

HPV vaccines? Still needed

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The human papilloma virus (HPV) was at one time deemed benign, with few variants¹⁻³. Further research revealed 150 serologically identifiable varieties, some benign, but many having oncogenic genes⁴. Vaccines against some of the latter varieties are Gardasil (Merck, Kenilworth, NJ, U.S.A.) and Cervarix (GlaxoSmithKline, Brentford, U.K.), introduced and recommended for girls before their sexual debut⁵. Some theological leaders were against vaccination, believing that vaccination leads to promiscuity⁶. To reduce residual host infection pools, inoculation advice eventually included boys⁷. Most vaccines successfully impart life-long immunity. Consequently, the earlier the vaccination, the longer and stronger the likelihood of preventing HPV morbidity.

Protection and New Vaccine

Anamnestic responses to viral antigens rapidly boost immunity and prevent disease recrudescence⁸⁻¹⁰. Early immunity to HPV is derived from 4 HPV varieties⁹⁻¹¹, and the available HPV vaccines have been successfully used in national vaccination campaigns¹⁰. Cervarix protects against HPV-16 and HPV-18; Gardasil, a quadrivalent vaccine, protects against HPV-16, HPV-18, HPV-6, and HPV-11. The additional HPVs (6 and 11) addressed by the Gardasil formulation are causally related to genital condylomata and recurrent respiratory papillomatosis. Other HPVs involved in oncogenesis are HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58.

Antibody induction is rarely complete with a single administration, and small significant groups fail to respond adequately, needing triple inoculation to reach efficacy⁹⁻¹¹. Moreover, the existing protection from early vaccines has limits, and a new broader-based HPV vaccine called V503 (with activity against 9 HPV varieties) was therefore developed. In 2014, the vaccine developer, Merck, made a Biologics License Application for registration of the product¹³, which is now under review by the U.S. Food and Drug Administration.

DISCUSSION

The causes of many cancers have been defined. For example, asbestos induces mesothelioma, radiation induces neoplasias, aniline dyes cause urogenital carcinogenesis, nitrosamines precipitate oncogenesis in the gut, petrochemicals act as carcinogens, genes (*BRCA*, for instance) predispose carriers to certain types of cancer, tobacco generates lung-cancer, and alcohol stimulates neoplastic change¹⁴.

Surgery, chemotherapy, and radiation remain the main therapies for established cancer, but they have limited success, with significant morbidity and mortality.

Despite the definition of many cancer causes, absolute cures remain stubbornly obscure. Prophylaxis remains the most desirable approach, and for cause-defined cancers, prevention with immunity is successful. High-levels of anti-HPV-16 and -18 antibodies persist for up to 7 years, and boosters are recommended. The HPV vaccinations stimulate immunomodulation and contribute to the prevention and lowered prevalence of HPV-positive head-and-neck squamous cell carcinomas and urogenital cancers. Accordingly, vaccination is now advised for all boys and girls before their sexual debut¹⁵⁻¹⁷. Transmission of HPV can occur during sexual activity or orogenital contact, and even during social kissing or inhalation of spray from sneezes or coughs by HPV carriers^{18,19}. After barrier methods of contraception diminished in the mid-1950s (yielding to major use of contraceptive hormone pills), sexual behaviors and mores changed, and HPV, together with other sexually transmitted infections, became more prevalent.

CONCLUDING REMARKS

Vaccination protection lasts decades and takes a long time to wane^{9,10}. Human papilloma viruses are implicated in cancers other than anogenital neoplasias²⁰⁻²². Vaccination against HPV should be considered essential for all and should become part of the battery of inoculations received in the first decade of life¹². Without HPV vaccination, a HPV pandemic is predicted, and use of broad-based vaccines is desirable to optimize HPV prophylaxis^{23,24}. Clinical tests to detect HPV infection are available, and vaccines will protect against HPV morbidity²⁵. The HPV oncogenic protein p53 can be detected during histopathology examination²⁶, and a search for proteins to moderate protein p53 is needed. Because of the proven immune response, all adults who are not inoculated against HPV, who are sexually active, and who face the probability of more than one sexual partner, are well advised also to be vaccinated against HPV. Further research into the clinical management of HPV is needed.

The global cancer incidence is 14 million new cases annually, with a resultant mortality of 8 million individuals. Prophylaxis remains the main mission. In health care, anamnestic or freshly acquired immunity is used to prevent cancers from returning once patients are in remission²⁵. Traditional vaccines are given to healthy patients to induce immunity. ImMucin (Vaxil Israel, Rehovot, Israel) is given to people who are already sick, and yet it behaves like a drug with biologic effects, acting like a cross between a drug and a vaccine as a two-pronged hybrid therapy. Targeting viruses predisposing to cancer is what vaccines can accomplish; they also create immunity against viruses

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implicated in oncogenesis. Vaxil Israel claims that their immunity works against mutated cells with initial neoplastic changes, consequently lowering the incidence of early cancers without affecting healthy cells. Vaxil Israel reports success with multiple myeloma and has tried the same approach on other cancers²⁵.

CONFLICT OF INTEREST DISCLOSURES

I have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and I declare that I have none.

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REFERENCES

- Jensen AB, Link CC, Lancaster WD. Section II. Papillomavirus etiology of oral cavity papillomas. In: Hooks JJ, Jordan GW, eds. *Viral Infections in Oral Medicine*. Oxford, U.K.: Elsevier Science and Technology; 1982: 132–46.
- SV40-based gene delivery vectors [in Ch. 15, Polyomaviruses]. In: Norkin LC. *Virology: Molecular Biology and Pathogenesis*. Washington, DC: ASM Press; 2010: 419–43.
- Lajer CB, von Buchwald C. The role of human papillomavirus in head and neck cancer. *APMIS* 2010;118:510–19.
- Touyz LZG. Human papilloma virus (HPV)—a biological and clinical appraisal: 2013. *Science Postprint* 2013;1:e00001.
- Forman D, de Martel C, Lacey CJ, et al. Global burden of human papillomavirus and related diseases. *Vaccine* 2012;30(suppl 5):F12–23.
- Touyz SJJ, Touyz LZG. The kiss of death: HPV rejected by religion. *Curr Oncol* 2013;20:e52–3.
- Touyz LZG. Human papilloma virus inoculation: why only girls? *Curr Oncol* 2009;16:2.
- Croignani P, De Stefani A, Fara GM, et al. Towards the eradication of HPV infection through universal specific vaccination. *BMC Public Health* 2013;13:642.
- Schiller JT, Castellsagué X, Garland SM. A review of clinical trials of human papillomavirus prophylactic vaccines. *Vaccine* 2012;30(suppl 5):F123–38.
- Malagón T, Drolet M, Boily MC, et al. Cross-protective efficacy of two human papillomavirus vaccines: a systematic review and meta-analysis. *Lancet Infect Dis* 2012;12:781–9.
- Safaeian M, Porras C, Pan Y, et al. on behalf of the cvt group. Durable antibody responses following one dose of the bivalent human papillomavirus L1 virus-like particle vaccine in the Costa Rica Vaccine Trial. *Cancer Prev Res (Phila)* 2016;6:1242–50.
- Liu X, Feng A, Cui Y, Tobe RG. Prevention of human papillomavirus (HPV) infection and cervical cancer in China: how does HPV vaccination bring about benefits to Chinese women? *Biosci Trends* 2013;7:159–67.
- Merck and Co. FDA Accepts for Review Merck's Biologics License Application for V503, Investigational 9-Valent Human Papillomavirus Vaccine [press release]. Whitehouse Station, NJ: Merck Co.; 2014. [Available online at: <http://www.mercknewsroom.com/news-release/research-and-development-news/fda-accepts-review-mercks-biologics-license-application-v>; cited 14 June 2016]
- American Cancer Society (ACS). What causes cancer? [Web page]. Atlanta, GA: ACS; 2016. [Available online at: <http://www.cancer.org/cancer/cancercauses>; cited 25 October 2015]
- Zhao FH, Lewkowitz AK, Hu SY, et al. Prevalence of human papillomavirus and cervical intraepithelial neoplasia in China: a pooled analysis of 17 population-based studies. *Int J Cancer* 2012;131:2929–38.
- Li J, Huang R, Schmidt JE, Qiao YL. Epidemiological features of human papillomavirus (HPV) infection among women living in Mainland China. *Asian Pac J Cancer Prev* 2013;14:4015–23.
- Syrjänen S. Current concepts on human papilloma virus infections in children. *APMIS* 2010;118:494–509.
- Touyz LZG. Lips, kissing and oral implications. *Jnl Aesthetic Dentistry* 2009;29–34.
- Chaturvedi AK, Engels EA, Pfeiffer RM, et al. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *J Clin Oncol* 2011;29:4294–301.
- Nasman A, Attner P, Hammerstedt L, et al. Incidence of human papilloma virus (HPV) positive tonsillar carcinoma in Stockholm, Sweden: an epidemic of viral-induced carcinoma? *Int J Cancer* 2009;125:362–6.
- Heng B, Glenn WK, Ye Y, et al. Human papilloma virus is associated with breast cancer. *Br J Cancer* 2009;101:1345–50.
- Bender E. Developing world: global warning. *Sci Am* 2014;311:S18–19. [Republished as: Bender E. Developing world: global warning. *Nature* 2014;509:S64–5]
- Pashley NR. Can mumps vaccine induce remission in recurrent respiratory papilloma? *Arch Otolaryngol Head Neck Surg* 2002;128:783–6.
- Massad LS, Einstein MH, Huh WK, et al. on behalf of the 2012 ASCCP Consensus Guidelines Conference. 2012 Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *Obstet Gynecol* 2013;121:829–46.
- Neff J. New Israeli Cancer Vaccine Triggers Response in 90% of Cancer Types [Web article]. Herzliya, Israel: NoCamels.com; 2015. [Available at: <http://nocamels.com/2015/01/new-vaccine-for-cancer/>; 14 June 2016]
- Immunological memory [in Ch. 4, Host defenses and viral counter measures] and T antigens and neoplasia [in Ch. 15, Polyomaviruses]. In: Norkin LC, ed. *Virology: Molecular Biology and Pathogenesis*. Washington, DC: ASM Press; 2010: 136–7;401–5.