Cervical Cancer: Latest Update on Screening and Prevention

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Outline
- Cervical cancer in Alabama
- Screening for Cervical cancer
- How can you provide more services to underserved women?
- Prevention of Cervical cancer through vaccination

Cervical Cancer
- 13,240 new cases in 2018
- 4,170 deaths related to cervical cancer
- Risk factors:
  - HPV high risk positivity
  - HIV or other immunosuppression
  - Smoking
  - Poor access to care, no recent screening

Cervical Cancer in Alabama 2017
Alabama ranks 9th in cervical cancer incidence (new cases) and 1st in cervical cancer mortality (deaths) in the United States.

<table>
<thead>
<tr>
<th></th>
<th>Alabama</th>
<th>United States</th>
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<tbody>
<tr>
<td></td>
<td>Incidence</td>
<td>Mortality</td>
</tr>
<tr>
<td>ALL Women</td>
<td>8.6</td>
<td>3.2</td>
</tr>
<tr>
<td>White</td>
<td>8.2</td>
<td>2.7</td>
</tr>
<tr>
<td>African American</td>
<td>10.6</td>
<td>5.2</td>
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Note: Rates are per 100,000 and age-adjusted to the 2000 US Standard Population. Data years include 2002-2006. Data is determined by lowest number being the worst and highest number being the best. States only include data for those states meeting high-quality standards for 2002-2006 and include data from states and jurisdictional cancer registries participating in SEER, NPCR, or both, in the U.S. and the Canadian Cancer Registry in Canada and underlying United States mortality data provided by NCHS (www.cdc.gov/nchs). ACS 2009 Supplemental Data.
Cervical cancer in Alabama

Screening for Cervical cancer

How can you provide more services to underserved women?

Prevention of Cervical cancer through vaccination

Case #1

- 32 yo F G2P2 presents with a new pap of squamous cell carcinoma
  - Last pap was 4 years ago – ASC-H
  - No symptoms
  - Normal periods

- Could this have been prevented 4 years ago?
  - What was her HPV status?
  - Did she even come in for follow-up?
  - What else could have been done after treatment?

Screening detects CIN3 (“pre-cancer”)

Treating CIN3 prevents cancer

Goal of screening is to detect CIN3 and prevent cervical cancer

Current Guidelines

<table>
<thead>
<tr>
<th>Screening Population</th>
<th>ACS/ASCCP/ASCP/ACOG Recommendations (2012)</th>
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<tbody>
<tr>
<td>Age &lt;21 years</td>
<td>No screening</td>
</tr>
<tr>
<td>Age 21–29 years</td>
<td>Pap test alone (no HPV test) every 3 years</td>
</tr>
<tr>
<td>Age 30–65 years</td>
<td>Pap + HPV co-test every 5 years recommended</td>
</tr>
<tr>
<td>Age &gt;65 years</td>
<td>No screening if:</td>
</tr>
<tr>
<td></td>
<td>- Adequate prior screening</td>
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<tr>
<td></td>
<td>- No history of CIN2+ in the past 20 years</td>
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<tr>
<td>Post-hysterectomy</td>
<td>No screening if:</td>
</tr>
<tr>
<td></td>
<td>- Cervix removed</td>
</tr>
<tr>
<td></td>
<td>- No history of CIN2+ in the past 20 years</td>
</tr>
<tr>
<td></td>
<td>NOTE: Evidence of adequate prior screening NOT required</td>
</tr>
</tbody>
</table>

Long-term persistent HPV is especially high risk

- 8,656 women age 20–29
- Co-testing years 1 & 3
- Followed 12 years for CIN3+
- Risk of CIN3+
  - Persistent HPV16+: 47%  
  - Persistent HPV+: 19%  
  - HPV−: 2%
- HPV history is an important risk modifier

All women with persistent High risk HPV develop CIN 2 or greater
### Comparison of Three Screening Strategies

<table>
<thead>
<tr>
<th>ATHENA trial</th>
<th>≥ 25yo, 42,209 women</th>
<th>3-year cumulative incidence rate of CIN3+</th>
</tr>
</thead>
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<table>
<thead>
<tr>
<th>Risk of CIN3+ if negative (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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<tbody>
<tr>
<td>Cytology alone</td>
<td>0.8 (0.5-1.1)</td>
<td>47.8 (41.6-54.1)</td>
</tr>
<tr>
<td>Cytology + HPV cotest</td>
<td>0.3 (0.1-0.6)</td>
<td>61.7 (56.0-67.5)</td>
</tr>
<tr>
<td>Primary HPV</td>
<td>0.3 (0.1-0.7)</td>
<td>76.1 (70.3-81.8)</td>
</tr>
</tbody>
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Conclusions:
- Greater number of CIN3+ cases detected with primary HPV screening or cotesting
- Greater reassurance of low CIN3 risk with a negative hrHPV test vs negative pap test
- Able to predict future risk of CIN with HPV testing

Wright TC et al. Gyn Onc 2014

### Observational Studies

- Meta-analysis
  - 4 RCTs cotesting vs. cytology: 1 RCT hrHPV vs. cytology
  - Including hrHPV → 40% decrease incidence of ICC

- 4 cohort studies
  - Similar findings to RCT
  - hrHPV- → very low rates of CIN3+ regardless of cytology results
  - Minimal risk of missing ICC with negative hrHPV or cotest

### Cervical pre-cancer in U.S. females

- 1.4 million new cases of low grade cervical dysplasia
- 330,000 new cases of high grade cervical dysplasia
  - 30% will progress
  - LEEP vs Cone
  - Follow-up

### New ASCCP risk-based guidelines

- Patient’s current test results and past history
- Risk matrix is used to calculate her risk of CIN2/3
- Computer program generates risk score
- Recommends next step in management

### HPV vaccination after treatment

- Cheraldi et al 2018
  - Prospective cohort study 20-45
  - Received 1st dose 1 month post LEEP, 2 subsequent doses
  - Patients self-selected cohort
  - 248 vaccinated → 2 recurred
  - 276 followup only → 11 recurred
  - 81.2% reduction in recurrence with vaccination

Schiffman JL. Lower Genit Tract Dis 2017
Different strategies may be needed to further decrease cervical cancer incidence and mortality in these areas/populations.

Self-sampling with primary hrHPV testing
- Particularly in under-screened populations with low interaction with the healthcare system.

HPV testing plus Pap over 30
- NOT reflex - need to know the HPV status of nl pap.

HR HPV + – look hard for disease

Consider “look and LEEP” strategy for HSIL paps

Consider vaccination after treatment

Await upcoming screening guidelines.

Alabama received a grade of “F” as an overall grade in women’s health and ranked 50th.

Cervical cancer in Alabama

Screening for Cervical cancer

How can you provide more services to underserved women?

Prevention of Cervical cancer through vaccination

High incidence and mortality rates of cervical cancer despite high participation in screening.
- Disconnect between screening and mortality

New Tools:
- HPV vaccination (lower than ideal)
- HPV testing

Opportunities available to partner with APDH and others for coverage, follow-up


Alabama Breast and Cervical Early Detection Program

State and Federal dollars to improve access to screening and diagnostic services for women by defraying the cost of these services from the patient.

ADPH provides: patient recruitment, targeted outreach, population health and systems change implementation services, professional development and provider outreach and support services

Selecting patients for ABCEDP
- Women have to qualify financially and be approved
- Must occur prior to screening appointment
- Can include uninsured and underinsured
- Have to be reapproved every year
- Reimbursement is at Medicare rate.
**Clinical breast examinations**

**Screening tests:**
- Pap
- Pelvic examinations
- HPV testing
- Mammogram

**Follow-up testing:**
- Cervical: colposcopy, biopsies, LEEP, conization
  - *If precancer or cancer is found, pt qualifies for emergency Medicaid to cover cost of treatment*
- Breast cancer: repeat imaging, ultrasound, biopsy
  - *If precancer or cancer is found, pt qualifies for emergency Medicaid to cover cost of treatment*

**Follow-up testing:**
- Counseling visit for all high grade abnormal pap tests and colposcopy results
- LSIL pap results / CIN 1 biopsy results not covered for separate counseling visit
  - Follow-up plan for LSIL/CIN 1 is repeat HPV test in 1 year
  - LEEP or conization procedure, as indicated
  - Referral to treatment and patient navigation services

**Services covered include:**
- Heart disease, stroke, and diabetes risk factor screening
  - BP
  - Weight/BMI/waist & hip circumference
  - Lipid panel, HbA1c, glucose
  - Health behavior assessment
  - Referral and follow-up
  - Counseling and links to community programs for nutrition, physical activity, and tobacco cessation resources

**Women who qualify for BCN also qualify for the Wise women Program.**

**What’s at Stake**
- Higher Mortality rates for breast and cervical cancers in Alabama
- Higher Incidence rates
- Increased late stage diagnosis of cancers
- Ability to treat some preventable cancers
- All people having the ability to have better health outcomes

**What needs to happen?**
- Increased number of women enrolled in ABC prior to screening
- Increased number of Wise Woman participants
- Increased treatment of preinvasive disease
- Increased follow-up of abnormal paps (due to patient coverage and navigation)
- Increased number of colposcopy providers in Alabama

**Outline**
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Case #2

- 27 yo F G4P4 with a pap of HSIL and biopsy proven squamous cell carcinoma
  - On visualization of the cervix she has a 8 cm lesion on anterior lip of cervix
  - Pelvic exam, consistent with parametrial extension
  - Imaging confirms Stage IV diagnosis

- How could this have been prevented?
  - Age at first pregnancy was 16
  - Gardasil recommended at age 11–12 up to age 26

HPV vaccine myth #1
Cervical cancer is just not as big a deal as other vaccine preventable diseases

HPV vaccine myth #2
I don't know anyone with cervical cancer. It's pretty rare.

HPV vaccine myth #3
There's not enough time to be sure it works.
Vaccine type prevalence, NHANES
Later vaccine era compared to pre-vaccine era

It works!: Impact of HPV vaccination
Proportion of Australian born females and males diagnosed as having genital warts at first visit, by age group, 2004-11

HPV vaccination reduces risk of CIN2+

Vaccination protects against Cancer!

HPV vaccine myth #4
Paps are just as good at preventing cervical cancer so we don’t need to vaccinate.
I have concerns about HPV vaccine safety.

- HPV vaccine safety studies have been very reassuring.
- 106 studies on 2.5 million people in 6 countries.
- As safe as every other vaccine.
- To date, we have not observed any signal that shows that HPV vaccination causes...
- Clinicians can reassure parents who may have concerns, that HPV vaccination is safe.

HPV Vaccination in United States

<table>
<thead>
<tr>
<th>13-17 yo</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females 2017</td>
</tr>
<tr>
<td>&gt;1 dose</td>
<td>68.6%</td>
</tr>
<tr>
<td>HPV UTD</td>
<td>53.1%</td>
</tr>
</tbody>
</table>

HPV Vaccination is Recommended

- HPV vaccination is safe.
- HPV vaccination works.
- HPV vaccination lasts.

Girls & Boys Age 11-12 can start HPV vaccination at age 9.
Preteens should finish HPV vaccine series before 13.

- Plus girls 13-26 years old who haven’t started or finished HPV vaccine series.
- Plus boys 13-26 years old who haven’t started or finished HPV vaccine series.

Reasons parents won’t vaccinate for HPV

- Not sexually active
- Not recommended
- Safety concern/Side...
- Not needed or...
- Lack of knowledge

Percent: Stokley et al. MMWR, 2014.
Provider recommendation in vaccination

- Overall uptake of HPV vaccine: 66.5% US (46.9–92.1%)
- If provider recommended vaccination: 74.4% (58.9–92.8%)
- No provider recommendation: 39.9% (16.0 – 88.6%)
- Any provider counts!
  - Obstetrician
  - Pharmacist
  - Dentist

Championing the HPV Vaccine

- Obvious
  - Giving presentations to groups of doctors, patients, parents
  - Sharing medically factual information on social media
  - Recommending HPV vaccine to patients and families
  - Connect HPV cancer survivors to advocacy opportunities

- Maybe not so obvious
  - Policy change to encourage vaccination
  - Vaccination in pharmacies
  - School-based vaccination programs
  - Quality metrics connected to payment
  - Coalition building through cancer center networks and others

Conclusions

- The burden of HPV-related disease continues to increase in Alabama and US

- Screening with pap testing only not enough
  - HPV testing
  - HPV vaccination

- We can do more to improve vaccination rates
  - Start in your own practice
  - Use social media
  - Build partnerships
  - Be a resource to your family/friends/relatives