



## ASC POSITION STATEMENT CERVICAL CANCER SCREENING AND PREVENTION

The American Society of Cytopathology (ASC) and its membership are committed to supporting women's health and working collaboratively with other pathology and clinical professionals to effectively prevent cervical cancer in the United States. The ASC supports innovations in technology and changes in testing and management based on scientific and clinically-validated advancements.

### Cervical Cancer Screening and Prevention

#### (1) Papanicolaou Test:

- The Papanicolaou (Pap) test and the dedication of professionals including cytotechnologists and pathologists have significantly benefited women's health by reducing the incidence of, and mortality from, cervical cancer. It is the most successful cancer screening tool in medical history.
- Analogous to other medical tests, the Pap test has an inherent false negative rate associated with sample collection and laboratory interpretation.
- Multiple advances have occurred within the test itself and its role in cervical cancer screening, which include: pre-analytic (collection, slide preparation, staining techniques); analytic (automation and computer-assisted screening); HPV testing (triage, co-testing and primary screening), reporting terminology and clinical management guidelines.
  - **Liquid based technology**
    - Currently ThinPrep® (Hologic, Marlborough, MA) and SurePath® (Becton-Dickinson/TriPath, Burlington, NC) are the predominant liquid-based Pap test types used in the US.
    - Liquid-based Pap tests provide a more standardized presentation than conventional smears and decrease the number of pre-analytic problems including transfer of sample, excess blood/inflammation, and air-drying.
    - Liquid-based Pap tests allow for the performance of ancillary studies, such as HPV and STI (Chlamydia, Gonorrhea and Trichomonads) tests directly from the same vial.
    - The standardized presentation of liquid -based Pap tests allows the incorporation of computer imaging technology.
    - Liquid-based technologies have been shown in multiple studies to have sensitivity for squamous intraepithelial lesions (SIL) equal to or greater than the conventional smear, however meta-analyses do not indicate an overall increase in HSIL detection. (1)
  - **Computer imaging technology**

- The Food and Drug Administration (FDA) has, thus far, approved two devices to assist in cervical cytology screening:
  - The Hologic ThinPrep™ Imaging System involves automated pre-screening and presentation to the cytotechnologist of the most abnormal 22 fields of view (FOV) on the slide by using coordinates identified by the imaging system. The slide is reviewed with a microscope equipped with a motorized stage and physically linked to the imager, thus allowing a dual review: one full review from the ThinPrep Imager and another review from an experienced cytotechnologist.
  - The B.D. FocalPoint™ GS Imaging™ System incorporates initial computer image analysis followed by presentation of 11 fields of view of the most likely abnormal cells to the cytotechnologist via a microscope equipped with a motorized stage and a physical link to the image; the system thus allows for a full screen by the imager and at least a partial review of the slide by an experienced cytotechnologist. Following initial cytologist review the slide may be archived safely with a partial review (field of view-only) if no potential abnormality is identified, or triaged to a full manual review if potential abnormality is noted.

## (2) HPV Testing

- **Background**
  - Human papillomavirus (HPV) has been established as a necessary cause for almost all cervical cancers. (2)
  - Cervical cancer is caused by high-risk-HPV types, with approximately 70% of cervical cancers due to infection by HPV 16 and 18.
  - The majority of low-grade HPV related cervical lesions spontaneously regress without treatment.
  - Persistent infection with high risk HPV types is essential in progression to cervical cancer.
  - The non-carcinogenic or low risk-HPV (LR-HPV) subtypes, such as 6 and 11, are associated with genital warts but have no role in cervical cancer screening.
- **HPV Detection Methods**
  - In the US, there are currently 4 FDA-approved HPV assays, specifically Digene Hybrid Capture 2© High-Risk HPV DNA test ( Qiagen Group); Cervista© HPV HR and Cervista© HPV 16/18 (Hologic, Inc); Aptima© HPV Assay and Aptima© HPV 16-18/45 Genotype Assay (Hologic, Inc); and cobas© HPV Test (Roche Molecular Systems, Inc). (3)
  - ASC endorses that all HPV testing should be performed using methods that are appropriately validated. (4)

- The testing laboratory should be CLIA-approved and participate in regular proficiency testing, perform all required verification and continually monitor quality assurance. (7)
- As with any laboratory test, the sensitivity of HPV testing is not 100%. A subset of carcinomas, both squamous and glandular, and other tumor types may not be detected by HPV testing. (5)
- **Current clinical applications of high-risk HPV testing, endorsed by professional organizations include (6):**
  - Co-testing with cytology in women between 30 and 65 years of age.
  - Reflex testing on equivocal or low-grade cytological abnormalities (ASC-US in patients 21 and over, and LSIL in postmenopausal patients).
  - Genotyping for HPV 16/18.
  - Follow-up of women with abnormal cytological and HPV screening results, negative after colposcopically-guided biopsies.
  - Post-treatment follow-up of cervical intraepithelial neoplasia (CIN).

### **(3) Laboratory regulations**

- The ASC supports and endorses compliance with CLIA and laboratory accreditation quality assurance requirements for gynecologic cytology screening. (7)
- The ASC advocates for reasonable cytotechnologist workload limits to ensure the quality of screening. (8,9)

### **(4) Cervical cancer prevention by vaccination**

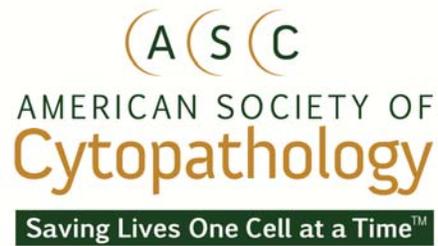
- The ASC supports universal HPV vaccination of adolescents and catch-up vaccination to prevent cervical cancer.
- Currently two vaccines are commercially available: Cervarix® (bivalent/HPV 16 and 18) and Gardasil® (quadrivalent/HPV types 6, 11, 16 and 18).
- As of 2014, vaccine uptake is relatively low in the US. (10,11)
- Women fully or partially vaccinated should continue to be screened following the same cervical cancer screening guidelines as those for the general population. (12)

### **(5) US Screening and management guidelines**

- The ASC supports current cervical cancer screening and management guidelines promulgated through national medical organizations such as the US Preventive Services Task Force, the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology. (12,13,14)

### **(6) Current cervical cancer screening options in the US:**

- Cytology alone for women 21 years of age and older.
- Cytology with reflex HPV testing following an interpretation of atypical cells of undetermined significance (ASC-US).



- Cytology and HPV co-testing of women 30 to 65 years of age.
- Primary HPV screening of women 25 years of age or older: primary screening with HPV testing alone was approved by the FDA in 2014 only for cobas® HPV Test (Roche Molecular Systems, Inc) on specimens prepared with ThinPrep® (Hologic, Marlborough, MA)
  - There is currently limited data in the US for primary HPV testing as a stand-alone screening modality.(16)
  - Direct comparisons to co-testing are insufficient in the literature at this point in time.(17)
  - Interim management guidelines by US professional societies are pending publication as of September 2014 (15)

**Summary statement:** (18)

- The ASC endorses worldwide screening as well as HPV vaccination for all women to prevent, detect and reduce cervical cancer incidence and mortality.
- The ASC does not endorse any specific Pap or HPV testing modality or any specific vendor(s).
- At the current time, the ASC upholds the use of routine cytology with HPV co-testing as the screening strategy most likely to diminish the adverse effects of either false negative cytology or false negative HPV screening test results. However, the choice of cervical screening method may vary for a variety of reasons. Patient and provider preference, geographic, demographic, and socio-economic considerations may all affect the choice of screening modality in a specific country, area, or practice setting.
- The ASC recognizes that cervical cancer screening in the United States remains opportunistic, (not organized with a recall system), with far from uniform test accessibility and patient compliance. As participation in screening and prevention is the key to reduction in cervical cancer morbidity and mortality, the ASC advocates for screening and vaccination access for all women with consideration of all acceptable screening modalities, patient compliance, test accessibility and overall cost.
- The overriding goal of the ASC and its pathologist and cytotechnologist members is to provide the highest level of quality care to the patients we serve, reiterating that no screening test is perfect.

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*Approved by the ASC Executive Board, September 16, 2014*