Prevention and Early Detection of Common Gynaecological Cancers

Comprehensive Guideline for Primary Care Physicians

National Cancer Control Programme
Ministry of Health
Sri Lanka

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Message of The Director General of Health Services

Chronic non-communicable diseases including cancer are the leading causes of death globally, killing more people each year. Although cancer has often been regarded principally as a problem of the developed world, more than half of all cancers occur in the developing countries. Cancer is an increasingly important factor in the burden of diseases in Sri Lanka.

Furthermore, according to the available data in Sri Lanka, the incidences of gynaecological cancers such as cervical, ovarian and uterine carcinomas have shown an increasing trend over the years, Cervical cancer is the second most common cancer among women and is the most frequent cause of death from gynaecological cancers.

The health care system in Sri Lanka has initiated programmes to detect gynaecological cancers early, mainly screening of cervical cancer. Nevertheless, late detection is a major problem in controlling these gynaecological cancers. Therefore, it is a necessity to publish a guideline for primary healthcare doctors to detect the common gynaecological cancers at correct time and it will facilitate in delivering better care at grass root level.

I would like to thank all the staff at National Cancer Control Programme for initiating this activity and the experts who contributed in developing this utmost important guideline.

Dr.Palitha Mahipala

Director General of Health Services

Message of The Deputy Director General of Health Services

(Medical Services 1)

Cancer being the second leading cause of mortality, it is important to increase knowledge about the causes of cancer, and interventions to prevent and manage the disease among health care personnel. Cancer can be reduced and controlled by implementing evidence-based strategies for prevention, early detection and timely management of patients with cancer. Many cancers have a high chance of cure if detected early and treated adequately.

The burden of cancer among females is increasing at an alarming rate. The gynaecological cancers including cervical and ovarian cancers lie within the five top most common cancers among females according to the cancer registry in Sri Lanka. Therefore developing a comprehensive guideline on prevention and early detection of common gynaecological cancers for primary care physicians is a need to mitigate gynaecological cancers which has an increasing trend.

Early detection of precancerous stages and morbidities of these gynaecological cancers, and timely referral for specialized care units are important strategies to curtail the cancer burden in Sri Lanka. Strengthening capacities of primary care physicians on these aspects by providing a comprehensive guideline will help out to achieve these objectives and strategies effectively.

I am sincerely grateful to the staff of National Cancer Control Programme, who worked tirelessly to create this vital publication. Furthermore, I would like to express my appreciation for all the experts involved in bringing this guideline a success.

Dr. Lakshmi Somathunga

Deputy director General (Medical Services I)

Preface

Director, National Cancer Control Programme

According to the cancer incidence data, the common gynaecological cancers including cervical, ovarian and uterine cancers are increasing in Sri Lanka. Cervical cancer is the second most common cancer accounting for 12% of newly diagnosed cancer among females with an age standardized incidence rate of 9.6 per 100,000 population. Ovarian cancer is the fourth commonest cancer accounting for 8% of newly diagnosed female cancers with an age standardized rate of 6.7 per 100,000 population (Cancer Incidence data, Sri Lanka, 2006).

With the increasing incidence, the deaths due to gynaecological cancers have also been increased. Furthermore, over 85 per cent of cervical cancer cases and deaths occur in developing countries where effective screening, diagnosis and treatment is limited or absent.

Reinforcing capacities of primary care medical officers on early detection of these gynaecological cancers and ensuring appropriate referral for specialized care are of paramount important in reducing both morbidity and mortality of these cancers. Therefore developing a guideline for primary care physicians is a necessity. Experts in several areas including consultant gynaecologists, consultant pathologists, consultant venereologists, consultant community physicians and public health staff actively took part during the course of developing this guideline. I would like to thank the experts for their generous contribution in making this activity a success.

I hope this guideline will help to improve the knowledge and skills needed by primary care physicians, in order to offer quality services as well as strengthening the referral pathway for prevention and early detection of common gynaecological cancers in Sri Lanka.

Dr.Neelamani Paranagama

Director, National Cancer Control Programme

Technical Guidance

List of experts provided technical guidance for developing guideline

National Cancer Control Programme(NCCP)		
1.	Dr. Neelamani Paranagama	Director, NCCP
2.	Dr. Eshani Fernando	Deputy Director, NCCP
3.	Dr. Chiranthika Vithana	Consultant Community Physician, NCCP
4.	Dr. Suraj Perera	Consultant Community Physician ,NCCP
5.	Dr. Varuni Bandara	Senior Registrar, NCCP
6.	Dr. Anoja Dheerasinghe	Registrar, NCCP
7.	Dr. Haleema Naseemdeen	MO, NCCP
8.	Dr. Harshani Amaradasa	MO,NCCP
9.	Dr. Anushyanthan Sivappiragasam	MO, NCCP
Family Health Bureau (FHB)		
1.	Dr. Deepthi Perera	Director, FHB
2.	Dr. N.Mapitigama	Consultant Community Physician ,FHB
3.	Dr. Achini Thilakarathne	Medical Officer, FHB
4.	Ms. Ramya Jayasekara	RSPHNO, FHB
Ministry of Health Sri Lanka		
1.	Dr. Indra Kumari Fernando	Director, Primary Health Care
2.	Dr. Thalatha Liyanage	Director, Non-communicable disease
Sri Lanka College of Obstetricians & Gynaecologists		
1.	Professor Hemantha Senanayaka	Professor in Obstetrics and Gynaecology, Faculty of Medicine, University of Colombo
2.	Dr. Kanishka Karunarathna	Director, Senior Consultant Gynaecologist, National Cancer Institute, Maharagama
1.	Dr. Samanthi Premarathne	Consultant Gynaeoncologist
2.	Dr. Harsha Atapattu	Consultant Gynaecologist (ROG), DGH Kalutatra

College of General Practitioners of Sri Lanka		
1.	Dr Kamal Fernandopulle	Family Physician
2.	Dr. Shreen Willatgamuwa	GP
College of Oncologists of Sri Lanka		
1.	Dr. Sujeewa Weerasingha	Consultant Oncologist, National Cancer Institute, Maharagama
College of Pathologist of Sri Lanka		
1.	Professor Dilani Lokuhetti	Professor in Pathology, Faculty of Medicine Colombo
2.	Professor Kamani Samarasingha	President, College of Pathologist Sri Lanka, 2013
3.	Dr. A.A.H.Priyani	Secretary, College of Pathologist Sri Lanka, 2013
National STD/AIDS Control Programme		
1.	Dr. Sisira Liyanage	Director, National STD/AIDS Control Programme
2.	Dr. Janaki Vidanapathirana	Consultant Community Physician, National STD/AIDS Control Programme
3.	Dr. Geethani Samaraweera	SR, Venereology, National STD/ AIDS Control Programme
University of Colombo(UOC)		
1.	Dr. Piyusha Atapattu	Senior lecturer in Department of Physiology , Faculty of Medicine, UOC
Field Health Services		
1.	Dr. Ramani Ramanayaka	DCMOH/MCH, Colombo (CMC)
2.	Dr.Chandani Denawaka	AMOH, Kaduwela

Abbreviations

ASCUS	Atypical squamous cells of undetermined significance
ASCUS high grade	Atypical squamous cells of undetermined significance high grade
ASCUS low grade	Atypical squamous cells of undetermined significance low grade
CA-125	Cancer Antigen 125
CIN	Cervical Intraepithelial Neoplasia
HPV	Human Papillomavirus
HRT	Hormone Replacement Therapy
HSIL	High grade squamous intra epithelial lesions
LLETZ	Large loop excision of the transformation zone
LSIL	Low grade squamous intra epithelial lesions
MOH	Medical officer of health
NILM	Negative for intraepithelial lesion or malignancy
OCP	Oral contraceptive pills
PID	Pelvic inflammatory disease
SCJ	Squamo-columnar junction
STIs	Sexually transmitted infections
TVS	Trans-vaginal ultrasound
VIA	Visual inspection: with acetic acid
VILI	Visual inspection: with Lugol's iodine

Chapter 1

Introduction

1.1 Scope and objectives of the guideline

The aim of this guideline is to direct the primary care physicians on prevention and early detection of common malignancies in the female genital tract: namely cervical, ovarian and uterine cancers and thereby to reduce the burden of cancer in the country. It focuses on improvement of the knowledge and skills of primary health care physicians, to offer quality services by providing recommendations.

1.2 The target audience

This guideline is intended to be used by the primary care physicians in Sri Lanka including Medical Officers of outpatient departments of hospitals, Medical Officers of Health (MOOH) and General Practitioners (GPs).

1.3 Expected output

By developing this guideline, it is expected to detect cervical cancers at a pre-malignant stage and ovarian and uterine carcinomas at an early stage. Furthermore, down staging of cancers at diagnosis will be achieved by early detection and timely referral. Ultimate aim is to decrease the morbidity and mortality associated with gynaecological cancers.

1.4 Situation of gynaecological malignancies in Sri Lanka

Cervical cancer is the second commonest malignancy among females with an age-standardized incidence rate of 9.6 per 100,000 population in 2006. It accounts for 12% of newly diagnosed cancers among females. Ovarian cancer is the fourth commonest malignancy with an age-standardized rate of 6.7 per 100,000 population accounting for 8% of female cancer incidence. Uterine cancer stands as the eighth commonest with an age-standardized rate of 2.8 per 100 000 population consisting 3% fall newly diagnosed female malignancies (National Cancer Control Programme, 2012).

Chapter Two

Prevention and Early Detection of Cervical Cancer

Ninety per cent of cervical cancers are squamous cell carcinomas and the other 10% are adeno-carcinomas. Squamous cell carcinoma arises from the metaplastic squamous epithelium of the transformation zone and adeno-carcinoma arises from the columnar epithelium of the endo-cervix.

2.1 The squamo-columnar junction of the cervix

The cervix is lined by both stratified non-keratinising squamous and columnar epithelium. These two types of epithelia meet at the squamo-columnar junction(SCJ)(Figure 2.1).

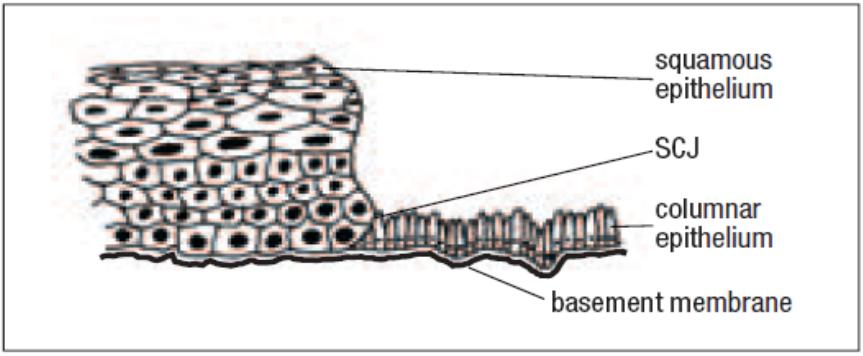

Figure 2.1- Squamo-colomnar junction (SCJ) of the cervix

Adapted from : Sellors JW, Sankaranarayanan R. *Colposcopy and treatment of cervical intraeplthellal neoplasia: a beginners manual* Lyon, France, IARC Press, 2002

Position of the SCJ in relation to the external os tends to vary over a woman's lifetime. It depends upon factors such as age, hormonal status, birth trauma, use of oral contraceptive pills (OCP) and physiological conditions such as pregnancy.

2.1.1 Squamous metaplasia and the transformation zone

The columnar epithelium of the cervix is gradually replaced by stratified squamous epithelium as a result of exposure to the acidic environment of the vagina. This normal replacement process is termed squamous metaplasia and it gives rise to a new SCJ. The mature new squamous epithelium closely resembles the original squamous epithelium. The newly formed SCJ and the original SCJ are distinct on examination. The area between the original and the new SCJ is called the transformation zone.

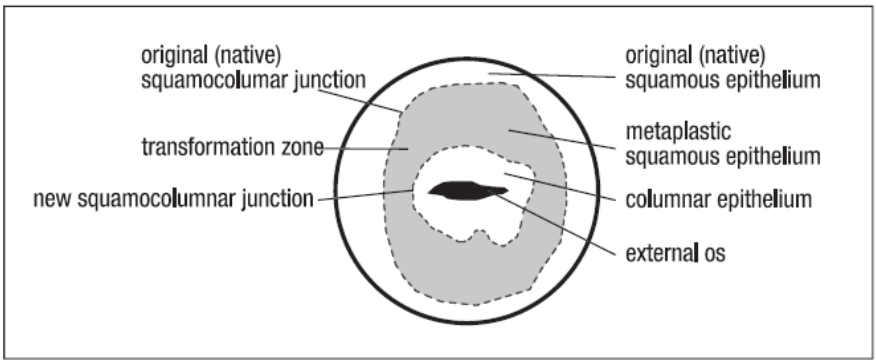

Figure 2.2 - Transformation zone of a cervix of a parous woman of reproductive age

Source: Sellors JW, Sankaranarayanan R. *Colposcopy and treatment of cervical intraeplthellal neoplasia: a beginners manual* Lyon, France, IARC Press, 2002

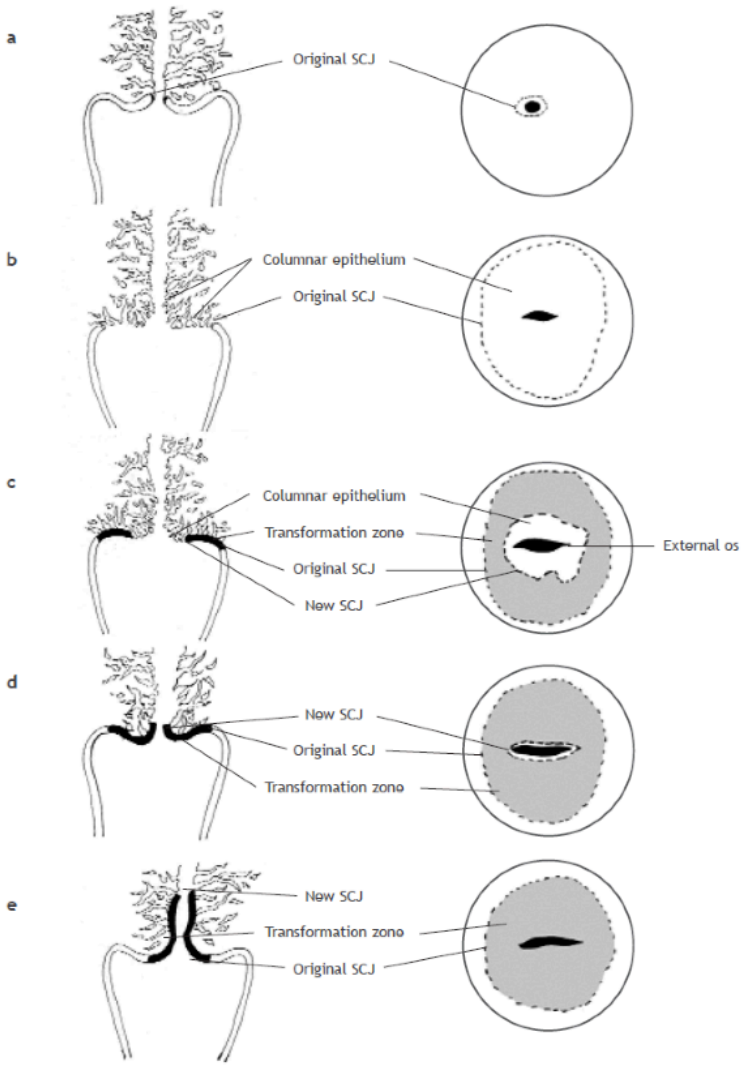

Figure 2.3 - Location of the squamo-columnar junction (SCJ) and transformation zone: (a) before menarche; (b) after puberty and at early reproductive age; (c) in a woman in her 30s; (d) in a peri-menopausal woman; and (e) in a post-menopausal woman

Source: Sellor JW & Sankaranarayanan, Celospy and treatment of Ceovicol intra-epithlat neoplasia a biginers manual, Lyon , France, IARC Press, 2002

2.2 Development of cervical carcinoma

Primary cause of carcinoma of cervix is the persistent infection with one or more of the oncogenic types of Human Papillomavirus (HPV). It is reported that HPV serotypes16 and 18 are found in 70% of all cervical cancers.

However, most HPV infections are transient, regardless of the serotype, with only a few of them persisting and even fewer progressing to precancerous lesions or invasive carcinoma.

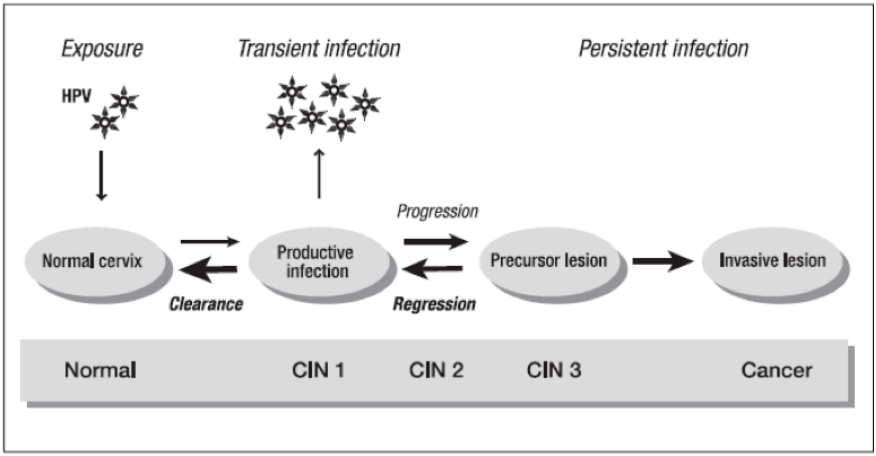

Figure 2.4 –Natural history of cervical cancer

CIN : cervical intraepithelial lesion
Adapted from : *Cervix cancer screening* Lyon, IARC Press, 2005 (IARC Handbooks of Cancer Prevention Vol. 10)

It may take 10–20 years for the precursor lesions caused by HPV to develop into invasive carcinoma. Therefore, most cervical cancers can be prevented by early detection and treatment at the level of pre-cancerous lesions.

2.3 Classification of cervical lesions

Sri Lankan guideline of classification for cervical cytology was adapted from the Bethesda system (Family Health Bureau, 2010).

Categories included in Modified Bethesda Classification adapted for Sri Lanka:

1. Negative for intraepithelial lesion or malignancy (NILM)
2. Low grade squamous intra epithelial lesions (LSIL)
3. High grade squamous intra epithelial lesions (HSIL)
4. Atypical squamous cells of undetermined significance (ASCUS)
   - Atypical squamous cells of undetermined significance - low grade (ASCUS low grade)
   - Atypical squamous cells of undetermined significance - high grade (ASCUS high grade)
5. Glandular cell atypia
6. Benign endometrial cells in a woman > 40 years
7. Squamous or glandular malignancy

Table 2.1:Cytological and histological classifications of cervical lesions

Cytological classification (used for screening) Bethesda system	Histological classification (used for diagnosis) Cervical Intraepithelial Neoplasia (CIN)
Normal	Normal
ASCUS	Atypia
LSIL	CIN 1 including flat condylomata
HSIL	CIN 2
HSIL	CIN 3
Invasive carcinoma	Invasive carcinoma

*Mild dysplasia, moderate dysplasia and severe dysplasia in previous cytological classification are equal to LSIL(CIN 1), HSIL(CIN 2) and HSIL(CIN 3) respectively

2.4 Risk factors for cervical carcinoma

HPV infection is the necessary cause of cervical cancer.
Other risk factors classified

1. Co-factors favouring infection with HPV:
    - Commencement of sexual activity at an early age
    - Multiple sexual partners
    - A partner who participate in high risk sexual activities
    - Poor socio-economic status-poor hygiene
    - Immunosuppression- acquired or primary (immunosuppressive drugs taken after organ transplant and HIV infection)
2. Co-factors favouring persistence of HPV infection:
    - High Parity
    - Tobacco smoking (both active and passive)
    - Immunosuppression- acquired or primary
    - Poor socio-economic status
    - Poor nutritional status
    - Prolong usage of oral contraceptive pills (slight increase in risk is observed with usage for > 5 years, whereas usage for > 10 years shows increased risk)

2.5 Clinical features of cervical carcinoma

Women with pre-cancerous lesions are usually asymptomatic. Symptoms begin when a pre-cancer becomes a true invasive cancer.

Common early symptoms are:

- Inter-menstrual bleeding/post-menopausal bleeding
- Post-coital bleeding
- Abnormal vaginal bleeding
- An unusual vaginal discharge
- Excessive sero-purulent discharge

➢ *If symptoms are present, it is essential to do a speculum examination*
➢ *Pap smear is mandatory even if the cervix looks normal*

However, in Sri Lanka majority (70%) of cervical cancers are diagnosed at an advanced stage (Stage III and IV)

2.6 Prevention of cervical carcinoma

Cervical cancer is a preventable and early-detectable at pre-cancerous stage. Therefore, it is very important to implement strategies to prevent the development of the cancer and to identify and manage it at pre-cancerous stage.

2.6.1 Community awareness on behavioural change

It is important to increase the public awareness on risk factors. Strategies aiming at establishing personal abstinence and changing risky behaviours should be started early in life, preferably at school.

Messages to be conveyed to the public should include:

- HPV vaccination before commencing sexual life
- Limiting sexual relationship to one mutually trusted partner
- Use of condoms in high risk sexual relationships though condoms give only partial protection from HPV
- Improvement in socio-economic status
- Cessation of tobacco smoking
- Continued participation in cervical cancer screening tests

2.6.2 HPV vaccine

HPV vaccines have been developed for protection against HPV infections. They are designed for prophylactic use only; they do not clear existing HPV infection or treat HPV related diseases.

Currently, two HPV vaccines are available:

- Bi-valent vaccine against HPV serotypes 16 and 18
- Quadri-valent vaccine against HPV serotypes 6, 11, 16 and 18

Both vaccines need to be administered in 3 doses intramuscularly (IM) over a period of six months.

- The quadri-valent vaccine is given at baseline and again after 2 months and 6 months
- The bi-valent vaccine is given at baseline and again after 1 month and 6 months
- Vaccines are indicated to be used in females 9-26 year of age before the onset of sexual activity

- However, this vaccine is not available in the government health services though it is available in the private sector.

Women, who have received HPV vaccination, should continue to participate in screening tests for cervical cancer.

2.6.3 Screening for cervical carcinoma

Screening for cervical carcinoma is one of the most effective strategies in controlling cervical cancer. Screening is done for asymptomatic population. It takes about 10-20 years for pre-cancerous lesion to develop into an invasive cancer. If precancerous lesions are identified and treated early, development of cervical cancer can be prevented. Detection of invasive cancer at an early stage leads to 5-year survival rate of approximately 92% and dramatically reduces cervical cancer mortality. It is recommended to screen women over 30 years by the World Health Organization (WHO).

Screening tests for cervical carcinoma:

1. Cytology: conventional (Pap Smear test) or liquid-based cytology

   Conventional Pap Smear is the screening method practiced in Sri Lanka
2. HPV DNA test

   (Still not available in Sri Lanka)
3. Visual inspection: using acetic acid (VIA) or Lugol's iodine (VILI) (Not done in Sri Lanka)

Informed consent is a must before a woman is screened for cervical cancer.

However, if there is a lesion ideal test is biopsy even though the smear is negative.

Cervical cancer screening includes:

- Taking a history, to assess whether the woman has specific risk factors or suggestive symptoms.

History

Ask the client about:

- Age, education, number of pregnancies, births and living children, last menstrual period, menstrual pattern, previous and present contraception
- Previous cervical cancer screening tests, their dates and results
- Medical history including any medications or drug allergies
- Social history, including factors that may increase her risk of cervical cancer
- Sexual history including age of sexual initiation and of first pregnancy, number of partners, previous sexually transmitted infections (STIs), and any behaviours that may suggest an increased risk of cervical carcinoma
- Any symptoms and signs of cervical malignancies and other illnesses

The screening test iinvolves a speculum examination (Annex 1).

A bimanual vaginal examination should be performed only after the cervical smear has been taken.

2.6.3.1 Conventional Pap Smear test

- A sample of cells is taken from the transformation zone of the cervix using a wooden spatula with an extended-tip and a cyto-brush.
- Ideally, two smears should be prepared on two glass slides.
- Each smear should be labelled clearly.
- The entire transformation zone should be sampled as almost all high-grade lesions develop in this zone.
- Then the smears should be immediately fixed in a 95% alcohol solution to preserve the cells. Fixed and air-dried slide is sent to a cytology laboratory to determine whether the cells are normal or abnormal and to classify appropriately.

Pap Smear test takes less than 5 minutes to perform; it is not painful and could be performed in an outpatient set up.

- The results of the Pap Smears will be reported to the clinic. The client should be informed of the results and followed-up as recommended.
- It is better to postpone taking a Pap Smear test if the woman is menstruating, having clinically evident acute inflammation, or pregnant.
- The accuracy of cytological testing depends on the quality of the services, including sampling practices and preparation and interpretation of smears in the laboratory.

Management of vaginal /cervical infections at primary care level

- If the woman is having symptoms of a vaginal or cervical infection, it should be treated before obtaining the Pap Smear.
- If there is any suspicion of a sexually transmitted infection (STI), best option is to refer to an STI clinic of the closest hospital.
- If the patient is not willing to attend a STI clinic, manage the client according to the guideline issued by National STD/AIDS Control Programme (Annex 11).

Places where Pap tests are performed:

- Well woman clinics in MOH areas
- Well woman clinics/gynaecological clinics in government hospitals
- National Cancer Institute, Maharagama
- National Cancer Control Programme, Cancer early detection centre, Narahenpita,
- General Practice
- Private hospitals

Target group for Pap Smear test

- Any woman over 30 years of age who is / had been sexually active
- For women who had undergone regular Pap Smear screening, further testing is not indicated after 65 years, if last two previous Pap Smears screening results have been negative.

Pap Smear screening should be continued in the following patients:

- *Patients who have undergone hysterectomy for a pre-cancerous conditions of the cervix (vault Smear)*
- *Patients who have undergone a subtotal hysterectomy*

Technique for obtaining Pap Smear

- Explain the client that the Pap Smear is not a diagnostic test, but a screening test to detect a precancerous lesion so that development of cervical cancer can be prevented
- The technique of obtaining Pap Smear is mentioned in Annex 111.

Recommendation for management and follow up (Source: Family Health Bureau 2010)

- For women with normal Pap Smear test - repeat Pap test after five years
- For women with abnormal Pap Smear test- adhere to the following guideline

Guideline on clinical management of those screened based on cytology report.

Satisfactory- When endo-cervical and metaplastic cells are lacking, the woman should be further evaluated to see whether she is pregnant, postmenopausal or on OCP.

Unsatisfactory- repeat the smear immediately

Cytological Types

1. **Negative for intraepithelial lesion or malignancy (NILM)**

   - Repeat the smear in 5 years
   - Inflammation- Treat only if a specific organism is identified or if the client is symptomatic. Clients with non- specific inflammatory smears without symptoms should not be treated.
   - All other reactive changes-As medical officers at primary health care level, offer treatment if possible. Refer if further management is needed.

2. Low grade squamous intra epithelial lesions (LSIL)

- Two repeat smear six month apart
- If repeat smear is negative- normal follow up
- If repeat smear is positive-refer to a gynaecologist for Colposcopic biopsy

3. High grade squamous intra epithelial lesions (HSIL)

- Refer to a gynaecologist for histological diagnosis. Colposcopy and large loop excision of the transformation zone (LLETZ) or cold knife conisation are recommended. If colposcopy biopsy is positive and if the lesion is adequately excised already, medical officer at primary health care level should obtain a follow up smear after 3 months. If the follow up smear is positive, refer the patient back to the gynaecologist. If the smear is negative, it should be repeated at 3 and 6 months intervals.
- If biopsy is negative, medical officer at primary health care level should obtain a follow up smear and act accordingly.

4. Atypical squamous cells of undetermined significance (ASCUS)

- ASCUS High Grade- Refer for Colposcopy
  If colposcopic biopsy is positive treat as for HSIL. In case of a negative biopsy, follow up with 3 smears, 3 months apart.
- ASCUS Low Grade-Medical officer at primary health care level to follow up and repeat smear in 6 months.

5. Glandular cell atypia

- Refer to a gynaecologist to investigate for cervical or endometrial lesions based on clinical details.

6. Benign endometrial cells in a woman aged > 40 years

- Refer to a gynaecologist to investigate based on clinical details

7. Squamous or glandular malignancy

- Urgent gynaecological referral for appropriate management is needed.

Table 2.2-Mangement of cervical lesions classified according to Modified Bethesda Classification System

(Source: Family Health Bureau, 2010)

Category	Recommendation
Negative	Routine re-screening If inflammatory-treat and follow up
LSIL (CIN 1)	Follow up by medical officer at primary health care level Two repeat smears 6 months apart If negative routine follow up If positive- refer gynaecologist
HSIL (CIN 11 or 111)	Refer to a gynaecologist for Colposcopy
ASCUS-low grade	Follow up by medical officer at primary health care level Repeat smear in 6 months
ASCUS-high grade	Refer to a gynaecologist for Colposcopy
Glandular cell atypia	Refer to a gynaecologist
Squamous or glandular malignancy	Urgent referral

Follow up of high risk women need more frequent (once a year) screening even if the Pap Smear results are negative

The women under the following categories should be considered as high-risk to offer yearly pap smears:

- Those on immunosuppressive drug treatment (including patients who had organ transplants)
- Those infected with HIV
- Those having Systemic Lupus Erythematosus (SLE)
- Those on chronic corticosteroid treatment
- Those with other HPV related malignancies such as cancers of the anus and vulva

2.6.3.2 HPV DNA-based screening methods

- New screening procedures are based on the detection of high-risk
- HPV DNA in vaginal or cervical smears.
- Detection of high-risk HPV does not necessarily mean that a pre-cancerous lesion or cancer is present; it indicates simply that there is HPV infection.
- HPV test has a greater sensitivity for CIN 2 and above lesions
- This test is not available in Sri Lanka, yet.

2.6.3.3 Visual methods

These methods identify abnormalities of the cervix by inspection of the cervix without magnification, after application of dilute acetic acid (vinegar) or Lugol's iodine.

Visual inspection using acetic acid

When 5% acetic acid is applied to abnormal cervical tissue, it temporarily turns aceto-white.

Visual inspection using Lugol's iodine

If iodine is applied to the cervix, precancerous and cancerous lesions appear as well defined, thick, and mustard or saffron-yellow in colour. Normal squamous epithelium stains brown or black, and columnar epithelium retains its normal pink colour.

2.6.3.4 Counselling after screening

As soon as the screening procedures are over, the woman should be informed about:

- Whether examination looks normal or abnormal
- When the results will be available
- The date of the next appointment

Women should be informed about the results and follow up when the report is available:

- The result of the test and what it means
- If normal, when they need to return for next screening
- If inadequate or not normal, how to be followed up
- Place and date for follow-up

2.7 Methods of diagnosing cervical pre-cancer

All women with a positive or abnormal screening test should be followed up as mentioned in 2.6.3.1.

Standard practice for diagnosis: colposcopy and biopsy

2.7.1 Colposcopy

Colposcopy is the examination of the cervix, vagina and vulva using a colposcope. A colposcope provides magnification and allows the cellular patterns in the epithelial layer and surrounding blood vessels to be examined. Application of dilute acetic acid and Lugol's Iodine highlight abnormal areas, which facilitates biopsying.

Please follow the guideline in annex v for referral for colposcopy

Even if colposcopy is not available, a cone biopsy may have a place.

2.8 Treatment of pre-cancer

Management of patients depends on the results of the colposcopic examination, biopsy and endo-cervical curettage. Most precancerous lesions can be treated by methods such as cryotherapy, cold-coagulation or LLETZ and cold knife conisation.

If colposcopy is not available there, cold knife cone biopsy should be offered.

2.9 Treatment of cervical cancer

Treatment will be decided at the tertiary care level. Modes of treatment usually consist of surgery and chemo-radiotherapy.

Chapter 3

Prevention and Early Detection of Ovarian Cancer

Most ovarian tumours are benign.

3.1 Types of ovarian tumours

There are 3 main types of ovarian tumors:

- Epithelial tumours
- Germ cell tumours
- Sex cord stromal tumours

About 90% of ovarian cancers are epithelial in origin.

3.2 Risk factors for ovarian carcinomas

- Increasing age
- Family history of ovarian cancer
- Personal history of breast cancer
- Nulliparity
- Sub-fertility
- Use of hormone replacement therapy (HRT) for menopause-related symptoms or especially prolonged use (over 5 years) of estrogens unopposed by progesterone
- Family history of breast cancer-
  Mutations in the genes BRCA1 increase the risk of breast and ovarian cancer while mutations in BRCA 2 genes increase the risk of breast, ovarian, endometrial and colonic cancers.

Factors reducing the risk

- Increasing parity
- Breast feeding
- OCP use (reduce the risk by about 60%)
- Hysterectomy or tubal ligation

3.3 Methods for early detection

- Ask woman to consult a doctor when she has symptoms

- Ovarian cancer symptoms are non-specific.
  - ➢ Majority may have only dyspeptic symptoms.
  - ➢ Other symptoms include abdominal distention or pain, loss of appetite, and urinary symptoms (urgency, frequency).
  - ➢ Occurrence of gastric symptoms (heart burns, dyspepsia etc.).
  - ➢ If a post menopausal female complains of sudden onset of these symptoms more attention should be paid in to exclusion of an ovarian malignancy.

Most of these symptoms are common to other less serious conditions.

Majority of ovarian cancers are diagnosed at an advanced stage as symptoms are being non-specific. Prompt attention to symptoms may improve the chance of early diagnosis and successful treatment.

Tests for early detection of ovarian cancer

- Routine trans-vaginal ultrasound scan (TVS) and serum Cancer Antigen 125(CA-125) are not useful for early detection of ovarian cancer.
- Any woman having above mentioned symptoms persistently should be referred to a gynaecologist to exclude an ovarian malignancy.

Once a year screening is indicated with pelvic examination, TVS and CA-125 in the following categories of the women who are at high risk of developing ovarian cancer:

- Three or more relations with a Lynch Syndrome related malignancies (colorectal, endometrial, ovarian and breast cancers)
- First degree relative suffering from ovarian cancer

Chapter 4

Prevention and Early Detection of Endometrial Cancer

4.1 Types of endometrial carcinomas

The most common endometrial cancer is endometrial adenocarcinoma.

Histological classification is as follows.

- Endometrioid (75%–80%).
    - Ciliated adenocarcinoma.
    - Secretory adenocarcinoma.
    - Papillary or villoglandular.
    - Adenocarcinoma with squamous differentiation.
        - Adenoacanthoma.
        - Adenosquamous.
- Uterine papillary serous (<10%).
- Mucinous (1%).
- Clear cell (4%).
- Squamous cell (<1%).
- Mixed (10%).
- Undifferentiated.

4.2 Risk factors for endometrial carcinoma

- Increasing age
- Early menarche and late menopause
- Use of HRT containing exogenous estrogens unopposed by progesterone
- Nulliparity
- Subfertility
- Polycystic ovarian disease/syndrome

- Endometrial hyperplasia with cellular atypia
- A certain type of ovarian tumors, the granulosa-theca cell tumor, secreting estrogen
- Family history of uterine, colon and breast cancer
- Personal history of breast cancer
- Obesity
- Pre-existing diabetes
- Tamoxifen used in treatment of breast cancer

Factors reducing the risk

- Increasing parity

4.3 Symptoms of endometrial carcinoma

- Peri or post-menopausal vaginal bleeding
- Abnormal vaginal bleeding

- *Even a single episode of post postmenopausal vaginal bleeding (vaginal bleeding after one year of menopause) should be investigated.*
- *All women with abnormal vaginal bleeding should be referred to a gynaecologist.*

4.4 Methods of early detection

There is no screening test recommended for endometrial carcinoma.

The best ways to identify endometrial cancer is to recognize symptoms early. Majority of the uterine cancers present due to early onset symptoms such as:

- Post-coital bleeding
- Heavy irregular vaginal bleeding before menopause(pus like and bloody)

If a woman complains of symptoms, she should be referred to a gynaecologist. About 70% of endometrial cancers are diagnosed at an early stage.

Trans-vaginal ultrasound scan, hysteroscopy and endometrial biopsy can be used to detect endometrial cancer.

Occasionally Pap Smear done for screening for cervical cancer may reveal endometrial cells.

Chapter 5

Other Malignancies of Female Genital Tract

5.1 Types

The following malignancies related to female genital tract are less commonly seen

Uterus:

- Leiomyosarcoma
- Endometrial stromal tumours including stromal sarcomas
- Carcinosarcoma
- Tumours of trophoblast including chriocarcinoma

Vuvar cancers

- Squamous cell carcinoma
- Melanoma
- Verrucous carcinoma
- Basal cell carcinoma
- Other – adenocarcinoma, sarcoma

Vaginal

- Squamous cell carcinoma
- Adenocarcinoma – clear cell, papillary, mucinous, adenosquamous
- Sarcoma – eg:sarcomabotryoides
- Melanoma

Fallopian tubes:

- Adenocarcinoma of the fallopian tube

5.2 Methods of early detection

There are no recommended methods of early detection.

Annex 1

Steps of pelvic examination

(Source: World Health Organization 2006)

The following equipment and supplies should be available:

- Papers and pencil
- Soap and water for washing hands
- Source of light to examine the cervix
- Examination table or couch covered by clean paper or cloth
- Disposable or high-level disinfected examination gloves
- Cusco's Specula of different sizes, high-level disinfected
- High stool
- Dustbin for clinical waste

Before the examination

- Have all necessary equipment and supplies ready.
- Ensure the speculum used is at a comfortable temperature.
- If planning to do a Pap Smear test, inform the woman what it is, what it is for, and when you expect to have the results.
- Ask the woman if she has any questions and answer them truthfully.
- Explain what the pelvic examination consists of and show the woman a speculum.
- Ask the woman to empty her bladder and ask her to remove her underwear (waist down).Be particularly sensitive to her sense of modesty about uncovering normally clothed areas, or if the examination is perceived to be invasive.
- Position the woman on the examination table.

Performing a pelvic examination

There are three components:

- An external genital examination
- A speculum examination
- A bimanual examination

Examination using Cusco's Speculum

- Before putting the speculum examine external genitalia-using a gloved hand to gently touch the woman, look for redness, lumps, swelling, unusual discharge, sores, tears and scars around the genitals and in-between the skin folds of the vulva. These can be signs of a sexually transmitted infection (STI).

- Hold the Cusco's speculum blades together and insert speculum directly as the vagina is a structure flat antero-posteriorly.
- Gently open the blades and look for the cervix.
- Move the speculum slowly and gently until you can see the entire cervix. Tighten the screw so it will stay in place.
- Check the cervix, which should look pink, round and smooth. There may be small yellowish cysts, areas of redness around cervical os or a clear mucoid discharge; these are normal findings.
- Look for any abnormalities, such as:
    - Vaginal discharge and redness of the vaginal walls, which are common signsof vaginitis. If the discharge is white and curd-like, there is a possibility of yeast infection,
    - Ulcers, sores or blisters. Genital ulcers may be caused by syphilis, chancroid, herpes virus or, in some cases, cancer. Sores and blisters are usually caused by herpes virus,
    - Easy bleeding when the cervix is touched with a swab or amuco-purulent discharge, which are signs of a cervical infection,
    - An abnormal growth or tumour, which might be cervical carcinoma.
- Loosen the screw of the speculum, gently pull the speculum towards you until the blades are clear of the cervix, close the blades and remove the speculum

Bimanual vaginal examination including test for cervical motion tenderness should be performed only after the cervical smear has been taken.

Bimanual vaginal examination

Test for cervical motion tenderness:

- Put the pointing and the middle finger of your gloved hand in the woman's vagina. Turn the palm of your hand up. Feel the cervix to see if it is firm and round.
- Then put one finger on either side of the cervix and move the cervix gently while watching the woman's facial expression.
- If this causes pain, (you may see the woman grimace), this indicates cervical motion tenderness, and she may have an infection of the uterus, tubes or ovaries (pelvic inflammatory disease - PID). If her cervix feels soft, she may be pregnant.

Bimanual vaginal examination

- Feel the uterus by gently pushing on her lower abdomen with your other hand. This moves the uterus, tubes and ovaries closer to the fingers inside her vagina. The uterus may be tipped forwards or backwards.
- When you find the uterus, feel for its size and shape. It should feel firm, smooth and smaller than a lemon.
  - If the uterus feels soft and large, the woman is probably pregnant.
  - If it feels lumpy and hard, she may have a fibroid or another growth.
  - If it hurts her when you touch it, she may have an infection.
  - If it does not move freely, she may have scars from an old infection/ endometriosis
- Feel the tubes and ovaries.
  - If these are normal, they will be difficult to feel.
  - If you feel any lumps that are bigger than an almond or that cause severe pain, she may have an infection or other condition needing urgent treatment.
  - If she has a painful lump and her period is late, she may have an ectopic pregnancy; in this case, she needs medical help right away.
- Move your finger to feel the inside of the vagina. Make sure there are no unusual lumps, tears or sores.
- Ask the woman to cough or push down as if she were passing stool. Look to see if something bulges out of the vagina (uterine prolapse).

After the examination

- Place used equipment in disinfectant solution and discard the gloves into the clinical waste bin.
- Wash your hands with soap and water.
- Record all findings on the woman's chart.
- Tell the woman if her examination was normal or if you noted anything unusual or abnormal. Explain what any abnormality you noted might mean.
- If you noted any signs that might indicate a STI, refer to STI clinic of the closest hospital. In case of non-compliance, treat the woman and her partner immediately (follow national guidelines). Provide condoms and teach them how to use them.
- If you find something that needs urgent treatment or that cannot be handled at your centre, refer the woman to a higher level of care.
- Give her a date to return for follow-up if necessary

Annex 11

Management of Vaginal Discharge

(Source: National STD/AIDS Control Programme, 2000 & 2012)

A spontaneous complaint of a change in vaginal discharge (in terms of quantity, colour or odour) is most commonly due to vaginitis/vaginosis but may also be due to cervicitis.

Commonest causes of vaginal discharge

- ***Trichomonas vaginalis*** infection
- Bacterial vaginosis
- ***Candida albicans*** infection
- ***Neisseria gonorrhoeae*** and/or ***Chlamydia trachomatis*** infections of the cervix may present with abnormal vaginal discharge.

The symptom of a vaginal discharge is highly indicative of vaginal infection, but is a poor predictor of cervical infection.

Among women with a vaginal discharge, assessment of risk may help to identify women with a higher risk of cervical infection.

Risk factors associated with cervicitis

- Having multiple partners
- Having a partner with symptoms suggestive of STI
- Recent change of partner

are frequently associated with cervicitis.

Women with a vaginal discharge and a positive risk assessment should therefore, be treated for gonococcal and chlamydial cervicitis as well as for vaginitis/vaginosis.

Physiological discharge

- Healthy women may have a variable amount of clear white discharge from vagina.
- It usually increases before and after menstruation, and becomes more watery when she is in the mid cycle.
- It also increases during pregnancy, while taking OCP and when an intrauterine device is in place.

Symptoms of individual infections

1. **Trichomoniasis**

This is caused by the flagellated protozoan ***Trichomonas vaginalis***. It is an STI in adults.

Symptoms

- The majority tend to be asymptomatic
- Some have symptoms characterized by a **diffuse, yellow–green, offensive vaginal discharge and vulval itching.**

Figure 1: Trichomoniasis

Management of sexual partners

- The sexual partner/s should be notified and treated.
- Patients should be advised to avoid sexual intercourse until both the index patient and the partner/s have completed treatment.

2. **Bacterial Vaginosis**

Bacterial vaginosis is a clinical syndrome resulting from replacement of the normal hydrogen peroxide producing Lactobacillus species in the vagina with high concentrations of anaerobic bacteria, such as ***Gardnerella vaginalis*** and ***Mycoplasma hominis***. The cause of the microbial alteration is not fully understood. Bacterial vaginosis is an endogenous reproductive tract infection.

Symptoms

- More than 50% are asymptomatic
- Unpleasant, fishy, malodorous, thin, homogenous, grey vaginal discharge.

  The odour, which is a result of metabolic by-products produced primarily by anaerobic bacteria is exacerbated during menstruation and also following intercourse due to the alkaline nature of blood and semen.
- Increased vaginal discharge
- Vaginal itching and irritation

Management of sexual partners

- Treatment of sexual partners has not been demonstrated to be of benefit.

It is recommended that predisposing factors such as use of antiseptic/ antibiotic vaginal preparations or vaginal douching should be reduced or eliminated.

3. **Candidiasis**

In the majority of cases, vulvo-vaginal candidiasis is caused by ***Candida albicans***.

Symptoms

- Up to 20% of women with the infection may be asymptomatic.
- Itching of the vulva, soreness and a non-offensive vaginal discharge, which may be curd like.
- Clinical examination may reveal vulval erythema (redness) or excoriations from scratching and oedema of the vulva.

Management of sexual partners

- Vulvo-vaginal candidiasis is usually not acquired through sexual intercourse.
- Treatment of sexual partners is not recommended, but may be considered for women who have recurrent infection.
- A minority of male partners may have balanitis, which is characterized by erythema of the glans penis or inflammation of the glans penis and foreskin (balanoposthitis).

Management of recurrent candidiasis

- Predisposing factors such as use of antibiotics and antiseptic/ antibiotic vaginal preparations or vaginal douching should be reduced or eliminated.

Other underlying factors for recurrent vulvo-vaginal candidiasis include uncontrolled diabetes mellitus, immune suppression and use of corticosteroids.

4. **Gonococcal cervicitis**

The endocervical canal is the primary site of urogenital gonococcal infection in women.

Symptoms

- Majority are asymptomatic
- Discoloured vaginal discharge, sometimes with associated vaginal and vulval irritation
- Dysuria
- Increased frequency of passing urine
- Intermenstrual bleeding
- Menorrhagia

Many infected females have cervical abnormalities such as

- Erythema/oedema of the cervix
- Cervical ectopy
- Induced cervical bleeding
- A muco-purulent / purulent discharge from cervical os

Primary care physicians should refer the patient to closest STI clinic on suspicion of a STI.
If there is any doubt of her compliance in her going to the referral centre, follow the syndromic management.

Syndromic Management

Syndromic management is based on the identification of syndromes and treatment for these. Syndromes for STI consist of symptoms and easily recognized signs such as urethral discharge/dysuria, genital ulcer/ulcers, vaginal discharge and lower abdominal pain. The syndrome is identified on clinical grounds (history and an examination) and treatment for each

syndrome is directed towards the most common organisms responsible for the syndrome.

Recommended syndromic treatment

1. **Treatment for vaginitis (Bacterial or Trichomoniasis)**
   Metronidazole 400mg orally twice daily for 7 days
   or
   Tinidazole 500mg orally twice daily for 5 days
2. **Treatment for vaginal candidiasis**
   Miconozole or clotrimazole 200mg vaginal pessaries intravaginally daily at night for 3days
   or
   Clotrimazole, 500mg vaginal pessaries intravaginally as a single dose
   or
   Nystatin vaginal pessaries 100 000 units intravaginally once daily at night for
   14 days
3. **Treatment for cervicitis (due to** *Neisseria gonorrhoeae* **(NG)and/or** *Chlamydia trachomatis)*
   Cefixime 400mg orally in a single dose
   or
   Ceftriaxone 250 mg intramuscular injection, as a single dose

   PLUS
   Azithromycin, 1g orally as a single dose
   or
   Doxycycline 100mg orally, twice daily for 7 days
   or
   Erythromycin, 500mg orally, 4 times daily for 7 days

Annex III

Pap smear-cervical cytology

(Source: Family Health Bureau, 2010)

Cytological testing involves collection of exfoliated cells from the cervix and microscopic examination of those cells after staining.

Labelling and obtaining a cervical smear

- Cervical screening should be done after clearly explaining the importance of the procedure and the steps to the client.
- Clients should be instructed not to douche on the day of the examination. She should not be using any intra vaginal medication at the time of testing. A cervical smear should not be performed if she has bleeding or obvious infection is present. In case of an infection, cervical smear should be performed only after appropriate treatment.
- Before starting the procedure, all necessary equipment and supplies should be available at hand. The glass slides should be correctly labelled. The Coplin jar filled with 95% ethanol / isopropyl alcohol should be kept ready.

Labelling of slides

This is a very important aspect, as incorrect labelling of slides will result in erroneous reports or even a mix up of results of several patients.
Please ensure that the following precautions are taken:

- An identification mark should be made on each slide using a diamond pencil before the smear is made.
- Before the smear is made, ensure that the slide is labelled according to the instructions given. The same identification number must be written on the accompanying referral form (Annex 1V)

Obtaining a cervical smear

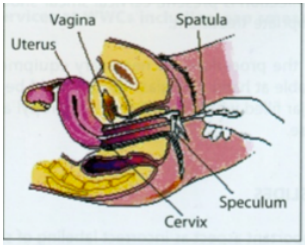

Figure 1: Visualization of the cervix

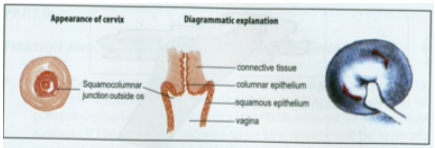

Figure 2: Smear taking

Figure 1- Visualization of cervix and Pap Smear taking

- The dorsal position is suitable for smear taking and a source of good illumination should be available at the foot end of the bed.
- A speculum of suitable size should be chosen for examination. It may be slightly moistened with water before insertion. The use of other lubricants or antiseptics should be avoided.
- Once the speculum is inserted the ecto-cervix should be clearly visualized.
- The thinner extended prong (narrow end) of the spatula should be inserted into the cervical os and rotated 360 degrees clockwise while keeping it opposed to the cervix (Figures 1 and 2). Since there is a tendency to slip over certain areas, a reverse anticlockwise rotation towards the opposite direction should also be performed immediately.
- In the case of a large patulous or multi-parous cervix, the broader end of the spatula is the most suitable to take the smear. This requires thorough scraping of the ecto-cervix over the whole area, using the broad, flat end of the spatula in backwards and forwards movement.
- Postmenopausal or postconisation os, with no visible squamo-columnar junction demands careful sampling of the canal. In this situation, an additional sample may be taken with an endo-cervical brush.

Bimanual vaginal examination should be performed only after the cervical smear has been taken.

Spreading the smear

The material collected on the spatula should be quickly and evenly spread on the relevant slide.

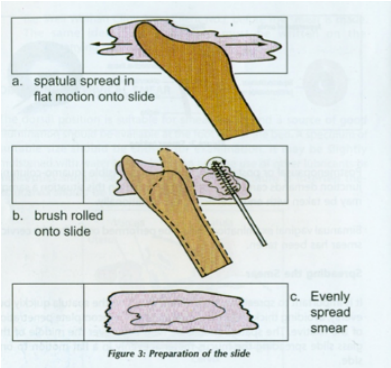

Figure 2-Slide preparation in Pap Smear test

Fixation and transportation of cervical smears

- The smear should be wet fixed without air drying. The slide should be fixed immediately to prevent drying by immersing it in a jar of 95% alcohol. Handle the slide only by the labelled end of it.
- The fixation can be carried out in a Coplin's jar filled with alcohol. Do not put more than 5 smears into the same Coplin jar.
- The slides should be wet fixed in alcohol for 30 minutes, taken out, air dried for 30 minutes and then transporting to the laboratory within next 7 days.
- If alcohol sprays are used, ensure that the whole smear is covered with the spray. Ideally, the alcohol in the Coplin jar used for fixation should be discarded after each fixation, but due to practical problems, alcohol in the jar can be used to fix about 20 slides and changed.
- Transporting the slides "dry" can be carried out in readymade wooden boxes. Adequate measures should be taken to ensure that the slides do not break during transport.
- It is very important that each slide is accompanied by a duly completed referral form(Annex 1V).A common form indicating the number of slides sent, and the place from where it is being sent should accompany the set of slides, which is sent to the laboratory for screening.
- A blue colour referral form should be filled and sent with all repeat smears of positive cases. This will enable the cyto-screener to prioritize the screening and screen these slides first.

Annex IV

Referral form for Pap smear cytology

REFERRAL FORM

MOH Area

1. Full Name :
2. Age :
3. Address / Contact No :
4. NID No. :
5. Identification No (Same as the slide) :
6. Name of the Clinic :
7. LRMP : Date Month Year
8. Specimen Type :

Present First Smear Date

Follow up

Previous Date Slide No :

Normal Abnormal

Diagnosis of previous smear :

Treatment

9. Symptoms

Discharge

Post- Coital Bleeding

Inter- menstrual Bleeding

post- menopausal Bleeding

Other (Specify)

10. Appearance of Cervix

Normal

Abnormal (Comment)

Malignant

Cervicitis

polyps

11. Condition

Pregnant

Post-natal (12/52)

IUCD inserted

Oral contraceptive

Menopause

Other hormones (Specify)

Comments : .....

.....

.....

Date . ..... Signature : .....

Designation : .....

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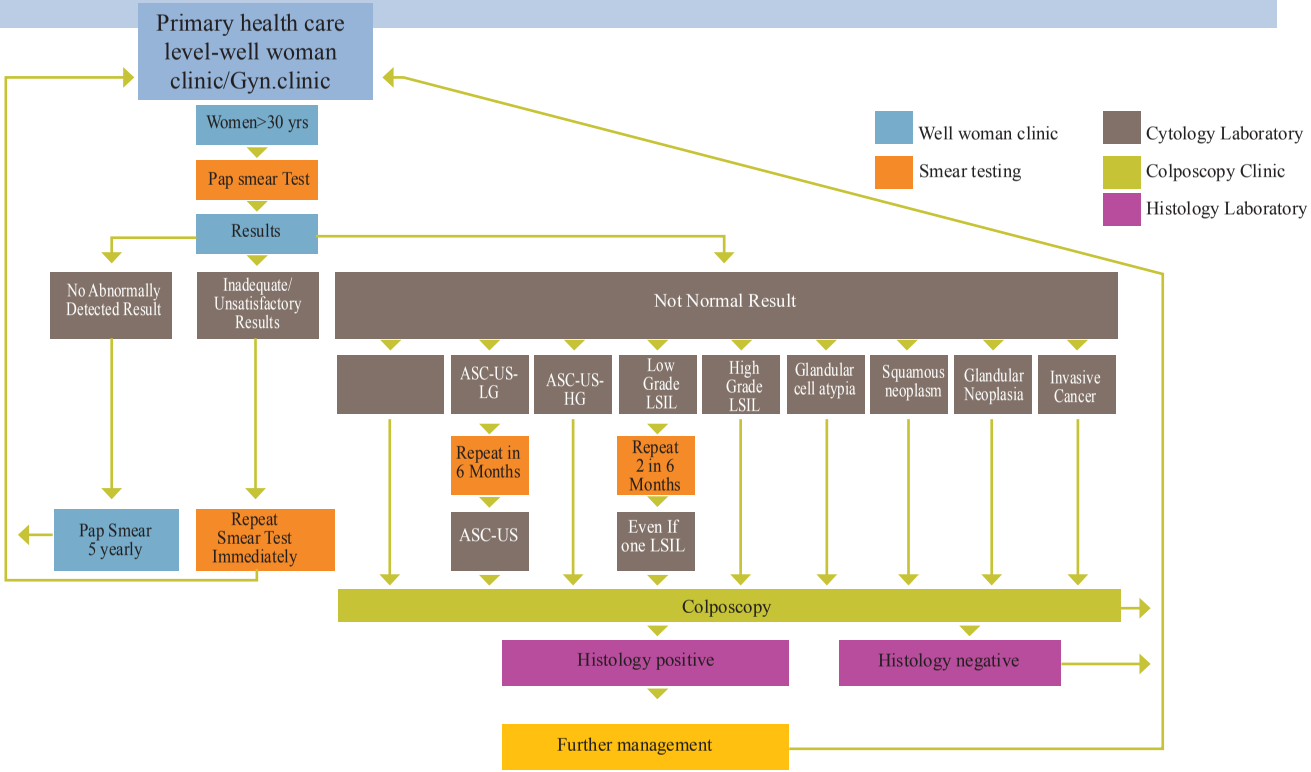
Annex V
Referral Pathway for Colposcopy



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