HPV & OROPHARYNGEAL CANCERS

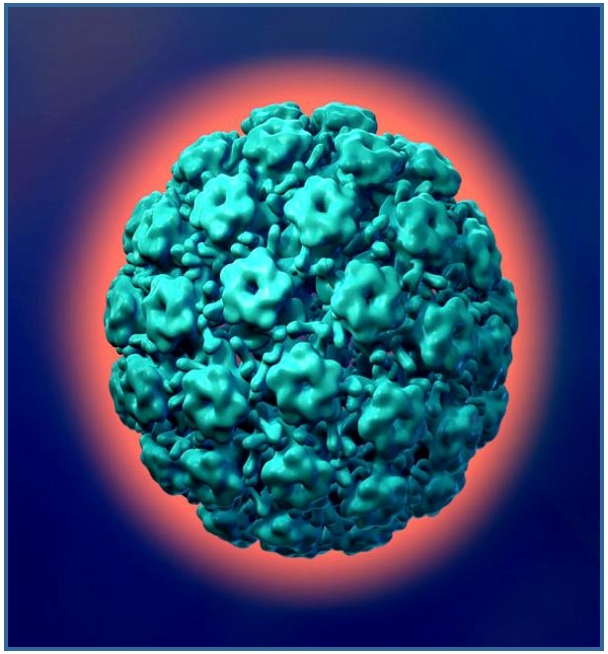
Tahereh Soori

Infectious Diseases Specialist

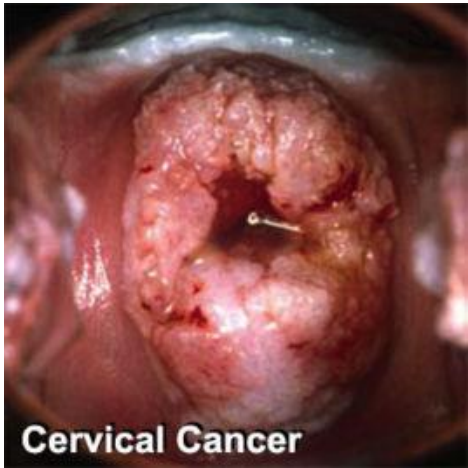
Associated Professor

Tehran University of Medical Sciences

Ethiology



- Non envelope virus, Double stranded circular DNA genome
- 55 nm diameter, Icosahedral capsid with 72 capsomers ,7900 base pairs



HISTORY

- First discovered in skin cells in the 1950s, HPV is now understood to infect basal keratinocytes in the skin or mucosal membranes.

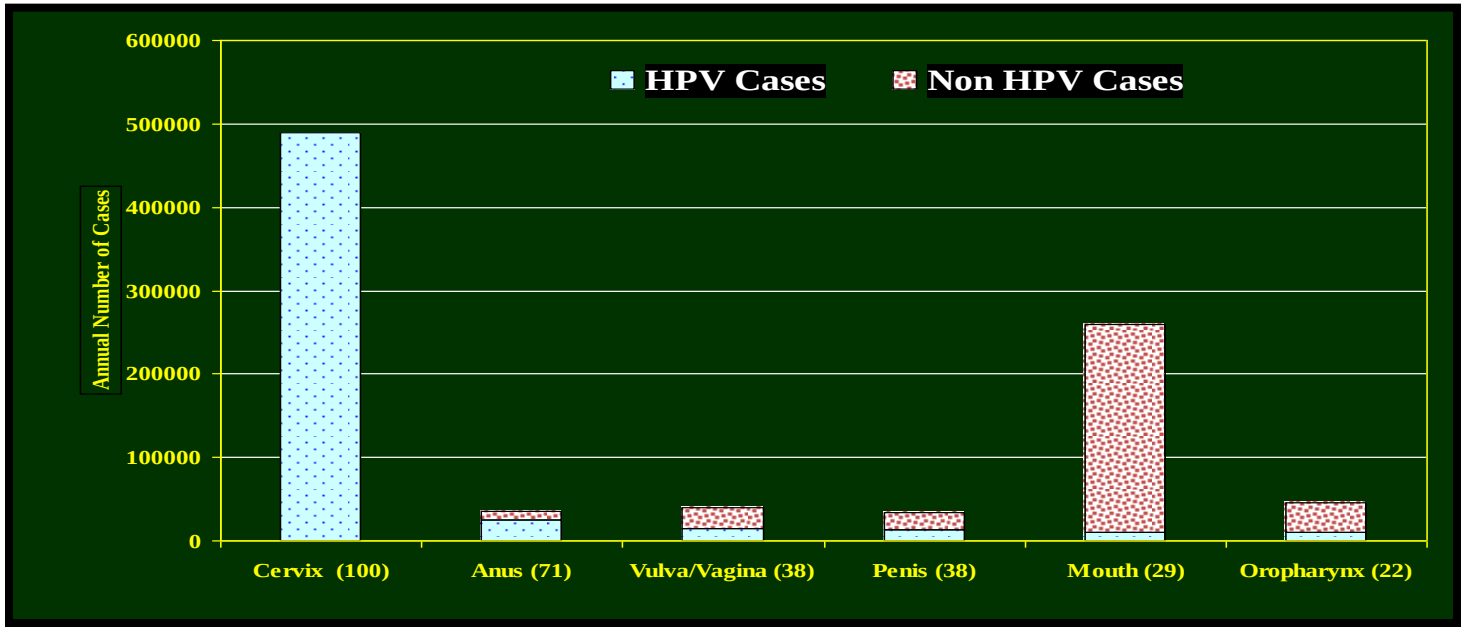
- The role of HPV in carcinogenesis of the cervix was elucidated by **Harald zur Hausen**, for which he received the **2008** Nobel Prize in Medicine .

HPV

- ~100 types identified
- ~30–40 anogenital ,**ORAL**
  - ~15–20 oncogenic
    - HPV **16** and **18** types account for majority of worldwide cervical acancers and are associated in nasopharyngeal cancers(16)
    - Other High-Risk HPV Types: 31,33,35,39,45, 51, 52, 56, 58, 59, 68,82
  - Nononcogenic types
    - HPV **6** and **11** are most often associated with external anogenital warts. **These two types are responsible for >90% of genital warts or oral cavity warts.**
    - Other Low Risk HPV Types: 40,42,43,44, 54, 61, 72, 73, 81

Risk not well established yet: 26, 53, 66

Worldwide incidence and distribution of cancers attributable to HPV



HPV has been found to cause cancer of the ***cervix, anus, penis, vulva, vagina, and oropharynx,*** as well as benign genital and oral warts, respiratory papillomatosis

Epidemiology

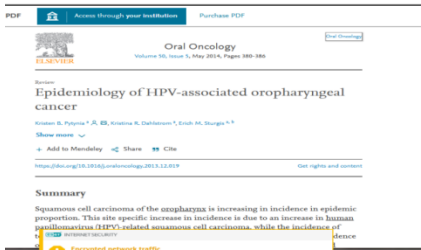
- **HPV in the world**
  - The most common STI
  - Prevalence:5%

- **HPV in Iran:**
  - prevalence among Iranian women (Tehran, Shiraz, Gorgan, Bushehr) : 7.4%
  - Another study was 9.4% of healthy women
  - General population 2.8% are HPV 18/16 infected
  - 58.5% , 76% of cervical cancers are related to HPV16/18

Epidemiology

- The incidence of HPV-positive OPSCC is increasing markedly, and it is not hyperbole to call this an **epidemic**.
- Approximately 25% of head and neck squamous cell carcinoma (HNSCC) worldwide are associated with high-risk human papillomaviruses (HPV).
- estimated 85,000 cases of oropharyngeal cancer worldwide
- at least 22,000 of these were HPV positive
- Within 6 years there was a 225% population-level increase in HPV-positive OPSCC in the United States and a concomitant 50% decrease in HPV-negative OPSCC

majority of HPV-related OPSCC cases are caused by HPV16.


PDF Access through your institution Purchase PDF

Oral Oncology

Epidemiology of HPV-associated oropharyngeal cancer

Summary

Squamous cell carcinoma of the oropharynx is increasing in incidence in epidemic proportion. This site specific increase in incidence is due to an increase in human papillomavirus (HPV)-related squamous cell carcinoma, while the incidence of

Natural History of Low-risk HPV Types

Median time to wart development after infection is **6–10 months** (range up to **18 months**) previously ***2.9 months***

Transient productive viral infection leads to minor cellular abnormalities and the development of low-grade lesions

Clearance

Recurrence rate is >25% within the first 3 month

Natural History of High-risk HPV Infection and Potential Progression to Cancer

Clearance

persistent infection is the most important risk factor for the development of cancer precursor lesions.

Only a minority(< 1%) of HPV infected individuals develop cancer

HPV** Natural **History

- Median time to **clearance of HPV**
- (including oncogenic and nononcogenic types).

- in women was 9.4 months.
- in men was 7.5 months

HPV neither correlates with nor predicts survival in NPC.

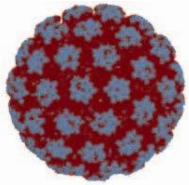
we could not draw a definitive conclusion as to the prognostic significance of HPV in NPC.

HPV-positive HNSCCs have a more favorable outcome and greater response to therapy.

Routes of HPV Transmission

Probability of HPV transmission per coital act ranged from 5 to 100% (median = 40%)

Primary



Less Common

Sexual Routes

Genital Contact
- sexual intercourse
- genital-genital
- manual-genital
- oral-genital

Most important risk factor is the number of sex partners (lifetime and recent)

Non-sexual Routes

Extragenital
- fomites (?)
  - undergarments
  - surgical gloves
  - biopsy forceps

Hypothesized

surgical gloves, biopsy forceps

Vertical
mother
↓
neonate (at birth)
↓
respiratory papillomatosis

Rare; types 6 & 11

HPV TRANSMISSION

- Oral lesions are transmitted through orogenital sexual contact.
- The presence of lesions in children should raise the possibility of sexual abuse, although it is possible that HPV may be transmitted by non-sexual contact.
- Recent evidence supports their horizontal, mouth-to-mouth, transmission.
- asymptomatic patients< patients with clinical lesions

- Family members of people with genital warts are not at additional risk in personal close contacts.

- **Recuurent laryngeal papillomatosis may occure in adults with oral sex.**

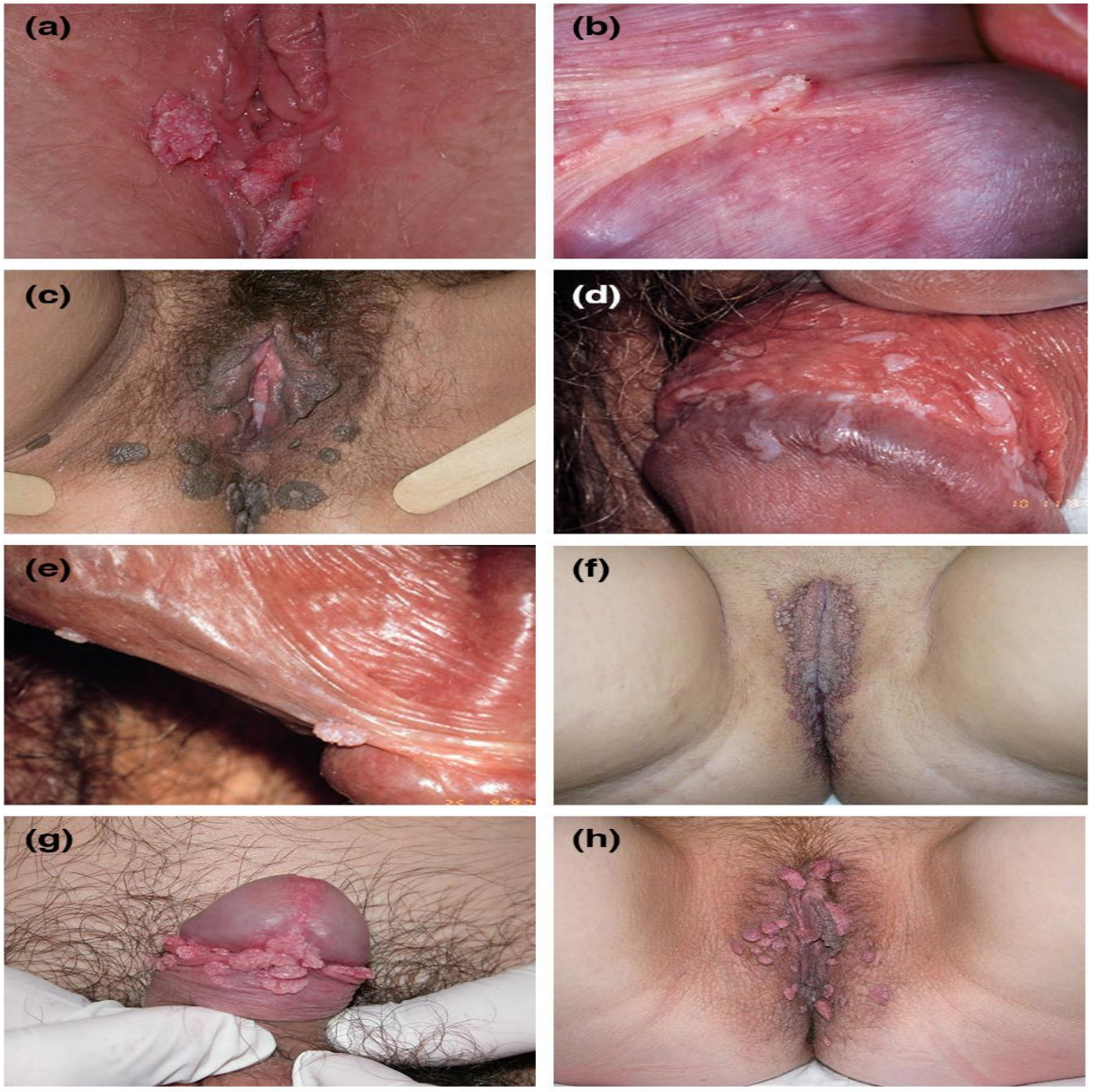
- Newer studies suggest a vertical transmission rate of approximately 20–30%. The majority of neonatal infections are cleared by the first year of life, with one study showing a 100% clearance rate

- **Role of C/S in prevention of baby infection is unknown and not recommended.**

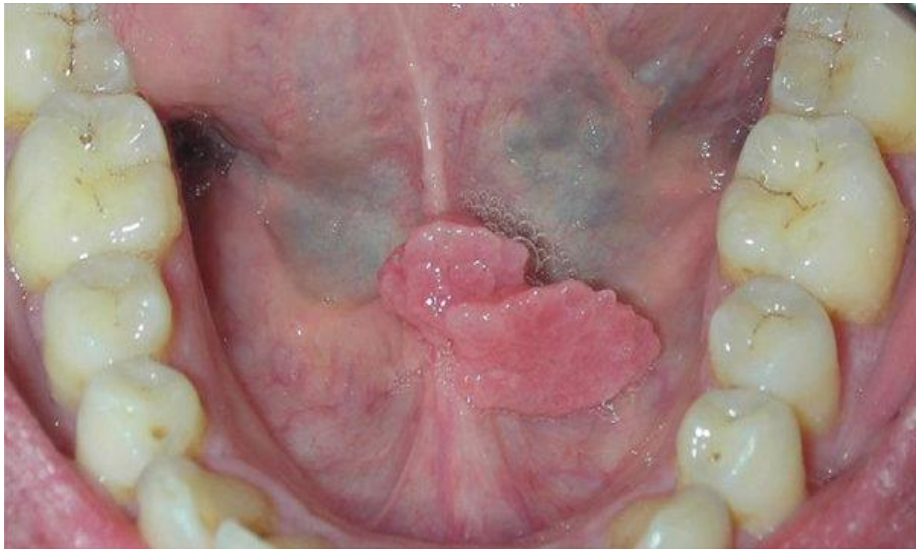
HPV Occupational Exposure

- Electrosurgical and laser
  - *The first report was a 44-year-old surgeon*
  - *The second case report was a 28-year-old gynecologic surgical nurse*

Clinical manifestation



HIV TEST



The most common intraoral sites of involvement include the labial mucosa, lingual frenulum and soft palate

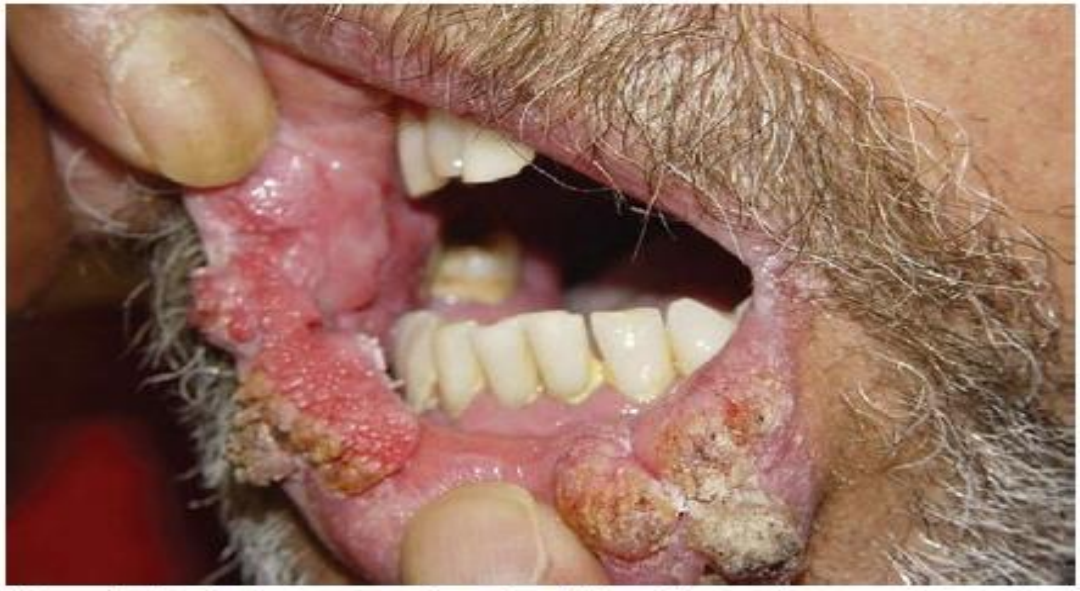


Figure 5: Condyloma accuminata in a HIV positive patient.

.

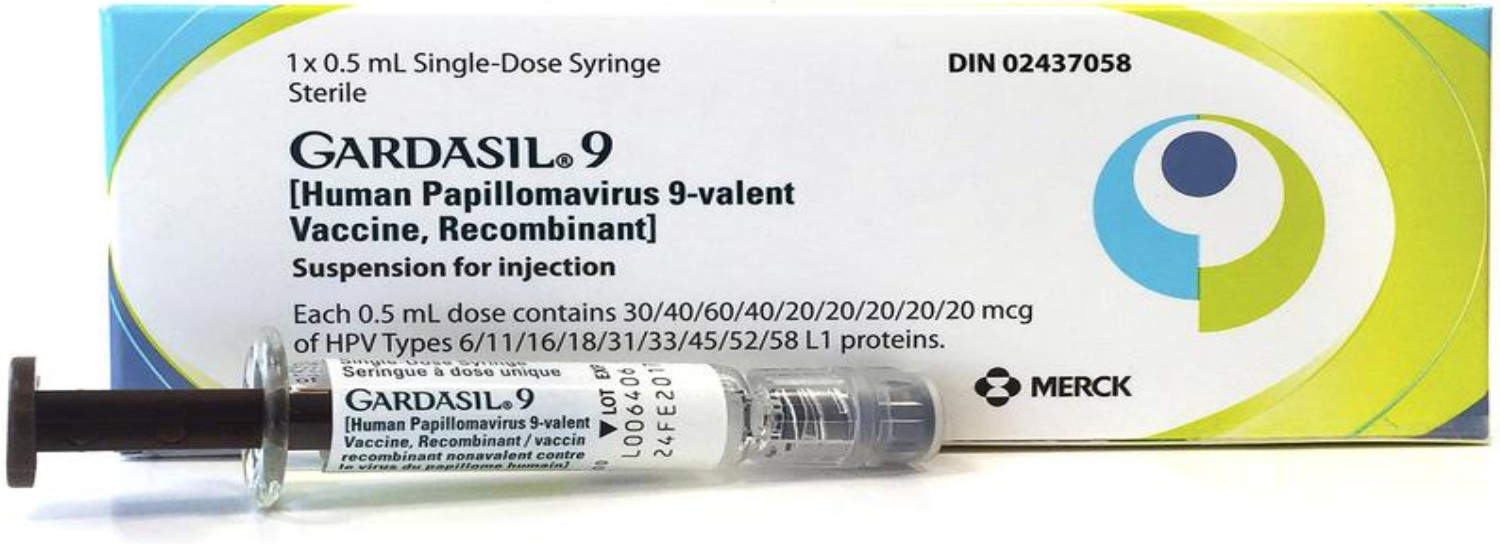
Recommended and Alternative Regimens for Treatment of External Anogenital Warts

Recommended Regimen	Dosing
Imiquimod 5% cream	Topically every night at bedtime for 3 times/wk up to 16 wk
Imiquimod 3.75% cream	Topically every night at bedtime up to 16 wk
Podofilox 0.5% solution or gel	Topically twice daily × 3 d followed by 4 d off for up to 4 cycles
Sinecatechins 15% ointment	Topically 3 times daily, for up to 16 wk
Bichloracetic acid 80%–90%	Applied once every 1–2 wk
Cryotherapy	Applied once every 1–2 wk
Surgical removal	
Trichloroacetic acid 80%–90%	Applied once every 1–2 wk


HPV
VACCINE


GARDASIL®
Vaccin Papillomavirus Humain [Types 6, 11, 16, 18] [Recombinant, adsorbé]
Humaner Papillomvirus-Impfstoff [Typen 6, 11, 16, 18] [rekombinant, adsorbiert]
Humaan papillomavirusvaccin [type 6, 11, 16, 18] [recombinant, geadsorbeerd]
Suspension injectable en seringue préremplie.
1 seringue préremplie unidose de 0,5 ml avec dispositif de protection de l'aiguille et 2 aiguilles.
Voie intramusculaire (IM)
Injektionssuspension in einer Fertigspritze
1 Dosis zu 0,5 ml in einer Fertigspritze mit Kanülenschutzvorrichtung und 2 Kanülen
Intramuskulär (i.m.) verabreichen
Suspensie voor injectie in een voorgevulde injectiespuit met beschermingsmiddel tegen de naald en 2 naalden
Intramusculair (i.m.) gebruik
1 dosis, 0,5 ml
sanofi pasteur MSD

6 11 16 18 31 33 45 52 58



預防90%
子宮頸癌

世界衛生組織
WHO認可

9歲以上
男女適用

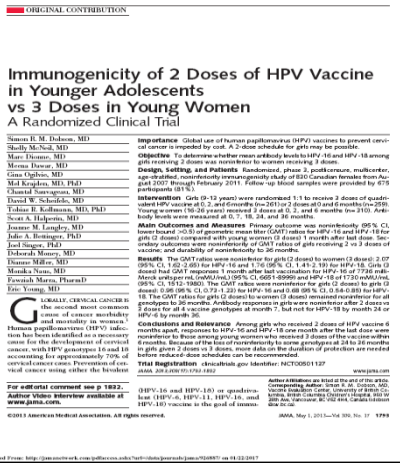
加衛苗®
2億支
已被接種

0 2 6
6個月內注射
3針長效預防


پاپیلوگارد®
NOVIN
Papilloguard®
NOVIN
NOVIN

Dosage and Administration

- intramuscularly (IM)
- deltoid region
- anterolateral area of the thigh
- 0.5 mL doses
- 0,2,6 month
- stored at 2-8 C
- Observation for 15 minutes after administration .
- If the vaccine schedule is interrupted, the vaccination series does not need to be restarted.



ORIGINAL CONTRIBUTION

Immunogenicity of 2 Doses of HPV Vaccine in Younger Adolescents vs 3 Doses in Young Women

A Randomized Clinical Trial

Precautions and Contraindications

- persons with a history of immediate hypersensitivity to any vaccine component.
- persons with a history of immediate hypersensitivity to yeast.
- ***HPV vaccines are not recommended for use in pregnant women .***
- If a woman is found to be pregnant after initiating the vaccination series, the remainder of the 3-dose series should be delayed until completion of pregnancy.
- Pregnancy testing is not needed before vaccination.
- If a vaccine dose has been administered during pregnancy, no intervention is needed.

Human Papillomavirus Vaccine Recommendations From the Advisory *Committee* on Immunization Practices

Population PLHA	Age Group, y	Recommendation
Females	11-12 (may start at 9)	Routine vaccination with either 2vHPV, 4vHPV, or 9vHPV
	13–26	Routine vaccination with either 2vHPV, 4vHPV, or 9vHPV[a]
Males	11–12 (may start at 9)	Routine vaccination: 4vHPV or 9vHPV
	13–21	Routine vaccination: 4vHPV or 9vHPV
	22–26	4vHPV or 9vHPV may be administered
MSM and HIV^+	22–26	Routine vaccination: 4vHPV or 9vHPV

2 doses younger than 15

9 of 12 studies reported **decreased disease recurrence** and decreased disease burden


THANKS