Natural history of oral papillomavirus infection in men

In *The Lancet*, Aimeé Kreimer and colleagues present one of the first natural history studies of oral human papillomavirus (HPV) infection. As part of the wider HPV Infection in Men (HIM) study, the researchers investigated 1626 adult men from three countries (Brazil, Mexico, and the USA), a population of substantial interest since the burden of HPV-driven oropharyngeal cancer is highest in middle-aged men and its incidence is increasing. They report that 4.4% (95% CI 3.5–5.6) of these men acquired an oral HPV infection within 1 year, and suggest that within 2 years more than 15% of men could acquire an oral HPV infection. Although this reported incidence is substantially lower than that of genital HPV infection, this study suggests that oral HPV infections are fairly common in men.

Another major finding is that more than half of the 81 incident oral HPV infections cleared within 1 year. This finding suggests that most oral HPV infections clear quickly, similar to genital HPV clearance, which in turn suggests that a one-time measurement of prevalent oral oncogenic HPV infection is unlikely to be a good marker (ie, probably has poor predictive value) for either oral HPV persistence or cancer development. However, this study had a fairly short follow-up period and few incident oncogenic oral HPV infections, so further investigation is necessary. If these results for oral HPV incidence and clearance are substantiated, a large proportion of men would seem to be likely to acquire oral HPV infection at some point in their lifetime, but persistent infection could be much rarer.

Oral sex has been suggested as the primary mode of oral HPV acquisition, since cross-sectional and case-control studies have shown that having many oral sex partners is associated with increased prevalence of oral HPV and with increased odds of HPV-driven oropharyngeal cancer. Interestingly, the HIM study investigators did not identify an association between incidence of oral HPV and having participated in oral sex in the past 6 months. However, their study did not have data for lifetime number of oral sex partners and whether the participant’s recent oral sex partners were new, which might be stronger risk factors than a binary yes-or-no measure of recent oral sex. A man who performs oral sex on a long-term partner or spouse might be less likely to acquire a new oral HPV infection because long-term monogamous partners are less likely to have an infection or because they might have been exposed in the past and developed antibodies that protect them from future acquisition of the same HPV type. Indeed, the HIM study investigators note that being married or cohabiting was associated with a roughly three-times increased hazard of incident oncogenic HPV, which suggests that sex with newer partners could be important for transmission. Further examination of oral HPV transmission is needed to understand whether other behaviours, such as rimming (oral–anal contact), autoinoculation, and open-mouth kissing, contribute to acquisition of infection.

Several explanations could account for why the incidence of oral HPV reported by the HIM study investigators is lower than the incidence of genital HPV. Other investigators have reported lower prevalence of performing oral sex than having vaginal sex. Similarly, the median number of lifetime sex partners is lower for oral sex than for vaginal sex, but whether behavioural changes alone can account for the difference in incidence of oral and genital HPV infection is unclear. Alternatively, oral sex might not be as efficient a transmitter of HPV as vaginal or anal sex, because of the flow of saliva or the location of susceptible mucosal epithelium at back of the throat. Additionally, in the HIM study, many infections that cleared quickly would not have been detected by the 6-month sampling schedule, so incidence of oral HPV might be underestimated in this study. Indeed, investigators of another recent study reported high rates of oral HPV clearance within 4 months, and we have previously reported that clearance of oral HPV might be quicker than clearance of anal HPV. Furthermore, since more than half of the incident oral HPV infections in the HIM study cleared before the first 6-month follow-up visit, time to clearance might be shorter than the investigators estimate.

The report from the HIM study investigators is an important contribution to our understanding of the natural history of oral HPV infection. Identification of how oral HPV is acquired can be challenging since longitudinal follow-up with detailed sexual questions is necessary, and the sexual behaviours in question are often concurrent with each other and with other risk behaviours. Further investigation of oral HPV acquisition
and persistence is necessary, especially in men, since the burden of oropharyngeal cancer is higher and uptake of HPV vaccines is lower in men than in women.

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GD’S has received research funding from Merck. DCB declares that he has no conflicts of interest.