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E6/E7 mRNA HPV Testing

Recently, a variety of new HPV assays have been developed, targeting E6/E7 mRNA, rather than DNA. The rationale is that E6 and E7 gene expression is upregulated when HPV DNA is integrated into the host genome, and the hope is that detection of this mRNA will correlate with HPV-induced oncogenesis. While E6/E7 gene expression is certainly important in the biology of HPV infection, the clinical utility of these assays has not been established.

When evaluating the clinical utility of mRNA testing, the first factor to consider is that the various mRNA assays differ markedly in their performance characteristics. The most commonly used methods for mRNA testing consist of flow cytometric methods and nucleic acid amplification (NAAT).

Flow cytometric E6/E7 assays are promoted based on the increased specificity relative to DNA assays, but the sensitivity of these E6/E7 assays is markedly inferior to current DNA assays (Roche, Digene, and Cervista). The inadequate sensitivity of the flow cytometric assays renders them inappropriate for use in a cervical cancer screening program.

In contrast to the flow cytometric assays, the E6/E7 NAAT assays appear to show sensitivity and specificity that closely approximate the performance of current high-risk DNA assays, but the strength of evidence is far greater for the more well established DNA assays. Furthermore, these E6/E7 assays do not provide the additional predictive power of 16/18 genotyping without the need for supplementary testing.

In summary, E6/E7 mRNA assays may be useful in a research setting, helping to elucidate the mechanisms of HPV-related oncogenesis, and these assays may eventually find clinical utility as a supplement to current DNA assays. At present however, E6/E7 mRNA assays cannot provide equivalent sensitivity and predictive power when compared to current high-risk and genotyping DNA assays.

In our view, the Roche Cobas DNA assay, providing both high-risk and genotyping results, offers the optimum clinical utility.