HKCOG Guidelines

Number 3

revised
November 2002

Guidelines on the Management of An Abnormal Cervical Smear

published by The Hong Kong College of Obstetricians and Gynaecologists

A Foundation College of Hong Kong Academy of Medicine

1 INTRODUCTION

In this revision of the Guidelines on the Management of An Abnormal Cervical Smear, 2 major recent developments were addressed. The first is the revision of the Bethesda System in 2001 where new categories mainly in atypical squamous and glandular cells were introduced (1). The second is on the use of HPV as an adjunct in cervical cytology.

2 RATIONALE FOR CERVICAL SCREENING

2.1 Cervical carcinoma, 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.

2.2 Cervical cytology screening can reduce the incidence and mortality of cervical carcinoma. Its effectiveness is increased when it forms part of an organized programme of screening [1].

2.3 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].

3 TARGET POPULATION AND SCREENING INTERVAL

3.1 The target population encompasses all women from age 25 or the time of commencing sexual activity (whichever is later) until they reach 65 years of age. In view of the rarity of cervical carcinoma in women below 25 years of age and the relatively high proportion of cytological abnormalities that spontaneously regress, screening before this age is less cost-effective and could result in unnecessary interventions. Nevertheless, women aged below 25 years with high risk profile may be screened. Screening may be discontinued in women aged 65 or more if 3 previous consecutive smears are normal. Women over 65 years who have never had a cervical smear, or who request a cervical smear, should be screened.

Taking a smear during pregnancy may induce bleeding and cause anxiety to the woman and hence this is not the best time to perform cervical screening.

3.2 The percentage reduction in the cumulative incidence of cervical cancer is 93% with an 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 is less costly and does not significantly reduce the efficacy of preventing invasive cervical cancer compared to that achieved with annual screening[3]. Screening at 3-yearly intervals, after 2 consecutive normal annual smears, is recommended. However annual screening is advised for persons at high risk of developing cervical carcinoma more rapidly eg. immunosuppressed women.

3.3 Particular emphasis should be given to recruit those women at greatest risk of developing cervical cancer - those who have never had a cervical smear, and those who have not had one for more than 3 years.

4 METHODS OF SCREENING AND OPTIMIZATION OF EFFECTIVE SCREENING METHOD

There are various methods of screening for cervical cancer. These include 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 standard method for cervical cancer screening and the following discussion mainly concentrates on this method. Nevertheless, it must be understood that the cervical smear test, like any other screening test, has inherent limitations and is neither 100% sensitive nor 100% specific.

4.1 Cervical cytology sample collection

4.1.1 The quality of the smear has a major influence on the sensitivity of the cervical smear. The presence of inflammatory cells, blood or debris, the type of cell collector used and the skill of the operator will affect the quality of the smear. Taking smears during menstruation should be avoided.

4.1.2 Use of a broom type device will optimize cell sampling from the endocervical canal and ectocervix and thus the transformation zone but it is more expensive than the Ayres' spatula.

4.1.3 Despite adequate collection of cervical cells, poor and uneven transfer of cells to the slide may hamper assessment because of insufficient cells or a thick smear. Mucus, blood or inflammatory cells may also obscure the cervical cells.

4.1.4 The smear should be immediately and properly fixed after the slide is prepared, either in 95% alcohol or using a spray fixative.

4.1.5 Liquid based preparations minimize the problems mentioned above and have reduced the rate of unsatisfactory smears but at a price**.** Liquid based specimens should be collected according to the manufacturer's instructions.

4.1.6 Factors that are important and can affect the interpretation of a smear include age, hormonal status, use of hormonal contraceptives or an IUCD, pregnancy and the date of last menstrual period. Such information should be indicated on the request form. The sample should be properly labeled.

4.1.7 The use of estrogen in postmenopausal women and the treatment of pre-existing infection may improve the quality of a smear.

4.2 Laboratory screening

4.2.1 Smears should be screened in a laboratory run by competent and qualified personnel and with documented good quality control.

4.2.2 Good quality control measures should include an approved re-screening programme in the laboratory.

5 REPORTING OF ABNORMAL SMEARS

5.1 Various terminologies have been used in the reporting of cervical smears. An understanding of the meaning of a smear report is essential for proper management of abnormal results.

5.2 Most laboratories in Hong Kong report cervical smears using the current Bethesda system (TBS) [4]. The strength of this system is that it provides 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 a cervical screening program.

5.3 The cytological terms low- and high-grade squamous intraepithelial lesion (LSIL and HSIL) correlate with, but is not diagnostic of, the histological diagnosis of HPV/CIN I and CIN II/III respectively.

5.4 The term Atypical Squamous Cells (ASC) applies to cytological changes that are suggestive of squamous intraepithelial lesion but are qualitatively or quantitatively insufficient for a definitive diagnosis. TBS 2001 further indicate cases more likely to have high grade lesions using the term ASC-H as compared to ASC-US (undetermined significance).

6 MANAGEMENT OF AN ABNORMAL CERVICAL SMEAR

6.1 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.

Cervical Smear	Significance	Suggested actions
Normal (± inflammation)	0.1% CIN II-III	Normal screening program (Once every 3 years after 2 normal annual smears)
ASC- US	5-17% CIN II-III[5] 0.1-0.2% invasive	Repeat smear in 4-6 months. Refer for colposcopy if abnormality persists.
ASC-H	24-94% CIN II-III[5]	Refer for colposcopy and biopsy
Low grade squamous intraepithelial lesion (LSIL)	15-30% CIN II-III[5] 0.1% invasive	Refer for colposcopy and biopsy
High grade Squamous Intraepithelial lesion (HSIL)	70-75% CIN II-III[5] 1-2% invasive	Refer for colposcopy and biopsy
HSIL-cannot exclude invasion		Early referral for colposcopy and biopsy
Invasive cancer	53.8% invasive	Biopsy if frank growth, otherwise early referral for colposcopy and biopsy
Abnormal glandular cells (AGC- endocervical /endometrial *)		Refer for colposcopy and biopsy, endocervical sampling, cone biopsy and endometrial sampling may be required. * for AGC- endometrial cells -endometrial sampling first
AGC-NOS	9-41% CIN2-3,AIS,Ca[5]	
AGC-favor neoplasia	27-96% CIN2-3, AIS, Ca[5]	
AIS	48-69% AIS[5] 38% Adenocarcinoma[5]	
Endometrial cells on smear in		
a/ women after menopause	28% benign pathology, 12% significant pathology[6] (hyperplasia,endometrial carcinoma, sarcoma)	Investigation recommended
b/ women greater or equal to 40 years of age		Interpret the smear result together with the clinical findings to determine the management
c/ women < 40 years of age		Treat as normal

6.2 Colposcopy examination

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

Histological confirmation of the colposcopic diagnosis is advisable before treatment. In patients with a colposcopic diagnosis of high-grade lesion, a "see and treat" approach [7] 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.

6.3 Role of HPV typing

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

6.3.2 High risk HPV can be found in around 50% of ASCUS and 82-85% of LSIL [8-9] HPV typing in triaging patients with ASCUS is an alternative to repeat cytology at 6 months in decision for colposcopy referral [8] . On the other hand, HPV typing has limited advantage in triaging patients with LSIL for colposcopy because over 80% of LSIL has high risk HPV[9].

6.3.3 High risk HPV can be detected by polymerase chain reaction (PCR) and dot-blot, or commercial kits.

6.3.4 The use of HPV typing alone in primary screening for cervical cancer is not recommended.

6.4 Treatment for CIN and basis of treatment

6.4.1 Majority of low grade lesions (HPV, CIN I) will regress spontaneously over 2 years and immediate treatment may not be necessary[10-11]. About 15% of 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 followed-up with smears every 6 months until having 3 consecutive normal results. Annual smear is then recommended for two times before returning to routine screening programme.

In patients with CIN 1 lesion involving more than 2 quadrants of the cervix or if the patient is unable or unwilling to return for follow-up, then treatment should be considered. If the lesion persists for more than 2 years, treatment is recommended.

6.4.2 The reason for treating high-grade cervical intraepithelial neoplasia (CIN II or III) is that these lesions could progress to invasive cancer if left untreated. The time of progression to cancer is variable and can take from months to years[1]. The risk of CIN III progressing to an invasive lesion is about 12% over a period of 10 years[12].

6.4.3 Treatment for CIN can be carried out under local anaesthesia on an outpatient basis in 90% patients.

6.4.4 Ablative methods including electrocoagulation diathermy, cryosurgery, cold coagulation and laser vaporization, are undesirable because they do not provide a specimen for histology examination.

The current recommended method is the loop electrosurgical excision procedure (LEEP). This has the advantage of providing a tissue specimen that is generally of sufficient quality for histological exclusion of occult invasion. Complications include intraoperative and postoperative bleeding (1-8%), infection, cervical stenosis (1%), cervical deformity and cervical incompetence[12] and rarely injury to vagina, bladder and ureter.

6.4.5 Hysterectomy is not recommended for the treatment of CIN II/III unless there are concomitant gynaecological problems that warrant a hysterectomy.

6.4.6 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.

6.4.7 After treatment for HSIL, patients should be followed up by cervical cytology for 3 times at 4 to 6-months intervals and then annually for 5 years, then return to routine screening interval.

7 RECALL SYSTEM

7.1 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.

7.2 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.

8 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. The College has guidelines on standard of colposcopy services and program on colposcopy service audit.

REFERENCE LIST

1 Laara E, Day NE, Hakama M. Trends in mortality from cervical cancer in the Nordic countries: association with organised screening programmes. Lancet 1987;1:1247-9.

2 Barron, B. A. and Richart, R. M. Statistical model of the natural history of cervical carcinoma. II:estimates of the transition time from dysplasia to carcinoma in situ. J Natl Cancer Inst. 1970; 45: 1025-1030.

3 WHO, Bulletin of the World Health Organisation, 1986; 64:607-618.

4 Solomon, D.; Davey, D.; Kurman, R.; Moriarty,A.; O'Connor, D.; Prey, M.; Raab, S.; Sherman, M.; Wilbur, D.; Wright Jr, D.; Young, N. The 2001 Bethesda system – Terminology for reporting results of cervical cytology. JAMA 2002, 287:2114-2119.

5 Wright, T.C.; Cox, J.T.; Massad, L.S.; Twiggs, L.B.; Wilkinson, E.J. 2001 Consensus guidelines for the management of women with cervical cytological abnormalities. JAMA 2002, 287:2120-2131.

6 Ashfaq R, Sharma S, Dulley T, Saboorian MH, Siddiqui MT, Warner C Clinical relevance of benign endometrial cells in postmenopausal women. Diagn Cytopathol 2001 Oct;25(4):235-8.

7 Ferenczy A, Choukroun D, Arsenean J, Loop electrosurgical excision procedure for squamous intraepithelial lesions of the cervix: advantages and protential pitfalls Obstet Gynecol 1996; 87: 322-337.

8 Solomon D, Schiffman M, Tarone R; ALTS Study group. Comparison of three management strategies for patients with atypical squamous cells of undetermined significance: baseline results from a randomized trial. J Natl Cancer Inst 2001 Feb 21;93(4):293-9.

9 The Atypical Squamous Cells of Undetermined Significance/Low-Grade Squamous Intraepithelial Lesions Triage Study (ALTS) Group. Human papillomavirus testing for triage of women with cytologic evidence of low-grade squamous intraepithelial lesions: baseline data from a randomized trial. J Natl Cancer Inst 2000 Mar 1;92(5):397-402.

10 Lee SS, Collins RJ, Pun TC, Cheng DK, Ngan HY. Conservative treatment of low grade squamous intraepithelial lesions (LSIL) of the cervix. Int J Gynaecol Obstet 1998;60:35-40.

11 Oster AG. Natural history of cervical intraepithelial neoplasia; a critical review. Int J Gynecol Pathol 1993;12(2): 186-192.

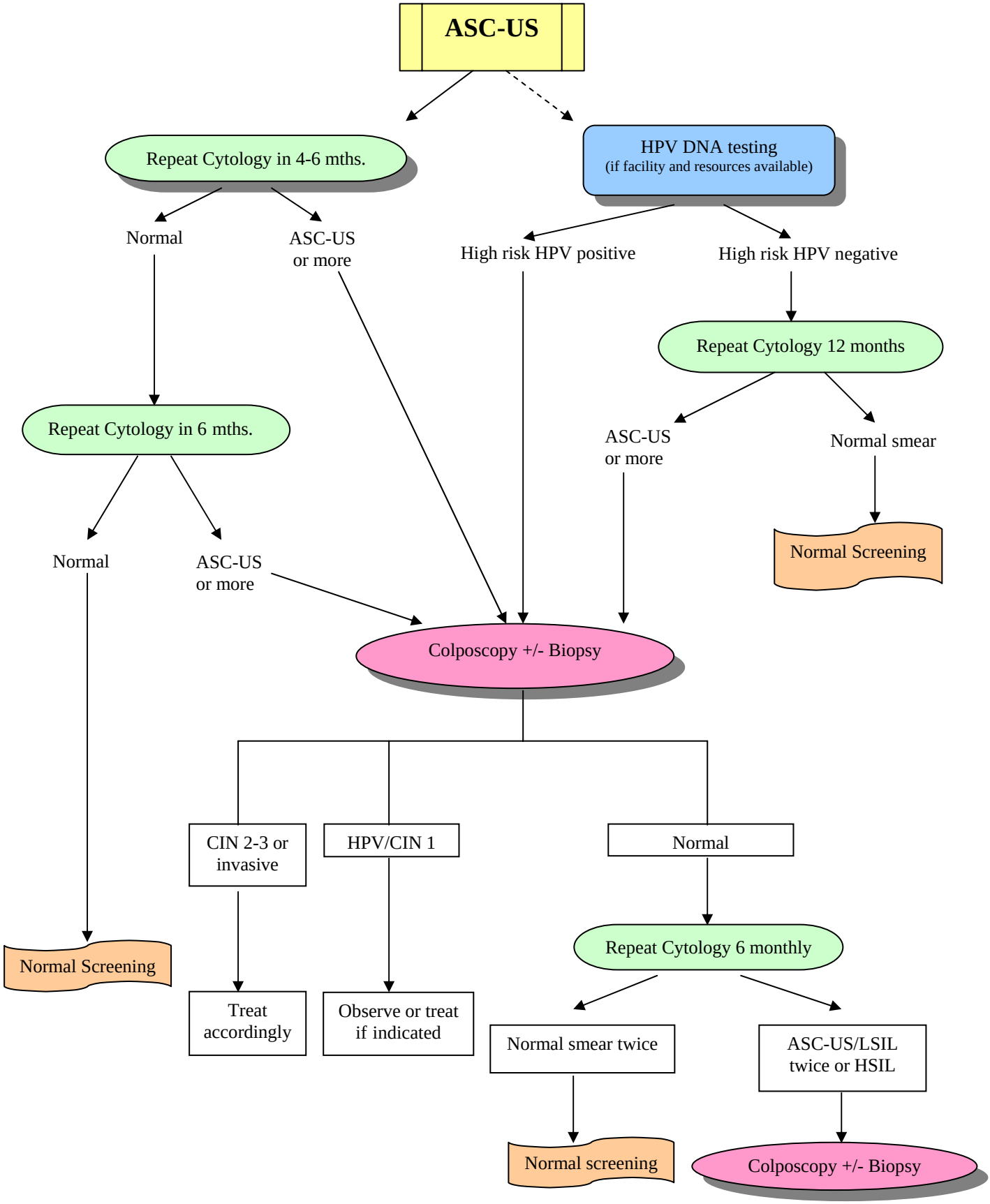
12 Spitzer M, Chernys AE, Seltzer VL. The use of large-loop excision of the transformation zone in an inner-city population. Obstet Gynecol 1993;82:731-5.

ACKNOWLEDGEMENT:

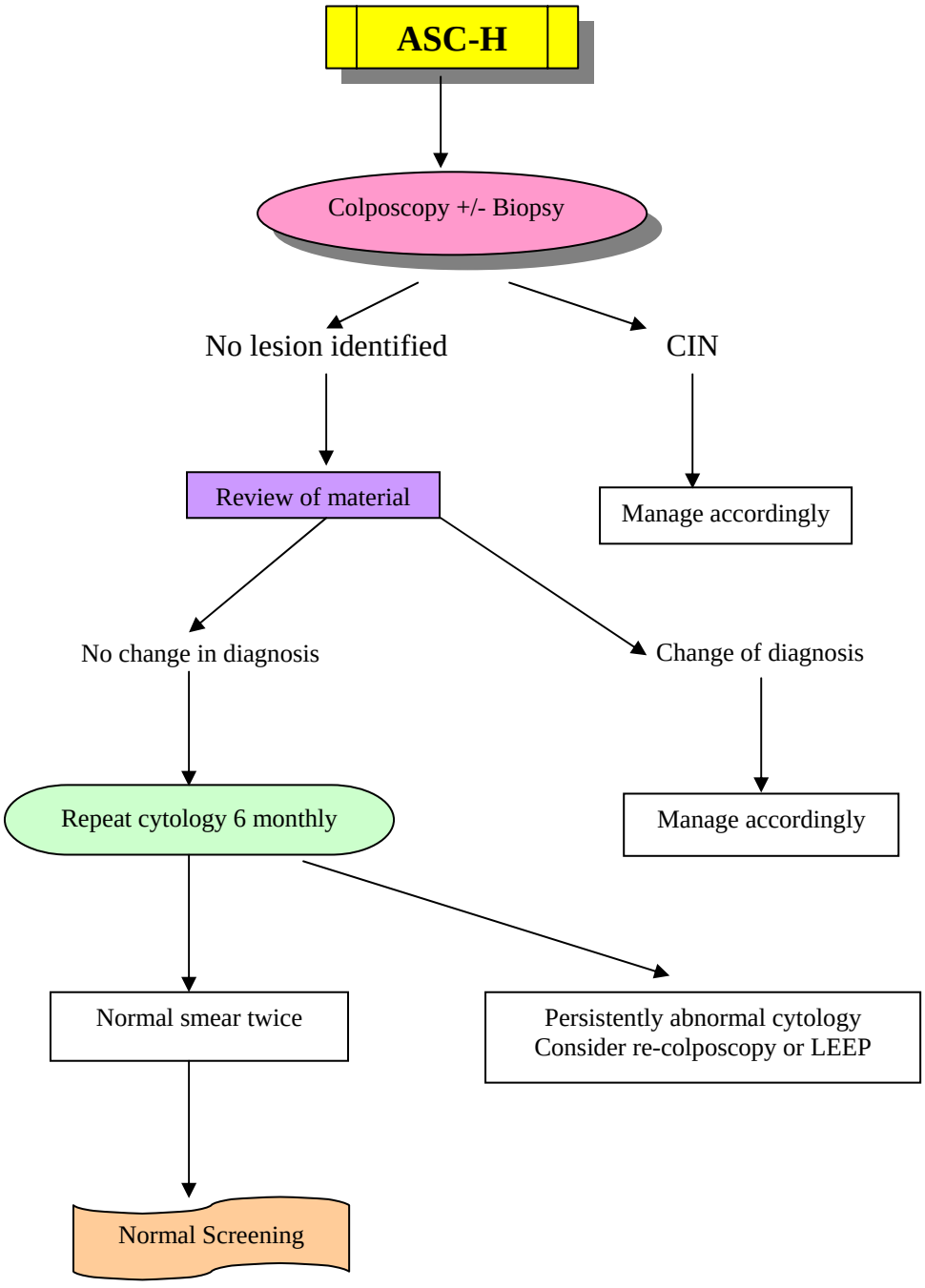
This document was revised by Professor HYS Ngan, Dr RJ Collins, Dr ANY Cheung, Dr M Chan, Dr S Fan, Dr TC Pun, Dr TH Cheung, Dr MYW Cheung and Dr TY Ng and was endorsed by the Council of the Hong Kong College of Obstetricians and Gynaecologists.

This guideline was produced by the Hong Kong College of Obstetricians and Gynaecologists as an educational aid and reference for obstetricians and gynaecologists practicing in Hong Kong. The guideline does not define a standard of care, nor is it intended to dictate an exclusive course of management. It presents recognized clinical methods and techniques for consideration by practitioners for incorporation into their practice. It is acknowledged that clinical management may vary and must always be responsive to the need of individual patients, resources, and limitations unique to the institution or type of practice. Particular attention is drawn to areas of clinical uncertainty where further research may be indicated.

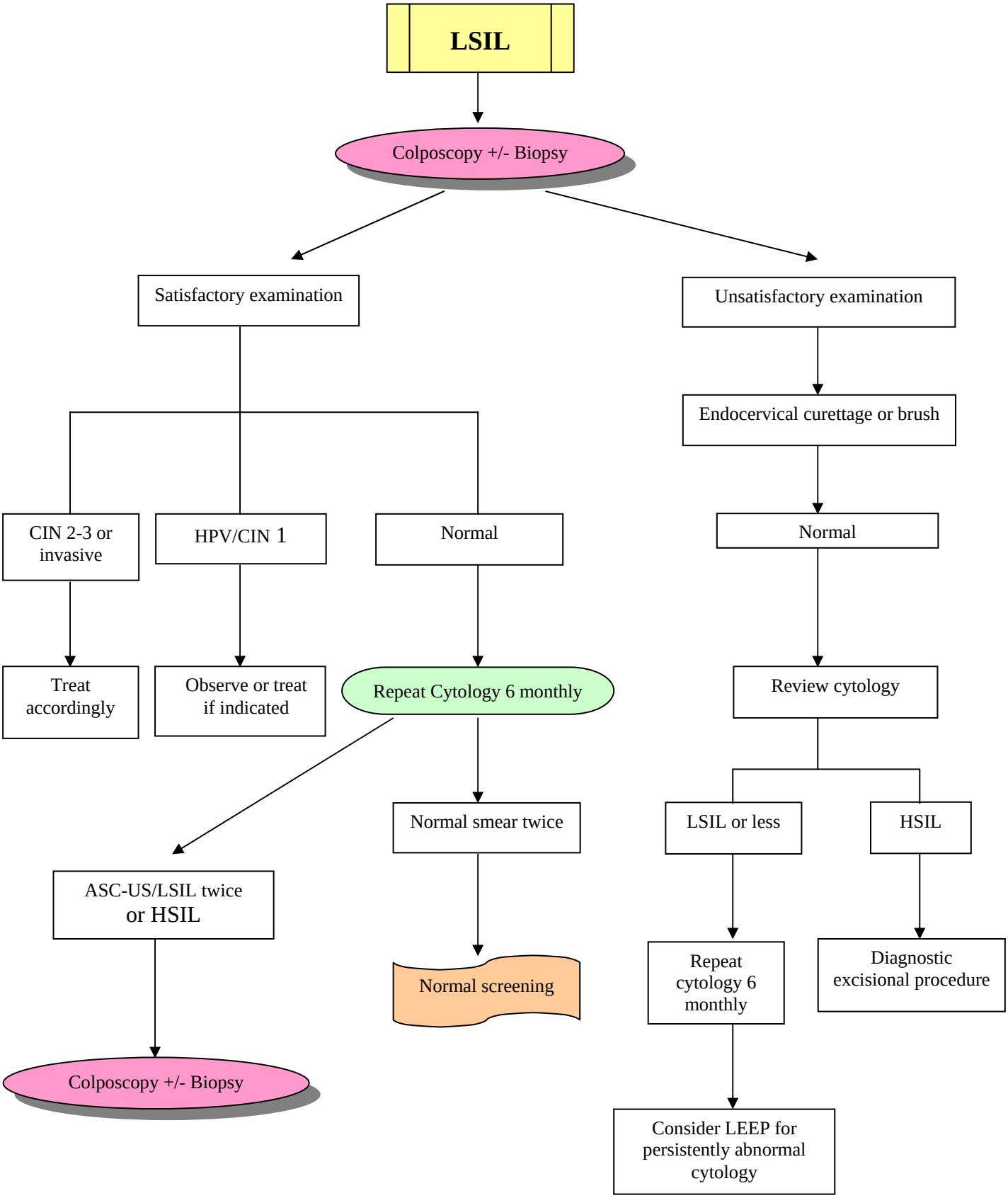
Management of Women with Atypical Squamous Cells of Undetermined Significance (ASC-US)



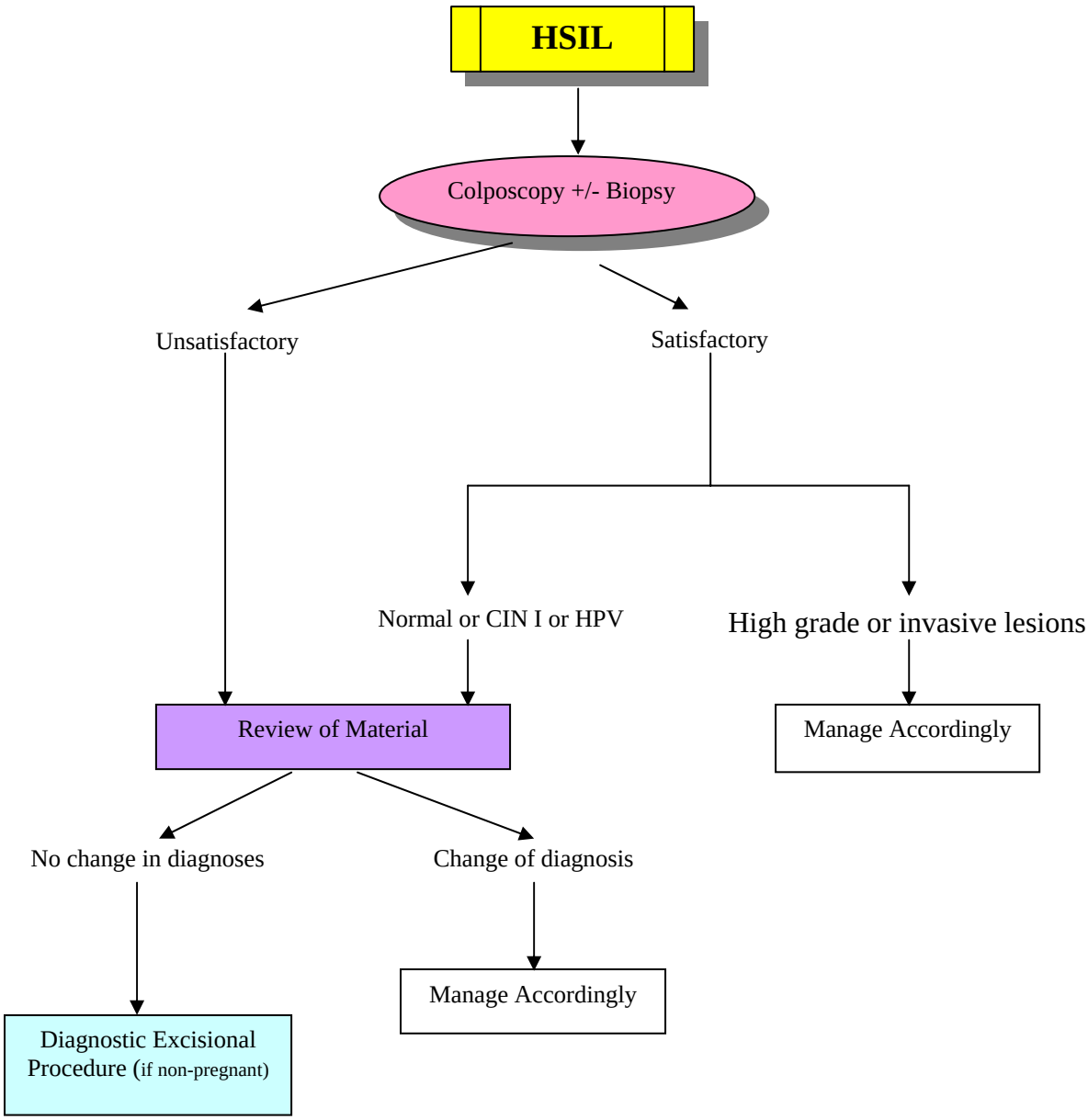
Management of women with Atypical Squamous Cells-Cannot Exclude High grade SIL (ASC-H)



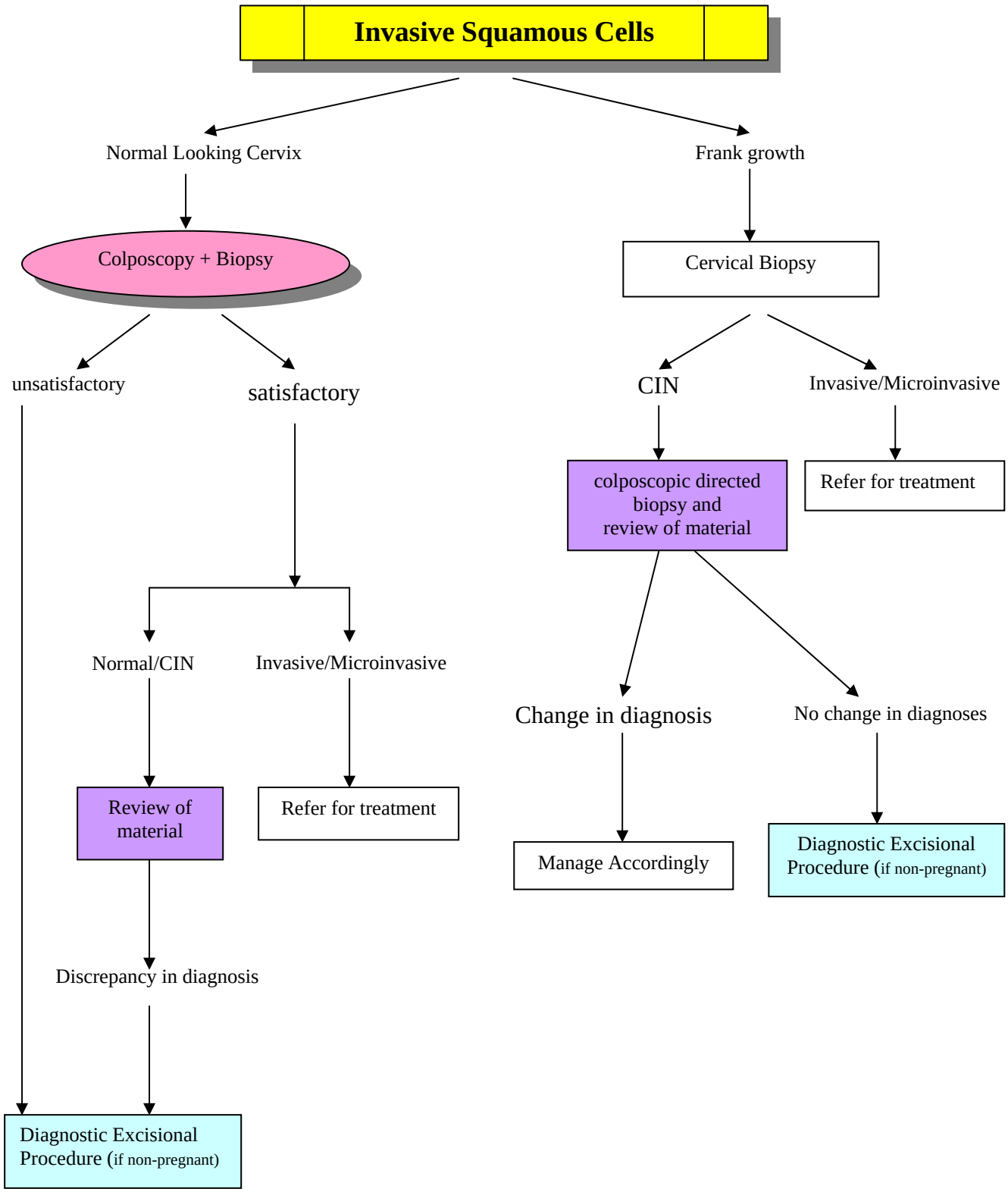
Management of women with Low Grade Squamous Itraepithelial Lesion(LSIL)



Management of women with High Grade Squamous Intraepithelial Lesion (HSIL)



Management of women with Smears showing Invasive Squamous Cells



Management of women with Smears showing Atypical Glandular Cells