Society of Gynecologic Oncologists of the Philippines (Foundation), Inc.

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Algorithm for the Cervical Cancer Screening Using Papanicolaou Smear & Direct Visual Inspection

**PAP SMEAR**

- Age: 3 years after onset of sexual activity
- NOT indicated after hysterectomy for benign disease
- Interval Annual with conventional cytology OR every 2 years with liquid-based cytology. THEN At or after age 30 after 3 consecutive normal smears, may decrease screening interval every 2-3 years

**ABNORMAL PAP SMEAR**

Follow Algorithm for Abnormal Pap Smear

**VIA***

(+) VIA

**Colposcopy + Biopsy + ECC**

**Outright biopsy**

**PRE-MALIGNANT**

Follow Algorithm for Premalignant Lesions

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* VIA = Visual inspection by Acetic Acid
** Acceptable in areas where colposcopy is not available

**FIGURE 1**

**IMPORTANT NOTE:** The algorithms apply for practitioners with training in colposcopy. For those with no training in colposcopy, please refer to a Gynecologic Oncologist.
Algorithm for the Management of Abnormal Pap Smear

ABNORMAL PAP SMEAR

ASCUS

LSIL*2

ASC-H

HSIL

AGUS*1

CARCINOMA
No gross lesion

(+)
Gross Lesion

HPV Typing if available *3

Repeat Pap smear after 4-6 months

Colposcopy ± biopsy ± ECC

NORMAL

Abnormal Smear

Pap Smear Colposcopy Ff up q 3-6 months

Normal

CIN I

CIN II

CIN III/CIS

MIC CA / Invasive CA

BIOPSY

Definitive Treatment (Refer to Gyne-Onco)

*1 For AGUS, if ECC is negative, fractional curettage is recommended.
*2 If LSIL was obtained by liquid based cytology, colposcopy is optional
*3 A (+) HPV typing would mandate immediate follow up and colposcopy

FIGURE 2
Cervical Cancer

Algorithm for the Management of Pre-Malignant Lesions

According to the 2002 ASCCP Guidelines TH± BSO as primary treatment for biopsy proven CIN 1, 2 or 3 is UNACCEPTABLE. However, in exceptional cases where the following conditions apply TH±BSO may be considered:

1. poor patient follow-up
2. concurrent benign conditions: myoma uteri, PID, ovarian cyst

*Comments:
1. Must differentiate between (+) and (-) margins after a cone or LEEP
The Clinical Practice Guidelines for Cervical Cancer

I. INCIDENCE:
   • Age Standardized Rate – 20.0/100,000¹
   • Age Incidence:
     - PGH and Rizal province between 40 and 60 years old
     - Same observation nationwide and worldwide
     - Age specific incidence (Rizal province) between 30 and 35 years old

II. RISK FACTORS
   • Multiple sexual partners
   • Early sexual activity
   • Multiparity
   • History of sexually transmitted infection
   • History of such infection in the sexual partner
   • Smoking history - 40 pack years

<table>
<thead>
<tr>
<th>RISK FACTORS</th>
<th>Relative Risk</th>
</tr>
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<tbody>
<tr>
<td>HIV</td>
<td>Very High</td>
</tr>
<tr>
<td>Moderate Dysplasia on Pap Smear within 5 years</td>
<td>Very High</td>
</tr>
<tr>
<td>Intercourse within one year of menarche</td>
<td>16</td>
</tr>
<tr>
<td>No prior screening</td>
<td>10</td>
</tr>
<tr>
<td>HPV (depending on subtype)</td>
<td>2.5 - 3.0</td>
</tr>
<tr>
<td>Six or more lifetime sexual partners</td>
<td>5</td>
</tr>
<tr>
<td>Low socioeconomic class</td>
<td>5</td>
</tr>
<tr>
<td>Race (black vs. white)</td>
<td>2.5</td>
</tr>
<tr>
<td>Smoking</td>
<td>2</td>
</tr>
<tr>
<td>Oral contraceptive pill use</td>
<td>1.2 - 1.5</td>
</tr>
<tr>
<td>Barrier contraception</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*DEFINITION: The Relative Risk Factor (RR) of a disease is the ratio of the incidence in people with the risk factor (exposed persons) to the incidence in people without the risk factor (unexposed persons). The farther the RR is from 1.0, the greater the difference in risk between the two groups.²

III. PRIMARY PREVENTION
   • Monogamous sexual relationship between husband and wife
   • Delay in onset of sexual intercourse
   • NOTE: There is a greater than twofold risk of cervical cancer for those starting intercourse at ages 14-15 versus those over 20 years.³
   • Use of barrier contraceptives like condoms (for male and female) and diaphragms
   • Prompt and adequate treatment of sexually transmitted infections
   • HPV Vaccination - for females 9-26 years old, may be given.

IV. SECONDARY PREVENTION
A. RECOMMENDED SCREENING⁴
   • When to start screening
     Approximately 3 years after onset of sexual activity
   • When to discontinue screening
     Age ≥70 years with an intact cervix plus a history of ≥3 consecutive normal smears & no history of abnormal cytology within the 10-year period prior to 70
   • Note:
     For high risk patients (≥1 risk factor), annual Pap smear is still recommended even if the ACS guidelines for discontinuation of screening is satisfied.
   • Screening after hysterectomy
     Not indicated following hysterectomy for benign disease

Note:
1. CIN 2/3 are exceptions to these benign conditions and warrant screening even after hysterectomy
2. For post-hysterectomy (for benign disease) high risk patients, annual Pap smear is still recommended to screen for vaginal intra-epithelial neoplasia (VAIN)

   • Screening interval
     Annual with conventional cytology OR Every 2 years with liquid-based cytology
     THEN
     At or after age 30, after 3 consecutive normal smears, may decrease screening interval every 2-3 years

B. CERVICAL CANCER SCREENING USING PAPANICOLAOU SMEAR & DIRECT VISUAL INSPECTION
   • Please refer to Figure 1.

V. CLINICAL PRESENTATION
A. Early symptoms:
   1. Vaginal bleeding - most important symptom
      a. induced by sexual intercourse or internal examination
      b. intermenstrual
      2. Vaginal discharge

B. Late symptoms:
   1. bone pain
   2. urinary and bowel disturbances
   3. leg edema

VI. DIAGNOSIS
A. Minimal requirements for diagnosis
   1. cervical punch biopsy for those with grossly evident tumor
   2. colposcopy and colpo-guided biopsies following investigation of an abnormal Pap smear
   3. pelvic examination including rectovaginal examination

B. Optional examinations (but are included in the clinical staging as recommended by FIGO)
   1. Blood examinations including CBC, Liver function tests, renal function tests
   2. Chest x-ray
   3. KUB-IVP
   4. Cystoscopy/ proctosigmoidoscopy

VII. MANAGEMENT OF ABNORMAL PAP SMEAR
   • Please refer to Figure 2.

VIII. MANAGEMENT OF PRE-MALIGNANT LESIONS
   • Please refer to Figure 3.

IX. FIGO CLINICAL STAGING FOR CERVICAL CANCER (Figure 4)

Stage I: Carcinoma strictly confined to the cervix; extension to the uterine corpus should be disregarded.

Stage IA: Invasive cancer identified only microscopically. All gross lesions even with superficial invasion are stage lb cancers. Invasion is limited to measured stromal invasion with a maximum depth of 5 mm and no wider than 7 mm.

Stage IA1: Measured invasion of the stroma no greater than 3 mm in depth and no wider than 7 mm in diameter

Stage IA2: Measured invasion of stroma greater than 3 mm but no greater than 5 mm in depth and no wider than 7 mm in diameter

Stage IB: Clinical lesions confined to the cervix or preclinical lesions greater than Stage IA.
Cervical Cancer

Stage IB1 Clinical lesions no greater than 4 cm in size.
Stage IB2 Clinical lesions greater than 4 cm in size
Stage II Carcinoma that extends beyond the cervix but has not extended onto the pelvic wall. The carcinoma involves the vagina but not as far as the lower third.
Stage IIA No obvious parametrial involvement. Involvement of up to the upper two thirds of the vagina.
Stage IIB Obvious parametrial involvement, but not onto the pelvic sidewall.
Stage III Carcinoma that has extended onto the pelvic sidewall. On rectal examination, there is no cancer free space between the tumor and the pelvic sidewall. The tumor involves the lower third of the vagina. All cases with a hydronephrosis or nonfunctioning kidney should be included, unless they are known to be due to other causes.
Stage IIIA No extension onto the pelvic sidewall but involvement of the lower third of the vagina
Stage IIIB Extension onto the pelvic sidewall or with hydronephrosis or nonfunctioning kidney
Stage IV Carcinoma that has extended beyond the true pelvis or has clinically involved the mucosa of the bladder / or rectum
Stage IVA Spread of the tumor onto adjacent pelvic organs
Stage IVB Spread to distant organs

X. CLASSIFICATION OF CERVICAL TUMORS

A. EPITHELIAL TUMORS

(Modified WHO histological classification)

1. Squamous cell carcinoma
   a. Microinvasive squamous cell carcinoma
   b. Invasive squamous cell carcinoma
      1. Large cell keratinizing
      2. Large cell non-keratinizing
      3. Small cell type
   c. Verrucous carcinoma
   d. Warty (Condylomatous) carcinoma
   e. Papillary squamous cell (Transitional) carcinoma
   f. Lymphoepithelioma-like carcinoma

2. Adenocarcinoma
   a. Mucinous adenocarcinoma
      1. Endocervical type
      2. Intestinal type
      3. Signet-ring type
   b. Endometrioid adenocarcinoma
      1. Endometrioid adenocarcinoma with squamous metaplasia
      2. Clear cell adenocarcinoma
      3. Minimal deviation adenocarcinoma
   c. Serous adenocarcinoma
   d. Mesonephric carcinoma
   e. Well-differentiated villoglandular adenocarcinoma

3. Other Epithelial tumors
   a. Adenosquamous carcinoma
   b. Glassy cell carcinoma
   c. Mucoidoid carcinoma
   d. Adenoid cystic carcinoma
   e. Adenoid basal carcinoma
   f. Carcinoïd-like tumor
   g. Small cell carcinoma
   h. Undifferentiated carcinoma
   i. Clear cell adenosquamous carcinoma

B. MESENCHYMAL TUMORS AND MIXED EPITHELIAL-MESENCHYMAL

1. Leiomyosarcoma
2. Endocervical stromal sarcoma
3. Embryonal rhabdomyosarcoma
4. Alveolar soft-part sarcoma
5. Adenosarcoma
6. Malignant mixed mesodermal tumor

C. MISCELLANEOUS TUMORS

1. Primary malignant melanoma
2. Primary choriocarcinoma
3. Lymphoma
4. Leukemia
5. Primary germ cell tumor

XI. MANAGEMENT OF CERVICAL CANCER

A. GENERAL GUIDELINES

1. Cervical cancer is diagnosed by biopsy. In the presence of a gross lesion, there is no need for a Papanicolaou smear or a fractional curettage.
2. Cervical cancer is staged clinically.
3. If clinically indicated, protocistosigmoidoscopy and cystoscopy should be done to rule out invasion.
4. Special work-ups may include computed tomography, magnetic resonance imaging, PET scan and bone scan.
5. Once the diagnosis of invasive cancer is made, the patient should be referred to a gynecologic oncologist.
6. In selected cases, primary Radical Hysterectomy with Pelvic Node Dissection must be performed by a gynecologic oncologist.
7. For advanced disease, concurrent chemotherapy and radiotherapy is the minimum standard of treatment.

B. Staging

Stage I

Stage IA Tumors limited to the cervix, no macroscopic stromal invasion
Stage IB1 Clinical lesions no greater than 4 cm in size.
Stage IB2 Clinical lesions greater than 4 cm in size
Stage IIA No obvious parametrial involvement. Involvement of up to the upper two thirds of the vagina.
Stage IIB Obvious parametrial involvement, but not onto the pelvic sidewall.
Stage III Carcinoma that has extended onto the pelvic sidewall. On rectal examination, there is no cancer free space between the tumor and the pelvic sidewall. The tumor involves the lower third of the vagina. All cases with a hydronephrosis or nonfunctioning kidney should be included, unless they are known to be due to other causes.
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Stage IIIB Extension onto the pelvic sidewall or with hydronephrosis or nonfunctioning kidney
Stage IV Carcinoma that has extended beyond the true pelvis or has clinically involved the mucosa of the bladder / or rectum
Stage IVA Spread of the tumor onto adjacent pelvic organs
Stage IVB Spread to distant organs

C. Treatment

1. Radical hysterectomy
2. Partial hysterectomy
3. Radiation therapy
4. Chemotherapy

D. Prognosis

1. Stage IA: 5-year survival rate is 90-95%
2. Stage IB: 5-year survival rate is 70-80%
3. Stage IIA: 5-year survival rate is 50-60%
4. Stage IIB: 5-year survival rate is 30-40%
5. Stage III: 5-year survival rate is 10-20%
6. Stage IV: 5-year survival rate is 5-10%
IX. FIGO CLINICAL STAGING FOR CERVICAL CANCER

Figure from FIGO Annual Report on the Results of Treatment, 1999

Figure 4
## Cervical Cancer

### Available Vaccine in the Philippines

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<thead>
<tr>
<th>HPV VACCINES</th>
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<tbody>
<tr>
<td><strong>HPV vaccine types 16 &amp; 18</strong></td>
</tr>
<tr>
<td><em>(Recombinant, ASO4 adjuvanted)</em></td>
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<tr>
<td><strong>Cervarix</strong></td>
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<tr>
<td><strong>Quadrivalent HPV vaccine</strong></td>
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<td><strong>Gardasil</strong></td>
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