

## Genital and oral carriage of human papillomaviruses in women with high grade squamous intraepithelial lesion and their male partners

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Human papillomaviruses (HPVs) are the main risk factor for cancer of the uterine cervix, and may also play a role in rectal, penile as well as head and neck cancer. A major way of HPV transmission is sexual contact, oropharyngeal HPVs may derive from oral sexual contact with genitally infected partners. The aim of the present work was to explore genital as well as oral HPV status in women with high grade squamous intraepithelial lesion (HSIL) and in their male partners.

Thirty-three women (median age 27; range 19-59) with cytologically confirmed HSIL and their male partners (median age 31, range 23-65) were enrolled; informed consent was collected from all participants. Exfoliated cells from the oral and genital mucosa were collected by cytobrush and placed immediately in dry ice. All samples from the couples were collected within a month to assess simultaneous carriage of HPVs. HPV detection was performed by MY/GP consensus nested PCR, HPVs were genotyped by sequencing and virus copy numbers were determined using real-time PCR. Prevalence data were compared by chi-square test or sign test, as appropriate. Log copy numbers were compared using Kruskal-Wallis test with Bonferroni correction. ANOVA and Yule's coefficient was used to test for association of HPV status with that of the partner.

As expected, the majority of women with HSIL proved to be HPV positive in the genital mucosa (28/33). Their oral mucosa, however, showed significantly lower HPV carriage (7/33,  $p < 0.001$ ); all orally positive women carried HPV in the genital mucosa. Similarly, males carried HPV in their genital mucosa more frequently than in the oral mucosa (17/33 vs. 7/33,  $p = 0.035$ ), but oral carriers were not always positive in their genital sample. Females carry HPV more frequently than males in their genital ( $p = 0.004$ ) but not in their oral samples. The most frequently encountered genotype was HPV16 in both sexes, but high risk genotypes HPV18, 31, 33, 51, 56, 66, 82 and low risk HPV11, 55, 61, 72, 81, 83 and 84 were also found. The genotype was the same in the genital and oral mucosa of 7/7 and 5/7 females and males, respectively.

Average copy numbers in positive females were significantly higher in the genital than in the oral mucosa ( $1.3 \times 10^5$  vs  $1.5 \times 10^3$ /ug DNS,  $p = 0.003$ ), while in males the copy numbers were comparable ( $8.2 \times 10^3$  vs  $1.8 \times 10^2$ /ug DNS). Females had higher copy numbers than males in the genital ( $p < 0.001$ ), but not in the oral mucosa. There were no differences in copy numbers of females with HPV positive or negative partners.

In couples, females are more frequently carriers than males in the genital ( $p < 0.002$ ), but not in the oral mucosa. In the genital mucosa 15, while in the oral mucosa three pairs shared the same HPV genotype, but neither genital nor oral carriage was found to be associated statistically with the status of the partner.

Though transmission between oral and genital mucosa as well as transmission between sexual partners is plausible, proving this association statistically needs higher sample sizes with enrolment of more couples.

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