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, in an 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 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. For example, in a study presented at the International Papillomavirus Workshop in 1991, and published in 1992, Southern blotting and polymerase chain reaction (PCR) methodologies were used to demonstrate a high concordance between self collected and physician collected specimens. The authors of this paper concluded that self administered lavage represented an extremely promising technique for obtaining samples for HPV testing. As the clinical value of HPV testing has become increasingly appreciated, and the technology for identifying HPV types has been refined, particularly with the introduction of Hybrid Capture II®, interest in self testing has grown. Several recent studies have demonstrated the feasibility of self testing methodologies, with one study, which concentrated on patients at high risk of cervical disease, showing a sensitivity of 93% for both self collected vaginal specimens and direct cervical smears. This study was based on self collection using a cytobrush to acquire vaginal epithelial cells rather than the more traditional approach of cervicovaginal lavage. Other studies have also evaluated the use of vaginal tampons and Dacron swabs. Relatively good concordance was found between HPV testing of self collected vaginal tampons and physician collected cervicovaginal lavage. Moreover, the comparison of self collected Dacron swabs with clinician acquired cervical samples showed excellent agreement (k value > 0.65). This agreement was not affected by age, menopausal status, or clinic in this multicentre study. One of the major potential applications of this approach is for HPV testing in resource poor settings. A study on a large number of women in rural Uganda has demonstrated the feasibility of using self collected vaginal swabs for HPV testing in population screening. Similarly, a study in previously unscreened South African women showed that HPV testing of self collected vaginal Dacron swabs was as sensitive as testing of clinician acquired Papanicolaou smears in this large study population of women over the age of 35 years. As these authors point out, this sort of approach may not only be of value in resource poor areas, but may also contribute in parts of the developed world where underscreening accounts for a large number of invasive cervical carcinomas.

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 compared 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 specimen. This study also assessed the attitude of women to the self collection methods: almost 100% of respondents found urine sampling acceptable, approximately 93% found vulvar sampling acceptable, and 88% found vaginal sampling 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

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

- Human papillomavirus (HPV) testing of self collected samples is not only feasible but produces reasonable results.
- Although self collected samples are generally inferior to clinician collected cervical samples, in certain situations these samples may be useful, such as resource poor settings and unscreened populations.
- The testing of self collected urine specimens is more acceptable to patients than self collected vaginal specimens but is significantly less sensitive for the detection of HPV, overall and in the context of less sensitive for the detection of HPV.
- All of these approaches refer simply to self collection and not self testing.

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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.


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REFERENCES


