Human papilloma virus

Reproductive block

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1. WHAT IS HPV
2. HPV RELEATED INFECTIONS
3. PREVELANCE IN U.S AND SAUDI ARABIA
4. TYPES OF VACCINES AVILABLE
5. TIME OF VACCINATION
6. DOSES AND ADMINISTRATIONS
7. DURATION OF PROTECTION
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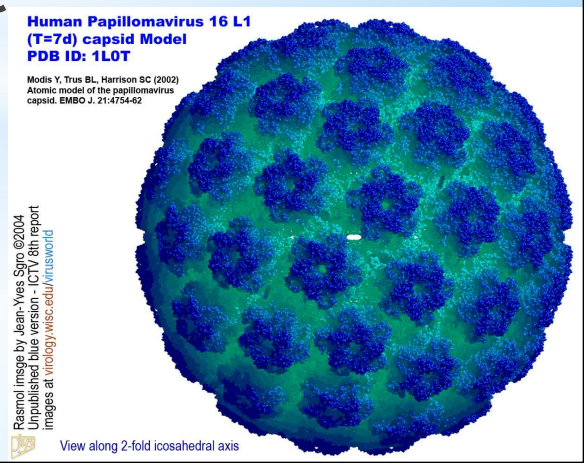
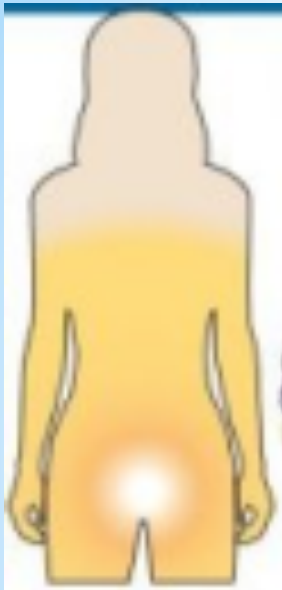
Human papillomavirus

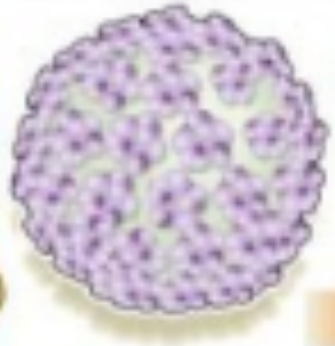
- ✓DNA virus from the papillomavirus family
- ✓over 150 types are known
- ✓More than 40 types are transmitted through sexual contact and infect the anus and genitals.
- ✓ spread by sustained direct skin-to-skin contact with vaginal and anal sex
- ✓It does not spread via common items like toilet seats
- ✓cannot be cultured without living tissue



Human papilloma virus (HPV)

Sexually transmitted HPV infections are common and often asymptomatic, untreated cases in women are the main cause of cervical cancer





- A sexually transmitted virus that causes cancer
- More than 100 types of HPV have been found so far
- 15 have been identified as putting women at high risk for cervical cancer

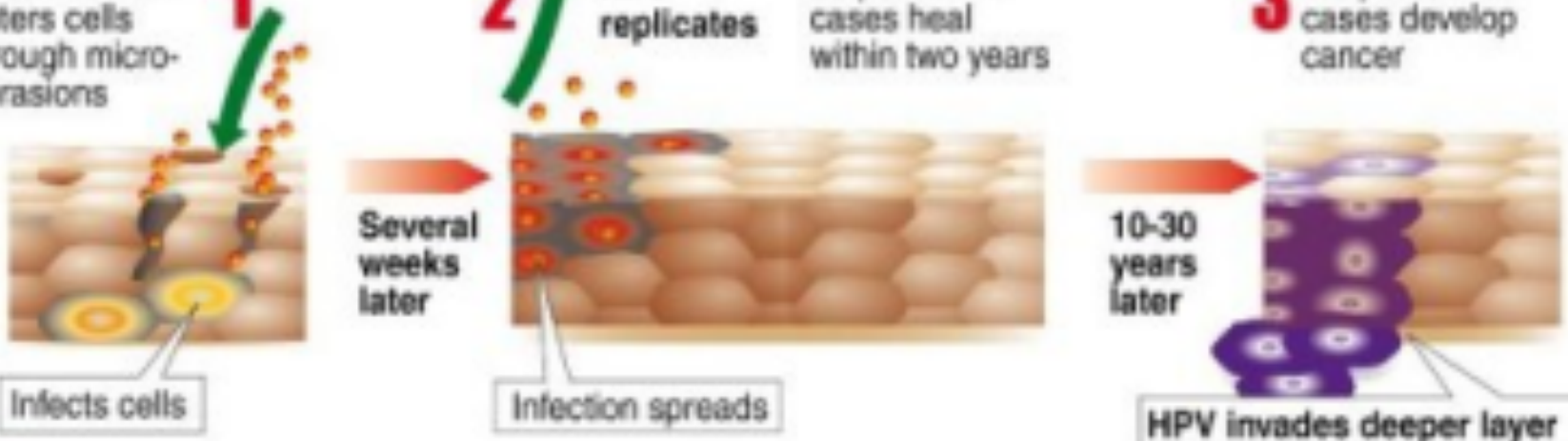
Cervical cancer

1 Virus in cervix enters cells through micro-abrasions

2 **HPV replicates**

90 percent of cases heal within two years

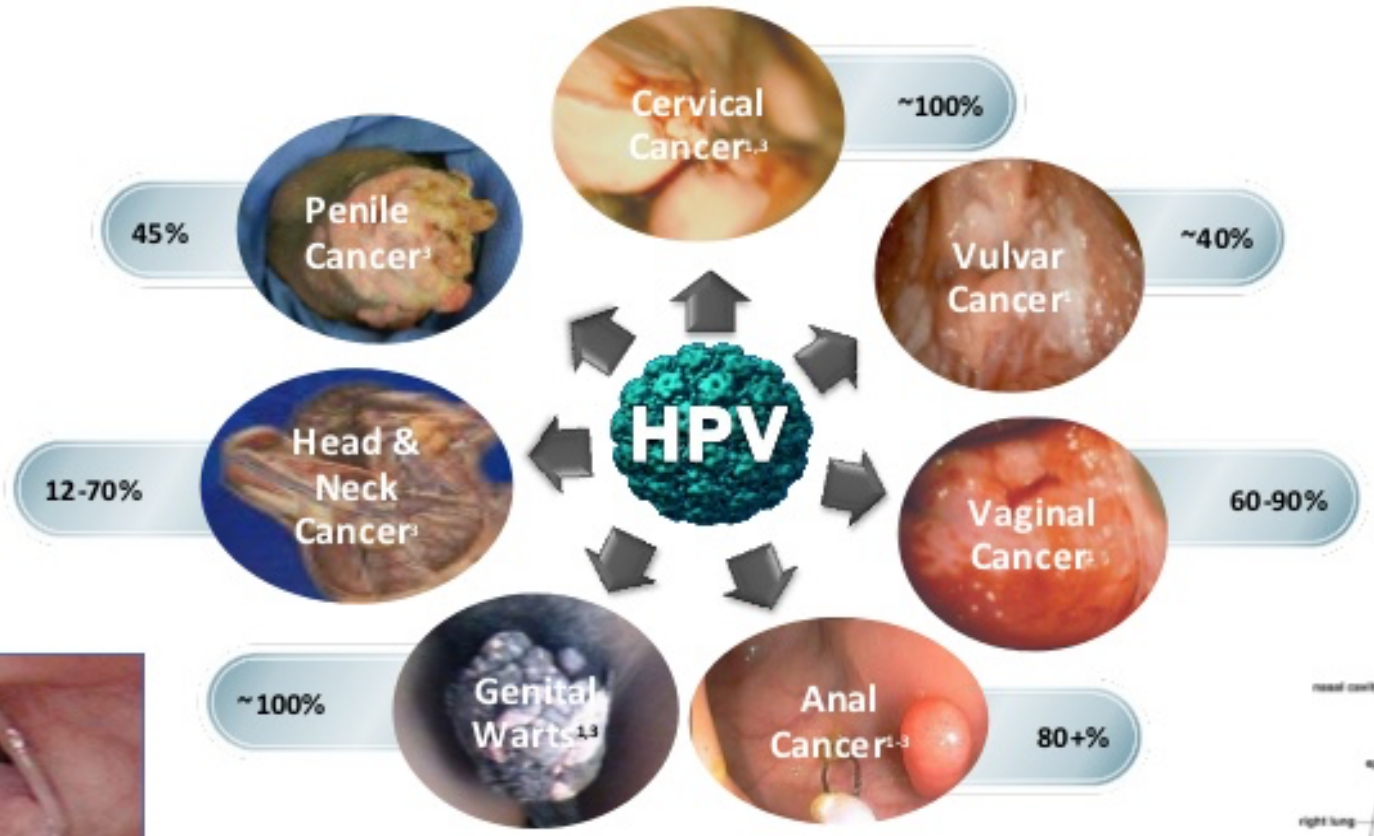
3 0.8 percent of cases develop cancer

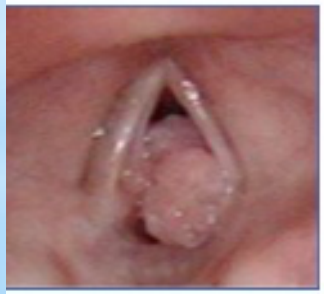


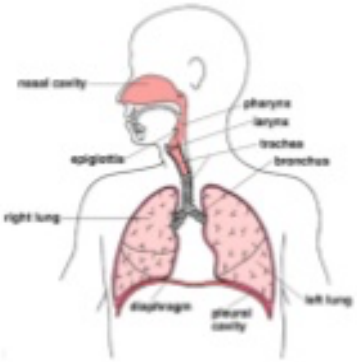
AFP

Source: Nobel/FDA

HPV causes more than cervical cancer







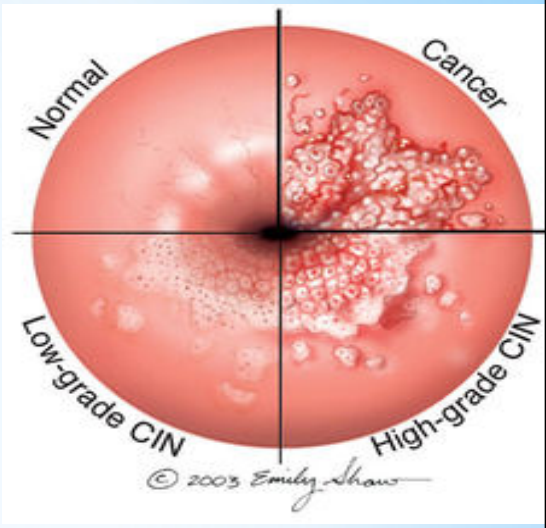
Percentages represent cases atrributable to HPV infection

Braaten KP et al. Rev Obstet Gynecol. 2008;1:2–10.

Hoots BE et al. Int J Cancer. 2009;124:2375–2383.

IARC. IARC monographs on the evaluation of carcinogenic risks to humans. Human papillomaviruses. Vol 90. Lyon, France: IARC, 2007.

DISEASE ASSOCIATIONS:



❖HPV-related disease in females

➢ **Cervical cancer and precursor lesions**

-The 3rd most common female cancer worldwide

-IN U.S

-THE ANNUAL INCIDENCE OF CIN

0.4 % :CIN 1 0.5% : CIN 2/3

-HPV 16 ,18 :

70% : cervical cancer

50 % :CIN

-HPV types 31, 33, 45, 52, and 58 :

19 % cervical cancers

in Saudi Arabia:

- Approximately 152 new cases of CC are diagnosed every year
- 55 women die from the disease annually
- ranking number 12 between all cancers in females
- accounts only for 2.4% of all new cases, despite the lack of national screening programs

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Human papillomavirus prevalence and type distribution among women attending routine gynecological examinations in Saudi Arabia

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Abstract

Background: Cervical cancer (CC) is caused by persistent infection with high-risk (HR) human papillomavirus (HPV) types. In Saudi Arabia which has a population of 6.5 million women over the age of 15 years, approximately 152 new cases of CC are diagnosed and 55 women die from the disease annually. Nevertheless current epidemiological data for HPV in this population are limited. This study evaluated the prevalence and type distribution of HPV and documented the awareness of HPV infection and health-related behavior among Saudi and non-Saudi women attending routine examination.

Methods: This was an observational, epidemiological cross-sectional study conducted between April 2010 and December 2011 at three hospitals in Saudi Arabia. Cervical samples from women aged ≥15 years, who were attending routine gynecological examinations were collected and tested for HPV-DNA by polymerase chain reaction and typed using the SPF_{10} DEIA/LiPA25 system. Two questionnaires on health-related behavior and awareness of HPV infection were completed.

Results: A total of 417 women, mean age (standard deviation) 41.9 (±10.4) years, were included in the final analysis, of whom 77% (321/417) were Saudi nationals. HPV-DNA was detected in 9.8% women (41/417, 95% confidence interval [CI]: 7.1-13.1). The prevalence of any HR-HPV by age was: 25–34 years: 3.0%; 35–44 years: 4.5%; 45–54 years: 3.2%; >55 years: 10.9%. The most prevalent HR-HPV-types were: HPV-68/73 (5 cases); HPV-18 (4 cases); HPV-16 (3 cases). The most prevalent low risk (LR) types were HPV-6 (4 cases); HPV-42, HPV-53 and HPV-54 (2 cases each). The prevalence of HPV was higher among non-Saudi nationals vs. Saudi nationals (16.7% vs. 7.8%, $P = 0.0234$). No statistically significant risk factors were identified: 32.2% (101/314) women were aware of HPV and 89.9% (285/317) showed an interest in HPV vaccination.

Conclusion: The overall prevalence of HPV was 9.8% in Saudi Arabia, but was higher in women over 55 years, as well

- This was an observational, epidemiological cross-sectional study conducted between April 2010 and December 2011 at three hospitals in Saudi Arabia

- **Result :**

1. The prevalence of HPV : 9.8% in Saudi Arabia, but was higher in women over 55 years, as well as in non-Saudi nationals.
2. The most prevalent HR-HPV-types were:

HPV-68/73 ---(5 cases)

HPV-18 ----(4 cases)

HPV-16 (3 cases)

The most prevalent low risk types were

HPV-6-- (4 cases)

HPV-42, HPV-53 and HPV-54 (2 cases each).

- **Vulvar and vaginal cancer and precursor lesions —**
- rare cancers globally

IN U.S

- estimated incidence of 27,000 vulvar cancers and 13,000 vaginal cancers in 2008

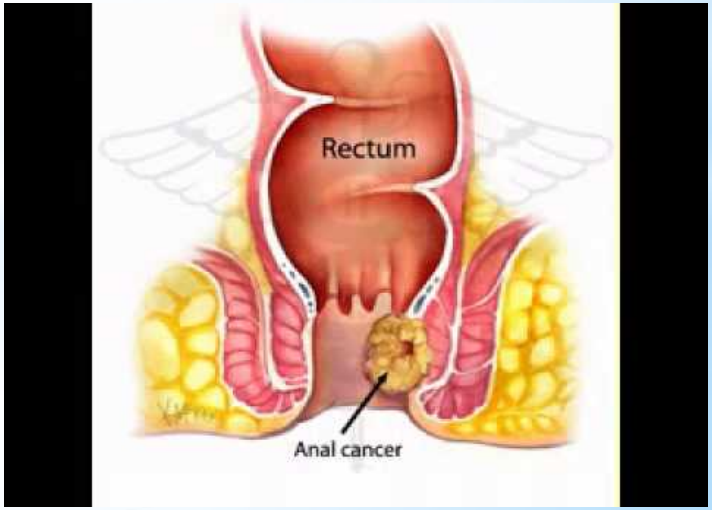
- the attributable fraction due to HPV infection has been estimated to be 43 % for vulvar and 70 % for vaginal cancer

❖HPV-related disease in females and males

➢Anal cancer and precursor lesions —

- rare cancer globally

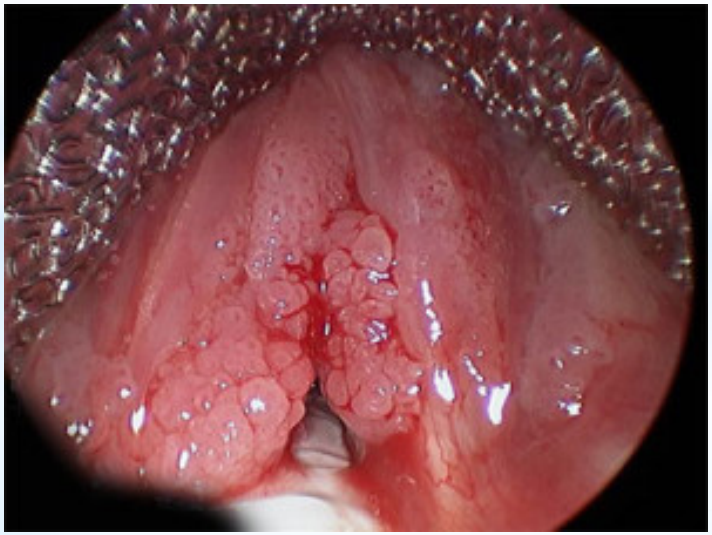
- HPV types 16 and 18 cause around 70 to 85 % of anal cancers and precancerous lesions (ie, anal AIN grade 2 and grade 3



Genital warts –

- HPV types 6 and 11 cause 90 percent of genital warts.

- IT is associated with physical and psychological morbidity and have a high rate of treatment failure AND treatment of recurrent episodes is costly



➢Oro-pharyngeal cancer –

- HPV infection may also play a role in the pathogenesis of squamous cell carcinomas of the head and neck.

- primarily found in the oropharynx and base of the tongue , tonsil AND larynx

❖HPV-related diseases in males

➢Penile cancer and precursor lesions –

- It is rare globally

- HPV 16 and HPV 18 cause approximately 35 to 40 % of penile cancers and 70-80 % of HPV-positive penile cancers

Three different vaccines have been developed against HPV :

FDA licensed Gardasil in June 8, 2006.

- ✓ a quadri-valent HPV vaccine, targets HPV types 6, 11, 16, and 18
- ✓ It is approved for the prevention of cervical cancer and cervical and vulvar intra epithelial neoplasia in young women
- ✓ both men and women from the ages of 9 to 26 for the prevention of genital warts, anal cancers, and anal intraepithelial neoplasias.
- ✓ In October 2018, it was approved too for women at age 27-45 y.

Among HPV-naïve populations, the efficacy for preventing CIN : 97 to 100 %

In the overall population of study participants (with or without prior HPV infection) the efficacy : 44 % after a mean follow-up period of 3 years.

* The National Cancer Institute
Reviewed: November 2, 2016

is approved In December 2014, the United States' Food and Drug Administration (FDA) for women and girls aged 9 to 26 and men and boys aged 9 to 15.

- ✓ a 9-valent vaccine, targets the same HPV types as the quadri-valent vaccine (6, 11, 16, and 18) as well as types 31,33, 45, 52, and 58 .

- ✓ An international trial reported the efficacy of this vaccine in approximately 14,000 females aged 16 to 26 years who were randomly assigned to receive the vaccine :

1. Among HPV-naïve populations, the efficacy of 9-valent vaccine for preventing CIN2 or more severe disease, VIN2 or 3, and VaIN2 or 3 associated with HPV types 31, 33, 45, 52, and 58 was **97 %**

The National Cancer Institute
Reviewed: November 2, 2016

-a bivalent vaccine, targets HPV types 16 and 18

-is approved for girls and women aged 9 to 25 for the prevention of cervical cancer and CIN.

- One large randomized clinical trial in more than 18,000 young females aged 15 to 25 years demonstrated the efficacy of bivalent HPV vaccine .

Among HPV-naïve patients, the efficacy of the vaccine for preventing CIN2 or more severe disease due to HPV types included in the vaccine was **93 %**

When?

American Cancer Society (ACS) guidelines

should be routinely offered to

1. females aged 11 to 12 years; immunization may begin at 9 years of age .

2. catch-up vaccination for females aged 13 to 26 who have not been previously vaccinated or completed their vaccine series.

IMMUNIZATION IN SPECIAL PATIENT POPULATIONS

What about ?
Pregnant females?

According to CDC RECOMMENDATIONS

- ✓ **not recommended**

given that safety in this setting has not been thoroughly evaluated .

- ✓ If a woman is found to be pregnant after initiating the vaccination series, the remainder of the three-dose regimen should be delayed until after completion of the pregnancy

- In quadri valent HPV vaccine trials, the composite rate of adverse pregnancy outcome (spontaneous abortion, late fetal death, congenital anomaly) was similar for the 3819 females who became pregnant and controls who did not receive the vaccine (22.6 versus 23.1 percent)

- Similarly reassuring findings have been reported for the bivalent HPV vaccine and for the 9-valent HPV vaccine , although data are more limited

- Safe in lactating females as it dose not affect the infant breast feeding

Immunization in females with pre-existing cervical abnormalities or genital warts

- A history of genital warts, abnormal cytology, or +VE HPV DNA test result is not evidence of prior infection with any or all of the vaccine HPV types

- vaccination can still provide protection against infection with HPV vaccine types not already acquired.
- assessment with Pap testing or screening for existing HPV infection is NOT indicated as part of the determination for HPV vaccine candidacy.

- these patients should be advised that vaccination will have no therapeutic effect on pre-existing HPV infection or CIN , and the potential benefit of HPV vaccination is not as great as if they were vaccinated before they started having sex.

Transplant recipients and HIV-infected patients

According to CDC RECOMMENDATIONS

- Studies of the HPV quadrivalent vaccine in HIV-infected adult men and women aged 16 to 23 years , boys and girls aged 7 to 12 years suggest that it is both immunogenic and safe in these populations.

- efficacy data are not yet available.

- For solid organ transplant recipient

It is safe to be given 3 to 6 months following trasplantation

VACCINE DOSE AND ADMINISTRATION

According To CDC GUIDELINES ON DEC 2016

Immunization schedule — In the United States, as of 2016, the recommended dosing schedule depends on the age of the patient

- Individuals younger than 15 years should receive two doses of HPV vaccine at least six months apart.

Individuals 15 years or older should receive three doses of HPV vaccine over a minimum of 24 weeks.

- The minimum interval between the first two doses is 4 weeks and the minimum interval between the second and third doses is 12 weeks.

- The Gardasil and Gardasil 9 are typically administered in three doses at time zero, and at two and six months of follow-up.
- Cervarix follow a similar three-dose schedule for those older than 15 years, the bivalent vaccine is typically administered in three doses at time zero, and at one and six months of follow-up.

Interrupted schedules

if the vaccination series is interrupted for any length of time, it can be resumed without restarting the series.

For how long ?

Duration of protection ?

- IN ALL CLINICAL TRIALS Persistent antibody levels and protection against HPV infection have been reported up to 10 years following vaccination .

- Of note, the precise level of antibody needed for protection against infection is unknown.

- Further data will become available in the future as female and male participants in vaccine studies are followed over time.

* CDC GUIDELINES DEC2016

Results:

- HPV-16 and -18 antibodies peaked at Month 7 and gradually plateaued at Months 18–24 and remained stable through 6.4 years

- Mean antibody levels at the last time point were several fold higher than those associated with natural infection.

- The study predict that HPV-16 and -18 mean antibody levels will remain well above those associated with natural infection for at least 20 years

Vaccine safety

All vaccines use virus-like particles (VLPs) which mimic the viral capsid.

VLPs do not contain genetic material and are produced in biologic systems, which have well-established safety records