

# Prevention of Human Papilloma Virus Infection and Related Lesions

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# Introduction

Genital HPV is a common highly contagious virus transmitted through genital contact mostly during vaginal and anal sex. About 100 types of HPV are known but only 40 can infect the genital areas of both sexes.

At least 50% of sexually active people will get HPV some time in their lives. About 6.2 million/year get HPV in the USA. Most of these new cases occur in women & men around 20s. According to the American CDC, by the age of 50, 80% of American women will have contracted at least one strain of HPV.

About 11,000 American women are diagnosed with cervical cancer/year, and 3,700 die/ year of the disease.

## Introduction (Cont.)

Most HPV infections clear spontaneously within 6 to 24 months & the risk for progression to pre-invasive and invasive cancer is highest among women with persistent infection beyond this period.

Type 16 HPV is the most common cause of invasive cancers of the cervix (accounts for 70% together with type 18) & other anogenital cancers. Persistent infection with low-risk HPV types 6 and 11 has been linked to low-grade cervical cancer (CIN lesions), genital warts & respiratory papillomatosis.

## Introduction (Cont.)

There is no treatment for HPV but there are treatments for the health problems that it may cause, such as anogenital warts and cancers of the cervix, vulva, vagina and anus.

The HPV vaccine is made up of proteins from the outer coat of the virus. It stimulates the immune system to produce specific antibodies to fight the virus.

# Types of Vaccines

1. Bivalent: Cervarix (GlaxoSmithKline): it protects against types 16 and 18 which are responsible for about 70% of cases of cervical cancers.
2. Quadrivalent HPV vaccine Gardasil (Merck & Co, Inc): highly effective in the prevention of persistent HPV infection, cervical cancer precursor lesions, vaginal and vulvar cancer precursor lesions, and anogenital warts due to HPV types 6, 11, 16, or 18 in girls and women who are not infected.

# Candidates for Vaccination

The vaccine is best effective when given before the girl/woman is sexually active. This is because it is most effective in girls/women who have not yet acquired any of the four HPV types covered by the vaccine. It is recommended for 9-26 year-old girls/women.

Sexually active women may get less benefit from the vaccine since they may have already acquired one or more HPV type(s) covered by the vaccine.

## Dose and effectiveness

- The vaccine series consists of 3 shots over a 6-month period. The second and third doses should be given 2 & 6 months after the first dose. It is essential that girls/women get all doses of the vaccine as it is not known how much protection is provided with a single or 2 doses.
- The vaccine is more than 95% effective in preventing diseases caused by the HPV types covered by the vaccine including precancers lesions & genital warts. However, it is less effective in young women who had already been exposed to one of the HPV types covered by the vaccine. The vaccine does not treat existing HPV infections, warts, precancers or cancers.

# Immunity

- The length of vaccine protection is not known. Studies have shown that women continued protected up to five years. Because the vaccine has been only available for few years, more research is needed to determine the time limit for protection and whether a booster dose is needed years later.
- The vaccine does not protect against all types of HPV. Therefore, about 30% of cases of cervical cancers and 10% of genital warts will not be prevented and consequently, women should continue their regular Pap smear screening test for cervical cancer.

# Side Effects

They are minor side effects and usually require no treatment.

- Pain: the most common side effects at the injection site. Other local side effects include swelling, redness and itching.
- High fever and dizziness.
- Allergic reaction: difficult breathing, skin rash, wheezes and hives.
- Nausea, vomiting, and diarrhea.
- Joint pains.

# Side Effects (Cont.)

- Interactions with many drugs:
  - Anticoagulants: e.g. Heparin, Enoxaparin and Warfarin
  - Immunosuppressants. Because the vaccine works by stimulating the immune response, immunosuppressant may not allow the immune system to form sufficient antibodies to fight the virus. Examples are:
    - Azathioprine
    - Certain monoclonal antibodies: Examples are:
      - Abatacept (Orencia) Adalimuma (Humira)
      - Muromonab-CD3 (Orthoclone OKT®3)
    - Corticosteroids: e.g. Betamethasone, Cortisone, Dexamethasone, Hydrocortisone, Prednisolone, Prednisone & Triamcinolone
    - Cyclosporine
    - Lenalidomide
    - Methotrexate
    - Nelarabine
    - Thalidomide
    - Trimetrexate (NeuTrexin®)

# Recommendations For Pregnant Women

For pregnant women, the current recommendation is that pregnant women should complete their pregnancy before getting the vaccine.

If a woman finds out she is pregnant after she has started getting the vaccine series, she should complete her pregnancy and deliver prior to finishing the 3-dose series.

# The Future With Males

Studies are now underway to find out if the vaccine works to prevent HPV infection in males.

The vaccine may prevent genital warts and rare cancers (e.g. penile) and anal cancer as well as the indirect health benefits for girls/women.

# Cervical Screening After Vaccination

Vaccinated women still should keep their regular cervical cancer screening performed at the scheduled time for the following reasons:

- The vaccine does not protect against all types of HPV that cause cervical cancer. About 30% of cases will continue to occur.
- Some women may not get all 3 doses of the vaccine or may not get them at the proper time interval.
- Women who had HPV infection with any of the 4 strains in the vaccine may not get its full benefit.
- The vaccine may change the epidemiology of infection and other equally oncogenic serotypes could replace the four serotypes targeted by the vaccine.

# Alternative Approaches To Prevent HPV

- Total abstinence is the best but not practical as a long term strategy.
- Monogamy: but only if both partners have been abstinent and they remain strictly monogamous. If any of the partner has had previous partner(s) and got infected, he/she might transmit infection to his current monogamous partner.
- Consistent use of condoms may reduce the risk of genital warts and cervical cancer.

# Therapeutic Vaccines

- Research in this aspect focuses on the main HPV oncogenes, E6 and E7. The expression of both oncogenes is required to promote the growth of cervical cancer cells and cells within warts. The development of immune responses against the two oncogenes might eradicate established tumors.
- A Mexican pharmaceuticals company, ORBI in Mexico City, is expected to release a therapeutic vaccination in 2008 called ONCOVAC.

**Thank You**