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GUIDELINES

FOR EARLY DETECTION AND PERIODIC SCREENING OF BREAST AND CERVICAL CANCERS

IN PRIMARY HEALTH CARE SETTINGS IN IRAQ

DISCLAIMER
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List of Abbreviations	
ACS	American Cancer Society
AGC	Atypical Glandular Cells
AIS	Adenocarcinoma In Situ
ASC-H	Atypical Squamous Cells cannot exclude High-grade squamous intraepithelial lesion
ASCUS	Atypical Squamous Cells of Undetermined Significance
ASR	Age-Standardized Rate
BSE	Breast Self-Examination
CBE	Clinical Breast Examination
CDC	Centers for Disease Control
CIN	Cervical Intraepithelial Neoplasia
CNB	Core Needle Biopsy
EMR	Eastern Mediterranean Region
EMRO	Regional Office of the Eastern Mediterranean
FNAC	Fine Needle Aspiration Cytology
HIV	Human Immunodeficiency Virus
HPV	Human Papillomavirus
HSIL	High-grade Squamous Intraepithelial Lesion
IARC	International Agency for Research on Cancer
INBCRP	Iraqi National Breast Cancer Research
LBC	Liquid Based Cytology
LEEP	Loop Electrosurgical Excision Procedure
LSIL	Low-grade Squamous Intraepithelial Lesion
MoH	Ministry of Health
MoHESR	Ministry of Higher Education and Scientific Research
MRI	Magnetic Resonance Imaging
OCP	Oral Contraceptive Pills
TBS	The Bethesda System
TZ	Transformational Zone
VIA	Visual Inspection by Acetic Acid
VILI	Visual Inspection by Lugol's Iodine
WHO	World Health Organization

Introduction

The Iraqi Ministry of Health (MoH) is fully committed to improve the quality of health care provided to all women. This implies an integrated preventive and therapeutic health services through a network of primary, secondary, and tertiary health care facilities. The MoH and in collaboration with Iraqi Cancer Board has given special attention to the program of screening and management of breast and cervical cancer among all women in the country. These two diseases are more prone for early detection with relatively simple and cost-effective measures. Additionally, the outcome of treatment and probability of cure is dramatically higher as these malignances discovered at early stages. Based on above; it becomes necessary to provide protocols that can arrange the work with such services.

The major aim of these guidelines is reduction of mortality from these diseases and improvement of quality of life of treated women. Simple instructions have been supplemented on mode of primary prevention from affection with these malignancies. All this work has been done in order to reach the final goal which is "Health for all".

1. The National Cancer Control Programs

The aim of the National Cancer Control Programs proposed by the World Health Organization (WHO) is a reduction of both the incidence of the disease and the associated morbidity and mortality. Its achievement requires understanding of the social and economic factors which governs the disease process. The following are the basic approaches to Cancer Control:

1. ***Prevention:*** includes attempts to minimize or eliminate exposure to carcinogenic agents in order to reduce individual susceptibility to their effect. This could be achieved by lifestyle modification or various forms of active intervention, e.g., trials with the antiestrogen drug (Tamoxifen) to control breast cancer.
2. ***Early Detection and Screening:*** increasing awareness of the signs and symptoms of cancer contributes to its early diagnosis. When tests for cancer of specific sites are available, screening of apparently healthy individuals can disclose cancer in early stages when treatment would be effective.
3. ***Treatment and Palliative Care:*** cancer treatment is becoming increasingly effective with the results that survival rates in certain types now exceeds 5 years for many patients in developed countries. However, the 5-year survival rate is only 10 % or less in other developing regions of the world mainly due to unavailability of treatment and delay in seeking medical advice.

Of the above available approaches to Breast and Cervical Cancer Control, prevention needs too much time before an impact is expected to be applicable at present. Treatment is hampered by the late stage of presentation in many countries. ***Thus, Early Diagnosis and Screening, especially when combined with adequate therapy offer the most immediate hope for a reduction in breast cancer mortality.***

2. Early Detection and Breast Cancer Control Activities in Iraq

2.1 The National Program for Early Detection and Down Staging Breast Cancer In Iraq:

In 2000 a National Program for Early Detection and Down Staging of Breast Cancer was initiated by the Ministry of Health (MoH) in collaboration with the Ministry of Higher Education and Scientific Research (MoHESR) and WHO since 2000. Referral centres and specialized clinics for early detection of breast cancer were established in all 18 governorates. The work started in 4 main specialized centres (Baghdad (2), Basrah, Ninawa) in addition to 16 specialized clinics for early detection of breast cancer in the major hospital of each governorate in Iraq.
Within these centers and clinics, breast cancer early detection techniques are promoted including:

- Clinical Breast Examination (CBE),
- Breast Self-Examination (BSE),
- Mammography,
- Ultrasonography (U/S)
- Fine Needle Aspiration Cytology (FNAC).

Follow-up committees have been organized for these activities at the governorate level that include in their membership: specialized surgeons, pathologists, radiologists, nurses and primary health care workers. The program plan of action has been expanded both horizontally and vertically and at the present time it has incorporated the primary health care sector.

The main objectives of this program are:

1. Down staging breast cancer at the time of presentation in Iraq where opportunities for cure are higher.
2. Promoting general public awareness on the risk factors of breast cancer, signs and symptoms of the disease and the available screening tools.
3. Decreasing the morbidity and mortality rates of breast cancer – as a long term objective.
4. Reducing the financial burden of breast cancer management.

That national early detection program, supervised by MoH, has a national policy and protocols and follows a multidimensional approach to achieve its goals represented in ensuring provision of high quality diagnostic and treatment services and capacity building of the health staff working in this field in addition to encouraging public health education of the Iraqi women.

2.2 The Iraqi National Breast Cancer Research Program:

In an attempt to address the aforementioned information needs on the clinical profile of breast cancer patients, and emphasizing the role of research as one of the basic pillars in the adoption of the cancer control strategy, an “Iraqi National Breast Cancer Research Program - INBCRP” was established by the Iraqi Ministry of Higher Education and Scientific Research in 2009. In collaboration with the International Agency for Research on Cancer (IARC) and WHO/EMRO, the Iraqi researchers developed a comprehensive information system to document the demographic characteristics, clinicopathological presentations and management outcomes of breast cancer patients in Iraq.

2.2.1 Strategic Target of the INBCRP

(Available at: www.bccru.uobaghdad.edu.iq)

1. Raising awareness of the general population to the common signs and symptoms of cancer in general and breast and cervical cancers in particular through promoting media campaigns, public health programs, broadcasting of TV spots, distribution of educational material, pamphlets, guidelines manuals, and relevant references.
2. Updating knowledge of health cadre to the concept of cancer research and early detection of breast and cervical cancers concentrating upon the impact of CBE, BSE, mammography, breast ultrasonography, fine needle aspiration & Pap smear cytology, colposcopy and HPV detection as screening modalities
3. Promoting Research on the topics of cancer control
4. Conducting comparative demographic and clinicopathological research studies on the behavior of mammary carcinoma in different countries in the EMR.
5. Training and upgrading skills of the health professionals working in the fields of early detection of cancer in general and breast and cervical cancers in particular. The target group are pathologists, radiologists, surgeons, gynecologists, nurses and cyto- & radio-technicians
6. Strengthening counseling skills of the health professionals and enhancing the referral and information health care systems

3. Cervical Cancer Screening Program in Iraq

The program of screening and early detection of cervical cancer and precancerous changes has been introduced recently in Iraq. In the first step, this program is planned to be implemented in Baghdad, Ninawa, Basra, and Babil. The ambition is the inclusion of this work within the preventive health care services in all governorates.

3.1 Objectives of the program:

1. Direct objectives:

a. Increase awareness about cervical cancer and healthy behavior for the prevention of disease in women aged 21 – 50 years.
b. Screening all women aged 21 - 50 years of attendees of health centers before the expansion of services to include all other age groups and before decrease the specified time period between screening procedures.

2. Remote objective: reduction of mortality rate due to cervical cancer

3. 2 Policy of the program

1. Perform screening for women aged 21 – 50 years.
2. Concentrate on high risk groups.
3. Instruct the gynecological departments to treat women with moderate and severe cellular changes and referring those with advanced or metastasized cancers to the oncological

centers and units for the treatment and providing palliative treatment. Monthly statistics should be introduced to the sections of cancer control in directorate of health.

4. Training the health workers on performing Pap smear and providing counseling for the women on the protection from cervical cancer.
5. Establishment of an effective referral system and supporting it with continuous supervision.
6. Ensuring a good quality of screening services (performing, saving, and reading the smear, returning the cytological reports within appropriate time, follow-up, and management)
7. As the appropriate counseling is an important and essential element within the control services of cervical cancer. Consequently, the health workers should be encouraged and trained to institute a good relationship with the women, and discuss their fairs and concerns. This will insure the delivery of information that the women need, in addition to their cooperation with the management and follow up.
8. Encourage the application of service to high risk group women by accessing them in their workplaces and gatherings, and at their presence to the health center for any reason.
9. Collect statistics about the services provided to facilitate the activities of monitoring and evaluation of the program and to achieve the long-term objective.
10. Sending monthly statistics with the work of cervical cancer early detection units and primary health care centers involved with the program to the directorate of health/section of cancer control and then to the cancer board/section of early detection.
11. Ensure strong management and support for program strategies at all levels of the health system.

4. Establishing a "Research Unit for Early Detection of Breast and Cervical Cancers" as a nucleus for a "National Centre of Excellence for Cancer Research"

In order to accomplish the strategic targets of the Iraqi National Cancer Research Program and aiming to support the provision of relevant health services to the Iraqi women in collaboration with MoH, the MoHESR established a Breast and Cervical Cancer Research Unit in Baghdad University Medical College in 2010. That research unit was is in charge of supervising all the activities of the program that were executed by the follow-up committees belonging to National Cancer Research Program at the level of each Iraqi governorate. Membership of those specialized committees comprises Professors and experts in the fields of Pathology, Radiology, Surgery, Public Health, Gynecology, Oncology and Nursing.

As the objectives of the research program were extended to include the control of all cancers affecting the Iraqi population, 2012 the “Breast & Cervical Cancer Research Unit” was promoted to the level of an “Iraqi National Cancer Research Center” following the support and endorsement of the Scientific Research Board authority of the MoHESR.

In January 2012, WHO/EMRO in collaboration with the Iraqi National Cancer Research Program, IARC, Susan G Komen for the Cure and IAEA/PACT - organized a Consultative Meeting to discuss the plan of action for implementing a “Regional Comparative Breast Cancer Research Program in the EMR” (Sharm Al-Sheikh, Cairo). The roles of the international collaborating agencies in that project were clearly defined and the expected outcomes of the

program were illustrated. The “online” information system data base, supervised by the Screening Group of IARC, is currently operating in a major cancer facility within each of the four countries participating in that project; i.e., Iraq (National Cancer Research Center, Baghdad University), Egypt (National Cancer Institute of Cairo), Jordan (King Hussein Cancer Center) and Lebanon (Lebanese Cancer Society).

Part One

Women Screening for Breast Cancer

1. Epidemiology

1.1Worldwide burden of breast cancer:

Breast cancer is the most common cancer among women in the world, comprising 23% of the female cancers. It is also the leading cause of cancer-related deaths, case-fatality rates being highest in low resource countries. (Anderson BO et al 2008).

In 2008 the total number of newly diagnosed breast cancer cases worldwide was 1.38 million, and the total number of deaths from the disease was 458,367; 59% of the mortality rates were recorded in less developed regions of the world. Considerable differences in the pattern of distribution and incidence rates of breast cancer from region to region are observed. In more developed and less developed regions of the world, the recorded incidence of age-standardized rates (ASRs) are 66.4 and 27.3 per 100,000 women respectively; being as low as 26 per 100,000 women in AFRO, SEARO and WPRO and reaching 62.7 per 100,000 women in EURO. In general ASR are greater than 80 per 100,000 in developed regions of the world (except Japan) and less than 40 per 100,000 in most of the developing regions (Globocan 2010).

The largest increase in cancer incidence among the WHO regions in the next 15 years is likely to be in the Eastern Mediterranean Region (EMR) (WHO/EMRO, 2009); where breast cancer is reported as the commonest type of female malignancy in almost all national cancer registries (Globocan 2010).

1.2 Survival rates

Breast cancer survival rates vary greatly worldwide, ranging from 80% or over in North America, Sweden and Japan to around 60% in middle-income countries and below 40% in low-income countries (Coleman et al., 2008). In general, breast cancer ranks as the fifth cause of death from cancer overall (458 000 deaths), but it is still the most frequent cause of cancer death among women in both developing (268 000 deaths) and developed regions (189 000 deaths) – (Globocan 2010).

The low survival rates in less developed countries can be explained mainly by the lack of early detection programs, resulting in a high proportion of women presenting with late-stage disease, as well as by the lack of adequate diagnosis and treatment facilities. Additionally, the poor survival in the EMR reflects as well the limited breast cancer awareness among women and primary care practitioners, the poorly accessible health care services and/or other socioeconomic barriers.

1.3 Situation in Iraq

In Iraq, breast cancer is the commonest type of malignancy among the Iraqi population in general. It accounts for more than one third of the registered female cancers according to the latest Iraqi Cancer Registry which shows a trend for the disease to affect younger age groups. The number of new cases reported in 2009 was 2906, with an incidence rate of 9.43/100 000 population in both sexes and 18.45/100 000 in female population (Iraqi Cancer Registry 2010).

Within the last two decades, there has been an obvious increase in the incidence rates of breast cancer, which became one of the major threats to Iraqi female health. Many cases in Iraq tend to be diagnosed at advanced stages with a likely prevalence of more aggressive tumor behavioral forms illustrated pathologically; thus yielding a high mortality incidence ratio (Alwan NA 2000,). According to Globocan 2010, it has been estimated that breast cancer is responsible for 23% of mortalities from malignancies among Iraqi females.

A study conducted in Iraq on 721 women presenting with palpable breast masses demonstrated that 14.3% were diagnosed with cancer. Approximately one third of the breast cancer patients presented at age 40–49 years; 71.9% came from urban areas; and 75% were married. History of lactation was reported in 63.1% and hormonal therapy in 29%. Positive family history was recorded in 16.2%. Although the lump was detected by the patient herself in 90.6% of cases, only 32% sought medical advice within the first month; accordingly classifying 47% of these patients in advanced stages (III and IV). (Alwan NA - 2010)

Another study applied on a sample of educated women affiliated to two prominent universities in Iraq documented that almost 75% of the participants believed that the best way to control breast cancer was through early detection and other possible preventive measures. In spite of the finding that most participants (90.9%) had heard of BSE, however, only 48.3% practiced this maneuver; the most common reason behind not doing so was lack of knowledge of how to perform the technique correctly. (Alwan NA – 2012)

The findings of these studies justify increasing efforts for establishing comprehensive breast cancer control programs in Iraq focusing on early detection and promoting public awareness.

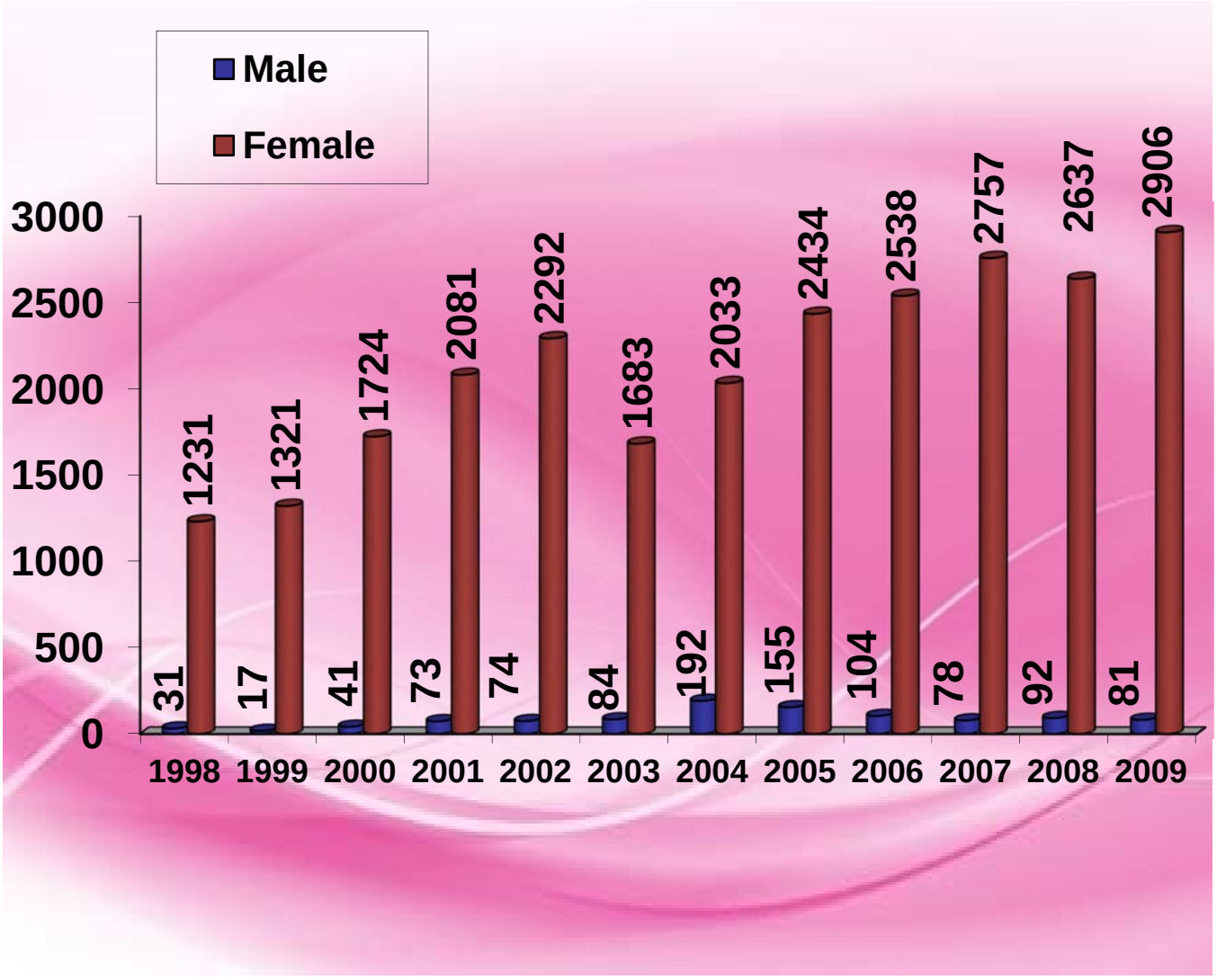


Figure 1: Number of new cases of breast cancer in Iraq (1998-2009)

(Iraqi Cancer Registry 2009)

Table 1: The commonest Cancers by Site in Iraqi Females

(Iraqi Cancer Registry Report 2009)

Primary Site	No. of Cases	% of total	Incidence Rate
1.Breast	2906	36.10	18.45
2. Brain &Other CNS	431	5.35	2.74
3.Bronchus & Lung	419	5.20	2.66
4. Leukemia	402	4.99	2.55
5.Colorectal Cancer	314	3.90	1.99
6.Ovary	307	3.81	1.95
7.N.H.Lymphoma	279	3.47	1.77
8.Skin	257	3.19	1.63
9. Stomach	231	2.87	1.47
10. Urinary Bladder	214	2.66	1.36

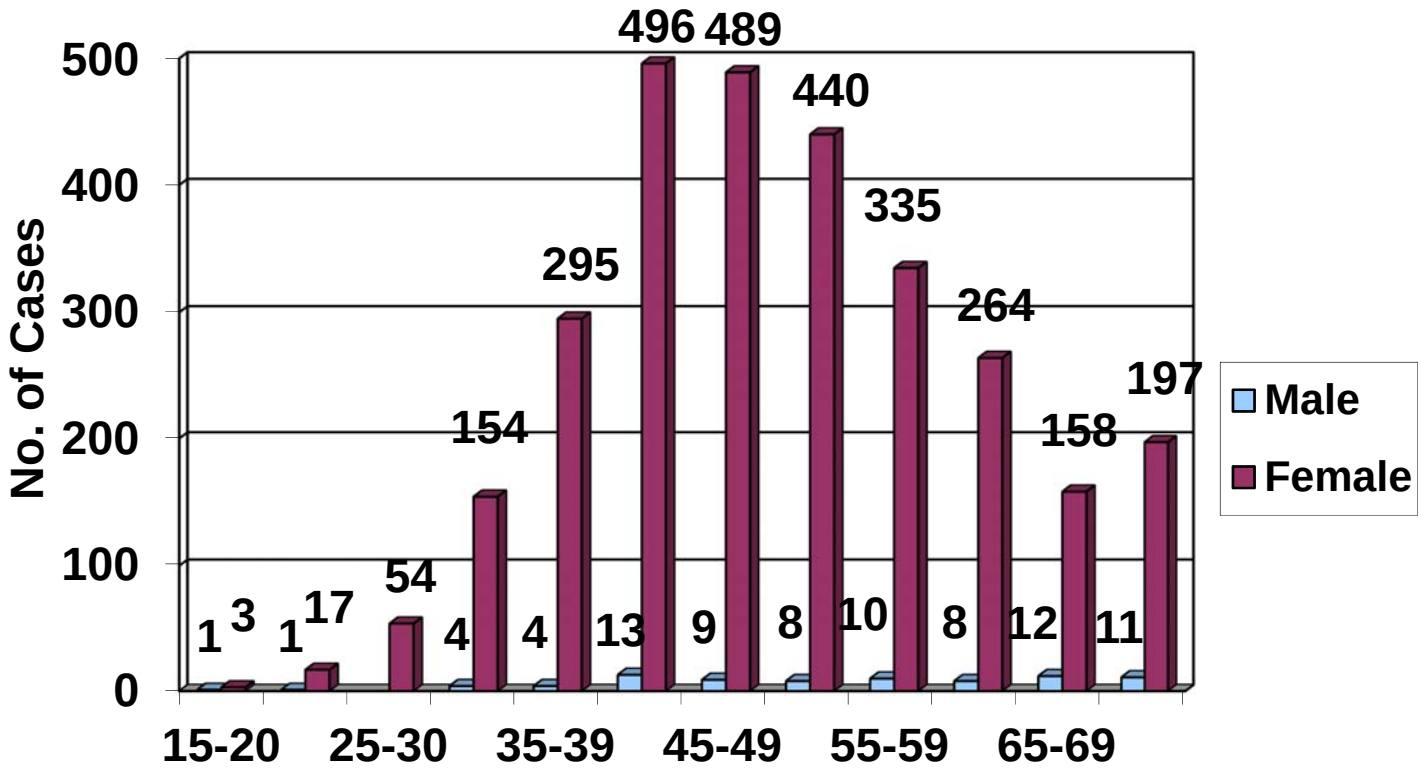


Figure 2: Breast cancer in Iraq according to age groups
(Iraqi Cancer Registry 2009)

2. Anatomy, Physiology & Pathology of the Female Breast

The female breast is in the unique position of being a gland which is non-functioning except during lactation. However, its extreme sensitivity to hormonal influences disposes it to a number of pathological conditions.

The size and structure of the breast vary with the age, sex, hormonal status and heredity of the individual. The areola is the circular pigmented area that contains sebaceous glands. In its center, the elevated nipple is covered by wrinkled skin lined by stratified squamous epithelium. It contains 15-20 lactiferous ducts (lined by two-layered cuboidal cell mucosa) which branch successively distally, leading eventually into the terminal ducts. Before puberty, this complex system ends blindly but at menarche, it proliferates distally giving rise to 30-epithelium lined ductules or acini. Each terminal duct and its ductules compose the terminal duct lobular unit. The ductules are covered by cuboidal and myoepithelial lining cells. In addition to ramifying ducts, the female breast consists of connective and adipose tissue.

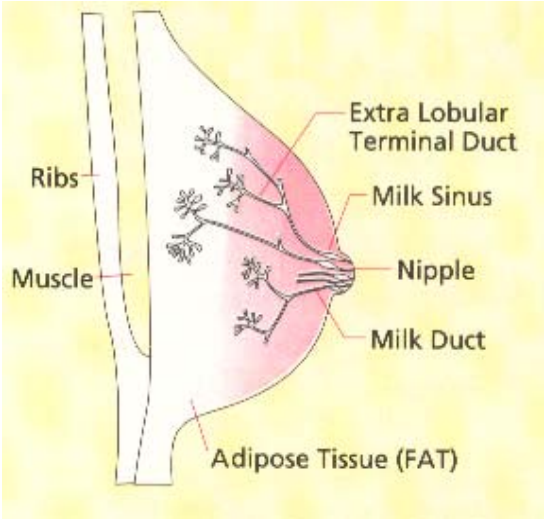


Figure 3: Anatomy of breast

2.1. Pathological classification of breast diseases

2.1.1 Benign Lesions:

A. Inflammatory and Related lesions:

- ***Acute Infections (Pyogenic Mastitis and Breast Abscess)***
- ***Chronic Infections & Granulomatous Inflammations***
- ***Non-Infective Inflammatory Lesions (Mammary Duct Ectasia , Fat Necrosis, Galactocele and Fibrocystic Changes or Cystic Mastopathy)***

<u>Fibrocystic Changes (Cystic Mastopathy)</u>

This is a pleomorphic disorder in which variable morphological patterns are encountered in different patients, different areas within the same lesion and even in different microscopical fields within the same slide. It develops in females between puberty and menopause and considered the commonest cause for a lump in the breast. Patients usually present with ill-defined tender thickness of the breast tissue, palpable lumps or physiological nodularity which may vary during the period of the menstrual cycle. It has been postulated that those changes are related to imbalance between estrogens and progestins (with excessive estrogenic stimulation). **Fibrocystic Changes are of clinical significance for 3 reasons:**

1. Some variants may clinically mimic carcinoma.
2. They may coexist with carcinoma.
3. They may predispose to the development of carcinoma.

In general, it is possible to distinguish 3 dominant patterns of morphological changes:

a. Cystic Formation and Fibrosis (Simple Fibrocystic Changes)

***b. Epithelial Hyperplasia (Epitheliosis)*:** It is the histological variant that increases the risk of subsequent development of malignancy; especially if it is associated with atypia.

c. Adenosis and Sclerosing Adenosis

B. Benign Tumors:

- ***Fibroadenoma***
- ***Adenomas***
- ***Intraductal Papilloma***

2.1.2 Malignant Lesions

A. Non Invasive Carcinomas:

- ***Intraductal Carcinoma***
- ***In Situ Lobular Carcinoma***

B. Invasive Carcinomas:

- ***Invasive Ductal Carcinoma – NOS (Not Otherwise Specified)***
  This is the most common type exhibiting marked increase in dense fibrous stroma giving the tumour a hard consistency (*Scirrhous*). On palpation, this manifest as stony hard nodules, this may have infiltrative attachments to the chest wall and skin resulting in dimpling and nipple retraction. Histologically, there are anaplastic duct cells arranged in glands, cords or solid nests. Because of the remarkable fibrosis, aspirates may yield only few cancer cells. Therefore a tissue biopsy may be recommended to confirm the cytological diagnosis.
- ***Lobular Carcinoma***
  This cancer starts in the milk glands (the lobules) and then spreads through the wall of the lobules. It can then spread (metastasize) to other parts of the body. About 1 in 10 invasive breast cancers are of this type.
- ***Medullary Carcinoma***
- ***Colloid (Mucinous) Carcinoma***
- ***Papillary Carcinoma***
- ***Tubular Carcinoma***
- ***Apocrine Carcinoma***
- ***Adenoid Cystic Carcinoma***
- ***Paget's Disease of the Nipple***
- ***Secretory (Juvenile) Carcinoma***
- ***Inflammatory Carcinoma***

2.2 Staging of breast cancer

In 1972, according to Denoix and the Committee of the Clinical Staging of the International Union Against Cancer (UICC), a new method was widely used by different centers. That staging system was adopted in 1989 by the American Joint Committee on Cancer (AJCC). The classification depends upon the size of the primary tumor (T), extent of regional lymph node metastases (N) and distant metastases (M). The designation TNM has been chosen for clinical staging and pTNM refers to pathological staging.

Clinical staging is important for precise individualized treatment planning, estimation of prognosis and end results comparisons with the pathological stage which is determined after definitive surgery. However clinical staging is less accurate than the pathological since there is a tendency to overestimate the size of the primary tumor and inaccurately assess the axillary lymph nodes for the presence of metastatic carcinoma.

2.3. Histopathological grading of mammary carcinoma

It is well known since a long time that the evolution of Breast Cancer depends on the degree of anaplasia (tumor differentiation). Different systems of grading have been successfully applied for better evaluation of cancer evolution. The rationale for grading lies in the fact that the latter has important influence on prognosis. After many trials, the classification of Scarff, Bloom and Richardson (SBR) was proved to be the most currently used and recommended by the WHO (Scarff and Toronti, 1968). It comprises the description of three characters:

A. *The Degree of Tubular Differentiation*: Score (1) is given to forms of generalized tubuliform or papillary formation. Score (3) is recorded when there is no differentiation and Score (2) is for intermediate type.

B. *The Nuclear Pleomorphism*: (3) points are given to cases having marked nuclear irregularity; (2) points when the nuclei are fairly uniform in size, shape and staining and (1) point is given if the nuclei are near to normal.

C. *The Mitotic Activity*: This is estimated after examination of at least 20 fields at magnification of 400. If at maximum only one mitosis is found, it is given (1) point. If on the opposite at least 3 mitoses are found in one field, it will be given (3) points.

Box 1: TNM classification of breast cancer

T-	**Primary**	**Tumor**
	Tx	Primary tumor cannot be assessed.
	To	No evidence of primary tumor.
	Tis	Carcinoma in situ.
	T_1	Tumor 2 cm or less in greatest dimension
		T_{1a} 0.5 cm or less in greatest dimension
		T_{1b} more than 0.5 cm but not more than 1 cm in greatest Dimension.
		T_{1c} more than 1 cm but not more than 2 cm in greatest dimension.
	T_2	Tumor more than 2 cm but not more than 5 cm in greatest dimension.
	T_3	Tumor more than 5cm in greatest dimension.
	T_4	Tumor of any size with direct extension to chest wall or skin.
		T_{4a} with fixation to chest wall (including ribs, intercostal muscles and serratus anterior muscle but not pectorals muscle.
		T_{4b} with edema (including peau d'orange), ulceration of skin, or satellite skin nodules on same breast.
		T_{4c} Both T_{4a} and T_{4b}
		T_{4d} Inflammatory carcinoma.
N-	**Regional**	**Lymph Nodes**
	N_x	Regional lymph nodes cannot be assessed (e.g. previously removed).
	N_0	No regional lymph node metastasis.
	N_1	Metastasis to movable ipsilateral axillary node (s).
		N_{1a} only micrometastasis (not larger than 0.2 cm)
		N_{1b} Metastasis to lymph node (s), any larger than 0.2 cm.
	N_2	Metastasis to ipsilateral axillary node (s) fixed to one another or to other structures.
	N_3	Metastasis to ipsilateral internal mammary lymph node (s).
M-	**Distant**	**Metastasis**
	M_x	Presence of distant metastasis cannot be assessed.
	M_0	No distant metastasis
	M_1	Distant metastasis (including metastasis to supraclavicular lymph nodes).

STAGE GROUPING	(according to the TNM classification)		
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II A	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
Stage II B	T2	N1	M0
	T3	N0	M0
Stage III A	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1, N2	M0
Stage III B	T4	Any N	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

(Adapted from UpToDate.-Tumor node metastasis (TNM) staging classification for breast cancer)

Table2: Staging and Survival Rates of Breast Cancer

Stage	Type	5-years survival rate
0	Ductal carcinoma in situ or lobular carcinoma in situ	92%
I	Invasive carcinoma 2 cm or less in size (including carcinoma in situ with micro invasion) without nodal involvement and no distance metastasis	87%
II	Invasive carcinoma < 5 cm without nodal involvement but with movable axillary nodes and no distance metastasis	75%
III	Invasive carcinoma < 5 cm in size with nodal involvement and fixed axillary nodes	46%
IV	Any form of breast cancer with distance metastasis	13%

(Adapted from American Cancer Society – Breast Cancer)

3. Etiology

The exact etiology of breast cancer is still unknown, but there are certain risk factors that are linked to the disease, although many women with risk factors never develop breast cancer. Instead, risk factors help to identify women who may benefit most from screening or other preventive measures.

Most of the data obtained point to three sets of influences that may be important in increasing breast cancer risk; which are g***enetic predisposition, hormonal imbalance and environmental factors.***

3.1. Risk factors:

3.1.1 Non- modifiable risk factors:

- **Increasing Age**: The chance of getting breast cancer goes up as the woman gets older.
- **Gender**: Simply being a woman is the main risk for breast cancer as it is nearly 100 times more common in women than men.
- **Family history and Genetic risk factors**: A family history of breast cancer elevates the breast cancer risk. Both maternal and paternal history of breast cancer is relevant. A history of male breast cancer in the family is a red flag for the presence of a gene mutation. Additional clues that a gene mutation may be present are a history of breast cancer in young women in the family, bilateral breast cancers, a history of ovarian cancer in the family and multiple relatives with cancers.

  About 5% to 10% of breast cancers are linked to mutation in certain genes. The most common gene changes are those of the BRCA1 and BRCA2 genes. Women with these gene changes have up to an 80% chance of getting breast cancer during their lifetimes.
- **Personal history of breast cancer:** A woman with certain type of breast cancer in one breast has a greater chance of getting a new cancer in either the other breast or in another part of the same breast. This is different from recurrence which might occur later.
- **Earlier breast radiation**: Women who have had radiation treatment to the chest area (as treatment for another cancer) earlier in life have a greatly increased risk of breast cancer.
- **Menstrual periods**: Women who began menses earlier (less than 12 years of age) or went through late menopause (after age55) have a greater probability of breast cancer.
- **Density of breasts on mammogram.** Risk of breast cancer is approximately five times greater in women with extensive dense tissue in the breasts compared to those with little or no dense tissue.

3.1.1 Modifiable risk factors

- **Reproductive factors**: The risk of breast cancer is somewhat increased among women who never had children or had their first child after age 30.
- **Treatment with Diethylstilbestrol (DES)**: women who received DES have slightly increased risk of developing breast cancer.
- **Hormonal Replacement therapy**: women on hormonal replacement therapy after menopause have higher risk to develop breast cancer.

- **Oral contraceptive pills**: most studies on oral contraceptive pills did not show increased risk of developing breast cancer. Other studies found slightly elevated risk of developing breast cancer with OCP use, risk was highest in women who started using OCP as teenagers. However, 10 or more years after stopping OCP, their risk returned to the same level as women who had never used them.
- **Obesity:** it is associated with two-fold increase in risk in post-menopausal women. However, for unknown reason, obesity in premenopausal women is associated with mild decrease in breast cancer.
- **Regular alcohol consumption**: moderate consumption of alcohol beverages increase risk of breast cancer.
- **Physical activity**: moderate physical activity is associated with lower risk of breast cancer.

Table 3: Relative Risks for Breast Cancer by Specific Risk Factor:

Factor		Relative risk	Group most at risk
Age		over 10-folds	risk increase with age above 50
age at menarche		3	menarche before 11
age at first completed pregnancy		3	first child in early 40s
Economic status	country	5	high-income developed
	socioeconomic status	2	professional or managerial occupational group (self, current family or family of origin)
Body weight and diet	before menopause	0.7	BMI > 35
	after menopause	2	BMI > 35
	diet	1.5	high saturated fat intake
alcohol consumption		1.3	prolonged intake above recommended daily limit

(Adapted from McPherson et al., 2000)

4. Early Detection and Screening for Breast Cancer

The detection of a breast mass in an apparently healthy woman before it is palpable is a technique that saves lives and saves breasts. All women are candidates for screening since all women are at risk for breast cancer development. Current incidence data suggests that nearly 10% of American women will develop this disease at a time in their life spans.

Educational messages about breast cancer that increased public and professional awareness of the problem are largely responsible for the earlier presentation of cases which has come about in most developed countries, during the twentieth century. Thus, breast cancer screening programs, which are usually accompanied by public education, have a most favorable effect on the early diagnosis of the disease. There is good evidence from randomized trials in Sweden and the USA and from case-control studies in Italy and the Netherlands that screening by mammography alone or in conjunction with physical examination can reduce mortality in women over the age of 50.

4.1 Diagnostic Approaches to Breast Lesions:

Thus, excluding surgical procedures, there are 3 major techniques commonly used to evaluate breast masses: physical examination, mammography and fine needle aspiration (FNA) cytology. The accuracy of each diagnostic modality varies. It has been estimated that from 8 to 38% of breast carcinomas cannot be detected by palpation alone. When mammography was added to physical examination, up to 85% were detected preoperatively. By adding FNA, 93 to 100% of carcinomas were accurately diagnosed.

4.2 Physical Breast Examination and Breast-Self Examination:

This is an inexpensive, non-invasive method of detection that can be taught to patients. Although degrees of competence, profession and thoroughness vary, it has been shown that approximately 60-90% of all breast cancers are usually found either by the patient herself during Breast Self-Examination (BSE) or by the examining physician through Physical Breast Examination (PBE).

Breast cancer is usually first discovered as a solitary, painless mass. The older the patient with a single breast mass, the more likely it is to be cancer, especially if the patient has a positive family history in a first degree relative (High-Risk patient). When these masses are first palpated they could be deceptively mobile and thus could be false negatively interpreted as fibrocystic changes. It has been suggested that a lesion must be 1-2cm. in diameter before it may be palpated and that it can take up to 10 years to reach a size of 1 cm. Unfortunately, most cancers are found accidentally by the patient herself when the mass is already 3-4 cm. in diameter and by that time 50-70% of the cases would have spread to the axillary nodes.

4.2.1 Clinical Breast Examination (CBE)

A CBE is a physical examination of the breast performed by health professional, (such as physicians, community nurses, midwives). The efficacy of clinical breast examination is dependent upon a number of factors: proper positioning of the patient, thoroughness of the search, use of a vertical strip technique, proper positioning and movement of the fingers, and examination duration of at least 5 minutes per breast. Repeating the CBE can be a useful diagnostic tool when

breast asymmetry is detected, as asymmetry is commonly transient. Persistence of an abnormality increases the pretest probability of the disease. CBE still detected about 5 percent of cancers that were not visible on mammography.

Family physicians in Iraq are expected to do CBE for women starting from the age of 20 years, as a part of her routine check-up every 2-3 years, increasing to once a year from the age of 30 years and above.

Steps to perform Clinical Breast Examination CBE

The patient should be examined in both the upright and supine positions. She must be disrobed from the waist up allowing the examiner to visualize and inspect the breasts.

Inspection: should be done while the patient is in three standing positions;

1- Arm relaxed at the sides
2- Hands pressed firmly on the waist (to contract the pectoral muscles so that any other areas of retraction can be visualized) and leaning forward
3- Arms over the head so the lower part of the breast can be inspected.

What to look for?

- Changes in breast contour such as; swelling, changes in color and shape
- Change in the direction of the nipple
- Dimpling or puckering of the skin
- "Orange peel" appearance of the breast skin

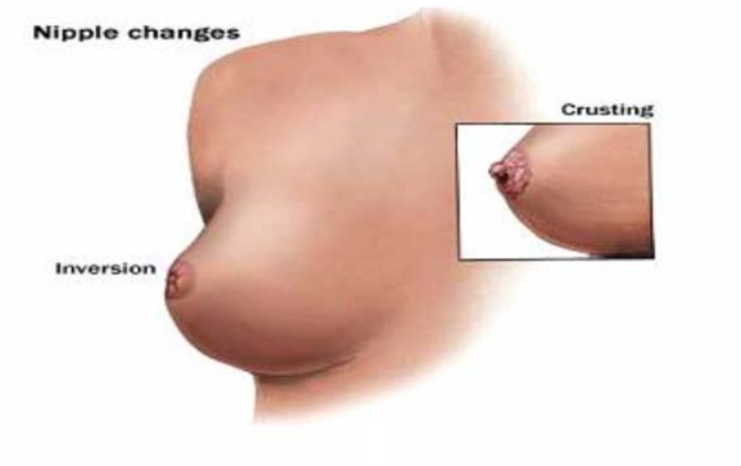


Figure 4: Possible breast changes observed during inspection

Palpation: should be done with the three middle finger pads; it should cover the whole area of each breast including the lymph nodes, underarms and upper chest from collarbone to below the breasts and from the armpits to the breastbone.

Three search patterns are commonly described Figure (5):

1. Vertical strip pattern - this pattern examines the breast tissue in overlapping vertical strips across the chest wall. This pattern is probably superior for ensuring that all breast tissue is examined.
2. Concentric circle method – the breast is examined in larger or smaller concentric circles.
3. Radial spoke method - wedges of tissue are examined beginning at the periphery toward the nipple in a radial pattern.

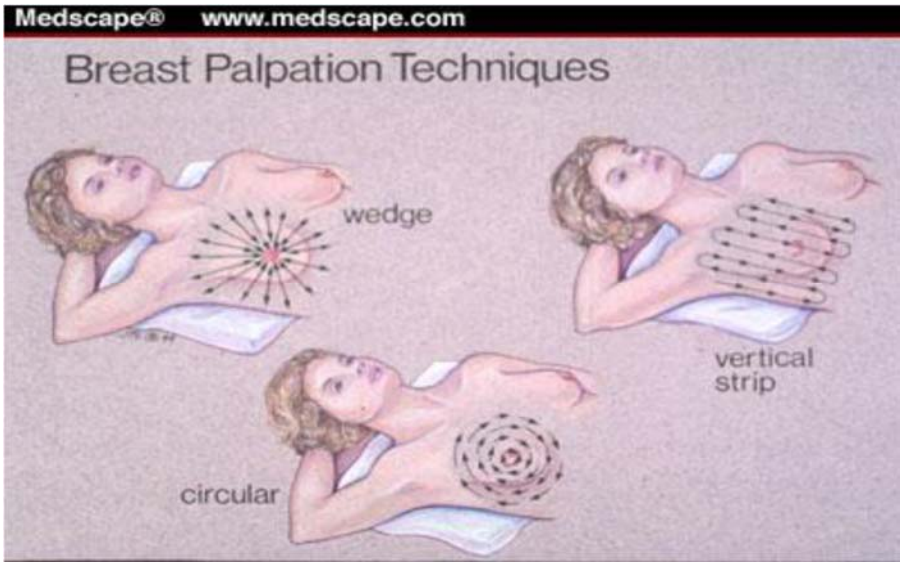


Figure 5: Techniques of breast palpation

Squeeze the nipple for any nipple discharge. Be careful not to compress the breast between fingers as it may result feeling a lump which does not exist. The location of the patient's concern as well as any abnormality found on examination should be documented. The size of any mass should be measured in centimeters with a tape measure and its location, mobility, and consistency recorded.

It is very helpful to record the location of any abnormality by documenting both the position on the breast and the distance in centimeters from the areola. In this manner, the precise location can be easily identified on subsequent follow-up examinations, by you or other practitioners. The "clock" system can be used for documentation, comparing the breast to a clock and using the location on the clock to indicate the location of a lesion (e.g. 1 o'clock position). The entire examination should be clearly and completely documented in detail including significant negatives, even if it is completely normal.

4.2.2 Breast Self-Examination (BSE):

Educational information on the technique of BSE can be accomplished utilizing commonly available pamphlets, instrumental video tapes or one-to-one personal teaching by a physician or a

nurse. The steps of BSE are demonstrated in a handy pullout guide provided by the cancer institutes. During the examination women should look for:

- Breast assymetry.
- Thickening, dimpling or skin retraction.
- Nipple retraction or surface changes as redness, ecchymosis or excoriation.
- Spontaneous nipple discharge.
- Any lump or nodularity which has not been noted previously during earlier exams.

This test is preferred to be done after the end of menstruation and more specifically after 7-10 days from the start of menstrual cycle as the breasts are not swollen or tender.
If the woman is lactating, she should perform the test after being sure from emptying the breasts from milk. For pregnant and postmenopausal women, they should localize certain day from each month for doing the test periodically, e.g. the first day from each month.

In view of the relatively high prevalence of breast cancer in Iraq in younger age groups and due to the late stage at presentation, Iraqi females are advised to perform BSE once each month, beginning at the age of 20 and continue each month throughout a women's life time.

Steps to Perform Breast Self-Examination BSE

General Ground Rules:

1. Use flat part of fingers.
2. Use powder or soap solution to allow fingers to slide smoothly over skin.
3. Palpate breast in systematic fashion to not miss any part.
4. Check nipples for discharge or skin changes.
5. Always palpate axillary lymph nodes (palpable nodes suspicious for cancer) and axillary tail of breast.

Inspection:

Step 1: Begin by looking at your breasts in the mirror with your shoulders straight and your arms on your hips. What **should** you look for: Color, shape, size of both breasts that are evenly shaped without visible distortion or swelling.
If you see any of the following changes, bring them to your doctor's attention:

- Dimpling, Puckering and Bulging of the Skin.
- A nipple that has changed Position or pushed inward instead of Sticking Out (inverted nipple).
- Redness, Soreness, rash, or swelling.

Step 2: Raise the arms overhead or put the hands behind the head and look for the same changes.
Step 3: Put your hands in the middle of the abdomen and push downward with the shoulders stretched forward to look for the shape of your Breasts.

Palpation:

Step 4: Examine each breast separately and feel for any new lumps, changes, or irregularities. Use the palmar aspect of the fingers (i.e., the pads of the fingers not the tips) moving in a circular or grid-like pattern.

Step 5: Examine the tail of both Breasts. The nipple should also be examined during this time. First, squeeze the nipple and check for any discharge.

Step 6: Lie down with a pillow or folded towel under the right shoulder and place the right arm behind the head. Check the entire breast and armpit area. The exam should then be repeated on the left breast, using the finger pads of the right hand.

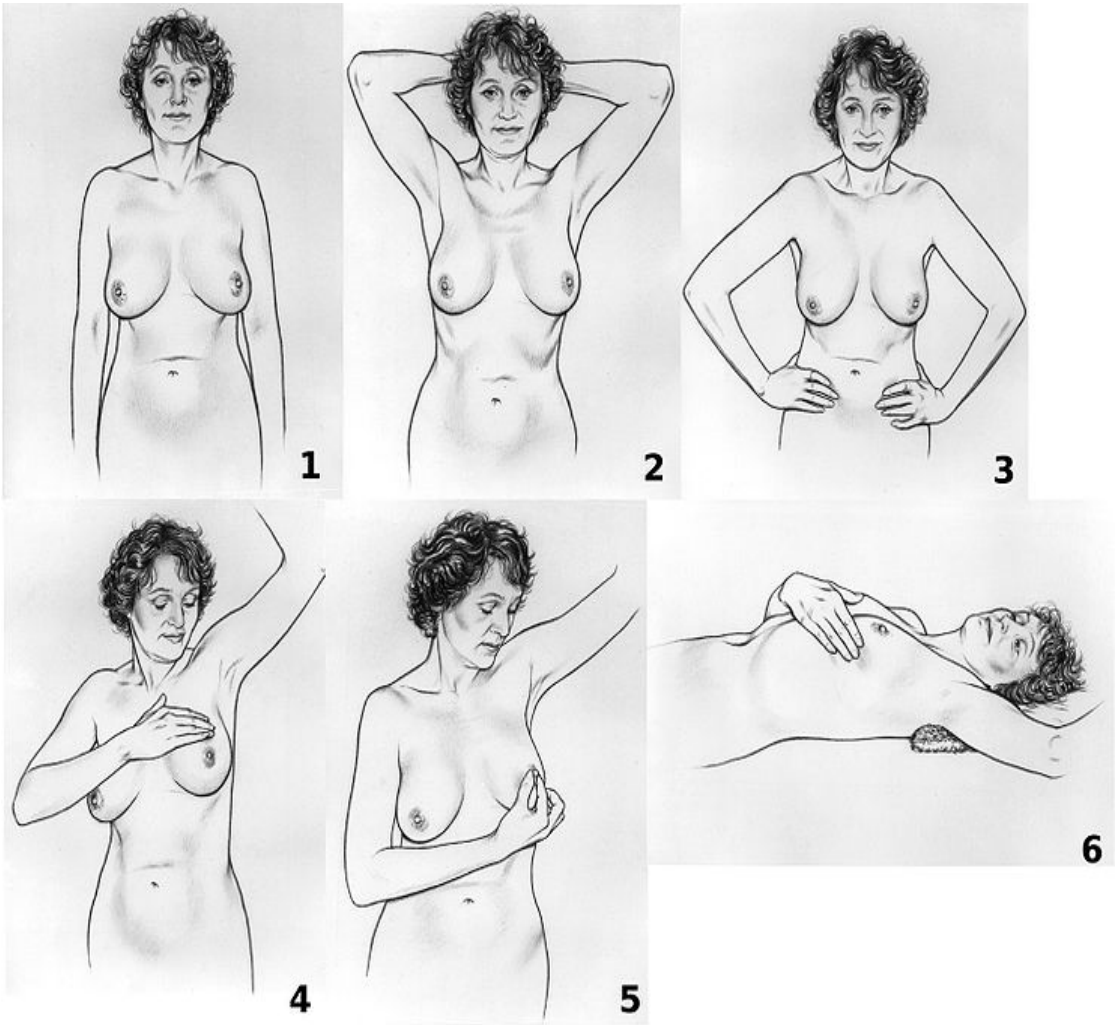


Figure 6: Steps of breast self-examination

4.3 Mammography:

This is an X-ray study of the breast utilized since 1940. Today, radiologists can produce high quality images at greatly reduced radiation exposures. The typical picture of breast carcinoma is an irregular specular opacity and tiny calcifications, with a retraction and thickening of the overlying skin.

Mammography is the only proven method for detecting non-palpable (occult) cancers as well as "Minimal" breast cancers. Included within this category are the lobular carcinoma in situ, non-invasive intraductal carcinoma and minimal invasive carcinoma: either lobular or intraductal, with a mass no greater than 0.5 cm. in diameter. Studies estimate that the sensitivity of mammography is between 68 and 94 %, and specificity is between 82 and 98.5%.

(Steriotactic Needle Biopsy of Mammographically Detected Breast Lesions):

For study of impalpable lesions revealed by mammography, a stereotactic technique of needle aspiration was first developed at the Karolinska Hospital in Sweden. The patient is placed prone on a special table, whereby the breast is positioned in an aperture in the table top and held in a stereotactic compression device that allows stereoradiographs to be taken with a superimposed coordinate system. An instrument holder fitted with a cannula 1.mm. thick and an internal stainless steel screw needle is then attached to the device. The cannula is inserted into the mammary tissue and cellular material is sampled with the needle. After the sampling, a small piece of stainless steel suture thread is introduced into the lesion to serve as a marker for later identification during surgery.

Now it is agreed upon that all women should have a baseline mammography at the age of 35. Women under 50 should be screened once every 1-3 years. After 50, annual examination is considered.

It is worthwhile mentioning that mammogram in younger women is usually difficult to interpret. The breast of younger women contain more glands and ligaments than do those of older women, resulting in dense breast tissue that can obscure the cancer. With age, breast tissue becomes fatter and has fewer glands, making it easier to interpret mammograms to detect changes.

As Iraqi breast cancer is more commonly diagnosed in premenopausal women, it is advisable that all primary health care physicians refer women for screening mammography at the age of 40 years. After that age, annual screening is recommended specifically in high risk women.

There is no specific upper age at which mammography screening should be discontinued. Rather, the decision to stop regular mammography screening should be individualized based on the potential benefits and risks of screening in the context of overall health status and estimated longevity. As long as a woman is in good health and would be a candidate for breast cancer treatment, she should continue to be screened with mammography

4.3.1 Risks and limitations of mammography:

- **Radiation Risk:** It is thought that ionizing radiation increases the risk of breast cancer development after a latent period of 10 years, that the risk is cumulative, and that the risk is greatest for adolescent exposure and decreases with increasing age at exposure. In those aged over 50, the risk of cancer induction is, 1:100,000 per single view examination.
  Many people are concerned about exposure to x-rays, but the level of radiation use in

modern mammograms does not measurably increases the risk for breast cancer.

- **False positive mammograms:** 5-15% of screening mammograms require more testing such as additional special views or ultrasound. Most of these tests turn out to be normal. However if there is an abnormal finding, a biopsy or follow-up may have to be performed which increase the anxiety in a false positive mammography finding women.
- **False negative mammograms:** While mammograms will detect most breast cancers, a small percentage will be missed. This should be very low especially if rigorous quality assurance programs are instituted in centers commissioned to offer this service. Overall 10% of diagnostic mammograms are false negatives, with approximately twice that rate for younger women and half that rate for woman over age 65.

Note: The small percentage of breast cancers that are not identified by mammography may be missed for any of the following reasons:

1. High breast density
2. Faster tumor growth rate
3. Inadequate positioning of the breast
4. Failing of interpretation: inability to observe small early signs of abnormalities

4.4 Other Imaging Techniques:

4.4.1 Ultrasonography

Ultrasound images are produced from reflected high-frequency sound waves, without exposure to ionizing radiation. The technique has been used in our specialized early detection breast cancer centers and clinics as an important screening tool in line with mammography to characterize suspected lesions specifically in premenopausal females where the sensitivity of mammography is low. It is highly specific in distinguishing a solid from a cystic mass and in diagnosing suspicious axillary nodes.

4.4.2 Magnetic resonance imaging (MRI)

MRI uses magnetic fields instead of x-rays to produce very detailed, cross-sectional images of the body. The sensitivity of MRI as screening tool for breast cancer is over 95% but its specificity is low, with a range of 53%-70%. While MRI is more sensitive in detecting cancers than mammograms, it also has a higher false-positive rate, which results in more call-backs and biopsies. Although low specificity and high cost of MRI restricted its use in routine screening, it has been increasingly used in the screening of high-risk individuals and in excluding local recurrence. .

Screening with both mammography and MRI might rule out cancerous lesions better then mammography alone in women who are known or likely to have an inherited predisposition to breast cancer.

4.5 Other Non-Imagining Techniques

4.5.1 Fine Needle Aspiration Cytology (FNAC):

In general, the definitive diagnosis of a breast mass can be established by: *open biopsy, tissue core needle (Tru-cut) biopsy, or fine needle aspiration biopsy.* Compared to FNAC, Tru-cut biopsy is a more traumatic procedure which should be performed under local anesthesia. It requires more time and special equipment that are more expensive. Pain, discomfort and bleeding are common complications.

FNAC, on the other hand, provides many advantages to the surgeons. It is an easy, reliable, cost effective diagnostic technique which can give rapid results. The procedure could be performed in an office setting without anesthesia. It is usually not more painful than a venipuncture and can be repeated immediately if the acquired material is inadequate.

The National Health Service Breast Cancer Screening Program (NHSBSP) displayed that recently many centers wished to include FNAC as an additional test to provide pre-operative diagnosis of breast cancer and to reduce the number of operations for benign breast lesions. This has major cost and morbidity saving implications for the management of breast diseases, both in screening and symptomatic practice.

Equipment and Procedure of FNAC:

When reduced to its simplest terms, FNAC consists of:

1. Using a needle and syringe to remove material from a mass.
2. Smearing it on a glass slide.
3. Applying a routine stain.
4. Examining it under the microscope.

4.5.2 Core Needle Biopsy (CNB):

This procedure involves the uses of a larger gauge needle (18-14) to remove a piece of tissue. It provides a specific histological diagnosis which could be interpreted by a general pathologist/. It is associated with slightly greater discomfort and higher cost than FNA. Bleeding and hematoma are common complications. It is important to ensure that there is agreement between the imaging appearance and the biopsy results. If the results are not concordant or any abnormality is found on the core biopsy, excisional biopsy will be required to ensure an accurate diagnosis.

Note: Both FNAC and CNB were reported to have equal sensitivity, positive predictive value for malignancy, and equally low rates of samples inadequate for diagnosis.

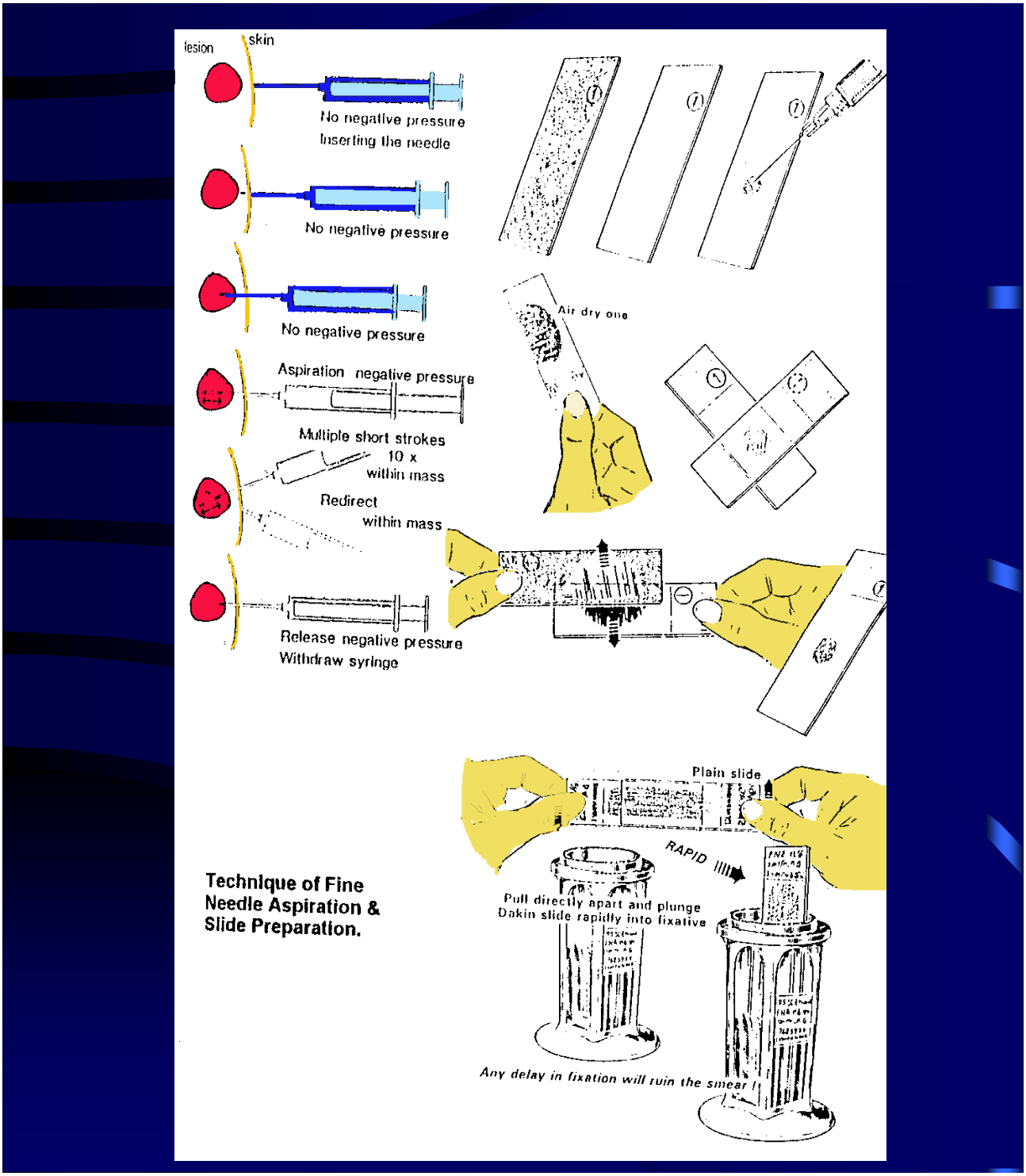


Figure 7: Technique of fine needle aspiration cytology

4.6 Triple Assessment Diagnostic Test:

The triple test uses a combination of physical examination, imaging studies, and FNA cytology as an alternative to surgical excision to establish that a breast mass is benign. The triple test is considered to identify the mass as benign if the physical examination, mammogram, and FNA all indicate a benign process. If the lesion cannot be visualized on mammogram or if the FNA contains insufficient cells for diagnosis, the triple test cannot be confirmatory for a benign lesion.

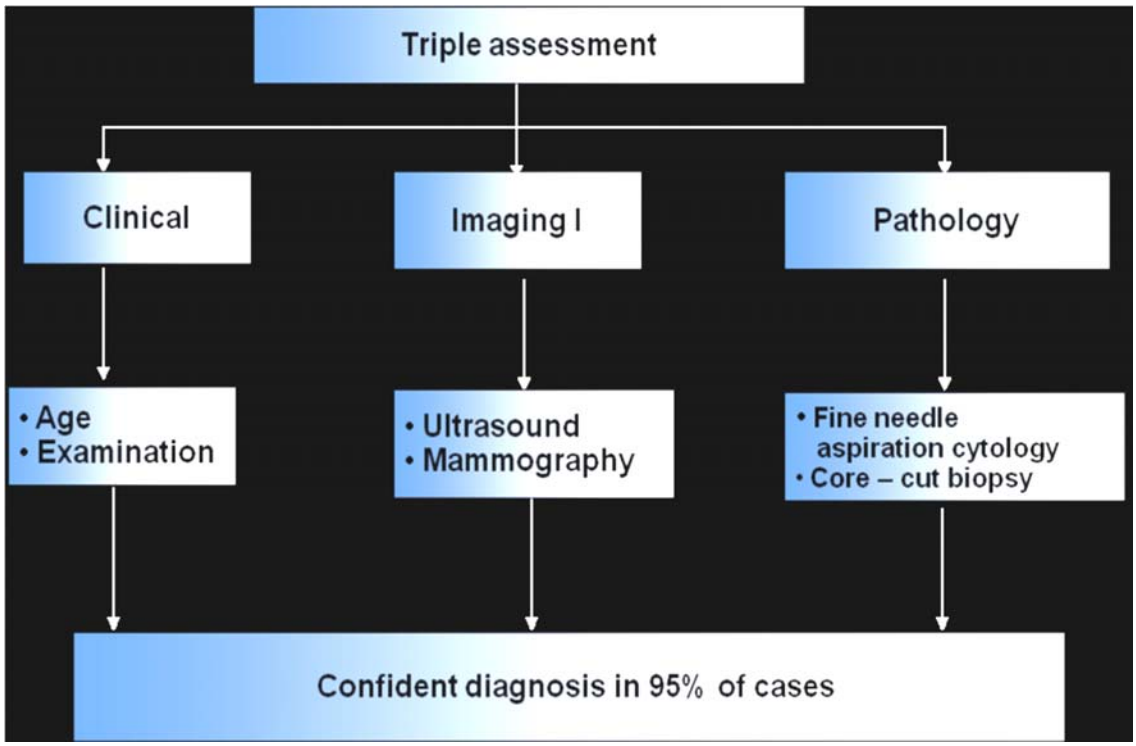


Chart 1: Triple Assessment Technique

4.7 Breast Cancer Screening in High Risk Women

There are a proportion of women who might have a higher risk of developing breast cancer than others. Those include:

1. Women who have personal history of breast cancer (specifically in a first degree relative).
2. .Women who have history of other premalignant breast lesions (eg, atypical ductal or lobular epithelial hyperplasia).
3. Women who have mutations in BRCA1 and BRCA2 genes.

4. Women who had been exposed to radiation during early years of life especially in the chest region.
5. Women with very dense breast tissues.

In these groups of women, early detection of breast cancer should follow the next schedule:

- Breast self-examination is performed monthly since the age of twenty years and continues throughout lifetime.
- Clinical breast examination is performed annually since the age of twenty and continues thereafter throughout lifetime.
- Screening mammogram is performed every 3 years at the age group 30-39 years, then it should performed annually from the age of 40 years and continue throughout lifetime. However, Ultrasound examination is recommended annually starting from the age of 30 years.

Table 4: Schedule of Iraqi Program for Screening for Breast Cancer

A. For Low Risk Women				
Test	**Age (in years)**			
	20 - 29	**30 -39**	**40 - 49**	**≥ 50**
BSE	Monthly	Monthly	Monthly	Monthly
CBE	Every 2- 3 years	Every year	Annually	Annually
Mammogram	---------	---------	Every 2 years	Annually
B. For High Risk Women				
Test	**Age (in years)**			
	20 - 29	**30 -39**	**40 - 49**	**≥ 50**
BSE	Monthly	Monthly	Monthly	Monthly
CBE	Annually	Annually	Annually	Annually
Mammogram	---------	Every 3 years *(with Annual Ultrasound)*	Annually	Annually

5. Management of Specific Breast Symptoms and Signs

Regardless of the type breast problems, the goal of evaluation is to rule out cancer and address the patient's complaints. Clinical features that are found from history or physical examination and should take special consideration are summarized in the following box

Box 2: Breast Complaints and Clinical Signs that should not be ignored

1. lumps, hard knot or thickening inside the breast or underarm area
2. swelling, warmth, redness or darkening of the breast
3. change in the size or shape of the breast
4. dimpling or puckering of the skin
5. itchy, scaly sore or rash on the nipple
6. retraction of the nipple or other parts of the breast
7. nipple discharge that starts suddenly, specifically if bloody
8. new pain in one spot that does not go away

5.1 Palpable mass, nodularity or asymmetry:

The first step in the evaluation of a palpable abnormality is to determine index of suspicion for benign versus malignant disease (the pretest probability of disease).

Low level of suspicion encompasses prominent nodularity, asymmetric thickening, and non – discrete possible mass. This can be followed with repeat exam in 1-2 months. If the abnormality persists or progresses on repeat examination, further diagnostic testing is indicated (the woman should be referred to a breast specialist).

Distinct mass should be interpreted as being intermediate or high index of suspicion. This should be evaluated with diagnostic testing. Both needle aspiration (FNA) and urgent diagnostic imaging are acceptable methods for evaluation, but there are several reasons to begin with diagnostic imaging. The procedure is associated with risks of tissue disruption or hematoma that may reduce mammographic sensitivity.

FNA should not be done for persistent asymmetric thickening, as FNA has very low sensitivity in that setting. Mammographic sensitivity is better, but also variable, in evaluating asymmetric thickening. If the mammographic reading indicates anything other than —"normal" or —"probably benign abnormality" then the patient is referred to the surgeon for further management.

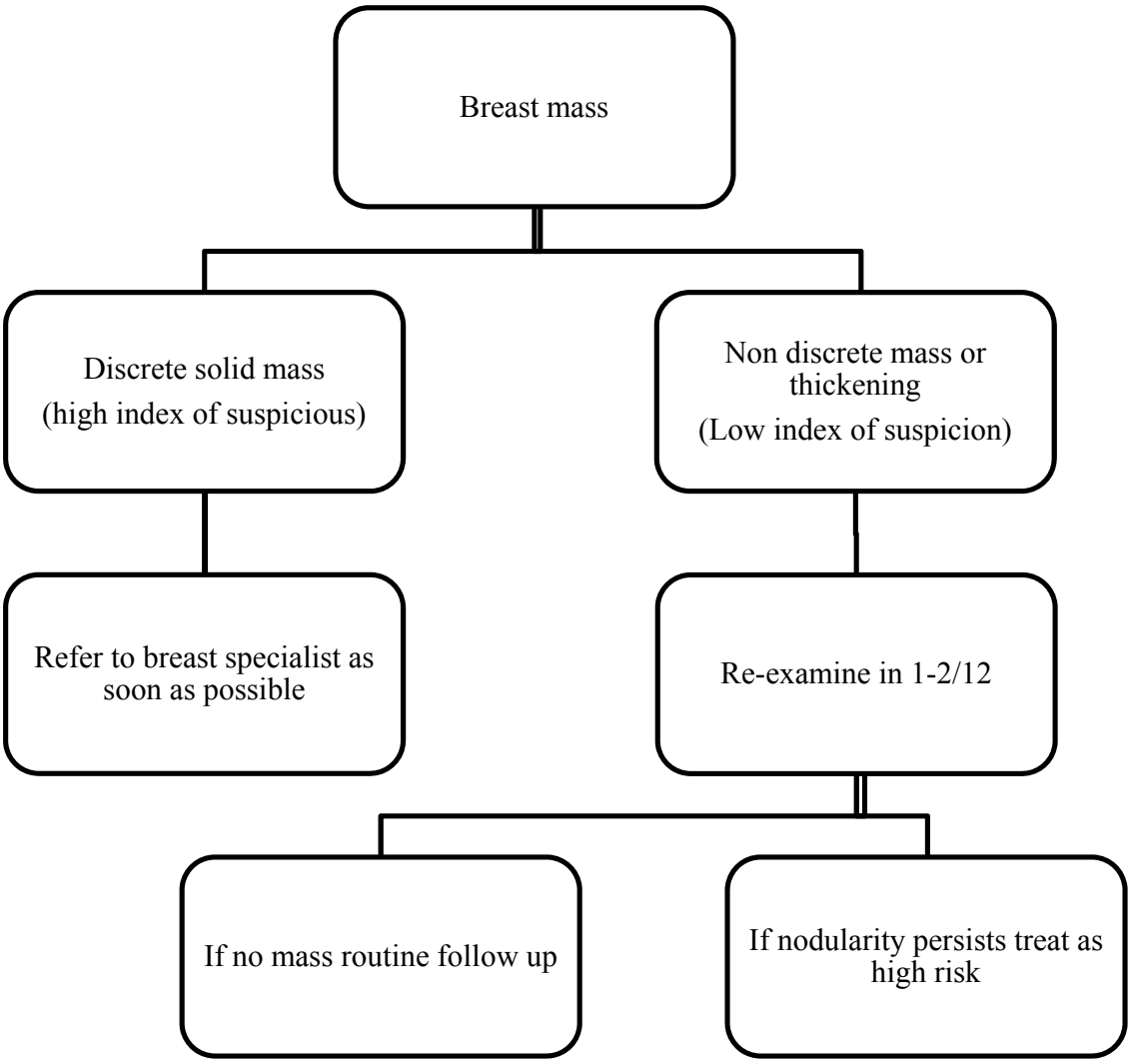


Chart 2: Breast Mass Management in Primary Health Care Center

5.2 Other breast abnormalities on physical exam:

1. A fluctuant ***painful mass*** suggests probable abscess and the patient should be urgently referred to a breast specialist for surgical intervention.

2. ***Erythematous changes*** in the breast raise the consideration of mastitis or inflammatory breast cancer. If there is no mass, a short course of antibiotic therapy for presumed mastitis is indicated. Close follow-up is important to insure resolution. Persistent inflammation warrants immediate referral to a breast specialist.

3. ***Nipple symptoms*** such as burning or itching in association with abnormalities on physical exam are concerning for Paget's disease. Exam findings may include persistent scaling or ulcer with serous fluid drainage or bleeding. Whereas the majority of cases of Paget's occur in association with mammographically detectable breast cancer, up to 40% may have negative mammogram. All suspicious nipple changes should be referred to a breast specialist.

5.3 Breast pain

Breast pain or mastalgia is a common patient complaint and can be divided into two groups.

- ***Cyclic mastalgia***: common in younger women occurs prior to the menses, increasing in severity until onset of menstrual bleeding. It is usually bilateral and may be felt as a heaviness or soreness and be poorly localized with radiation to axilla.
- ***Noncyclic mastalgia*** occurs in older women (most common in 40's and 50's) and may be constant or intermittent. It is often unilateral, more focal, and may be felt as a sharp or burning pain. Important historical factors include timing and features of pain, emotional stress, medications and family history.

Many women present to their provider's office because of fears that their pain is a sign of breast cancer, but breast cancer is rarely associated with breast pain in the absence of mass or physical exam changes. If pain is focal and persistent, however, referral to a breast specialist is indicated.

A thorough breast exam is essential. If an abnormality is found, referral for diagnostic breast imaging is appropriate. In cases where no focal pain is present and no abnormality is found on exam, reassurance is sufficient. Women can be reassured that as many as 60-80% of cases resolve spontaneously. A large portion of patients are satisfied with reassurance alone and require no further intervention.

Non-pharmacologic intervention should be reviewed and include instruction for a well-fitting bra. Relaxation techniques, warm compresses or cold packs, gentle massage and a diet low in fat may decrease pain.

A large number of medications have been implicated in breast pain, including hormonal medications such as contraceptives and postmenopausal hormone replacement, antidepressants and several cardiac / antihypertensive medications including spironolactone and digoxin. If these medications are related temporally, a change in dose or medication may be helpful.

Caffeine avoidance and vitamin E supplementation have been advocated as therapeutic measures in women with breast pain. Unfortunately, studies failed to demonstrate a therapeutic benefit for them.

If pharmacologist treatment is desired, a trial of evening primrose oil, 1000 mg bid (or its active ingredient gamma linoleic acid 160 mg bid) for 3 – 6 months is indicated. Research has shown varied success in treatment, but it is a low cost, low risk intervention. Oral or topical NSAIDs also can be used for general pain relief. Topical NSAIDS have been shown in randomized trials to be effective in reducing mastalgia.

If these are not successful and patient continues to have significant pain requiring intervention, referral to a breast care specialist is indicated. Available therapies at that point primarily include hormonally active medicines, including progesterone; Danazol, and bromocriptine, however, side effects tend to limit their tolerability.

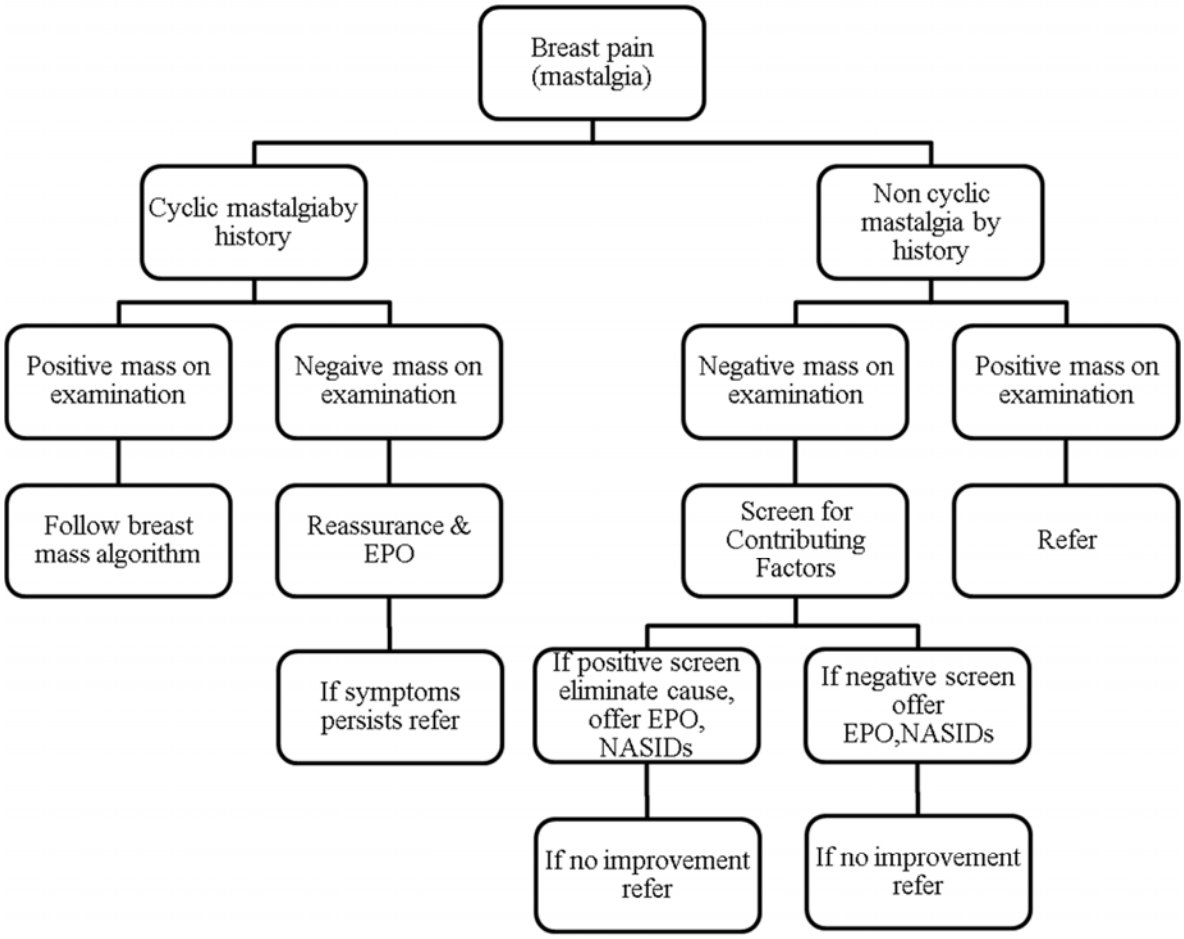


Chart 3: Breast Pain Management at Primary Health Care Center

5.4 Nipple discharge

Nipple discharge is not uncommon in premenopausal women. Galactorrhea is the most common type of discharge and is usually bilateral, expressible from multiple ducts, sticky and milky to yellowish in color.

A bloody nipple discharge could be pathognomonic of Intraductal Papilloma or Ductal Carcinoma. That could be confirmed by nipple discharge cytological study.

Otherwise, primary care providers can generally evaluate and manage this condition without further imaging or referral.

- Pregnancy needs to be ruled out.
- Prolactinoma or other conditions that reduce dopamine inhibition of prolacin secretion in the hypothalamic pituitary pathway can be screened with prolactin level.
- Medication effect is the most common etiology. Discuss the pros and cons of continuing the medication with the patient.
- Hypothyroidism and renal failure are medical conditions associated with galactorrhea.
- If no physiologic cause of elevated prolactin is found, MRI imaging of the hypothalamus / pituitary and referral to an endocrine specialist is appropriate.

Otherwise, women with this complaint may be reassured and counseled that nipple stimulation (sexual activity, jogging, poorly fitted bras, and repeated attempts to express discharge) may induce galactorrhea.

Green, gray, milky or black, discharge is all consistent with fibrocystic breast disease or ductal ectasia and is benign characteristics.

However, spontaneous discharge (without nipple manipulation), presence of a suspicious mass, or discharge from a single duct or in a postmenopausal woman are of concern and should lead to referral. Serous discharge could be suspicious for malignancy.

If one does cytological testing, a negative result is not definitive, but a positive result is very significant.

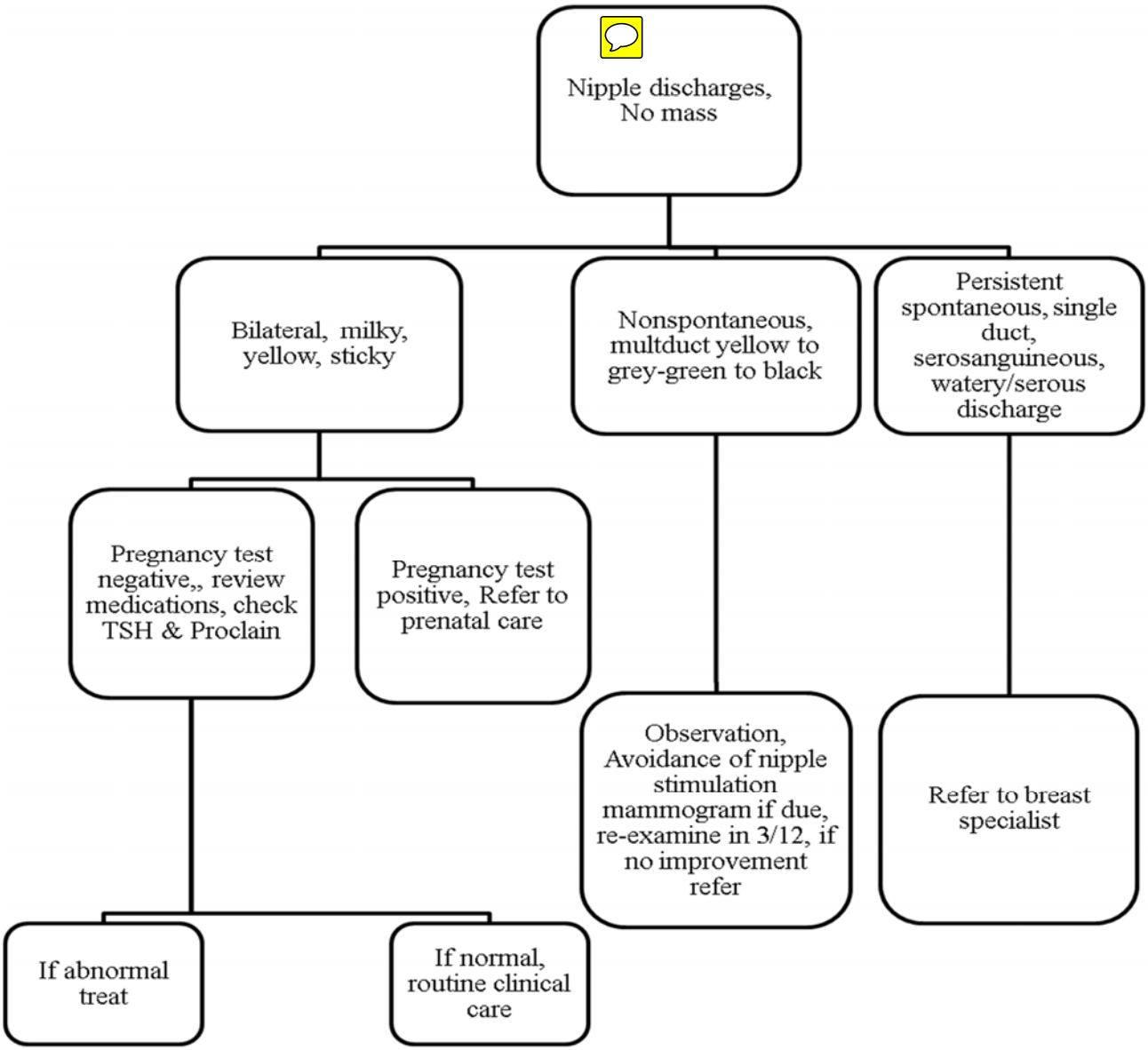


Chart 4: Management of Nipple Discharge in Primary Health Care Center

6. Referral Guidelines

The following conditions and clinical cases should be referred to secondary care level:

1. ***Lump***: breast lump in the following patients:
   - Discrete lump with a discrete lump of high index of suspicion for breast cancer (hard, irregular, fixed, decrease mobility)
   - Asymmetrical nodularity that persist at review after menstruation
   - Abscess
   - Persistently refilling or recurrent cyst
2. ***Pain:*** intractable pain not responding to simple measures such as wearing a well-fitting bra, and over the counter analgesics.
3. ***Nipple discharge***
   - Bilateral spontaneous discharge sufficient to stain clothes in patients aged < 50 years
   - Blood stained discharge in patients aged < 50 years (ASP referral if discharge is unilateral)
   - Any nipple discharge in patients over 50 years of age
4. ***Patients with breast signs or symptoms which are highly suggestive of cancer include:***
   - ulceration
   - skin nodule
   - skin distortion
   - nipple eczema
   - recent nipple retraction or distortion (less than 3 months)
   - unilateral nipple discharge which stains clothes

NOTE: The following women could be managed in primary health center:

- Younger women less < 35 years with long standing tender lumpy breasts.
- Postmenopausal women with symmetrical nodularity if no localized abnormality.
- Younger girls with tender developing breasts.
- Women with moderate degree of breast pain who do not have a discrete palpable lump.
- Women aged less than 50 with nipple discharge from more than one duct, intermittent - not blood stained.
- Women with long standing nipple retraction.
- Women with simple skin lesions, e.g. sebaceous cysts, should be managed as when present elsewhere.

7. Prognosis of Breast Cancer

7.1 Factors affecting the prognosis in breast cancer

1. Lymph node status
2. Tumor size
3. Tumor grade
4. Tumor stage
5. Tumor type (where are the cancer cells and how do they look in the lab)
6. Tumor characteristics:
   a) Hormone receptor status (estrogen and progesterone receptor status)
   b) HER2/neu status
   c) Proliferation rate
7. Tests for metastases

7.2 What is metastasis?

When breast cancer has spread to the lymph nodes, tests are done to check for metastasis (when the cancer spreads to other organs, such as the bones, lungs or liver). Although the cancer starts in the breast, it can be carried to other parts of the body through the lymph fluid and/or the blood. Once breast cancer spreads, prognosis is poorer. Many patients with metastases have been treated for breast cancer in the past and then cancer recurs and spread.

More than 50% of American breast cancer patients (American Cancer Society: Breast Cancer Facts) and over 70% of Iraqi patients (Alwan N, 2000 & 2010). have metastatic breast cancer when they are first diagnosed.

7.3 Signs of and tests for metastasis

Shortness of breath, chronic cough, and weight loss and bone pain can be symptoms of metastases. Tests must be done to confirm or rule out metastases. The three main tests are:

- A blood test to check for spread to the liver or bones
- Bone scans to test for spread to the bone
- X-ray/CT scans to test for spread to the chest, abdomen and liver
- Positron emission tomography (PET) and other tests for metastases may be done, depending on a person's symptoms and the findings from the three main tests.

8. Treatment of Breast Cancer

Treatment decisions are made by the patient and her treating team after consideration of the optimal treatment available for the stage and biological characteristics of the cancer, the patient's age and preferences, and the risks and benefits associated with each treatment protocol. Most women with breast cancer will have some type of surgery. Surgery is often combined with other treatments such as radiation therapy, chemotherapy, hormone therapy, and/or biologic therapy.

Types of Treatment

8.1 Surgery

The primary goal of breast cancer surgery is to remove the cancer from the breast and to assess the stage of the disease. Several types of breast surgery have been developed in order to provide the best results with minimum damage:

- Lumpectomy
- Mastectomy
- Breast reconstruction

8.2 Radiation therapy

Radiation therapy (also known as radiotherapy) uses targeted, high-energy X-rays to kill cancer cells. The goal of radiation therapy is to kill any cancer that might be left in or around the breast.
Radiation therapy is vital after lumpectomy (also called breast conserving surgery), since much of the breast tissue is left intact. It lowers the chances of the cancer returning in the breast by about 50 percent]. Many women who have a mastectomy do not need radiation therapy. However, in some cases, radiation is used after mastectomy to treat the chest wall and the lymph nodes around the collarbone and in the armpit (axillary nodes).
Radiation therapy is typically given for 5 to 7 weeks. Radiation to the breast is almost always recommended after a lumpectomy, and in some circumstances, following mastectomy.

Side effects of Radiotherapy:

1. Fatigue often described as feeling worn out or exhausted, skin changes, erythema, pruritus, skin breakdown and infection.
2. Xeroderma, dryness & peeling of the skin, moist reaction, sores or ulcers.

8.3 Chemotherapy

Chemotherapy drugs kill or disable cancer cells. Chemotherapy is a treatment option for most types of breast cancer. The decision to use chemotherapy is based on the tumor stage and certain tumor characteristics, as well as your age, overall health and personal preferences.

Chemotherapy after breast surgery (adjuvant chemotherapy)

For those with early breast cancer, chemotherapy is usually given after breast surgery (called adjuvant chemotherapy) but before radiation therapy. Adjuvant chemotherapy helps lower the risk of recurrence by getting rid of cancer that might still be present in the body.

Chemotherapy before breast surgery (neoadjuvant chemotherapy)

Chemotherapy is sometimes used before surgery (called neoadjuvant or preoperative chemotherapy). In women with large tumors who need a mastectomy, neoadjuvant chemotherapy may shrink the tumor enough that a lumpectomy becomes an option.

In women with locally advanced breast cancer, neoadjuvant chemotherapy can reduce the size of the tumor in the breast and/or in the lymph nodes, and make it easier to surgically remove the cancer.

8. 3.1 Chemotherapy drugs

Many of the drugs used to treat early breast cancer and locally advanced breast cancer are different than those used to treat metastatic breast cancer. Although each of the drugs listed below (table 5) is effective on its own, combining different drugs makes them even better at killing cancer cells.

Table 5: Chemotherapy drugs for early and locally advanced breast cancer

Drug (abbreviation)	Brand name
Cyclophosphamide (C)	Cytoxan
Docetaxel (T)	Taxotere
Doxorubicin (A)	Adriamycin
Epirubicin (E)	Ellence
5-Fluorouracil (5FU or F)	Adrucil
Methotrexate (M)	Maxtrex
Paclitaxel (T)	Taxol

8. 4 Other modalities of treatment

8.4.1 Hormone therapies: e.g. tamoxifen, aromatase inhibitors, and ovarian suppression (therapies that stop the ovaries from producing hormones)

8.4.2 Targeted therapies: e.g. Trastuzumab (Herceptin), Lapatinib (Tykerb) and other tyrosine-kinase inhibitors

9. Follow-Up of Treated Patients

9.1 Physical health follow-up

Follow-up services include those coping with the direct physical side effects and problems associated with breast cancer treatment. Follow-up of patients after conservative treatment includes a periodic physical examination and mammography every six months during the first two years and every year thereafter. Local recurrences occur for approximately 1% of the target population per year. Therefore, continued screening for the early detection of local relapses improves long-term survival after breast cancer treatment, especially mastectomies.

As important, is educating the woman and her family in the early detection of any signs of recurrence or possible metastasis of the cancer to other areas of the body. Symptoms such as bone pain, shortness of breath, excessive tiredness, unexpected bleeding and the suchlike, should be pointed out as possible signs of concern.

9.2 Mental health follow-up

For women diagnosed with breast cancer, follow-up services should also include interventions to deal with the emotional and psychological issues that are raised as a result of a diagnosis. The word cancer still brings with it a magnitude of fear and anxiety not associated with many other diseases. Breast cancer is an illness where the mortality and morbidity rate are clearly defined and where most women, especially those in developing countries, understand that their survival rate may not be strong. Women also continue to be the focal point of family life and an illness that threatens their life and ability to function significantly impacts the emotional well-being of the family unit.

It is therefore of utmost importance that any treatment and follow-up program for women with breast cancer include a strong psychosocial component that builds upon the strengths of the family, offers community and other normal forms of support during the most difficult stages of the illness, and assists the family in making the journey in a productive and positive manner.

10. Prevention of Breast Cancer

There is no sure way to prevent breast cancer. But there are things all women can do that might reduce their risk and help increase the odds that if cancer does occur, it is found at an early, more treatable stage.

1. Both increased body weight and weight gain as an adult are linked with a higher risk of breast cancer after menopause.
2. Alcohol also increases risk of breast cancer. Even low levels of alcohol intake have been linked with an increase in risk.
3. Many studies have shown that moderate to vigorous physical activity is linked with lower breast cancer risk.
4. A diet that is rich in vegetables, fruit, poultry, fish, and low-fat dairy products has also been linked with a lower risk of breast cancer in some studies. But it is not clear if specific vegetables, fruits, or other foods can lower risk. Most studies have not found that lowering fat intake has much of an effect on breast cancer risk.
5. Women who choose to breastfeed for at least several months may also reduce their breast cancer risk.
6. Not using hormone therapy after menopause can also help in avoiding raising the risk.
7. It's not clear at this time whether chemicals that have estrogen-like properties (like those found in some plastic bottles or certain cosmetics and personal care products) increase breast cancer risk. If there is an increased risk, it is likely to be very small. Still, women who are concerned may choose to avoid products that contain these substances when they can.

Part Two

Women Screening for Cervical Cancer

1. Epidemiology

Cervical cancer is the second most common malignancy in women worldwide, with only breast cancer occurring more commonly. The frequency varies considerably between developed and developing countries, however. Thus, cervical cancer is the second most common cancer in developing countries, but only the tenth most common in developed countries. Similarly, cervical cancer is the second most common cause of cancer-related deaths in women in developing countries but is not even among the top 10 causes in developed countries.

Internationally, more than 500,000 new cases are diagnosed each year; rates vary widely, ranging from an annual incidence of 4.5 cases per 100,000 in Western Asia to 34.5 per 100,000 women in Eastern Africa. In industrialized countries with well-established cytology screening programs; the incidence of cervical cancer ranges from 4 to 10 per 100,000 women.

The last estimate of cervical cancer death rate is 273 000 deaths every year. Of the new cases 80% occur in underdeveloped countries. And it account for 2.7 million of life lost among women between the age of 25-64 years worldwide; some 2.4 million occur in developing area and only 0.3 million in developed countries. Cervical cancer death rates have been decreasing, but the disease still accounted for 200,000 deaths in 2010; in developing countries, 46,000 of these women were aged 15-49 years, and 109,000 were aged 50 years or older and in underdeveloped countries, 75% of the affected women are presented with advance stage, while 75% of the affected women in developed counties were presented at an early stage and for that cure can be expected.

1.1 Age-related demographics

The Centers for Disease Control and Prevention (CDC) surveillance of screening-detected cancers (colon and rectum, breast, and cervix) in the United States from 2004 to 2006 reported that the incidence of late-stage cervical cancer was highest among women aged 50-79 years. However, cervical cancer may be diagnosed in any woman of reproductive age.

Indeed, rates of cervical adenocarcinoma have been increasing in women under 40 years of age. These cases are less easily detected with Pap test screening, and survivorship is low because cases tend to be detected at a late stage. Moreover, the HPV types causing adenocarcinoma are different from the types causing squamous carcinoma. HPV 16, which is a stronger carcinogen than other HPV types, has been found more frequently in younger women than in older ones.

1.2 The situation in Iraq

In Iraq, the annual incidence and mortality of cervical cancer is estimated at 2.1 and 1.4 per 100000 respectively, with the total number of newly diagnosed cases equals to 311 and the total

number of death equals to 212. This figure gives a cumulative risk of 0.3% for women ages 0-74 years. (WHO/ICO HPV Information center/Iraq)

In Iraq the age – specific demography of cervical cancer shows a steady increase in incidence rates starting from the age of 45 till 65 years where it plateaus later on. However, still 43% of newly diagnosed cases occur in women below 45 years, owing to the large proportion of this age group among Iraqi population. (WHO/ICO HPV Information center/Iraq)

Although the incidence rates of this cancer in Iraq are relatively low, as in the most other Islamic countries, the majority of the cases usually present in advanced stages with poor prospects of cure. According to the latest Iraqi Cancer Registry; cervical cancer ranks 15th among the most common female cancers. The low incidence of cervical carcinoma in Iraq and other Islamic countries compared to the western world could be mainly attributable to the act of circumcision, the strict observance of religion and the presence of principles and laws that forbid illegal extramarital relationships (Alwan N, EMHJ 2001, www.bccru.uobaghdad.edu.iq. 2012)

Unlike many other cancers, cervical carcinoma usually develops slowly and passes through readily detectable and treatable precancerous conditions termed "Cervical Intraepithelal Neoplasia CIN". A WHO pilot study demonstration project that was initiated to screen for CIN lesions in Iraq displayed that , as more than two—thirds of the Iraqi patients have late diagnosis, a feasible control strategy would be to encourage Iraqi women to seek screening for CIN. By using colposcopy, Pap smear cytology and Human Papilloma virus detection as screening tools, the study demonstrated that no lesion was missed when the three methods were used in concert (Alwan N, EMHJ, 2001).

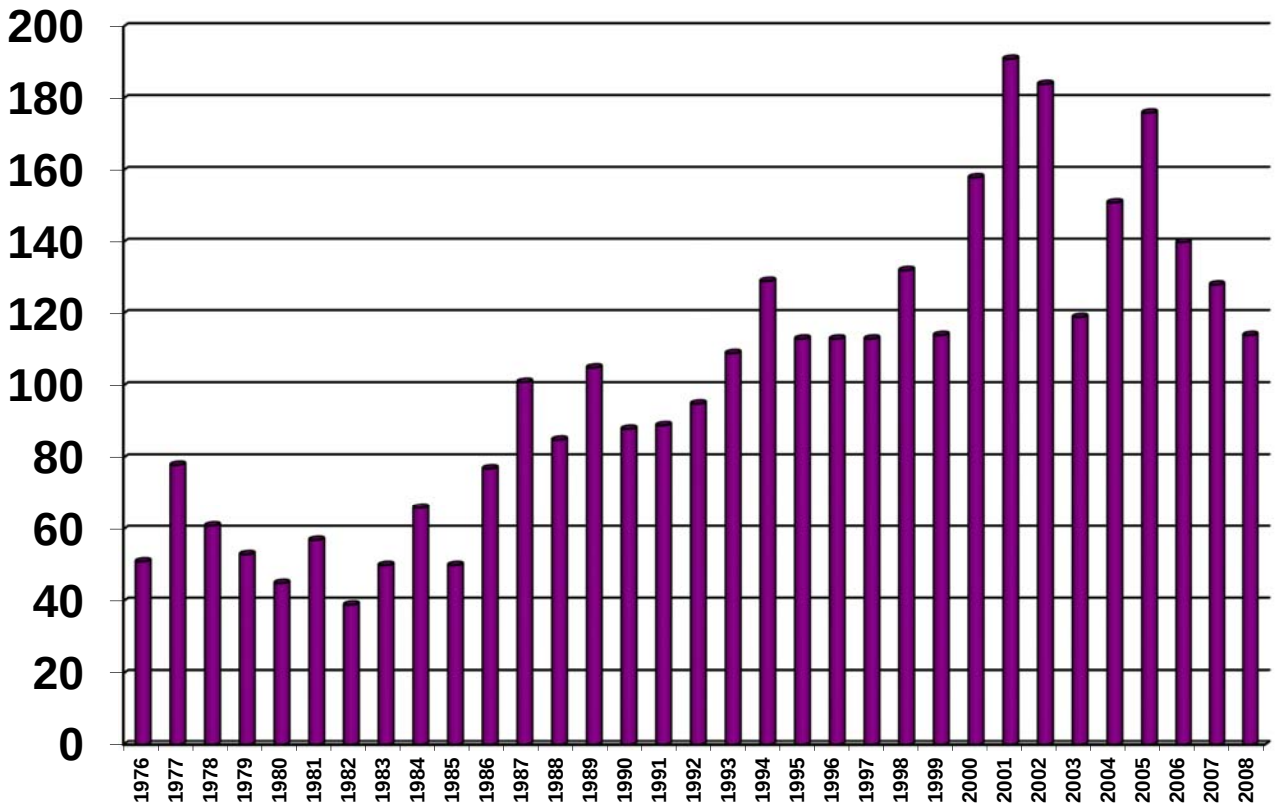


Figure 8: Number of new cases of cervical Cancer in Iraq (1976 – 2008)

2. Anatomy, Physiology, and Pathology of Cervix

The cervix is the lower part of the uterus (womb). It is sometimes called the *uterine cervix*. The body of the uterus (the upper part) is where a baby grows. The cervix connects the body of the uterus to the vagina (birth canal). The part of the cervix closest to the body of the uterus is called the *endocervix*. The part next to the vagina is the *exocervix (or ectocervix).* The 2 main types of cells covering the cervix are *squamous* cells (on the exocervix) and *glandular* cells (on the endocervix). The place where these 2 cell types meet is called the *transformation zone*. Most cervical cancers start in the transformation zone.

2.1 The transformation zone

The transformation zone is a dynamic area, usually located on the ectocervix. At times, the distal edge of the transformation zone extends into the upper vagina. The transformation zone, by definition, is the area between the original squamocolumnar junction and the current squamocolumnar junction. The transformation zone is that portion of the cervix that originally was columnar epithelium and through a process of squamous metaplasia is now squamous epithelium. Squamous metaplasia occurs continuously; however, this process is most active during fetal development, around the time of menarche, and during pregnancy. Local hormonal changes, as reflected by vaginal pH, influence this process.

Understanding the transformation zone is of utmost importance because cervical cancer and its precursors typically begin within the transformation zone.

2.2 Precancerous changes of cervix

Most cervical cancers begin in the cells lining the cervix. These cells do not suddenly change into cancer. Instead, the normal cells of the cervix first gradually develop precancerous changes that turn into cancer. These changes can be detected by the Pap test and treated to prevent the development of cancer.

The change from cervical pre-cancer to cervical cancer usually takes several years in the vast majority of cases. For most women, pre-cancerous cells will go away without any treatment. Still, in some women pre-cancers turn into true (invasive) cancers. Treating all precancers can prevent almost all true cancers. Pre-cancerous changes are separated into different categories based on how the cells of the cervix look under a microscope (Table 6).

Table 6: Cervical precancer: different terminologies used for cytological and histological reporting

Cytological classification (used for screening)		Histological classification (used for diagnosis)	
Pap	**Bethesda system**	**CIN**	**WHO descriptive classifications**
Class I	Normal	Normal	Normal
Class II	ASC-US ASC-H	Atypia	Atypia
Class III	LSIL	CIN 1 including flat condyloma	Koilocytosis
Class III	HSIL	CIN 2	Moderate dysplasia
Class III	HSIL	CIN 3	Severe dysplasia
Class IV	HSIL	CIN 3	Carcinoma in situ
Class V	Invasive carcinoma	Invasive carcinoma	Invasive carcinoma

(Adapted from WHO, comprehensive cervical cancer control: a guide to essential practice-2006)

*CIN: cervical intraepithelial neoplasia; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; ASC-US: atypical squamous cells of undetermined significance; ASC-H: atypical squamous cells: cannot exclude a high-grade squamous epithelial lesion.

The CIN classification has almost universally replaced the world health organization classification, with CIN I, 2 and 3 corresponding to mild, moderate and severe dysplasia/carcinoma *in situ,* respectively. A revised classification has been introduce with high grade lesions (CIN 2 and 3) which are likely to behave as cancer precursors and low grade lesions (CIN I and HPV-associated changes) with unknown but a likely low progressive potential.

The progressive potential of high grade lesions or CIN 3 has been calculated to be 18% at 10 years and 36% at 20 years. Woman with abnormal cytology after initial management of carcinoma *in situ* of cervix were almost 25 times more likely to develop invasive carcinoma than woman who have normal follow- up cytology. Thus, immediate treatment of CIN3 is needed once diagnosed.

2.3 Types of cervical cancer

There are 2 main types of cervical cancers: *squamous cell carcinoma* and *adenocarcinoma*. About 80% to 90% of cervical cancers are squamous cell carcinomas. These cancers are from the squamous cells that cover the surface of the exocervix. Under the microscope, this type of cancer is made up of cells that are like squamous cells. Squamous cell carcinomas most often begin where the exocervix joins the endocervix, i.e. the transformation zone.

Most of the other cervical cancers are adenocarcinomas. Cervical adenocarcinomas seem to have becoming more common in the past 20 to 30 years. Cervical adenocarcinoma develops from the mucus-producing gland cells of the endocervix. Less commonly, cervical cancers have features of both squamous cell carcinomas and adenocarcinomas. These are called *adenosquamous carcinomas* or mixed carcinomas.

Although almost all cervical cancers are either squamous cell carcinomas or adenocarcinomas, other types of cancer also can develop in the cervix. These other types, such as melanoma, sarcoma, and lymphoma, occur more commonly in other parts of the body.

2.4 Staging

The current system of staging for cervical cancer is based on the International Federation of Gynecology and Obstetrics (FIGO) classification. This staging system is a clinical approach based on findings from clinical assessment or examination of patients under anesthesia, which may be supplemented by chest radiography, excretory urography, cystoscopy, and proctoscopy

Table 7: Staging and Survival Rates of Cervical Cancer

Stage	Type	5-years survival rate
0	The cancer cells are only in the cells on the surface of the cervix (the layer of cells lining the cervix), without growing into (invading) deeper tissues of the cervix.	93%
I	The cancer has grown into (invaded) the cervix, but it is not growing outside the uterus. The cancer has not spread to nearby lymph nodes or distant sites.	80-93%
II	The cancer has grown beyond the cervix and uterus, but hasn't spread to the walls of the pelvis or the lower part of the vagina.	58-63%
III	The cancer has spread to the lower part of the vagina or the walls of the pelvis. The cancer may be blocking the ureters (tubes that carry urine from the kidneys to the bladder). OR The cancer has spread to lymph nodes in the pelvis (N1) but not to distant sites.	32-35%
IV	The cancer has spread to nearby organs or other parts of the body.	15-16%

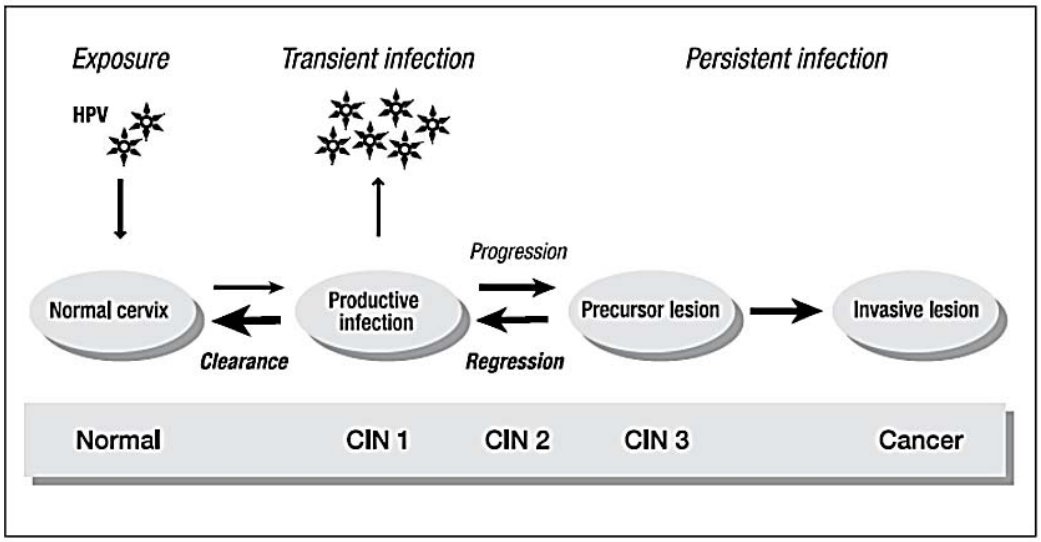
(Adapted from American cancer society – Cervical cancer)

3. Etiology

3.1 Natural history of cervical cancer

Cervical cancers are caused by human Papilloma viruses (HPV). These viruses are tissue-specific DNA viruses that are easily transmissible and highly prevalent.
HPV is the most common sexually transmitted infection with about 630 million people believed to be infected with HPV worldwide. Fortunately, the vast majority of HPV infections are transient: they clear as a result of natural immune responses, becoming undetectable after 6 to 18 months. However, precancer can develop if infection persists, and precancerous cells can become cancerous over time.

Figure 2.7 Natural history of cervical cancer



CIN: cervical intraepithelial lesion

Adapted from: *Cervix cancer screening*. Lyon, IARCPress, 2005 (IARC Handbooks of Cancer Prevention, Vol. 10).

Figure 9: Natural history of cervical cancer

Human Papilloma virus induces cellular changes at the basal layer of squamous epithelium of the cervix at the transformation zone. These changes are called cervical intraepithelial neoplasia (CIN). These changes tend to regress to normal within one year or very slowly progress to more severe abnormalities and eventually to cervical cancer .Persistence and progression to cancer may take several years (10-20 years) to develop. This long natural history makes it liable for early detection and treatment at its precancer lesions, if women were screened, diagnosed and treated early.

3.2 Cancer-causing HPV types:

Human papillomaviruses comprise a large family of viruses, with more than 100 types known. Some infect the genital tract and of these, some have a high potential for causing cancer (oncogenic types), whereas others cause non-cancerous conditions.

- Oncogenic HPV types cause a variety of anogenital and other cancers, such as oral cancer.
- Nononcogenic HPV types cause genital warts, abnormal cervical cytology, recurrent respiratory papillomatosis, or infections that go unnoticed and eventually clear up.
- HPV 16 and 18 are oncogenic types associated with about 70 percent of all cervical cancer cases. At least 11 other HPV types cause cancer, though less commonly. Among these, HPV 45 and 31 each account for about 4 percent of cervical cancer cases.

(Outlook volume 27 number 2)

3.3 Risk Factors

1. Women having a child at age less than 20 years increase the risk of cervical cancer and cervical intraepithelial neoplasia (CIN3) especially in pre-menopausal grand multiparous women.
2. Women who have had a high number of live births are more likely to develop cervical cancer. The reasons not yet were fully established.
3. Cigarette smoking is the only nonsexual behavior consistently and strongly correlated with cervical dysplasia and cancer, increasing risk two– to four– fold. Cervical cancer may develop more readily in smokers as the toxins in cigarettes concentrate in the cervical mucus. As well as having a direct oncogenic effect, smoking decreases local immune resistance. As a result, once infected, sexually active women who smoke are more likely to develop persistent HPV infection, which in turn increases the possibility of developing cervical cancer.
4. Women with other sexually transmitted infections (e.g. HSV, Chlamydia), were more likely to develop cervical cancer, possibly mediated by inflammatory cytokine responses or independent effects on the female reproductive system including the cervix.
5. Increasing numbers of sexual partners provides the opportunity for more HPV transmission to occur between partners.
6. Intrauterine devices are not linked to any increase in cervical cancer risk. A reduced of risk of cervical cancer is associated with copper IUCD use.
7. Diaphragm and condom use not associated with risk of cervical cancer but spermicidal may offer some protection.

Table 8: Relative risks for cervical cancer by specific risk factor

Risk factor	Relative risk*
HIV (human immunodeficiency virus) infection	Very high
Moderate dysplasia on Pap smear within past 5 yr	Very high
Intercourse within 1 yr of menarche	16
No prior screening	10
HPV infection (depending on subtype)	2.5-30
Six or more lifetime sexual partners	5
Low socioeconomic class	5
Black race (compared with white race)	2.5
Smoking	2
Oral contraceptive use	1.2-1.5
Barrier contraceptive use	0.6

(Adapted from Institute for Clinical Systems Improvement. Health care guideline: cervical cancer screening / Institute for Clinical Systems Improvement. June 2002)

*A relative risk of 1 indicates no increased probability of a negative outcome, whereas a relative risk of less than 1 means an actual protective effect may be present. A relative risk of 10 means a 10-fold increase.

4. Means of Early Detection of Premalignant Lesions

Basically there are three means for early detection of cervical cancer: the visual inspection, cytology and HPV testing. These are either used individually or in combination.
The recommendations for each means are summarized below:

4.1 Visual inspection methods (VIA, VILI):

This involves staining of the cervix with either acetic acid or Lugol's iodine and search for certain abnormalities in staining of cervix.

- A single visit approach combining VIA and cryotherapy is safe, acceptable, feasible and cost effective in developing countries with low resources, which minimize loss to follow up.
- A three to five year screening interval should be considered for VIA negative women between the ages of 25-49. VIA-positives are offered cryotherapy at the time of screening to maximize program effectiveness. Post-cryotherapy, these women are seen in 12 months for a repeat screening.
- Women under 25 years of age should be screened only if they are at high risk for disease. VIA is not appropriate for women over 50 years. For HIV positive women, annual screening is recommended.
- A minimum of a once in a lifetime screening with VIA (and appropriate treatment) has the potential to reduce cancer risk by one third.
- Mid-level providers may be trained for VIA and cryotherapy. Effective training and quality assurance program are essential to ensuring the effectiveness of VIA. This is especially true as VIA is Known to have a lower specificity than other methods thus creating the potential for over treatment if inspection is not carefully and consistently supervised.

4.2 Cytology:

Involves scraping the cervix, immediately fixing the scrape on a slide and sending it to a competent cytology lab to be stained and read.

- Cytology is currently the most common manner of screening for cervical cancer. New screening methods are now being introduced in conjunction with or as replacement to cytology
- Cytological cervical sampling can be conducted by a physician, mid-level provider. Self-sampling is being explored as effective option. Reviewing cervical samples must be conducted by a trained cytologist.
- Where resources permit, initiation of cytological screening should occur between 21-25 or 3 years after the initiation of sexual activity.
- Interval screening should follow regional standards but not be longer than 5 years in women under 60.

- In low to middle-resource settings, the use of cytology as a population based screening method has not proven effective due to an unattainable reliance on health infrastructure, information systems and physician/cytologist time.
- For these reasons, the expansion of cytology-based screening programs in low-income countries is not recommended. Other screening approaches covered in this document could be more appropriate and effective in controlling cervical cancer.

4.3 HPV TESTING:

This means is becoming more widely applied in combination with either visual inspection methods or cytology because means of detecting HPV in cervical specimen are becoming increasingly available and take shorter time for results to appear making it suitable to increase the specificity of other tests.

Cervical cancer is a rare outcome of HPV infection. HPV is a common and mainly sexual transmitted infection. It can be found in almost all cases of cervical cancer. However, most HPV infection will not progress to CIN or cancer. The invasive disease doesn't develop unless there is persistent of HPV (DNA) and it has been proposed as the first ever identified 'necessary cause' of a human cancer. Out of the 80 known HPV genotypes, 30 are known to infect the genital tract. From these, 20 have been identified as carcinogenic with type 16 & 18 found most commonly in malignant lesion.

- HPV testing is the most sensitive screening test for detection of CIN2/3 and cervical cancer.
- Sub-optimal specificity of HPV testing results in an increased number of women referred for further evaluation. It could be a limitation in settings where colposcopy is not available.
- HPV testing is cost-effective for primary screening in women 30 years and over, and for triage of abnormal cytology in younger women.
- The high negative predictive value of HPV testing permits longer inter-screening periods and a reduction in the number of screening visits needed over a lifetime.
- Introduction of a faster, simpler and more affordable HPV test currently used in demonstration projects will benefit areas with limited resources.

Table 9: Sensitivity and specificity of cervical cancer early detection methods

	Sensitivity	Specificity	Reference
VIA	55	90	ACCP_cxca_screening_2011
Cytology	88	95	
HPV testing	98	85	
VIA	76	81	Goldie et al ; cost effectiveness of cervical cancer screening in developing countries ; N Engl J Med 2005;353:2158-68.
cytology	63	94	
HPV testing	88	93	

4.4 Colposcopy:

This is not a means of early detection of cervical cancer but it provides better inspection of cervical abnormalities and directed biopsy after triaging the woman with abnormal cervical changes or tests to the referral center or hospital.

- Colposcopy is essential for the assessment of abnormal cytology findings in order to make a diagnosis of preinvasive cervical neoplasia.
- Using acetic acid and magnification, the trained colposcopist determines severity of the neoplasia based on color and characteristics of observed cervical changes.
- Training and equipment for the procedure is expensive and requires maintenance that could be prohibitive in low-resource settings.
- The low sensitivity and low positive predictive value make colposcopy an insufficient tool for cervical screening. It should be only used for the assessment of abnormal cytology.
- Recent findings challenge the use of colposcopy as the "gold standard" in detection. Four guardant cervical biopsies from the squamocolumnar junction and endocervical picked up more lesions. More study is needed to confirm these findings.
- Use of colposcopy after identification of high-risk HPV has been recommended by the American Society of Colposcopy and Cervical Pathology (ASCCP). The role of colposcopy after VIA or VILI is used as the primary screening tool is less certain.

4.5 The single visit approach (=screen- and -treat = see-and -treat) for early detection and management

- Recent evidence suggest that the approach taken to screening can be as, or more important than the test used, in determining impact on cancer outcomes.
- In the single visit approach, screening and treatment are performed at the same visit to minimize the chance of abnormal results going unmanaged.
- This requires that the screening test provide rapid and accurate results and an appropriate, effective, adequate method of treatment are available to women with abnormal tests in the same sitting.
- Over the past several years, a variety of screening and treatment options have been considered for use within the single visit approach - Cytology, HPV, testing and Visual Inspection with Acetic Acid (VIA).
- At present, the most accessible and effective modality for the single visit approach is visual inspection with acetic acid (VIA) followed by cryotherapy of positive cases. In the near future, other screen technologies, such as HPV testing might become available and accessible for use within this approach.

5. The 2001 Bethesda System for Management of Cervical Abnormalities

The Bethesda System (TBS) for reporting cervical or vaginal cytologic diagnoses was introduced in 1988 and revised in 1991 to establish uniform terminology and standardize diagnostic reports. In addition, it introduced a standardized approach for reporting if an individual specimen is adequate for evaluation. TBS 2001 was developed through a process that involved committee review of the literature, solicitation of expert opinions, and discussion of the proposed changes on an interactive Web site.

In 2006, a group of experts met to develop revised evidence-based consensus guidelines for the 2001 Bethesda system. Recommendations for managing atypical squamous cells of undetermined significance and low-grade squamous intraepithelial lesion (LSIL) are essentially unchanged. Changes were made for managing these conditions in adolescents for whom cytological follow-up for 2 years was approved. Recommendations for managing high-grade squamous intraepithelial lesion (HSIL) and atypical glandular cells (AGC) also underwent only minor modifications. More emphasis is placed on immediate screen-and-treat approaches for HSIL. Human papillomavirus (HPV) testing is incorporated into the management of AGC after their initial evaluation with colposcopy and endometrial sampling.

The 2004 Interim Guidance for HPV testing as an adjunct to cervical cytology for screening in women 30 years of age and older was formally adopted with only very minor modifications.

5.1 Terminology in reporting results of cervical cytology

5.1.1 Specimen Adequacy

- Satisfactory for evaluation indicates that specimen has all the following:
  - Appropriate labeling and identifying information
  - Relevant clinical information
  - Adequate numbers of well-preserved and well-visualized squamous epithelial cells
  - An adequate endocervical/T.Z. component

- Unsatisfactory for evaluation ... (specify reason)
  - Specimen rejected or not processed (specify reason)
  - Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormality because of (specify reason)

5.1.2 Interpretation/Result

The specimen is considered negative for intraepithelial lesion or malignancy: when there is no cellular evidence of neoplasia. The examiner should state also whether or not there are organisms or other non-neoplastic findings.

The following information outlines the main aspects that may be detected in Pap smear:

A- Organisms:

- Trichomonas vaginalis
- Fungal organisms morphologically consistent with Candida species

- Shift in flora suggestive of bacterial vaginosis
- Bacteria morphologically consistent with Actinomyces species.
- Cellular changes (cytopathologic changes multinucleated giant cells) consistent with Herpes simplex virus

B- Other non-Neoplastic findings:

Reactive cellular changes associated with: inflammation (includes typical repair), radiation, intrauterine contraceptive device (IUD), glandular cells status post hysterectomy and atrophy.

C- Epithelial cell abnormalities:

1- Squamous cells

- Atypical squamous cells (ASC)
  - of undetermined significance (ASC-US)
  - cannot exclude HSIL (ASC-H)
- Low grade squamous intraepithelial lesion (LSIL) encompassing: human papilloma virus (HPV)/mild dysplasia/CIN 1
- High grade squamous intraepithelial lesion (HSIL) encompassing: moderate and severe dysplasia, Carcinoma in situ (CIS); CIN 2 and CIN 3
- Squamous cell carcinoma

2- Glandular cells:

- Atypical glandular cells (AGC) (*specify endocervical, endometrial, or not otherwise specified NOS*).
- Atypical glandular cells, favour neoplastic (*specify endocervical or not specified*).
- Endocervical Adenocarcinoma In Situ (AIS)
- Adenocarcinoma.

3- Others (List not comprehensive)

- Endometrial cells in women 40 years of age or over

Notes:

- The most common cervical cytological abnormality is atypical squamous cells (both ASC-US and ASC-H), assigned to around 3 - 4% of smears.

- Findings of endometrial cells are usually benign, but if the finding is not associated with menses or occurs in postmenopausal women who are not on hormone replacement therapy, it may indicate a risk for an endometrial abnormality. In menstruating women, endometrial cells generally are no longer present seven days after the first day of the last menstrual period.

Box 3: The 2001 Bethesda System for Reporting Cervical Cytologic Diagnoses

Specimen adequacy
Satisfactory for evaluation
  Presence or absence of endocervical or transformation zone components or other quality indicators such as partially obscuring blood or inflammation
Unsatisfactory for evaluation (specify reason)
  Specimen rejected or not processed (specify reason)
  Specimen processed and examined, but unsatisfactory for evaluation of epithelial abnormalities (specify reason)
General categorization (optional)
Negative for intraepithelial lesion or malignancy
Epithelial cell abnormality
Other
Interpretation/result
Negative for intraepithelial lesion or malignancy
  Organisms
    Trichomonas vaginalis
    Fungal organisms morphologically consistent with Candida species
    Shift in flora suggestive of bacterial vaginosis
    Bacteria morphologically consistent with Actinomyces species
    Cellular changes consistent with herpes simplex virus
  Other non-neoplastic findings (optional to report)
    Reactive cellular changes associated with:
      Inflammation (includes typical repair)
      Radiation
      Intrauterine contraceptive device
  Glandular cells status posthysterectomy
  Atrophy
Epithelial cell abnormalities
  Squamous cell
    Atypical squamous cells (ASC)
      ASC of undetermined significance (ASC-US)
      ASC, cannot exclude high-grade squamous intraepithelial lesion (ASC-H)
    Low-grade squamous intraepithelial lesion (LSIL)
      Encompassing: human papillomavirus, mild dysplasia, and cervical intraepithelial neoplasia (CIN) 1
    High-grade squamous intraepithelial lesion (HSIL)
      Encompassing: moderate and severe dysplasia, carcinoma in situ, CIN 2, and CIN 3
    Squamous cell carcinoma
Glandular cell
    Atypical glandular cells (AGC)
      Specify endocervical, endometrial, or glandular cells not otherwise specified
    Atypical glandular cells, favor neoplastic
      Specify endocervical or not otherwise specified
    Endocervical adenocarcinoma in situ (AIS)
    Adenocarcinoma
Other (list not comprehensive)
  Endometrial cells in a women 40 years or older
Automated review and ancillary testing (include if appropriate)
Educational notes and suggestions (optional)

(Adapted from Solomon D et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology)

5.2 Management and Interactions Taken for Abnormalities:

1- Specimen Adequacy:

- Absence of an endo-cervical cell/transformation zone (EN/TZ) component, to repeat Pap test in 12 months and not to wait longer.
- A specimen is considered "partially obscured" when 50 to 75 percent of the epithelial cells cannot be visualized. Specimens in which more than 75 percent of the cells are obscured are designated unsatisfactory. Women with partially obscuring blood or inflammation should have a repeat test in six months.
- A specimen is considered "unsatisfactory" for evaluation to repeat Pap test within two to four months. If the cells are obscured by inflammation and a specific infection is identified, treatment should be given before repeating the Pap test.

2- Interpretation/Result:

A- Organisms:

- Trichomonas: treat asymptomatic women with trichomonads noted on liquid-based cervical cytology, but with conventional Pap smears, the diagnosis should be confirmed by wet prep.
- Bacterial vaginosis; cervical cytology is not a reliable diagnostic method for bacterial vaginosis, so it need confirmation with clinical testing before treatment.
- Actinomyces is typically in women who have an intrauterine device.

B- Other non-neoplastic findings

- Reactive changes/inflammation: The cervical cytology sampling does not need to be repeated unless the patient is HIV positive, in which case it should be repeated in four to six months.
- Hyperkeratosis on an otherwise negative cervical cytology test is may be related to infection or trauma with inflammation, such as from use of a diaphragm. We repeat the cervical cytology test in 6 to 12 months, depending upon whether the patient is at increased risk for CIN, such as immune-compromised or age less than 30.
- Inflammatory: mild no need to treat or repeat. Moderate and sever inflammatory evaluate for other infections, e.g. gonorrhea and Chlamydia; and do KOH. If any of the preceding is positive treat accordingly and repeat after 3 months. If all test negative, repeat after 6 months. Persistent inflammatory changes refereed to secondary care for colposcopy.

6. Management of Cervical Lesions

6.1 Management of cytology with Atypical Squamous Cells of Undetermined Significant (ASC-US) in Primary Care.

1-For non-adolescent women (chart5 below), there are three acceptable management schemes for evaluation of ASC-US;

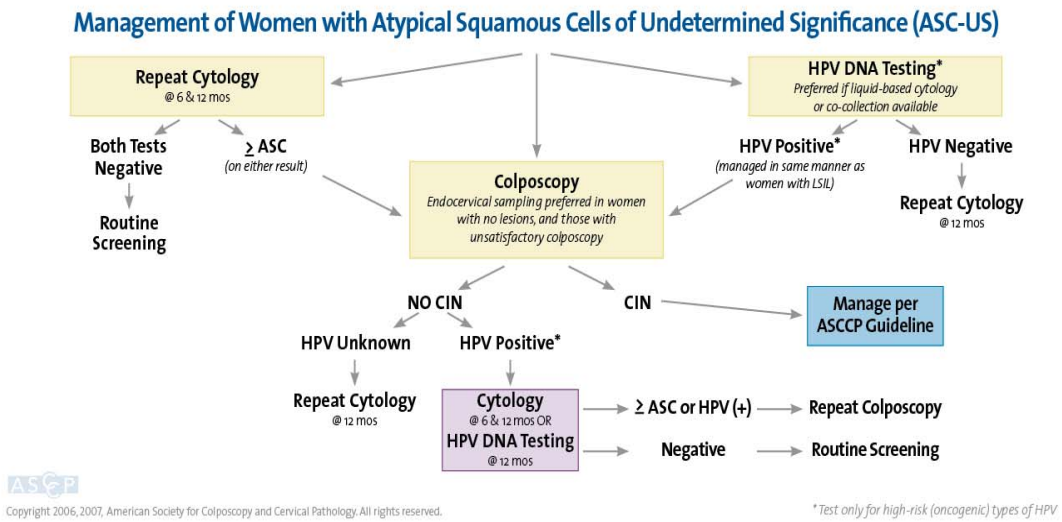


Chart 5: Management of Women with Atypical Squamous Cells of Undetermined Significant (ASC-US)

i. **Reflex HPV test:** Women with a positive test for high risk types of HPV DNA are evaluated by immediate referral to colposcopy.
HPV negative ASC-US is usually due to disturbances in maturation or cellular changes related to inflammation or atrophy repeat cervical cytology in 12 months. If HPV testing remains negative at 12 months, return to routine screening intervals, based on her age and prior screening history.
Some women have persistent HPV negative and ASC-US. This is most likely due to inflammation or atrophy. Such women can be followed with annual cervical cytology if there are no symptoms of postcoital or abnormal uterine bleeding and if a pelvic examination is normal.

ii. **Repeated cytology in 6 and 12 months** and, if normal, routine screening may be resumed. A second abnormal smear (ASC-US or greater) is evaluated with colposcopy.

iii. **Immediate referral to colposcopy**, colposcopy is expensive, can be uncomfortable, and potentially leads to over-diagnosis and over-treatment.

2- Adolescents (see chart6): Pap testing is not recommended for women 20 years old or younger, but if they do have Pap test results that show ASC-US, they are likely to be observed without treatment.

In adolescents (20 years old or younger), the prevalence of transient HPV infection (and transient cytological abnormality) is very high while the prevalence of invasive cancer is near zero. For this reason, adolescents with ASC-US are best managed with follow-up cytology at 12 months (persistence for 24 month do colposcopy). If cytology HSIL or higher referred.

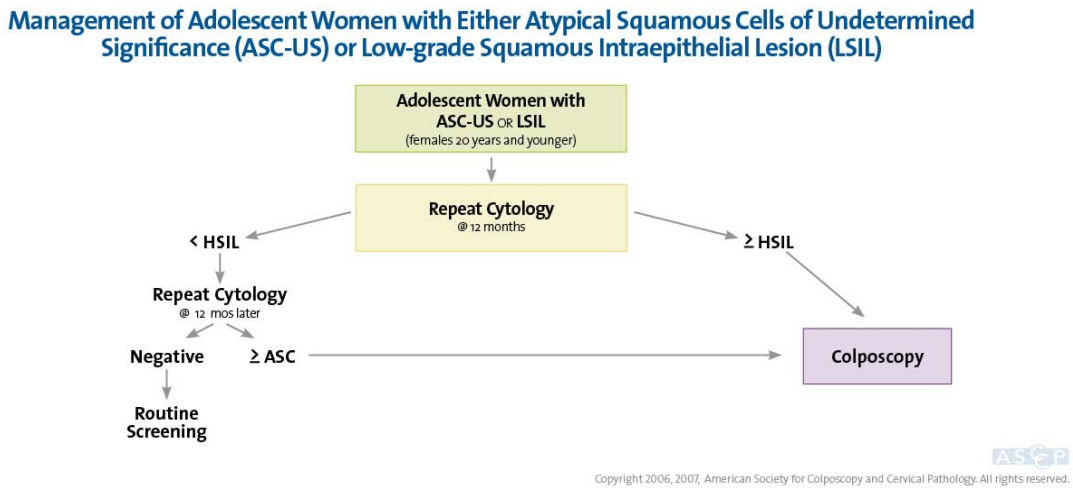


Chart 6: Management of Adolescent Women with either Atypical Squamous Cells of Undetermined Significant (ASC-US) or Low-grade Squamous Interaepithelial Lesion (LSIL)

3- Pregnant women: pregnant women with ASC-US are managed in the same way as non-pregnant women, except endocervical curettage is not performed. However, it should be noted that pregnancy-related physiologic and anatomic changes result in the production of more metaplastic cells and reactive changes and inflammation make diagnosis of ASC more challenging in this population.

4- Infection or reactive changes: The presence of infection or reactive changes does not preclude further evaluation of ASC-US. When an infectious organism is identified antibiotic therapy is generally indicated for symptomatic infections, as well as some asymptomatic infections .After treatment of the infection, evaluation of ASC-US is performed.

5- Postmenopausal women: Postmenopausal women are managed in the same way as pre-menopausal women. Cellular changes (e.g., nuclear enlargement) associated with postmenopausal vaginal atrophy may be mistaken for ASC. In the past, estrogen administration followed by repeat cytology was suggested to help distinguish atypical atrophic epithelium,

which matured into normal squamous epithelium with estrogen therapy, from true intraepithelial neoplasia, which is not affected by estrogen. However, this is no longer recommended.

6- Immunosuppressant: Immune-suppressed women, including women who are HIV positive, with ASC-US can be managed the same as women in the general population .They are not at increased risk of CIN 2, 3.

6.2 Referral guidelines

Conditions of cervix and results of cytological examination that necessitate referral to secondary care level are summarized in the following box.

Box 4: Criteria for Referring to Secondary Care Level in Cervical Coditions

A. The patient presented with symptoms suggestive of cervical cancer
   1. Vaginal bleeding after intercourse, between periods (inter-menstrual), or after menopause.
   2. Water or bloody discharge from vagina that may be heavy and have a foul odor.
   3. Pelvic pain or pain during sexual intercourse.

B. On cytology:
   1. Women (including adolescents) with ASC-H or more and glandular cells on cytological should be referred for Secondary care for colposcopy and endocervical curettage.
   2. Women with ASC-US who have:
      a. A positive reflex test for high risk types of HPV DNA. Those should be evaluated by immediate referral to colposcopy.
      b. Recurrent abnormal smear (ASC-US or greater). Those are evaluated with colposcopy.

6.3 Modalities of treatment of premalignant cervical lesions:

6.3.1 Ablative Techniques:-

1. Cryotherapy, or freezing the area by the application of probes; anesthesia is not usually required.
2. Cold coagulation, usually without, or with some local anesthesia.
3. Electrodiathermy, under either local or general anesthesia.
4. Carbon dioxide (CO2) laser evaporation, usually with local analgesia.

6.3.2 Excisional techniques

1. Cold knife biopsy
2. Laser cone biopsy
3. Large loop diathermy (LLETZ or LEEP)
4. Hysterectomy: abdominal or vaginal.

The most common modes of treatment are the cryotherapy (ablative) and the LLETZ (excisional).

Cryotherapy:

- Cryotherapy is an acceptable, affordable, safe and effective treatment of ectocervical CIN in both low- and high-resource settings.
- Compared to the equipment and supplies required for LEEP, cryotherapy costs much less and does not require electricity.
- Accessibility to treatment is increased since primary health care personnel other than physicians can be trained to perform cryotherapy under monitoring and supervision.
- In suitable patients cryotherapy cures 90% of CIN overall but is not recommended for lesions involving the endocervix or vagina.
- Pending answers to questions on the risk of transmission and acquisition of STI's and HIV during the post-cryotherapy healing period, patients are advised to avoid intercourse or to use condoms at least one month.

Cervical conization (LLETZ or LEEP):

- Cervical conizatin is safe and effective in the management of CIN 2/3
- Cold knife cone and loop electrosurgical excision procedures appear to be equally effective in the treatment of cervical dysplasia.
- Follow up after cervical conization should be based on pathology results and the resource setting.
- The "see-and-treat" approach is cost-effective in low resource settings.
- Cervical conization should be avoided in pregnancy unless there is invasive cancer.

Table 10: Follow up of Women Treated for Preinvasive Cervical Abnormalities

Modalities of treatment	Histology/Pre-treatment smear history	Follow up
After conservative treatment	Low grade CIN	6, 12 and 24 months and then routine screening
After conservative treatment	High grade lesion	6, 12 and annual cytology for 9 years and then routine screening
After hysterectomy	(CIN2, CIN3, CGIN)	No vault smear
After hysterectomy	Routine recall in last10 years, No CIN	Vault smear 6 months after hysterectomy
After hysterectomy for CIN	Less than 10 years, Routine recall, No CIN	Vault smear 6 and 8 months after hysterectomy
After hysterectomy for CIN	Complete excision of CIN	Follow up as if the cervix is still in situ

(Ref: Wai: BJMP: 2008:1(2): 18-22).

6.4 Management of cervical cancer

The options for treating each patient with cervical cancer depend on the stage of disease. The stage of a cancer describes its size, depth of invasion (how far it has grown into the cervix), and how far it has spread.

Although the choice of treatment depends largely on the stage of the disease at the time of diagnosis, other factors that may influence the options are our age, general health, individual circumstances, and patient preferences. All risks and side effects of the various treatments should be fully understood by patients before making a decision.

The 3 main methods of cancer treatment are surgery, radiation therapy, and chemotherapy. Sometimes the best treatment approach uses 2 or more of these methods. Patient recovery is the goal of cancer care team. If a cure is not possible, the goal may be to remove or destroy as much of the cancer as possible to help for living longer and feeling better. Sometimes treatment is aimed at relieving symptoms. This is called *palliative treatment*.

6.4.1 Follow-up care

When treatment ends, the doctors will still want to watch the patient closely through regular follow-up appointments. During these visits, doctors will ask questions about any problems and perform thorough examination, including regular pelvic exams and Pap tests. Lab tests and x-rays or other imaging tests may also be done looking for signs of cancer and long term effects of treatment.

7. Cervical Cancer Prevention

Cervical cancer (not precancer) prevention is based on 2 essential points:

1. Primary prevention which is based mainly on vaccination and could be supported by certain modifications in lifestyle
2. Secondary prevention which is the cervical screening and early detection of cervical precancerous lesions (this is discussed previously)

7.1 HPV vaccine:

Currently there are two types of vaccines worldwide against HPV as follows:

1. Gardasil (Merk): this is a quadrivalent vaccine against HPV types 16, 18,6,11.

2. Cervarix (GSK): this is a bivalent vaccine against HPV types 16, 18.

The current recommendations for both vaccines and vaccination in general are:

- Both new vaccines are prophylactic vaccines preventing HPV-16 and -18 primary infections. They do not clear existing HPV infection or treat HPV-related diseases.
- Both vaccines induce high serum neutralizing antibody levels against HPV 16 and 18 in more than 99% of females who are naïve to specific HPV types.
  Neutralizing antibodies correlate with vaccine efficacy. There may be some cross immunity against 31/45 as well.
- Efficacy against surrogate markers such as persistent HPV type-specific infection and precancer lesions such as CIN 2 or higher is more than 90% for both vaccines.
- International and national bodies have reviewed the safety and efficacy data for both vaccines and approved their use in over 100 countries.
- Current evidence and WHO recommendations supports HPV vaccination of young adolescent girls (9 or 10 through 13 years of age) prior to onset of sexual debut to prevent cervical cancer in later life.
- Both vaccines continue to show good safety profiles similar to other commonly administered vaccines. Most common adverse events reported that are statistically significant for both vaccines are injection site pain, swelling or erythema.
- National level introduction schemes and demonstration projects have shown a high level of acceptability and coverage rates when HPV vaccines are delivered through school-based programs. Similar levels of success have been demonstrated in both high and low-resource settings.
- Cervical cancer screening and treatment for precancer should continue as per national guidelines as the currently available vaccine prevents infection caused by HPV 16 and HPV 18.

Still vaccination and screening are complementary strategies, and synergy in a cost- effective manner will be required for the next few decades. Both vaccines are expensive so it is important to know the prevalence of cervical HPV in the community and do a careful cost effectiveness

study before introducing the vaccine in the community. The cost per single dose ranges around 100 USD.

8.2 Sexual contact:

Completely avoiding all sex or sexual contact is an impractical way to prevent infection with HPV. Condoms provide partial protection, but not complete protection because they do not cover all areas of the genitals. Having a limited number of sexual partners may reduce the risk of HPV infection.

3- Stop smoking:

Women who smoke cigarettes are at increased risk of developing cervical cancer .Women who smoke and have an abnormal Pap smear can reduce their risk of cervical cancer by quitting smoking.

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Annex 1

Performance Checklist for Breast Examination

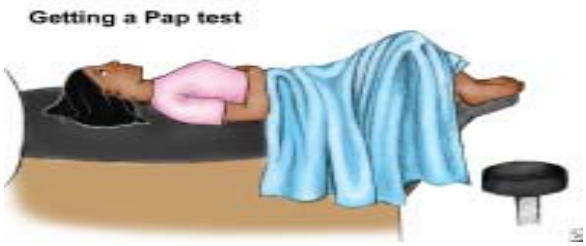
Task	Achieved		Comments
	Yes	No	
1. Welcome the client			
2. Explain breast examination procedure, and answer questions.			
3. Wash hands and dry completely.			
4. Examine breasts visually for: • symmetry • dimpled area • localized skin changes • nipple abnormalities.			
5. Place lotion or jelly on breast if desired to reduce friction			
6. Palpate each breast, beginning at periphery and working toward center, using small, circular motions: • Masses or nodules. • Irregular thickening. • Tenderness			
7. Palpate each axilla: • axillary tail of breast. • axillary lymph nodes or masses.			
8. Palpate and examine each nipple: • retraction or other abnormality, • scaling or eczema of surface of nipple, • discharge on gentle squeezing.			

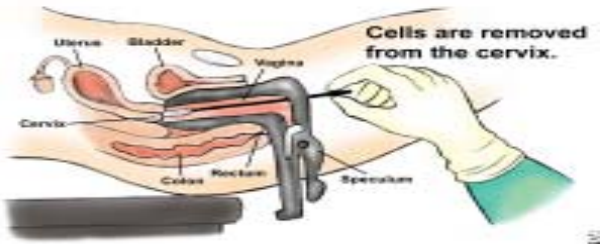
Task	Achieved		Comments
	Yes	No	
9. Inform the client that the procedure is over and she can rest comfortable.			
10. Discuss findings of examination with woman.			
11. Thank the woman and teach her how to perform Breast Self-Examination (BSE).			

Annex 2

Performance Checklist for Cervical Cytology (Pap smear)

I. General Principles			
Task	**Achieved**		**Comments**
	Yes	**No**	
1. Welcome the client			
2. Explain your plan of action			
3. Obtain client history			
4. Assess risk factors			
5. Assess eligible criteria to participate in the screening program			
6. Wash your hands			
7. Obtain the vital signs (blood pressure and pulse rate)			
8. Assess general appearance			

II. Pre-Procedure Preparation			
Task	**Achieved**		**Comments**
	Yes	**No**	
1. Assure that all equipments and instruments are ready, functioning and clean/sterile if needed: - 3 glass slides. - Spatula/brush. - Speculum. - Latex Gloves. - Fixator (alcohol, hair spray). - Pen for labeling.			
2. Assure that the couch is clean with a towel/draw sheet or disposable paper roll is placed.			
3. Request the client to lie on the examination table on her back with her knees up and bent and her feet in stirrups (rests).  			
4. Cover the client's lower half with a cloth to provide sense of comfort and feeling of privacy.			
5. Adjust the side light to the suitable angle.			

III. Procedure			
Task	**Achieved**		**Comments**
	Yes	**No**	
1. Explain the procedure to the client and assure her that it will only take a minute, but that there will be a slight discomfort from the speculum insertion.			
2. Clean the vagina with antiseptic solution (front to back using each cotton swab once).			
3. Ask the client to take a deep breath to ease the insertion of the speculum into the vagina.			
4. Inspect the vagina and the cervix carefully.			
5. Obtain a sample of mucus and cells from the cervix and endocervix (the opening of the cervix) using a wooden scraper or a small cervical broom. 			
6. Spread the obtained cervical cell sample into three glass slides evenly and sprayed with a fixative. This sample is sent to the lab for close and careful examination under a microscope.			
7. Assure the name of the client is being documented with the cytology form.			

8. Inform the client that the procedure is over and she can rest comfortable.			
9. Thank the client and instruct her when to come back for result.			

Steering committee members involved in the preparation of the Guidelines for Early Detection and Periodic Screening of Breast and Cervical Cancers in Primary Health Care Settings in Iraq

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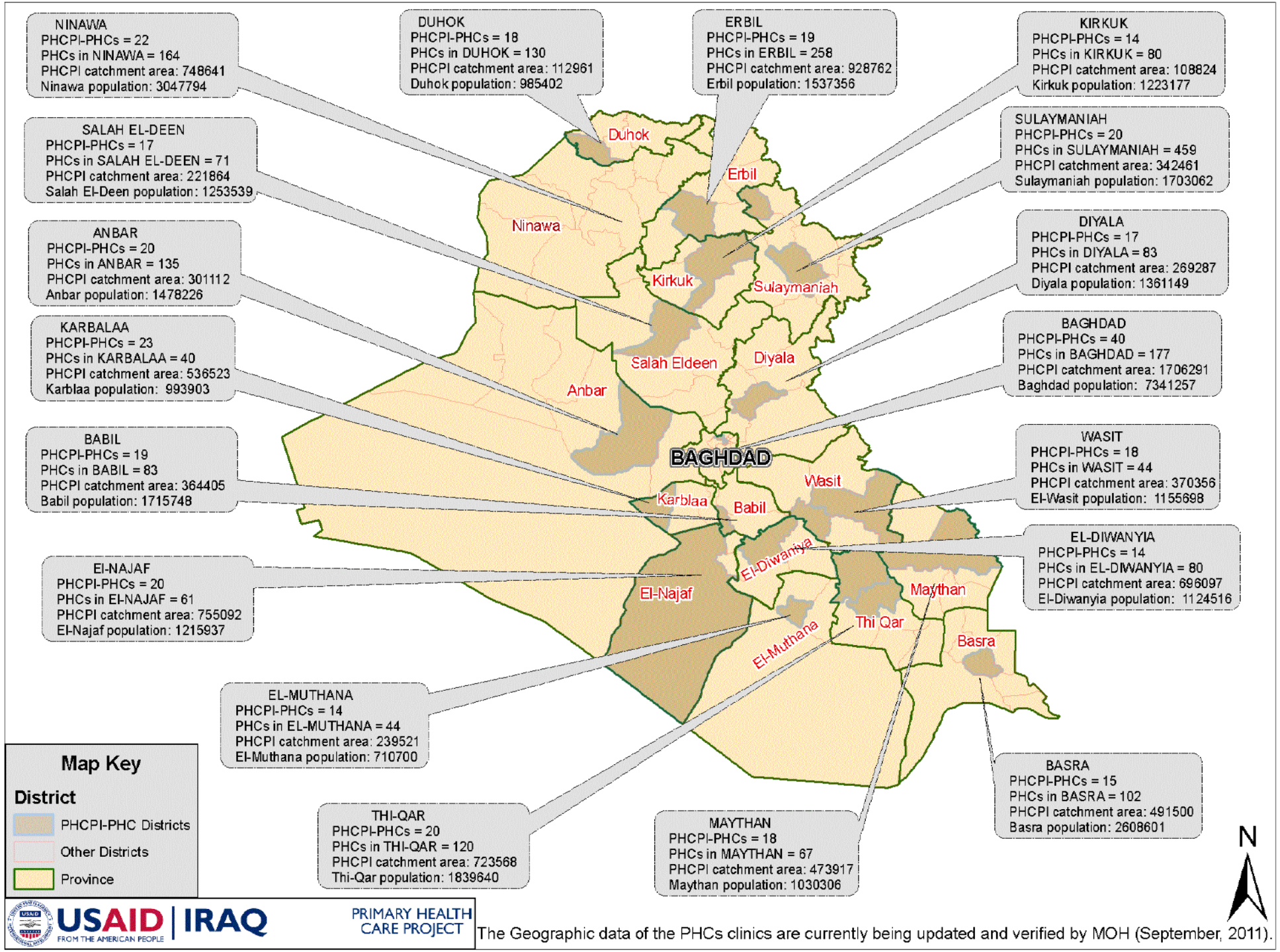
PHCPI-PHCs population mapped to IRAQ population



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PRIMARY HEALTH CARE PROJECT

The Geographic data of the PHCs clinics are currently being updated and verified by MOH (September, 2011).

U.S. Agency for International Development
Primary Health Care Project In Iraq
http://phciraq.org/
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