Cervical Cancer Update 2013

New Screening and Follow-up Guidelines of Abnormal Pap Smears

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Onset, Massachusetts

R. Mimi Secor, MS, MEd, FNP, FAANP

- FNP for 35 years specializing in Women’s Health
- Newton Wellesley ObGyn, Massachusetts
- National Speaker, Consultant
- 2013 Lifetime Achievement Award, Mass Coalition of NPs
- Co-author 2012, “Fast Facts About The Gyn Exam for NPs”
- Co-author, 2010. “Advanced Health Assessment of Women; Skills & Procedures” both by Springer publishing
- Visiting Scholar - Boston College
- Fellow in AANP, American Assoc. of Nurse Practitioners
- Board of Director, NPACE, Natick, Massachusetts
- Worked in Bethel, Alaska for 7 years (1992-1999)

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Disclosure

Speaker- Genpath Lab
Objectives (No pharm credits)

- Discuss current epidemiology of cervical cancer. 10 minutes
- Describe updated cancer screening guidelines and rationale for these guidelines. 20 minutes
- Explain new 2013 ASCCP follow-up guidelines for abnormal Pap smear findings. 30 minutes

HPV 2013 Update: What's New?

- Vaccine Update: NEW for Boys, Men
- Cervical Cancer Screening Guidelines: New 2012
- F/u of Abnormal Pap Guidelines: New 2013
- External Genital Warts:
  - : May harbor high grade lesions
- Anal Cancer Screening: Controversial
- Oral Cancer Association: The New STI
HUMAN PAPILLOMA VIRUS, HPV

Estimated Prevalence of STDs in the US
20 Million New Infections a Year!

<table>
<thead>
<tr>
<th>Condition</th>
<th>Estimated Prevalence</th>
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<tbody>
<tr>
<td>Human Papillomavirus</td>
<td>20 Million</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>3 Million</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1.25 Million</td>
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<tr>
<td>HIV/AIDS</td>
<td>1.2 Million</td>
</tr>
<tr>
<td>Genital Herpes</td>
<td>50 Million+</td>
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A Little Coitus Never “Hoitus”

Teens “hooking up”
Friends with “benefits”
Married men, having sex with men
living on the “down low”

References:
HPV: Introduction

- Most common STI in US
- Cause of cervical cancer
- Associated with external genital warts, and cancer of the penis, vagina, vulva, anus & oropharynx!

<table>
<thead>
<tr>
<th>Site</th>
<th>Total Cancers</th>
<th># Cases Attributable to HPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>11,150</td>
<td>11,150 (100%)</td>
</tr>
<tr>
<td>Penis</td>
<td>1,280</td>
<td>512 (40)</td>
</tr>
<tr>
<td>Vulva/Vagina</td>
<td>5,630</td>
<td>2,252 (40)</td>
</tr>
<tr>
<td>Anus</td>
<td>4,650</td>
<td>4,185 (90%)</td>
</tr>
<tr>
<td>Airway</td>
<td>24,540</td>
<td>6,380 (26%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>47,250</td>
<td>24,479 (12%)</td>
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**HPV Vaccine Update: Girls & Boys**

**Ages 9-26; Three Doses @ 0, 2, 6 months**

- **Girls, Women:** 2 doses may provide protection, ? duration
  - Quadrivalent (Gardasil): FDA approved 2006
    HPV Vaccine 6, 11, 16, 18, by Merck
  - Bivalent (Cervarix): FDA approved 2009
    HPV Vaccine 16, 18, by Glaxo Smith Kline

- **Boys, Men:**
  - Quadrivalent (Gardasil) for MEN: Ages 9-26 years
    - FDA approved 2009
    - Prevents Genital Warts, MAY prevent "Anal Cancer"

**Recommendations by CDC & ACIP**
Advisory Committee on Immunization Practices of CDC

**NEW- March, April 2012:**
Cervical Cancer Screening Guidelines

**Citations:**
  [e-pub ahead of print].
  (http://www.annals.org/content/early/2012/03/14/0003-4819-156-12-201206190-00424.full?sid=46a1b16f-88a2-4347-9c5e-76cb86a6720e)
### 2012: NEW Cervical Cancer Screening Guidelines

- **Ages 21-29***
  - 1st Pap at age 21
  - Repeat every 3 years*

- **Age >30 years:*** if low risk
  - Pap and HPV = Primary screening
  - If both negative, repeat every 5 years
  - Pap ONLY = every 3 years

- **Age 65 years:** MAY STOP (if negative history)

*Low Risk = NO history of CIN 2, CIN 3, HIV+, immunocompromised, DES

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### Age to START Screening for Cervical Cancer

**Age 21**


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### Clinical Uses of HPV Testing

- **High-risk types: NEW 2012**
  - ASC-US management in women age ≥21 years old
  - Pap plus HPV for screening women ≥30 years
  - Primary Screening, Co-testing
  - HPV testing ALONE is NOT recommended
Guidelines: Screening Post-Hysterectomy

ACS, ACOG, USPSTF Guidelines

• Recommend *against* routine screening if hysterectomy performed for benign disease
• AND who have no history of high-grade CIN


Guidelines: Age may *Stop* Cervical Cancer Screening

• 65 years old


2013 ASCCP: Essential Changes

• More strategies incorporate “Co-testing” to reduce follow-up visits
• Women aged 21-24 yrs are managed conservatively!
ASCPC 2013: Essential Changes

CIN 2+
- The pathway to long-term follow-up of treated and untreated CIN 2+
- Is more clearly defined by incorporating “Co-testing”

Acknowledgement: Thanks to ASCCP for permission to reprint their 2013 Algorithms for Follow-up of Abnormal Pap Smears

Cytology Normal (NILM) but EC/TZ Absent, Insufficient
Unsatisfactory Cytology

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

  - Repeat Cytology after 3-6 months

- Repeat Cytology
  - Abnormal
  - Manage per ACOG guideline
  - Normal
  - Routine screening (HPV unknown) or
    - Cervical (if 3-5 years HPV+)

  - Unsatisfactory
  - Colposcopy

- Other to evaluate

Women > 30, Cytology Neg, HPV Positive

- Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive

  - Repeat Cytology
    - HPV negative
    - HPV positive

  - HPV DNA Typing
    - HPV 16 or 18 Positive
    - HPV 16 and 18 Negative

  - Colposcopy
  - Repeat Cytology
    - ≥ 1 year

  - Manage per ACOG guideline

Secor 2013 Copyright
Atypical Glandular Cells, AGC: Clinical Significance

- **Uncommon** abnormality (0.4% in 2003)
- More common in "Older" women ≥ 40 years
- 3-17% have **invasive cancer** including:
  - Adenocarcinomas of cervix, endometrium, ovary & fallopian tube
- Thorough workup required
  - ECC, EMB, US, Colposcopy, etc.

Best Follow-up after Treatment of CIN? Pap alone or Pap AND HPV?

- F/u for 20 years after High-Grade CIN Treatment
- "Short term monitoring post-treatment of women with combined HPV testing AND cytology at 6 months and 24 months seems to be sufficient to detect post-treatment cervical disease." Pap AND HPV!
- BMJ 2012 Nov;345:e6855 (Free)
  http://click.jwatch.org/cts/click?q=227%3B67752576%3BqOmRKGX%2B8u0fJHY0GbGw2Be58k0UnPklWclcFopp%2Bco%3D
- BMJ 2012 Nov;345:e7086 (Free)
  http://click.jwatch.org/cts/click?q=227%3B67752576%3BqOmRKGX%2B8u0fJHY0GbGw2TFTv3lXwKe1WclcFopp%2Bco%3D

Young Women w Biopsy-confirmed CIN 2, 3: CIN 2- Observe, CIN 3- Treat
Diagnosed w Adenocarcinoma in-situ AIS: during Diagnostic Excisional Procedure

Anal Cancer Screening
New and Controversial

In memory of Farrah Fawcett
### HPV-Associated Anal Lesions
High-grade precursor lesions = Anal intraepithelial neoplasia (AIN)

- 80% associated with high-risk HPV 16, 18
- 4,650 estimated cases in US 2007

~ Annual mortality: 260 men die, 430 women die

- Men Having Sex with Men/MSM
  - Cancer rate 35 per 100,000
  - Equal to cervical cancer rate before Paps!

### Anal Cancer: Risk Factors

- Men having sex with men/MSM
- HIV infection
- IV Drug use
- ≥15 lifetime sexual partners
- Receptive anal intercourse, unprotected
- History of CIN, Cervical Intraepithelial Neoplasia
- Cigarette smoking


### Anal Screening Recommendations
No Universal Guidelines

- NOT recommended by CDC, USPSTF, ACS, or ISDA or the National Guidelines Clearinghouse

- Yearly: per New York Dept. of Health
  - HIV positive: Every 6 months 1st year screened
  - Men having Sex with Men/MSM
  - History of genital warts
  - History of CIN 2,3, Cervical intraepithelial Neoplasia

New York State Dept of Health. www.hsguidelines.org
Anal Pap Procedure:
Position Patient on Side, or in Gyn Stirrups

- Use Dacron swab (+/- May use cytobrush)
  - Pre-moistened with tap water
- Insert 5 cm (about 2”)
  - Spiral motion, firm pressure, rotate 360 degrees
  - Circling 1 direction, DON’T reverse
- Gradually withdrawn over 10 sec (rotating)
- Agitate in liquid fixative for 15 seconds
- No reflex HPV testing available

http://www.analcancerinfo.ucsf.edu/
http://www.aids.about.com/cs/conditions/a/analpape.htm

Lower Anogenital Squamous Terminology (LAST) Histopathology Diagnosis

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

Low-Grade Squamous
Intraepithelial Lesion (LSIL)

High-Grade Squamous
Intraepithelial Lesion (HSIL)

Manage like CW1

Manage like CW2,3
Anal Condylomata: NEW July 2010
How Often Do Anal Warts Harbor High-Grade Neoplasia?

- Retrospective cohort, n = 319
- Among Men having Sex with Men, MSM
  - 50% HIV+, 50% HIV-
- High-grade lesions were frequently present
  within Anal Condylomata
  - If HIV positive = 47%
  - If HIV negative = 26%

- Appear benign on exam!
- Refer for: Anoscopy, Biopsy

Differential Diagnosis of Genital Warts: Biopsy When in Doubt!

- Biopsy any atypical lesion: Before treatment
  - Immunosuppressed patients
  - Unresponsive to treatment
- Neoplastic lesions include:
  - Bowenoid papulosis, Bowen's disease
  - Squamous cell carcinoma
  - Vulvar intraepithelial neoplasia (VIN)
  - Anal intraepithelial neoplasia (AIN)
  - Giant condyloma (Buschke-Löwenstein tumor)
  - Dysplastic nevi

Imiquimod, (Zyclara) 3.5% cream: FDA Approved for Genital Warts

- Applied daily x 8 weeks
- Complete clearance 43.8% (statistically significant) versus placebo 22.7%
- Efficacy greater in Women than Men
- Side effects:
  - Itching 2.5%, burning 5.8%, pain 6.8%
  - 31% needed rest periods due to side effects
- www.ZyclaraCream.com
Head and Neck Cancer
New HPV Risk Confirmed in 2007

Our Daughter, Katherine with Neighbor
Who Died from Oropharyngeal Cancer 2009

HPV and Oral Carcinoma
New Risk Confirmed in 2007, 7% positive

- 35,000 cases per year in US (Men 25,000: Women 10,000)
- Up to 15,000 New cases per year HPV related!
- Up to 60% HPV related

- ~47,000 oral cancer cases from 1973 to 2004
  ~17,500 cases HPV related

"Incidence Trends for Human Papillomavirus-Related and -Unrelated Oral Squamous Cell Carcinomas in the United States."


Dr. Maura Gillison, Ohio State, Columbus, OH tel 866.203.9386
Oropharyngeal Cancer
HPV 16 infection increases risk 50 fold!

- Major Risk Factors:
  - Tobacco, Alcohol, etc.
- HPV HR types: 7% of US population infected!
  - Oral sex
  - **Only takes 1 partner**
  - Not a cancer of promiscuity
  - Number of lifetime sex partners
  - **Age of 1st coitus, 50% HPV+ within 3 years**

- Younger age than non-HPV cancers < 60 years

Oropharyngeal Cancer Symptoms
No Diagnostic Algorithm

**History**
- Unilateral persistent sore throat > 2 weeks
- Ear pain
- Speech changes
- Tongue numbness
- Lymph node in neck, unexplained

**Exam:**
- White leukoplakia, white patch along gum line
- Erythroplasia; flat patch, subtle, high risk
- Ulcers

Presentation: White Lesion
Oral Cancer

Potential Screening Techniques for Oral Cancer

Current
- Annual
- Clinical exam with visual inspection
- Refer for tissue biopsy

Future
- Oral cytology (Pap smear)
- Oral HPV testing (ongoing research)
- Brush biopsy
- Visual assistance devices

American Cancer Society Guidelines

“...the cancer-related check-up should include examination for cancers of the thyroid, testicles, cervix, ovaries, lymph nodes, oral cavity, and skin, as well as health counseling...”

Smith RA, CA Cancer J Clin. 2003

Thank You and Good Luck!

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www.MimiSecor.com
www.ReachMD.com

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QUESTIONS

Bibliography and Resources

- www.cdc.gov/std/treatment (new 2006 guidelines)
- cdc.gov/std/hpv (Gardasil pt education)
- Herpesdiagnostics.com (Herpes-Select serology)
- Asccp.org, ACS.org, Digene.com (Pap guidelines)
- Asha.org (great patient education materials)

Bibliography

- http://depts.washington.edu/nmpc/online_training/index.html#clinicalslides
- www.cdc.gov/ stds/treatment