

Cervical cancer screening in pregnancy

Impact of the latest ASCCP guidelines

By Alan G. Waxman, MD, MPH, and Meggan M. Zsemlye, MD

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EDUCATIONAL OBJECTIVES

After participating in this activity, physicians should be able to:

- Explain why a prenatal visit may be a good opportunity to review whether a woman should have a Pap test.
- List the revised ASCCP Consensus Guidelines for the Management of Cytological Abnormalities and Cervical Intraepithelial Neoplasia that relate to pregnant women and adolescents.
- Describe strategies for managing adolescents, pregnant or non-pregnant, with positive Pap smear results.
- Explain the physiological changes to the cervix in pregnancy that make a colposcopy examination challenging.

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Significantly fewer women are getting cervical cancer—and dying from it—thanks to the widespread use of the Pap test over the past 50 years.¹ Since at least the mid-1960s, a Pap test has been a routine part of prenatal care and the post-partum visit.²

While pregnancy, per se, does not increase a woman's risk of developing cervical cancer, it gives you a chance to assess whether a patient has had a Pap within the recommended screening intervals. Our goals in this article are to discuss the timing of cervical cytology screening in pregnancy and the latest recommendations for managing abnormal Pap tests during pregnancy and to offer some helpful tips for performing colposcopy in pregnancy.

Some 42% of cervical cancers are diagnosed during the reproductive years (ages 15–44).³ It should come as no surprise, therefore, that invasive cervical cancer has been reported in up to 0.1% of prenatal patients at large referral centers. The rate of preinvasive CIN 3 is much higher.⁴ Most women diagnosed with cervical cancer have not had a Pap test within the previous 5 years, if ever.⁵

HPV testing and research sparked the revision of the ASCCP's 2001 Consensus Guidelines. Here's what you need to know about the major changes in recommendations for managing pregnant women with abnormal cytology results.



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Pap tests during pregnancy


Does every woman need a Pap test as part of her prenatal care? Clearly, the Pap history of every new prenatal patient must be carefully reviewed. If she has not had a Pap within the recommended screening interval for her age and history, the initial prenatal exam is the ideal time to perform it. On the other hand, if a woman wouldn't be due for a Pap test were she not pregnant, adding a cytology exam at this time does little to prevent cervical cancer. There's no good evidence that pregnancy increases the risk of developing cervical lesions in human papillomavirus (HPV)-positive women, nor does existing dysplasia progress more rapidly during pregnancy.⁶

The American College of Obstetricians and Gynecologists and the American Cancer Society agree that a woman should have her first Pap test at age 21 or about 3 years after the onset of vaginal intercourse.^{7,8} Cytology screening should continue annually until age 30 if conventional cytology is used. If *liquid-based* cytology is used, however, the American Cancer Society allows for Pap tests every other year during this period. After age 30, if the previous three Pap test results

were reported as negative for intraepithelial lesion or malignancy, the interval between Pap tests may be extended to 2 to 3 years. HPV DNA testing may be added to Pap screening at age 30.^{7,8} As noted above, there's no evidence to suggest modifying these screening intervals during pregnancy.

The technique for performing the Pap test in pregnancy is no different than for a nonpregnant patient, although a bit of additional gentleness is appropriate, as the tissue is likely to bleed more easily. Both broom device and Ayre spatula with cytobrush can be safely used,⁹ but avoid a moistened cotton swab; it's less sensitive than the first two.⁴

Be sure to alert the pathologist to your patient's pregnancy by noting it on the cytology requisition, because otherwise several cytologic findings particular to pregnancy can be mistaken for neoplastic abnormalities. For example, degenerated decidual cells and clusters of cytotrophoblast cells might mimic high-grade squamous intraepithelial lesions (HSIL). Also, syncytiotrophoblast cells with perinuclear cavitation and nuclear atypia are occasionally mistaken



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DR. WAXMAN is Professor and DR. ZSEMLYE is Associate Professor, Obstetrics and Gynecology, University of New Mexico, Albuquerque, NM.

for HPV changes, and Arias-Stella reaction may produce cells that appear similar to adenocarcinoma.⁴

Managing abnormal Paps in pregnancy

The widespread clinical use of HPV testing and recent research into HPV and cervical cancer prompted new evidence-based management guidelines. These were developed in a September 2006 consensus conference sponsored by the American Society for Colposcopy and Cervical Pathology (ASCCP), with representation from 29 professional organizations.¹⁰ This revision of the ASCCP's 2001 Consensus Guidelines has had a substantial impact on the management of pregnant women with abnormal cervical cytology.

Gravidas: a "special population."

Pregnant women are considered a special population under the 2006 ASCCP Guidelines.¹⁰ Those with cervical cytology showing abnormal squamous cells of undetermined significance (ASC-US) should be managed the same way as nonpregnant women with ASC-US. The three acceptable follow-up methods in patients older than 20 are:

- 1 repeat Pap testing in 6 months,
- 2 testing for the presence of high-risk HPV, or
- 3 immediate triage to colposcopy.

A repeat Pap showing ASC-US or worse or a positive HPV test should trigger referral to colposcopy. More than three-quarters of reproductive-aged women with cytologic evidence of low-grade squamous intraepithelial lesions (LSIL) will test positive for high-risk HPV.¹¹ Therefore, HPV DNA testing is neither cost effective nor clinically useful as a triage test for LSIL in pregnant women.

While colposcopy is the preferred option in pregnant women older than 20


with HPV-positive ASC-US or LSIL, it is also acceptable to defer colposcopy until 6 or more weeks' postpartum. All women with a Pap result of ASC-H (atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion) should have colposcopic evaluation.

Teens: another "special population."

Adolescents, pregnant or not, are also considered a special population. Their risk for invasive cervical cancer is extremely low, 0.1 per 100,000.³ On the other hand, the prevalence of HPV is very high in sexually active young women, as are the chances for acquiring new HPV infections. Therefore, the finding of a positive HPV-DNA test before age 21 has little clinical utility and should not be ordered. But if an HPV test is inadvertently ordered and found to be positive, disregard the result. Moreover, most dysplasias in this age group regress spontaneously over time.^{12,13}

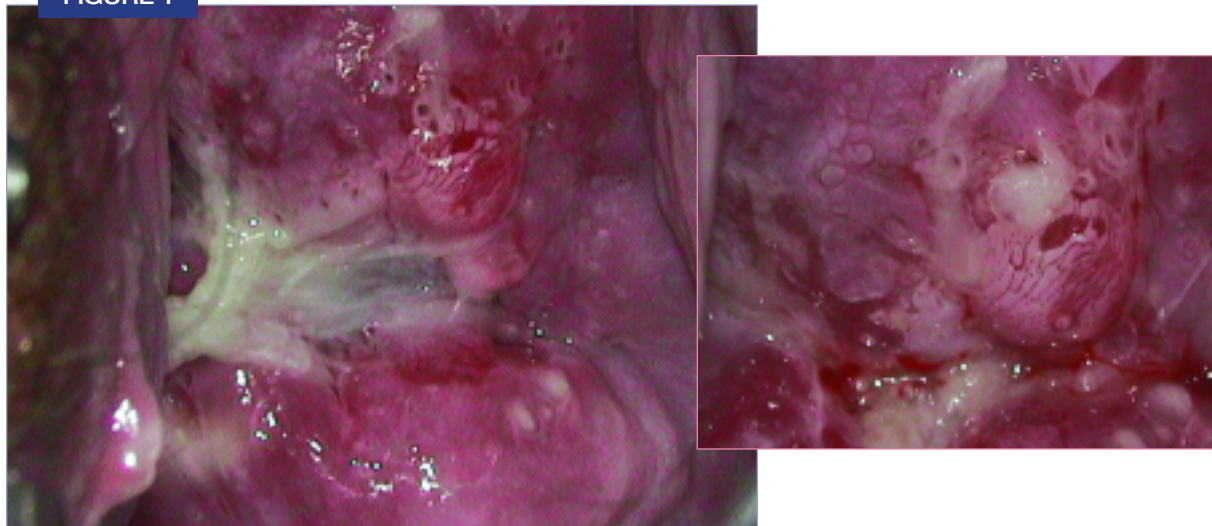
With this in mind, and given recent findings of increased prematurity risks in women who become pregnant after being treated for dysplasia,^{14,15} the 2006 Consensus Guidelines recommend a very conservative strategy for abnormal Pap tests in this age group. (For an algorithm outlining these steps, see Wright TC Jr, Massad LS, Dunton CJ, et al. 2006 consensus guidelines for the management of women with abnormal cervical screening tests. *J Low Genit Tract Dis.* 2007;11:201-222, or go to the following page on the ASCCP Web site: www.asccp.org/consensus/cytological.shtml.)

Adolescents, pregnant and nonpregnant, with ASC-US or LSIL should simply be followed with repeat cervical cytology annually for 2 years. Colposcopy should not be performed unless the first of these repeat Paps shows HSIL or worse or the second repeat Pap result an additional 1 year later is ASC-US or worse. This safely allows time for HPV infections and dysplasia to spontaneously regress without overtesting and overtreatment. At the same time, this strategy



Disregard the result if an HPV DNA test for a patient <21 years is inadvertently ordered and is positive. . .

FIGURE 1



Colpophotograph showing the cervix of a 31-year-old G3, P2 carrying twins at 20 weeks' gestation was taken after 5% acetic acid was applied. The patient's Pap test was reported as HSIL. She smokes half a pack of cigarettes per day and is HIV negative. Note the acetowhite epithelium with neovascularization from both dysplasia and pregnancy. A coarse mosaic pattern is present with atypical vessels. A biopsy of the area in the inset (right) showed only CIN 2. She delivered prematurely at 29 weeks' gestation. A LEEP performed 3 months postpartum was negative for dysplasia.

permits timely diagnosis when high-grade lesions persist.

A cytology result of HSIL in a pregnant woman of any age should trigger referral to colposcopy (Figure 1). Ideally, perform this colposcopy only if you're experienced in performing colposcopy in pregnant patients. Biopsy of lesions that appear consistent with HSIL or cancer is preferred, but it's acceptable to biopsy other lesions.¹⁰ Reassure patients that there's no evidence that colposcopy, with or without biopsy, is dangerous during pregnancy. In contrast, endocervical curettage is not acceptable in pregnancy (Table 1). Unless you've diagnosed CIN 2 or worse on colposcopy, follow-up with cytology and colposcopy is recommended no sooner than 6 weeks' postpartum.

If, on the other hand, you diagnose CIN 2 or 3 during pregnancy, cytology and colposcopy may be repeated, but no more often than every 12 weeks. And don't repeat the biopsy unless the lesion appears worse on repeat colposcopy or

TABLE 1

Colposcopy in pregnancy

- Perform only if an experienced colposcopist.
- Don't rely on your colposcopic impression.
- Colposcopy is preferred with HPV-positive ASC-US or LSIL, but may be deferred until postpartum.
- Biopsy (recommended) if HSIL Pap.
- If HSIL, wait at least 12 weeks before repeating colposcopy, and then biopsy only if lesion appears worse.
- Do NOT perform endocervical curettage in pregnancy (contraindicated).
- Barring cancer, defer treatment until after postpartum assessment.

ASC-US—atypical squamous cells of undetermined significance

LSIL—low-grade squamous intraepithelial lesions

HSIL—high-grade squamous intraepithelial lesions

Source: Based on data from Wright TC, et al.¹⁰

TABLE 2

Tricks of the trade for performing colposcopy in pregnancy

- Use the largest speculum that can be comfortably inserted.
- Hold back obscuring vaginal sidewalls with vaginal sidewall retractor or condom over the speculum.
- Use 5% acetic acid to help coagulate the obscuring mucus.
- Use the ring forceps to gently remove some of the mucus. (Overly aggressive attempts will result in bleeding.)¹
- Carefully examine each quadrant of the cervix. It's easy to miss subtle changes with an enlarged cervix.
- Remember, the ring forceps make an excellent endocervical speculum.
- Don't hesitate to biopsy if a high-grade lesion is suspected. The colposcopic impression is insensitive; cancers might be missed without biopsy.
- Biopsies are safe and you can minimize bleeding by using a two-handed technique: biopsy with one hand and hold a small cotton swab with Monsel's at the ready in the other.

the initial Pap is suspicious for invasive cancer. Avoid diagnostic excision procedures (LEEP or cold knife conization) during pregnancy unless you suspect invasive cancer. Likewise, do not treat cervical lesions unless invasive cancer is diagnosed.¹⁶

Manage a Pap diagnosis of atypical glandular cells (AGC) in pregnancy the same way you would for a non-pregnant patient, except that endocervical curettage is contraindicated.¹⁰ This is somewhat problematic, as it is disease in the endocervical canal that is of interest. Colposcopy is unreliable for diagnosing adenocarcinoma in situ of the cervix (AIS). On the other hand, most lesions uncovered by a Pap

diagnosis of AGC are squamous. They are usually located adjacent to the squamocolumnar junction and therefore should be diagnosed on biopsy. Biopsy-proven adenocarcinoma in situ (AIS) in pregnancy may be managed the same way as high-grade squamous dysplasia (CIN 2,3). While vaginal delivery at term is usually allowed, it's advisable to consult with a gynecologic oncologist.

Colposcopy technique in pregnancy

The physiologic changes to the cervix as pregnancy progresses can make the colposcopy examination challenging for even the most experienced colposcopist (Table 1 and 2).

- ▶ The cervix becomes increasingly larger, softer, and more elastic. High estrogen levels evert the endocervix. This can be of practical advantage when the colposcopy exam is not satisfactory. If the patient is early in her pregnancy, repeating the exam in 4–6 weeks generally exposes the entire squamocolumnar junction.
- ▶ Along with increasing eversion of the cervix come proliferation and hyperplasia of endocervical papillae. The tips of these papillae commonly undergo metaplasia and acetowhitening.
- ▶ Nabothian cysts proliferate.
- ▶ The hyperplastic endocervical tissues secrete increased amounts of tenacious, obscuring mucus.
- ▶ The increasingly elastic vaginal sidewalls may intrude on the colposcopist's visual field.
- ▶ The colposcopic impression is less reliable in pregnancy. Neovascularization is enhanced and produces prominent mosaic and punctuation pattern, which may herald only low-grade dysplasia. Decidualization of the cervical stroma can produce nodules mistaken for cancer.

Do a Pap at the prenatal exam if she has not had one within recommended screening intervals. . .



**A thorough
colposcopy exam
should precede
postpartum
treatment. . .**

Spontaneous regression of high-grade dysplasia has been observed after delivery. One team of researchers followed 153 women, of whom 82 had CIN 2 on antepartum biopsy and 71 had CIN 3.¹⁷ Some 68% of those with antepartum CIN 2 and 70% of those with CIN 3 regressed to CIN 1 or negative on postpartum exam. Only 7% of those with CIN 2 progressed to CIN 3, and none developed cancer. The rate of regression was the same among those who delivered by cesarean as those who delivered vaginally.

Other investigators reported a 34.2% postpartum regression rate in 77 women with carcinoma in situ (CIN 3) in pregnancy. Two patients developed microinvasive carcinoma.¹⁸ A thorough colposcopy exam should therefore precede postpartum treatment. This exam should be deferred until at least 6 weeks after

delivery to allow regression of the cervical changes of pregnancy.

In conclusion, since the common ages for new diagnoses of cervical cancer overlap the ages at which women conceive, the timing of Pap screening is no different in pregnancy than in the nonpregnant state. Once you find a cytologic abnormality, however, pregnancy requires you to modify management to minimize morbidity and discomfort while maximizing the opportunity for timely diagnosis of cancer and premalignant changes. You can safely defer treating all but frankly invasive cancer until after delivery at term. If invasive cancer is diagnosed, both a gynecologic oncologist and maternal-fetal medicine subspecialist should be involved in discussing when and how delivery should take place. ◀

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