

Guidelines on the Management of An Abnormal Cervical Smear

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1 RATIONALE FOR CERVICAL SCREENING

- 1.1 Cervical cancer, which is largely preventable, still affects about 500 women and causes the death of about 150 women in Hong Kong each year (Hong Kong Cancer Registry). Despite a decrease in age standardized incidence, it is the 4th commonest malignancy in females and ranks 7th as a cause of cancer death in females.
- 1.2 Cervical cytology screening can reduce the incidence and mortality of cervical cancer. Its effectiveness is increased when it forms part of an organized programme of screening ¹.
- 1.3 The long latency which normally exists between the emergence of precursor lesions and occurrence of invasive, life threatening disease provides the foundation of the screening program for cervical cancer ².

- 2.2 Screening at 2 or 3-yearly intervals does not significantly reduce the chance of finding invasive cervical cancer below that found using annual screening and it results in considerable reduction in cost ³. The percentage reduction in the cumulative incidence of cervical cancer is 93% with annual or biannual screening interval, 91% if performed every 3 years, 84% if performed every 5 years and 64% if performed every 10 years. Screening at 3-yearly intervals, after 2 consecutive normal smears are obtained by annual screening, is recommended. However in persons at higher risk for carcinoma of the cervix, eg. immunosuppressed women, annual screening is advised.
- 2.3 Particular emphasis should be given to recruit those women at greatest risk for cervical cancer and women who have never had a cervical smear, or those who have not had one for more than 3 years.

2 TARGET POPULATION AND SCREENING INTERVAL

- 2.1 The target population encompasses all women from the time of commencing sexual activity until they reach 65 years of age. Screening may be discontinued in women aged 65 or more if previous smears have been consistently normal, although the upper limit beyond which screening ceases to be effective is unknown. Women over 65 years who have never had a cervical smear, or who request a cervical smear, should be screened.

3 METHODS OF SCREENING AND OPTIMIZATION OF EFFECTIVE SCREENING METHOD

There are various methods of screening for cervical cancer including cervical cytology, cervicography, HPV typing and polar probe. Apart from cervical cytology, the effectiveness of the other methods has not been established in cervical cancer screening. At the moment, cervical cytology remains the gold standard for cervical cancer screening. The following discussion mainly concentrates on this method.

3.1 Cervical cytology sample collection

- 3.1.1 The quality of the smear has a major impact on the sensitivity of the cervical smear. The presence of inflammatory cells, blood or debris, the type of instrument used and the skill of the operator may affect the quality of the smear. Avoid taking a smear during menstruation.
- 3.1.2 Use a device that will optimize sampling of the endocervical canal and ectocervix and thus the transformation zone and is cost effective. The broom type device is more expensive but gives better yield of endocervical cell than the conventional Ayres' spatula.
- 3.1.3 Despite adequate collection of cervical cells, poor transfer of cells to the slide may result in samples which are too thick or uneven for assessment. The cervical cells may be obscured by mucus, blood or inflammatory cells.
- 3.1.4 The smear should be fixed properly, either in 95% alcohol or using a spray fixative, immediately after the slide is prepared.
- 3.1.5 Factors that are important and can affect the interpretation of a smear include age, hormonal status, use of OC pills, pregnancy, presence of IUCD, and date of last menstrual period. Such information should be provided on the request form. Ensure proper labelling of the sample.
- 3.1.6 Liquid based preparations have assisted in decreasing the problems mentioned in above and have reduced the unsatisfactory smears rate but at a price.

- 3.1.7 The use of estrogen in postmenopausal women and the treatment of pre-existing infection may help to improve the quality when a smear needs to be repeated.

3.2 Laboratory screening

- 3.2.1 Smears should be screened by a laboratory with documented good quality control.
- 3.2.2 Random re-screening of 10% of negative cases, targeted re-screening and rapid re-screen are methods used in quality control.
- 3.2.3 Computer assisted re-screening and primary screening are now available but at a cost.

4 REPORTING OF ABNORMAL SMEARS

- 4.1 Various terminology is used in the reporting of cervical smears. An understanding of the meaning of a smear report is essential for proper management of abnormal results.
- 4.2 Most laboratories in Hong Kong are now reporting cervical smears using The Bethesda system (TBS) ⁴. A strength of this system is that it requires an evaluation of the adequacy of the specimen and encourages a descriptive diagnosis of abnormalities. For uniformity, this should be the default reporting system in the cervical screening program.
- 4.3 The cytological terms low- and high-grade squamous intraepithelial lesion (LSIL and HSIL) correlate with the histologic diagnosis of HPV/CIN I and CIN II/III respectively.
- 4.4 The term Atypical Squamous Cells of Undetermined Significance (ASCUS) applies to squamous cell abnormalities that cannot be accounted for by reactive changes but do not fulfill the criteria for a specific squamous lesion. Some patients with ASCUS will harbour HSIL or rarely invasive cancer.

5 MANAGEMENT OF AN ABNORMAL CERVICAL SMEAR

5.1 Criteria for referral for colposcopy

The decision to refer for colposcopy depends on the likelihood that a patient has CIN II/III or more advanced disease. The following table is a guide to this decision.

<u>Cervical Smear</u>	<u>Significance</u>	<u>Suggested actions</u>
Normal	0.1% CIN II-III ⁵	Normal screening program (Once every 3 years after 2 normal annual smears)
Inflammatory	may mask HGSIL or invasive cancer	Treat confirmed infection. Repeat smear in 3-6 months and refer for colposcopy if abnormality persists.
ASCUS	in persistent ASCUS: 14% CIN II-III** 0.7% microinvasive 0.2% invasive	Repeat smear in 3-6 months. Refer for colposcopy if abnormality persists.
Low grade squamous intraepithelial lesion (LSIL)	13.4% CIN II-III* 0.1% microinvasive	Refer for colposcopy and biopsy
High grade Squamous Intraepithelial lesion (HSIL)	69.5% CIN II-III* 2.3% microinvasive 3.5% invasive	Refer for colposcopy and biopsy
Invasive cancer	53.8% microinvasive* or invasive	Biopsy if frank growth, otherwise early referral for colposcopy and biopsy
Abnormal glandular cells of undetermined significance (AGUS)	17% HG, 5% AIS 2% invasive adenocarcinoma ⁶	Refer for colposcopy and biopsy, then cone biopsy and D & C may be required.
Endometrial cells at inappropriate time	(if menopause) 7% adenocarcinoma ⁵ 13% hyperplasia 38% endometrial polyp	Investigate for endometrial pathology.

*1996 Hong Kong colposcopy data, some data with colposcopy performed only after persistent ASCUS

**Hong Kong colposcopy data includes persistent ASCUS at second or third smears

5.2 Colposcopy examination

The colposcopist's role is to examine the transformation zone, define the extent of the lesion, and to biopsy the most abnormal area for a tissue diagnosis. In addition to the cervix, the vagina should also be inspected.

Histological confirmation of the colposcopic diagnosis is advisable before treatment. In patients with a colposcopic diagnosis of high grade lesion, a "see and treat" approach⁷ ie. perform loop excision without a biopsy, is adopted by some colposcopists. Although this practice decreases the need for another visit, it carries the risk of over-treating patients with low-grade lesions. The rate of overtreatment depends on the expertise of the colposcopist.

5.3 Role of HPV typing

5.3.1 Patients who present with ASCUS and LSIL and are positive for high risk HPV-types, are more likely to progress to high grade lesions (CIN II-III or invasive cancer).

5.3.2 HPV typing allows identification of such patients and thus may facilitate triage for colposcopy.

5.3.3 Molecular identification methods use the polymerase chain reaction (PCR) and dot-blot, or commercial kits such as *Digene Hybrid Capture*.

5.3.4 The role of HPV typing in screening for cervical cancer is not yet well established.

5.4 Treatment for CIN and basis of treatment

5.4.1 Since 85% of low grade lesions (HPV, CIN I) will regress over 2 years without treatment, these patients can be observed⁸. About 15% of

these patients may progress to CIN II or III and require treatment later.

If a low-grade lesion is confirmed by colposcopy and biopsy, the patient can be regularly followed-up every 6 months until the smear returns to normal. After that, the patient can be followed annually. If the smears are normal for 5 consecutive years, the patient can return to the routine screening programme.

If the patient is unable or unwilling to return for follow-up, then treatment should be considered. If the lesion persists without treatment for more than 2 years, options for treatment should be discussed with the patient.

5.4.2 Treatment for CIN can be carried out under local anaesthesia on an outpatient basis.

5.4.3 The reason for treating high-grade cervical intraepithelial neoplasia (CIN II or III) is that these lesions are likely to progress to invasive cancer if left untreated. The time of progression to cancer is variable and can take from months to years¹. The risk of CIN III progressing to an invasive lesion was > 12%⁹.

5.4.4 If a high-grade lesion is found, and obvious invasive cancer has been excluded, local treatment can be performed with a success rate of more than 90%.

Ablative methods include electrocoagulation diathermy, cryosurgery, cold coagulation and laser vaporization and all suffer the disadvantage of not producing a specimen for histology examination.

The currently preferred method is the loop electrosurgical excision procedure (LEEP). This has the advantage of providing a tissue specimen that is generally of sufficient quality for histologic exclusion of occult invasion. Complications include intraoperative and postoperative bleeding (1-8%), infection, cervical stenosis (1%), cervical deformity and cervical incompetence¹⁰.

- 5.4.5 Hysterectomy is not recommended for the treatment of CIN II/III unless there are concomitant gynaecological problems that warrant a hysterectomy or if the patient is unreliable for follow-up surveillance.
- 5.4.6 After treatment for HSIL, patients should be followed up by cervical cytology for 3 times at 6-monthly intervals and then annually.
- 5.4.7 The diagnosis and indication for treatment, treatment procedures and possible treatment complications, should be discussed with the patient before colposcopic examination and treatment. All counselling, cytology / histology / colposcopy results, consent, and the management plan should also be documented. Patients with high grade lesions should be informed of the result as soon as possible and preferably within 4 weeks.

6 RECALL SYSTEM

- 6.1 It is a good practice that a record system is available to keep track of the outcome of patients with an abnormal smear. A recall system should ideally be in place to make sure patients with abnormal smears are properly managed.

- 6.2 A recall system to remind women with normal cytology that they are due for another cervical smear will optimize the efficacy of a screening programme.

7 AUDIT

The results of the management of abnormal smears should be audited regularly. Auditing should include the quality of treatment, the quality of service, the adequacy of follow-up and the clinical outcome. Reference on what can be audited could be found in the "Standard and quality in colposcopy, NHSCSP publication No.2, January 1996, edited by David Luesley".

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