Cervical Cancer Screening and HPV

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Disclosures

• I have no conflicts of interest to disclose
• Slides courtesy of: Dr. Sarah Morgan

I. Background: History

1. The Pap test was developed by George Papanicolaou as a research method in understanding the menstrual cycle.

2. Papanicolaou soon recognized its potential for finding cervical cancer early and presented his findings in 1923.

3. American Cancer Society (ACS) promoted the Pap test during the early 1960s and it became widely used.
I. Background: Cervical Cancer¹, 4

- Cervical cancer historically was a leading cause of death in US women.
- The mortality rate from cervical cancer has declined by 70% since routine Pap screening was implemented.

![Graph showing US Death Rate from Cervical Cancer, per 100,000³](image)

I. Background: Cervical Cancer¹

**Current Disease Burden in the US:**
- In 2017 approximately 12,820 women will be diagnosed with cervical cancer.
- Approximately 4,210 will die from the disease.
- Being rarely or never screened is the major contributing factor to most cervical cancer deaths in the US today.

I. Background: Cervical Cancer¹

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I. Background: Cervical Cancer¹

I. Background: HPV

- 12,109 new cases of cervical cancer²
- 4092 deaths in 2010
- 330,000 new cases of high-grade cervical dysplasia (CIN 2/3)³
- 1.4 million new cases of low-grade cervical dysplasia (CIN 1)⁴
- 1 million new cases of genital warts⁰
I. Background: Cervical Cancer

Worldwide, cervical cancer is the 4th leading cause of cancer deaths in women. 80% of cervical cancer deaths occur in developing countries.

I. Background: HPV

- >100 types identified
- 30–40 anogenital
  - Oncogenic types include: 16, 18, 31, 33, 35, 39, 42, 51, 52, 56
  - "HPV 16 (54%) and HPV 18 (13%) account for the majority of cervical cancers"***
  - Non-oncogenic types include: 6, 11, 40, 42, 43, 44, 54
  - "HPV 6 and 11 are most often associated with external anogenital warts"***

Human Papilloma Virus (HPV): Non-enveloped DS DNA virus

Who gets HPV?

- Half of women within 3 yrs of starting sex
  - 31% get HPV 16
  - 20% get HPV 18
- 80% of women by age 25
- Nearly 100% of women with > 5 lifetime partners
- Nearly 100% of infections “clear" by 1 year

I. Background: HPV

1. Infection of the host cell.
2. Virus DNA is released within the nucleus
3. Numerous cellular transcription factors interact with the non-coding viral regulatory region (LCR), starting transcription of the two transforming early genes (E6 and E7).
4. The transforming proteins interact with the cellular anti-oncogenic regulator p53 disrupting the cell cycle.

HPV 16 Genome

CIN1 CIN2 CIN3 Cervical Cancer

<table>
<thead>
<tr>
<th>CIN1</th>
<th>CIN2</th>
<th>CIN3</th>
<th>Cervical Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower 1/3 of epithelium</td>
<td>Lower 2/3 of epithelium</td>
<td>&gt;2/3 to full thickness of epithelium</td>
<td>Invasive Carcinoma</td>
</tr>
<tr>
<td>Mildly atypical cellular changes</td>
<td>Moderately atypical cellular changes</td>
<td>Preservation of epithelial maturation</td>
<td>Severely atypical cellular changes</td>
</tr>
<tr>
<td>p16 negative</td>
<td>p16 positive</td>
<td>p16 positive</td>
<td></td>
</tr>
</tbody>
</table>
Cervical cancer is typically the culmination of a years-long process that begins with an infection with a carcinogenic HPV type.

I. Background: HPV

- Initial HPV Infection
- Persistent Infection
- CIN 1
- CIN 2/3
- Cervical Cancer

Cofactors: Viral, host, environmental

36 month cumulative incidence of CIN2-3 among women with HPV-16 or HPV-18 infection: 27.2%

II. Current Recommendations for Screening

“The guidelines are based on a systematic evidence review, contributions from six working groups, and a recent symposium co-sponsored by the ACS, American Society for Colposcopy and Cervical Pathology (ASCCP), and American Society for Clinical Pathology (ASCP), which was attended by 25 organizations.”

“The guidelines generally advise a reduction in the number of tests women get over their lifetime to better ensure that they receive the benefits of testing while minimizing the harms.”

II. Recommendations for Screening: Caveats

- These recommendations apply to women who have a cervix, regardless of sexual history.
- They do NOT apply to women who have received a diagnosis of a high-grade, precancerous cervical lesion or cervical cancer.
- They do NOT apply to women with in-utero diethylstilbestrol (DES) exposure.
- They do NOT apply to women who are immunocompromised.

II. Recommendations for Screening

A. Pap Screening
B. hrHPV Screening
II. A. Pap Screening

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;21</td>
<td>No screening</td>
</tr>
<tr>
<td>21-29</td>
<td>Cytology screening every 3 years</td>
</tr>
<tr>
<td></td>
<td>HPV testing/cotesting should not be used for screening in this age group</td>
</tr>
<tr>
<td>30-65</td>
<td>Cytology with HPV co-testing every 5 years</td>
</tr>
<tr>
<td></td>
<td>Acceptable: cytology every 3 years</td>
</tr>
<tr>
<td>&gt;65</td>
<td>No screening IF adequate prior screening negative</td>
</tr>
</tbody>
</table>

Starting Screening

- Recommend screening starting at 21 YO regardless of sexual activity

Stopping Screening

- Women with history of CIN2 or a more severe diagnosis should continue screening for at least 20 years
- Women who have had hysterectomy do not need screening if they do not have a cervix and do not have a history of CIN2 or a more severe diagnosis
- Women over 65 YO may discontinue screening if they have an adequate negative prior screening history

II.B. hrHPV Screening

- Because of equivalent or superior effectiveness, **primary hrHPV screening can be considered** as an alternative to current US cytology-based cervical cancer screening methods.
- Cytology alone and cotesting remain the screening options specifically recommended in major guidelines.
- **Primary hrHPV screening should not be initiated prior to 25 years of age**
- **Rescreening after a negative primary hrHPV screen should occur no sooner than every 3 years**

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A negative hrHPV test provides greater reassurance of low CIN3+ risk than a negative cytology result
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II.B. hrHPV Screening: USPSTF Draft Guideline

- The USPSTF recommends:
  - Screening for cervical cancer **every 3 years with cervical cytology alone** in women ages 21 to 29 years.
  - Either screening **every 3 years with cervical cytology alone or every 5 years with high-risk human papillomavirus (hrHPV) testing alone** in women ages 30 to 65 years

www.uspreventiveservicestaskforce.org
II.B. hrHPV Screening

“ACOG and the American Society for Colposcopy and Cervical Pathology issued a joint statement reaffirming their support for testing for both every five years, or screening with a Pap alone every three years.”

II.B. hrHPV Screening

COMMITTEE OPINION

Cervical Cancer Screening in Low-Resource Settings

- A prospective cluster randomized study in rural India showed an approximate 50% reduction in cervical cancer mortality and late-stage disease with a single lifetime HPV DNA screening test compared with controls
- Cultural obstacles to successful cytology screening in the U.S. Affiliated Pacific Islands potentially could be overcome with HPV testing of self-collected specimens. Self-collected specimens have similar HPV detection rates as those collected by clinicians. The sensitivity of testing on self-collected HPV specimens has been shown to be comparable with cytology and almost as high as physician-collected HPV specimens

III. Workup of Cytologic Abnormalities

A. Unsatisfactory cytology
B. Absent endocervical cells
C. +hrHPV with normal cytology
D. ASCUS
E. LSIL
F. ASC-H
G. HSIL
H. AGC

I. Special populations
   i. 21-24 YO
   ii. Pregnancy
   iii. Menopausal women
   iv. Adolescents

III.A. Unsatisfactory Cytology

1. HPV unknown (any age)
2. HPV negative (≤30)
3. HPV positive (≥30)
   - Repeat Cytology 2-4mos
   - Colposcopy

III.B. Absent Endocervical Cells (NILM)

21-29 YO
- HPV negative
- HPV unknown
- HPV testing "preferred"
- Repeat Cytology 3 yrs
- Manage per Guideline

≥30 YO
- HPV negative
- HPV unknown
- Repeat Cytology 3 yrs
- HPV positive

Routine Screening

www.asccp.org
III. C. +hrHPV with negative cytology

**Women ≥30 YO**

- +hrHPV
  - Repeat Cotesting 1 year
- HPV DNA Typing
  - +hrHPV OR ≥ASCUS
  - HPV-16 or -18 positive
  - HPV-16 and -18 negative
  - Repeat Cotesting 1 year
- +hrHPV OR ≥ASCUS
  - Colposcopy
  - Manage per Guideline
- Repeat Cotesting 3 years

- Negative Cytology AND HPV negative
  - Repeat Cotesting 1 year
  - Cytology AND HPV negative
  - Repeat Cotesting 3 years

- Negative Cytology WITH Negative HPV
  - Repeat Cotesting 1 year
  - Negative Cytology AND Negative HPV
  - Repeat Cotesting 3 years

- Positive HPV
  - Repeat Cotesting 1 year
  - +hrHPV OR ≥ASCUS
  - Colposcopy
  - Manage per Guideline

- Unknown HPV
  - Repeat Cotesting 1 year
  - Unknown HPV
  - Repeat Cotesting 3 years

- Negative Pap and HPV
  - Repeat Cotesting 1 year
  - Negative Pap and HPV
  - Repeat Cotesting 3 years

- colposcopy
  - Manage per Guideline

III. D. ASCUS

- ASCUS
  - Repeat Cytology 1 year
  - ASCUS
  - Repeat Cytology 3 years
  - ASCUS
  - Repeat Cytology (routine screening)
  - Manage per Guideline
  - Repeat Co-testing 3 years

- Negative
  - HPV testing
  - “preferred”

- ≥ASCUS
  - Colposcopy
  - Manage per Guideline

- Positive
  - Repeat Co-testing 3 years

III. E. LSIL

- Negative HPV
  - Repeat Cotesting 1 year
  - Negative HPV
  - Repeat Cotesting 3 years

- Unknown HPV
  - Repeat Cotesting 1 year
  - Unknown HPV
  - Repeat Cotesting 3 years

- Positive HPV
  - Repeat Cotesting 1 year
  - Positive HPV
  - Repeat Cotesting 3 years

- +hrHPV OR ≥ASCUS
  - Colposcopy
  - Manage per Guideline

- ≥ASCUS
  - Manage per Guideline

III. F. ASC-H

- Positive OR Negative HPV
  - Colposcopy
  - Manage per Guideline

III. G. HSIL

- Immediate Excisional Biopsy (LEEP) OR Colposcopy
  - Manage per Guideline

III. H. AGC

**Practical tip:** Colpo with ECC AND EMB with few exceptions

- Atypical Endometrial Cells
  - Endometrial AND Endocervical Sampling
  - Endometrial Pathology
  - No Endometrial Pathology
  - Colposcopy
  - Manage per Guideline

- Manage per Guideline

Options vary if patient is pregnant or is 21-24 YO
III. H. AGC

All other categories/NOS

Colposcopy

**AND endometrial sampling IF ≥35YO OR risk factors for endometrial hyperplasia**

Manage per Guideline

Practical tip: Colpo with ECC AND EMB with few exceptions

III.I. Special Populations: 21-24 YO– ASCUS or LSIL

ASCUS or LSIL

Repeat Cytology at 12 mos

Positive HPV testing (ASCUS only)

ASC-H/HSIL/AGC

Negative/ASCUS/LSIL

Repeat Cytology at 12 mos

≥ASCUS

Colposcopy

Negative x2

Manage per Guideline

Routine Screening

III.I.i. Special Populations: 21-24 YO– ASCUS or LSIL

ASCUS or LSIL

Repeat Cytology at 12 mos

Reflex HPV testing (ASCUS only)

ASC-H/HSIL/AGC

Negative/ASCUS/LSIL

Repeat Cytology at 12 mos

≥ASCUS

Colposcopy

Negative x2

Manage per Guideline

Routine Screening

III.I.ii. Special Populations: Pregnant Women– LSIL

Pregnant Woman

LSIL

Defer Colpo to 6 weeks PP

No CIN 2-3

Colposcopy

CIN 2-3

FU Postpartum

Manage per Guideline

III.I.iii. Special Populations: Postmenopausal Women– LSIL

HPV Negative

Repeat Cytology 12 mos

HPV Positive

≥ASCUS

Colposcopy

Negative

Repeat Cytology 12 mos

No CIN

CIN

Colposcopy

OR

LSIL Postmenopause

Repeat Cytology 6+12 mos

≥ASCUS

Return to Normal Screening

Manage per Guideline

III.I.iv. Special Populations: Adolescents

WHY ARE YOU DOING A PAP??

• Repeat cytology 12 mos
• If <HSIL continue to follow q12 mosx2
• If persistent ≥LSIL at 24 mos → colposcopy
• If HSIL → colposcopy
• Do NOT do HPV cotesting: because of high prevalence it is not clinically significant
• Ignore HPV status if you happen to know it

WHY ARE YOU DOING A PAP??

• Repeat cytology 12 mos
• If <HSIL continue to follow q12 mosx2
• If persistent ≥LSIL at 24 mos → colposcopy
• If HSIL → colposcopy
• Do NOT do HPV cotesting: because of high prevalence it is not clinically significant
• Ignore HPV status if you happen to know it
IV. Colposcopy: ASCCP Standards

<table>
<thead>
<tr>
<th>Component</th>
<th>Minimum Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-colposcopy</td>
<td>Evaluate and document at least the following:</td>
</tr>
<tr>
<td>Evaluation</td>
<td>• Indication for colposcopy</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy status</td>
</tr>
<tr>
<td></td>
<td>• Menopausal/menstrual status</td>
</tr>
<tr>
<td></td>
<td>• Hysterectomy status</td>
</tr>
<tr>
<td>Examination</td>
<td>Obtain informed consent</td>
</tr>
<tr>
<td></td>
<td>• Examine vulva and vagina grossly</td>
</tr>
<tr>
<td></td>
<td>• Examine cervix with magnification after application of 3-5% acetic acid</td>
</tr>
<tr>
<td>Documentation</td>
<td>Document findings at least in text format:</td>
</tr>
<tr>
<td></td>
<td>• Document SCJ</td>
</tr>
<tr>
<td></td>
<td>• Document Colposcopic findings (AWE Y/N, Lesions Y/N)</td>
</tr>
<tr>
<td></td>
<td>• Document Impression (Normal/L SIL/H SIL/Cancer)</td>
</tr>
<tr>
<td>Biopsy</td>
<td>• If indicated, take biopsies at SCJ</td>
</tr>
<tr>
<td></td>
<td>• Document whether or not endocervical sampling performed</td>
</tr>
<tr>
<td>Post-procedure</td>
<td>• Make arrangements to notify patient of results</td>
</tr>
</tbody>
</table>

Assessment of Colposcopy Adequacy

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix Visibility</td>
<td>Fully/Not Fully Visible</td>
</tr>
<tr>
<td>SCJ Visibility</td>
<td>Fully/Not Fully Visible</td>
</tr>
<tr>
<td>Abnormal Findings</td>
<td>Low-grade features</td>
</tr>
</tbody>
</table>

Abnormal Colposcopic Findings

<table>
<thead>
<tr>
<th>Features</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-Grade AWE</td>
<td>Thin/translucent</td>
</tr>
<tr>
<td></td>
<td>Rapidly fading</td>
</tr>
<tr>
<td>Vascular Patterns</td>
<td>Fine mosaic</td>
</tr>
<tr>
<td></td>
<td>Fine punctuation</td>
</tr>
<tr>
<td>Margins/Border</td>
<td>Irregular/geographic contour</td>
</tr>
<tr>
<td></td>
<td>Condylomatous/raised/papillary</td>
</tr>
<tr>
<td></td>
<td>Flat</td>
</tr>
<tr>
<td>High-Grade AWE</td>
<td>Thick/dense</td>
</tr>
<tr>
<td></td>
<td>Rapidly appearing/slowly fading</td>
</tr>
<tr>
<td></td>
<td>Cuffed gland openings</td>
</tr>
<tr>
<td></td>
<td>Variegated red and white</td>
</tr>
<tr>
<td>Vascular Patterns</td>
<td>Coarse mosaic</td>
</tr>
<tr>
<td></td>
<td>Coarse punctuation</td>
</tr>
<tr>
<td>Margins/Border</td>
<td>Sharp border</td>
</tr>
<tr>
<td></td>
<td>Inner border sign (internal margin)</td>
</tr>
<tr>
<td></td>
<td>Ridge sign</td>
</tr>
<tr>
<td></td>
<td>Peaking edges</td>
</tr>
<tr>
<td></td>
<td>Contour flat</td>
</tr>
<tr>
<td></td>
<td>Fused papillae</td>
</tr>
</tbody>
</table>

Suspicious for Invasive Cancer

<table>
<thead>
<tr>
<th>Features</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical Vessels</td>
<td></td>
</tr>
<tr>
<td>Irregular Surface</td>
<td></td>
</tr>
<tr>
<td>Epithelial lesion</td>
<td></td>
</tr>
<tr>
<td>Necrosis</td>
<td></td>
</tr>
</tbody>
</table>

Biopsies

<table>
<thead>
<tr>
<th>General Guidance</th>
<th>Number of Biopsies</th>
<th>Reasoning</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple biopsies</td>
<td>At least 2, and up to 4 biopsies</td>
<td>A single biopsy, targeting the &quot;worst appearing&quot; lesion may miss up to 1/3 of prevalent precancers</td>
<td>Britain 2016, Canada 2012, Gage et al, Stoler et al, Pretorius et al, Wentzensen et al</td>
</tr>
</tbody>
</table>
V. Subsequent management of CIN

A. CIN1 or No Lesion preceded by “lesser abnormalities” (LSIL)

B. CIN1 preceded by ASC-H or HSIL

C. CIN 2 or 3

D. CIN 2 or 3 in Young Women

E. CIN 2 or 3 in Young Women

F. AIS

G. AGC

V.A. Subsequent Management: CIN1 or No Lesion preceded by “lesser abnormalities”

Follow-up Without Treatment

- HPV negative AND Cytology negative
- Age-appropriate re-test 3 yrs

If persistent 22 yrs: Testing OR Treatment

- No CIN
- CIN 2/3
- CIN 1

- Manage per Guideline

V.B. Subsequent Management: CIN1 preceded by ASC-H or HSIL

Pap/Cotesting at 12 and 24 mos

- HPV negative
- AND Cytology negative
- HPV+ OR Any Cytologic Abnormality except HSIL

- Age-specific re-test in 3 years

- HPV negative AND Cytology negative

- Routine Screening

- Pap/Cotesting at 12 and 24 mos

- HPV negative AND Cytology negative

- HPV+ OR Any Cytologic Abnormality except HSIL

- Age-appropriate re-test 3 yrs

- Colposcopy

- Management

- Manage per Guideline

V.C. Subsequent Management: CIN 2 or 3

Pap/Cotesting at 12 and 24 mos

- HPV negative AND Cytology negative

- HPV+ OR Any Cytologic Abnormality except HSIL

- Age-appropriate re-test 3 yrs

- Colposcopy

- Management

- Manage per Guideline

V.D. Subsequent Management: CIN1 in Women 21-24 YO—after ASCUS/LSIL

Repeat Cytology at 12 mos

- ASC-H or HSIL

- Repeat Cytology at 12 mos

- Negative

- Repeat Cytology at 12 mos

- ASCUS

- Colposcopy

- Follow per Guideline

V.D. Subsequent Management: CIN1 in Women 21-24 YO—after HSIL/ASC-H

Inadequate Colposcopy

- Adequate Cytology

- Pathology Review

- HSIL at 6 or 12 mos

- Negative x2

- Other Results

- Manage per Guideline

Adequate Colposcopy

- Diagnostic Excisional Procedure

- Repeat Cytology at 12 mos

- (≥1 year)

- Pathology Review

- Manage per Guideline
V. E. Subsequent Management: CIN 2 or 3 in Young Women

- Observation: Repeat Colpo+Cytology at 6 and 12 mos
  - Negative Cytology AND Normal Colpo x2
  - Normal Colpo and Cytology negative
  - Worsening Colpo OR HSIL on cytology OR Colpo impression=HSIL ±1 year
  - Repeated excision or ablation of T-zone
  - Positive excision results

- Treatment using Excision or Ablation of T-zone
  - 2ASC OR HPV+
  - Repeat Colpo and Biopsy
  - Progression to CIN1 OR persistent CIN 2/3 at 24 mos

- Negative PAP
  - AND HPV neg
  - Repeated excision/recommended

- Worsening colposcopy

- Hysterectomy preferred

V. F. Subsequent Management: AIS

- Hysterectomy preferred OR Fertility Sparing Conservative Management
  - Margins positive OR ECC positive
  - Repeat excision/recommended

- Reevaluation at 6 mos* OR Reevaluation 6 mos*
  - Margins and ECC negative

- Long-term follow-up
  - Repeat Cytology with combination of:
    - COtast+Colpo+ECC

V. G. Subsequent Management: AGC

- Initial Cytology Favor neoplasia OR AIS
  - No Neoplasia
  - Diagnostic Excisional Procedure With Endocervical Sampling
    - Manage per Guideline

- Practical Tip: CKC with ECC and D+C

- 12 ASCUS OR HPV+

- Pap and Cotest at 12 and 24 mos
  - Both negative

- Pap and Cotest 3 years
  - Both negative

- Repeat Screening

- CIN 2/3 BUT no Glandular Neoplasia
  - Manage per Guideline

- Pap and Cotest at 12 and 24 mos
  - Both negative

- Pap and Cotest 3 years
  - Both negative

- Repeat Screening

- Manage per Guideline

VI. HPV Vaccine

- Formulations in US
  - Cervarix
  - Gardasil
  - Gardasil 9

<table>
<thead>
<tr>
<th>Type</th>
<th>Cervarix</th>
<th>Gardasil</th>
<th>Gardasil 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV types</td>
<td>16, 18</td>
<td>6, 11, 16, 18</td>
<td>6, 11, 16, 18, 31, 33, 45, 52, 58</td>
</tr>
<tr>
<td>Licensing</td>
<td>October 2009–Females</td>
<td>June 2006–Females</td>
<td>December 2014–Females and Males</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Hypersensitivity to</td>
<td>Hypersensitivity to</td>
<td>Hypersensitivity to</td>
</tr>
<tr>
<td>Dosing Schedule</td>
<td>3-dose series: 0, 1, 6 months</td>
<td>3-dose series: 0, 2, 6 months</td>
<td>3-dose series: 0, 2, 6 months</td>
</tr>
</tbody>
</table>
VI. HPV Vaccine: ACIP Recommendations

**ACIP recommendations**

**Who should get the HPV vaccine?**
- For girls and women, recommended either at 15-18YO for those who were not previously vaccinated
- For boys and men, recommended until age 21

**Who should be screened for HPV**
- Women age 21 - 65 years
- High-risk sexual partners of women with abnormal CIN
- For cervical cancer screening, a Cervical Cancer Screening

**Who should not be screened for HPV**
- Women who have had a hysterectomy with removal of the cervix

VI. HPV Vaccine: Trends in CIN

**2007-2014 Following HPV Vaccine Implementation:**
- Significant reduction in all CIN 1-3 for women 15-19YO
- Significant reduction in CIN 2 for women 20-24YO
- Downtrend in CIN1 in women 20-24 YO

IV. HPV Vaccine: Adverse Reactions

<table>
<thead>
<tr>
<th>Vaccine/Reaction Type</th>
<th>Reaction</th>
<th>Rate/doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quadrivalent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Local/Mild</td>
<td>Injection site reaction</td>
<td>83 per 100</td>
</tr>
<tr>
<td></td>
<td>Erythema and swelling</td>
<td>25 per 100</td>
</tr>
<tr>
<td>- Local/Severe</td>
<td>Injection site erythema and/or swelling &gt; 2 inches in size and pain severe</td>
<td>5.7 per 100</td>
</tr>
<tr>
<td>- Systemic/Mild</td>
<td>Pyrexia</td>
<td>13 per 100</td>
</tr>
<tr>
<td></td>
<td>Urticaria</td>
<td>3 per 100</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>26 per 100</td>
</tr>
<tr>
<td></td>
<td>Myalgia</td>
<td>1 per 100</td>
</tr>
<tr>
<td></td>
<td>Arthralgia</td>
<td>1 per 100</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal disorders</td>
<td>17 per 100</td>
</tr>
<tr>
<td>- Systemic/Severe</td>
<td>Anaphylaxis</td>
<td>1.7 – 2.6 per 10^7</td>
</tr>
</tbody>
</table>

IV. HPV Vaccine: Adverse Reactions

<table>
<thead>
<tr>
<th>Vaccine/Reaction Type</th>
<th>Reaction</th>
<th>Rate/doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivalent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Local/Mild</td>
<td>Injection site pain</td>
<td>78 per 100</td>
</tr>
<tr>
<td></td>
<td>Swelling</td>
<td>26 per 100</td>
</tr>
<tr>
<td></td>
<td>Redness</td>
<td>30 per 100</td>
</tr>
<tr>
<td>- Systemic/Mild</td>
<td>Fatigue</td>
<td>33 per 100</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>30 per 100</td>
</tr>
<tr>
<td></td>
<td>Myalgia</td>
<td>28 per 100</td>
</tr>
<tr>
<td></td>
<td>Itching</td>
<td>10 per 100</td>
</tr>
<tr>
<td></td>
<td>Arthralgia</td>
<td>13 per 100</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal symptoms</td>
<td>13 per 100</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>3 per 100</td>
</tr>
<tr>
<td></td>
<td>Rash</td>
<td>1 per 100</td>
</tr>
<tr>
<td></td>
<td>Urticaria</td>
<td>0.46 per 100</td>
</tr>
</tbody>
</table>

IV. HPV Vaccine

**Summary of Recommendations:**
- It is crucial that OB/GYNs & other providers educate parents and patients on the benefits and safety of HPV vaccination
- CDC and ACOG recommend routine vaccination with HPV vaccine for girls and boys.
- The target age for vaccination is 11-12 year for girls and boys.
- The 9-valent HPV vaccine has been added to the ACIP recommendations for girls and boys.

VII. Pearls: Principles of Screening

1. Clinicians should not screen average risk women younger than age 21 for cervical cancer
2. Clinicians should start screening average risk women for cervical cancer at age 21 ONCE every 3 years with cytology alone
3. Clinicians should not screen average risk women for cervical cancer with cytology more than ONCE every 3 years.
4. Clinicians may use combination of cytology and HPV testing once every 3 years in average risk women aged 25 who prefer screening less often than every 3 years.
5. Clinicians should not perform HPV testing in average risk women younger than 30 years.
6. Clinicians should stop screening average risk women older than 65 for cervical cancer if they have had 3 consecutive negative cytology results or 2 consecutive negative cytology results plus HPV within 10 years with the most recent test performed within 5 years.
7. Clinicians should not screen average risk women of any age for cervical cancer if they have had a hysterectomy with removal of the cervix.
VII. Pearls: Resources

ACOG App
ASCCP App
www.asccp.org

ACOG
By Fountainhead
Mobile Solutions
ASCCP Mobile
By ASCCP

References