Cervical Cancer Screening Update

Melissa Hartman, DO
Women’s Health
<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendation</th>
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<tr>
<td>ACS (2011)</td>
<td>Age 21 or 3 years after first intercourse q 1-2 years Age &gt;30 screen q 3 years if 3 normal consecutive paps</td>
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<td>ACP (2008)</td>
<td>Begin at age 21 or 3 years after first intercourse q 1-3 years</td>
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<td>NCI (2003)</td>
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<td>After Hysterectomy</td>
<td>No screening</td>
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<tr>
<td>HPV vaccinated</td>
<td>Follow age-specific recommendations</td>
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</table>
Diagram of the TZ

- TZ
- Most Distal Cervical Crypt Opening
- SCJ
- Area of Ectopy
Lubricants do NOT interfere with pap smears. (LOE=1b)
Conventional Pap vs Liquid Based Cytology

- ACOG reports both are acceptable
- USPSTF says evidence is inconclusive (I)
- Metanalysis Data
  - Thin Prep is not superior to conventional pap for detection of CIN 2 or worse
  - Thin Prep is less specific → Leading to more false positive results with ASCUS

When should we stop screening?

- **ACS**: Women who are >70 yo and who have had 3 or more consecutive normal paps within 10 yrs

- **USPSTF**: recommends against screening in women >65 yo if they have had adequate recent screening and are not at high risk (D)

- **ACOG**: no upper age to end screening
When should we stop screening?

- 20% of cervical cancers occur in women over age 65

- Progression from HPV infection to cervical cancer is 10-20 years

Human Papilloma Virus – Etiology of Cervical Cancer

- Carcinogenic types
  - 16, 18, 45 & 56

- Intermediate
  - 31, 33, 35, 39, 51 & 59

- Non-cancer inducing
  - 6, 11, 42, 43, 44
HPV

- 80% of sexually active people will get HPV at some time in their lives

- >90% are self-eliminating over 18 mos

- Testing is 83-100% sensitive
How can patients decrease their risk of Cervical Cancer?

- HPV Vaccine (70% decrease)
- Condoms (50% decrease)
- Monogamous relationships
- Abstinence
Gardasil®

- The vaccine, Gardasil®, protects against HPV types 6, 11, 16, 18
- About 30% of cervical cancers will not be prevented by the vaccine
- Ideally, females should be immunized before sexual activity
- Recommendation:
  - Girls 11-12 yo
  - Boys in 2009 ACIP gave permissive recommendation
  - Approved for ages 9-26
- 3 shot series over 6 months
- Less than 1/3 of girls 13-17 have received one dose
The Gardasil 9® vaccine protects against HPV strains: 16, 18, 31, 33, 45, 52, 58, 6, 11

Approved for males and females age 9-26 yo

3 shot series over 6 mo

Due to the added strains it is thought to significantly reduce the risk for cervical cancer and genital warts
The vaccine Cervarix® protects against HPV strains 16 & 18

Approved for females 9-25 yo

3 shot series over 6 months
Cervical Carcinogen Cofactors

- **Smoking**: 2-3 fold
- **BCPs**: >10 yr use increase 4 fold – possibly b/c people using BCPs are generally more sexually active
- **Multiple Pregnancies**: >7
- **Low SE status**
- **Immunocompromised**: HIV and HPV co-exist 90% of the time, it is usually more resistant to treatment and more likely to progress
- **Infections**: Gonorrhea, Chlamydia
- **Folate deficiency**: 5 fold
- **Family history**: 2-3 fold

JAOA. 2008. 108 (2) 65-70
Lancet 2002, 359 (9312) 1085
ACS www.cancer.org/docroot/CRI/content/CRI_2_4_2X_what_are_the_risk_factors_for
Risk Factors for Cervical Cancer

- Early age of intercourse:
  - <16 yo = 16 fold

- Multiple Sexual Partners:
  - >3 partners = 6 fold
  - >6 partners = 12 fold

- STD’s

- DES exposure:
  - Taken off market in 1971, causes clear cell vaginal CA and adenosis

- Sex with high risk male
- Uncircumcised partner
- Not using condoms
- Smoking
  - 2-3 fold increase
2001 Bethesda System

- ASC – Atypical Squamous Cells
  - ASC-US
  - ASC-H

- LSIL

- HSIL

- AGC-Atypical Glandular Cells
  - AGC-NOS
  - AGC-Favor Neoplasia
  - AIS (Adenocarcinoma in situ)
HPV in “Older Women”

- 71% of ♀ age 18-22 with ASCUS are HPV +
- 31% of ♀ >29 are HPV +
- 20% of ♀ >40 are HPV +

- Even with normal paps, older women with HPV are twice as likely to develop CIN 3 within 10 years

ASCCP 2013 Cervical Cancer Screening Guidelines
Unsatisfactory Pap

Unsatisfactory Cytology

- **HPV unknown (any age)**
- **HPV negative (age ≥30)**
- **HPV positive (age ≥30)**

**Repeat Cytology after 2-4 months**

- **Abnormal**
  - Manage per ASCCP Guideline
- **Negative**
- **Unsatisfactory**
  - Routine screening (HPV-/unknown) or Cotesting @ 1 year (HPV+)

**Colposcopy**
Endocervical Transformation Zone absent/insufficient

**Cytology NILM* but EC/TZ Absent/Insufficient**

- **Ages 21-29+**
  - HPV negative
    - Routine screening
  - HPV testing (Preferred)

- **Age ≥30 years**
  - HPV unknown
    - Repeat cytology in 3 years (Acceptable)
    - HPV positive or
      - HPV testing
      - 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
>30 yo Cytology neg, HPV+

**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

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

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

  - Negative
  - > ASC
  - Routine Screening

- **HPV Testing**
  - Preferred

  - HPV Positive
    - (managed the same as women with LSIL)
  - HPV Negative
    - Repeat Cotesting @ 3 years

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

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

Manage per ASCCP Guideline

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ASC-US or LSIL: 21-24 yo

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
  - Negative, ASC-US or LSIL
    - Repeat Cytology @ 12 months
      - Negative x 2
        - > ASC
          - Colposcopy
    - ASC-H, AGC, HSIL
- HPV Positive
- Reflex HPV Testing Acceptable for ASC-US only
  - HPV Negative
    - Routine Screening

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LSIL

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

**LSIL with negative HPV test**
- among women ≥ 30 with cotesting
  - Preferred: Repeat Cotesting @ 1 year
    - Cytology Negative and HPV Negative
      - Repeat Cotesting @ 3 years
  - Acceptable: ≥ ASC or HPV positive

**LSIL with no HPV test**
- Colposcopy

**LSIL with positive HPV test**
- among women ≥ 30 with cotesting
- Non-pregnant and no lesion identified
- Inadequate colposcopic examination
- Adequate colposcopy and lesion identified
- Endocervical sampling “preferred”
- Endocervical sampling “preferred”
- Endocervical sampling “acceptable”

- No CIN2,3
  - Manage per ASCCP Guideline

- 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
Normal cervix in pregnancy with metaplasia, nabothians and gland openings. The SCJ is visualized.
Low grade CIN in a pregnant patient with faint acetowhite changes, geographic margins and fine mosaic. There is metaplasia proximally. The SCJ is not completely visualized.
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.
ASC-H and HSIL: 21-24 yo

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
        Persist for 24 months with no CIN2,3 identified
        - Biopsy
          - CIN2,3
            Manage per ASCCP Guideline
            - Diagnostic Excisional Procedure*
        - CIN2,3
          Persist for 1 year
          - Biopsy
            - CIN2,3
              Manage per ASCCP Guideline for young women with CIN2,3

Two Consecutive Cytology Negative Results and No High-grade Colposcopic Abnormality

Routine Screening

*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
High grade CIN from 9 to 12 o'clock with dense acetowhite changes, sharp margins and punctuation at 12 o'clock. Ectropion is also present. Mucus at 8 o'clock obscures visualization of the SCJ.
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.
Papillary adenocarcinoma with raised surface contour and bleeding.
AGC Management

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

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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
- CIN2,3
- 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.

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CIN1 Preceded by ASC-H or HSIL

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*
  - HPV(-) and Cytology Negative at both visits
  - HPV(+) or Any cytology abnormality except HSIL
  - Age-specific Retesting in 3 years*

- **Diagnostic Excision Procedure**
  - HSIL at either visit

- **Review of cytological, histological, and colposcopic findings**
  - Manage per ASCCP Guideline for revised diagnosis

*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
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

≥ ASC

Colposcopy

≥ 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)*

- **Adequate Colposcopy**
  - Either Excision† or Ablation of T-zone*
    - **Cotesting** at 12 and 24 months
      - 2x Negative Results
        - Repeat cotesting in 3 years
      - Any test abnormal
        - Colposcopy With endocervical sampling

- **Inadequate Colposcopy or Recurrent CIN2,3 or Endocervical sampling is CIN2,3**
  - **Diagnostic Excisional Procedure†**

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

†If 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.

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CIN2 and CIN3: Young Women

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
- Either test abnormal

**Treatment using Excision or Ablation of T-zone**

- Colposcopy worsens or High-grade Cytology or Colposcopy persists for 1 year
  - Repeat Colposcopy/Biopsy Recommended
- CIN3 or CIN2,3 persists for 24 months
  - Treatment Recommended

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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

- **Margins Negative**
  - Re-evaluation*  
    - @ 6 months — acceptable
  - Long-term Follow-up

* Using a combination of co-testing and colposcopy with endocervical sampling

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Progression of Dysplasia

Contribution of Dr Sauder, 2006
## Natural History of CIN

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<th>Regress</th>
<th>Persist</th>
<th>Progress to CIN3</th>
<th>To Cancer</th>
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<tr>
<td><strong>CIN 1</strong></td>
<td>60%</td>
<td>30%</td>
<td>10%</td>
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<td><strong>CIN 2</strong></td>
<td>40%</td>
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<td><strong>CIN 3</strong></td>
<td>33%</td>
<td>&gt;56%</td>
<td>--</td>
<td>20%</td>
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Endometrial Cells on Pap

- Normal in first 14 days of cycle
- Abnormal in post-menopausal women or during last half of cycle
- Will need endometrial biopsy in older women or if out of cycle
- Benign glandular cells seen on pap if woman is s/p hysterectomy is of no clinical significance and does not warrant biopsy
Hyperkeratosis

- Reactive mechanism to physical, chemical or inflammatory trauma

- Repeat pap in 6 months with HPV (C)

- Chechini et al found no CIN in 269 pts
Leukoplakia of the cervix.
Indications for Colposcopy

- Abnormal Pap
- Repeated minimally abnormal pap
- Suspicious lesion seen or palpated
- Genital warts
- History of sexual abuse
- History of DES exposure
- Post-coital bleeding
Post-Coital Bleeding

- Refer to colposcopy

- 25% have underlying pathology
  - 5% cancer
  - 15% dysplasia
  - 5% polyps
Normal cervix with ectropion, metaplasia and a polyp at the os.
Condyloma of the cervix and vagina with irregular surface contour and snow acetowhite changes. The SCJ is not visualized.
Reminder of the 2012 AAFP/USPSTF/ASCCP/AC CP Consensus Guidelines
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<td>Women with a history of ≥CIN2 should continue routine screening for at least 20 y</td>
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<td>HPV vaccinated</td>
<td>Follow age-specific recommendations</td>
<td>Same as unvaccinated women</td>
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Two SCJs are visualized in a patient with uterus didelphius. Metaplasia and gland openings are noted around each SCJ.