ejpmr, 2017,4(12), 135-140

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A BREIF REVIEW ON HUMAN PAPILLOMAVIRUS: A DNA VIRUS FROM THE PAPILLOMAVIRUS FAMILY

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Article Received on 01/10/2017 **Article Revised on 22/10/2017** **Article Accepted on 14/11/2017**

ABSTRACT

Human Papillomavirus (HPV) is the most common sexually transmitted infection (STI). HPV is a different virus than HIV and HSV (herpes). HPV is so common that nearly all sexually active people get it at some point in their lives. There are many different types of Human Papillomavirus (HPV). Some types can cause health problems including genital warts and cancers. But there are vaccines that can stop these health problems from happening. HPV is transmitted through intimate skin-to-skin contact. You can get HPV by having vaginal, anal, or oral sex with someone who has the virus. It is most commonly spread during vaginal or anal sex. Human Papillomavirus (HPV) is so common that nearly all men and women get it at some point in their lives. Human Papillomavirus (HPV) can be passed even when an infected person has no signs or symptoms. Genital warts usually appear as a small bump or groups of bumps in the genital area. They can be small or large, raised or flat, or shaped like a cauliflower. A healthcare provider can usually diagnose warts by looking at the genital area. Human Papillomavirus (HPV) Cancers include cancer of the cervix, vulva, vagina, penis, or anus. HPV infection can also cause cancer in the back of the throat, including the base of the tongue and tonsils.

KEY WORDS: HIV and HSV.

INTRODUCTION

Human Papillomavirus Infection is an infection by *human papillomavirus* (HPV).[4] Most HPV infections cause no symptoms and resolve spontaneously.[1] In some people, an HPV infection persists and results in warts or precancerous lesions.[2] The precancerous lesions increase the risk of cancer of the cervix, vulva, vagina, penis, anus, mouth, or throat. Nearly all cervical cancer is due to HPV with two types, HPV16 and HPV18, accounting for 70% of cases.[1][6] Between 60% and 90% of the other cancers are also linked to HPV.[3,5-6] HPV6 and HPV11 are common causes of genital warts and laryngeal papillomatosis.[1]

Infection

Human Papillomavirus (HPV) infection is caused by *human papillomavirus*, a DNA virus from the papillomavirus family, of which over 170 types are known.[7] More than 40 types are transmitted through sexual contact and infect the anus and genitals.[3] Risk factors for persistent HPV infections include early age of first sexual intercourse, multiple partners, smoking, and poor immune function.[1] HPV is typically spread by sustained direct skin-to-skin contact with vaginal and anal sex being the most common methods.[3] Occasionally, it can spread from a mother to her baby during pregnancy.[8] It does not spread via common items like toilet seats.[8] People can become infected with more than one type of HPV.[8] HPV only affects humans.[4][9]

HPV vaccines can prevent the most common types of infection.[3] To be most effective, they should be used before an infection occurs and are therefore recommended between the ages of nine and 13.[1] Cervical cancer screening, such as with the Papanicolaou test (pap) or looking at the cervix after using acetic acid, can detect early cancer or abnormal cells that may develop into cancer.[1] This allows for early treatment which results in better outcomes.[1] Screening has reduced both the number and deaths from cervical cancer in the developed world.[10] Warts can be removed by freezing.[4]

HPV is the most common sexually transmitted infection globally.[4] Most people are infected at some point in their lives.[3] In 2012, about 528,000 new cases and 266,000 deaths occurred from cervical cancer worldwide.[11] Around 85% of these occurred in the developing world.[1] In the United States, about 27,000 cases of cancer due to HPV occur each year.[8] About 1% of sexually active adults have genital warts.[8] While cases of warts have been described since the time of ancient Greece, their viral nature was not discovered until 1907.[12]

Signs and Symptoms

Notable HPV[13] Types And Associated Diseases

Over 170 types of HPV have been identified, and they are designated by numbers.[7][14]

Some HPV types, such as HPV-5, may establish infections that persist for the lifetime of the individual without ever manifesting any clinical symptoms. HPV types 1 and 2 can cause common warts in some infected individuals. HPV types 6 and 11 can cause genital warts and laryngeal papillomatosis.[1] HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 are considered carcinogenic.[15-18]

WARTS

Figure Showing the Warts in the Body

Papilloma

Skin infection ("cutaneous" infection) with HPV is very widespread.[19] Skin infections with HPV can cause noncancerous skin growths called warts (verrucae). Warts are caused by a rapid growth of cells on the outer layer of the skin.[20] While cases of warts have been described since the time of ancient Greece, their viral cause was not known until 1907.[12]

Genital Warts

HPV infection of the skin in the genital area is the most common sexually transmitted infection worldwide.[11] Such infections are associated with genital or anal warts (medically known as condylomata acuminata or venereal warts), and these warts are the most easily recognized sign of genital HPV infection.[21-23]

The strains of HPV that can cause genital warts are usually different from those that cause warts on other parts of the body, such as the hands or feet, or even the inner thighs. A wide variety of HPV types can cause genital warts, but types 6 and 11 together account for about 90% of all cases.[24][25] However, in total more than 40 types of HPV are transmitted through sexual contact and can infect the skin of the anus and genitals.[3] Such infections may cause genital warts, although they may also remain asymptomatic.

Laryngeal Papillomatosis

In addition to genital warts, infection by HPV types 6 and 11 can cause a rare condition known as recurrent laryngeal papillomatosis, in which warts form on the larynx[26] or other areas of the respiratory tract.[27][28] These warts can recur frequently, may interfere with breathing, and in extremely rare cases can progress to cancer. For these reasons, repeated surgery to remove the warts may be advisable.[27][29]

Cancer

Hpv-Induced Cancers[30]

About a dozen HPV types (including types 16, 18, 31, and 45) are called "high-risk" types because persistent infection has been linked to cancers such as cancer of the oropharynx, vulva, vagina, cervix, penis, and anus.[31] These cancers in common involve sexually transmitted infection of HPV to the stratified epithelial tissue.[1][2][30] Individuals infected with both HPV and HIV have an increased risk of developing cervical or anal cancer.[31]

HPV is believed to cause cancer both by integrating into DNA and in non-integrated episomes.[36] Some of the "early genes" carried by the HPV virus, such as genes E6 and E7, act as oncogenes that promote tumor growth and malignant transformation. Furthermore, HPV can induce a tumorigenic process through integration into a host genome which is associated with alterations in DNA copy number.[32-38]

Cervical Cancer

Nearly all cases of cervical cancer are associated with HPV infection, with two types, HPV16 and HPV18, present in 70% of cases.[1][6][39-42] HPV type 16 is the most malignant strain, present in 41 to 54% of all cervical cancers,[39][43] and in many cases of vaginal/vulvar cancer,[44] penile cancers, anal cancers, and cancers of the head and neck.[45]

Genital Cancers

Studies show a link between HPV infection and penile and anal cancers. Sexually transmitted HPVs are found in a large percentage of anal cancers.[30] Moreover, the risk for anal cancer is 17 to 31 times higher among gay and bisexual men than among heterosexual men[46-48][49] - though one survey did not find a difference between the HPV infection rate of men who had sex with men versus those who had sex only with women.[50] Anal PAP smear screening for anal cancer might benefit some subpopulations of men or women engaging in anal sex.[51] No consensus exists, though, that such screening is beneficial, or who should get an anal Pap smear.[52][53]

Immuno-Compromised Individuals

In very rare cases, HPV may cause epidermodysplasia verruciformis in individuals with a weakened immune system. The virus, unchecked by the immune system, causes the overproduction of keratin by skin cells, resulting in lesions resembling warts or cutaneous horns.[54]

Cause

Sexually transmitted HPV is divided into 2 categories: low-risk and high-risk. Low-risk HPVs cause warts on or around the genitals. Type 6 and 11 cause 90% of all

genital warts and recurrent respiratory papillomatosis that causes benign tumors in the air passages. High-risk HPVs cause cancer and consist of about a dozen identified types. Type 16 and 18 are two that are responsible for causing most of HPV-caused cancers. These high-risk HPVs cause 5% of the cancers in the world. In the United States, high-risk HPVs cause 3% of all cancer cases in women and 2% in men.[55]

Diagnosis

There are multiple types of HPV, sometimes called "low-risk" and "high-risk" types. Low-risk types cause warts and high-risk types can cause lesions or cancer.[56] Health guidelines recommend HPV testing in patients with specific indications including certain abnormal Pap test results.

Cervical Testing

According to the National Cancer Institute, "The most common test detects DNA from several high-risk HPV types, but it cannot identify the type(s) that are present. Another test is specific for DNA from HPV types 16 and 18, the two types that cause most HPV-associated cancers. A third test can detect DNA from several high-risk HPV types and can indicate whether HPV-16 or HPV-18 is present. A fourth test detects RNA from the most common high-risk HPV types. These tests can detect HPV infections before cell abnormalities are evident.

Mouth Testing

Studies have found heightened HPV in mouth cell samples from people with squamous cell carcinoma of the mouth. Studies have not found significant HPV in mouth cells after sampling with toothbrushes (5 of 2,619 samples)[58] and cytobrushes (no oral transmission found).[57]

Testing Men

Research studies have tested for and found HPV, including high-risk types (i.e. the types found in cancers), on fingers, mouth, saliva, anus, urethra, urine, semen, blood, scrotum and penis. However, most research tests have used Dacron swabs and custom analysis not available to the general public.[59-61]

Prevention

The HPV vaccines can prevent the most common types of infection.[3] To be effective they must be used before an infection occurs and are therefore recommended between the ages of nine and thirteen. Cervical cancer screening, such as with the Papanicolaou test (pap) or looking at the cervix after using acetic acid, can detect early cancer or abnormal cells that may develop into cancer. This allows for early treatment which results in better outcomes.[1] Screening has reduced both the number and deaths from cervical cancer in the developed world.[10] Warts can be removed by freezing.[4] Methods of reducing the chances of infection include sexual abstinence, condoms, vaccination, and microbicides.

Treatment

There is currently no specific treatment for HPV infection.[61-65] However, the viral infection, more often than not, clears to undetectable levels by itself.[66] According to the Centers for Disease Control and Prevention, the body's immune system clears HPV naturally within two years for 90% of cases.[64,66] However, experts do not agree on whether the virus is completely eliminated or reduced to undetectable levels, and it is difficult to know when it is contagious.[1,54]

Follow up care is usually recommended and practiced by many health clinics.[1,55] Follow-up is sometimes not successful because a portion of those treated do not return to be evaluated. In addition to the normal methods of phone calls and mail, text messaging and email can improve the number of people who return for care.[1,56]

REFERENCES

1. "Human papillomavirus (HPV) and cervical cancer". WHO. June 2016. Archived from the original on 5 August 2016. Retrieved 10 August 2016.
2. Ljubojevic, Suzana; Skerlev, Mihael. "HPV-associated diseases". Clinics in Dermatology, 2014; 32(2): 227-234.
3. "What is HPV?". CDC. 28 December 2015. Archived from the original on 7 August 2016. Retrieved 10 August 2016.
4. Milner, Danny A. (2015). Diagnostic Pathology: Infectious Diseases. Elsevier Health Sciences. p. 40. ISBN 9780323400374. Archived from the original on 11 September 2017.
5. "The Link Between HPV and Cancer". CDC. September 30, 2015. Archived from the original on 9 November 2015. Retrieved 11 August 2016.
6. Bzhalava, D; Guan, P; Franceschi, S; Dillner, J; Clifford, G., "A systematic review of the prevalence of mucosal and cutaneous human papillomavirus types", Virology, 2013; 445(1-2): 224-31.
7. "Human Papillomavirus (HPV) Questions and Answers". CDC. 28 December 2015. Archived from the original on 11 August 2016. Retrieved 11 August 2016.
8. "Pink Book (Human Papillomavirus)" (PDF). CDC.gov. Archived (PDF) from the original on 21 March 2017. Retrieved 18 April 2017.
9. Sawaya, GF; Kulasingam, S; Denberg, TD; Qaseem, A; Clinical Guidelines Committee of American College of, Physicians (16 June 2015). "Cervical Cancer Screening in Average-Risk Women: Best Practice Advice From the Clinical Guidelines Committee of the American College of Physicians.". Annals of Internal Medicine, 2015; 162(12): 851-9.
10. World Cancer Report 2014. World Health Organization, 2014; 5.12.
11. Tyring, Stephen; Moore, Angela Yen; Lupi, Omar (2016). Mucocutaneous Manifestations of Viral Diseases: An Illustrated Guide to Diagnosis and Management (2 ed.). CRC Press. p. 207. EHPV, archived from the original on 17 December 2014.

12. Chaturvedi, Anil; Maura L. Gillison (4 March 2010). "Human Papillomavirus and Head and Neck Cancer". In Andrew F. Olshan. Epidemiology, Pathogenesis, and Prevention of Head and Neck Cancer (1st ed.). New York: Springer.
13. Muñoz, N; Bosch, F. X.; De Sanjosé, S; Herrero, R; Castellsagué, X; Shah, K. V.; Snijders, P. J.; Meijer, C. J.; International Agency for Research on Cancer Multicenter Cervical Cancer Study Group, "Epidemiologic classification of human papillomavirus types associated with cervical cancer", The New England Journal of Medicine, 2003; 348(6): 518–27.
14. Kumar, Vinay; Abbas, Abul K.; Fausto, Nelson; Mitchell, Richard (2007). "Chapter 19 The Female Genital System and Breast". Robbins Basic Pathology (8 ed.). Philadelphia: Saunders.
15. Palefsky, Joel M.; Holly, Elizabeth A.; Ralston, Mary L.; Jay, Naomi (February 1988). "Prevalence and Risk Factors for Human Papillomavirus Infection of the Anal Canal in Human Immunodeficiency Virus (HIV)–Positive and HIV-Negative Homosexual Men" (PDF). Departments of Laboratory Medicine, Stomatology, and Epidemiology Biostatistics, University of California, San Francisco. The Journal of Infectious Diseases Oxford University Press. Archived from the original on 15 January 2013. Retrieved 2 March 2014.
16. Muñoz N, Castellsagué X, de González AB, Gissmann L; Castellsagué; De González. "Chapter 1: HPV in the etiology of human cancer". Vaccine, 2006; 24(3): S1–S10.
17. Antonsson A, Forslund O, Ekberg H, Sterner G, Hansson BG. "The ubiquity and impressive genomic diversity of human skin papillomaviruses suggest a commensalic nature of these viruses". J. Virol. 2000; 74(24): 11636-41.
18. Mayo Clinic.com, Common warts, http://www.mayoclinic.com/print/common-warts/DS00370/DSECTION=all&METHOD=print Archived 17 October 2011 at the Wayback Machine.
19. De Koning MN, Quint KD, Bruggink SC, Gussekloo J, Bouwes Bavinck JN, Feltkamp MC, Quint WG, Eekhof JA. "High prevalence of cutaneous warts in elementary school children and ubiquitous presence of wart-associated HPV on clinically normal skin". The British Journal of Dermatology. 172: 196–201.
20. Lountzis NI, Rahman O (2008). "Images in clinical medicine. Digital verrucae". N. Engl. J. Med., 2014; 359(2): 177.
21. MedlinePlus, Warts, https://www.nlm.nih.gov/medlineplus/warts.html#cat42 Archived 5 June 2016 at the Wayback Machine. (general reference with links). Also, see
22. Greer CE, Wheeler CM, Ladner MB, Beutner K, Coyne MY, Liang H, Langenberg A, Yen TS, Ralston R. "Human papillomavirus (HPV) type distribution and serological response to HPV type 6 virus-like particles in patients with genital warts". J. Clin. Microbiol, 1995; 33(8): 2058-63.
23. "Human Papillomavirus". Medscape. Archived from the original on 29 November 2016.
24. "Photos of larynx Papillomas — Voice Medicine, New York". Voicemedicine.com. Archived from the original on 12 June 2010. Retrieved 29 August 2010.
25. Sinal SH, Woods CR. "Human papillomavirus infections of the genital and respiratory tracts in young children". Seminars in Pediatric Infectious Diseases, 2005; 16(4): 306–16.
26. Wu R, Sun S, Steinberg BM. "Requirement of STAT3 activation for differentiation of mucosal stratified squamous epithelium". Mol. Med., 2003; 9(3–4): 77–84. PMC 1430729.
27. Moore CE, Wiatrak BJ, McClatchey KD, Koopmann CF, Thomas GR, Bradford CR, Carey TE. "High-risk human papillomavirus types and squamous cell carcinoma in patients with respiratory papillomas". Otolaryngol. Head Neck Surg., 1999; 120(5): 698-705.
28. Parkin DM. "The global health burden of infection-associated cancers in the year 2002". Int. J. Cancer, 2006; 118(12): 3030-44.
29. Pahud, BA; Ault, KA (December 2015). "The Expanded Impact of Human Papillomavirus Vaccine". Infectious Disease Clinics of North America (Review), 2015; 29(4): 715-24.
30. "Archived copy". Archived from the original on 24 August 2012. Retrieved 24 August 2012.(subscription required)
31. Schiffman M, Castle PE (2005). "The promise of global cervical-cancer prevention". N. Engl. J. Med., 2005; 353(20): 2101-4.
32. Alam S, Conway MJ, Chen HS, Meyers C. "Cigarette Smoke Carcinogen Benzo[a]pyrene Enhances Human Papillomavirus Synthesis". J Virol. 2007; 82(2): 1053-8.
33. Lu B, Hagensee ME, Lee JH, Wu Y, Stockwell HG, Nielson CM, Abrahamsen M, Papenfuss M, Harris RB, Giuliano AR (February 2010). "Epidemiologic factors associated with seropositivity to human papillomavirus type 16 and 18 virus-like particles and risk of subsequent infection in men". Cancer Epidemiol. Biomarkers Prev, 2010; 19(2): 511-6.
34. Liu, Ying. "Comprehensive mapping of the human papillomavirus (HPV) DNA integration sites in cervical carcinomas by HPV capture technology". Oncotarget, 2015; 7: 5852–5864.
35. Parfenov, Michael. "Characterization of HPV and host genome interactions in primary head and neck cancers". Proceedings of the National Academy of Sciences, 2014; 111: 15544-15549.
36. Karagas MR, Waterboer T, Li Z, Nelson HH, Michael KM, Bavinck JN, Perry AE, Spencer SK, Daling J, Green AC, Pawlita M. "Genus β human papillomaviruses and incidence of basal cell and squamous cell carcinomas of skin: population based case-control study". BMJ. 2010; 341: 2986.
37. Baseman JG, Koutsky LA. "The epidemiology of human papillomavirus infections". J. Clin. Virol., 2005; 32(Suppl 1): S16-24. Overall, these DNA-

based studies, combined with measurements of type-specific antibodies against HPV capsid antigens, have shown that most (>50%) sexually active women have been infected by one or more genital HPV types at some point in time [S17].
38. Cohen J. "Public health. High hopes and dilemmas for a cervical cancer vaccine". Science, 2005; 308(5722): 618-21.
39. Ault KA (2006). "Epidemiology and Natural History of Human Papillomavirus Infections in the Female Genital tract". Infectious Diseases in Obstetrics and Gynecology. 2006: 1-5.
40. Kreimer, Aimee R.; Clifford, Gary M.; Boyle, Peter; Franceschi, Silvia (1 February 2005). "Human papillomavirus types in head and neck squamous cell carcinomas worldwide: a systematic review". Cancer Epidemiology, Biomarkers & Prevention, 2005; 14(2): 467-475.
41. Noel J, Lespagnard L, Fayt I, Verhest A, Dargent J. "Evidence of human papilloma virus infection but lack of Epstein-Barr virus in lymphoepithelioma-like carcinoma of uterine cervix: report of two cases and review of the literature". Hum. Pathol, 2001; 32(1): 135-8.
42. "Vulvar Intraepithelial Neoplasia: Varied signs, varied symptoms: what you need to know". www.advanceweb.com. Archived from the original on 16 July 2012. Retrieved 5 August 2009.
43. Bolt J, Vo QN, Kim WJ, McWhorter AJ, Thomson J, Hagensee ME, Friedlander P, Brown KD, Gilbert J. "The ATM/p53 pathway is commonly targeted for inactivation in squamous cell carcinoma of the head and neck (SCCHN) by multiple molecular mechanisms". Oral Oncol. 2005; 41(10): 1013-20.
44. Greenblatt, R. J. "Human papillomaviruses: Diseases, diagnosis, and a possible vaccine". Clinical Microbiology Newsletter, 2005; 27(18): 139-145.
45. Freitas LB, Chen Z, Muqui EF, Boldrini NA, Miranda AE, Spano LC, Burk RD (2014-07-01). "Human Papillomavirus 16 Non-European Variants Are Preferentially Associated with High-Grade Cervical Lesions". PLOS ONE. 9: e100746.
46. "HPV and Men — CDC Fact Sheet". Centers for Disease Control and Prevention (CDC). 3 April 2008. Archived from the original on 17 October 2009. Retrieved 13 November 2009.
47. Frisch M, Smith E, Grulich A, Johansen C. "Cancer in a population-based cohort of men and women in registered homosexual partnerships". Am. J. Epidemiol, 2003; 157(11): 966-72. Archived from the original on 19 May 2009. However, the risk for invasive anal squamous carcinoma, which is believed to be caused by certain types of sexually transmitted human papillomaviruses, a notable one being type 16, was significantly 31-fold elevated at a crude incidence of 25.6 per 100,000 person-years
48. Thomas W. Gaither; et al. "The Influence of Sexual Orientation and Sexual Role on Male Grooming-Related Injuries and Infections". J Sex Med., 2015; 12(3): 631–640.
49. Chin-Hong PV, Vittinghoff E, Cranston RD, Browne L, Buchbinder S, Colfax G, Da Costa M, Darragh T, Benet DJ, Judson F, Koblin B, Mayer KH, Palefsky JM. "Age-related prevalence of anal cancer precursors in homosexual men: the EXPLORE study". J. Natl. Cancer Inst., 2005; 97(12): 896-905.
50. "AIDSmeds Web Exclusives : Pap Smears for Anal Cancer? — by David Evans". AIDSmeds.com. Archived from the original on 7 July 2011. Retrieved 29 August 2010.
51. Goldie SJ, Kuntz KM, Weinstein MC, Freedberg KA, Palefsky JM (June 2000). "Cost-effectiveness of screening for anal squamous intraepithelial lesions and anal cancer in human immunodeficiency virus-negative homosexual and bisexual men". Am. J. Med., 2000; 108(8): 634–41.
52. Gillison ML, Koch WM, Capone RB, Spafford M, Westra WH, Wu L, Zahurak ML, Daniel RW, Viglione M, Symer DE, Shah KV, Sidransky D. "Evidence for a causal association between human papillomavirus and a subset of head and neck cancers". J. Natl. Cancer Inst. 2000; 92(9): 709–20.
53. Gillison ML. "Human papillomavirus and prognosis of oropharyngeal squamous cell carcinoma: implications for clinical research in head and neck cancers". J. Clin. Oncol. 2006; 24(36): 5623-5.
54. D'Souza G, Kreimer AR, Viscidi R, Pawlita M, Fakhry C, Koch WM, Westra WH, Gillison ML (2007). "Case-control study of human papillomavirus and oropharyngeal cancer". N. Engl. J. Med., 2007; 356(19): 1944-56. Archived from the original on 12 May 2007.
55. Ridge JA, Glisson BS, Lango MN, et al. "Head and Neck Tumors" Archived 20 July 2009 at the Wayback Machine. in Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ (Eds) Cancer Management: A Multidisciplinary Approach Archived 4 October 2013 at the Wayback Machine.. 11 ed. 2008.
56. "Oral Cancer on the rise among non-smokers under 50" (PDF). California Dental Hygienists' Association. Archived from the original (PDF) on 24 January 2011. Retrieved 10 January 2011.
57. Chaturvedi, Anil K.; Engels, Eric A.; Pfeiffer, Ruth M.; Hernandez, Brenda Y.; Xiao, Weihong; Kim, Esther; Jiang, Bo; Goodman, Marc T.; Sibug-Saber, Maria (10 November 2011). "Human papillomavirus and rising oropharyngeal cancer incidence in the United States". Journal of Clinical Oncology, 2011; 29(32): 4294-4301.
58. Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, Kim E, Jiang B, Goodman MT, Sibug-Saber M, Cozen W, Liu L, Lynch CF, Wentzensen N, Jordan RC, Altekruse S, Anderson WF, Rosenberg PS, Gillison ML (October 2011). "Human Papillomavirus and Rising Oropharyngeal

Cancer Incidence in the United States". Journal of Clinical Oncology, 2011; 29(32): 4294-301.
59. Ernster JA, Sciotto CG, O'Brien MM, Finch JL, Robinson LJ, Willson T, Mathews M (December 2007). "Rising incidence of oropharyngeal cancer and the role of oncogenic human papilloma virus". The Laryngoscope, 2007; 117(12): 2115-28.
60. Kidon MI, Shechter E, Toubi E (January 2011). "[Vaccination against human papilloma virus and cervical cancer]". Harefuah (in Hebrew), 2011; 150(1): 33-6, 68.
61. Lechner M, Frampton GM, Fenton T, Feber A, Palmer G, Jay A, Pillay N, Forster M, Cronin MT, Lipson D, Miller VA, Brennan TA, Henderson S, Vaz F, O'Flynn P, Kalavrezos N, Yelensky R, Beck S, Stephens PJ, Boshoff C, Boshoff G. "Targeted next-generation sequencing of head and neck squamous cell carcinoma identifies novel genetic alterations in HPV+ and HPV- tumors". Genome Medicine, 2013; 5(5): 49.
62. "Lung Cancer Risk Rises in the Presence of HPV Antibodies". Lung Cancer Risk Rises in the Presence of HPV Antibodies. Archived from the original on 27 April 2012.
63. "Lung Cancer Patients More Likely to Have High-Risk Human Papillomavirus". NPIN. Archived from the original on 27 July 2012.
64. Syrjanen K, Syrjänen S, Kellokoski J, Karja J, Mäntyjarvi R. "Human papillomavirus (HPV) type 6 and 16 DNA sequences in bronchial squamous cell carcinomas demonstrated by in situ DNA hybridization". Lung, 1989; 167(1): 33-42.
65. Carpagnano GE, Koutelou A, Natalicchio MI, Martinelli D, Ruggieri C, Di Taranto A, Antonetti R, Carpagnano F, Foschino-Barbaro MP (11 October 2011). "HPV in exhaled breath condensate of lung cancer patients". British Journal of Cancer, 2011; 105(8): 1183-90.
66. Klein F, Amin Kotb WF, Petersen I (July 2009). "Incidence of human papillomavirus in lung cancer". Lung Cancer, 2009; 65(1): 13-8.