Cervical cancer is preventable, but it is the second most common gynecologic cancer worldwide and the third most common cancer in women in the United States (American College of Obstetricians and Gynecologists [ACOG], 2003). Approximately 11,070 new cases and 3,870 deaths from cervical cancer occurred in 2008 in the United States (American Cancer Society [ACS], 2008). The incidence and mortality rates of cervical cancer are higher among women who do not obtain regular cervical cancer screening (ACS; Centers for Disease Control and Prevention, 2005).

Cervical cancer screening with the Papanicolaou (Pap) smear has been identified as an effective method of prevention (Berman, 2006; Camillo, 2006; Farley, McBroome, & Zahn, 2005; Feldman, 2003; Sirovich, Feldman, & Goodman, 2008; Solomon, Breen, & McNeel, 2007). The Pap smear detects precancerous lesions, for which effective treatments exist (Brink, Snijders, Meijer, Berkhof, & Verheijen, 2006; Feldman; Miller et al., 2003; Valdespino & Valdespino, 2006). The five-year survival rate for localized cervical cancer is 92%, whereas women with invasive cervical cancer have a five-year relative survival rate of only 72% (ACS, 2008). However, the relative survival rate is 100% if precancerous lesions are detected and treated (ACS).

A clinician recommendation is one of the strongest predictors of adherence with Pap smear testing (Markovic, Kesci, Topac, & Matejic, 2005; Ruffin, 2003). Yet despite the recommendations depicted in Table 1, Pap smear intervals are inconsistent among clinicians. Some clinicians have extended the screening interval among 35-year-old women with three documented negative Pap smears (Murphy, Schwarz, & Dyer, 2008), whereas other clinicians admit to uncertainty regarding Pap smear interval (Feldman, 2003; Shell & Tudiver, 2004) and continued annual Pap smear testing among low-risk women (Murphy et al.; Saint, Gildengorin, & Sawaya, 2005; Sawaya et al., 2003). Low-risk women are those who comply with regular cervical cancer screening, have no history of cervical cancer, and are not immunocompromised (Feldman).

The purpose of this article is to review the optimal screening interval for low-risk women who are 30 years of age or older and have an intact cervix. That age group is of particular interest because, although cervical cancer is diagnosed most commonly in the fifth decade of life, the average age of diagnosis is 47 years, and approximately half of the cases are diagnosed in women who are younger than 35 years of age (Waggoner, 2003).

Paradigm Shift

High-risk human papillomavirus (HPV) has been implicated in abnormal Pap smear results (Vo et al., 2004) and in cervical cancer (Denny & Wright, 2005; Merck & Co., Inc., 2006; Waggoner, 2005) (see Figure 1). Infection with HPV may be transient (ACOG, 2003; Berman, 2006; Goldie, Kim, & Wright, 2004; Sykes, Reddy, & Peddic, 2005) or persistent (Brink et al., 2006). Additionally, a long latency period occurs between infection with the virus and cervical cancer (Berman; Sirovich et al., 2008; Waxman, 2004).

Newer liquid-based cytologic tests (e.g., ThinPrep®, Cytcorporation; Sure Path™, BD Diagnostics) that facilitate HPV testing are in use (Walling, 2003). They may be used alone or in conjunction with cytology (Denny & Wright, 2005). The newer tests are more sensitive than the regular or conventional Pap smear (Biscotti et al., 2005; Mariani, 2004; Mayrand et al., 2007).

Literature Review

A literature review for 2003–2008 was conducted to determine evidence-based practice recommendations regarding optimal cervical cancer screening intervals for women 30 years or older with an intact cervix. Nonexperimental studies are used in the discussion because no randomized clinical trials are available to assist in determining cervical cancer screening intervals (Van den Akker-van Marle, van Ballegooijen, & Habbema, 2003; Sirovich et al., 2008). The reviewed studies did not provide the required evidence because: (a) most studies involved triennial cervical cancer screening using predominantly the conventional Pap smear with or without three previous consecutive negative results, and (b) only...
one study compared conventional Pap smear with liquid-based cytology and reflex HPV DNA testing and liquid-based cytology with HPV testing among women who were 30 years of age or older. Investigators in three studies found an increased risk of cervical cancer when the screening interval was extended to three years. Sawaya et al. (2003) used the Markov model to estimate the rate of progression of cervical dysplasia to cervical cancer among 30- to 64-year-old women (N = 31,728) who obtained annual Pap smears compared to those who obtained triennial Pap smears. The investigators found that if a Pap smear was obtained triennially with mostly the conventional method, after three or more negative results, women who were 30–44 and 45–59 years of age had an increased risk of cervical cancer of 2 per 100,000 and 1 per 100,000, respectively (Sawaya et al.). No increased risk was found for cervical cancer among the 60- to 64-year-old women. The study adds to the preponderance of evidence regarding the efficacy of annual screening with the conventional Pap smear and new evidence for annual screening with the newer liquid-based cytology.

During a matched case-control study of women with at least two consecutive negative Pap smears (N = 1,416), investigators found a significantly increased relative risk of invasive squamous cell cervical cancer at two-year (p = 0.013) and three-year intervals (p = 0.007) compared to a one-year interval (Miller et al., 2003). No significant difference was found between two- and three-year intervals (Miller et al.). The investigators agreed on a small absolute risk of developing invasive cervical cancer during the three years after a negative smear (Miller et al.). The authors recommended the use of newer cytologic tests in evaluating optimal screening intervals.

Priest et al. (2007) conducted a descriptive study among women younger than 80 years of age who were diagnosed with invasive cervical cancer (N = 371). The investigators found that 50% of cases of cervical cancer were present among women who were not screened within the previous three years.

All three of the studies provide supporting evidence for the efficacy of the annual conventional Pap smear in reducing the risk of cervical cancer. Therefore, the recommendation by the U.S. Preventive Services Task Force (2006) that women may obtain triennial screening using the conventional Pap smear is not supported by the evidence. Furthermore, because of the low sensitivity of conventional Pap smears, clinicians should perform them frequently to prevent cervical cancer (Priest et al., 2007). The sensitivity of newer liquid-based cytology alone and in combination with HPV DNA testing is higher than that of the conventional Pap smear; cytology with HPV DNA has a sensitivity of 100% (Mariani, 2004; Mayrand et al., 2007). Therefore, whenever they are used in screening for cervical cancer, less frequent screening likely will be necessary because fewer false-negative results will occur.

Goldie et al. (2004) used a state transition mathematical model to simulate the natural history of HPV and cervical cancer. The investigators found that the lifetime reduction of cervical cancer was higher among women 30 years of age or older who obtained triennial screening with liquid-based cytology and HPV DNA testing (90%–92%) compared with annual screening with the conventional Pap smear (89%). That is the only study identified that incorporated all three testing methods in Table 1.

## Conclusion

Insufficient evidence exists in the literature to make any practice recommendation regarding the ACOG and ACS guidelines in Table 1. To determine screening interval, clinicians should consider the natural history of cervical cancer and the sensitivity of the Pap test (Miller et al., 2003; Sirovich et al., 2008). Based on the aforementioned premise, clinicians can accept the recommendations of the ACS and ACOG, but further research should evaluate the new guidelines. Additionally, clinicians should educate women regarding continuing annual gynecologic visits and perform annual risk assessment. Risk assessment

\[
\text{Figure 1. Light Microscopy of Cervical Smear Cells Showing Typical Cytologic Indicators of Infection With Human Papillomavirus}
\]

\[
\text{Note. Copyright 2009 by Roger Dachez/Photo Researchers, Inc. Used with permission.}
\]
allows clinicians to determine whether a woman's low-risk status has changed. Women who engage in sexual activity at an early age and those who have multiple sexual partners are more likely to be infected with the oncogenic strains of HPV, which are the primary cause of cervical cancer (ACS, 2008). HPV infection may persist and progress to cancer in women who are immunosuppressed, smoke cigarettes, have poor nutrition, are multiparticuous or use oral contraception over a long period of time (ACS). Therefore, women should be assessed for the presence or absence of those factors.

Author Contact: Denise M. Linton, DNSc, FNP, BC, can be reached at dlinton@lsuhsc.edu, with copy to editor at CIONEditor@ons.org.

References


