Self testing for human papillomaviruses

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Is it feasible and what samples should be used?

A great deal has been written about the potential value of human papillomavirus (HPV) testing, particularly in the context of cervical screening programmes. Much of the published literature has focused on the assessment of specific patient groups, particularly women with mildly abnormal cervical smears, and the attempt to identify those women at greatest risk of either possessing or developing a high grade intraepithelial lesion which, according to current guidelines, requires treatment. Much of the value of HPV testing is dependent upon its high sensitivity for the detection of high grade disease and also the high negative predictive value of testing women both with low grade cytological abnormalities and in the context of primary screening. However, the duration of protection of a negative result is not yet known. These points are among those covered by the systematic review of the role of HPV testing within a cervical screening programme, published in 1999, and form the basis of many of the conclusions of that report. One of the other recommendations put forward was that HPV testing could potentially be applied to self collected cervical samples. In particular, this could help to improve coverage of the screened population by encouraging those who do not attend for routine cervical smears to provide samples for testing themselves. This issue is addressed in the study by Nobbenhuis et al in this issue of JCP, in which both a self collected cervicovaginal lavage specimen and a cervical smear were analysed cytologically and by HPV DNA testing. There was poor correlation between the cytology results of the self collected specimens and the cervical smear, but relatively high concordance between high risk HPV detection in the two specimen types.

The concept of HPV testing of self collected samples is not new. An alternative sample that may be applicable to HPV testing, and is easier to collect than cervical/vaginal specimens, is urine. HPV particles were identified in the urine of a pregnant woman as long ago as 1979. The feasibility of detecting HPV DNA in the urine of women with cervical neoplasia was demonstrated in a small study that showed absolute concordance between biopsy/scrape and urine for the presence or absence of HPV-16 DNA. However, comparison of HPV DNA detection by type specific PCR in cervical smears and paired urine samples showed that the sensitivity of HPV detection in urine was lower than that in cervical material. In an interesting recent study, using the hybrid capture methodology, a variety of self collected samples were compared in a consecutive series of 200 women referred to a colposcopy clinic for the investigation of cervical cytological abnormalities. High risk HPV types were found in almost 90% of the self collected vaginal samples from women shown to have high grade lesions but in only 62% of vulvar samples and 45% of urine samples. These sensitivities compare with 98% sensitivity for the cervical brush sample collected by a physician and should be compared with the negative predictive values, which parallel the sensitivities ranging from almost 99% for the cervical brush sample through 90% for the self collected vaginal swab, 80% for the self collected vulvar swab, and 76% for the self collected urine sample. This study also assessed the attitude of women to the self collection methods: almost 100% of respondents found urine sampling acceptable, approximately 93% found vaginal sampling acceptable, and 88% found self collection methods acceptable. Another study, which focused on adolescent girls, found a similar pattern. The HPV prevalence, this time using PCR, for any HPV, was 90% in the cervical swabs but only 73% in the urine specimens. These investigators also used Hybrid Capture II, which demonstrated a significantly higher viral load in the cervical specimens than in the urine specimens. Interestingly, the prevalence of HPV in both the cervix and the urine was significantly higher in those adolescents with intraepithelial neoplasia than in normal adolescents. Overall, therefore, testing of self collected urine specimens is more acceptable to patients than self collected vaginal specimens but is significantly

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Abbreviations: HPV, human papillomavirus; PCR, polymerase chain reaction. 

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less sensitive for the detection of HPV, both overall and in patients with high grade disease.

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The available data, including those of Nobbenhuis et al., indicate that HPV testing of self collected samples is not only feasible but produces reasonable results. Although it seems clear from these studies that self collected samples are generally inferior to clinician collected cervical samples in terms of sensitivity and negative predictive value, there are situations in which these samples may be useful, particularly in the context of resource poor settings and unscreened populations. However, it is important to appreciate that all of these approaches refer simply to self collection and do not indicate self testing. The analytical phase of HPV testing still requires laboratory based protocols for either PCR or hybrid capture.


References