AMERICAN SOCIETY OF CYTOPATHOLOGY

ASC Statement on New Technologies in Cervical Cytology Screening

Cervical cytology is arguably the most cost-effective cancer prevention test in medicine. For over five decades, the national standard for cervical cancer screening has been the Papanicolaou (Pap) test, which is largely responsible for the dramatic 90% decrease in mortality and 70% decrease in cervical cancer overall.

Although the Pap test has been extremely successful in decreasing mortality from cervical cancer, it has limitations. Similar to other medical tests, the Pap test has an inherent false negative rate associated with the process of patient compliance, sample collection and laboratory interpretation. Several technologies have been developed, and others are in development, in an effort to improve upon the accuracy of cervical cancer screening. These include, but are not limited to liquid-based technologies, computer-assisted screening and Human Papillomavirus (HPV) testing.

Liquid-based collection and processing provide a more representative sampling than conventional smearing of the specimen on a glass slide. These technologies have been shown in multiple studies to have sensitivity for squamous epithelial lesions (SIL) equal to or greater than the conventional smear. Certainly the liquid based collection methods decrease or eliminate a number of pre-analytic sample problems including difficulties in collection, air drying and inflammation.

Computer-assisted rescreening of all specimens initially screened as negative improves sensitivity as compared to a single manual screen with random 10% rescreening. The Food and Drug Administration (FDA) has approved two devices to assist in cervical cytology screening. One method incorporates initial computer evaluation followed by manual rescreening of the most likely abnormal cases; the least abnormal cases need no review. The other methodology involves an automated screening and presentation of digitized images of the most abnormal field to a reviewer for interpretation.

Certain high-risk oncogenic Human Papillomavirus types appear to be essential for the development of cervical cancer. Several methodologies including polymerase chain reaction (PCR), DNA-RNA hybrid capture and oligonucleotide probes are available to detect the presence of and/or subtyping of HPV DNA in gynecologic cytology. The current methods involve testing on residual material from liquid based cytology. It is well recognized that HPV testing is useful in the triage of patients with a cytologic interpretation of Atypical Squamous Cells of Uncertain Significance (ASC-US). There is literature to suggest that HPV testing can also be used as a stand-alone test for follow-up of patients after treatment or colposcopy and as an adjunct to cytology in the primary screening of women over 30 years of age. Population-based, primary screening with HPV testing is not currently recommended because of the presence of widespread transient infection in the population and problems with test specificity.

The continuing elucidation of the role of HPV in the development of cervical cancer has brought to light many potential biomarkers, which may play significant role in the integration of the viral genome into a host cell and a cell's neoplastic transformation. The

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literature reports variable analytic sensitivities and specificities for many of these markers. Further studies will hopefully help explain the molecular mechanisms involved and the clinical value of these markers.

Effective HPV vaccines have been developed. Currently they are intended to be used in a female population previously unexposed to HPV. The incidence of neoplastic cervical disease should decrease, and the cervical screening intervals should increase, as the vaccinated population becomes sexually active. Clinical trials assessing the efficacy of vaccine in men and HPV exposed older women are underway.

Cervical cytology and diagnostic pathology in general are in a period of transition. The conventional Pap smear, which has been the national and international standard for decades, continues to be an accepted screening modality; however, new technologies expand the range of available screening options. These technologies may provide greater sensitivities for the detection of SIL, but at increased cost. On the other hand, increased test sensitivity may allow for more effective screening strategies and patient management that could offset the increased cost of the technology.

Clinicians and laboratories should utilize cervical cytology screening paradigms that are most appropriate for their patient populations and clinical practice. These decisions must be continually reevaluated as science and technology evolve and as clinical studies provide scientific data on cost-effective strategies to further reduce morbidity and mortality from cervical cancer.

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