

## *How oral sex behaviors can lead to cancer*

The sexual revolution in the Western world during much of the 1960s drastically changed behaviors and attitudes towards sexuality. The advent of the birth control pill, the acceptance of non-marital sex, a younger age at first intercourse, and having multiple sexual partners dramatically transformed sexual practices and norms in the last decades<sup>(1)</sup>. One of the consequences was an upwards trend in the incidence of sexually transmitted diseases (STD), as human immunodeficiency virus (HIV), chlamydia, gonorrhea, and syphilis are efficiently transmitted during sexual contacts. The consequences of the sexual revolution are felt today as more and more individuals engage in vaginal, anal and oral sex, often without protection. More than one million people worldwide acquire a sexually transmitted infection every day<sup>(2)</sup>.

The aforementioned changes in sexual mores also redefined sexual intercourse to include oral sex as a common variation of the act. Long considered safer than genital intercourse, because it avoids unwanted pregnancies, oral sex practices have become more common among adults and adolescents, in both heterosexual and homosexual relationships<sup>(3)</sup>. According to the U.S. Centers for Disease Control and Prevention, 85% of sexually active adults, and 33% of adolescents reported having oral sex at least once with a partner of the opposite sex<sup>(4)</sup>. Oral sex is not without danger, since many STDs are caught through unprotected oral sex behaviors. However, of all STDs that can infect mouth and throat, one virus has received major attention by the public and healthcare providers recently, the human papillomavirus (HPV).

Although awareness about risky oral sexual behaviors such as cunnilingus, fellatio and anilingus and their consequences have increased, the population and healthcare providers are still insufficiently educated about oral HPV infection and head-and-neck cancer (HNC) risk. In the general population, between 0.8 and 44.7% of individuals are aware that HPV is a risk factor for oral cancer<sup>(5)</sup>. For medical and dental professionals, the awareness is between 26 and 88%<sup>(5)</sup>. Indeed, many health professionals reported that it is difficult to respond to questions and concerns from patients because of their limited knowledge about the role of HPV in oral cancers<sup>(6)</sup>. There is a need for educational interventions for healthcare providers on how HPV can cause HNCs, because of the compounded stigma that comes from being diagnosed with a dreadful disease and then learning that it was the person's own sexual behavior that led to it. It is not simple for the general population to seek information from credible sources<sup>(5)</sup>.

Historically, HPV was first known for its role in cervical carcinogenesis, and consequently, it has long been perceived as a viral infection of concern mainly to women. HPV is causally associated with several anogenital cancers such as vaginal, vulvar and anal cancers, but nowadays it is clear that HPV infection can also cause a subset of HNCs<sup>(7,8)</sup>. Oral HPV infection is relatively uncommon in the general population, with a prevalence of 4.5%<sup>(9)</sup>. In analogy with genital infections, a high proportion of oral HPV infections

clear within 6 to 18 months<sup>(10)</sup>, but persistent infections can progress to neoplastic lesions of the head and neck<sup>(11,12)</sup>. We can differentiate two types of HNCs according to their respective risk factors: those related to smoking and drinking habits, not related to HPV<sup>(13)</sup>, accounting for the majority of HNCs, and the HPV-positive HNCs, mainly oropharyngeal cancers (OPC). The etiological role of HPV in these cancers varies by HNC subsite, but also differs in different parts of the world<sup>(14)</sup>. Overall, nearly 30% of HNCs are caused by oral HPV infection, mainly with the HPV16 genotype<sup>(15,16)</sup>. In the last decades, an increase in HPV-positive HNC incidence has been observed in both sexes, with a five-fold higher incidence rate in men<sup>(17-20)</sup>. Indeed, HPV-positive HNC is particularly common among young white men with high socioeconomic status<sup>(21,22)</sup>. By 2020, it is expected that HPV-positive OPC will become the most common HPV-related cancer, surpassing cervical cancer<sup>(7)</sup>.

The question of how oral sex can transmit HPV infection and cause mouth or throat cancers has great relevance. The most plausible explanation for HPV transmission to the oral cavity is through orogenital or oroanal contact during oral sex<sup>(3)</sup>. An increased incidence of oropharyngeal cancer has been reported in many countries, and it is associated with having multiple oral sex partners or oral sex at an earlier age<sup>(23)</sup>. Oral HPV infection is also associated with higher number of genital sexual partners, younger age at first intercourse, and history of genital warts<sup>(24)</sup>. Fortunately, oral HPV acquisition rates are low, and infections can clear within a year<sup>(25)</sup>. Interestingly, differences seem to exist in the gender directionality of transmission. Men acquire oral HPV infection more easily via orogenital contact than women do when practicing oral sex on male genitals<sup>(10,26)</sup>.

Knowing that oral sex behaviors lead to oral HPV infection — which then increases risk of HNCs — is relevant for HNC prevention, since a significant proportion of HPV-positive oral cancers could be prevented by reducing oral infection. The use of condom and dental dam to avoid the direct contact of the mouth with the partner's anogenital sites can lower the chances of getting oral HPV infection. A related question is: does HPV vaccination confer the same protection? Chaturvedi et al.<sup>(27)</sup> provide new evidence on HPV vaccination and prevention of oral infections. Their study included 2,627 American men and women aged 18 to 33 years enrolled in the National Health and Nutrition Examination Survey. The authors estimated the effects of HPV vaccination on the burden of oral infections. The protective effect of vaccination was striking; the prevalence of oral HPV infection was reduced by 88.2% in vaccinated adults who reported the receipt of one or more dose(s) of the quadrivalent HPV vaccine, targeting HPV 6, 11, 16 and 18, compared to those ones not vaccinated. On the other hand, an important concern raised was the low uptake of the vaccine in the general population (29.2% in women vs. 6.9% in men). The limited knowledge of healthcare professionals and the general population

on the relationship between oral sex practices, oral HPV infection, and risk of OPC are possible explanations for that. These results are the first line of evidence in support of a future reduction on the burden of HPV-positive HNCs. In light of this evidence, HPV vaccination for oral HPV prevention should be seen and promoted as an additional benefit, especially in men<sup>(21,22)</sup>. Men are generally not targeted for vaccination except for Australia, the United States, and Canada, which adopted this policy in 2012. Unfortunately, even in these countries coverage in men is still low<sup>(28)</sup>.

There are numerous research efforts on the way to learn how we can prevent oral HPV infection, and longitudinal studies are warranted to better understand the natural history of oral HPV infection, the risk factors for oral HPV acquisition and persistence, and the development of HNCs. But one thing is certain: there are fewer options to prevent oral HPV infection and ultimately HPV-positive HNCs than there are for cervical HPV infection and cervical cancer. The latter can also be prevented via screening and treatment, as an established public health practice, an option that unfortunately does not exist for HNCs. Definitely, prevention starts by informing both the general population and healthcare providers about the relationship between oral sex behaviors, oral HPV infection acquisition and transmission, and cancer risks. Meanwhile, promoting safer oral sex practices and HPV vaccination of both sexes could be the only options to prevent oral HPV infections, as well as HPV-related HNC burden in future generations. While healthcare providers deliver these health promotion messages, it also helps to counsel patients about the benefits of smoking cessation and alcohol drinking in moderation.

### Conflict of interests

The authors have no conflicts of interest on the topic and contents of this editorial. Dr. Franco has served as occasional consultant or advisory board member to companies involved with HPV diagnostics (Qiagen, Roche, Gen-Probe, BD, Abbott), HPV vaccination (GSK, Merck), and cervical cancer screening or control (3M, Ikonisys, Cytyc). His institution has received unconditional grants from Merck and Roche to supplement publicly funded investigator-initiated studies in his unit. His unit's entire research program has been funded by the Canadian Institutes of Health Research (CIHR), U.S. National Institutes of Health, National Cancer Institute of Canada, Cancer Research Society, Canadian Cancer Society Research Institute, and Fonds de Recherche Quebec-Santé (FRQS). No funding was received by the authors for the writing of this editorial.

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