Cervical Cancer Prevention FACT SHEET

ACCP Alliance for Cervical Cancer Prevention

HPV Testing: Promise and Challenges

Human papillomavirus (HPV), one of the most common sexually transmitted infections (STIs), is the primary cause of cervical cancer.[1] HPV infection is a necessary but not sufficient precursor to cervical cancer. While the cumulative lifetime incidence of HPV infection is 70 to 80 percent in many countries, the vast majority of women with HPV infection will not develop cancer[2,3] (see the ACCP fact sheet, *Natural History of Cervical Cancer*). Worldwide, interest is growing in the potential uses for HPV DNA testing in cervical cancer prevention programs. HPV testing indicates whether a woman is infected with high-risk HPV types and thus at increased risk of cervical cancer. The test's relatively high sensitivity for detecting high-grade squamous intraepithelial lesions (HSIL) in older women makes it particularly appealing.[4-6]

Optimal uses of HPV testing in cervical cancer prevention programs are not yet clear, but proposed uses include triage for women with Pap smear findings of atypical squamous cells of unknown significance (ASCUS), surveillance of women treated for high-grade lesions, primary screening for high-grade lesions, and as an adjunct test to Pap smear screening.[4,5,7] The cost-effectiveness and usefulness of these approaches have not been clearly outlined and require further research.

Techniques for detecting HPV

HPV cannot be cultured reliably in a laboratory setting; therefore, HPV testing relies on molecular techniques that detect HPV DNA in cervical cell samples. Because there are so many HPV types with differing carcinogenic potential, HPV tests are designed to determine if one or more high-risk types are present in a specimen. Descriptions of two broadly recognized techniques for detecting specific HPV types follow.

Signal-amplified nucleic acid assay

The one commercially available HPV test, Digene Corporation's Hybrid Capture II (HC II) assay, uses signal amplification to detect HPV DNA. It provides sensitivity for detecting HPV DNA approaching that of polymerase chain reaction (PCR) (see below). HC II detects 13 high-risk HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) and is standardized and highly reproducible.

Performing the HC II test involves a laboratory process that produces light signals roughly proportional to the amount of HPV DNA present in the specimen. The process requires equipment ranging from basic laboratory supplies to technologically advanced equipment, such as a special computer. These requirements currently make the use of HC II too costly and difficult to implement in many low-resource settings.

Target-amplified techniques

Target-amplified HPV assays, such as PCR, produce highly concentrated samples of a specific DNA genetic sequence. The DNA samples are then probed to identify which specific HPV genotypes are present. PCR is the most common target-amplified technique; its inherent strength lies in its capacity to detect

Self-collection of samples

Studies indicate that women can successfully obtain self-collected vaginal specimens for use in HPV DNA detection. Self-sampling may be more acceptable to women, resulting in increased program effectiveness due to better population coverage. Studies evaluating the HC II test found that self-collected samples were less specific but as sensitive as conventional cytology for detecting HSIL in women aged 35 or older.[6] In addition, self-collection was acceptable to women and showed sufficient sensitivity to warrant further evaluation.[8,9] The impact of self-sampling on program effectiveness has yet to be evaluated, however.

Key recommendations

- Further research is needed to develop HPV test technologies that are feasible for use in low-resource settings and that accurately predict a woman's risk of developing high-grade lesions and need for further testing. Ideally, an HPV diagnostic would require minimal supporting equipment and would provide inexpensive, accurate, and rapid detection.
- Further research and education on self-collection and other sampling methods are needed so that providers and women perform the procedures correctly.
- Effective education and counseling messages need to be developed for providers to use when counseling women who are at risk of or diagnosed with HPV infection.

very small amounts of HPV DNA. The considerable skills, equipment, and costs involved, however, generally make PCR inappropriate for large screening programs in low-resource settings.

Test characteristics

Both HC II and PCR techniques for detecting HPV DNA require transport of the sample (and use of a transport medium) to the laboratory, storage, and processing time in the laboratory. These requirements will have programmatic implications. While HPV is an objective test with rapid turnaround, the test results are not immediate. In addition, quality-control mechanisms for HPV testing need further evaluation.

Test performance

Research suggests that HPV DNA testing has potential as a primary screening method among women aged 30 and older. Among these women, the sensitivity of a single lifetime HC II test for detection of high-grade dysplasia has been 80 to 90 percent (higher than for cytology), and specificity has ranged from 57 to 89 percent.[5,6,10] The test also has a high negative-predictive value. In addition, HC II may be more effective than conventional cytology or visual inspection with acetic acid for screening post-menopausal women. When used to detect HSIL, however, the test is only moderately specific, particularly among women younger than age 30.

Programmatic issues

Women who test positive for carcinogenic types of HPV may experience great anxiety about developing cancer despite being at very low risk. There currently is no cure for HPV infection, prevention is very difficult, and there is no way to clearly predict which HPV-infected women are likely to develop cancer. In addition, cervical cancer's association with sexual activity carries a stigma in many parts of the world, and women may be reluctant to seek screening if it is associated with taking what could be seen as an STI test. A desire to avoid unnecessary client concern may leave providers with difficult decisions regarding how they should describe the test to women. These issues must be taken into account when considering initiating HPV testing. Qualitative research on women's information needs may help address these concerns and guide the development of culturally appropriate counseling messages.

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