Oral Sexual Behaviors and the Prevalence of Oral Human Papillomavirus Infection

Aimée R. Kreimer
National Cancer Institute, National Institutes of Health, Bethesda, Maryland

(See the brief report by D’Souza et al., on pages 1263–9.)

In this issue of the Journal, D’Souza et al. [1] demonstrate that oral sexual behaviors are associated with the detection of prevalent oral human papillomavirus (HPV) infection. With their study, D’Souza and colleagues have taken an additional step toward improving our understanding of the epidemiologic profile of oral HPV transmission. HPV is an important human carcinogen that is increasingly implicated in human cancers occurring at multiple anatomical sites [2]. Over the past decade, there has been accumulating molecular and epidemiologic evidence demonstrating that HPV causes a subset of head and neck cancers, specifically in the oropharynx [3, 4]. This evidence mandates the need for additional novel research along multiple areas of the disease continuum. Important research topics include (1) elucidating the natural history and epidemiologic profile of oral HPV infection in healthy individuals, (2) determining whether the HPV vaccine is efficacious in preventing oral HPV infections and related diseases, and (3) determining whether the HPV status of the tumor should be used in clinical decision-making pertaining to treatment.

D’Souza et al. [1] used 2 distinct populations and differing study methods to evaluate associations between self-reported sexual behaviors and detection of prevalent oral HPV infection. The oral HPV point prevalence was 2.9% among 210 college-aged men and 4.8% among 332 controls in a hospital-based case-control study. Although these percentages are not statistically different, it is noteworthy that the point prevalence among college-aged men (median age, 19 years) was lower than that in the older hospital-based control group (median age, 57 years); this finding has been observed in previous studies [5, 6]. This finding does not parallel the striking inverse trend of decreasing cervical HPV prevalence with increasing age [7]. Differences in the methods of specimen collection in the study (specifically, the addition of the use of an oropharynx brush in the hospital-based case-control study. Although these percentages are not statistically different, it is noteworthy that the point prevalence among college-aged men (median age, 19 years) was lower than that in the older hospital-based control group (median age, 57 years); this finding has been observed in previous studies [5, 6]. This finding does not parallel the striking inverse trend of decreasing cervical HPV prevalence with increasing age [7]. Differences in the methods of specimen collection in the study (specifically, the addition of the use of an oropharynx brush in the hospital-based case-control study, compared with the use of oral rinse and gargle alone by college-aged men) may have accounted for some of this difference, as a result of the improved sensitivity of detection of oral HPV infections in the hospital-based study. In addition, the hospital-based controls may have come from a higher-risk population, and, therefore, findings for this group would not be reflective of the true prevalence among older adults. Similarly, older adults may be more likely to have persistent infection detected, which could also inflate the point prevalence. Alternatively, it may be that the natural history of oral HPV infection actually differs from that of the cervix. This finding highlights the importance of developing and standardizing specimen collection, storage, and testing methods that reliably measure infection with high sensitivity, and it strongly argues for additional large, well-designed studies to better understand the natural history of oral HPV infection.

Despite the use of different study designs and populations, as well as different questionnaire variables assessing exposure, the findings that sexual behaviors and, specifically, oral sex are associated with prevalently detected oral HPV infection are consistent in the 2 populations. In addition, open-mouthed kissing (inquired about in the study of college-aged men only) was significantly associated with oral HPV infection. Even among the men who reported never having had oral sexual contact, more kissing partners significantly increased the risk of oral HPV infection, suggesting the independence of kissing as a risk factor for oral HPV infection.

Although the finding that oral HPV may be transmitted through kissing is intriguing, it is based on a small sample size (6 infections in men from the college study and even smaller numbers in the subset of individuals who reported no...
oral sexual behaviors). Caution must be used in interpreting the findings, until their replication in larger studies can allow for effective evaluation of the independent effects of various behaviors on oral HPV infection. That being said, if such common behaviors as kissing have the potential to transmit a cancer-causing infection, this could have implications for public health interventions. Fortunately, the overwhelming majority of oral HPV infections are likely to clear with no intervention, as is the case for cervical infections [8].

The fact that oral HPV infection is present in a subset of the population yet oropharyngeal cancers are exceedingly rare supports this hypothesis of viral clearance. Reductions in oral HPV16 infection and persistence will become more important as the rates of HPV-associated oropharyngeal cancers continue to increase over time [9, 10].

Public health messages targeting behavior modification have been difficult to implement successfully in the past. An alternative prevention measure is primary prevention using prophylactic HPV16/18 vaccines that, when administered to HPV16/18-naive women [11, 12], confer near-complete protection against these HPV infections at the cervix, as well as at extracervical sites, including the vulva and vagina [13]. Although we are optimistic that the HPV vaccine will protect against oral HPV infections in similar fashion, a direct evaluation is necessary. Importantly, if, as observed for cervical HPV infections, vaccine efficacy against oral HPV infections is high and vaccination does not treat or aid in the clearance of existing infections [14], these new data from D’Souza and colleagues suggest that vaccine programs may need to reconsider the timing of administration. To date, vaccination before sexual debut has been considered ideal for the prevention of genital HPV infection. The Centers for Disease Control and Prevention Advisory Committee on Immunization Practices has recommended vaccinating adolescent girls between the ages of 11 and 12 years (with catch-up vaccination performed to 26 years of age) [15]. Because current recommendations might straddle age at initiation of oral sex, decreasing the age when vaccination occurs may need to be considered. Although earlier vaccine administration is important to protect against oral infections, covering girls through the peak years of cervical HPV infection (age, 15–25 years) [7] will remain the most critical aspect of vaccine administration planning. Of note, currently available data demonstrate that the durability of protection (at the cervix) lasts at least 5 years [11, 12].

Given our vast knowledge of cervical HPV infection, it has been theorized that oral infections are likely the result of oral-genital contact. The present study confirms and expands on that theory by demonstrating that not only are oral sexual behaviors important, but more common behaviors, such as kissing, may also transmit HPV infection to the oral region. If the vaccine protects against oral HPV infections to a degree akin to what is observed for cervical infections, program development and cost-benefit analyses should consider both the epidemiologic profiles of oral and cervical HPV, in concert with vaccine durability, to produce evidence-based recommendations for future HPV vaccine administration.

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References