠٨ to ٢٠١٢ data from the Center for Disease Control and Preventions (CDC's) National Program of Cancer Registries and the National Cancer Institute's Surveillance , Epidemiology ,and End Results program provides estimates of cancers attributable to HPV .

Table 1
Annual cancers attributable to human papillomavirus—United States, 2008–2012

Cancer	Average Number of HPV-Associated Cancers		Average Number of Cancers Attributable to HPV	
	Female	Male	Female	Male
Anal	3260	1750	3000	1600
Cervical	11,771	0	10,700	0
Oropharyngeal	3100	12,638	2000	9100
Penile	0	1168	0	700
Vaginal	802	0	600	0
Vulvar	3554	0	2400	0
Total	22,487	15,556	18,700	11,400

Adapted from Viens LJ, Henley SJ, Watson M, et al. Human Papillomavirus-Associated Cancers - United States, 2008-2012. MMWR Morb Mortal Wkly Rep 2016;65(26):661–6.

The American Cancer Society estimation about new cases :

Some data about anogenital warts :

AVAILABLE VACCINES FOR PREVENTION

Before ٢٠١٧ there were ٣ types of vaccine available to protect against HPV in the united states :

The difference between vaccines :

The Advisory Committee on Immunization Practices (ACIP) recommendation about best age for vaccination :

Why the vaccine is most effective when administered before initiation of sexual activity ?

Males vaccination :

٢ dose series and ٣ dose series :

Table 2
Advisory Committee on Immunization Practices updated recommendations March, 2015

	Bivalent (Ceravix)	Quadrivalent (Gardasil)	9-Valent (Gardasil-9)
Manufacturer	GlaxoSmithKline	Merck	Merck
HPV types	16, 18	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58
Recommended age[a]	Female patients 11–26 y	Female patients 11–26 y Male patients 11–21 y[b]	Female patients 11–26 y Male patients 11–21 y[b]

[a] HPV vaccine may be given as young as age 9 years.
[b] Immunization through age 26 years is recommended for men who have sex with men; men who are immunocompromised, including infection with HIV; and all men desiring protection against HPV.

Adapted from Petrovsky E, Bocchini JA Jr, Hariri S, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the advisory committee on immunization practices. MMWR Morb Mortal Wkly Rep 2015;64:300–4.

IMMUNOGENICITY

Younger individuals have more robust antibody responses to the HPV vaccine.

Antibody response decrease with older age at vaccination .

Studies to date demonstrate long-term immune memory following the standard ٣-dose series with no evidence of waning immunity .

EFFICACY AND SAFETY

Cervical cancer develops over many years . Therefore it is not a feasible endpoint for vaccine efficacy studies .

CIN-٢ :

Nearly ١٠٠% of those in the vaccine groups were protected against CIN٢caused by HPV ١٦ and ١٨ and genital warts due to HPV ٦ and ١١ and from vulvar, vaginal , and anal dysplasia due to HPV types in the vaccine.

Table 3
HPV dosing and timing of 9-valent vaccine[24]

Age at 1st Dose	Regimen	Minimum Time bw 1st & 2nd Dose	Minimum Time bw 2nd and 3rd Dose	Minimum Time bw 1st and 3rd Dose
9–14 y	2-dose	24 wk	NA	NA
15–26 y	3-dose	4 wk	12 wk	24 wk

Advisory Committee on Immunization Practices (ACIP) Meeting 10/20/16

Prevalence of vaccine type HPV:

Clinical trials of the ٩vHPV vaccine have demonstrated greater than ٩٠% efficacy against new persistent cervical infections and CIN٢ due to additional ٥ HPV types in the vaccine .

Is it safe to revaccinate those who received ٤vHPV vaccine with a ٣-dose series .

Side effects :

VACCINE UPTAKE

The CDC uses annual National Immunization Survey-Teen (NIS-Teen) to monitor vaccine coverage . Data from the most recent survey in ٢٠١٥ showed that ٤٩,٨ of male and ٦٢٠٨ of female adolescents between the age of ١٣and ١٧ years had received at least one dose of the HPV series .

Furthermore only ٢٨,١% of boys and ٤١,٩% of girls received all three HPV doses .

TABLE 4
National Immunization Survey: teen coverage results 2008–2015

Vaccine	2008	2009	2010	2011	2012	2013	2014	2015
Tdap after 10 y of age, %	40.8	55.6	68.7	78.2	84.6	86.0	87.6	86.4
≥3 doses HepB, %	87.9	89.9	91.6	92.3	92.8	93.2	91.4	91.1
≥2 doses MMR, %	89.3	89.1	90.5	91.1	91.4	91.8	90.7	90.7
≥2 doses of Varicella, %	34.1	48.6	58.1	68.3	74.9	78.5	81.0	83.1
≥1 MCV4, %	41.8	53.6	62.7	70.5	74.0	77.8	79.3	81.3
HPV								
Females								
≥1 dose, %	37.2	44.3	48.7	53.0	53.8	57.3	60.0	62.8
≥3 doses, %	17.9	26.7	32.0	34.8	33.4	37.6	39.7	41.9
Males								
≥1 dose, %	—	—	1.4	8.3	20.8	34.6	41.7	49.8
≥3 doses, %	—	—	—	1.3	6.8	13.9	21.6	28.1

Data from Reagan-Steiner S, Yankey D, Jeyarajah J, et al. National, regional, state, and selected local area vaccination coverage among adolescents aged 13–17 years - United States, 2015. MMWR Morb Mortal Wkly Rep 2016;65:850–8.

NIS-Teen data from ٢٠١٣ demonstrated that , for parents of both boys and girls, not receiving a recommendation to vaccine and not knowing enough about the HPV vaccine were among the top ٥ reasons for not having their child vaccinated against HPV.

In a study researchers asked parents how important they thought various vaccines were to their childs health

Some states and local areas have much better HPV vaccine uptake than the country as a whole . Those that have been successful in improving vaccine coverage have used several strategies :

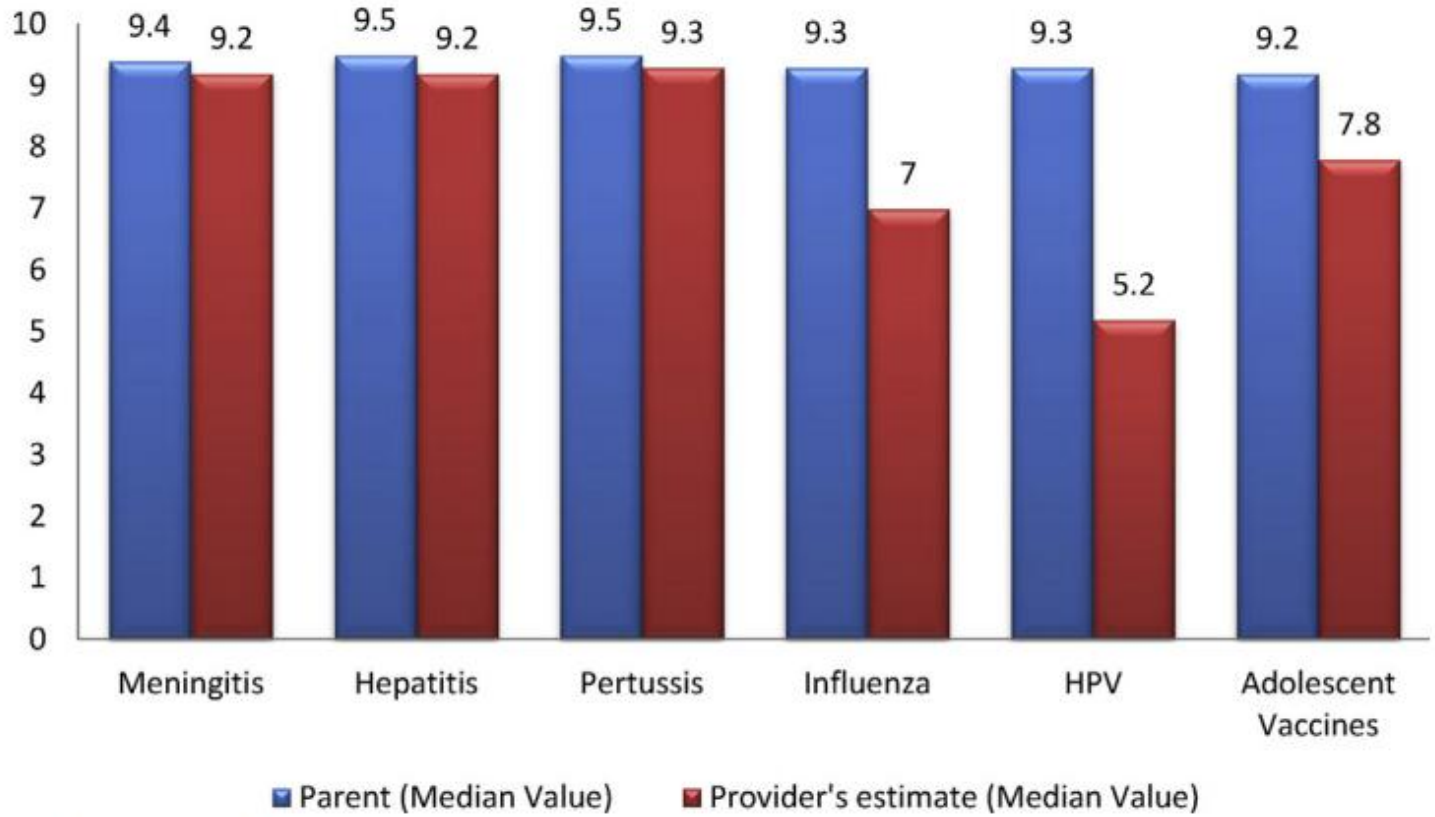

Fig. 1. Clinicians underestimate the value parents place on HPV vaccine. (*From* Centers for Disease Control. You are the key to HPV cancer prevention. Available at: https://www.cdc.gov/vaccines/ed/hpv/index.html. Accessed December 2, 2016.)

SUMMARY

Rates of cancers attributable to hpv are rising . The morbidity and mortality of these cancers place an unnecessary burden of disease on the US population and on the US health care budget . A safe and extremely effective vaccine is available to prevent many of these cancers .

Studies have shown that the health care providers recommendation to immunize is the most important factor in the parents decision. Parents of all adolescent boys and girls should receive a strong and unequivocal recommendation to vaccinate their child against HPV at the ١١- or ١٢ – year – old well-child visit . This recommendation should be consistent with the recommendation to receive the Tdap and MCV٤ vaccine . Ideally, adolescents will complete their HPV vaccine series by the ١٣th birthday .this will lead to greater immune response and protect most adolescents before they are exposed to sexually transmitted HPV .

THANKS FOR YOUR ATTENTION