Introduction

Cytology
Since the publication of the 2006 consensus guidelines, new cervical cancer screening guidelines have been published and new information has become available which includes key cervical cancer screening and follow up, and cervical precancer management data over a nine year period among more than 1 million women cared for at Kaiser Permanente Northern California. Moreover, women under age 21 are no longer receiving cervical cancer screening and cotesting with high-risk HPV type assays, and cervical cytology is being used to screen women 30 years of age and older. Therefore, in 2012 the American Society for Colposcopy and Cervical Pathology (ASCCP), together with its 24 partner professional societies, Federal agencies, and international organizations, began the process of revising the 2006 management guidelines. This culminated in the consensus conference held at the National Institutes of Health in September 2012. This report provides updated recommendations for managing women with cytological abnormalities. A more comprehensive discussion of these recommendations and their supporting evidence was published in the Journal of Lower Genital Tract Disease and Obstetrics and Gynecology and is made available on the ASCCP website at www.asccp.org.

Histopathology
Appropriate management of women with histo-pathologically diagnosed cervical precancer is an important component of cervical cancer prevention programs. Although the precise number of women diagnosed with cervical precancer each year in the U.S. is not known, it appears to be a relatively common occurrence. In 2001 and 2006, the American Society for Colposcopy and Cervical Pathology and 28 partner professional societies, federal agencies, and international organizations, convened processes to develop and update consensus guidelines for the management of women with cervical precancer. Since then, considerable new information has emerged about management of young women, and the impact of treatment for precursor disease on pregnancy outcomes. Progress has also been made in our understanding of the management of women with adenocarcinoma in-situ, also a human papillomavirus (HPV)—associated precursor lesion to invasive cervical adenocarcinoma. Therefore, in 2012 the ASCCP, together with its partner organizations, reconvened the consensus process of revising the guidelines. This culminated in the September 2012 Consensus Conference held at the National Institutes of Health. This report provides the recommendations developed for managing women with cervical precancer. A summary of the guidelines themselves—including the recommendations for managing women with cervical cytological abnormalities — are published in JLGTD and Obstetrics & Gynecology.
Although the guidelines are based on evidence whenever possible, for certain clinical situations limited high-quality evidence exists. In these situations the guidelines are based on consensus expert opinion. Guidelines should never be a substitute for clinical judgment. Clinical judgment should always be used when applying a guideline to an individual patient since guidelines may not apply to all patient-related situations. Finally, both clinicians and patients need to recognize that while most cases of cervical cancer can be prevented through a program of screening and management of cervical precancer, no screening or treatment modality is 100% effective and invasive cervical cancer can develop in women participating in such programs.

The 2001 Bethesda System terminology is used for cytological classification. This terminology utilizes the terms low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL) to refer to low-grade lesions and high-grade cervical cancer precursors respectively. For managing cervical precancer, the histopathological classification is two-tiered applying the terms cervical intraepithelial neoplasia grade 1 (CIN 1) to low-grade lesions and CIN2,3 to high-grade lesions. If using the 2012 Lower Anogenital Squamous Terminology (LAST), CIN1 is equivalent to histopathological LSIL and CIN2,3 is equivalent to histopathological HSIL. Please note that cytological LSIL is not equivalent to histopathological CIN 1 and cytological HSIL is not equivalent to histopathological CIN2,3. The current guidelines expand clinical indications for HPV testing based on studies using FDA-approved, validated HPV assays. Management decisions based on results using HPV tests not similarly validated may not result in outcomes intended by these guidelines. HPV testing should be restricted to high-risk (oncogenic) HPV types. Testing for low-risk (non-oncogenic) HPV types has no role in evaluating women with abnormal cervical cytological results. Therefore, whenever “HPV testing” is mentioned in the guidelines, it refers to testing for high-risk (oncogenic) HPV types only.

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Unsatisfactory Cytology

- **HPV unknown (any age)**
  - Abnormal: Manage per ASCCP Guideline

- **HPV negative (age ≥30)**
  - Repeat Cytology after 2-4 months
    - Negative: Routine screening (HPV-/unknown) or Cotesting @ 1 year (HPV+)
    - Unsatisfactory: Colposcopy

- **HPV positive (age ≥30)**
  - Unsatisfactory: Colposcopy
Cytology NILM* but EC/TZ Absent/Insufficient

Ages 21-29+

HPV negative

Routine screening

HPV unknown

HPV testing (Preferred)

Age ≥30 years

Repeat cytology in 3 years (Acceptable)

HPV positive or

Cytology + HPV test in 1 year

Genotyping

Manage per ASCCP Guideline

*Negative for intraepithelial lesion or malignancy
*HPV testing is unacceptable for screening women ages 21-29 years
Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

- Repeat Cotesting @ 1 year
  - Acceptable
  - Cytology Negative and HPV Negative
  - Repeat cotesting @ 3 years

- HPV DNA Typing Acceptable
  - HPV 16 or 18 Positive
  - HPV 16 and 18 Negative
  - Repeat Cotesting @ 1 year

Colposcopy

- Manage per ASCCP Guideline
Management of Women with Atypical Squamous Cells of Undetermined Significance (ASC-US) on Cytology*

**Repeat Cytology**
- @ 1 year
- Acceptable

- Negative
- > ASC

**Routine Screening**

**Colposcopy**
- Endocervical sampling preferred in women with no lesions, and those with inadequate colposcopy; it is acceptable for others

**HPV Testing**
- Preferred

- HPV Positive
  - (managed the same as women with LSIL)

- HPV Negative
  - Repeat Cotesting @ 3 years

**Manage per ASCCP Guideline**

*Management options may vary if the woman is pregnant or ages 21-24.
*Cytology at 3 year intervals

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Management of Women Ages 21-24 years with either Atypical Squamous Cells of Undetermined Significance (ASC-US) or Low-grade Squamous Intraepithelial Lesion (LSIL)

Women ages 21-24 years with ASC-US or LSIL

Repeat Cytology @ 12 months Preferred

- HPV Positive
  - Reflex HPV Testing
    - Acceptable for ASC-US only
    - HPV Negative
      - Routine Screening

- HPV Negative
  - Repeat Cytology @ 12 months
    - Negative, ASC-US or LSIL
      - Routine Screening
    - ASC-H, AGC, HSIL
      - Colposcopy

- Negative x 2 > ASC

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Management of Women with Low-grade Squamous Intraepithelial Lesions (LSIL)*‡

**LSIL with negative HPV test** among women ≥ 30 with cotesting

- Repeat Cotesting @ 1 year
  - Cytology Negative and HPV Negative
  - Repeat Cotesting @ 3 years

**LSIL with no HPV test**

- Acceptable
- Colposcopy
  - ≥ ASC or HPV positive
  - Non-pregnant and no lesion identified
  - Inadequate colposcopic examination
  - Adequate colposcopy and lesion identified

**LSIL with positive HPV test** among women ≥ 30 with cotesting

- Endocervical sampling “preferred”
- Endocervical sampling “preferred”
- Endocervical sampling “acceptable”

- CIN2,3
  - Manage per ASCCP Guideline

- No CIN2,3
  - Manage per ASCCP Guideline

* Management options may vary if the woman is pregnant or ages 21-24 years
‡ Manage women ages 25-29 as having LSIL with no HPV test

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Management of Pregnant Women with Low-grade Squamous Intraepithelial Lesion (LSIL)

**Pregnant Women with LSIL**

- **Colposcopy Preferred**
  - **No CIN2,3^**
    - Postpartum follow-up
  - **CIN2,3**
    - Manage per ASCCP Guideline
- **Defer Colposcopy** (Until at least 6 weeks postpartum) Acceptable

^ In women with no cytological, histological, or colposcopically suspected CIN2,3 or cancer
Management of Women with Atypical Squamous Cells: Cannot Exclude High-grade SIL (ASC-H)*

Colposcopy
Regardless of HPV status

No CIN2,3

Manage per
ASCCP Guideline

CIN2,3

Manage per
ASCCP Guideline

* Management options may vary if the woman is ages 21-24.
Management of Women Ages 21-24 yrs with Atypical Squamous Cells, Cannot Rule Out High Grade SIL (ASC-H) and High-grade Squamous Intraepithelial Lesion (HSIL)

**Colposcopy**
(Immediate loop electrosurgical excision is unacceptable)

- **No CIN2,3**
  - Observation with colposcopy & cytology *
    - @ 6 month intervals for up to 2 years
  - Other results
  - HSIL
    - High-grade colposcopic lesion or HSIL
      - Persists for 1 year
      - Biopsy
      - Manage per ASCCP Guideline for young women with CIN2,3

- **CIN2,3**

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*If colposcopy is adequate and endocervical sampling is negative. Otherwise a diagnostic excisional procedure is indicated.

*Not if patient is pregnant
Management of Women with High-grade Squamous Intraepithelial Lesions (HSIL)*

**Immediate Loop Electrosurgical Excision**

Or

**Colposcopy** (with endocervical assessment)

No CIN2,3

CIN2,3

**Manage per ASCCP Guideline**

* Management options may vary if the woman is pregnant, postmenopausal, or ages 21-24

* Not if patient is pregnant or ages 21-24
Initial Workup of Women with Atypical Glandular Cells (AGC)

All subcategories (except atypical endometrial cells)

Colposcopy (with endocervical sampling) and Endometrial sampling (if ≥ 35 yrs or at risk for endometrial neoplasia*)

Atypical Endometrial Cells

Endometrial and Endocervical Sampling

No Endometrial Pathology

Colposcopy

*Includes unexplained vaginal bleeding or conditions suggesting chronic anovulation.
Subsequent Management of Women with Atypical Glandular Cells (AGC)

Initial Cytology is AGC - NOS

No CIN2+, AIS or Cancer

- Cotest at 12 & 24 months
  - Both negative: Cotest 3 years later
  - Any abnormality: Colposcopy

CIN2+ but no Glandular Neoplasia

- Manage per ASCCP Guideline

Initial Cytology is AGC (favor neoplasia) or AIS

No Invasive Disease

- Diagnostic Excisional Procedure*
  - *Should provide an intact specimen with interpretable margins. Concomitant endocervical sampling is preferred.
Management of Women with No Lesion or Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 1 (CIN1) Preceded by “Lesser Abnormalities”

Follow-up without Treatment

- Cotesting at 12 months
  - HPV(-) and Cytology Negative
- Age appropriate retesting 3 years later
  - Cytology negative +/- HPV(-)
  - Routine screening

≥ ASC or HPV(+)

Colposcopy

No CIN

- Manage per ASCCP Guideline

CIN2,3

If persists for at least 2 years → Follow-up or Treatment

CIN1

- If persists for at least 2 years → Follow-up or Treatment

* “Lesser abnormalities” include ASC-US or LSIL Cytology, HPV 16+ or 18+, and persistent HPV

∞ Management options may vary if the woman is pregnant or ages 21-24.

+ Cytology if age <30 years, cotesting if age ≥30 years

† Either ablative or excisional methods. Excision preferred if colposcopy inadequate, positive ECC, or previously treated.
Management of Women with No Lesion or Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 1 (CIN1) Preceded by ASC-H or HSIL Cytology

- **Cotesting at 12 and 24 months**
- **Diagnostic Excision Procedure**
- **Review of cytological, histological, and colposcopic findings**

**Flowchart:**
- If HPV(-) and Cytology Negative at both visits, perform Age-specific Retesting in 3 years.
- If HPV(+) or Any cytology abnormality except HSIL, proceed to Colposcopy.
- If HSIL at either visit, proceed to Colposcopy.

- *Only if colposcopy was adequate and endocervical sampling is negative*
- ^ Except in special populations (may include pregnant women and those ages 21-24)
- *Cytology if age <30, cotesting if age ≥30 years*

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Management of Women Ages 21-24 with No Lesion or Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 1 (CIN1)

After ASC-US or LSIL

Repeat Cytology @ 12 months

< ASC-H or HSIL

Repeat Cytology @ 12 mos

Negative

Routine Screening

> ASC-H or HSIL

Colposcopy

After ASC-H or HSIL

Manage per ASCCP Guideline for Women Ages 21-24 with ASC-H or HSIL using postcolposcopy path for No CIN2,3

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Management of Women with Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 2 and 3 (CIN2,3)*

*Management options will vary in special circumstances or if the woman is pregnant or ages 21-24

1If CIN2,3 is identified at the margins of an excisional procedure or post-procedure ECC, cytology and ECC at 4-6mo is preferred, but repeat excision is acceptable and hysterectomy is acceptable if re-excision is not feasible.

Adequate Colposcopy

Either Excision† or Ablation of T-zone*

Cotesting at 12 and 24 months

2x Negative Results

Repeat cotesting in 3 years

Routine screening

Inadequate Colposcopy or Recurrent CIN2,3 or Endocervical sampling is CIN2,3

Diagnostic Excisional Procedure†

Any test abnormal

Colposcopy With endocervical sampling

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Management of Young Women with Biopsy-confirmed Cervical Intraepithelial Neoplasia — Grade 2,3 (CIN2,3) in Special Circumstances

Young Women with CIN2,3

Either treatment or observation is acceptable, provided colposcopy is adequate. When CIN2 is specified, observation is preferred. When CIN3 is specified, or colposcopy is inadequate, treatment is preferred.

Observation — Colposcopy & Cytology
@ 6 month intervals for 12 months

- 2x Cytology Negative and Normal Colposcopy
  - Cotest in 1 year
  - Both tests negative
  - Cotest in 3 years

- Colposcopy worsens or High-grade Cytology or Colposcopy persists for 1 year
  - Either test abnormal
  - Repeat Colposcopy/Biopsy Recommended

Treatment using Excision or Ablation of T-zone

- CIN3 or CIN2,3 persists for 24 months
- Treatment Recommended
Management of Women Diagnosed with Adenocarcinoma in-situ (AIS) during a Diagnostic Excisional Procedure

Hysterectomy — Preferred

Conservative Management
Acceptable if future fertility desired

Margins Involved or ECC Positive

Re-excision Recommended

* Using a combination of cotesting and colposcopy with endocervical sampling

Margins Negative

Re-evaluation* @ 6 months — acceptable

Long-term Follow-up

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Interim Guidance for Managing Reports using the Lower Anogenital Squamous Terminology (LAST) Histopathology Diagnoses

Low Grade Squamous Intraepithelial Lesion (LSIL)*

Manage like CIN1

High Grade Squamous Intraepithelial Lesion (HSIL)*

Manage like CIN2,3

*Histopathology Results only.

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Definitions

- **Colposcopy** is the examination of the cervix, vagina, and, in some instances the vulva, with the colposcope after the application of a 3-5% acetic acid solution coupled with obtaining colposcopically-directed biopsies of all lesions suspected of representing neoplasia.

- **Endocervical sampling** includes obtaining a specimen for either histopathological evaluation using an endocervical curette or a cytobrush or for cytological evaluation using a cytobrush.

- **Endocervical assessment** is the process of evaluating the endocervical canal for the presence of neoplasia using either a colposcope or endocervical sampling.

- **Diagnostic excisional procedure** is the process of obtaining a specimen from the transformation zone and endocervical canal for histopathological evaluation and includes laser conization, cold-knife conization, loop electrosurgical excision procedure (LEEP), and loop electrosurgical conization.

- **Adequate colposcopy** indicates that the entire squamocolumnar junction and the margin of any visible lesion can be visualized with the colposcope.

- **Endometrial sampling** includes obtaining a specimen for histopathological evaluation using an endometrial aspiration or biopsy device, a “dilatation and curettage” or hysteroscopy.

Terms Utilized in the Consensus Guidelines

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