The Latest Pap Guidelines

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Learning Objectives

• Use current Pap guidelines in practice
• Understand the difference between HPV reflex testing and HPV co-testing
• Understand Pap recommendations after hysterectomy
Incidence and Mortality of Cervical Cancer

• US estimates for 2014
  – 4020 deaths from cervical cancer
  – 12,360 new cases of cervical cancer

Natural History of HPV Infection

HPV Infection → Transient Infection → Persistent Infection → Low-Grade Dysplasia (CIN 1) → High-Grade Dysplasia (CIN 2/3) → Invasive Cancer

- Persistent Infection: > 2 years
- Low-Grade Dysplasia (CIN 1): 2-5 years
- High-Grade Dysplasia (CIN 2/3): 9-15 years
- Transient Infection: ~1 year

Pagliusi, 2004
Who Gets Cervical Cancer?

• Being rarely or never screened is the major contributing factor to most cervical cancer deaths

• Descriptors
  – Minorities
  – Low socio-economic status
  – Born in a foreign country
    • Living in the US < 10 years
  – No medical home

Data from: US Census, National Center for Health Statistics, Behavioral Risk Factor Surveillance System, and National Health Interview Study, CDC
Are There System Failures?

- Patient doesn’t come in for screening
- Providers do not screen the patient at visits
- Abnormal screen not investigated
- Patient doesn’t get appropriate therapy for abnormalities
- Patient gets cervical cancer
Are There System Failures?

Pap results 3-36 months prior to diagnosis
n=833

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<td>ASC-US</td>
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<td>Glandular cells</td>
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Spitzer et al, 2002
Terminology for Glandular Cells

<table>
<thead>
<tr>
<th>Bethesda System 1991</th>
<th>Bethesda System 2001</th>
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<tr>
<td>Glandular cells</td>
<td>Glandular cells</td>
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<tr>
<td>Endometrial cells, benign in a postmenopausal woman</td>
<td>AGC (endocervical or endometrial glandular cells)</td>
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<tr>
<td>AGUS</td>
<td>AGC-favor neoplasia</td>
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<tr>
<td>Endocervical adenocarcinoma</td>
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<td>Extrauterine adenocarcinoma</td>
<td>Endocervical</td>
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<td>Adenocarcinoma NOS</td>
<td>Endometrial</td>
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</table>

Spitzer et al, 2002
The 2001 Bethesda System

• Specimen Adequacy
  – Presence or absence of endocervical cells
  – Processing issues

• General Categorization (optional)

• Interpretation/Result
  – Negative for intraepithelial lesion or malignancy
    • Organisms and/or other non-neoplastic findings (e.g., atrophy)
  – Epithelial cell abnormalities (squamous and glandular)
  – Other malignant neoplasms (specify)

Spitzer et al, 2002
Why so many changes?

Abnormal Paps
CIN
AIS

- ASCUS-LSIL
  + HPV testing
- CIN 1
  - Adolescents & young women
  - Unsatisfactory test
  - HPV testing with screening
Goals of Cervical Cancer Screening

• Prevent the morbidity and mortality from cervical cancer
• Prevent the overzealous management of precursor lesions that most likely will regress or disappear and for which the risks of management outweigh the benefits
Possible Harms of Screening

- Anxiety over a positive test
- Stigma of an STI
- Pain and bleeding from procedures
- Treatment-related pregnancy complications
- Surrogate marker for harm – number of colposcopies
Strength of Recommendations

- **Recommended** – good data to support use when only one option is available
- **Preferred** – option is the best when there is more than one option
- **Acceptable** – one of multiple options when there is either data indicating that another approach is superior or when there are no data to favor any single option
- **Not recommended** – weak evidence against use and marginal risk for adverse consequences
- **Unacceptable** – good evidence against use
Management and Screening Intervals Based on Cancer Risk

- < 0.1% risk – f/u in 5 years
- 0.1-2% risk – f/u in 3 years
- 2-5% risk – f/u in 6-12 months
- > 5% risk - colposcopy
- CIN 3+, SCCa or AIS - treatment
Who Has <0.1% Risk?

• Women undergoing routine screening
  – Not in follow-up for abnormalities
• Adequate visualization of the cervix
• Directed sampling with acceptable collection instruments
Initiation of Screening

• Age 21
  – Risk of cervical cancer in women ≤ 25 years
    • 1.4/100,000 women
    • 55,000 Pap tests must be done to find 1 cervical cancer
  – Risk of cervical cancer in women 15-19 years is 1-2/1,000,000 women
  – HPV is common
  – Most lesions regress without intervention
  – Age of coitarche is not a factor
Screening Intervals

• Ages 21 to 29
  – Pap test every 3 years
  – Reflex HRHPV testing – only for ASCUS
    • Reflex testing means if the Pap shows ASCUS, then the lab will automatically do a HRHPV test
    • If the Pap has any other result than ASCUS, no HRHPV test will be performed

<table>
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<th>Reflex HRHPV Testing</th>
<th>Pap</th>
<th>HRHPV Performed</th>
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<tr>
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<td>Negative</td>
<td>No</td>
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<tr>
<td>ASCUS</td>
<td>Yes</td>
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<td>&gt; LSIL</td>
<td>No</td>
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HRHPV - Reflex vs. Cotest

Pap with HRHPV Reflex Testing

- Negative or > LSIL
- ASCUS
  - HRHPV Test

Pap with HRHPV Co-Testing

- Pap
  + HRHPV
Screening Intervals

• Ages 30 to 65
  – Pap test and HRHPV cotesting every 5 years is PREFERRED
  – Pap test with reflex HRHPV testing every 3 years is acceptable
Rationale for Cotesting

• Detection of prevalent CIN 3 is increased
• Enhances detection of adenocarcinoma/AIS
• Minimizes the number of colposcopies
Screening Intervals

• Rationale for longer Pap intervals
  – Cancer risk 18 mos after 3 negative Paps = 1.5/100,000
  – Cancer risk 36 mos after 3 negative Paps = 4.7/100,000
  – Risk of CIN3+ after 1 year ≈ Risk of CIN3+ after 3 years
Discontinuation of Screening

- Age $\geq 65$
  - Adequate negative prior screening
    - $\geq 3$ consecutive, satisfactory negative Pap tests or 2 consecutive negative HPV tests within the last 10 years and most recent test within 5 years
    - AND no CIN 2+ within the last 20 years
- Severe co-morbid or life-threatening illnesses
- Do not resume for any reason, even for a new sexual partner
Rationale for Discontinuation at Age 65

- CIN 2+ is rare after age 65
- HPV risk remains only 5-10% and is unlikely to lead to cancer within the remaining lifetime

Chen HC et al. JNCI 2011;103:1387-96
Rodrigues AC et al. JNCI 2009;101:721-8
When NOT To Stop At 65 Years

• History of CIN 2, CIN 3, AIS or cancer
  – Continue routine screening for at least 20 years, even if the patient is past 65 years of age
Screening after Hysterectomy

• Discontinue after hysterectomy with removal of cervix as long as there’s no history of CIN 2, CIN 3, AIS or cancer in the last 20 years
• Vaginal cancer is rare – 7/1,000,000/yr
• Risk of a Pap abnormality after hysterectomy is 1%
Resources

- [www.asccp.org](http://www.asccp.org)
- ASCCP App for iOS and Android