Cervical Cancer Screening: How to Manage the Positive Screening Tests

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Disclosures

• No financial relationships or conflict of interest to disclose
Background

• Most of HPV infections are transient, only few are persistent

• HPV infection is common in teenagers, but cervical cancer is rare at this age

• Most young women have an effective immune system, it can:
  • Clear the infection with an average of 12 months
  • Resolve spontaneously most cervical HPV lesions
Background

• **CIN 1** has a high rate to regression to normal cells.

• **CIN 2** represents a mix of LSIL and HSIL.
  • The use of biomarkers are useful in this situation (p16).

• **CIN 3 and AIS** are clearly cancer precursors

THE KEY TO EFFECTIVELY MANAGING CERVICAL ABNORMALITIES IS TO DISTINGUISH TRUE CERVICAL CANCER PRECURSORS FROM BENIGN CERVICAL ABNORMALITIES WITH LITTLE PREMALIGNANT POTENTIAL
There are different possibilities of abnormal tests:

- Women 30 + years:
  - who are cytology negative but HPV positive
  - with ASC-H or HSIL cytology, but colposcopy with no lesion or biopsy-confirmed CIN 1
  - with ASC-US, ASC-H cytology and LSIL, HSIL, AGC confirmed by biopsy

- Young women with biopsy-confirmed CIN 2 or 3.
Modalities of Screening in Women > 30y
3 modalities are possible

**HPV Test:**
- Negative: retest in 3 years
- Positive: cytology and eventual colposcopy

**Cytology:**
- Negative: 1-1-3
- Positive: colposcopy

**Co-test HPV Test + Cytology:**
- Cyto and HPV negatives: retest in 5 years
- HPV +, cyto -: retest at 1 year
- HPV -, cyto +: review cytology
  - ASC-US or LSIL: repeat at 1 year
  - ASC-H or HSIL: colposcopy and EEC
- Cyto and HPV +: colposcopy

*Argentine Colposcopy Society Guidelines*
Risk factors

• Women with any of the following risk factors may require more frequent cervical cancer screening:

  • HIV infection
  • Immunocompromise (eg, solid organ transplant recipients, autoimmune disease)
  • Tobacco
  • Exposure to diethylstilbestrol in utero
  • Previous treatment for CIN 2, CIN 3, or cancer
Management of Women with ASC-US or LSIL

**TZ 1 - 2**
- No lesion or LSIL colposcopic lesion
- Cytology & colposcopy in 6 months
- Biopsy
- Manage Argentine Colpo Guidelines
- Routine screening

**TZ 3**
- No lesion or LSIL colposcopic lesion
- HSIL colposcopic lesion
- HSIL colposcopic lesion
- ECC
- Manage Argentine Colpo Guidelines
- Manage Argentine Colpo Guidelines
- Biopsy

If cytology informs ASC-US Triage with HPV Test is preferred

 Argentine Colposcopy Society Guidelines
Management of Women with ASC-H or HSIL

**COLPOSCOPY**

**T Z 1, 2, 3**

- No lesion
  - ECC
  - Negative
    - Review cytology: CONE if the diagnostic is confirmed

- LSIL or HSIL colposcopic lesion
  - Biopsy
  - Manage Argentine Colpo Guidelines

Argentine Colposcopy Society Guidelines
Management of Women with AGC

**No Lesion**
- **ECC**
  - NEGATIVE
  - Manage Argentine Colpo Guidelines

**LSIL or HSIL colposcopic lesion**
- **Biopsy and ECC**
  - POSITIVE
  - Manage Argentine Colpo Guidelines

**< 35y**
- Cytology & colposcopy every 6 months for 2 years
  - If negative: routine screening

**> 35y**
- Ultrasound and/or Endometrial Biopsy
  - If negative for endometrial pathology: cytocolposcopic assessment every 6 months for 2 years

ARGENTINE COLPO GUIDELINES

IFCPC 2017 World Congress
Management of Women with Biopsy confirmed LSIL (and cytology LSIL or minor)

**Cyto & Colpo FU**

- 2 years
  - Persistent Lesion
    - Evaluate risk factors to decide Treatment or FU
  - Progression to CIN 2+
    - Manage Argentine Colpo Guidelines

Argentine Colposcopy Society Guidelines
Management of Women with Biopsy confirmed LSIL (with cytology ASC-H / HSIL or major lesion suspected by colposcopy)

2 ways are possible

- **Repeat Cytology and perform new colposcopy**
  - Diagnostic change
  - Treatment according to diagnostic
  - Confirmed diagnostic
  - Excisional Procedure

- **Excisional Procedure in cases of**
  - ZT 3
  - ECC positive

(Argentine Colposcopy Society Guidelines)
Management of Women with CIN 2 - 3

**CIN 2**
- **p16**
  - Negative
    - Cytology & colposcopy in 6 months
    - 2 negative controls
    - Routine screening

**CIN 3**
- **Positive or p16 not possible to perform**
  - **< 25 or ZT1**
    - Cyto & colpo FU every 6 months for 2 years (if FU is possible) or excisional treatment
  - **> 25 or ZT 2, 3**
    - Excisional treatment

 Argentine Colposcopy Society Guidelines

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Pregnant Women

• L-SIL: cyto & colpo examination with biopsy if HSIL + is suspected and new evaluation at 6-8 weeks after delivery.

• H-SIL: cyto & colpo examination every 12 weeks with biopsy if more lesion is suspected. New evaluation at 6-8 weeks after delivery.
### Treatment of CIN 3

#### 2011 IFCPC Nomenclature

**Accepted in Rio World Congress, July 5, 2011**

Nomenclature Committee chairman: Jacob Bornstein MD

#### 2011 IFCPC colposcopic terminology of the cervix

<table>
<thead>
<tr>
<th>General assessment</th>
<th>Adequate/inadequate for the reason ... (i.e.: cervix obscured by inflammation, bleeding, scar)</th>
<th>Squamocolumnar junction visibility: completely visible, partially visible, not visible</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transformation zone types</strong></td>
<td>1, 2, 3</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Normal colposcopic findings</th>
<th>Original squamous epithelium:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mature</td>
</tr>
<tr>
<td></td>
<td>Atrophic</td>
</tr>
<tr>
<td>Cervical columnar epithelium</td>
<td>Ectopy</td>
</tr>
<tr>
<td>Metaplastic squamous epithelium</td>
<td>Nabothian cysts</td>
</tr>
<tr>
<td>Crypt (gland) openings</td>
<td>Decidua in pregnancy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormal colposcopic findings</th>
<th>General principles</th>
<th>Location of the lesion: Inside or outside the T-zone, Location of the lesion by clock position Size of the lesion: Number of cervical quadrants the lesion covers, Size of the lesion in percentage of cervix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (Minor)</td>
<td>Thin aceto-white epithelium, Irregular, geographic border</td>
<td>Fine mosaic, Fine punctuation</td>
</tr>
<tr>
<td>Grade 2 (Major)</td>
<td>Dense aceto-white epithelium, Rapid appearance of aceto whitening, Cuffed crypt (gland) openings</td>
<td>Coarse mosaic, Coarse punctuation, Sharp border, Inner border sign, Ridge sign</td>
</tr>
<tr>
<td>Non specific</td>
<td>Leukoplakia (keratosis, hyperkeratosis), Erosion</td>
<td>Lugo's staining (Schiller's test): stained/non-stained</td>
</tr>
</tbody>
</table>

#### Suspicious for invasion

- Atypical vessels
- Additional signs: Fragile vessels, irregular surface, Exophytic lesion, Necrosis, Ulceration (necrotic), tumor/gross neoplasm

#### Miscellaneous finding

- Congenital transformation zone, Condyloma, Polyp (Ectocervical/ endocervical) Inflammation,
- Stenosis, Congenital anomaly, Post treatment consequence, Endometriosis

#### 2011 IFCPC colposcopic terminology of the cervix – addendum

<table>
<thead>
<tr>
<th>Excision treatment types</th>
<th>Excision type 1, 2, 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Excision specimen dimensions</strong></td>
<td>Length - the distance from the distal/external margin to the proximal/internal margin</td>
</tr>
<tr>
<td></td>
<td>Thickness - the distance from the stromal margin to the surface of the excised specimen</td>
</tr>
<tr>
<td></td>
<td>Circumference (Optional)- the perimeter of the excised specimen</td>
</tr>
</tbody>
</table>
Post Treatment FU: During 20 years

- Cyto & Colpo every 6 months during 2 y, if -ve routine screening

- Cotest (HPV Test + cytology) at 6 – 12 months
  - Negative:
    - Repeat cotest in one year, if negative repeat cotest every 5 years
  - Positive:
    - Pap test or HPV test +: colposcopy
    - HPV test + but PAP and colposcopy -: cyto & and colpo FU every 6 months
ACOG recommendations

• Major recommendations with consistent scientific evidence include the recommended screening and the follow-up

  • For women with ASC-US, reflex HPV testing is preferred

  • For women with HPV-positive ASC-US, whether identified on reflex HPV testing or co-testing, colposcopy is recommended

  • For women with LSIL and no HPV test or a positive HPV test result, colposcopy is recommended

  • For women with a histologic diagnosis of cervical intraepithelial neoplasia (CIN) 2, CIN 3, or CIN 2,3 and adequate colposcopic examination, both excision and ablation are acceptable treatment modalities, except in pregnant women and young women
CONCLUSIONS

• In countries where HPV testing is available for routine screening:
  • Colposcopy may be required for women with positive HPV results or with repeated unsatisfactory cytological findings that are missing endocervical or transformation zone components.
  • If either Pap smear or HPV testing are positive, co-testing is integrated into follow-up care; colposcopy, HPV DNA typing, or both may be indicated.
Thank you!!

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