

## HPV AND HEAD NECK MALIGNANCIES— ROLE OF VACCINATION

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### INTRODUCTION

**Human papillomavirus** is a DNA virus from the papillomavirus family, of which over 170 types are known (1) Most HPV infections cause no symptoms and resolve spontaneously. In some people, an HPV infection persists and results in warts or precancerous lesions. The precancerous lesions increase the risk of cancer of the cervix, vulva, vagina, penis, anus, mouth, or throat (2) Over the last decade it has become clear that human papillomavirus (HPV) not only causes genital and anal cancers, but also causes a subset of head and neck squamous cell carcinoma (HNSCC). HPV causes an estimated ~30,000 oropharyngeal cancers, HPV is detected in ~25% of all HNSCC (Kreimer et al., 2005), and the majority of these HPV-associated HNSCC are oropharyngeal (tonsillar and base of tongue) squamous cell cancers. (3) In fact, HPV is now the major cause of oropharyngeal cancer in developed countries, detected in 45–90% of cases (D'Souza et al., 2007a; Kreimer et al., 2005; Nasman et al., 2009). HPV has also been detected in a smaller subset of laryngeal (24%) and oral cavity (23%) cancers (Kreimer et al., 2005).

HPV is detected in the tumor of these oropharyngeal cancers, where it is localized to the cell nuclei, transcriptionally active, clonal, and not found in the surrounding benign tissue (Gillison et al., 2000). Epidemiologic evidence for the role of HPV in oropharyngeal cancer is equally strong. The exact mechanism of carcinogenesis is not known but is very similar to carcinogenesis of cervical cancer and infection takes many years to develop malignancy.

Maura Gillison (4) states that Head and neck cancers are now known to be etiologically heterogeneous, with a predominant subset attributable to tobacco and alcohol use, and a distinct subset attributable to HPV infection. In 2007, IARC stated that there is sufficient evidence to conclude that HPV 16 is a cause of Oropharyngeal cancers. The epidemiology of

head and neck squamous cell carcinoma (HNSCC) has changed dramatically over the past two decades. As tobacco use, traditionally the most important risk factor for HNSCC, has decreased in the U.S., the incidence of tobacco-associated HPV-unrelated HNSC has also decreased (Chaturvedi et al., 2008; Ryerson et al., 2008). In stark contrast, the incidence of HPV-associated oropharyngeal cancers overall is increasing. (3) He also states that evidence to date suggests that incidence rates of oropharyngeal cancers attributable to HPV are rising in several regions around the world, predominantly among men however there is no evidence that the biological behavior of HPV-positive cancer with regard to better prognosis is different for men and women. He further states that there is a growing body of evidence that the natural history of oral HPV infection is significantly different among men and women like prevalence of oral HPV 16 infection was > 5-fold higher in men and Oral HPV infection had a bimodal age distribution among men but not among women also smoking significantly increased the odds of oral HPV infection among women but not among men, and married women, but not married men, had significantly lower odds of infection

The HPV infection has both sexual and non sexual modes of transmission, former being predominant

<b>HPV ROUTES OF TRANSMISSION*</b>		
(When your skin or mucosa comes in contact with an infected person's skin or mucosa) like:		
SEXUAL ROUTE	NON- SEXUAL ROUTE	
By having vaginal, anal, or oral sex with someone who has the virus. It is most commonly spread during vaginal or anal sex.	EXTRAGENITAL	VERTICAL
	<b>FORMITES</b> <ul style="list-style-type: none"> <li>● UNDERGARMENTS</li> <li>● SURGICAL GLOVES</li> <li>● INSTRUMENTS</li> <li>● CONTACT WITH AN INFECTED PERSON'S SKIN</li> </ul>	MOTHER TO CHILD IN PREGNANCY
(*Centers for disease control and prevention)		

Nigel Field et al (5) states that there is good evidence for sexual acquisition of oropharyngeal HPV infection, and an intriguing hypothesis is that the increase in HPV-associated HNSCC might be driven in part and predated by changes in population sexual behavior however acquisition and persistence of oral HPV infection, and the evidence for changes in sexual behaviour driving

increases in HPV-associated HNSCCs is still circumstantial. There is now interest in developing a valid and reliable test to determine the HPV status of oropharyngeal tumours.

Gypsyamber D'Souza (3) states that besides sexual behavior, several other risk factors have been consistently associated with increased odds of prevalent oral HPV like;

- ñ Smoking and HIV-infection are both associated with significantly increased oral HPV prevalence, suggesting that tobacco-related and HIV-related immunosuppression may impact oral HPV natural history.
- ñ Oral HPV prevalence higher in men than women in several studies suggest a possible hormonal differences in immunity in men and women (Klein, 2000).
- ñ Oral HPV prevalence also appears to increase with older age which is unusual for a sexually transmitted infection, possible causes of this pattern includes decreased oral HPV clearance with older age or re-expression of latent infections that become re-expressed due to age related changes in the immune system's ability to control these infections.

### HPV VACCINATION

**Akanksha Rathi (6) states that** the need of vaccination arises as natural HPV infection induces a very weak immune response and may not lead to protection from reinfection. On the other hand, the vaccine produces robust immune response. Two different vaccines that have been developed to prevent infection from HPV 16 and 18 and one of these offers added protection against HPV 6 and 11 (which cause genital warts). The quadrivalent and bivalent vaccines have been licensed for use in several countries including India.

A recent Study results suggest that vaccination against the human papillomavirus (HPV) may sharply reduce oral HPV infections that are a major risk factor for oropharyngeal cancer, a type of head and neck cancer. The study of more than 2,600 young adults in the United States found that the prevalence of oral infection with four HPV types, including two high risk, or cancer causing, types, was 88% lower in those who reported receiving at least one dose of an HPV vaccine than in those who said they were not vaccinated but he also states that the potential impact of current HPV vaccines on oral HPV infections that lead to cancer has not yet been rigorously tested in clinical trials, although he also states that HPV vaccines are strongly recommended for oropharyngeal cancer prevention (3)

The vaccination schedule is as under

<b>VACCINATION SCHEDULE*</b> (Preferably before first sexual contact)	
9 - 14 years old - 2-dose series	First dose: now
	Second dose: 6 to 12 months after the first dose
15 - 26 years of Age – 3 -dose series	First dose: now
	Second dose: 1 to 2 months after the first dose
	Third dose: 6 months after the first dose
*HPV vaccine – Medline Plus – US National Library of Medicine	

### Points to note about the Vaccine

1. In randomized double blind studies, the bivalent vaccine was found to have 87.5% efficacy in preventing persistent infection due to HPV 16/18 and 92% efficacy in preventing HPV 16/18 associated cytological abnormalities on intention-to-treat analysis.(6)
2. In India HPV vaccine is not yet included in national immunization program.
3. Till date the vaccine has not found any safety issue that would alter its recommendations for the use of the vaccine.
4. Vaccination is not given in pregnancy.
5. The government of Delhi recently announced introduction of HPV vaccine for grade 5 girls studying in government & government-aided schools.
6. The vaccine is costly (Gardasil-3000 INR per shot & Cervarix-2000 INR per shot).(5)
7. If you already have an HPV infection, getting the HPV vaccine can't treat it, but it can protect you from getting other types of HPV (7)
8. The molecular mechanism underlying vaccine efficacy in the head and neck is similar to that in the anogenital tract. (4) Data available so far support a hypothesis that vaccination would generate serum immunoglobulin-derived salivary immunoglobulin which has the potential to prevent incident oral HPV infection
9. Vaccination is important because HPV-induced HNSCC has important clinical implications as this subset of cancers responds better to chemotherapy and radiotherapy (82% vs 55% response rate for HPV negative cases) and has a better disease-free and overall survival (95% vs 62% at 2 years). Patients with HPV-induced HNSCC have a lower incidence of second primary tumors, as well as decreased risk (or cumulative incidence) of relapse.(8)

## CONCLUSION

Human papillomavirus is a DNA virus from the papillomavirus family and it not only causes genital and anal cancers, but also causes a subset of head and neck squamous cell carcinoma. It has both sexual and non sexual modes of transmission, former being predominant. Other factors associates with higher risk of HPV induced carcinogenesis are -- Smoking and HIV-infection, male sex and older age. Vaccines are available to prevent HPV infection and are to be given to boys and girls between 14-26 years of age preferably before first sexual contact, and if you already have an HPV infection, getting the HPV vaccine can't treat it, but it can protect you from getting other types of HPV infections.

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