Editorial

Papanicolaou Testing and Colposcopic Screening

John E. Hocutt, Jr, MD, Richard R. Clark, MD, John L. Pfenninger, MD, and Patricia Queripel

Wilmington, Delaware, and Midland, Michigan

For the last 40 years, the Papanicolaou test has been used as a screening procedure for cervical cancer. Although few would doubt its effectiveness in decreasing the morbidity and mortality associated with invasive cancer of the uterine cervix, its accuracy and ultimate usefulness as a definitive screening tool have been recently questioned.[1–4] In comparison to the Papanicolaou test, colposcopy is a more sensitive technique for the identification of early cervical intraepithelial neoplasia (CIN) and the human papillomavirus (HPV).[1,2,5] Colposcopy is even more effective if used in conjunction with the Papanicolaou test. In a recently published article in the *Journal of the American Medical Association*, Koss stated: ". . . an optimal cancer detection system should probably consist of a cervical smear and colposcopy."[4]

As reported in their article in *The Journal of Family Practice*, Shepherd and Lynch[5] have begun the data collection we so desperately need to compare the effectiveness of the Papanicolaou test with that of colposcopic biopsy. They rightfully point out that such comparison involves many factors including the laboratory, the patient, the clinician, and the disease process and, therefore, a very large number of patients must be studied before definitive conclusions can be made. However, their small study did not include a colposcopic examination of women who had "normal" Papanicolaou tests. There may be risk in following only the 16% of patients with CIN I as detected by Papanicolaou tests until we have conclusive data on the rate of progression of koilocytosis to dysplasia and on the number of cases of CIN not detected by Papanicolaou smears. The data Shepherd and Lynch have started to collect are vital to the practicing family physician who must decide how to screen and follow patients who are at higher risk for developing cervical cancer.

From the Department of Family Medicine, Medical Center of Delaware, Wilmington (Drs Hocutt and Clark and Ms Queripel), and The National Procedures Institute, Midland, Michigan (Dr Pfenninger). Requests for reprints should be addressed to John E. Hocutt, Jr, MD, Medical Center of Delaware, Department of Family Medicine, 2002 Foulk Rd, Suite C, Wilmington, DE 19810.

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In this issue of the Journal, Pfenninger[6] has provided insight on colposcopic examinations of women who had abnormal Papanicolaou tests or high-risk clinical histories. In his study, cervical dysplasia was a very frequent finding in the young female population, and family practice residents were found to be quite effective as beginner colposcopists. Many of the Papanicolaou tests did not demonstrate the dysplasia that was discovered on follow-up colposcopy. Data on colposcopic examination of patients who had normal Papanicolaou tests would be very informative.

One way to protect patients while collecting the above clinical information is to use colposcopy in conjunction with the Papanicolaou smear to screen patients. We have recently performed both Papanicolaou testing and colposcopic screening on 44 sequential patients. The high incidence of HPV and CIN found by screening colposcopy and the low incidence rate found by Papanicolaou testing was disturbing in our small series. Of the 20 patients in whom HPV was detected by biopsy (a prevalence rate of 48%), Papanicolaou tests had detected HPV in only three.

The Papanicolaou test continues to be the screening method of choice for invasive cancer of the uterine cervix, but it does have several drawbacks.[4,7] It is a relatively insensitive method for detecting HPV and CIN I. Early detection of HPV types 16 and 18 (the ones most often found on cervical biopsy and believed to be the most frequent precursor for cervical cancer[8–10]) or CIN is likely to be critical in our efforts to reduce or eliminate cervical cancer.[11]

It has been argued that although the Papanicolaou test may not be very sensitive in detecting the early stages of CIN, it is unlikely that more serious pathology (CIN III or beyond) is undetected.[2] Since the introduction of routine Papanicolaou testing, the incidence and mortality from invasive cervical cancer has decreased dramatically.[12] However, we may be on the verge of a reversal of this trend as a result of the recent epidemic of cervical HPV and CIN.[13–17]

Less than 4% of all cancer deaths in the United States in 1990 were due to cervical cancer.[12] Although screening with Papanicolaou tests has helped to bring us to this point, it has not led to the eradication of cancer of the uterine cervix in any of the populations in which it has been studied.[4] Beral predicted a 60% increase in cervical cancer and a 70% increase in mortality in women under the age of 50 years by the mid-1990s.[17] The British Medical Association concluded that more than a 70% increase in mortality from cervical cancer was possible by the 1990s in Great Britain[18] in spite of routine Papanicolaou testing. Such figures parallel increases in HPV and CIN noted over the past 15 years in Great Britain and the United States, and could be modified by earlier detection and treatment.

De Villiers et al evaluated 9295 routine smears obtained from three gynecologic hospitals.[19] They examined these for HPV using filter in situ hybridization, and found that of the 8755 negative cytologic smears, 9% were positive for HPV DNA (whereas only 2% of the abnormal smears were suggestive of HPV). The majority of these were HPV types 16 and 18. The authors went on to conclude that the 9% DNA-positive figure was probably an underestimate of the actual rate of HPV infection by a factor of two or three. In light of De Villiers' data, the 48% prevalence of HPV seen in our data may be within the anticipated norm. In addition, a report in 1989 by the American College Health Association presented data supportive of a 40% to 50% prevalence of HPV in the reproductive age group.[19]

It is unclear how frequently or how quickly HPV without evidence of concomitant dysplasia progresses to cervical cancer. Nash reported in 1987 that one third of 45 cases of biopsy-confirmed HPV of the cervix progressed to CIN within 1 year.[20] Mitchell, in 1986, reported that of 846 women with HPV, 30 progressed to histologically proven carcinoma in situ within 6 years. Fifty others had cytologic evidence of dysplasia, but a biopsy had not been performed on these patients at the time the article was published.[21] Other studies have shown that more serious lesions may coexist with HPV and may not be initially apparent on cytologic evaluation.[22]

The Papanicolaou test also has limited sensitivity in the early identification of CIN. Our study identified five patients with CIN I histologically, but none of these were identified cytologically by Papanicolaou test on an adequate specimen. A study by Giles involving 200 asymptomatic women noted a prevalence of 5% for CIN detected by cytology alone; but when colposcopy was also used, the prevalence increased to 11%.[2] There was a 58% false-negative rate for smaller lesions (ie, CIN I and II) with the Papanicolaou test. These data support that of Fetherston who stated that the false-negative rate for a single Papanicolaou smear in women with lesions confirmed histologically can be as high as 50%.[23]

The importance of earlier identification of CIN lies in the anticipated earlier treatment and closer monitoring for advanced lesions. CIN should be treated in order to prevent the development of invasive cervical carcinoma.[11]

The idea of using a diagnostic tool such as the colposcope as a screening device will almost certainly be challenged. It does not fit the usual requirements of a screening test because it is labor-intensive, not widely available, and expensive. However, by changing the manner in which the colposcope is used and by increasing the number of practitioners proficient in its use, it could become a true screening technique.

If family physicians include a brief colposcopy screening examination, at no additional charge, with their regular pelvic examination of sexually active women, then those with colposcopic abnormalities could be identified and brought back for a complete examination. The cost for women without abnormalities would not increase. The follow-up examination should follow the protocol normally used for evaluation of an abnormal Papanicolaou smear.

A model for addressing the problem of overwhelming a subspeciality with additional screening has already been clinically tested. A somewhat similar situation existed 10 years ago when screening and diagnostic flexible sigmoidoscopy were introduced. It quickly became evident that gastroenterologists alone were not able to perform the number of necessary routine screening and diagnostic flexible sigmoidoscopy examinations. Family physicians skillfully stepped in to fill the void. Likewise, family physicians should have little trouble incorporating screening and diagnostic colposcopy into their patient services.

Colposcopy is quickly becoming a standard of care for family physicians. In a survey of family medicine residencies in the fall of 1989, 384 programs were contacted; 280 provided responses (Clark RR and Walters DT. Wilmington Hospital, The Medical Center of Delaware, unpublished data, 1990). Eighty-nine percent of respondents stated that their residents were trained in or exposed to colposcopy as a part of the residency program. Thirty-nine percent said that their residents were taught colposcopy in the family practice office, while 50% said that residents were taught outside the office.

The high prevalence of HPV and CIN leads us to the following conclusions:

1. We are in the midst of an epidemic of HPV and CIN. This epidemic may alter the prevalence of cervical carcinoma unless changes in screening practices occur.
2. Identification of cervical HPV is important and the

Papanicolaou test alone is inadequate for timely detection. Colposcopic examination is necessary to identify the majority of individuals infected with the virus.

3. Early identification of CIN (ie, CIN I and II) is preferable to later identification (CIN III) and is more likely to occur if a "screening" colposcopic examination is combined with the Papanicolaou test.

The US Preventative Services Task Force states that ample evidence exists that early detection and "treatment of precursor cervical intraepithelial neoplasia can lower mortality from cervical cancer."[24]

Screening colposcopy may be quite effectively used by family physicians to significantly increase the diagnostic accuracy of pelvic examinations. The prevalence of HPV in a family physician's practice is likely to be much higher than most physicians expect. The importance of earlier HPV detection than the Papanicolaou test provides needs further study. Screening colposcopy may not only be the first step in uncovering the extent of a precancerous problem, but may also provide the initial data needed to formulate a clinical plan to deal with the problem.

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