THE 'PAP' OR CERVICAL SMEAR AND THE ROLE OF COLPOSCOPY IN SCREENING FOR CARCINOMA OF THE CERVIX

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ABSTRACT

Cervical cancer is the commonest female genital tract cancer in Singaporean women with an annual age-standardized rate of 17.4 per 100,000. High risk factors are early sexual intercourse, multiple sexual partners and cigarette smoking. Population screening with annual cervical (Pap) smears after beginning sexual activity until age 35 and at 5 year intervals after that can reduce both incidence and mortality rate from invasive cervical cancer. Benign, premalignant and malignant conditions may be identified in smears. The term cervical intra-epithelial neoplasia (CIN) reflects better the continuum of change in precursor lesions and is preferred over the older dual terminology of dysplasia/carcinoma-in-situ for precursors of cervical cancer. Colposcopy is essential for evaluation of all patients with abnormal cervical smears. Colposcopy is used to identify the site, severity and extent of abnormality as well as to aid directed biopsy, plan treatment and allow use of conservative methods to treat the precursor lesions. Colposcopy however, has no role as a primary screening precedure for cervical cancer but instead cervical smears are used for screening.

Key Words: cervical cancer, cervical/Pap smears, screening, colposcopy

INTRODUCTION

Cancer of the cervix is the commonest female genital tract malignancy in Singaporean women with an Age-Standardized Rate (ASR) per 100,000 per year of 17.4(1). About 100 women die from cervical cancer each year in Singapore(2) and most of these deaths are theoretically preventable if the disease can be detected in the pre-invasive stage of carcinoma-in-situ. Screening programmes for cervical cancer are designed to detect malignant and premalignant cervical changes at a phase when effective and curative treatment may be offered. In several places where well planned and conducted screening programmes exist, both the incidence and mortality from invasive cervical cancer have shown a definite decrease(3).

Who should be screened for cervical cancer?

Women who have started to have sexual intercourse are at risk of developing the precursor lesions or invasive cervical cancer. Factors associated with high risk of developing cervical cancer are the following:

- Early sexual intercourse (in teenage years)
- Multiple sexual partners
- Early pregnancy
- Urban population
- Low socio-economic status
- Cigarette smoking

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How frequently should screening be done?

The second Walton report(4) from Canada recommends annual smears for all sexually active women from age 18 till 35, whereas a 3 year interval was recommended in the first report, a change mainly due to an increased risk of early age of first coitus and multiple sexual partners. If smears remain normal, then a 5 year interval is recommended until age of 60. In the USA, 2 initial smears are recommended at an interval of one year and if normal, then subsequent smears at 1 but no more than 3 year intervals. With increasing reports of rising incidence of cervical cancer in younger women and rapidly progressive forms of the disease, a 1 year interval would be ideal below the age of 35 to detect precursor lesions. It would also seem wise to start screening soon after sexual intercourse is begun since Human Papillomavirus (HPV) may be an etiologic factor in cervical carcinogenesis. Those with HPV infection may then be identified and recruited earlier since it may be difficult to distinguish between the cytologic changes of HPV infection and precursors of cervical cancer.

How is screening done and how should a cervical/"Pap" smear be taken?

Screening is by taking of a Papanicolaou or "Pap" smear of the cervix by scraping the entire circumference of the squamo-columnar junction and sampling the endocervix. The "Pap" smear should be taken before a digital/bimanual vaginal examination to avoid trauma to the cervix. The vaginal speculum should be introduced without lubricants or minimal amount which would not contaminate the cell sample; alternatively, water may be used as lubricant. The posterior vaginal pool (fornix) cytologic sample is no longer taken as described by Papanicoloau due to consistently high false-negative rates hence the preferred term of cervical smear rather than "Pap" smear. An ectocervical scrape and an endocervical sample instead represent the best method of obtaining cervical cytology. The wooden Ayre spatula is the most widely used sampling device to obtain the ectocervical sample, the endocervical sample is best obtained either with a saline moistened cotton swab or a spatula with one prong longer than the other [eg, Wolfendale Spatula(5)].

Each sample is smeared evenly and thinly on one half of one glass slide. Too scanty and too thick smears must be avoided. The slide must be quickly fixed with absolute alcohol or other fixative before it air-dries or interpretation is difficult due to blurred cell details.

Is screening effective in reducing the incidence and mortality from cervical cancer?

Well conducted screening programmes decrease both the incidence of and mortality rate from cervical cancer in the screened population(3). In unscreened populations the risk of developing cervical cancer is 10 fold or more higher than in screened populations. There is a 50-75% decrease in the mortality rate from cervical cancer when women participate regularly in screening programmes. Regular screening with cervical smears detects premalignant lesions and invasive cancers at an earlier stage allowing conservative therapy in the former and more effective as well as highly curative therapy in the latter. The reduction in risk is clearly related to the proportion of women at risk who are screened. In Norway where only 5% of women participate, there is a slight increase in the risk of developing cervical cancer whereas in Finland, Iceland and Louisville in Kentucky, USA with almost 100% coverage the incidence of invasive cervical cancer and deaths from it have decreased. The incidence of cervical cancer has decreased in British Columbia from 39.3 in 1959 to 13/100,000 in 1973, in North East Scotland from 35.3 in 1959-1961 to 9.1/100,000 in 1979-1981 and in Sweden from 40-45 in 1967 to 12 per 100,000 in 1979. Where screening programmes do not show a decreased incidence of cervical cancer, the incidence may have increased if not for screening. Rescreening the same woman is associated with a diminishing return in terms of prevention and instead persuading women who have never had cervical smears to have the first smear is much more valuable. Protection from invasive cervical cancer is lost quite rapidly in the following 2-3 years following a single negative smear but protection is much greater after increasing number of negative smears(3); therefore regular continued screening is required for protection form cervical cancer.

What is a satisfactory cervical smear and what causes false-negative smears?

Endocervical cell presence indicates that the columnar epithelium has been sampled and by implication the squamo-columnar junction (SCJ) which is the upper limit of the transformation zone (TZ), an area of the cervix in which cervical neoplasia originates. The presence of immature metaplastic cells in the smear also indicate that the TZ has been sampled. Absence of endocervical cells may be due to receeding of the SCJ to within the cervical canal (most often in postmenopausal women) or inadequate sampling. Alternatively, in pregnancy or in those on oral contraceptives due to decreased cohesion the cells may not form sheets in smears. Smears with inadequate cells, excessive inflammatory cells or blood may be unsuitable for interpretation. Other factors that contribute to false-negative smears are inadequate fixation, air-dried smears, obscuring/lubricating substances, or those that are too thick. In a screening programme improper labelling, undercall by cytotechnicians as well as fatigue of screeners also contribute to false-negative smears.

What cell types are seen in the normal cervical smear?

In a normal smear ectocervical squamous epithelial cells, sheets of columnar endocervical cells, inflammatory cells, microorganisms (trichomonads and monilial hyphae or yeast forms) and spermatozoa may be seen together with some erythrocytes. Adequate estrogen levels cause epithelial maturation and superficial as well as intermediate squamous cells exfoliate, whereas in the presence of estrogen and progesterone or when progesterone predominates, exfoliated cells are mainly intermediate type squamous cells. Parabasal cells exfoliate in the absence of ovarian hormones since the epithelium is thin and does not mature. Endometrial cells may be seen during and soon after menstruation and up to 10 days from the start of the menstrual cycle or in endometritis, IUCD users, in those with menstrual cycle disorders and in presence of endometrial hyperplasia. In postmenopausal patients with endometrial cells in the smear an endometrial currettage is mandatory to exclude an endometrial malignancy. Cervical smears are inappropriate for endometrial cancer screening since only 30-40% of patients with endometrial cancer have malignant cells in their smear and also are of no value to screen for ovarian cancer.

What are the abnormalities identifiable in a cervical smear?

Abnormalities in the smear may be those which are benign, those with neoplastic potential [the dysplasias/cervical intraepithelial neoplasias (CIN)] and those from malignant conditions. Benign conditions such as Trichomonas vaginalis, candida organisms and postmenopausal atrophy cause degenerative and atypical changes in the epithelial cells. The spectrum of nuclear changes extend from mild to severe inflammatory change to dyskaryosis. Dyskaryotic cells may be derived from cervical cancer precursor lesions which may be any grade of CIN or microinvasive cancers. Herpes simplex infection causes severe cytopathic effects of multinucleate cells, nuclear chromatin abnormalites and giant cell formation. Human papillomavirus (HPV) infection causes koilocytosis and binucleation, nuclear hyperchromasia and keratinization of squamous cells.

Why the term "CIN" rather than dysplasia?

There is increasing preference for cervical intraepithelial neoplasia (CIN) terminology which reflects better the continuum of change in the spectrum of precursor lesions to describe changes in cervical epithelium. These changes were previously referred to as mild dysplasia (CIN 1), moderate dysplasia (CIN 2) and severe dysplasia and carcinoma-in-situ (CIN 3)(6). CIN nomenclature is preferred because it avoids the artificial and unrealistic division between severe dysplasia and carcinoma-in-situ since they are not distinct clearly definable entities but both have chromosomal aneuploidy, abnormal mitotic figures and similar precursor potential. Pathologists are unable to consistently differentiate between severe dysplasia and carcinoma-in-situ in practice. The dual terminology of dysplasias and carcinoma-in-situ led to lack of therapeutic individualization and overtreatment of small carcinoma-in-situ lesions by hysterectomy and undertreatment of large severely dysplastic lesions with conization or electro/cryo therapy.

What are the terms used to describe CIN in smear reports?

CIN is identified by cells with an increased nuclear: cytoplasmic (N:C) ratio and immature cytoplasmic differentiation. Dyskaryosis, a cytologic term, describes the nuclear characteristics of malignancy in cells from tissues with any grade of CIN. Dyskaryotic changes may however be seen in cells derived from only CIN or from an invasive carcinoma, though in the latter changes are usually much more marked. Another system of cytologic terminology used refers mainly to cytoplasmic changes in cells rather then nuclear changes, when the terms superficial cell, intermediate cell and parabasal cell dyskryosis are used as being equivalent to mild, moderate and severe dysplasia/carcinoma-in-situ respectively(7). Yet another terminology used in smear reports is of dysplasia, which however is a histologic term referring to cytologic changes in cells seen from the expected histologic condition present in the tissues from which the cells derive. This

terminology presumes an ability of the cytologist to predict from cytologic changes the histological lesions from which the abnormal cells arise. When CIN 3 or malignant cells are reported the physician/gynaecologist must be aware that cytologists cannot distinguish reliably between an in-situ lesion, a microinvasive or an invasive cervical carcinoma. The distinction between these 3 conditions is however critical and therefore a cervical biopsy for histology is required to determine the true nature of the lesion. The cytological terms in common use and the expected histological correlations are shown in Table 1.

Table 1
CYTOLOGICAL TERMS AND HISTOLOGICAL CORRELATIONS

Cytology (alternative cytological terms)	Histological correlation (equivalent terms)
Mild dyskaryosis (superficial cell dyskaryosis, mild atypia[2])	Mild dysplasia (CIN[1] 1)
Moderate dyskaryosis (intermediate cell dyskaryosis, moderate atypia)	Moderate dysplasis (CIN 2)
Severe dyskaryosis[3] (parabasal cell dyskaryosis, severe atypia)	Severe dysplasia and carcinoma in situ (both of which are included in CIN 3)
Malignant cells[3]	Invasive cancer

[1]CIN = Cervical intraepithelial neoplasia

[2]Atypia is less precise than the preferred term dyskaryosis

[3]Severe dyskaryosis may refer to cells from CIN 3 or invasive carcinoma unless there is other definite evidence of an invasive lesion, in which case malignant cells may be reported. Some cytologists report malignant cells when a smear is consistent with carcinoma in situ (CIN 3); while others use the term malignant cells only when cells of suggestive of an invasive lesion are present.

[Reproduced with permission from Hudson (1985)]

What is the role of colposcopy in diagnosis of cervical cancer and its precursors?

With greater implementation of cervical cancer screening, there is an increasing problem of how to best manage patients with abnormal smears. In the past, standard investigation and treatment has been surgical cervical cone excision or hysterectomy. With the increasing number of young, often nulliparous women with precursor lesions, cone biopsy is an excessively morbid procedure with potentially serious immediate and future complications with regard to fertility and pregnancy and hysterectomy solely for cervical cancer precusors is nearly always overtreatment. Colposocopy fulfills a critical role because it allows localisation of the abnormal area in the cervix from which abnormal cells arise and allows a conservative approach to management which is shown in Figure 1.

What is colposcopy and how does it influence management?

Colposcopy uses a binocular microscope with strong illumination to examine the cervical epithelium and subepithelial vascular patterns at magnifications from 5x to 50x. It is an outpatient clinic technique requiring no anaesthesia which allows visualization of the cervical epithelium of the transformation zone from which cervical neoplasia or its precursors arise. A directed punch biopsy is taken for histological assessment from the most severely abnormal area. Expert colposcopists can reliably

FIGURE 1
THE ROLE OF COLPOSCOPY IN MANAGEMENT OF PATIENTS WITH ABNORMAL CERVICAL SMEARS
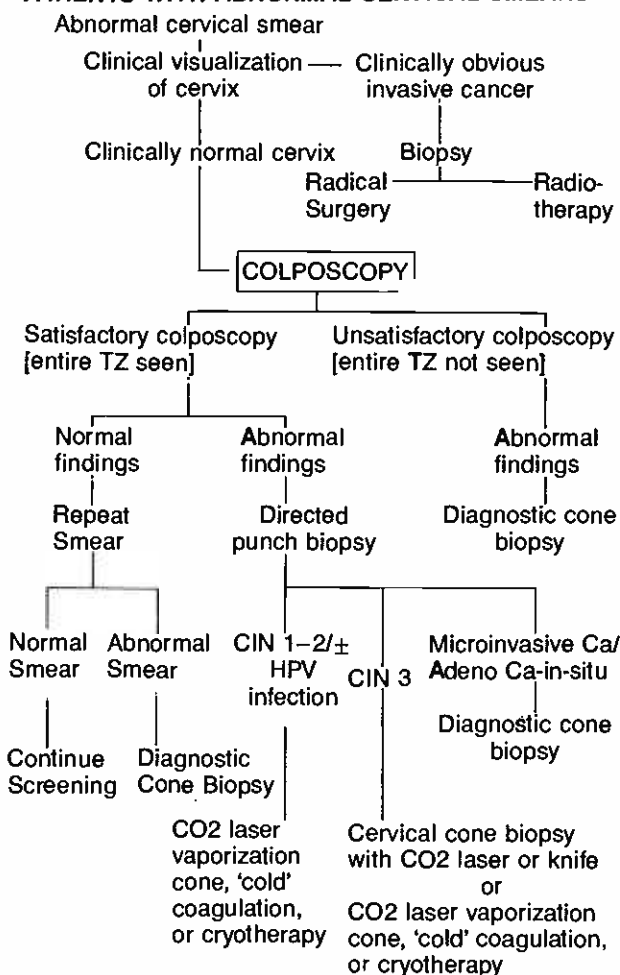
*TZ = Transformation done

predict the expected histological diagnosis(8) but treatment should await the histological report. If the entire transformation zone cannot be visualized or the cervical lesion extends into the endocervical canal or directed biopsy reports microinvasion or adenocarcinoma-in-situ, then a diagnostic (and often incidentally therapeutic) cervical cone biopsy is indicated. Cone biopsy is also indicated when cytology does not correspond to the colposcopic findings and indicates a possible invasive carcinoma or the patient not reliable for regular follow-up if destructive techniques were to be used. An additional use of colposcopy is for tailoring of the cone biopsy to suit the lesion(9). For a small ectocervical lesion a small cone or ring biopsy may be adequate while in the presence of endocervical extension the affected part of cervical canal is excised(9).

What is the role of colposcopy in screening for cervical cancer?

Colposcopy has little role as a screening tool for cervical cancer on a population basis because of the high degree of technical expertise, instrumentation and time required for an adequate examination whereas cervical smears can be used to screen far greater numbers of patients in the same time. However, colposcopy is essential to evaluate patients with abnormal cytology and ideally all patients with abnormal cytology should be seen and assessed by an expert colposcopist before any

treatment is planned (Figure 1). This is possible in most situations where adequate medical facilities exist and certainly in a local Singaporean context where patients can easily be referred locally for expert colposcopic assessment(8).

CONCLUSION

Cervical cancer screening with regular cervical smears done on a population basis has been shown to reduce both the incidence and mortality rate from cervical cancer. Proper smear taking techniques are essential to reduce the rate of false-negative smears. Colposcopy is not useful for cervical cancer screening on a population basis. It is essential however that all patients with abnormal cervical smears should be evaluated with colposcopy by an experienced colposcopist before any treatment is planned.

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