Editorial

The Adequate Cervical Smear: A Modern Dilemma

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Cervical cancer remains the only truly preventable gynecologic malignancy. Yet the goal of preventing cervical cancer deaths through use of the Papanicolaou smear remains elusive. Cervical cancer is the second most common cancer among women worldwide. Incidence and mortality rates for cervical cancer in most developed Western countries have steadily decreased since the 1950s. These decreases relate in part to the introduction of widespread cervical screening programs using cervical cytology in the 1960s. In the United States, cervical cancer incidence has fallen from 20,000 cases per year in 1960 to less than 14,000 cases per year in 1990. This decrease may be largely attributable to the success of widespread cytologic screening.

Against this background of an overall decline in the incidence of cervical cancer, the age-specific incidence rates for younger women show an alarming increase. This increase suggests that new risk factors are affecting younger generations, with varying timing and levels of impact in different countries.[1]

Furthermore, the increase in cervical cancer mortality in young women is coincident with a dramatic increase in the diagnosis and incidence of premalignant disease. This apparent change in the clinical presentation of cervical neoplasia demands continued and critical review of our approach to cervical screening.

The reference standard for screening for cervical neoplasia remains the Papanicolaou smear. When the discipline of exfoliative cytology was first launched in the late 1940s, the primary purpose of the Papanicolaou smear was to detect cervical cancer, which at that time was a scourge, almost the equal of breast cancer. It was soon realized that the Papanicolaou smear performed more efficiently in detecting intraepithelial precancerous lesions. An accepted dogma has therefore become that premalignant disease, detected by conscientious screening, can be managed by conservative therapeutic modalities that preserve fertility and reproductive capacity. With appropriate follow-up, the patient can be afforded a high degree of protection against the subsequent development of cervical cancer.

The occurrence of cervical cancer in women who have been screened and have received negative smear reports is increasingly viewed as an avoidable failure. A recent *Lancet* editorial entitled "Cancer of the Cervix: Death by Incompetence" stated that "all the necessary scientific facts for saving most of the lost lives have been known for twenty years."[2] This conviction has been widely communicated in both the medical and lay press. Worldwide, failures of the cervical screening process constitute one of the most litigious areas in women's health.

In recent years, intensive efforts have been made to improve the quality of cytologic samples provided for laboratory interpretations. Inadequate sampling and laboratory interpretation errors are the two major factors evident among women who have received negative cytologic reports shortly before the diagnosis of cancer. The false-negative rate of a single smear for high-grade squamous intraepithelial lesions (cervical intraepithelial neoplasia II to III) is widely accepted to be at least 20% to 30%. Even in the best laboratories, only about one third of these errors can be attributed to laboratory error. The remainder are due to specimen collection inadequacies.

Highly controlled sample collection is the most important factor in improving the reliability of cytologic diagnosis of cervical neoplasia. The quest for better cell samples has substantially changed the practice of cervical cytology over the past decade. A range of improved sampling instruments for collecting smears, including some specifically designed for sampling the endocervical canal (ie, Cytobrush, Cervex-Brush), have become available. Some laboratories now routinely issue such instruments to physicians who perform cervical smears.

Additionally, women whose smears lack an endocervical component but are otherwise normal are advised to have an early repeat test. "Endocervical component" refers to either endocervical columnar cells or transforma-

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ISSN 0094-3509

tion-zone, squamous metaplastic cells. This recommendation is based on cross-sectional analyses that show that women whose smears contain an endocervical component have a higher rate of reported abnormalities than women whose smears lack an endocervical component. This has been interpreted to imply that the presence of an endocervical component indicates an adequate sample. In fact, the new Bethesda System for reporting cervical smear diagnoses suggests that specimens from premenopausal women that lack an endocervical component should be reported as "less than optimal" or "unsatisfactory."[3]

The assumption underlying this classification and the recommendation of early repeat cytology is that important abnormalities may be missed on smears that lack an endocervical component. However, it should be noted that research in this area has produced no firm evidence of a higher frequency of diagnosis of squamous intraepithelial lesions (SIL) or invasive cancer in women whose previous cervical smears contained no endocervical component.

Kivlahan and Ingram (1985)[4] found no significant difference in the reporting of cervical epithelial disease on the second screening of women whose initial smear was negative and contained endocervical cells (3.3%) compared with women whose initial smear was negative but did not contain endocervical cells (3.0%). Vooijs et al (1984)[5] reported that among women whose entry smears included endocervical cells, the proportion reported as having cervical precancerous lesions at a second screening 3 years later was 1.0%. This compared with a proportion of 0.84% among women whose entry smear was reported as not including endocervical cells.

In a recent milestone study from the Victorian Cytology Service, Melbourne, Australia, Mitchell and Medley[6] reported results of a longitudinal analysis of 20,222 women who received negative cervical smear reports in 1987. The subsequent incidence of SIL was not significantly higher in women whose initial smear was negative but lacked an endocervical component compared with women whose initial report was negative with an endocervical component.

This is not intended to underemphasize the importance of careful sampling of cells from the cervix. In the 1990s, a Papanicolaou smear should be taken using an Ayre's type cervical spatula (wooden or plastic) and an endocervical brush. A saline-moistened cotton-tipped applicator is not optimal for endocervical sampling. The cotton-tipped applicator is difficult to insert into a tight endocervical canal, particularly in nulliparous or postmenopausal women or in the post-treatment patient. Furthermore, reliable transfer of adequate cell numbers from the cotton-wool mesh is difficult.

Both the Cytobrush and Cervex-Brush obtain superior samples with greater total numbers of cells, more frequent presence of an endocervical component, and greater numbers of endocervical or metaplastic cells. Care should be taken to use these instruments in a manner that ensures the most reliable sampling. An article in this issue of the Journal by Ferris et al[7] addresses the most appropriate use of the Cervex-Brush. If a spatula and Cytobrush are used, the ectocervical specimen is first collected and held without plating it onto a slide. The endocervical sample is then collected. Both specimens should be plated normally onto a single slide and promptly fixed. The brush specimen can be smeared over the spatula specimen or on a separate section of the slide. The single slide collection may reduce the backlog of Papanicolaou smears now found in some cytology laboratories.

The incidence of cervical adenocarcinoma and glandular intraepithelial neoplasia has greatly increased over the past two decades. These lesions may occur exclusively within the endocervical canal and mandate adequate endocervical sampling in cervical screening. Abnormal endocervical cells in a smear indicative of glandular neoplasia demand appropriate investigation and management.

The more widespread use of endocervical sampling instruments in cervical screening has greatly increased the numbers of endocervical columnar cells in smears. Some laboratories have had difficulties in interpreting these increased numbers of glandular cells, particularly in the presence of nonspecific inflammatory nuclear atypia. The frequency of reporting "atypical glandular cells" in Papanicolaou smears has significantly increased. This is a difficult diagnosis for the clinician. Glandular neoplasia must not be missed, but cytologic overcall can result in unnecessary and aggressive interference, such as cone biopsy. Therefore, the clinician should insist that the laboratory reevaluate the smear to determine whether the "atypia" seen is suggestive of glandular neoplasia. Such a smear may require referral for expert reevaluation.

If a cervical smear is carefully collected from the ecto- and endocervix, but is reported as lacking an endocervical component (as occurs in a small but significant proportion of smears), there is no compelling evidence that immediate or early repeat testing is of value. If the woman is identified for any reason as being at increased risk of cervical neoplasia, however, a repeat smear in 3 months is indicated.

Repeated testing incurs a significant financial burden in addition to anxiety about possible missed abnormalities. These are disproportionate to any likely benefit. Nonetheless, the clinician must deal with the patient apprehension and medicolegal implications of a smear reported as "unsatisfactory" or "less than optimal" on the basis of absent endocervical cells. There is no consensus

on what constitutes an adequate sample. This considerable dilemma for the patient and her physician is readily solved if the laboratory is willing to add a statement such as, "Presence or absence of endocervical cells is not the sole criterion of specimen adequacy," thus removing the requirement for early repeat cytology for patients where it is not otherwise indicated.

False-negative Papanicolaou smears have been studied for over 40 years. If these facts have been recognized for some decades, why has the issue become of such recent social and medicolegal importance? The explanation relates to a woman's expectations. Her expectation is that if she has cervical cancer or a significant precancerous lesion, it will be detected at that single screening visit rather than by serial testing involving delayed diagnosis with attendant risk of progression. This expectation is not unreasonable. However, it demands that health-care professionals perform cervical screening in a thoughtful and conscientious way so that the cytologic specimen contains cells from the cervical areas most often involved in disease states.

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