

## Review Article

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# Updates in Cervical Cancer Prevention

FARHAT HUSSAIN

### Summary :

*Cervical cancer is a totally preventable cancer in females. There is continuous effort ongoing to overcome the existing deficiencies in the screening and vaccination programme. The goal is to improve the situation so that maximum reduction in the incidence and mortality of cervical cancer can be achieved.*

### Introduction:

Cervical cancer is one of the few cancers in female that is almost preventable. Globally cervical cancer accounts for an estimated 5,85,000 new cases and 2,66,000 deaths in 2012<sup>1</sup>. Screening as well as vaccination is essential in the fight against cervical cancer. With the advancement of science and improvement in technologies there have been changes in screening and vaccination for cervical cancer to improve the existing deficiencies. Both the primary and secondary prevention efforts for cervical cancer has shown reduction in the incidence and mortality of the disease.

### Updates in screening tests :

#### Liquid Based Cytology :

Screening programmes have a vital role in cervical cancer prevention allowing early detection and treatment of precancerous lesions and early staged cancer. Pap's test, which is a well established tool for primary screening of cervical cancer has undergone changes in its technology to overcome its inherent limitations. The conventional Pap's smear, which was introduced in the early sixties is now being replaced by Liquid Based Cytology (LBC) in many developed countries. LBC has become the method of choice in USA, UK, New Zealand and is widely used in Australia, Sweden and Denmark. The Surepath and ThinPrep tests are two different methods for LBC and both are approved by the Food and Drug Administration (FDA). Conventional Pap's smear is associated with a high false negative rates which is linked up with both sampling and interpretation errors<sup>2</sup>. Two thirds of all false negatives are the result of cells not being collected or discarded in the sampling device and /or not being tested or

missed<sup>3</sup>. Review of evidence reveals that as many as 50% of precancerous lesions may be missed with a single conventional Pap test.

The liquid based Pap test differs from the conventional method because of its improved fixation, decreased obscuring factors and standardization of cell transfer. The sampling is free from operator dependent variation since processing is controlled by laboratory.

The collecting device is either combination of ayre's spatula and endocervical brush or a broom with detachable head. After collection of sample the device is rinsed or detachable head is dropped into the vial containing preservative, ensuring 100% of collected sample to be sent to the laboratory for processing. In SurePath method sample is centrifuged while in ThinPrep method sample is filtered. Both methods result in a well-preserved approximate monolayer of cells with a background devoid of blood, mucus and inflammatory cells. The end result is better specimen adequacy and improved cell morphology which leads to

- Increased detection rate of both low grade, high grade squamous intraepithelial lesions and glandular lesions.
- Decreased rate of ASC-H and ASCUSw 'x
- Significantly fewer "Unsatisfactory smears" reducing unnecessary repeat testing.

Overall there is better concordance with the simultaneous histopathological examination indicating increased accuracy. Moreover, LBC allows an opportunity to perform HPV DNA test with residual sample as a second line test without the need to recall the patient, which favorably influences the economy.

**HPV DNA Test:**

It is a screening test recently approved by FDA, which determines whether a woman has been infected with high risk HPV infection or not. HPV testing has been included in screening programs. HPV test is done by using a small soft broom like brush to collect cervical cells, which is immersed in a vial containing preservatives. The cap of vial is tightened with the brush in situ and sent to the laboratory for processing. HPV DNA test is more sensitive than other screening tests. Thus it has the advantage of allowing the screening interval to be extended to 10 years for screen negative women. The test is objective, reproducible and can be done in large numbers within a limited time by technicians after a short training period. But the test is highly expensive, which is an obstacle to its introduction in the screening programmes of most countries in South East Asia Region.

The US FDA have approved HPV DNA test as a primary screening tool for cervical cancer, meaning it may be used without a Pap test but current guidelines do not recommend HPV testing alone for primary cervical cancer screening. HPV DNA test is recommended in following situations —

- If the pap test is borderline abnormal or the report is ASCUS, HPV test is done as a triage test to decide whether the individual needs colposcopy or not.
- If the woman is 30 years or older HPV test may be used in conjunction with a pap test. This is called co-testing. Co-testing is recommended every 5 years as part of routine cervical cancer screening.

**HPV genotyping test:**

This test identifies the specific HPV type causing HPV infection. This gives a better understanding of a woman's risk of developing cancer so that plan for follow up screening and further testing can be done.

HPV genotyping is indicated if the pap's smear is normal but HPV test is positive for high risk. If HPV genotyping is positive for HPV 16 or 18, colposcopy is recommended. But if the test is negative for HPV 16 or 18, wait for 12 months and then repeat Pap test and HPV test. Thus HPV genotyping is not a primary screening test but is a test, which guides the subsequent follow up of patient.

**Updates in screening guidelines:**

National comprehensive Cancer Network (NCCN) updated the cervical cancer screening guidelines in 2012 based on American Cancer Society (ACS), American Society for Colposcopy and Cervical Pathology (ASCCP) and American Society for Clinical Pathology (ASCP) screening guidelines for the prevention and early detection of cervical cancer.

The major change in the screening guideline is as follows—

- Cervical cancer screening should begin at age 21 years
- Both conventional cytology and liquid based cytology can be used in screening.
- Women between 21 to 29 years should be screened by cytology alone every 3 years.
- Women between 30 to 65 years should be screened by cytology and HPV DNA test called co-testing every 5 years.
- If HPV test is not available or is not used the same group of women can be screened by cytology alone every 3 years.
- Women who are more than 65 years with previous screening reports negative or who have undergone hysterectomy for benign conditions do not need any further screening.
- Women who are HPV vaccinated should follow the same screening guidelines as unvaccinated women.

**Updates on HPV vaccination :****Update I:**

According to 'Immunization technical advisory committee of Centre for Disease Control and Prevention (CDC)' a 2- dose schedule is recommended if HPV Vaccine is initiated before 15<sup>th</sup> birthday<sup>10</sup> (0,6–12 months). This will provide similar protective efficacy compared to a 3- dose schedule but will allow potential cost savings.

Thus the new HPV immunization schedule for females will be as follows —

- Girls aged between 9 – 14 years are recommended a 2 dose schedule (0,6 – 12 months).
- For a 2 dose schedule, the second dose should be received 6 to 12 months after the first dose.

- HPV vaccine as part of routine immunization is recommended for females at age 11 or 12, but can begin as early as age 9.
- Vaccination is also recommended for older girls and younger females between 15 to 26 years who will be given a 3- dose schedule (0,1-2, 6 months).
- Vaccination is recommended through age 26 for women with deficient immune systems like HIV infection.

#### Update II:

All boys between 11 and 12 years will receive HPV vaccination like girls according to new guidelines<sup>11</sup>. The aim is to prevent HPV infection in males that can cause cancers of anus, penis and mouth/throat. This also prevents genital warts. Vaccinating males may also provide additional protection to females.

#### Update III:

In addition to Bivalent and Quadrivalent HPV vaccine, another HPV vaccine is approved by FDA in 10 December 2014 called HPV-9 or Gardasil – 9. It is available in United States and can be used for routine vaccination. It gives protection against HPV 6, 11, 16, 18, 31, 33, 45, 52 and 48. In addition to prevent genital warts it gives protection against cervical cancer, vaginal and vulval cancer in females, anal and throat cancer in males and females and penile cancers in male. Because it gives protection against 5 additional HPV types (when compared with quadrivalent vaccine) it gives additional 10% protection against HPV linked cancers including 15% of cervical cancer.

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