Cervical cancer screening

Abstract

In Malaysia, cervical cancer is the third most common cancer among women and the seventh-highest among the entire population (Malaysia National Cancer Registry report, MNCRR, 2007 – 2011). Almost all cervical cancers can be attributed to the presence of the human papilloma virus (HPV) infection. The good news is that it can be prevented via widespread vaccination with the HPV vaccine among the younger age groups and regular screening for pre-cancerous lesions of the cervix. Pre-cancerous lesions can be treated easily and this will prevent further development into cancer and can save lives.

Cervical cancer screening consists of either cervical cytology alone (conventional Pap test or the liquid-based cytology), or as a co-testing (combination of liquid-based cytology and HPV test at the same time) or as primary testing for presence of the HPV. Screening should start from age 25 years old if sexually active and up to age 65. The screening interval will depend on the type of screening test used and the results. For normal results, the interval varies from 3 to 5 years. In the future, primary screening with HPV test alone will be more common and this will allow lengthening of the screening interval to 5 years if the test is negative. If the HPV test is positive, cervical cytology can be used for triaging woman to either follow-up or direct referral for colposcopy.

Reasons for the test

- As part of routine cervical cancer screening.
- Investigate the cause of abnormal vaginal bleeding or discharge.
- Bleeding after sexual intercourse.

How to prepare for the test?

- Women should not be menstruating or have sperm present in the vagina from recent intercourse. Therefore, women should avoid sexual intercourse within a period of 24 hours prior to the procedure.
- Do not douche, use tampons, or use vaginal medications for at least 24 hours before having the test.
- The smear can be done during pregnancy. However, it is not routine and only done when there is an indication for it.

What to expect after the test?

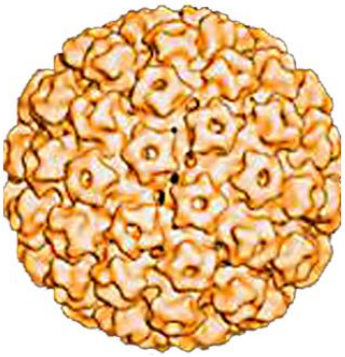
- There may be some slight bleeding or discharge following the test. Advise to use a tissue to wipe or wear a panty liner after the procedure.
- A positive test may indicate that there are some cells changes that need further investigations but do not necessarily indicate a pre-cancerous or a cancerous condition of the cervix. Further testing or a colposcopy or even a biopsy may be indicated to confirm the abnormality.
- Sometimes the smear report may indicate the presence of infection and treatment may be appropriate.

- One must be aware that the cervical cytology smear is not 100% accurate and the need for regular repeat smear as per recommended interval is important to ensure that the precancerous changes are not missed in the future.

Human Papillomavirus (HPV)

- Non enveloped double stranded DNA
- More than 200 types
- 15 are oncogenic
- Spread by direct skin to skin contact –sexual intercourse, oral or anal sex, any other contact involving the genital area (eg hand to genital, object - sex toys)

NIH FactSheet HPV and cancer Updated: January 22, 2021



Human Papillomavirus (HPV)

- High contagious - probability of infection : 50-80% via sex
- Most common STIs - 20 millions infected in US
- 80% of women will acquired HPV by age 50.

Koutsky et al 2000

- most HPV infection (90%) will clear within 2 years.

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 90

- Persistent infection with hrHPV, , is the cause of almost all cervical cancers
- HPV types 16 and 18 cause 70-80% of cervical cancer.

Fontham et al 2020

American Cancer Society Guidelines 2020

HPV testing

- uses molecular technique
- test for high risks and low risks HPV – can specify genotypes

Human papillomavirus: High- and low-risk types for causing cervical cancer

High-risk (oncogenic or cancer-associated) types
Common types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 69, 82
Low-risk (non-oncogenic) types
Common types: 6, 11, 40, 42, 43, 44, 54, 61, 72, 81

- Uses - a primary screening, as a triage (eg ASCUS) or co-testing
- Higher sensitivity but lower specificity

Saslow et al., 2012.

Currently, there are 3 options available for cervical cancer screening:

1. Cervical cytology alone – either conventional Pap smear (using slide fixed with alcohol) or liquid based cytology.
2. Testing for HPV alone – called the Primary HPV testing
3. Co-testing – meaning do both at same time

Liquid-based cytology:

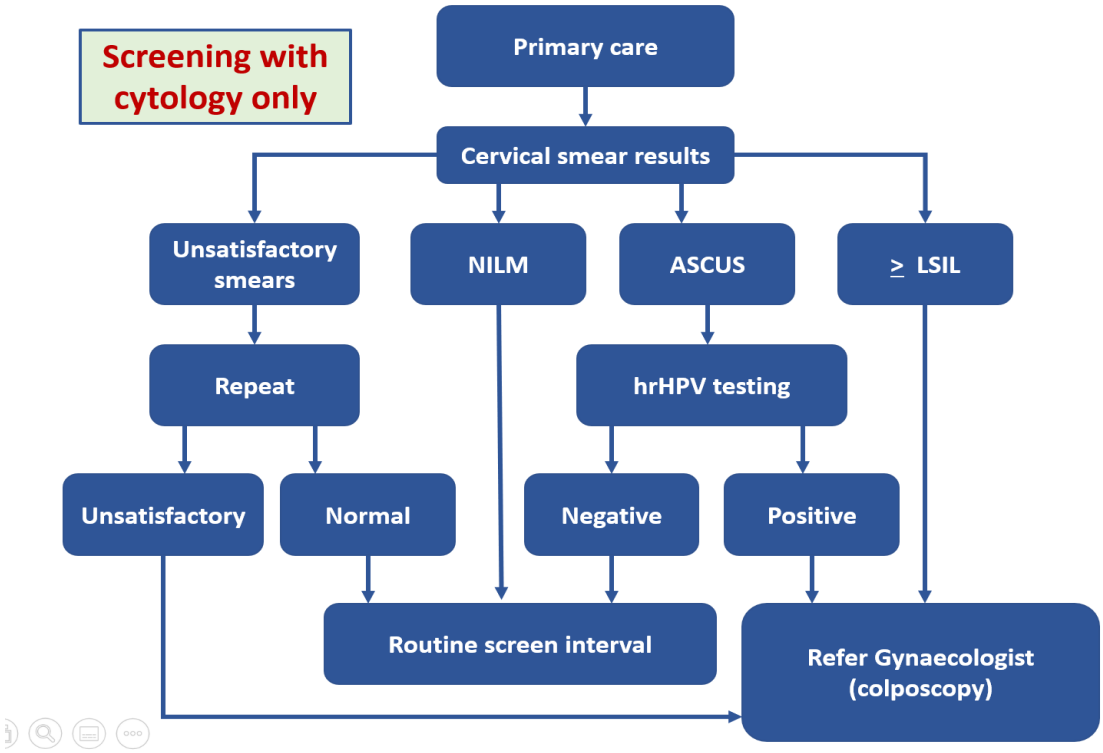
- Take sample from the cervix including transformation zone. It is important to follow the instruction as in user manual.
  - ✓ ThinPrep: 360 degrees rotation 3X. Rinse the brush vigorously inside the preservative vial by swirling and pushing against the vial wall 10 times. Discard the brush.
  - ✓ SurePath: 360 degrees rotation 5X in clockwise manner. Drop the detachable cytobrush head into the preservative vial

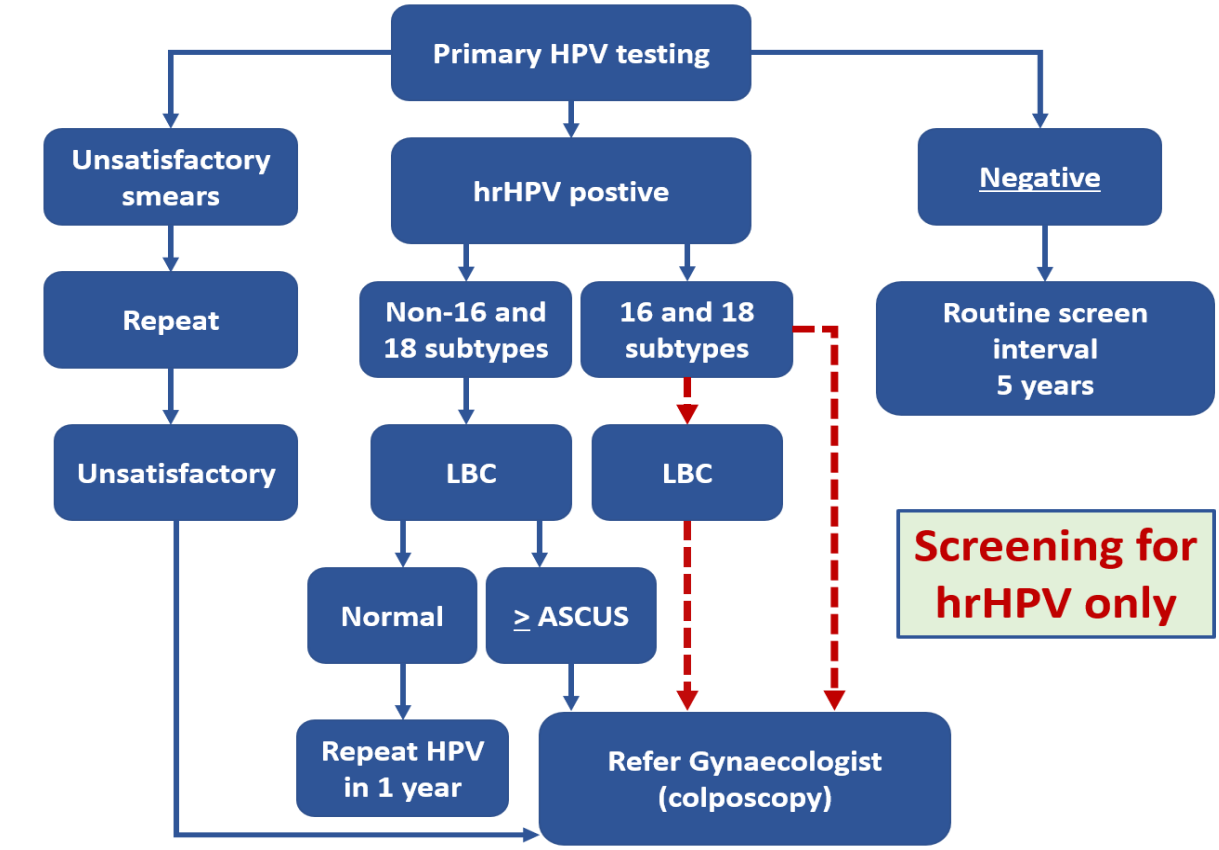
When to Start Screening

Recommendation for cervical screening			
Organisation	**When to start**	**When to stop**	**Intervals**
MOH Singapore 2019	≥ age 25 LBC ≥ 30 with LBC alone or HPV alone, or co-testing	69	• LBC alone – 3 years • HPV alone – 5 years • Co-testing – 5 years
HK COG 2016	≥ age 25 LBC ≥ 30 with LBC alone or co-testing	65	• If the first two consecutive annual LBC negative – 3 years • Co-testing - 5 years
American Cancer Society	≥ age 25 with LBC alone or HPV alone, or co-testing	65	• LBC – 3 years • HPV – 5 years • Co-testing – 5 years
MOH Malaysia 2019 **Wait for new MOH guidelines soon**	?? > age 25 or 30 LBC alone > Age 30 HPV alone or co-testing -	65	• If the first two consecutive • annual LBC negative - 3 years • Co-testing - 5 years • HPV – 5 years

Management of cervical Cytology Smear Report		
The 2014 Bethesda System		
Specimen adequacy	**Action Plan**	
Satisfactory for evaluation (with or without endocervical cells/Transformation zone component)	See Interpretation/Result & Action plan below.	
Unsatisfactory for evaluation:	Treat any infection if present. Give a short course of vaginal oestrogen cream in postmenopausal with atrophic changes. Repeat smear in 3 months	
Interpretation	**Action Plan**	
Negative for intraepithelial lesion or malignancy (NILM)	Satisfactory and no additional findings	Continue screening at normal interval.
	Infective / inflammatory changes	Treat specific infection if symptomatic or clinically indicated. Continue screening at normal interval.

Management of cervical Cytology Smear Report		
The 2014 Bethesda System		
Interpretation	**Action Plan**	
Epithelial Cells Abnormalities:		
Squamous cells	Atypical Squamous Cells of Undetermined Significance **(ASCUS)**	ASCUS - Options Perform hrHPV testing . If positive, refer for colposcopy. If negative, follow routine screening schedule.
	• Atypical squamous cells – cannot exclude HSIL **(ASC-H)** • Low Grade Squamous Intraepithelial Lesion **(LSIL)** • High Grade Squamous Intraepithelial Lesion **(HGSIL)**	Refer for colposcopy.
	Squamous cell carcinoma	Refer for biopsy or colposcopy.





GUIDELINES FOR PRIMARY HPV TESTING IN CERVICAL CANCER SCREENING IN MALAYSIA. MOH 2019

Women who have had a total hysterectomy for a benign condition and have no history of abnormal smears, do not need to continue to be screened if the cervix, was completely removed, and histologically is normal. Women with subtotal hysterectomy should continue screening as per guidelines.

Endocervical Cells - presence of endocervical and/or metaplastic cells indicates that the transformation zone is adequately sampled and allow microscopic examination of the glandular cells of the cervix. If the smear result is normal while lacking an endocervical component, there is no indication to repeat the smear earlier than the recommended screening interval, if the woman has a normal smear history. Endocervical cells may never be obtained in some women – such as in post menopausal, previous surgery to cervix.

References and further reading:

1. Management Guidelines for Abnormal Pap Smear & Preinvasive Disease of the Cervix (2019) by the Health Promotion Board Singapore for its Cervical Screen Programme. https://www.sccps.org/wp-content/uploads/2019/03/CSS-Clinical-Mgt-Guidelines-2019_March-Release.pdf
2. HKCOG Guidelines: Guidelines for Cervical Cancer Prevention and Screening November 2016. https://www.hkcog.org.hk/hkcog/Download/Cervical_Cancer_Prevention_and_Screening_revised_November_2016.pdf
3. Fontham, E. T. H., Wolf, A. M. D., Church, T. R., Etzioni, R., Flowers, C. R., Herzig, A., … Smith, R. A. (2020). Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. CA Cancer J Clin 2020;0:1-26.
4. Perkins, R. B., Guido, R. S., Castle, P. E., Chelmow, D., Einstein, M. H., Garcia, F., … Schiffman, M. (2020). 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. Journal of Lower Genital Tract Disease, 24(2), 102–131.
5. Guidelines for Primary HPV Testing in Cervical Cancer Screening in Malaysia 2019. https://www.ogsm.org.my/docs/GUIDELINES%20FOR%20PRIMARY%20HPV%20TESTING%20FOR%20CERVICAL%20CANCER%20SCREENING%20IN%20MALAYSIA.pdf

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