Overview

Despite a significant decrease in the incidence and mortality of cervical carcinoma in the United States, an estimated 12,200 women will be diagnosed with the disease in 2010, with 4210 expected deaths. High-risk groups include women without access to health care and those who have immigrated to the United States from countries where cervical cancer screening is not routinely performed. Because cervical cytology screening is the current method for early detection of this neoplasm, the purpose of these guidelines is to provide direction for the evaluation and management of cervical cytology.

These guidelines include recommendations on screening techniques, initiation, and frequency of screening, and management of abnormal screen-
ing results including colposcopy. Cervical cytology screening techniques include liquid-based cytology or conventional Papanicolaou (Pap) smears. Unless specifically noted, these techniques are collectively referred to as cervical cytology in this discussion.

Human papillomavirus (HPV) DNA testing for primary cervical cancer has been approved by the FDA; several diagnostic tests are available (e.g., HPV high-risk and HPV 16/18 DNA tests, Hybrid Capture 2 HPV DNA test). However, HPV DNA testing is not recommended in women younger than 21 years. HPV DNA testing for high-risk virus types can also be used as a component of both primary screening and workup of abnormal cytology results; it is not useful to test for low-risk virus types. (See HPV DNA Testing on page 1378 for more detail about these tests.)

Colposcopy, along with colposcopically directed biopsies, is the primary method for evaluating women with abnormal cervical cytologies. During a colposcopic examination, the cervix is viewed through a long focal-length dissecting-type microscope (magnification, 10–16x). A 4% solution of acetic acid is applied to the cervix before viewing. The coloration induced by the acid and the observance of blood-vessel patterns allow a directed biopsy to rule out invasive disease and determine the extent of preinvasive disease. If the entire squamocolumnar junction of the cervix is visualized (i.e., the entire transformation zone is seen), the examination is considered satisfactory and endocervical curettage (ECC) is unnecessary. Special considerations for colposcopy performed during pregnancy are also discussed (see page 1376).
SCREENING GUIDELINES FOR EARLY DETECTION OF CERVICAL CANCER\textsuperscript{a}

When to Start Screening
- Cervical cancer screening should begin at 21 years of age. Screening before age 21 should be avoided, because it may lead to unnecessary and harmful evaluation and treatment in women at very low risk of cancer.
- Sexually active adolescents (i.e., women aged < 21 y) should be counseled and tested for sexually transmitted infections, and should be counseled regarding safe sex and contraception. These measures may be performed without cervical cytology and, in the asymptomatic patient, without the introduction of a speculum.
- Both liquid-based and conventional methods of cervical cytology are acceptable for screening.

Frequency of Screening
- Cervical cytology screening is recommended every 2 y for women between ages 21 and 29 y.
- Co-testing using the combination of cytology plus HPV DNA testing is an appropriate screening test for women aged > 30 y. Any low-risk woman aged 2-30 y who receives negative test results on both cervical cytology screening and HPV DNA testing should be rescreened no sooner than 3 y subsequently.
- Women aged ≥ 30 y who have had 3 consecutive negative cervical cytology screening test results, have no history of CIN II or III, are not HIV infected, are not immunocompromised, and were not exposed to diethylstilbestrol in utero may extend the interval between cervical cytology examinations to every 3 y.
- Women who have been immunized against HPV 16 and 18 should be screened by the same regimen as nonimmunized women.
- Regardless of the frequency of cervical cytology screening, physicians also should inform their patients that annual gynecologic examinations may still be appropriate even if cervical cytology is not tested at each visit.

When to Discontinue Screening
- Women treated in the past for CIN II, CIN III, or cancer remain at risk for persistent or recurrent disease for at least 20 y after treatment and after initial posttreatment surveillance, and should continue to have annual screening for at least 20 y.
- Women who have had a hysterectomy with removal of the cervix and have a history of CIN II or III, or in whom a negative history cannot be documented, should continue to be screened even after their period of posttreatment surveillance. Although the screening interval may then be extended, no good data support or refute discontinuing screening in this population.
- In women who have had a total hysterectomy for benign indications and have no prior history of high-grade CIN, routine cytology testing should be discontinued.
- Because cervical cancer develops slowly and risk factors decrease with age, it is reasonable to discontinue cervical cancer screening between 65 and 70 y of age in women who have 3 or more negative cytology test results in a row and no abnormal test results in the past 10 y.

Cervical Cancer Screening Version 1:2011

INITIAL FINDINGS OF SCREENING EXAM

- Visible/suspicious lesion on cervix
- Cervical cytology/Pap test\(\text{c-d}\) unsatisfactory
- Cervical cytology/Pap test\(\text{c-d}\) negative for intraepithelial lesion or malignancy
- Cervical cytology/Pap test\(\text{c-d}\) negative and high-risk HPV DNA positive \(\geq 30\text{ y}\)
- Cervical cytology/Pap test\(\text{c-d}\) positive for epithelial abnormalities:
  - Atypical squamous cells (ASC)
  - Low-grade squamous intraepithelial lesions (LSIL)
  - High-grade squamous intraepithelial lesions (HSIL)
  - Atypical glandular cells (AGC)

FOLLOW-UP

- Biopsy
- Repeat cervical cytology/Pap should be done within 6-12 wk
- Treat infection if present and indicated
- Screening frequency based on screening guidelines; see Screening for Early Detection of Cervical Cancer (previous page)
- See Follow-up for High-Risk HPV DNA testing \(\geq 30\text{ y}\) (page 1362)
- See AGC Follow-up and Management (page 1370)

- If cancer, see NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Cervical Cancer*
- If no cancer, consider CKC and/or referral to gynecologic oncologist/specialist

- Biopsy visible lesion; diagnostic excision if no visible lesion
- If cancer, see NCCN Guidelines for Cervical Cancer*
- If CIN I-III, see page 1369

*In this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org.

\(\text{c-d}\): Referral to specialist with oncological expertise for complex clinical situations should be strongly considered. Examples of complex clinical situations include atypical glandular cells, adenocarcinoma in-situ, pregnancy, and persistent/recurrent dysplasia with desire for fertility preservation.

\(\text{ASC-US}\): Cervical cytology/Pap test results should be reported using the Bethesda System. See The Bethesda System 2001 (page 1375).

\(\text{ASC-H}\): Conventional Pap test or liquid-based technology is an acceptable method for primary screening.
Cervical Cancer Screening Version 1:2011

**SCREENING FINDINGS (Cytology positive)**

- **ASC-US**<sub>h</sub> or **LSIL**<sub>h</sub>
  - Repeat cervical cytology/Pap test at 12 mo

- **ASC-H**<sub>h</sub> or **HSIL**<sub>h</sub>
  - Colposcopy

- **AGC**
  - See AGC Follow-up and Management (page 1370)

**SCREENING FOLLOW-UP**

- **Negative or no biopsy done or CIN I**
  - Satisfactory colposcopy
    - CIN II
    - CIN II-III, NOS
    - LEEP, cryotherapy, CKC, or laser ablation

- **CIN III**
  - Negative or CIN I, CIN II
    - Perform ECC and cervical biopsy
    - CIN II-III, NOS
    - LEEP or CKC
  - Repeat cervical cytology/Pap test and colposcopy at 6 mo

- **Unsatisfactory colposcopy**
  - See Follow-up of LEEP, CKC, Cryotherapy, or Laser Ablation for CIN (page 1369)

**FOLLOW-UP FINDINGS**

- **Negative or no biopsy done or CIN I**
  - Repeat cervical cytology/Pap test at 24 mo
    - ASC-US, LSIL, or HSIL
    - Colposcopy<sup>g</sup>

**MANAGEMENT**

- **Negative**
  - Resume screening per guideline (See page 1360)

- **ASC-US, LSIL, or HSIL**
  - Repeat cervical cytology/Pap test at 24 mo
    - Negative or CIN I, CIN II
      - Repeat cervical cytology/Pap test and colposcopy at 6 mo
      - See Follow-up of LEEP, CKC, Cryotherapy, or Laser Ablation for CIN (page 1369)

**FOLLOW-UP FOR HIGH-RISK HPV DNA TESTING**

- **High-risk HPV test positive and cytology/Pap test negative**
  - See page 1361

- **High-risk HPV test positive or negative and cytology/Pap test positive**
  - See page 1361

**HCN Clinical Practice Guidelines in Oncology**

© JNCCN–Journal of the National Comprehensive Cancer Network | Volume 8 Number 12 | December 2010

---

**Notes:**

- Follow appropriate colposcopy findings pathway (i.e., satisfactory or unsatisfactory). If appropriate, see Colposcopy During Pregnancy (page 1376).
- **AgCN** = Cervical intraepithelial neoplasia
- **ECC** = Endocervical curettage
- **LEEP** = Loop electrosurgical excision procedure
- **CKC** = Cold-knife conization

---

**HPV DNA Testing:**

- HPV DNA testing is not recommended in adolescents or young women < 21 y.

---

**Abbreviations:**

- AGC = Adult Guidelines for Cervical Cancer Screening
- ASC-US = Atypical Squamous Cells of Undetermined Significance
- LSIL = Low-grade Squamous Intraepithelial Lesion
- ASC-H = Atypical Squamous Cells, cannot exclude HSIL
- HSIL = High-grade Squamous Intraepithelial Lesion
- CIN = Cervical intraepithelial neoplasia
- ECC = Endocervical curettage
- LEEP = Loop electrosurgical excision procedure
- CKC = Cold-knife conization
Cervical Cancer Screening Version 1:2011

**SCREENING FINDINGS (cytology positive)**

- **ASC-US**
  - Repeat cervical cytology/Pap test at 6 mo
  - Immediate colposcopy
  - HPV DNA testing for high-risk virus only (preferred if available as reflex testing on liquid-based cytology)

- **LSIL, ASC-H, or HSIL**
  - Repeat cervical cytology/Pap test at 6 mo
  - Colposcopy

- **AGC**
  - See AGC Follow-up and Management (page 1370)

**SCREENING FOLLOW-UP FINDINGS**

- Negative
  - Colposcopy
  - Repeat cervical cytology/Pap test at 6 mo

- Positive
  - Colposcopy

**FOLLOW-UP MANAGEMENT**

- Negative
  - Resume screening per guideline (see page 1360)

- Colposcopy

- ≥ ASC-US
  - Colposcopy

**Notes:**

6 The FDA approved HPV DNA testing for high-risk virus types; it is not useful to test for low-risk virus types. High-risk HPV DNA tests detect whether any of the 13 to 14 high-risk types of HPV are present, although the tests do not indicate which types are present.

1 In women with ASC-US who are HPV high-risk-positive, NCCN and the American Society for Colposcopy and Cervical Pathology (ASCCP) do not recommend using the HPV 16/18-specific DNA test (i.e., HPV genotyping) to screen for who should proceed to colposcopy (http://www.asccp.org/pdfs/consensus/clinical_update_20090408.pdf).

For colposcopy for ASC-US or LSIL, see page 1365, and for ASC-H or HSIL, see page 1367. If appropriate, see Colposcopy During Pregnancy (page 1376).
Cervical Cancer Screening Version 1:2011

**SCREENING FINDINGS**

<table>
<thead>
<tr>
<th>Follow-Up</th>
<th>Supervision</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASC-US</td>
<td>Immediate colposcopy</td>
</tr>
<tr>
<td>HPV DNA testing for high-risk virus only (preferred if available as reflex testing on liquid-based cytology)</td>
<td></td>
</tr>
<tr>
<td>Repeat cervical cytology/Pap test at 6 mo</td>
<td></td>
</tr>
</tbody>
</table>

**FOLLOW-UP FINDINGS**

- Negative or no biopsy done
- CIN 1
- Satisfactory colposcopy
- CIN II
- CIN III
- Microinvasive
- Cancer
- Colposcopy for ASC-US or LSIL

**MANAGEMENT**

- Negative
- Resume screening per guideline (see page 1360)
- Positive
- Colposcopy
- Negative
- Repeat cervical cytology/Pap test at 6 mo
- ≥ ASC-US
- Resume screening per guideline (see page 1360)
- ≥ ASC-US
- Repeat cervical cytology/Pap test at 6 mo
- LEEP, cryotherapy, CKC, or laser ablation
- LEEP, cryotherapy, CKC, laser ablation, or total hysterectomy
- See Follow-up of LEEP, CKC, Cryotherapy, or Laser Ablation for CIN (page 1369)
- See NCCN Guidelines for Cervical Cancer*
- See Cervical Biopsy and ECC Findings (page 1366)

*In this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org.

The FDA approved HPV DNA testing for high-risk virus types; it is not useful to test for low-risk virus types. High-risk HPV DNA tests detect whether any of the 13 to 14 high-risk types of HPV are present, although the tests do not indicate which types are present.

Follow appropriate colposcopy findings pathway (i.e., satisfactory or unsatisfactory). If appropriate, see Colposcopy During Pregnancy (page 1376).

CIN II may be followed without treatment in certain clinical circumstances at the discretion of the physician.

If appropriate for preexisting pathologic condition or quality of life.

---

© JNCCN–Journal of the National Comprehensive Cancer Network | Volume 8 Number 12 | December 2010

Version 1.2011, 08-26-10 ©2010 National Comprehensive Cancer Network, Inc. All rights reserved. These guidelines and this illustration may not be reproduced in any form without the express written permission of NCCN.
Cervical Cancer Screening Version 1:2011

Clinical trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated.

© JNCCN–Journal of the National Comprehensive Cancer Network | Volume 8 Number 12 | December 2010
Cervical Cancer Screening Version 1:2011

**COLPOSCOPY FINDINGS**

- Satisfactory colposcopy
- Lesion seen
  - Cervical biopsy negative
    - CIN I
    - CIN II
    - CIN III
  - Microinvasive
    - CKC
    - See NCCN Guidelines for Cervical Cancer
  - Cancer
    - LEEP, cryotherapy, CKC, or laser ablation for CIN
    - See Follow-up of LEEP, CKC, Cryotherapy, or Laser Ablation for CIN

- Unsatisfactory colposcopy
  - Repeat cervical cytology/Pap test, colposcopy, and ECC every 6 mo until 2 consecutive negative results
  - Perform ECC

**CERVICAL BIOPSY FINDINGS**

- Negative colposcopy/no biopsy
  - Repeat cervical cytology/Pap test, colposcopy, and ECC every 6 mo until 2 consecutive negative results
  - See NCCN Guidelines for Cervical Cancer

**MANAGEMENT**

- Repeat cervical cytology/Pap test, colposcopy, and ECC every 6 mo until 2 consecutive negative results
- Consider LEEP or CKC for definitive diagnosis
- LEEP or CKC for definitive diagnosis

**MANAGEMENT**

- Repeat cervical cytology/Pap test, colposcopy, and ECC every 6 mo until 2 consecutive negative results
- Consider LEEP or CKC for definitive diagnosis
- LEEP, cryotherapy, CKC, or laser ablation

- LEEP, cryotherapy, CKC, laser ablation, or total hysterectomy

- See Follow-up of LEEP, CKC, Cryotherapy, or Laser Ablation for CIN

*In this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org.

**ADULTS ≥ 21 Y**

- Colposcopy for ASC-H or HSIL
  - No lesion seen
    - Negative colposcopy/no biopsy
      - Repeat cervical cytology/Pap test, colposcopy, and ECC every 6 mo until 2 consecutive negative results
      - Perform ECC

- CIN I

- CIN II

- CIN III

- Microinvasive

- Cancer

- LEEP, consider fertility issues

**FOR ADOLESCENTS OR YOUNG WOMEN < 21 Y, SEE PAGE 1363**

- Repeat cervical cytology/Pap test, colposcopy, and ECC every 6 mo until 2 consecutive negative results
- Consider LEEP or CKC for definitive diagnosis
- LEEP, cryotherapy, CKC, or laser ablation for CIN

(If appropriate for preexisting pathologic condition or quality of life.)

- See NCCN Guidelines for Cervical Cancer

*In this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org.

**VERIFICATION NUMBER**

- CIN II may be followed without treatment in certain clinical circumstances at the discretion of the physician.
- If appropriate for preexisting pathologic condition or quality of life.
- Perform vaginal and vulvar colposcopy.
- If preceeding cervical cytology/Pap test was ASC-H, may consider follow-up.
**Cervical Cancer Screening Version 1:2011**

**ADULTS ≥ 21 Y**

**COLPOSCOPY FINDINGS**

- **ASC-H** → Perform ECC
- **Cervical biopsy negative**
  - **CIN I**
    - LEEP or CKC
    - See Follow-up of LEEP, CKC, Cryotherapy, or Laser Ablation for CIN (facing page)
  - **CIN II** → LEEP or CKC
  - **CIN III** → LEEP, CKC, or total hysterectomy
  - **Microinvasion** → CKC
  - **Cancer** → See NCCN Guidelines for Cervical Cancer*

**CERVOICAL BIOPSY FINDINGS**

- **Positive ECC** → LEEP or CKC
- **No lesion seen**
  - **Cervical biopsy negative**
    - **CIN I** → LEEP or CKC
    - **CIN II** → LEEP or CKC
    - **CIN III** → LEEP, CKC, or total hysterectomy
  - **Lesion seen**
    - Biopsy

**MANAGEMENT**

- **LEEP, CKC** → Repeat cervical cytology/Pap test, colposcopy, and ECC every 6 mo until 2 consecutive negative results
- **Consider LEEP or CKC for definitive diagnosis**
- **Repeat cervical cytology/Pap test, colposcopy, and ECC every 6 mo until 2 consecutive negative results**
- **or**
  - **Cervical biopsy negative**
  - **CIN I** → LEEP or CKC
  - **CIN II** → LEEP or CKC
  - **CIN III** → LEEP, CKC, or total hysterectomy
- **Microinvasion** → CKC
- **Cancer** → See NCCN Guidelines for Cervical Cancer*
- **LEEP, consider fertility issues** → LEEP or CKC

**Follow-up of LEEP, CKC, Cryotherapy, or Laser Ablation for CIN (facing page)**

---

*In this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org.

---

**CIN II** may be followed without treatment in certain clinical circumstances at the discretion of the physician.

**If appropriate for preexisting pathologic condition or quality of life.**

**Perform vaginal and vulvar colposcopy.**

---

Clinical trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated.

© JNCCN–Journal of the National Comprehensive Cancer Network | Volume 8 Number 12 | December 2010
Cervical Cancer Screening Version 1:2011

FINDINGS AT TREATMENT

CIN I with positive or negative margins or CIN II, III with negative margins

Follow-up of therapy for CIN: LEEP, CKC, cryotherapy, or laser ablation

CIN II, III with positive margins

Margin status unknown
- Cryotherapy
- Laser ablation

FOLLOW-UP

Cervical cytology/Pap test at 6 mo

Negative

≥ ASC-US

See Screening Follow-up (page 1364)

HPV DNA testing* at 12 mo

Negative

Resume screening per guideline (see page 1360)

≥ ASC-US

Resume screening per guideline (see page 1360)

Cervical cytology/Pap test at 6 mo and consider ECC (category 2B)

Negative

Resume screening per guideline (see page 1360)

≥ ASC-US

See Screening Follow-up (page 1364)

Reexcision (especially if invasion is suspected)

or

Consider hysterectomy (after consultation with specialist)

Negative

Resume screening per guideline (see page 1360)

≥ ASC-US

See Screening Follow-up (page 1364)

HPV DNA testing* at 12 mo

Positive

Colposcopy

Negative

Resume screening per guideline (see page 1360)

≥ ASC-US

See Screening Follow-up (page 1364)

Negative

Resume screening per guideline (see page 1360)

Positive

Colposcopy

*In this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org.

*The FDA approved HPV DNA testing for high-risk virus types; it is not useful to test for low-risk virus types. High-risk HPV DNA tests detect whether any of the 13 to 14 high-risk types of HPV are present, although the tests do not indicate which types are present.

*Follow appropriate colposcopy findings pathway (i.e., satisfactory or unsatisfactory). If appropriate, see Colposcopy During Pregnancy (page 1376).
Clinical trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated.
The FDA approved HPV DNA testing for high-risk virus types; it is not useful to test for low-risk virus types. High-risk HPV DNA tests detect whether any of the 13 to 14 high-risk types of HPV are present, although the tests do not indicate which types are present.

If atypical glandular cells favor neoplasia or adenocarcinoma in situ, follow CKC with endometrial sampling if not yet done.

Follow appropriate colposcopy findings pathway (see opposite page). If appropriate, see Colposcopy During Pregnancy (page 1376).
Cervical Cancer Screening Version 1:2011

ATYPICAL GLANDULAR CELLS: FOLLOW-UP AND MANAGEMENT

CERVICAL BIOPSY FINDINGS

ECC FINDINGS

FOLLOW-UP

MANAGEMENT

- Negative
  - Repeat cervical cytology every 6 mo until 2 consecutive negative results
  - Positive CIN I, II, III or AIS
    - Positive
      - Colposcopy
    - Negative
      - Resume screening per guideline (see page 1360)

- Positive CIN I, II, III or AIS
  - CKC

- Negative
  - HPV DNA testing at 12 mo
    - Negative
      - Resume screening per guideline (see page 1360)
    - Positive
      - Colposcopy

AGC

CIN II

- Negative
  - LEEP or CKC

- Positive CIN I, II, III or AIS
  - CKC

CIN III

- Negative
  - LEEP or CKC

- Positive CIN I, II, III or AIS
  - CKC

If CIN I, II, III, see page 1369
If AIS or cancer, see page 1373
If endometrial biopsy done, see page 1374

The FDA approved HPV DNA testing for high-risk virus types; it is not useful to test for low-risk virus types. High-risk HPV DNA tests detect whether any of the 13 to 14 high-risk types of HPV are present, although the tests do not indicate which types are present.

If atypical glandular cells favor neoplasia or adenocarcinoma in situ, follow CKC with endometrial sampling if not yet done.

Follow appropriate colposcopy findings pathway (see page 1370). If appropriate, see Colposcopy During Pregnancy (page 1376).
ATYPICAL GLANDULAR CELLS: ADENOCARCINOMA IN SITU MANAGEMENT

CKC FINDINGS

- Negative margins, fertility desired
  - Cervical cytology/Pap test ± ECC every 6 mo until hysterectomy
  - Requires consent/counseling
  - Strongly consider hysterectomy when childbearing completed

- Negative margins, fertility not desired
  - Strongly consider hysterectomy

- Positive margins, fertility desired
  - Reexcision to attain negative margins
  - Requires consent/counseling
  - Strongly consider hysterectomy when childbearing completed

- Positive margins, fertility not desired
  - Hysterectomy
  - Consider repeat CKC to rule out invasive disease prior to hysterectomy (category 2B)

- AIS (strongly consider referral to gynecologic oncologist/specialist)
  - Cervical cytology/Pap test ± ECC every 6 mo until hysterectomy

- Cancer
  - See NCCN Guidelines for Cervical Cancer*

*In this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org.
ATYPICAL GLANDULAR CELLS: ENDOMETRIAL BIOPSY FINDINGS

**ENDOMETRIAL BIOPSY FINDINGS**

- Negative
- Hyperplasia
- Atypical hyperplasia
- Cancer
- Unsatisfactory

**MANAGEMENT**

- Consider transvaginal ultrasound for endometrial stripe thickness if no other source for AGC has been explained
- Consider dilatation and curettage (D&C) or hormonal therapy
- D&C or Consider referral to gynecologic oncologist/specialist
- See NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Uterine Neoplasms*
- Consider D&C or Consider transvaginal ultrasound for endometrial stripe thickness if no other source for AGC has been explained in a postmenopausal woman

*To view the most recent version of these guidelines, visit the NCCN Web site at www.NCCN.org.

**Clinical trials**: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged. All recommendations are category 2A unless otherwise indicated.
Cervical Cancer Screening Version 1:2011

BETHESDA SYSTEM 2001

SPECIMEN TYPE: Indicate conventional smear (Pap smear) vs. liquid-based vs. other

SPECIMEN ADEQUACY
- Satisfactory for evaluation (describe presence or absence of endocervical/transformation zone component and any other quality indicators, such as partially obscuring blood or inflammation)
- Unsatisfactory for evaluation (specify reason)
  - Specimen rejected/not processed (specify reason)
  - Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality because of (specify reason)

INTERPRETATION/RESULT
NEGATIVE FOR INTRAEPITHELIAL LESION OR MALIGNANCY
(When there is no cellular evidence of neoplasia, state this in the Interpretation/Result section of the report, whether or not there are organisms or other non-neoplastic findings)
- Organisms:
  - Trichomonas vaginalis
  - Fungal organisms morphologically consistent with Candida spp
  - Shift in flora suggestive of bacterial vaginosis
  - Bacteria morphologically consistent with Actinomyces spp
  - Cellular changes consistent with Herpes simplex virus
- Other non-neoplastic findings (optional to report; list not inclusive):
  - Reactive cellular changes associated with
    - Inflammation (includes typical repair)
    - Radiation
    - Intrauterine contraceptive device (IUD)
  - Glandular cell status post hysterectomy
  - Atrophy
- OTHER
  - Endometrial cells (in a woman aged ≥ 40 y; specify if “negative for squamous intraepithelial lesion”)

EPITHELIAL CELL ABNORMALITIES
- Squamous cell
  - ASC
  - of undetermined significance (ASC-US)
  - cannot exclude HSIL (ASC-H)
  - LSIL
  - encompassing: HPV/mild dysplasia/CIN I
  - HSIL
  - encompassing: moderate and severe dysplasia, CIS, and CIN II and III
    - with features suspicious for invasion (if invasion is suspected)
  - Squamous cell carcinoma
- Glandular cell
  - Atypical
    - Endocervical cells (NOS or specify in comments)
    - Endometrial cells (NOS or specify in comments)
    - Glandular cells (NOS or specify in comments)
  - Atypical
    - Endocervical cells, favor neoplastic
    - Glandular cells, favor neoplastic
  - Endocervical adenocarcinoma in situ
  - Adenocarcinoma
    - Endocervical
    - Endometrial
    - Extrapelvic
    - not otherwise specified (NOS)
- OTHER MALIGNANT NEOPLASMS (specify)

Note: The NCI Bethesda System 2001 Web site includes additional information such as the definitions of terms used for this table and information about ancillary testing and automated review.

COLPOSCOPY DURING PREGNANCY

Recommendations for colposcopy and follow-up are the same as delineated in these guidelines except:

- Consultation or referral to colposcopist with experience in colposcopy during pregnancy
- No ECC
- Treatment for CIN (any grade) delayed until after pregnancy
- Colposcopy and cervical biopsy for LSIL and ASC-US can be deferred until 6 weeks postpartum
- Colposcopy and cervical biopsy should be limited to patients in whom high-grade neoplasia or invasive cancer is suspected
- Diagnostic limited excisional procedure is recommended only if invasion is suspected
- Brush cytology is safe during pregnancy
Techniques for definitive treatment of cervical abnormalities include excision with the loop electrosurgical excision procedure (LEEP), cold-knife conization (CKC), or total hysterectomy. Ablative procedures include laser ablation or cryotherapy.

Cervical Cancer Screening

Initiation and Frequency
The NCCN Guidelines for Cervical Cancer Screening Panel adopted the recent recommendations of the American College of Obstetricians and Gynecologists (ACOG) on the initiation and frequency of cervical cancer screening (see page 1360). Women should begin screening at 21 years of age, regardless of whether sexual intercourse has already occurred. Recent data indicate that cervical screening should be avoided in women younger than 21 years, because these women are at very low risk of cancer and because treatment can lead to complications (e.g., significant increase in premature births in women previously treated for dysplasia). However, adolescents who are immunocompromised (e.g., HIV infection, organ transplants, long-term steroid use) must undergo cervical screening. For example, those infected with HIV should be tested every 6 months during the first year and then annually. Cervical cytology screening should still be initiated in young women (≥ 21 years) who have been vaccinated against HPV 16 and 18, because other high-risk subtypes of HPV are oncogenic (e.g., HPV 31).

The onset of gynecologic care should not be based on the need for cervical screening. Thus, sexually active adolescents should receive counseling and testing for sexually transmitted diseases and should also receive counseling about safe sex and contraception. In asymptomatic adolescents, gynecologic care can be performed without using a speculum. After initiation, cervical screening should be performed every 2 years in women 21 to 29 years of age with either liquid-based cytology or conventional cervical cytology smears (i.e., Pap smears). However, women with high-risk factors (e.g., a history of cervical cancer, diagnosis of cervical intraepithelial neoplasia [CIN] II–III, in-utero exposure to diethylstilbestrol, and/or immunocompromised [e.g., HIV infection]) should undergo more frequent screening, usually annually, as determined by their physician. HPV DNA testing is not recommended in adolescents or younger women (i.e., < 21 years; see page 1363). HPV DNA testing is also not recommended as routine screening in women younger than 30 years and in women with atypical squamous cells with suspicion of high-grade dysplasia (ASC-H), low-grade squamous intraepithelial lesions (LSIL; except in postmenopausal women), or high-grade squamous intraepithelial lesions (HSIL) cytology (http://www.asccp.org/pdfs/consensus/clinical_update_20090408.pdf). See HPV DNA Testing on page 1378 for more detail.

Screening options for women 30 years and older include cervical cytology alone or cervical cytology combined with DNA testing for high-risk HPV types (i.e., combined testing). After a 30-year-old woman at low risk for cervical cancer has 3 or more consecutive (and technically satisfactory) cytologic examinations with normal (i.e., negative) findings, cervical screening may be performed less frequently (i.e., every 3 years, at the discretion of the physician). Combined cytology and HPV DNA testing should not be performed more often than every 3 years if both tests were negative. However, physicians should also inform their patients that annual gynecologic examinations may still be appropriate even if cervical cytology is not tested at each visit.

Women with high-risk factors (e.g., a history of cervical cancer, diagnosis of CIN II or III, in-utero exposure to diethylstilbestrol, and/or immunocompromised [e.g., HIV infection]) who are 30 years and older should receive more frequent screening, usually annually, as determined by their physician. Women who have had a hysterectomy with removal of the cervix should have annual screening with vaginal cytology if they have history of CIN II or III lesions or cancer, or if a negative history cannot be documented (see page 1360).

Combined cytology and HPV DNA testing seems to increase the detection rate of CIN III, which is a precursor of cervical cancer. Although some studies have used HPV DNA testing alone without cervical cytology for screening women aged 30 years and older, currently this strategy is not used in the United States. The appropriate screening interval for women with negative cytology who test positive for HPV DNA is shown on page 1362 and is described later (see Squamous Epithelial Cell Abnormalities in Adult Women Aged 21 Years or Older, page 1380).
Cervical Cancer Screening

Continue or Discontinue Screening

Cervical cytology screening should continue in women who have been vaccinated against HPV 16 and 18 (see page 1360). Women previously treated for CIN II, CIN III, or cancer should continue to undergo annual screening for at least 20 years after treatment and after initial postoperative surveillance, because they remain at risk for persistent or recurrent disease. Women who have had a hysterectomy with removal of the cervix should have screening for vaginal cancer if they have history of CIN II or III lesions or cancer, or if a negative history cannot be documented. Cervical cytology screening should continue for women with other high-risk factors (e.g., in-utero diethylstilbestrol exposure, immunocompromised [e.g., HIV infection]).

Screening for cervical cancer can be discontinued after total hysterectomy for benign disease, although efforts should be made to confirm through physical examination or pathology report that the cervix was completely removed. Screening for cervical cancer may be discontinued for women with an intact cervix who are aged 65 to 70 years and older with 3 or more negative cytology test results in a row and with no history of abnormal cervical cytology tests in the previous 10 years, because cervical cancer develops slowly, and risk factors decrease with age. Women with comorbid or life-threatening illness may discontinue screening.

HPV DNA Testing

Note that the recently approved HPV 16/18 and the HPV high-risk DNA tests are 2 different diagnostic tests (http://www.asccp.org/pdfs/consensus/clinical_update_20090408.pdf). The HPV high-risk DNA test detects whether any of the 14 high-risk (oncogenic) types of HPV are present, although it does not indicate which types are present. The HPV 16/18 DNA test detects whether HPV 16 or 18 is present, termed HPV genotyping. The American Society for Colposcopy and Cervical Pathology (ASCCP) provides information about HPV DNA testing (http://www.asccp.org/hpv.shtml#provider). The HPV 16/18 DNA test is not used alone; it is used together with the HPV high-risk DNA test. Currently, these tests should not replace other cervical cancer screening methods (i.e., regular Pap tests and gynecologic examinations; http://www.sgo.org/WorkArea/showcontent.aspx?id=2474).

The other high-risk HPV DNA test, Hybrid Capture 2 HPV DNA test (Digene HPV HC2 DNA Test), assesses whether women are positive for any of 13 high-risk types of HPV, although false-positive results can occur because of slight cross-reactivity with nononcogenic HPV subtypes. Note that the HC2 has no internal standard to determine sample adequacy. Data on the sensitivity of HC2 for disease detection are derived from studies that used it in the setting of co-collection with cytology. The performance characteristics of HC2 as a stand-alone test are unknown.

HPV Vaccines

Vaccination with the quadrivalent HPV vaccine provides protection against infection by certain types of HPV that cause cervical, vulvar, and vaginal cancer (types 16, 18) and genital warts (types 6, 11). After 3 years, the efficacy of the quadrivalent HPV vaccine was 99% for preventing CIN grades II and III caused by HPV 16 or 18 in women who were not previously infected with either HPV 16 or 18 before vaccination; however, efficacy was only 44% in those who had been infected before vaccination. Many agree that CIN III (which is essentially squamous cell carcinoma in situ [i.e., stage 0]) is the best marker for risk of progression to invasive cancer. Recent data suggest that 40% of CIN II lesions will regress after 2 years; however, CIN II lesions from HPV 16 seem less likely to regress. In addition, a meta-analysis reported that 22% of CIN II lesions progress to carcinoma in situ.

Although how long immunity lasts after vaccination is unclear, data suggest the quadrivalent HPV vaccine is effective for at least 5 years and up to 9.5 years. Recent data suggest that the quadrivalent HPV vaccine decreases abnormal Pap results, colposcopies, and cervical biopsies.

Another prophylactic HPV vaccine is the bivalent vaccine, which was recently approved in the United States for preventing cervical cancer and pre-cancerous lesions from HPV 16 and 18 in girls and women aged 10 to 25 years (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm187048.htm). The bivalent vaccine is also approved in more than 90 other countries.

The FDA also approved the HPV quadrivalent vaccine for use in girls and women aged 9 to 26 years (http://www.fda.gov/downloads/BiologicsBloodVaccines/Vaccines/ApprovedProducts/UCM111263.pdf). However, the vaccine is most
All women with cervical cytology tests reported as normal (i.e., negative for intraepithelial lesion or malignancy), unsatisfactory, or positive for invasive cancer are managed as shown on page 1361. A biopsy should be performed on any grossly visible or suspicious lesion on the cervix, because cervical cytology can be reported as negative when invasive cancer is grossly present. If the cervical cytology is positive for invasive cancer, a biopsy is recommend if a lesion is visible, or a diagnostic excision is recommended if no lesion is visible (see page 1369 or the NCCN Clinical Practice Guidelines in Oncology [NCCN Guidelines] for Cervical Cancer in this issue; to view the most recent version of these guidelines, visit the NCCN Web site at www.nccn.org). If the initial cervical cytology is negative and the cervix is grossly normal, then subsequent screening should be based on the recommendation for frequency discussed earlier (see page 1360). Cervical cytology tests reported as unsatisfactory should be repeated within 6 to 12 weeks. Underlying infection should be treated, if indicated, before obtaining the subsequent cytology. Combined testing using cervical cytology and HPV high-risk DNA testing is discussed in the following sections.

Squamous Epithelial Cell Abnormalities in Adolescents or Young Women (Age < 21 Years)

The management of squamous cell abnormalities requires special consideration in adolescents or young women (age < 21 years) because of both the high prevalence of HPV positivity in this age group and the frequent regression of LSIL lesions (see page 1363). For example, various studies have reported that a high percentage of young women will be HPV-positive within several years of initial sexual activity. These statistics indicate that HPV testing cannot be used to further triage management of squamous epithelial abnormalities in this population. Therefore, the algorithm specifically notes that HPV testing is not recommended in adolescents or women younger than 21 years. Although a small number of adolescents or young adults may have CIN III, progression to cancer is extremely rare in women younger than 21 years, and most instances of CIN III are detected on subsequent screening. Therefore, although colposcopy is routinely recommended for LSIL in women 21 years or older, younger patients may be initially followed up with repeat cytology.

ASC of Undetermined Significance or LSIL: Young
women (aged < 21 years) with ASC of undetermined significance (ASC-US) or LSIL should undergo repeat screening at 12 months. Those with negative cervical cytology results or with persistent ASC-US or LSIL should undergo repeat screening after 24 months. If the cytology results are negative after this 3-year period, then the patient can resume routine screening. If the cytology indicates ASC-US, LSIL, or HSIL, then colposcopy is recommended. Patients then follow the “satisfactory” or “unsatisfactory” colposcopy pathway for adolescents or young women (see page 1363). Colposcopy is also recommended if the first rescreen at 12 months shows ASC-H or HSIL.

**ASC-H:** Colposcopy is recommended if initial screening reveals ASC-H or HSIL, because of the increased risk for CIN II or higher. Further management depends on colposcopy findings. For a satisfactory colposcopy, repeat cervical cytology and colposcopy at 6 months are recommended if the findings are reported as CIN II or I-negative, or if no biopsy was performed. Options for patients with CIN II or III not otherwise specified (NOS) findings include 1) an ablative or excision procedure (i.e., laser ablation, cryotherapy, LEEP, or CKC); or 2) repeat cervical cytology and colposcopy at 6 months. Patients with unsatisfactory colposcopy results should undergo ECC and cervical biopsy, and should then be managed as shown on page 1363.

**Squamous Epithelial Cell Abnormalities in Adult Women Aged 21 Years or Older**

**ASC-US or LSIL:** The guideline offers 3 options for the management of ASC-US in adults (see page 1364). Unlike adolescents, HPV DNA testing for high-risk virus is informative in adult women because of the lower underlying prevalence. The inclusion of HPV testing as an option is based on the results of the ASCUS-LSIL Triage Study (ALTS) trial, which showed that HPV triage (“reflex” HPV testing for atypical Pap smears from liquid-based cytology) is at least as sensitive as immediate colposcopy for detecting CIN grade III and refers about half as many women to colposcopy. However, in women with ASC-US who are positive for oncogenic HPV high-risk DNA, the NCCN and ASCCP do not recommend the use of HPV 16/18–specific DNA testing (i.e., HPV genotyping) as a screen to determine who should proceed to colposcopy (http://www.asccp.org/pdfs/consensus/clinical_update_20090408.pdf). Only approximately 50% of CIN II-positive infections are associated with HPV 16 or 18. Thus, the risk of CIN II-positive disease is approximately 20% in women with ASC-US who are positive for other oncogenic HPV types (e.g., HPV 31, 45). Therefore, the NCCN and ASCCP recommend referring women with ASC-US who are positive for HPV high-risk DNA for colposcopy.

A second option is immediate colposcopy. A third option is to repeat the cervical cytology. If 2 consecutive cytology tests performed 6 months apart are negative, screening every 2 years may be resumed. However, if the repeat cytology test shows persistent ASC-US or greater, a colposcopic evaluation of the cervix is appropriate.

Women aged 30 years and older who are high-risk HPV DNA–positive but cytology negative have several options: 1) repeating both tests (i.e., cytology and high-risk HPV DNA) at 12 months; or 2) HPV genotyping (i.e., specific HPV 16/18 DNA test; see page 1362). Several studies suggest that it is appropriate and safe to wait 1 year before rescreening. Approximately 60% of women who are high-risk HPV–positive will become HPV-negative during follow-up. Data suggest that the incidence of CIN III-positive is 17% in women who are HPV 16-positive, 14% in those who are HPV 18-positive, and only 3% with other high-risk HPV types. Thus, it is also appropriate to use HPV genotyping because HPV 16 and 18 are more oncogenic than the other high-risk types of HPV, and patients with persistent HPV 16/18 infection are at greater risk.

**LSIL, ASC-H, or HSIL:** In adolescent patients, LSIL often regresses spontaneously; therefore, repeat cervical cytology is an effective triage strategy. In contrast, in adults, the ALTS trial showed that LSIL cytology is best managed with colposcopy initially, because no useful triage strategy was identified. Therefore, colposcopy is recommended in adults older than 30 years for all squamous lesions other than ASC-US (i.e., LSIL, ASC-H, HSIL). HPV DNA testing is not recommended in women with ASC-H, LSIL, or HSIL cytology. Note that cytologic LSIL is not the same as histologic CIN I; cytologic HSIL is not the same as histologic CIN II, III.

**Colposcopy for LSIL or ASC-US in Adult Women**

**Satisfactory Colposcopy for LSIL or ASC-US:** The first consideration in evaluating the colposcopy result is determining whether the colposcopy visual-
ized the entire transition zone of the cervix and was considered satisfactory (see page 1365). Unsatisfactory colposcopies are addressed in the next section. The ASCCP published 2 consensus guidelines: “2006 Consensus Guidelines for the Management of Women With Abnormal Cervical Cancer Screening Tests” and “2006 Consensus Guidelines for the Management of Women With Cervical Intraepithelial Neoplasia or Adenocarcinoma in Situ” (http://www.asccp.org/consensus.shtml).3,36

Women found to have negative findings or CIN I on cervical biopsy, or those who did not have a biopsy, after satisfactory colposcopic examination for ASC-US or LSIL may be followed up with a repeat cytology at 6 months or with HPV DNA testing for high-risk viruses at 12 months. Excision or ablation procedures are not recommended for these patients to avoid potential overtreatment. If negative cervical cytology is found at 6 and 12 months, a normal screening schedule can be reinstated, because most of these lesions will regress to normal.38 If ASC-US or greater is found on one of these examinations, the screening management recommendations should be followed (see page 1364). For patients followed by HPV DNA at 12 months, a positive result requires a colposcopy, whereas negative findings permit returning to a normal screening schedule. The ALTS trial suggested that after an initial diagnosis of CIN I or less with colposcopy, the most efficient test for identifying women with CIN grade II or III might be an HPV test alone at 12 months.50

If the cervical biopsy shows CIN II or III, further therapy is indicated, consisting of LEEP, cryotherapy, CKC, or laser ablation. However, CIN II may be followed up without treatment in certain clinical circumstances (e.g., young woman who desires fertility, is reliable about office visits, and prefers no treatment) at the discretion of the physician. Total hysterectomy may also be considered an option for CIN III, if indicated for preexisting pathologic conditions or enhancement of quality of life. The panel favored the use of CKC for patients in whom microinvasive cervical cancer was suspected.51 The LEEP has been associated with a cautery artifact that may compromise the pathologic evaluation of the tissue specimen. Diagnosis of microinvasive or invasive cancer at cervical biopsy requires treatment according to the NCCN Guidelines for Cervical Cancer (in this issue and at www.NCCN.org).

Unsatisfactory Colposcopy for LSIL or ASC-US: If the colposcopic examination is unsatisfactory for ASC-US or LSIL, ECC should be performed in addition to the directed cervical biopsy (see page 1366). If the cervical biopsy is negative (or no biopsy is performed) and the ECC findings are negative or CIN I, repeat cytologic examinations at 6 months or HPV DNA testing at 12 months can be performed. The same strategy as previously outlined for a satisfactory colposcopy should be followed. ECC with a diagnosis of CIN II or III requires LEEP or CKC for definitive diagnosis.52

A cervical biopsy result of CIN II requires a LEEP or CKC to establish a definitive diagnosis. If CIN III is identified, options include LEEP, CKC, or a total hysterectomy. However, in patients with CIN III, an initial LEEP or CKC is recommended before the total hysterectomy to confirm the diagnosis. CKC is performed for microinvasive biopsy findings; CKC or LEEP can serve as definitive treatment if the lesion is confirmed to be intraepithelial.31 A diagnosis of microinvasive or invasive cancer on cervical biopsy, LEEP, or CKC requires treatment according to the NCCN Guidelines for Cervical Cancer (in this issue and at www.NCCN.org).

Colposcopy for ASC-H or HSIL in Adult Women
All women diagnosed with ASC-H or HSIL on cytology require colposcopic evaluation. Again, management depends on whether the colposcopy is considered satisfactory or unsatisfactory (see either page 1367 or 1368). A LEEP or CKC is recommended for those with HSIL or with ASC-H and positive ECC who have unsatisfactory colposcopy results, with management as outlined (see page 1368). Patients with ASC-H who have a negative ECC with no lesion seen, however, can have cytology, colposcopy (including vaginal or vulvar colposcopy), and ECC repeated every 6 months until 2 results in a row are negative. Patients can resume regular screening after 2 consecutive negative results (see page 1360).

Management of those with a satisfactory colposcopy depends on whether a lesion is seen. ECC should be performed in those without a lesion or biopsy or with a negative colposcopy. If the ECC is negative, then the cytology, colposcopy (including vaginal or vulvar colposcopy), and ECC should be repeated in every 6 months until 2 results in a row are negative. If CIN I is identified on ECC, follow-up may be considered in women with a preceding ASC-H.

If a lesion is identified, 2 options are available,
A patient may choose a LEEP procedure as the first option, particularly if maintaining fertility is not an issue; this patient should then undergo follow-up as described in the next section (see page 1369). Biopsy is the second option. A negative cervical biopsy or CIN I lesion can be managed with either 1) a repeat cervical cytology, colposcopy (including vaginal and vulvar colposcopy), and ECC every 6 months (until 2 consecutive results are negative and then regular screening can resume); or 2) a LEEP or CKC can be considered for definitive diagnosis or for positive findings. A diagnosis of CIN II or III requires treatment with LEEP, cryotherapy, CKC, or laser ablation. However, CIN II may be followed without treatment in certain clinical circumstances (e.g., young woman who desires fertility, is reliable about office visits, and prefers no treatment) at the discretion of the physician. Total hysterectomy is another recommended option if the lesion is CIN III and if other indications for hysterectomy are present (e.g., symptomatic fibroids, persistent abnormal bleeding). Again, CKC should be performed for microinvasive biopsy findings, and any confirmed invasive cancers need treatment according to the NCCN Guidelines for Cervical Cancer (in this issue and at www.NCCN.org).

Follow-Up After Treatment of CIN

Surgical margins cannot be assessed after ablative procedures with cryotherapy or laser ablation; recommended follow-up for these patients consists of cervical cytology at 6 months or HPV DNA testing at 12 months (see page 1369). Treatment of those initially managed with excision (i.e., LEEP or CKC) depends on the status of the margins. Cervical cytology at 6 months or HPV DNA testing at 12 months is recommended for those with CIN II or III lesions with negative margins and for all CIN I lesions. For CIN II and III lesions with positive margins, options include 1) cervical cytology at 6 months; an ECC can be considered (category 2B); 2) reexcision, especially if invasion is suspected; or 3) consider hysterectomy. If repeat cervical cytology or HPV DNA testing is negative, screening as per the guidelines may be resumed (see page 1360). If HPV DNA testing is positive, then colposcopy is recommended. If the repeat cervical cytology identifies ASC-US or greater, then the screening recommendations should be followed as previously mentioned (see page 1364).

Atypical Glandular Cells

The finding of AGC on cervical cytology is associated with a clinically significant lesion in 45% of patients, including CIN, cervical adenocarcinoma in situ (AIS), cervical cancer, and endometrial, ovarian, and fallopian tube cancers (see page 1370). CIN is the most common finding; 3% to 17% of women have invasive cancer. Cervical cytologic screening methods are less useful for diagnosing AIS, because AIS affects areas of the cervix that are harder to sample (i.e., endocervical canal). However, liquid-based cytology seems to improve detection of abnormal glandular lesions (http://www.sgo.org/WorkArea/showcontent.aspx?id=952). Thus, all patients with a finding of AGC on cervical cytology and who are younger than 35 years with no risk factors for endometrial cancer should undergo colposcopy, ECC, and HPV DNA testing (if not already done). Risk factors for endometrial cancer include obesity, unopposed estrogen replacement therapy, polycystic ovarian syndrome, tamoxifen therapy, anovulation, or hereditary nonpolyposis cancer syndrome (HNPCC).

Patients aged 35 years or older and all those with atypical glandular endometrial cells, abnormal bleeding, or endometrial cancer risk factors should also undergo endometrial biopsy, along with colposcopy, ECC, and HPV DNA testing (if not already performed), as part of their initial evaluation. Management is then directed by the results of the cervical biopsy, ECC, and HPV testing. Additional management may be dictated by the results of the endometrial biopsy (see page 1374). Note that it is not appropriate to repeat cervical cytology in the initial triage of AGC. HPV DNA testing alone is also not appropriate in the initial triage of all subcategories of AGC.

If cervical biopsy and ECC identify CIN (I, II, or III) or AIS, further evaluation using CKC is indicated (see page 1372). However, a patient with an adequate colposcopic examination, a cervical biopsy revealing CIN I, and a negative ECC may be managed conservatively either with a repeat cervical cytology every 6 months until 2 consecutive negative results are obtained, or with HPV DNA testing at 12 months. Colposcopy is recommended for those with cervical cytology greater than ASC-US. For patients with cervical biopsy findings of CIN II or III but with a negative ECC result, LEEP or CKC is recommended (see page 1372).
The panel felt that most patients with a cervical cytology showing AGC and an abnormal cervical biopsy result or ECC should undergo CKC to both confirm the diagnosis and serve as potential treatment. The use of LEEP in patients with AIS has been associated with an increased incidence of positive excision margins in the tissue specimen. Therefore, CKC is the preferred diagnostic procedure in patients at risk for AIS or microinvasion. CKC should be followed by endometrial sampling if “AGCs favor neoplasia” or “AIS” is reported.

Management of AIS
The panel recommends that all patients with AIS should be strongly considered for referral to a gynecologic oncologist or similar specialist (see page 1373). Treatment choice depends on the patient’s desire for fertility. The definitive treatment for AIS is hysterectomy. Patients desiring to preserve fertility and who have a CKC specimen with negative margins of excision may be followed up conservatively with repeat cervical cytology with (or without) ECC every 6 months until hysterectomy, and should also receive counseling on the risks of this strategy. Hysterectomy should be strongly considered in these patients when childbearing is completed. Women with positive findings on cervical cytology/ECC should then be managed according to the options on page 1370. Those with negative findings can continue screening every 6 months.

However, clear margins of excision do not rule out persistent AIS, because approximately 30% of patients have residual disease on subsequent hysterectomy. If CKC margins are positive for abnormal glandular cells, a hysterectomy is recommended if the patient does not desire to remain fertile. Repeat CKC should be considered before hysterectomy to rule out invasive disease (category 2B).

Reexcision to attain negative margins is recommended for patients with positive margins who wish to remain fertile. These patients should also receive counseling regarding the risks of this strategy. Hysterectomy should be strongly considered in these patients when childbearing is completed.

Finally, patients with invasive adenocarcinoma on cervical biopsy, ECC, CKC, or endometrial biopsy should undergo treatment according to the NCCN Guidelines for Cervical Cancer (in this issue and at www.NCCN.org) and for Uterine Neoplasms (available at www.NCCN.org).

Management of Endometrial Biopsy
If the result of the endometrial biopsy is negative, transvaginal ultrasound to determine the endometrial stripe thickness may be considered if no other source for the AGC has been identified (see page 1374). If the endometrial biopsy result is hyperplasia, recommended options are either hormone therapy or consideration of a uterine dilatation and curettage (D&C). Patients with atypical hyperplasia on biopsy should undergo a D&C; additionally, referral to a gynecologic oncologist or similar specialist should be considered. For patients with unsatisfactory endometrial biopsy results, consider D&C or transvaginal ultrasound for endometrial stripe thickening if no other source of AGC has been identified in a postmenopausal woman. A diagnosis of endometrial cancer requires treatment according to the NCCN Guidelines for Uterine Neoplasms (available at www.NCCN.org).

Colposcopy During Pregnancy
During pregnancy, the recommendations for colposcopy and follow-up are the same as outlined previously, with the following exceptions:

- Brush cytology is safe during pregnancy; however, to avoid possible disruption of the pregnancy, ECC should not be performed.  
- Colposcopy and cervical biopsy during pregnancy should be limited to women in whom high-grade neoplasia or invasive cancer is suspected; LSIL and ASC-US can be deferred until 6 weeks postpartum.
- Treatment for CIN (any grade) should be delayed until after pregnancy.  

Because colposcopic evaluation in pregnant women can be problematic, consultation with or referral to an experienced colposcopist should be considered. A diagnostic limited excisional procedure is recommended only if invasive cancer is suspected (see page 1376).

References
Cervical Cancer Screening


Cervical Cancer Screening


### Individual Disclosures for the NCCN Cervical Cancer Screening Panel

<table>
<thead>
<tr>
<th>Panel Member</th>
<th>Clinical Research Support</th>
<th>Advisory Boards, Speakers Bureau, Expert Witness, or Consultant</th>
<th>Patent, Equity, or Royalty</th>
<th>Other</th>
<th>Date Completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nadeem R. Abu-Rustum, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>7/1/09</td>
</tr>
<tr>
<td>Susana M. Campos, MD, MPH, MS</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>12/3/09</td>
</tr>
<tr>
<td>Patrick J. Fahey, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>4/30/10</td>
</tr>
<tr>
<td>Michael Farmer, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>9/21/10</td>
</tr>
<tr>
<td>Rochelle L. Garcia, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>1/19/10</td>
</tr>
<tr>
<td>Anna Giuliano, PhD</td>
<td>None</td>
<td>Merck &amp; Co., Inc.</td>
<td>None</td>
<td>None</td>
<td>12/21/09</td>
</tr>
<tr>
<td>Howard W. Jones III, MD</td>
<td>None</td>
<td>Cytoc Health Corporation; Merck &amp; Co., Inc.; and Digene Corporation</td>
<td>None</td>
<td>None</td>
<td>4/6/10</td>
</tr>
<tr>
<td>Subodh M. Lele, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>9/30/09</td>
</tr>
<tr>
<td>Richard W. Lieberman, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>9/28/09</td>
</tr>
<tr>
<td>Stewart L. Massad, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>4/22/10</td>
</tr>
<tr>
<td>Mark A. Morgan, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>5/12/10</td>
</tr>
<tr>
<td>Edward E. Partridge, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>5/13/10</td>
</tr>
<tr>
<td>R. Kevin Reynolds, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>9/28/09</td>
</tr>
<tr>
<td>Helen E. Rhodes, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>11/16/09</td>
</tr>
<tr>
<td>Diljeet K. Singh, MD, DrPH</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>9/28/09</td>
</tr>
<tr>
<td>Karen Smith-McCune, MD, PhD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>11/25/09</td>
</tr>
<tr>
<td>Nelson Teng, MD, PhD</td>
<td>GOG</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>1/15/10</td>
</tr>
<tr>
<td>Cornelia Liu Trimble, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>1/12/10</td>
</tr>
<tr>
<td>Fidel Valea, MD</td>
<td>None</td>
<td>Genzyme Corporation; Merck &amp; Co., Inc.; and Covidien</td>
<td>None</td>
<td>None</td>
<td>12/10/09</td>
</tr>
<tr>
<td>Sharon Wilczynski, MD</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>9/29/09</td>
</tr>
</tbody>
</table>

Dr. Hughes has disclosed that she has a patent, equity, or royalty in Myriad Genetic Laboratories, Inc.; Affymetrix; and Qiagen NV. The remaining guidelines staff have disclosed that they have no conflicts of interest.