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Kissing and HPV: honest popular visions, the human papilloma virus, and cancers

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INTRODUCTION

Kissing is among the multitude of functions of the lips. It is a frequent act involving the lips, oral cavity, head and neck, and other parts of the face and body[1]. Peri-osculation is the designated term for kissing. Paleolithic troglodytes recorded kissing in cave paintings, and kissing is mentioned 46 times in the Bible.

Kissing assumes different forms as habits are influenced through cultural mores. An affectionate greeting among the Inuit in Northern Canada called a *kunik* involves pressing the nose and upper lip to cheek or forehead of the loved one. South Pacific Islanders were accomplished paramours long before European influence, and yet they never kissed as a habit. Globally, kissing is assumed to be totally innocent, without any disadvantages.

This article appraises kisses, groups the types of kisses, and discusses insights about the risks of transmitting infections between partners, with a focus on the human papilloma virus (HPV) and the association between HPVs and cancer. Suggestions on prophylaxis and safe kissing are presented.

Kissing and the Arts

Kissing has been interpreted by many artists. Peter Behrens painted *The Kiss* as a colored woodcut in 1898. Friedrich W. Kleukens created a mosaic called *The Kiss* in 1914. August Rodin sculpted his *The Kiss* in 1889. *The Kiss* (1907–1908) by Gustav Klimt is well known, as is *The Kiss* (1891) by Edouard Vuillard. Well-known and more contemporary kisses include Clark Gable and Vivien Leigh's in *Gone With the Wind* (1940); Rachel McAdams and Ryan Gosling's in *The Notebook* (2005), which was dubbed the Best Kiss by MTV that year; and Britney Spears and Madonna's at the MTV Video Music Awards in 2003. These kisses reflect the adulation and innocent nature of kissing, and how societies accept the practice as harmless.

Types of Kisses

Since at least Roman times, many varieties of kissing were known. At least 5 different types have been identified, and their Latin names still apply: gestural, cultural, osculum, basium, and saviolum (including orogenital).

There are two types of gesture kissing, the first being "air-kissing," which is approximation of cheek to cheek without contact. Human perception interprets a kiss if distances are less than 55 mm, with air between. Human warmth and odors (pheromones) are easily detected at that distance. Gesture air-kissing is a successful, hygienic way to avoid microbiologic transfer. The second gestural type is "hand and foot kissing" in which lips make contact with the body. Although this ancient custom implies high status, germ transfer through touching (shaking hands or hand kissing) combined with a lack of hand hygiene is cited as a reason for the spread of antibiotic-resistant nosocomial infections such as methicillin-resistant *Staphylococcus*. Consequently, after any kissing, it is advisable to disinfect contact areas with detergent, a practice common in hospitals.

Cultural kissing involves facial contact other than with the lips, such as the Inuit *kunik* described earlier. Indonesian and African tribes promote frontal cranial contact as a greeting. Whether lips are closed or open is irrelevant, and the bodily contact is short.

The osculum is the closed-lip peck on the cheek. It is often combined with gestural kissing, repeated on both sides of the face. Some Russian cultures repeat the gesture more than once when greeting and taking farewells.

The basium kiss is the mutual approximation of lips without opening the mouth. Slight pressure is momentarily maintained. Prolonging a basium kiss is reportedly satisfying to some.

The saviolum kiss is the mutual approximation of lips, with mouth opening and insertion of the tongue into a partner's mouth, that is known in Anglo-Saxon cultures as "French kissing." The participants alternate protruding their tongue into the partner's mouth while maintaining lip-to-lip contact. This kiss, considered the most passionate, is also sometimes described as a "tonsil-washer."

Orogenital contact is considered a saviolum kiss and is a form of sexual expression that commonly occurs in all types of partnerships: heterosexual,

homosexual, and lesbian. Fellatio and cunnilingus are orogenital activities for sexual gratification.

Viral transmission is facilitated through coitus, but some viruses, such as HPV, are also transmitted vertically from mother to child or through physical social activities such as hugging and play among siblings. Recurrent respiratory papillomatosis (RRP), a hyperproliferative condition of the respiratory mucosal tree, is caused by HPVs[2]. Kissing allows HPVs to infect other head-and-neck areas such as the oral and sinus cavities, the conjunctiva of the eyes, the ear canals, the oropharynx, and the tonsils. Although those sites are more rarely infected than is the genital tract, the resulting RRP infections are challenging to comprehend, to examine, to thwart, and to stop. *De novo* anogenital warts in children should raise suspicions of sexual abuse by infected adults[2,3].

PATHOLOGY REALITY CHECK

At least 15 species of α-HPVs are known. These mucotropic viruses infect the head-and-neck mucosae, the upper aerodigestive tract, and the anogenital region. Some HPVs are deemed low-risk (LR)—that is, non-oncogenic (for example, HPV 6 and HPV 11). Their high-risk (HR) counterparts such as HPV 16, HPV 18, HPV 51, and HPV 53 have high oncogenic potential. Each species consists of several different subspecies: LR HPV 11 has 10 subspecies; HR HPV 16 has 9; HR HPV 18 has 7; HR HPV 51 has 5; and HR HPV 53 has 6. Oncogenic types such as HR HPV 16 and HPV 18 cause high-grade dysplasias and neoplasias. The LR HPVs (HPV 6 and 11) are far less prevalent in genital cancers, but might be associated with RRP infection[2,3]. All HPVs share common structural features that allow for the immune response to successful target most of them[3,4].

Transmission of disease through kissing is accomplished by viral, bacterial, and (rarely) protozoal organisms[5]. Viral infections such as hepatitis, verruca vulgaris, Epstein–Barr viral mononucleosis[6], and HIV are transmitted not only through close sexual contact, but also through exchange of bodily fluids (saliva) from kissing. Once considered rarely transmissible by saliva, HIV is now acknowledged to be transmissible during intimate kissing. *Neisseria meningitides,* the organism that causes meningitis in the young, can be transmitted in the same manner.

The HPVs—harboured by men and women alike—cause most (but not all) labial, vulval, perineal, penile, and oral papillomata, and DNA typing shows that oral and cervical cancers derive from distinct, transmissible HPVs[7].

HPV VACCINATION

Preventing HPV disease is more desirable and effective than reversing established cellular reactions after HPV infection. Although there are natural constraints on HPV oncogenesis [such as production of the p53 and pRB (retinoblastoma) proteins], HR HPV E6 and E7 proteins can destabilize epithelial chromosomes. Inactivation of those two major suppressors (p53 and pRB) and other cellular proteins largely accounts for oncogenic induction by the HR HPVs[3]. A quadrivalent vaccine against genome-derived proteins—including the L1 virus-like particles from HPVs 6, 11, 16, and 18—constitutes effective immune prophylaxis against the development of HPV-associated cancers and mucosal warts.

Cervarix (GlaxoSmithKline, Brentford, U.K.) is a vaccine against HPV 16 and HPV 18, and Gardasil (Merck, Whitehouse Station, NJ, U.S.A.) is a quadrivalent vaccine against HPVs 16, 18, 6, and 11, the latter two HPVs being causally related to genital condylomata and RRP. Vaccines impart immunity against HPV-induced neoplastic change in most recipients[4,8].

IMPLICATIONS OF HPV AND CANCER

Because people practicing various forms of saviolum kissing transmit viable microbiota (such as HPV, HIV, and so on), it is important to further examine the implications of infection by HR HPVs.

Oncogenic Progression

Chronic infection with HR HPV is a necessary prerequisite for most cervical cancers, but invasive neoplasia does not always develop after infection with HR HPV. Although HR HPVs remain dormant for decades, cancer is uncommon among women (and men) because infection with HR HPV is frequently self-limiting. A decade or more passes before neoplastic changes transition to stage 1 dysplastic lesions (carcinoma *in situ* or intraepithelial carcinoma, also called CIN lesions). Infection with HPV develops in stages to frank cervical carcinogenesis as various biologic moderators change. Data from HR HPV *in vitro* studies and from clinical specimens reveal progressive models from dysplasia to neoplasia in oropharyngeal and cervical cancers. Those observations at early stages have allowed for a determination of which individuals are susceptible to developing cancer from specific HPV types. Susceptibility is determined by the genetic composition of the immune-moderating proteins. When an infected HPV dysplastic lesion results in DNA changes, transcription control of the HR HPV factors is produced from changes in the E6 and E7 oncogenes. Additional epigenetic modifications subsequently accumulate in grade 3 CIN basal and para-basal cells, producing evident cancers by altering moderators such as E2 and constraining growth factors such as p53 that control the E6 and E7oncogenes[3,4].

Other factors affecting cervical carcinogenesis derive from female hormones such as estrogen and progesterone. Modifiers resulting from inflammation (common in pelvic inflammatory disease in women)

and cytokines such as tumour necrosis factor α and the metalloproteases enhance the invasiveness of malignant cells. Identifying HR HPV infections early, and implementing aggressive vaccination and chemotherapy, might minimize malignant transformation[4].

Identification and Management

Most oral and laryngeal papillomata are caused by HPV 6 and HPV 11. Early detection and treatment optimizes prevention against the development of RRP. Because HPVs come in as many as 150 different types, it is salutary to recall that the currently available HPV vaccines are not absolute in preventing or curing existing HPV infections[4]. Great success has been reported through mass immunization[9], and immunization of both sexes is indicated to optimize epidemiologic immunity. Early detection of the E7 protein is feasible; the Cervimax monoclonal antibody kit [Cervimax, Vienna, Austria (http://www.cervimax.eu/IHC.html)] for immunohistochemical assay is used mainly for research, but shows clear immune-reactivity with E7 antigen. Thus, HR HPV, CIN, and cervical cancer could be determined early and be moderated by vaccination.

DISCUSSION

The current recommendation is to vaccinate before sexual activity starts, especially for girls. Because young males are reservoirs for sexually transmitted HPVs, boys should also be vaccinated. These vaccinations reduce the prevalence of cervical carcinomas. High-level antibodies against HPV 16 and HPV 18 persist for 7 years after vaccination, and booster vaccines are recommended before that period elapses. Vaccinations stimulate immunomodulating mechanisms and positively affect prevention and prognosis for HPV morbidity[4].

BEHAVIOR MODIFICATION

Promiscuity, including indiscriminate saviolum kissing, is fingered for transmission of viruses, especially HPVs. Saviolum kissing is not innocent or benign. Ideally, saviolum kissing and sexual intimacy should be restricted to life partners. Greater awareness of kissing as an infective source should be noted, and education about the risks from sexual practices should be included in sex-advice programs targeted at young people before their sexual debut.

CONCLUDING REMARKS

Many cancers have no established causation, and their exact causes remain obscure. Genetic susceptibility and preneoplastic conditioning by chemicals, physical radiation, infections, or chromosomal damage might predispose certain individuals to developing certain types of cancer. Viruses are but one causative factor in oncogenesis. Certain HPVs have been firmly implicated for specific kinds of cancer, and HPV-related cancers are being progressively defined. Putative HPV genomes are successfully being identified, deconstructed, and understood. As the various HPV constituents are elucidated, the hope is that novel, more effective vaccines will appear. Identifying vulnerable genomic loci and comprehending their molecular physiology could procure a safe, reliable, and totally effective cure against HPV neoplasia. Much is known about HPV; but precise biomolecular mechanisms relating to mutation, resistance, and carcinogenesis remains obscure. More research into HPV biology is needed[4].

CONFLICT OF INTEREST DISCLOSURES

The author has no financial conflict of interest to declare.

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