FOGSI FOCUS

Breast Diseases

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Foreword

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Message

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Dear FOGSIANS,

Greetings to each one of you. August is month dedicated to breastfeeding, especially the first week from 1st to 7th August is Breastfeeding Week, and we at FOGSI have dedicated the month to the problems associated with the breast. Being gynecologists, we are still debating whether the diseases of the breast fall in our domain or not. I would like to ask everyone one question, if a girl, lady, or a woman has any problem associated with the breast, whom will she go to first? If we say for the breastfeeding, the domain is ours, but for the rest whosoever, are we correct? The second question which I would like to raise is, why less and less of us obstetricians initiating breastfeeding, being mothers ourselves, being knowledgeable about the advantages for the baby and the mother too. My third question is, why being the proponents of women's health, we are not able to counsel women about being careful about their health and why is breast cancer already the major killer in our country? Simple measures like self-examination of the breast and mammography every three years could save many a lives. Dear friends, we have a lot of responsibilities on our shoulders and maybe we also think, why only us? I can only tell you, because "you are the chosen ones." Let us all take a pledge that we will execute our duties to the best of our capabilities and promote preventive care more than curative care. I will urge all of us to wear a pink ribbon all this month to remind us of our pledge.

My heartiest congratulations to Dr Kawita Bapat and her team for taking up this unique concept and focusing on the neglected issues of womanhood.

"My mission in life is not only to survive but to thrive and to do so we need some passion, some compassion, some humor, and some style."

Let us all passionately provide compassionate care with style and not let anything in this world deter us from doing so. Let us help women of our country to stay in the pink of their health.

Looking forward to seeing you all soon.

Jaideep Malhotra

Foreword

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President FOGSI and ICOG (2014–15)
President - MOGS (2013–14)

Dear Friends,

Hearty congratulations to Dr Kawita Bapat, Chair of FOGSI Breast Health Committee, and Dr Jaideep Malhotra, President FOGSI 2018, for putting their heads together and envisaging a brilliant conference and FOGSI FOCUS on this very important subject.

Kawita's conference "BREASTCON" will focus on the subject of breast health which is an often neglected subject. Breast health is an important component of a woman's overall wellness. Women frequently seek medical advice when they are concerned about breast discharge, lumps, size, pain, and skin changes. While many changes in the breast are related to hormone changes during menstruation, if there is something different it merits a visit to a gynecologist. The primary step a woman can take to maintain breast health is to take the time to understand the anatomy of the breast and schedule regular self-breast examination.

Yes, breast cancer is on the rise, so creating awareness for early detection is essential. Women can help with the early detection and treatment of breast cancer by playing an active role in their own health care. While there are some different opinions from medical organizations on the value of breast self-exams, all agree about the value of annual clinical breast exams, and the importance of regular mammograms after the age of 40–42 years.

General measures for prevention of any disease starts with a change to healthy lifestyle with plenty of physical activity, keeping weight control, healthy eating with plenty of fruit, vegetables and fiber, adequate sleep, and positive thinking. It is never too late to change oneself!

Globally, breast cancer is the most common female cancer, comprising 23% of all cancers that are newly diagnosed in more than 1.1 million women each year. It is also the most common cause of cancer-related death among women worldwide, with case fatality rates highest in low- and middle-income countries (LMCs). The annual global burden of new breast cancer cases is projected to be 1.5 million, with an ever-increasing majority from LMCs.

Evidence-based guidelines outlining optimal approaches to breast cancer detection, diagnosis, and treatment have been well-developed and disseminated in several high-resource countries. However, these guidelines define optimal practice, and, therefore, have limited utility in LMCs. Hence, there is a need to develop clinical practice guidelines oriented specifically toward LMCs, which take into consideration existing health care resources. So FOGSI can join hands with the Breast Health Global Initiative, a global health alliance of organizations and individuals which strives to develop, implement, and study evidence-based, economically feasible, and culturally appropriate guidelines for international breast health and cancer control for LMCs to improve breast health outcomes.

So friends, you will realize that this initiative by Dr Kawita Bapat is very important. Creating awareness and helping early detection and appropriate referral should be taken seriously by all FOGSIANS.

Wishing this initiative and BREASTCON all the best!

10th June, 2018.

Preface

Being a practicing gynecologist for 30 years. We routinely deal with breast disease in day-to-day practice as a primary physician.

Basic knowledge of breast disease is as important as any other health issue like cholesterol testing in menopause or any other problem of uterus and ovaries. In fact, identification of occult breast disease could be the most important contribution a gynecologist can make during routine examination.

Breasts are made up of hormone responsive tissues, which develop at time of puberty. It is an important reproductive organ that undergoes changes during pregnancy, lactation, and late reproductive years. It is an important sex organ that influences body image and sexual function.

The designation of obstetrician and gynecologists as a primary physician for women imposes responsibilities for breast. Breast cancer is not only disease entity of breast.

This FOGSI FOCUS is complete guide for healthy breast disease in different scenarios, right from pediatric to geriatric. This FOCUS has all the salient aspects of breast that we need to understand as gynecologist. At the end of these pages on breast, readers should gain proficiency in treating of breast diseases. This FOGSI FOCUS will definitely serve as an eye opener on the importance of treating breast diseases with a scientific approach.

I wish to thank the FOGSI president Dr Jaideep Malhotra for her invaluable support in publishing this FOGSI FOCUS and providing me an opportunity to make this paramount contribution to medical literature.

I owe my gratitude towards my husband Dr Surendra Bapat for his immense support in publishing this work of literature.

Kawita Bapat

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Breast: Gynecological Perspective

Kawita Bapat

INTRODUCTION

The obstetrician and gynecologist may be the primary physician, sometimes the only physician seen by women of childbearing age on a regular basis. Basic knowledge of breast disease is as important as any other health issue like cholesterol testing in menopause or any other problem of uterus and ovaries. In fact identification of occult breast disease could be the most important contribution a gynecologist can make during routine examination.

BREAST IS A GYNECOLOGICAL ORGAN

Breasts are made up of hormone responsive tissue, which develop at time of puberty. It is an important reproductive organ that undergoes changes during pregnancy, lactation, and late reproductive years. It is an important sex organ that influences body image and sexual function.

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GYNECOLOGIST AS PRIMARY PHYSICIAN

Breast disease affects many women and a large number of them visit gynecologists for benign conditions like abnormal development, adolescent problems, secretion, breastfeeding, cyclical mastalgia, fibroadenoma, nodularity, and nipple discharge. Underneath majority of these complaints are worries about development of breast cancer. Being a primary physician the importance of these complaints and disorders lies in their history, incidence, and discrimination, between benign and malignant disease. A large overlap exists between the symptoms of benign and malignant disease with the latter basically an asymptomatic disease.

The difficulty to diagnose breast cancer is a major cause for anxiety and uncertainty to both patient and physician.

One of the most common causes of cancer in women is cancer of breast. Given the incidence of mortality rate due to breast cancer, breast screening must be the part of primary care of all women attending a gynecologist.

An important future role for gynecologists in issues of breast health, Ideally, the optimal screening test for breasts will focus on the detection of preinvasive disease, without the potential to metastasize. Detection and effective management of such lesions will prevent major treatment related morbidity and breast cancer mortality.

The routine management of hyperplastic and preinvasive diseases in the breast in future hardly is only surgical, given the difficulty to detect and accurately excise such small lesions.

An important future role for gynecologists in issues of breast health these lesions represent disorders of growth, which are highly hormone responsive. The role of growth and hormonal manipulation, as well as medical and radiological follow-up will most likely increase. Given the current rapid development of designer drugs, hormones, the intricate interactions between different drugs, the hormonally sensitive tissues, involvement in this treatment plan will necessitate an in depth knowledge of hormonally sensitive organs, drugs, hormones, and hormone receptors.

Debatable issues whether gynecologist should develop:

- Proper ambulatory surgical facilities suitable for performing breast biopsies
- Perform biopsy for all true solid three-dimension masses
- Refer to oncosurgeon
- Breast disease both benign and malignant should be included in teaching program for gynecologists.

The American board does not recommend that every obstetrician and gynecologist must be trained to perform open surgery for breast cancer. However, emphasizes on

screening examination of breasts and recommends special training and workshops to be held for training in surgical treatment of breast disease.

NEW GUIDELINES

Women with average-risk (most women) should begin yearly mammography at the age of 50 years. At the age of 55 years women should have mammography every other year. Regular mammography should continue as long as woman is in good health.

Recommendations

- In many parts of the world the surgically trained gynecologic oncologist participates in treatment as well as detection and diagnosis of breast disease
- The fight against breast cancer requires insights and skills of all the physicians and scientists who can make a contribution in this field and multispecialty approach at one stop
- In this era of subspecialty, there is need for multidisciplinary approach to breast disorders especially cancer of breast
- Mammography has the ability to detect prepalpable invasive and preinvasive carcinoma breast
- Magnetic resonance imaging is extremely promising but expensive modality to diagnose early carcinoma breast
- The Federation of Obstetric and Gynecological Societies of India/International Conference on Obstetrics and Gynecology (FOGSI/ICOG) recommends that obstetricians and gynecologists should have:
  - Understanding of breast cancer
  - Basic knowledge of the steps required for diagnosis and treatment
- Breast cancer may be individualized depending on:
  - Extent of the disease
  - Individual tumor features.

CONCLUSION

Breast disease is as important as any other women's health issue. The identification of occult breast disease could be the most important contribution gynecologists make during the routine examination of women. Breast diseases should be included in the teaching program for gynecologists and should be covered thoroughly enough to enable the gynecologist to confidently make a diagnosis of both benign and malignant disease. We often address cosmetic concerns about breast and gynecologists often manage postpartum breast complications. The incidence of breast cancer is on the rise. Early detection is vital as prompt treatment gives a normal 5-year survival rate. Hence, breast examination should be an integral part of examination of all patients. Prompt detection is possible with both clinical breast examination supplemented with ultrasonographic examination. Given the incidence and mortality rates of breast cancer, breast screening must be the part of primary care for all women.

2

CHAPTER

Anatomy and Physiology of Breast

Sangeeta Jain, Vipin Jain, Surbhi Jain

Breast is a modified apocrine tubulo-alveolar gland, consisting of 15–20 lobes radiating out from nipple; which are separated from each other by adipose and collagenous connective tissue. These fibrous septae are called Suspensory (Cooper's) ligaments; anchoring inner skin layer to deep fascia, making compartments (Fig. 1). That is why incisions of an infected gland is made in radial direction. Prolongation of upper, outer quadrant of breast tissue under the axillary fascia forms "tail of Spence or axillary tail." Breast lies in a pocket of superficial fascia which enables it to be dissected in a relatively avascular plane.

Breast gets its arterial blood supply from internal thoracic artery, external thoracic artery, intercostal artery, and thoracoacromial artery. Drained by veins which form a ring around the base of nipple, called "circulus venosus," then to external and internal mammary veins. Breasts are supplied by anterior and lateral thoracic nerves derived from T3–T6 spinal segments.

Lymphatic drainage of breasts is very important because of anastomosing channels between both breasts. Glandular lymphatics drain anterior axillary (pectoral) nodes to central axillary nodes, then to apical nodes, to deep cervical nodes

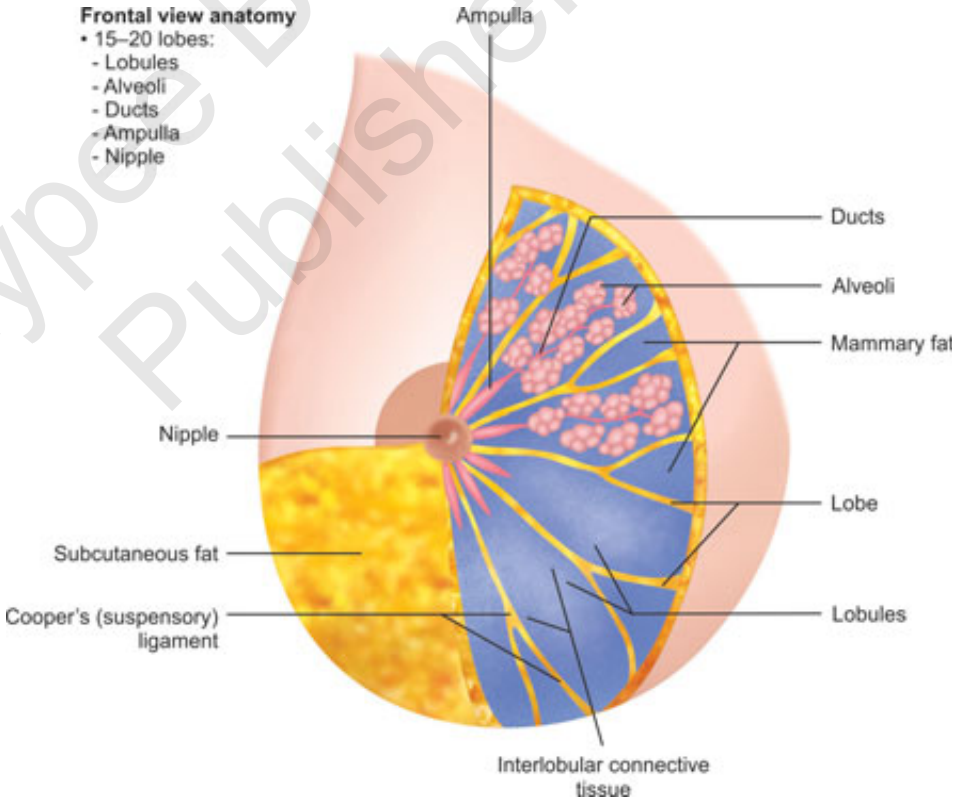

Figure 1: Frontal view of anatomy.

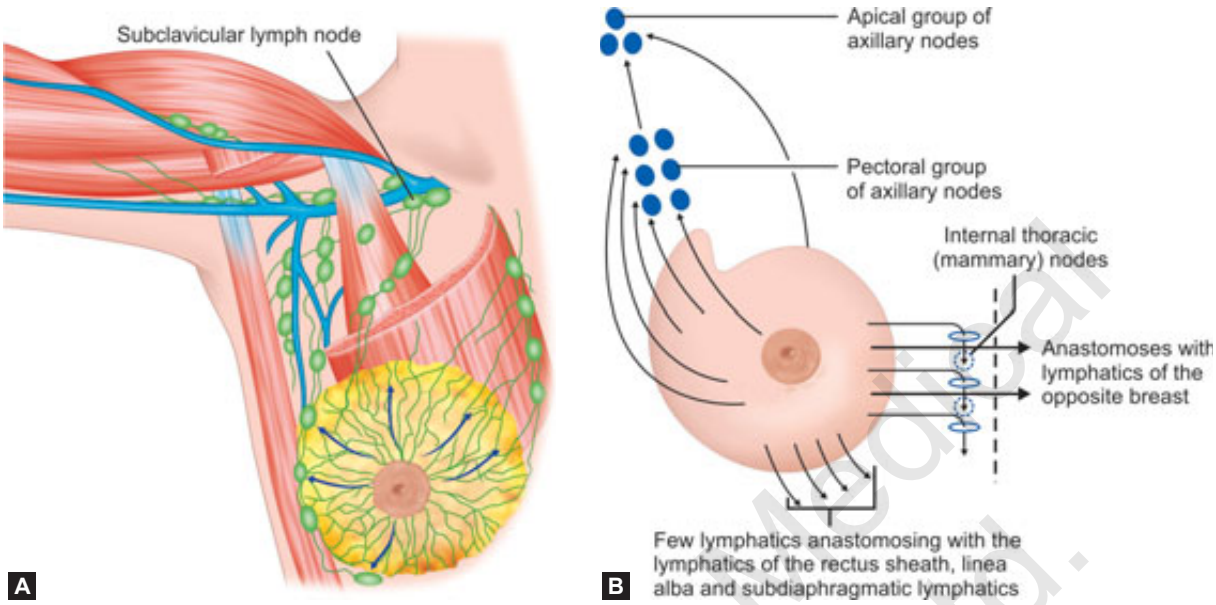

Figure 2: Surgical and line diagrams: Lymphatic drainage system of the breast.

and then subclavicular (subclavian) nodes. Medial quadrants drain into parasternal nodes. Superficial skin, areola, and nipples form large channels and drain to pectoral nodes. Seventy-five percent of lymph from breast drains into axillary lymph nodes (Fig. 2). In patients with localized cancer, a simple mastectomy, followed by radiotherapy to axillary lymph nodes is treatment of choice.

Lactogenesis is under endocrine control during pregnancy and for few weeks after birth, i.e., under the influence of prolactin, human chorionic somatomammotropin, growth hormone, cortisol, insulin, parathyroid hormone, etc. Once mother's milk comes in, milk synthesis is controlled locally, i.e., autocrine phase of lactogenesis starts. Montgomery tubercles present on areola enlarge during pregnancy and lactation and may produce a scent that guides baby to breast. Breast feeding provides a protective mechanism against breast carcinomas.

Surgically, breast is divided into upper lateral, upper inner, lower lateral, and lower inner quadrants. Sixty percent of breast carcinomas occur in upper lateral quadrant. Breast cancer is the most common cancer in the world. Simple self-breast examination after the periods can help females in detecting breast masses at the earliest and is the need of the hour.

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3

CHAPTER

Development of Breast

Dolly Mehra

INTRODUCTION

Mammary glands (breast) are distinguishing feature of mammals and a primary symbol of femininity in our culture. An understanding of the development of the mammary gland is essential to anyone asked to evaluate and treat aberrancies of such development.[1]

The mammary gland is considered to be a modified and highly specialized type of apocrine gland. The human breast consists of the parenchyma and stroma, originating from ectodermal and mesodermal elements respectively. Breast development occurs in distinct stages via complex epithelial-mesenchymal interactions, orchestrated by signaling pathways under the regulations of systemic hormones. The human breast houses the mammary gland that produces and delivers milk through development of extensive tree like network of branching ducts. It is characterized by extensive remodeling in adulthood, a factor that increases its susceptibility to carcinogenesis.[2]

EMBRYONIC STAGE

Mammary glands begin to develop early in embryonic life. They are derived from two thickened strips of epidermal ectoderm, the primitive mammary ridges or milk line, which appears during 6 weeks. The ridges extend from axilla to the inguinal region, but rapidly regresses except in the thorax, in the pectoral region at the fourth intercostal space.[3] The earliest stages of embryogenesis are largely hormone independent.[4,5]

Toward the end of first trimester, the mammary buds that persist in the thoracic region penetrate the underlying mesenchyme.[6] The primary buds begin to grow downwards into the underlying mesenchyme under the inductive influence of regulatory hormones secreted by the mesenchyme.[7] The primary bud enlarges moves to ventral position. Indentations appear along the basolateral margins to become sites for future secondary mammary outgrowths. The cells of primary mammary bud continue to evaginate into the underlying stroma and become surrounded by fibroblast like cells within the collagenous mesenchyme. So at the end of first trimester, a well-defined mammary bud penetrating into the upper dermis can be observed. Two type of epithelial cells (central and basal) can be seen.[8] The mesenchymal cells differentiate to form fibroblasts, smooth muscle cells, capillary endothelial cells and adipocytes.

In the second trimester, secondary epithelial buds appear from the indentations on the primary mammary bud. Each secondary epithelial bud which grows into the mesenchyme has a slender stalk and bulbous end.[8] These secondary epithelial buds canalize and coalesce forming secondary buds that give rise to lactiferous buds. The epithelial cells lining the lactiferous ducts are arranged into two layers with the layer adjacent to the lumen gaining secretory function while the basal layer differentiate into myoepithelial cells. By the end of second trimester, basic framework of gland is ready with tubular structure in a bed of dense fibroconnective tissue stroma. The surrounding areola is formed by the ectoderm.

Repeated branching of the secondary epithelial buds and canalization occurs in the third trimester.[8] The epidermis in the region of future nipple becomes depressed, forming the mammary pit.[9] The lactiferous ducts drain into the retroareolar ampullae that converge into the pit. The nipple is created with smooth muscles aligned in circular and longitudinal fashion. Due to complex interplay between fetal, placental and maternal hormones at the final weeks of gestation, the loose fibroconnective tissue stroma increase in vascularity.

At term approximately 15–20 lobes of glandular tissue have formed, each containing lactiferous duct that open onto the breast surface through the mammary pit. Both the surrounding skin and the fibrous suspensory ligaments of cooper that anchor the breast to pectoralis major fascia provide support to the breast.

INFANT BREAST

At birth the breast is usually palpable with varying amounts of tissue and no significant difference between the genders. Falling levels of maternal estrogen in neonate stimulate the neonatal pituitary gland to produce prolactin, which results in unilateral or bilateral breast enlargement and/or transient secretions from breast in neonates. Soon after birth, the nipples are everted because of proliferation of underlying mesoderm, areolae increase in pigmentation.

The first 2 years of life is a critical period for breast maturation.[10] Anzbagahan et al. described morphological and functional maturation stages from birth to 2 years of age. The morphological changes of the breast are depicted by the degree of glandular differentiation and functional maturation is characterized by secretory capacity of the lining epithelium.

After 2 years of age the infant breast remain relatively quiescent.[11]

PUBERTAL DEVELOPMENT

Sexually dimorphic development of breast first begins at puberty, under the influence of sex hormones, especially estrogens.[12] The actions of estrogen depends upon the presence of pituitary growth hormones and the ability of growth hormone to stimulate production of insulin-like growth factors (IGF-I) in the mammary gland.

The age of these pubertal changes varies from 8 and a half to 13 and a half years. Significant variations are seen in individual depending upon level of pubertal maturation, ethnicity and hormonal concentration.

Tanner described macroscopic stages of breast development at puberty:

- Stage 1: The preadolescent phase with only elevation of the papilla
- Stage 2: Formation of breast bud with elevation of the nipple as a small mound of breast tissue along with enlargement of the diameter of areola. This stage correlates with the entity of thelarche
- Stage 3: Further enlargement of breast and areola. Between Tanner stage 2 and 3, discrepancy in size between the breasts is commonly seen. This is at the age of 12.5 years
- Stage 4: There is enlargement of nipple and areola, leading to formation of secondary mound on the breast. Average age 13–14 years. Menarche occurs between stage 3 and 4.
- Stage 5: Recession of the areola occurs on the breast which results in loss of separation of contours. Average age is 15 years.

The average time spent between Tanner stage 2 and 5 is 4–4.5 years. The most marked increase in size and diameter of the nipples is seen between stage 3 and 5, the average increase in diameter is 5–6 mm.

CELLULAR CHANGES AT PUBERTY

Cellular changes occur at both stromal and parenchymal levels, during pubertal development but increase in fibrous and fatty tissue of stroma precedes the ductal changes. Under the influence of estrogen, first the stromal changes occur, following which ductal elongation and dichotomous branching occurs. The epithelium forms into a branching, bilayered ductal structures, consisting of an outer basal myoepithelial layer of cells and an inner luminal cell layers that can be divided into ductal luminal cells, lining inside of ducts and the alveolar luminal cells, which secrete milk during lactation. More alveoli are laid during each menstrual cycle, but significant degree of alveolar expansion only occurs during pregnancy.

Ductal elongation and complex branching originates at the site of the terminal end buds. The primary ducts that reach the nipple form a complex of subsidiary ducts. The primary ducts branch into segmental and subsegmental ducts. The subsegmental ducts lead to terminal duct formation, which further subdivides to form several terminal ductules or acini.[13] A collection of acini arising from terminal duct along with the surrounding intralobular stroma is termed a terminal duct lobular unit,which is the functional unit of breast.

As ductal elongation continues the remainder of the space in the breast is taken up by adipose tissue, blood vessels, immune cells and fibroblasts. Estrogen is responsible for ductal elongation and progesterone for side branching.

Human female breast has lobular development of four types. Lobular type 1 consists of a short terminal duct ending in a cluster of secretory cells called alveoli. Lobule type 2, 3, and 4 consists of a terminal duct branching into several ductules and an increasing number of alveoli.

The adult nulliparous breast is complete in stromal and ductal maturation by 18–20 years of age and it contains type 1 lobules. The mammary glands remain in this mature, but inactive state until pregnancy.

REGULATION OF BREAST DEVELOPMENT

Mutual and reciprocal interactions between epithelial and mesenchymal cells are responsible for prenatal, infant, and pubertal breast development. The mesenchyme has inductive properties that lead to the migration and changes in cell adhesion of epithelial cells. Hormonal influence on this paracrine interaction between the mesenchyme and parenchyma exists at all stages of development. The formation of lactiferous ducts is induced by placental hormone entering the fetal circulation. Other hormones implicated but not proven in prenatal and pubertal development are progesterone, growth hormone, IGF-1, estrogen, prolactin, adrenal corticoid and triiodothyronine. Epidermal growth factors receptors are commonly present in prenatal breast.

CONCLUSION

Development of human breast is distinctive due to the extensive remodeling it undergoes into adulthood. Development occurs in various stages under the influence of several hormonal signals. The study of human breast development is essential to understand various congenital and acquired disorders of breast.

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4

CHAPTER

Adolescent Breast Problems

Mumtaz Pulikkathodi

INTRODUCTION

Puberty is marked by prominent changes in the size, shape, and function of breasts. It is an important sign of transition to adulthood. Abnormalities or anomalies of normal breast development can result in poor self-esteem or make the adolescent feel self-conscious; however, most breast abnormalities in children and adolescents are otherwise benign.

Adolescent breast problems may be broadly classified into:

- Developmental abnormalities
- Abnormalities of size and symmetry
- Breast pain
- Discharge from the nipples
- Breast abscess
- Breast mass.

DEVELOPMENTAL ABNORMALITIES

Most of these problems present in the infancy itself when the apprehensive parents bring the infant for an expert opinion. The problem of accessory breast tissue becomes evident mostly during the pubertal age and is first detected then.

- Athelia–means the absence of a nipple
- Amastia–the absence of breast tissue is called amastia. It results from the obliteration of milk line during embryogenesis. It is often associated with other congenital anomalies
- Accessory breast tissue–type of breast tissue present decides the nomenclature. Polymastia refers to the presence of any accessory breast tissue. Polythelia refers to supernumerary (or accessory) nipples.

Even though accessory nipples are present at birth they are usually recognized later in life. The most common site of the accessory nipple is just inferior to the normal breast but may occur at any point along the milk line from the axilla to the groin where appropriate regression during embryonic development did not occur.

The most common site for polymastia is the lower axilla.[1] In most cases, accessory breast tissue consists of a small areola and nipple, and sometimes glandular tissue also may be present.

Treatment

Because of the association polythelia and renal anomalies;[2] in some studies, a renal ultrasound is indicated in children with supernumerary nipples. If a renal anomaly is detected, pelvic imaging is needed as concomitant genital abnormality is a possibility.

Supernumerary nipples usually are asymptomatic.[3] Surgical removal may be indicated for cosmetic purpose.

Surgical excision of polymastia also may be done to prevent painful swelling during pregnancy and/or the rare development of fibroadenoma or a tumor in accessory breast tissue.[4]

ABNORMALITIES OF SIZE AND SYMMETRY

Small Breasts

Small breasts are also referred to as hypomastia or micromastia. Conditions that should be ruled out in girls with small breasts are abnormalities of pubertal development, hypothyroidism, ovarian failure, and androgen excess. Adolescents with bilateral small breasts and otherwise normal sexual development should be considered normal and reassured.

Breast Asymmetry

It is a common presenting complaint among adolescents. It is normal to have some amount of asymmetry. It may be more pronounced between Tanner stage 2 and 4 when the breasts are developing and usually improves by Tanner stage 5. Despite this improvement, 2% of adult women have some degree of breast asymmetry.

Treatment involves counseling. The adolescent may be reassured. Wearing a padded brassiere will be of cosmetic help. Permanent solution or marked difference in size will be a prosthetic insert.

Juvenile Breast Hypertrophy

Juvenile breast hypertrophy means a spontaneous overgrowth of breast tissue. It is extremely uncommon. The etiology could be an abnormal response to gonadal hormones.[5] Negative remarks from peers and backache could be bothersome to the young girl. The differential diagnosis includes juvenile fibroadenoma, nonbreast cancers, and phyllodes tumors.[6]

Treatment is decided by the stage of patient's growth. A backache can be managed by a proper fitting supportive brassiere. Antiestrogen and progesterone may be tried to decrease breast growth.

Once the full growth is achieved reduction mammoplasty can be offered for cosmetic reasons and/or chronic back pain. It doesn't interfere with breastfeeding in future.

Breast Atrophy

Breast atrophy could be secondary to weight loss from chronic diseases or eating disorders and the size may be restored with weight gain.

Tuberous Breast

It is a variant of breast development in which the base of the breast is limited and the nipple and areola are overdeveloped. The etiology is unknown. The available surgical options vary depending on the location of the hypoplastic breast tissue.

BREAST PAIN

It is also called mastalgia or mastodynia. Can occur during exercise, pregnancy, oral contraceptive use, and in fibrocystic change. History taking is important in deciding the cause of pain and thus choosing the appropriate treatment modality.

- Cyclical premenstrual poorly localized pain is usually due to physiological swelling. Treatment would include reassurance, a supportive brassiere, analgesia with ibuprofen and oral contraceptive pills
- If associated with physical activity, may obtain some relief by using a sports brassiere
- If the pain is induced by caffeine intake limiting its usage would be helpful
- If the pain is localized look for nodularity and cyst
- Whether there is a history of recent use of oral contraception. Pain related to oral contraceptive usage usually improves after the first few months of usage. If there is no relief, may have to reconsider continuing oral contraceptives
- Usage of contraceptive implants can also cause mastalgia
- History of drug intake is important. Mastalgia can be caused by certain drugs (e.g., phenothiazines, exogenous hormones, and marijuana)

Examine the breasts and regional lymph nodes. Look for cysts, abscesses, or localized inflammation.[7] Palpation of the chest wall can help to identify extramammary causes of chest pain, such as inflammation of the costochondral junctions (Tietze syndrome).[8] Treatment is removing the underlying cause and adding analgesics.

NIPPLE DISCHARGE

Nipple discharge is uncommon in children and adolescents, and most cases are associated with benign causes. In clinical evaluation it is important to identify:

- The appearance of fluid, milky, purulent, serous, etc.
- Whether it is spontaneous or provoked by manipulation
- Whether the discharge is unilateral or bilateral (bilateral nipple discharge is always due to an endocrinologic or physiologic process)
- Whether the patient is taking any medications associated with nipple discharge (e.g., some antipsychotics and antidepressants, among others) (Table 1)

TABLE 1: Medications that cause hyperprolactinemia

Type of medicine	*Frequency of prolactin elevation*
Antipsychotics, first generation	
Haloperidol	High
Fluphenazine	High
Chlorpromazine	Moderate
Trifluoperazine	Moderate
Antipsychotics, second generation	
Paliperidone	High
Risperidone	High
Asenapine	Moderate
Olanzapine	Low
Clozapine	None or low
Antiemetic and gastrointestinal	
Metoclopramide	High
Domperidone	High
Prochlorperazine	Low
Antihypertensives	
Methyldopa	Moderate
Verapamil	Low
Opioid analgesics	
Methadone, morphine	Transient increase
Cyclic antidepressants	
Clomipramine	High
Amitriptyline	Low
Selective serotonin reuptake inhibitors	
Fluoxetine, fluvoxamine, paroxetine, and sertraline	None or low

- Cancers present with spontaneous bloody discharge arising from a single duct and are exceedingly rare in children and adolescents.[8]

Differential Diagnosis

Milky Discharge

- It is characteristic of galactorrhea, which is typically bilateral
- Causes: Pregnancy, postpartum or postabortion states, hypothyroidism, hypogonadism, overstimulation from manual manipulation, certain drugs, and prolactin-secreting tumors
- Hypothyroidism is the most common cause of galactorrhea in adolescents[9]
- Investigation to identify the cause include a pregnancy test, prolactin level, thyroid function studies, luteinizing hormone, and follicular-stimulating hormone. In doubtful cases fat staining can confirm it.[10]

Purulent Discharge

Suggests an infection of the breast (e.g., cellulitis or abscess) and should be sent for culture with sensitivity testing.

Serous or Serosanguineous Discharge

Nipple discharge may also be caused by intraductal papilloma, fibrocystic changes, or rarely cancer.

Bloody Discharge

Bloody discharge is rare in infants and young children.[11] The most common cause is mammary duct ectasia, chronic nipple irritation (e.g., jogger's nipple), and rarely breast cancer.

BREAST ABSCESS

During puberty when breast changes are maximum it is more prone to develop mastitis. Mastitis results from entry of pathogen to the ductal system. Predisposing events could be trauma (sexual activity, hair plucking, nipple piercing), obesity, and mammary duct ectasia. Patient presents with complaints of pain and swelling. Examination would reveal swelling, erythema, warmth, tenderness, and induration. Purulent nipple discharge may be present.[12]

Differential diagnosis is a hematoma or fat necrosis which result from direct trauma. Clinically the solid nature differentiates fat necrosis from mastitis. Fluctuation will be present in an abscess. Ultrasonography also helps in the diagnosis.[13]

Management

- Supportive therapy (application of warm compresses and provision of breast support)
- Antimicrobial therapy (if a gram stain is not available, empiric coverage for *Staphylococcus aureus* and group A *Streptococcus*)
  - Cephalexin 25–50 mg/kg per day orally in 2–4 doses
  - Clindamycin 30–40 mg/kg per day orally in 3–4 doses
  - Cloxacillin 25–50 mg/kg per day orally in four doses
- Drainage of breast abscess—breast abscess may require ultrasound-guided fine needle aspiration or incision and drainage. Care must be taken to avoid the breast bud and to minimize the risk of hypoplasia or scarring.

BREAST MASS

Most of the breast mass in adolescents are self-limited and benign. Some of the common benign breast lesions seen in adolescents include:

- Fibrocystic disease
- Fibroadenoma
- Giant fibroadenoma
- Phyllodes tumor
- Mammary duct ectasia.

Malignant breast lesions, which are extremely uncommon in adolescents include:

- Primary breast cancer
- Metastatic cancer
- Secondary cancer.

Fibrocystic Change

Fibrocystic changes of the breast are common in adolescents. The etiology is unknown, but thought to result from an imbalance between estrogen and progesterone.

They present with painful breasts before menstruation and report improvement during menstruation. On examination, the fibrotic tissue may be palpated and is generally found in the upper outer quadrants of the breast. A serosanguineous discharge may be present.[14] Ultrasonography may be helpful in the diagnosis. Mammography is not indicated to evaluate masses in the adolescents, because a large amount of glandular tissue present in adolescents makes mammography difficult to interpret.[15]

The treatment includes mild analgesia with ibuprofen. Oral contraceptives improve symptoms in 70–90% of women.

Juvenile Fibroadenoma

Juvenile fibroadenomas are the most common breast lesions in adolescents[16] and account for 30–50% of breast masses in adolescents.

Usually, they are asymptomatic but may cause discomfort for a few days before the onset of menstruation. Examination reveals rubbery, well circumscribed, and mobile masses of average size 2–3 cm. They are most frequently found in the upper, outer quadrants. These characteristic features help in clinical diagnosis. In equivocal cases, ultrasonography and/or needle aspiration are helpful.[17] Ultrasonographic evaluation reveals a solid avascular mass that is well circumscribed. Histologically, fibroadenomas consist of proliferating stroma.

Management includes careful follow-up and reassurance. Most fibroadenomas in adolescents decrease in size, and some completely disappear with time.[17]

The frequency of follow-up: Fibroadenomas <5 cm can be observed at 1–2 month intervals for growth or regression. When the mass regresses, observation at 3–4 month intervals for up to 2 years. If the ultrasound characteristics are entirely consistent with a fibroadenoma, the mass need not be biopsied or excised unless there is overriding clinical concern.

The decision to proceed with excision is based on family anxiety, history of breast cancer, and the patient's age. However, if there is growth of the lesion, the lesion is greater than 5 cm, or the lesion persists to adulthood, excisional biopsy is warranted.[17]

Disadvantages of excisional surgery include scarring at the incision site, dimpling of the breast from the removal of a tumor, damage to the breast's duct system, and mammographic changes (e.g., architectural distortion, skin thickening, and increased focal density).

Giant Fibroadenoma

Giant fibroadenomas grow rapidly to greater than 5 cm and may compress or replace normal breast tissue. They should be excised because they cannot be easily distinguished from phyllodes tumors by physical examination, ultrasonography, or mammography.[18]

However, it has been reported in girls as young as 10 years of age, most are benign. Patients present with a large breast mass that is usually painless; the overlying skin may be shiny and stretched from rapid growth. A bloody discharge may be present if the nipple is involved. Ultrasonographic findings that are suggestive, but not diagnostic, of phyllodes tumors include lobulations, a heterogeneous echo pattern, and an absence of microcalcifications. The recommended treatment is excision; more radical measures may be indicated for malignant lesions.

Mammary Duct Ectasia

Mammary duct ectasia is characterized by distention of subareolar ducts with fibrosis and inflammation. A nipple discharge (multicolored, sticky) may be present if the fluid in the cyst is dark, it may appear as a blue mass under the nipple (sometimes referred to as "blue breast") The blocked ducts can predispose to infection, leading to mastitis or breast abscess. In addition, penetration of the duct wall by lipid material may be associated with fever and acute local pain and tenderness.

Mammary duct ectasia often resolves spontaneously, sometimes with a residual subareolar nodule. Surgical excision may be warranted for persistent or recurrent symptoms or an associated persistent cyst.[19]

Primary Breast Cancer

Primary breast cancer is exceedingly rare in children and adolescents.[20] Surveillance Epidemiology and End Results data from 2011–2015 list an incidence of invasive breast cancer of 0.1/100,000 for females between 15 and 19 years. The most common type was juvenile secretory carcinoma (>80%), followed by intraductal carcinoma. Rhabdomyosarcoma and lymphoma also may occur as a primary tumor of the breast.

Clinical Features

The most common finding of breast cancer in adolescents is a hard, irregular mass which may or may not be fixed to the underlying tissue. Additional findings include skin or nipple retraction, skin edema (peau d'orange), nipple involvement, nipple discharge, and axillary or supraclavicular lymphadenopathy.[21]

Risk Factors

Effective and accurate counseling for adolescents and their parents regarding breast cancer prevention should be a routine component of preventive health services for adolescents. Risk factors for breast cancer that may affect adolescent patients include a personal history of cancer and exposure to radiation. Smoking, alcohol consumption, and limited physical activity have also been associated with breast cancer.

Personal history of cancer: Malignancies that occur in the adolescent breast are more likely metastatic from another malignancy than primary breast cancer.

Radiation exposure and childhood cancer: Exposure to ionizing radiation (e.g., radiation therapy to the chest) and childhood cancer are risk factors for secondary breast cancer in adolescents. Guidelines for survivors of childhood cancer generally recommend that girls who received chest radiation during treatment for childhood cancer begin breast cancer surveillance with mammography or magnetic resonance imaging 8 years after treatment or at age of 25 years, whichever occurs last.

Metastatic Cancer

In the adolescent age group, most malignant breast masses are metastatic from other cancers such as Hodgkin lymphoma, non-Hodgkin lymphoma, or neuroblastomas, hepatocellular carcinoma, and rhabdomyosarcoma.[22] Rhabdomyosarcoma is one of the most common primary cancers to metastasize to the breast, occurring in 6% of female patients with rhabdomyosarcoma. Metastatic breast cancer may cause dyspnea, generalized skin rash, limb swelling, back pain, and hepatomegaly.

Secondary Breast Cancer

It is another category of malignancy that arises as a consequence of irradiation of the chest wall. Usually, irradiation is carried as a part of management for some other condition, like lymphoma.

CONCLUSION

Majority of the breast abnormalities in the adolescent are benign and could be physiological. Even though the

common causes of breast pain in adolescent are improper support and fibrocystic disease, the possibility of assault and mastitis should be kept in mind. Hormone assay and history of drug intake to be considered in girls presenting with discharge through the nipple. A breast lump is mostly due to physiological nodularity. Though cancer is rare in adolescents, it is essential to observe the mass through one or two menstrual cycles and if found to be persisting imaging is recommended. Imaging helps to differentiate between cystic and solid lesions and sonography is the ideal imaging technique. Fibroadenoma is the common breast mass and is managed by surgical excision. Other indications for surgery is mainly for cosmetic purpose in asymmetry, small or large breasts.

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5

CHAPTER

Gynecomastia

Poonam Goyal

INTRODUCTION

Gynecomastia is enlargement of breast in males with firm tissue extending concentrically beyond nipples.[1,2]

This condition is an endocrine disorder and is usually benign in nature. It is self-limiting most of the times. However, it causes a lot of anxiety and patient seeks medical advice. A complete workup and evaluation for the cause is indicated in all.[1-3]

EPIDEMOLOGY AND PREVALENCE

It is the most important breast condition in males and should not be ignored. The prevalence of gynecomastia is reported to be between 32% and 62% due to the use of different diagnostic methods and different life styles.[1-5] In postmortem cases it is 40%. This wide variation is likely due to differences in what is considered to be normal subareolar glandular tissue, the diagnosing physician and most importantly variations in the age distribution of the patient populations. Pubertal gynecomastia usually begins at age of 10–12 years and peaks at the age of 13–14 years. It usually regresses within 18 months and is uncommon in males aged 17 years and older. The final peak occurs in older males; particularly in those aged 50–80 years,[5] with a prevalence of 24–65%. This is because of increase in adiposity with aging.

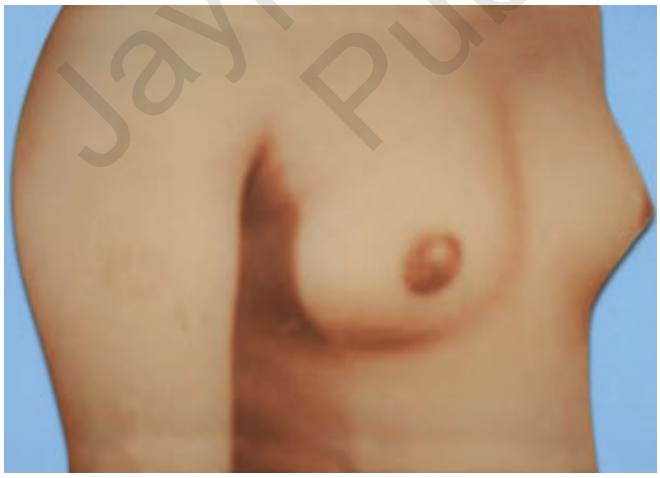


Figure 1: Male with gynecomastia.

SIGNS AND SYMPTOMS

The classic feature of gynecomastia is male breast enlargement more than 2 cm with soft, compressible, and mobile subcutaneous chest tissue palpated under the areola of the nipple in contrast to softer fatty tissue. This enlargement may occur on one side or both. Dimpling of the skin and nipple retraction are not typical features of gynecomastia. Milky discharge from the nipple may also be present and is seen in an individual with gynecomastia having a prolactin secreting tumor.[3,5] An increase in the diameter of the areola and asymmetry of chest tissue are other possible signs of gynecomastia.

DIAGNOSIS

A thorough history and examination of the patient is required.[6] For this in a male, evaluation of testicular development and penile size is done. Assessment of all secondary sexual characters is done. Gynecomastia is usually bilateral but may also be unilateral.

INVESTIGATIONS[6]

Complete blood check up with liver function, renal function, biomarkers for testicular function, thyroid function, and adrenal function are indicated. Additional tests include β-human chorionic gonadotropin (β-HCG),[7] 17-keto steroid, dehydroepiandrosterone, total testosterone, free testosterone,

follicule stimulating hormone (FSH), luteinizing hormone (LH), and estradiol.

Fine-needle aspiration cytology is done for differentiation of breast tissue from fat.

Mammography done only when malignancy is suspected.[8] Ultrasound of abdomen, testis is done if tumor is suspected to be the cause of gynecomastia. Ultrasonography of breast can also be done to confirm and see the extent of breast tissue.[7]

DIFFERENTIAL DIAGNOSIS

Condition must be differentiated from:

- Mastitis
- Breast cancer
- Pseudogynecomastia
- Lipoma
- Sebaceous cyst
- Dermoid cyst
- Hematoma
- Metastasis
- Ductal ectasia
- Fat necrosis.

CLASSIFICATION[9]

The spectrum of severity has been classified into following grades:

Grade 1: Minor enlargement of breast up to 2 cm, no skin excess.

Grade 2: Moderate enlargement of breast 2–5 cm, no skin excess.

Grade 3: Moderate enlargement of breast 2–5 cm with skin excess (Fig. 2).

Grade 4: Markedly enlarged breast >5 cm with skin excess (Fig. 3).

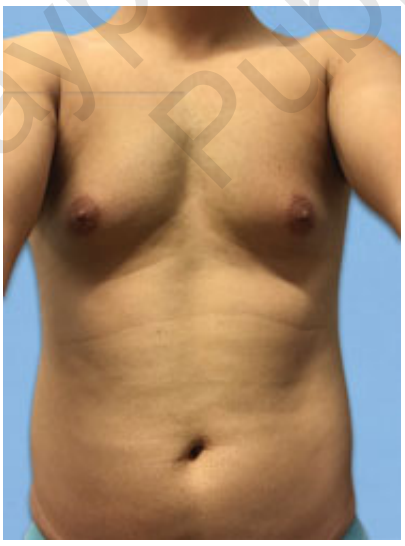


Figure 2: Grade 3 enlargement.

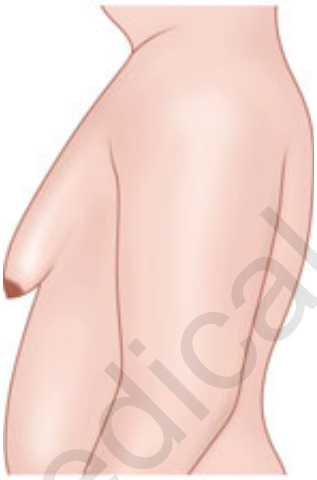


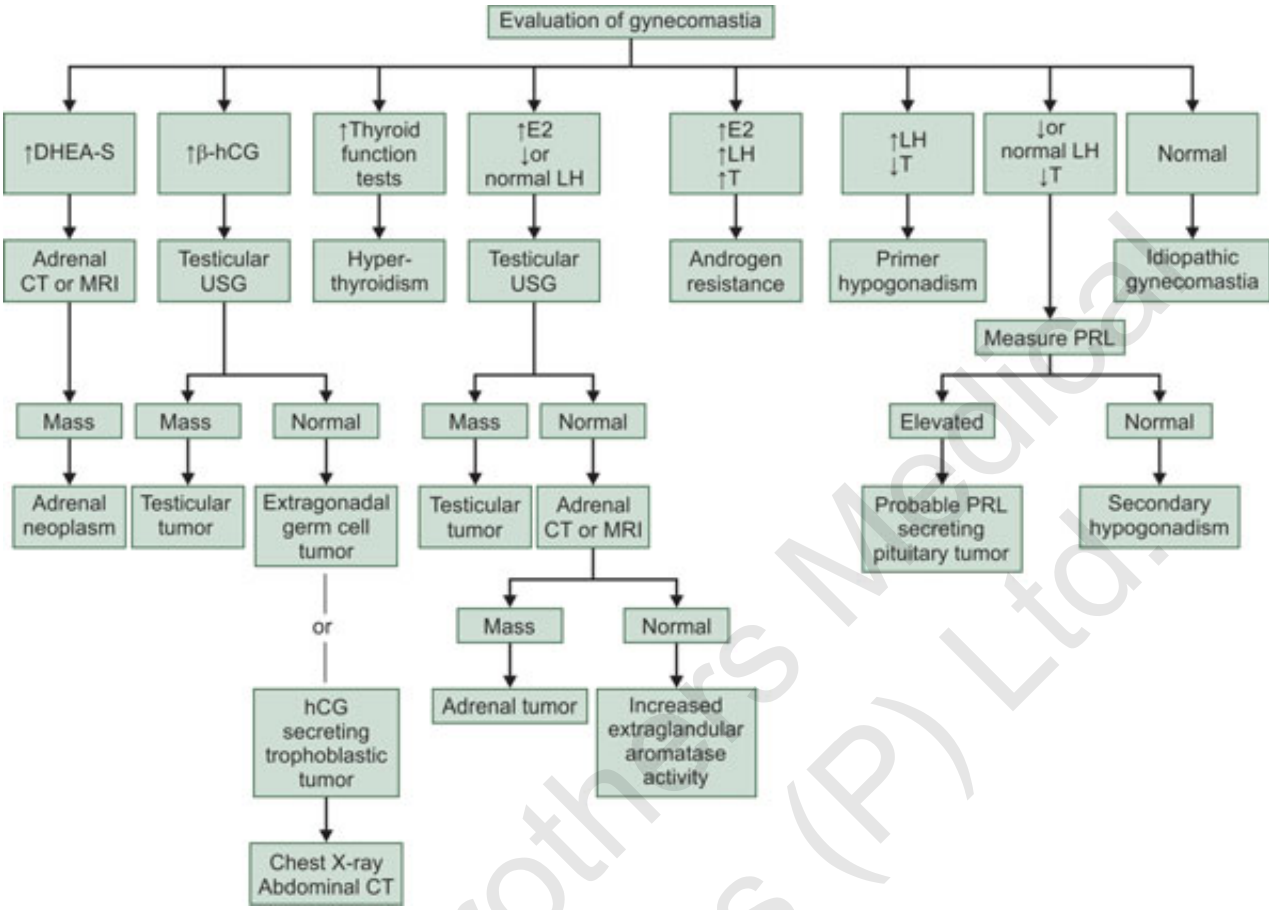
Figure 3: Grade 4 enlargement.

PHYSIOLOGICAL GYNECOMASTIA

Most of the neonates have breast tissue resulting from the transfer of maternal hormones via placenta. Another phase is pubertal, at around age of 14 years up to 60% boys are affected. There is surge of FSH, LH in conjunction with growth hormone and insulin like growth hormone. This stimulates testosterone production by Leydig cells.[5,10] Estrogen concentration increases 3-fold. Estrogen peaking occurs before testosterone concentration which will eventually increase up to >30-fold. Gynecomastia is thus from natural delay in onset of testosterone peak. All this resolves by itself with in period of 1–2 years. Finally, with increasing age because of natural decline in free testosterone level and increasing obesity there are chances of physiological gynecomastia.

EVALUATION OF THE CAUSES OF GYNECOMASTIA

- Nonphysiological gynecomastia develops with disorders or drugs associated with low testosterone levels or high estrogen and high sex hormone binding globulin levels which indirectly result in low free testosterone levels
- Low androgen levels: Hypogonadotrophic hypogonadism/Kallmann's syndrome, high prolactin state, pituatary disease, infection Klinefelter's syndrome,[11] congenital defects in testosterone synthesis, and neurological disease
- High androgens and high estrogen levels: Testicular feminization, β-HCG producing tumors, congenital adrenal hyperplasia, Leydig cell tumors[11]
- High estrogen levels: Abnormal aromatase,[12] feminizing adrenal carcinoma, sertoli cell tumor
- Hyperthyroidism: It causes increase in sex hormone-binding globulin which in turn decreases free testosterone levels. It leads to production of androstenedione and also of estrogens
- Other nonhormonal causes: Cirrhosis, renal compromise, starvation, systemic illness, and trauma



Flowchart 1: Hormones affecting breast tissue.

- Tumors: Testicular tumors with excess of aromatase activity,[13] germ cell tumors, lung and hepatic tumors. Oncology treatment with radiation or chemotherapy can damage Leydig cells further aggravating the problem
- Genetic: It runs in families where father and son both have aromatase mutation leading to excess of estrogens.[14,8]

EVALUATION OF A MALE WITH GYNECOMASTIA[4,5]

Drugs Affecting Male Breast[15]

- Drugs leading to low androgen levels: Ketoconazole, metronidazole, gonadotropin-releasing hormone (GnRH) agonists, cytotoxic drugs, and sipronolactone
- Drugs leading to high androgens and estrogens: Anabolic steroids, androgen containing contraceptives, excessive testosterone replacement
- Drugs leading to high estrogen levels: Estrogens, isoflavones, phytoestrogens, soy products, tea tree oil, clomiphene citrate, and digitalis
- Other drugs: Angiotensin converting enzyme inhibitors, alcohol, amphetamines, calcium channel blockers, reserpine, antiretroviral drugs, theophylline, cyclosporine, and diazepam

Figure 4: Body builder with gynecomastia.

- All these drugs affect only when they are used in high doses and that too for long time
- Most important is body builders (Fig. 4) who use androgens[16] and men with prostate cancer on GnRH agonists
- Some herbal creams and even lavender oil.

MANAGEMENT

- Physiological gynecomastia requires no treatment unless patient has irritation, pain, or significant embarrassment
- Identifying and withdrawing an offending drug
- Maintaining more stable levels of testosterone[16] with transdermal testosterone or biweekly injections. Danazol can be used but is less effective
- Antiestrogen treatment with tamoxifen 10–20 mg/day and men with prostate cancer can be treated with androgen receptor blockers instead of GnRH agonists.[17-19]

SURGERY

- Men with findings suspicious for malignancy or gynecomastia with persistent pain not relieved with drugs. Main aim is to achieve masculine thorax and smallest possible incision scar
- Liposuction is one of the option when adipose tissue is more and skin is taut
- Subcutaneous mastectomy[3] is done for excision of glandular tissue and redundant skin if any
- This technique involves direct resection of glandular portion with periareolar or transareolar approach
- Complications of surgery are infection, sensory changes, pain, breast asymmetry, and scarring. Most disturbing is poor cosmetic outcome.

PROGNOSIS

Gynecomastia itself is not harmful but it is the indication of some underlying cause like tumors or endocrine disorder.[20]

CONCLUSION

Gynecomastia is enlargement of breast in males which can be physiological or pathological. It can be because of various drugs. Treatment is according to the underlying cause. Surgery is indicated in few refractory cases or where cancer is suspected.

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6

CHAPTER

Breast Self-examination

Shraddha Agarwal

INTRODUCTION

Breast self-examination is a screening method used in an attempt to detect early breast cancer. The method involves the woman herself looking at and feeling each breast for possible lumps, distortions, or swelling.

Breast self-examination is one such technique that helps you get familiar with the size, shape, and texture of your breasts. The purpose of breast self-examination is not to identify breast cancer but to determine whether what you feel/see is normal or abnormal. Hormonal changes affect the size of breasts and can make them sensitive during your menstrual cycle. An ideal time to perform a breast self-examination is a few days after the monthly menstrual cycle ends, when the breast tissue is the least lumpy.[1]

Postmenopausal women should choose the most convenient or easily remembered time, such as the first or last day of the month.[2] Choose a day each month that will be easy to remember and make breast self-examination a regular part of your good health routine. Breast self-examination is also important in women with breast implants.

HOW TO DO A BREAST SELF-EXAM (FIG 1)?

Part 1: Look

Stand in front of a mirror and look closely at your breasts in the following three positions, viewing from the right and left as well as facing forward.

- Arms at your sides
- Arms raised above your head bending forward, and
- Place hands on your hips and hunch over. Check for changes in the following:
  - Shape: Compare one to the other. One breast may normally be larger than the other, but sudden changes in size should not occur
  - Skin: Check for rash, redness, puckering, dimpling, or orange-peel-textured appearance
  - Nipples: Check for any physical changes such as a sudden inversion, scaliness, redness, itching, swelling, or discharge
  - Vein patterns: Look for a noticeable increase in size or number of veins compared to the other breast.

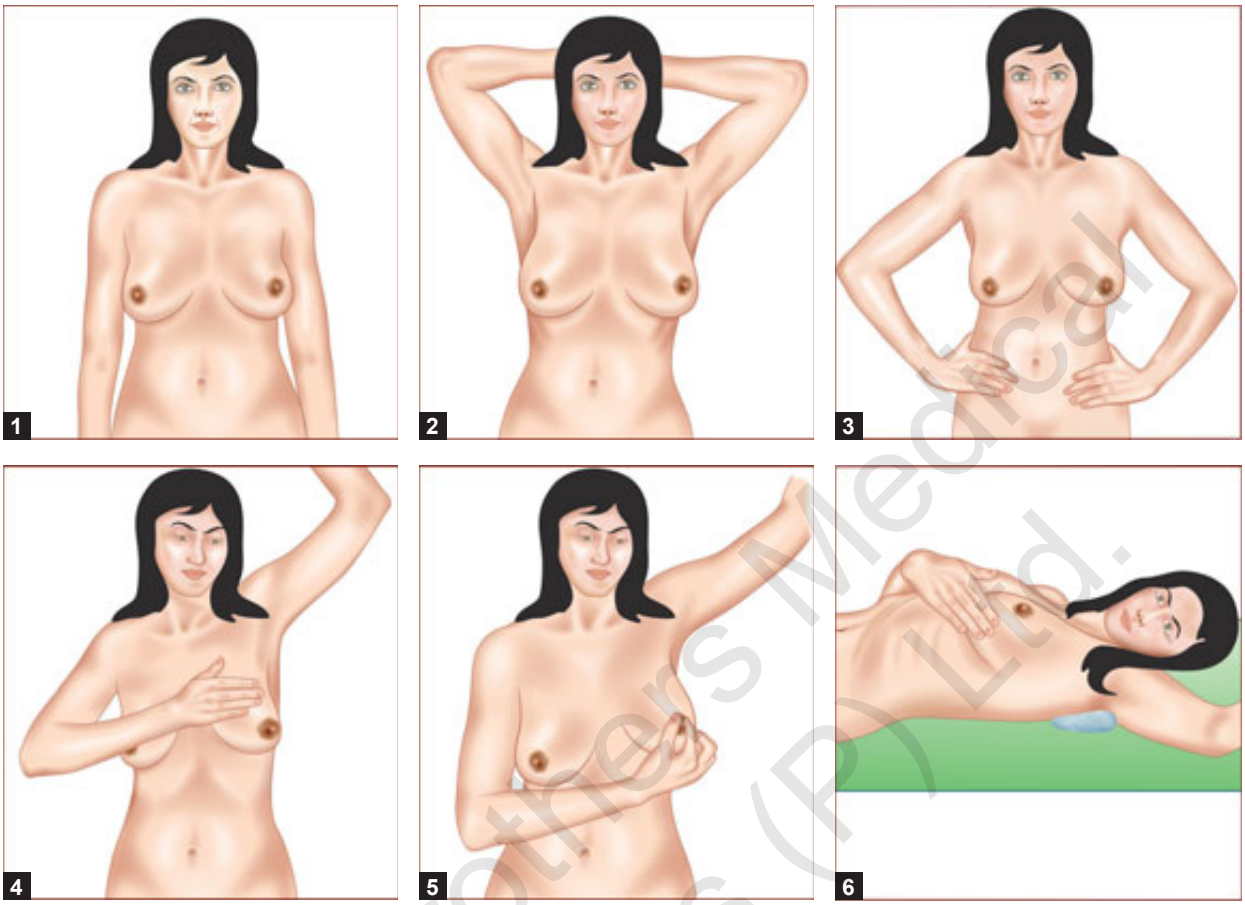
Part 2: Palpate

Using the flat pads of your three middle fingers (not the tips) move the pads of your fingers in little circles, about the size of a dime. For each little circle, change the amount of pressure so you can feel all levels of your breast tissue. Make each circle three times—once light, once medium, and once deep, before you move on to the next area (Fig. 2).

- Circles: Beginning at the outer edge of your breast use the flat part of your fingers, moving in circles slowly around the breast. Gradually make smaller and smaller circles toward the nipple. Be sure to cover the entire breast and check behind the nipple
- Wedges: Starting at the outer edge of the breast, move your fingers toward the nipple and back to the edge. Check your entire breast, covering one wedge-shaped area at a time
- Lines: Beginning at the outer edge of your breast move your fingers downward using a circular motion until they are below the breast. Then move your fingers slightly toward the middle and slowly move back up. Go up and down until you go over the entire breast area.

CURRENT RECOMMENDATIONS FROM THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS[3]

- Screening mammography every year for women aged 40–49 years
- Screening mammography every year for women aged 50 years or older



Steps 1-3 involve inspection of the breast with the arms hanging next to the body, behind the head and in the side
Step 4 is palpation of the breast,
Step 5 is the palpation of nipple
Step 6 is the palpation while lying down

Figure 1: A pictorial example of breast self-examination in six steps.

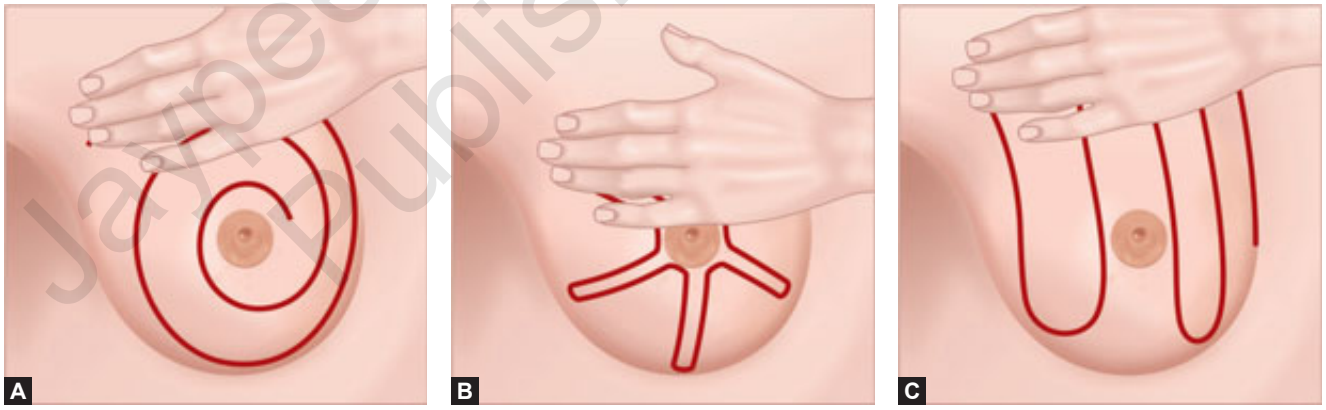


Figure 2: Methods of palpation. **A,** Circles; **B,** Wedges; **C,** Lines.

- Breast self-awareness has the potential to detect palpable breast cancer and can be recommended
- Clinical breast exam every year for women aged 19 years or older.

American Cancer Society states that women should be counseled, regarding the importance of being alert to breast changes (breast self-awareness).[4] Unlike breast self-examination, breast self-awareness does not include the recommendation for women to examine their breast on routine basis.

CONCLUSION

Over the years, there has been some debates on the importance of breast self examination in detecting cancer by different studies but still BSE is an essential and useful strategy to detect early breast cancers. It should be combined with clinical breast examination and mammography as and when required. Breast self examination should be taught to women of all ages by every gynaecologist as a part of their routine checkup.

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7

CHAPTER

Be Aware of Breast Early Detection Saves Life

Richa D Baharani, Pushpa Pandey, Sonam Baharani

INTRODUCTION

Breast cancer is the most common female cancer worldwide representing nearly a quarter of all cancers. There is significant increase in the incidence of cancer associated morbidity and mortality in Indian subcontinent as described in global and Indian studies. Earlier cervical cancer was most common in Indian woman but now the incidence of breast cancer has surpassed cervical cancer and is a leading cause of cancer death; although, cervical cancer still remains most common in rural India. A multidisciplinary approach to breast cancer including awareness programs, preventive measures, screening programs for early detection and availability of treatment facilities are vital for reducing both incidence and mortality of breast cancer in Indian women.

DEFINITION

Screening is looking for cancer before a person has any symptoms. This can help find cancer at an early stage.

METHODS

Screening modalities are as follows:

- Clinical breast examination
- Breast self-examination
- Mammogram
- Breast ultrasonography
- Magnetic resonance imaging (MRI)
- Thermography
- Tissue sampling
- Breast cancer susceptibility gene testing.

CLINICAL BREAST EXAMINATION

A clinical breast examination is the examination of breast by a doctor or other health professional. The doctor will carefully feel the breasts and under the arms for lumps or anything else that seems unusual. It should be done every 1–3 years starting at the age of 20 years and every year starting at the age of 40. It is recommended more frequently if one has strong family history of breast cancer. Breast examination is best performed soon after menstrual period.

BREAST SELF-EXAMINATION (FIG. 1)

The method involves woman herself looking at and feeling each breast for possible lumps, distortions, or swelling. It is a regular and repetitive monthly self-examination of the breast performed by a woman at the same time each month, in a predetermined manner. The concept of breast self-examination has not proven to be beneficial. A 2003 Cochrane review found screening by breast self-examination is not associated with lower death rates among women who report performing breast self-examination and does, like other breast cancer screening methods, increase harms, in terms of increased numbers of benign lesions identified and an increased number of biopsies performed. They conclude "at present, breast self-examination cannot be recommended". There was no high quality evidence looking at clinical breast examination.[1]

BREAST AWARENESS

It is about becoming familiar with the breasts and the way they change throughout a woman's life. It is a concept that encourages women to how their breasts look and feel normally, so that they gain confidence about noticing any change which might help detect breast cancer early. Breast awareness as a concept, is gaining increasing acceptance worldwide.[2]

Changes that one should be aware of:

- Painless lump or thickening that feels different from the rest of the breast
- Change in size: It may be that one breast has become noticeably larger or noticeably lower

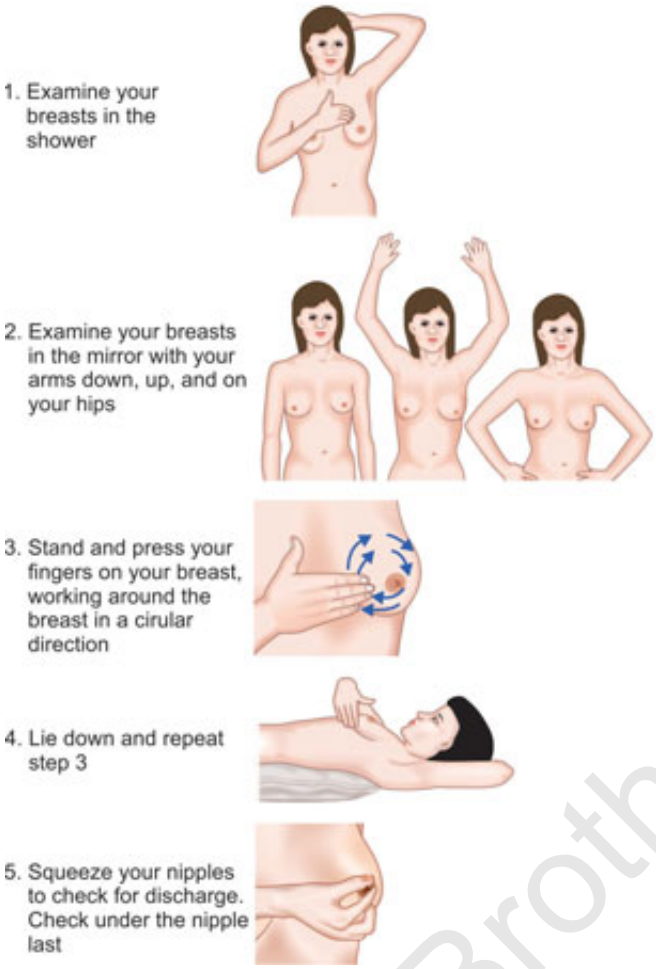

Figure 1: Breast self-examination.

- Recent retraction of the nipple
- Rash on or around the nipple
- Blood stained spontaneous discharge from one or both the nipples
- Puckering or dimpling of the skin overlying the breast
- A swelling under the armpit or around the collarbone (where the lymph nodes are present)
- Constant pain in one part of the breast or armpit.

The five point code of breast awareness:

1. Know what is normal for you
2. Know what changes to look and feel for
3. Look and feel
4. Report any changes to your doctor without delay
5. Have mammogram (X-ray of the breast) at least once in 2 years from the age of 40 years (ideally every year).

BREAST ULTRASONOGRAPHY

Ultrasound is particularly useful in young women with dense breasts in whom mammograms are difficult to interpret and in distinguishing cysts from solid lesions. It is not useful as a screening tool. Ultrasound of the axillary tissue is performed when cancer is diagnosed and guided percutaneous biopsy of any suspicious gland is to be performed.

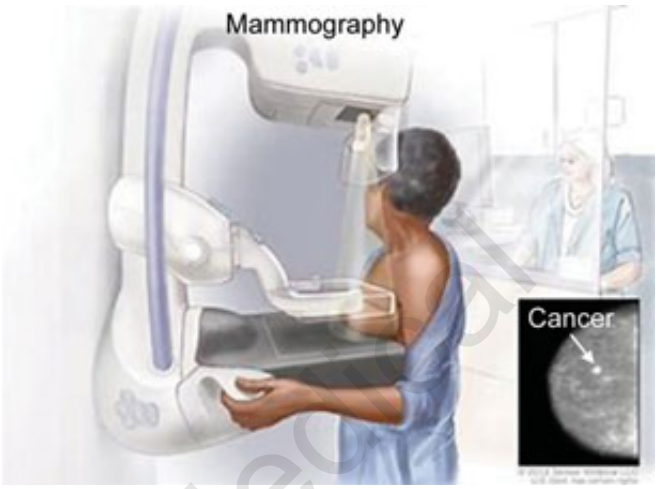

Figure 2: Mammography.

MAMMOGRAPHY

It is a common screening method relatively fast and wildly available. It is a type of radiography used on breasts. During mammography breast is pressed between two plates and X-rays are used to take pictures of breast tissue (Fig. 2).

It is of the following types:

- Screening mammography: For medical screening of apparently healthy women
- Diagnostic mammography: To aid in the diagnosis of women who is experiencing symptoms.

Mammograms are less likely to find breast tumors in women younger than 50 years than in older women,[3] this may be because younger women have denser breast tissue that appears white on a mammogram and tumors also appear white on a mammogram.[4,5] If suspicious signs are identified in the image, then the woman is usually recalled for a second mammogram, sometimes after waiting 6 months to see whether the spot is growing, or a biopsy of the breast is performed.[6] Normal mammogram does not exclude the presence of carcinoma, 5% breast cancer are missed, thus digital mammography is being introduced which allows manipulation of images and computer-aided diagnosis. Tomo-mammography is also being used as a more sensitive diagnosis.

MAGNETIC RESONANCE IMAGING (FIG. 3)

A kind of a body scan that uses a magnet and radio waves linked to a computer. The MRI scan will make detailed pictures of areas inside the breast. It is used along with mammograms to screen women who are at high risk for getting breast cancer, e.g.:[7]

- Certain gene changes such as in the *BRCA1* or *BRCA2* genes

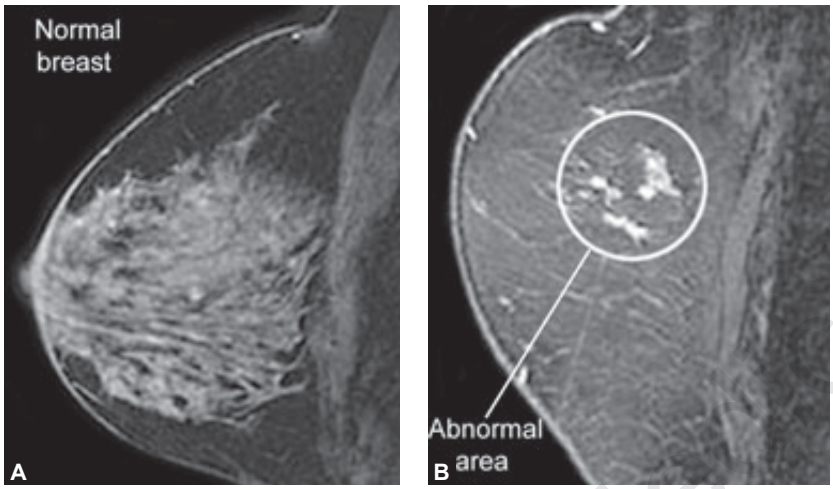

Figure 3: Magnetic resonance imaging of breast.

- A family history (first degree relative such as mother, daughter or sister) with breast cancer
- Certain genetic syndromes such as Li-Fraumeni or Cowden syndrome
- History of previous lumpectomy or breast biopsy surgeries
- Axillary metastasis with an unknown primary tumor
- It is useful in women with implants
- It differentiates scar from recurrence of cancer.

THERMOGRAPHY

It is a screening test being studied in clinical trials. Thermography is a procedure in which a special camera is used that senses heat to record the temperature of the skin that covers the breast. Tumor can cause temperature changes that may show up on the thermogram.

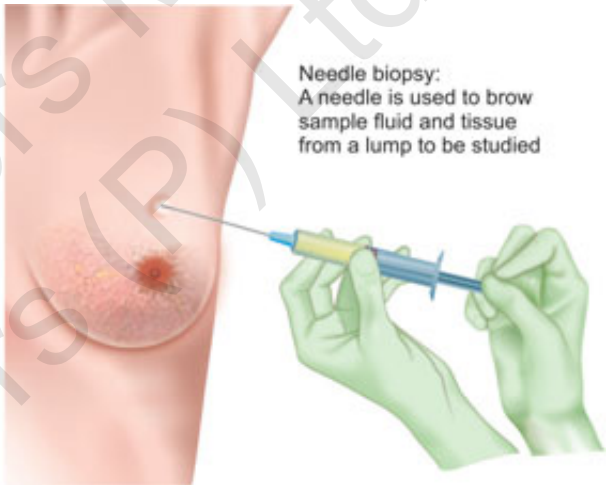

Figure 4: Fine needle aspiration cytology.

TISSUE SAMPLING

Cells are taken from breast tissue and checked under microscope. Three ways of taking tissue samples are being studied:

1. Fine needle aspiration–a thin needle is inserted into the breast tissue around the areola to take out sample of cells and fluid. It is an important part of the triple assessment of the palpable breast lump—clinical, radiological, pathological. It has reduced the number of open breast biopsies (Fig. 4)
2. Nipple aspiration: Use of gentle suction to collect fluid through the nipple. The nipple aspirate test is not indicated for breast cancer screening[8]
3. Ductal lavage: A hair size tube is inserted into the nipple and a small amount of saline is released into the duct. Saline picks up breast cells, it is sucked out and examined.

BRCA GENE TESTING

Genetic testing does not detect cancers, but may reveal a propensity to develop cancer. Women who are known to have a higher risk of developing breast cancer usually undertake more aggressive screening programs.

A clinical practice guideline by the US Preventive Services Task Force recommends against routine referral for genetic counseling or routine testing for BRCA mutations, on fair evidence that the harms outweigh the benefits. It also encourages a referral for counseling and testing in women who have a family history that indicates they have an increased risk of a BRCA mutation, on fair evidence of benefit. About 2% of American women have family histories that indicate an increased risk of having a medically significant BRCA mutation.[9]

DIAPHANOGRAPHY

Optical imaging, also known as diaphanography, multi-scan transillumination, and light scanning, is the use of transillumination to distinguish tissue variations. It is in the early stage of study.[10]

MOLECULAR BREAST IMAGING

Molecular breast imaging is a nuclear medicine technique that is currently under study. It shows promising results for imaging people with dense breast tissue and may have accuracies comparable to MRI.

It may be better than mammography in some people with dense breast tissue, detecting 2–3 times more cancers in this population. It however carries a greater risk of radiation damage making it inappropriate for general breast cancer screening. It is possible to reduce the dose of radiation used.

An earlier alternative technique suited for dense breast tissue, scintimammography is now not recommended by the American Cancer Society, which states, "This test cannot show whether an abnormal area is cancer as accurately as a mammogram, and it is not used as a screening test". Some radiologists believe this test may be helpful in looking at suspicious areas found by mammogram. However, the exact role of scintimammography is still unclear.[11,12]

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8

CHAPTER

Noncancerous Breast Conditions

Rita K Jha

INTRODUCTION

Female breasts are very complex. These are filled with parts called glands, fat, and fibrous tissue. They are constantly going through change from the time of their development through pregnancy and menopause.

Up to 30% of women suffer from a benign breast condition requiring treatment at sometime in their life. Many of these conditions can cause discomfort or pain and need treatment. Others don't need treatment. Many of them mimic the symptoms of breast cancer and need further evaluation.

Noncancerous breast conditions are generally associated with a number of factors. These include the makeup of the breast (fatty tissue versus dense or thick tissue), age, weight, family history, hormonal influence (including period of pregnancy, lactation, and menopause) having imbalance in the ratio of hormones, and infection/inflammation by liberating cytokines.

All these conditions are classified in following headings:[1]

- Congenital disorders–Amazia, polymazia, etc.
- Injury–Hematoma, traumatic fat necrosis, etc.
- Inflammation/infection–Mastitis leading to abscess, Mondor's disease, etc.
- Aberration of normal development and involution of the breast–Concept was first published by L.E. Hughes of Cardiff breast clinic in 1983 and was based on pathogenesis. It includes fibroadenoma, fibrocystic disease of the breast, mastalgia etc.
- Ductal ectasia/periductal mastitis
- Pregnancy related–Galactocele, puerperal abscess.

HOW THESE CONDITIONS ARE DIAGNOSED?[2]

- By recognizing some symptoms related to breast such as lump or swelling in the breast, pain in the breast, discharge from the nipple, etc.
- Sometimes examining doctor detects the problem during routine physical examination or screening
- By investigations like ultrasonography (USG)/mammography/fine needle aspiration cytology/biopsy.

Regarding diagnosis, The American Academy of Family Physician[3] recommends the following:

- A routine mammography every other year for women between 50 and 74 years of age
- The use of USG instead of a mammogram in young women with dense breast tissue and a lump
- Mammograms in women older than 40 years if a fine needle biopsy shows a solid lump. If the lump is cystic and can be drained successfully with a fine needle, no further evaluation is needed
- If the results from a physical exam and fine needle biopsy diagnose the breast condition as benign, a following physical exam should occur in 4–6 weeks.

CAN THESE CONDITIONS BE INFLUENCED/PREVENTED?

Noncancerous breast conditions cannot be prevented; however, following conditions may influence it:

- Drinking alcohol during teen years may increase the risk
- Eating foods which contain carotenoids like melons, carrots, sweet potatoes, squash, nuts, and beans during teen years lowers the risk
- Girls who are heavy at the age of 10 years have a lower risk
- Menopausal hormone therapy and a positive family history increase the risk.

There are a number of noncancerous breast conditions but those which require special mention in detail are as follows.

MASTALGIA[4]

Mastalgia, also known as mastodynia or breast pain, is a recognized organic condition though studied less thoroughly than other breast problems. Natural history—approximately

70–80% of women experience breast pain at some time in their lifetime. It accounts for 30–47% of breast clinical evaluation. In severe form, it interferes with sexual activity in about 48%, physical activity in 37%, social activity in 12%, and other activities in about 8% of the cases.

Types with Clinical Features

Cyclical

- Related to exaggerated premenstrual symptoms beginning in the luteal phase or 2nd half of the cycle
- Symptoms increase by the use of exogenous hormones like combined oral contrceptives (COC)/hormone replacement therapy (HRT)
- Associated with breast engorgement, nodularity in the breast, ache, heaviness, and tenderness that is bilateral
- More prevalent in younger women in 3rd or 4th decade of lives and accounts for 2/3rd of all breast symptoms
- Occurs usually due to benign mammary dysplasia.

Noncyclical

- Independent of menstrual cycle and is described as dragging or burning-like pain
- It may be intermittent or constant
- Is usually unilateral
- Occurs in relatively older women in 4th or 5th decade of life
- More difficult to treat than cyclical mastalgia.

Extramammary (Referred)

- Pain is perceived to be located in the breast but is actually located at an extramammary site
- Costochondritis (Tietze syndrome) is a manifestation of chest wall pain that is frequently interpreted as breast pain
- Other causes are chest wall muscular pain, herpes zoster infection, rib fracture, etc.

Management

- Reassurance: Firm reassurance that the symptoms are not associated with cancer helps in majority of women
- Support: The breasts has minimal structural support and is at significant risk for motion related displacement resulting in mastalgia and thus the use of external support appears to be effective in reducing breast pain and approximate fitting and supportive bra should be worn throughout the day and a soft bra as sports bra worn at night
- Reduction in methyl xanthene intake as caffeine in tea and chocolate, discontinuation of hormone therapy like COC/HRT, application of heat and cold pack, vitamin B6 intake in doses of 100 mg/day, and light breast massage reduces symptoms in some of the cases
- Topical nonsteroidal anti-inflammatory drugs in gel form is another option, a significant reduction in all types of pain is observed
- Low fat diet: In a study it has been seen that in 90% of women taking 15% dietary fat had relief of pain after 6 months compared to only 22% with 36% fat intake
- Evening primrose oil: Containing essential fatty acids gamma linoleic acid in adequate doses of 2–3 g/day has better relief from pain in about 50–70% of women. It is used as first line therapy. It appears to achieve higher response rate in those over 40 years of age than younger women. It works by its effects on prostaglandin synthesis. Occasional nausea and headache are its only side effects. Some author has suggested the use of wheat germ/corn oil because of less cost and comparable results
- Hormone modulating drugs including danazol, bromocriptin, tamoxifen, and depoprovera are recognized drug treatment for mastalgia. Though these drugs are associated with significant side effects that limit their general use
- Danazol: It is the only medication approved by United States Food and Drug Administration for mastalgia. It is started at doses of 100–200 mg twice daily in severe pain and tapered to a lower dose of 100 mg/day. Relief of symptoms occurs in about 70–80% of cases. Side effects like edema, weight gain, depression, headache, change in voice, and hirsutism are there and therefore, many patients stop the drug when the symptoms improve
- Bromocriptin: It is a dopamine antagonist that inhibits the release of prolactin. Elevated prolactin levels has been seen in mastalgia patients. In doses of 2.5 mg twice daily for 3–6 months is effective in about 45% of cases. Side effects are nausea, vomiting, and giddiness. Cabergoline is long acting with fewer side effects
- Goserelin: Is a potent synthetic analogue of luteinizing hormone-releasing hormone that causes reversible reduction in serum estrogen level and decrease in breast pain, it is an effective treatment of mastalgia and should be kept as second line therapy. It is given in doses of 3.6 mg monthly injection. Side effects include vaginal dryness, hot flushes, decreased libido, oily skin and hair, and decreased breast size
- Tamoxifen in doses of 10–20 mg/day demonstrated reduction in breast pain and the result was comparable to that of bromocriptine and danazol
- Restandol (testosterone undecanoate) in doses of 40 mg twice daily is effective. Androgenic side-effects after 3 months of treatment are often the limiting factor in its use
- Ablative surgery should never be contemplated for breast pain and any patient seeking this treatment should be referred to a psychiatrist.

Recommendations

- Education and reassurance is an integral part for the management of mastalgia and should be the first-line treatment
- The use of a well-fitting bra that provides good support should be considered for the relief of cyclical and noncyclical mastalgia

- A change in dose, formulation, or scheduling should be considered for women on HRT. HRT may be discontinued if appropriate
- Reducing caffeine intake, treatment with vitamin E and use of evening primrose oil are still under study to determine their effectiveness in the treatment of breast pain
- Flaxseed should be considered as a first-line treatment for cyclical mastalgia
- Topical non-steroidal anti-inflammatory gel, such as diclofenac 2%, should be considered for pain control in localized treatment of mastalgia
- Tamoxifen 10 mg daily or danazol 200 mg daily should be considered when first-line treatments are ineffective
- Mastectomy or partial mastectomy should not be considered as an effective treatment for mastalgia
- Cyclical Mastalgia occurring in relatively younger age-group is not a disease to be worried about; however, non-cyclical mastalgia in older women must be investigated to rule out cancer.

FIBRADENOMA[5] (BREAST MOUSE)

It is one of the most common benign tumors of breast and accounts for 50% of all breast biopsies. It occurs in young women (20–35 years), may occur in teenagers, and is rare after menopause. It arises from hyperplasia of a single lobule and is surrounded by a well-marked capsule. Patient notices a mass while showering or dressing. Swelling may enlarge during pregnancy and lactation. On examination a firm, smooth, rubbery, freely mobile lump, without inflammatory reaction usually ranging from 5 mm to 5 cm size can be palpated. Ultrasonographic imaging identifies well-defined smooth, solid mass with clearly defined margins. Regression occur spontaneously in about 15% of cases. No change is seen in about 75% and enlargement is noted in 5–10% of cases.

Management

Management is usually conservative unless there is evidence of enlargement. Large or growing mass must be excised. Excision is done through a cosmetically appropriate incision. Ultrasonography guided percutaneous vacuum assisted cryoablation can be done in smaller lesions.

FIBROCYSTIC DISEASE OF BREAST[6]

It is one of the most common lesion of breast referring to histological picture of fibrosis, cyst formation, and epithelial hyperplasia common in women of 35–55 years of age and presents bilaterally.

Most patients are asymptomatic but smooth mobile and potentially compressible lump accompanied by pain, tenderness or sometimes nipple discharge may be found in some of them especially in premenstrual phase.

Diagnosis

Smooth thin walled cysts with absence of internal echoes are seen on ultrasound examination. Benign cyst fluid is either straw colored or dark green or brown. Fibrocystic change and risk of breast cancer.

Fibrocystic disease as such is not associated with increased risk of breast cancer especially when it is non-proliferative. However, if there is histological evidence of epithelial hyperplasia with atypia, there is 5-fold higher risk. Risk is bilateral for lobular lesions and ipsilateral for ductal lesions. In cases with positive family history and atypia, there is 11-fold increased risk.

Management

Fibrocystic change is a normal evolutionary change in breast development and involution, and does not require specific treatment, other than good clinical examination and age appropriate imaging. The patients are advised to discontinue intake of coffee, tea, and chocolate. Analgesic can be given. Cyst can be aspirated and if they resolve completely, no further treatment is required.

Biopsy should be performed in presence of following findings:

- No fluid is obtained during needle aspiration
- Fluid is thick or bloody
- Cyst is complex
- There is intracystic mass
- Mass persists after aspiration
- Persistent mass is noted at any time during follow-up.

Depending on biopsy report further management is done.

DISCHARGE NIPPLE

Nipple may leak fluid for a variety of reasons. A clear or milky color represents hormonal influence. If it is green black, it states a blocked milk duct. If the discharge is bloody, it can be related to an injury, infection or tumor either benign or malignant. Treatment will depend on the underlying cause.

BACTERIAL MASTITIS[4]

It is the most common variety of mastitis and is associated with lactation in majority of cases. Infecting organism is penicillin resistant *Staphylococcus aureus* usually. Ascending infection from a sore and cracked nipple may initiate it. The affected breast presents the classical signs of acute inflammation. Later on abscess may form. Treatment is by an appropriate antibiotic and drainage of the abscess.

LIPOMA

These are common and are made up of mostly fat tissue. Can be felt as a lump and treatment is by surgical removal.

Less Common Conditions[7]

Amazia

Congenital absence of the breast, may occur on one or both sides.

Polymazia

Accessory breasts have been recorded in the axilla, groin, buttock, and thigh. They function during lactation.

Hematoma

Hematoma formation can give rise to a lump but resolves in most of the cases.

Traumatic Fat Necrosis

It may be either acute or chronic. Following injury, a painless lump appears that may mimic carcinoma. Biopsy is required for diagnosis and treatment is by surgical removal.

Tuberculosis of Breast

It is rare and can be associated with active pulmonary tuberculosis, can present with multiple chronic abscess and sinuses. Diagnosed by bacteriological and histological examination and treated by antituberculous chemotherapy.

Mondor's Disease

It presents as thrombophlebitis of superficial veins of breast and anterior chest wall, usually subsides; however, treatment is by restricted arm movements and analgesics.

Duct-ectasia/Periductal Mastitis

There is dilatation of the breast ducts associated with periductal inflammation. There is discharge from nipple. The fluid sets an irritant reaction in surrounding tissue leading to abscess or fistula formation. In the case of mass or nipple retraction, carcinoma must be excluded. Treatment is by antibiotics and surgery.

Galactocele

It is rare and usually presents as a solitary subareolar cyst dating from lactation.

Calcification

Small spots of calcium salts can be shown anywhere in breast tissue. These are not painful. Most are benign. However, some can be a sign of cancer. If in doubt, fine needle biopsy is required and treated accordingly.

Intraductal Papilloma

This is a wart like growth located inside the nipple, causing discharge. It is usually treated by surgery.

Gynecomastia

A man's breasts would seem swollen and feel tender and there is enlarged breast tissue. This does not need to be treated, unless severe pain is there. Hormonal treatment or tissue reduction surgery can be given.

Phyllodes Tumors[8]

These benign tumors, previously known as serocystic disease of Brodie, usually occur in women over the age of 40 years, but can occur in younger women. It presents as a large mobile tumor with an uneven surface. Histologically there is a wide variation in their appearance. Treatment is enucleation in young women. Elderly women need wide local excision.

CONCLUSION

Living with noncancerous breast condition can be emotionally hard. Women having them are worried about its turning to cancer. Though this is not the case in most instances, there still exists a small chance of its conversion. As gynecologists are the primary care physicians to women and the disease related to breasts are usually examined by them initially, a careful breast examination with regular screening should be part of every routine gynecological examination either in gynecological outpatient department, antenatal clinic, infertility clinic, postnatal clinic, or gynecological oncology clinic.

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9

CHAPTER

Establishment of Lactation

Shakuntla Kumar

INTRODUCTION

Lactation is the process by which milk is synthesized and secreted from the mammary glands of the postpartum female breast in response to an infant sucking at the nipple. Breast milk provides ideal nutrition and passive immunity for the infant, encourages mild uterine contractions to return the uterus to its prepregnancy size (i.e., involution), and induces a substantial metabolic increase in the mother, consuming the fat reserves stored during pregnancy. The mammary gland is an apocrine, milk-secreting gland with a compound tubuloalveolar architecture made up of cells from the ectoderm and mesoderm of the early embryo.[1,2]

INITIATION AND MAINTENANCE OF LACTATION

Pregnancy is marked by profound hormonal changes reflecting major secretory contributions from the placenta, the hypothalamus, and the pituitary gland, with contributions from a number of other endocrine glands (e.g., the pancreas, thyroid, and parathyroid). Increased estrogen and progesterone levels during pregnancy stimulate secretion of prolactin from the pituitary, whereas placental lactogen appears to inhibit the release of a prolactin-inhibiting factor from the hypothalamus. Prolactin, lactogen, estrogen, and progesterone all aid in preparing the mammary gland for lactation. Initially in gestation, an increased growth of ductule and lobuloalveolar tissue occurs in response to estrogen and progesterone. In the beginning of the second trimester, secretory material begins to appear in the luminal cells. By the middle of the second trimester, mammary development has advanced sufficiently to permit lactation to occur should parturition take place.

Once the infant is delivered, a major regulatory factor, the placenta, is lost and new regulatory factors, including the maternal-infant interaction and neuroendocrine regulation, are gained for control of lactation. Loss of placental hormone secretion results in an endocrine hypothalamic stimulation of prolactin release from the anterior pituitary gland, as well as neural stimulation of oxytocin from the posterior pituitary. The stimulation of the nipple by suckling activates a neural pathway that results in release of both prolactin and oxytocin. Prolactin is responsible for stimulating milk production, whereas oxytocin stimulates milkejection (the combination is known as the let-down reflex). Oxytocin also stimulates uterine contractions, which the mother may feel while she is breastfeeding; this response helps to restore the uterus to prepregnancy tone. Milk production and ejection are thus dependent on the complex interaction of stimulation by the infant's suckling, neural reflex of the hypothalamus to such stimulation, release of hormones from the anterior and posterior pituitary, and response of the mammary gland to these hormones to complete the cycle.

MILK SECRETION

Breast milk provides ideal nutrition and passive immunity for the infant, encourages mild uterine contractions to return the uterus to its prepregnancy size (i.e., involution), and induces a substantial metabolic increase in the mother, consuming the fat reserves stored during pregnancy. The pituitary hormone prolactin is instrumental in the establishment and maintenance of breast milk supply. It also is important for the mobilization of maternal micronutrients for breast milk. In addition to prolactin and oxytocin, growth hormone, cortisol, parathyroid hormone, and insulin contribute to lactation, in part by facilitating the transport of maternal amino acids, fatty acids, glucose, and calcium to breast milk.

Secretory initiation–stage I lactogenesis occurs during the 2nd half of pregnancy. High levels of circulating progesterone supplied by the placenta inhibit further differentiation. Small amounts of milk containing lactose and casein may be secreted after about 16-week's gestation, and lactose derived

from the breast begins to appear in maternal urine. During late pregnancy, many women are able to express colostrum.

Secretory activation–stage II lactogenesis or secretory activation is marked by the onset of copious milk production after delivery. This stage is triggered by the rapid decline in progesterone that follows delivery of the placenta and requires the presence of elevated levels of prolactin and cortisol as well as insulin.

Maintenance of lactation–lactation or galactopoiesis is the process of continued secretion of copious milk. It requires regular removal of milk and stimulation of the nipple, which triggers prolactin release from the anterior pituitary gland and oxytocin from the posterior pituitary gland. In the absence of milk removal, elevated intramammary pressure and accumulation of a feedback inhibitor of lactation reduce milk production and trigger mammary involution

Milk is produced as the result of synthetic mechanisms within the mammary gland, as well as the transport of components from blood. Milk-specific proteins are synthesized in the mammary secretory cells, packaged in secretory vesicles, and exocytosed into the alveolar lumen. Lactose is secreted into the milk in a similar manner, whereas many monovalent ions, such as sodium, potassium, and chloride, are dependent on active transport systems based on sodium potassium adenosine triphosphatases (Na^+/K^+-ATPases). In some situations, the mammary epithelium, which may behave as a "mammary barrier" between the interstitial fluids derived from blood and the milk because of the lack of space between these cells, may "leak," permitting direct diffusion of components into the milk. This barrier results in the formation of different pools or compartments of milk components within the mammary gland and is responsible for maintaining gradients of these components from the blood to the milk.

Lipid droplets can be observed within the secretory cells of the mammary gland and are surrounded by a milk fat globule membrane. These fat droplets appear to fuse with the apical membrane of the secretory cells and then to be either exocytosed or "pinched off" into the milk,[3] growing as they fuse with one another.[4] Some whole cells also are found in milk, including leukocytes, macrophages, lymphocytes, and mammary epithelial cells. The mechanisms by which these cells enter the milk are complex and include, among others, specific cellular receptor-mediated homing of antigen-specific lymphocytes. As the structure of the mammary gland is compartmentalized, so is that of the milk. The gross composition of milk consists of cytoplasm encased by cellular membranes in milk fat globule membranes (fat compartments made up of fat droplets), a soluble compartment containing water-soluble constituents, a casein-micelle compartment containing acid-precipitable proteins with calcium and lactose, and a cellular compartment. The relative amounts of these components change during the course of lactation, generally with less fat and more protein in early lactation than in late lactation.

Colostrum is the first postpartum milk that is produced and is generally very dense in protein and fat content and has an enriched amount of immunologic factors compared with mature milk. Colostrum gives way to a transitional milk during the first week of life, where water content increases. Mature milk is relatively constant during the next ensuing months until weaning. Mode of delivery appears to also influence macronutrient composition of colostrum, with vaginal delivery versus cesarean section being associated with higher protein content.[5]

In addition, there are strong influences of maternal diet on fatty acid profiles in colostrum and later milk.[6,7] Maternal age may also positively influence fat content in colostrum and may be related to increased fat synthesis or reduced water production.[8] Thus, the infant consumes a dynamic complex solution that has physical properties permitting unique separation of different functional constituents from one another, presumably in forms that best support growth and development.

LACTATION PERFORMANCE

Successful lactation performance depends on continued effective contributions from the neural, endocrine, and maternal-infant interactions that were initiated at the time of delivery. The part of this complex behavior most liable to inhibition is the mother-child interaction. Early and frequent attachment of the infant to the breast is mandatory to stimulate the neural pathways essential to maintaining prolactin and oxytocin release.

Lactation ceases when suckling stops; therefore any behavior that reduces the amount of suckling by the infant initiates weaning or the end of lactation. Introduction of water in bottles or of one or two bottles of formula a day may begin the weaning process, regardless of the time after parturition, but can be most damaging to the process when the mother-infant dyad is first establishing lactation. In some cases where breast milk has not come in and newborns have dropped greater than 5% weight, discrete amounts of supplemental formula may improve breastfeeding success.[9] There are physiologic consequences to women who never lactate. Parous women aged 50 years or younger who had never lactated had higher prevalence of hypertension, obesity, and diabetes. Long-term cancer risk for breast and ovarian cancer are also reduced in women who have lactated.[10,11]

CONCLUSION

To conclude it will be apt to state that the development of lactation, a hallmark of mammalian evolution, is designed to enhance the survival of the neonate of the species through a remarkable spectrum of immediate and long-term protective functions. Human milk contains a wide variety of soluble and cellular components with a diverse spectrum of biologic functions.

Vaginal delivery is seen to be associated with higher colostrum protein content. Hormonal activity induced by labor pain and uterine contractions might account for the alterations in the protein composition of human milk to facilitate optimal development of important physiologic functions in newborns.[5]

The passive transfer of the diversity of maternal biologic experiences to the neonate through the process of breastfeeding represents an essential component of the survival mechanism in the mammalian neonate. For millions of years, maternal products of lactation delivered through breastfeeding have been the sole source of nutrition and immunity during the neonatal and early infancy period for all mammals, including the human infant. During the past few centuries, however, human societies have undergone remarkable changes that have had a major impact on basic maternal-infant interaction, breastfeeding, and on our environment. Such changes include introduction of sanitation and nonhuman milk and formula feeds for neonatal nutrition, use of antimicrobial agents, introduction of processed foods, and exposure to newer environmental macromolecules and dietary antigens. These changes have had a profound impact on human homeostatic mechanisms that, at the same time, are opening up new insights into the importance of breastfeeding in the developing human neonate.

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10

CHAPTER

Breast Pumping: Bridging Motherhood and Work

Neerja Pauranik

INTRODUCTION

Breast pumps as means of expressing milk have not caught the imagination of lactating mothers and medical professionals alike in India for many obvious reasons. However, the same has been hailed as a 'quiet revolution' transforming the practice in the United States and other countries.[1] A real change has occurred with advent of good quality, very efficient electrical double breast pumps in the last two decades.[2]

Indications and Benefits of Breast Pump for Mother and Baby

Feeding, Work, and Leisure

Feeding the milk expressed by hands-free electric pump is a boon for mother and baby both, because most of the benefits of at breastfeeding accrue in this mode also. Breast pumps liberate mothers and enable them to work as per the need and also permit them the pursue of leisure activities.[3]

The fact that more women are entering work force for long hours each day and also that they cherish more independence need not be in conflict with the ideal of exclusive breast feeding for 6 months and extended supplemental feeds till around 2 years. The hands-free ease of ever improving breast pumps allows mother to do multitasking at homes too.

Tiding Over Brief Periods of Separation

It is made easy with the help of a breast pump. Many planned and unplanned exigencies like maternal ill health, accident, surgery, and travelling may interrupt the feeding, wherein machine expressed milk comes as a handy rescue. Parents will do well to have a stash of stored milk in home refrigerator. It serves as a cushion to fall back on.

Breast Pumps Serve the Family for Long

Breast pumps serve the family for long for up to 2 years or more. Many mothers who faithfully follow the advice of exclusive breast feeding for 6 months often resort to rather abrupt weaning and use of cow/buffalo milk or formula feed. They need not do so, if they keep expressing milk by pump.

The Machine Pumps Bonding

Use of breast pumps increase bonding in the family, by freeing up the mother for work and providing opportunity to father and other family members to feed the baby with expressed milk, preferably by cup, rather than bottle.

Pump Expression Enhances Lactation

Breast pumps help continued lactogenesis for as late as 2–3 years.

More the extraction, more the production. It is a virtuous cycle. The machine can be made to work on one idle breast when the baby is suckling on the other. Higher demands during periodic growth spurts and for twin babies may be tiring for a working woman. In occasional instances breast pumps may be used even before delivery to promote lactation and store some milk, provided there is no risk of initiation of labor. A few genuine cases of lactation failure may be helped by expression of milk by breast pump.

Power Pumping

Whenever there are issues with low milk yield, principle of demand and supply is applied. "Power pumping" is a practice that involves very frequent feeding of a baby who is experiencing a growth spurt during which the baby demands frequent, longer, and vigorous suckling. Power pumping is done for 1 hour each day or night. Pump for 20 minutes, then pause for 10 minutes, followed by pumping for 10 minutes, then rest for 10 minutes and then again pump for 10 minutes; therefore total 40 minutes pumping is performed in 1 hour, which ultimately leads to production of more milk.

Breast pumps are of great help for low birth babies and all those who cannot latch and suckle and those needing care in neonatal units. The current practice of feeding them "other milk" (cow or formula) is not the best option.

Machine Works in Harmony

Breast pump works in harmony with at breastfeeding and also with manual expression of milk. The expressed breast milk is the best medium to be added to cereals and other semi-solid foods for a rapidly growing toddler.

Pumping for Milk Banks

The silent revolution of breast pumping is proving to be a boon for another game changing development, that is, milk banking. The later works by collecting, screening, and distributing human milk donated by women. According to the World Health Organization, receiving milk from a human milk bank should be the first alternative for a baby whose mother is not able to breast feed. The ministry of Health and Family Welfare of India has planned a network of milk banks for 661 new born care units across the country. However, there is urgent need for good regulatory and monitoring system to be in place to ensure safety and quality of milk.[4]

Corollary Benefits to Mother

A longer period of feeding infants human milk represents a net increase in milk production, leading to greater caloric expenditure that could assist mothers in reducing postpartum weight.[5] It will also serve as a maternal insurance against breast, uterine, and cervical cancer.

Possible Harms and Problems

Improper use of breast pump can lead to mastitis, trauma, and nipple wounds.[6] During the process of pumping and storing human milk contamination may occur which may compromise its nutritional and anti-infective benefits. The sources of contamination may be many—nipple shields, valves, storage container, feeding vessel, and human hands. There may be leaching of undesirable substances from the container into the milk. Degradation of key milk components has been documented during storage. Thawing of frozen milk reduces anti-infective factors.[7]

The hazards of nipple confusion in bottle fed babies apply to all whether the milk is from formula or expressed by pump. Hence, it is desirable that expressed milk be fed by a sipper cup or spoon.

Some activists and die-hard proponents of breast feeding are concerned that while feeding the expressed milk may be fine in many respects, but it reduces mother baby bonding and other benefits of at breastfeeding. They are not amused by the prospect of many mothers never or seldom feeding their babies at-breast.[8]

Research

Not surprisingly, women who expressed their milk, had more education, were more often employed, and had a higher household income than those who did not.[9]

A recent Cochrane review (2016) included 41 trials out of which 22 (involving 1339 participants) contributed data for analysis to compare different methods of milk expression. Outcomes were maternal satisfaction or acceptability of milk, breast or nipple pain, quantity of expressed milk, nutrient quality of milk, and changes in prolactin and oxytocin. There were no statistically significant differences.[10]

Only one study from India in 1996 compared manual expression with nonelectric pump. It was seen that volume of milk increased significantly with the use of pump. The authors recommended combination of both.[11] The possible benefits or harms from wide spread practice of breast pumps merit careful study in India and improved national data collection (Box 1).

BOX 1 Suggested questionnaire for research

1. What are the reasons for expressing or not expressing milk with a pump?
2. How do mothers manage the integration of at the breast feeding with extended use of new pumps?
3. Does extended milk expression by pump actually leads to reduced postpartum weight?
4. Does longer period of milk expression by pump has similar benefits for maternal well being and health that are associated with feeding the baby at the breast?
5. What is the frequency of problems like mastitis, trauma, nipple wounds, pain from overstretching of breast?
6. Do infants really receive more human milk, if their mothers use breast pump?
7. How do women handle and store the expressed milk and what are the effects of there practices on composition of milk?
8. What are the medium and long-term correlations between composition of stored milk and infant health?
9. What are the consequences for infants who are fed expressed milk by bottle versus cup and does it lead to changes in overall feeding practices up to toddler age?
10. How to balance the benefits of foremilk and hind-milk by alternative reversing the sequence of at breast feeding and expressed milk?

The national immunization survey should be modified to include some of the above questions. At a minimum, the feeding at-breast should be distinguished from feeding expressed milk and the duration of each practice should be ascertained.

Advocacy, Awareness, and Education

Health care professionals, their associations and non-government organizations should seriously debate whether feeding expressed mothers milk in bulk volumes with the help of double breast electric pumps can be considered as an extension of "true breastfeeding".[12] The answer has to be "yes". Advocacy is needed for awareness and education about benefits and cost-effectiveness of electric pumps and milk banks. The targets of advocacy will include all expectant and lactating mothers, family members, and each and every health care professional. Pediatricians and obstetricians will have to shed their doubts, apathy, and inertia. So much is at stake. We have come a long way since mid-1990s when the movements like breastfeeding promotion network and baby friendly hospitals were launched. Technology gives

us new opportunities as well as challenges. Breast pumps are an important milestone is this journey. Another gift of technology is electronic social media which are playing exemplary role in bonding, sharing, helping, advocating, educating, and supporting women and significant others. Myriad groups on Facebook etc. have rapidly evolved. We must direct women in our follow-up to these resources.[13] The present author has published and distributed many volumes of health education literature in Hindi over last two decades.

CONCLUSION

Breast milk is a "Unique Living Fluid", the constituents of which are released in pulsatile fashion throughout the meal, day and night. It adjusts as per the needs of premature or low birth weight babies as well. Breast milk contains unique interferons and interleukins, which can treat infections of eye, ear, respiratory system, allergies, and dental problems. It provides protection of brand new intestinal mucosa and many other countless benefits, which are not mentioned in this chapter because of word limits. Breast milk can achieve much more than this, but it requires its own "warm chain" of support. We merely pay "lip service" to "breast is best" mantra. Mothers and more so their relatives need a warm chain of protection and skilled support, not "cold assurance that failure does not matter."[14]

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11

CHAPTER

Trouble Shooting of Breastfeeding

Alka V Kuthe

"There is a reason behind everything in nature."

–Aristotle

INTRODUCTION

The breast is a remarkable endocrine organ that experiences growth, differentiation, and lactation in response to a complex interplay of hormones and stimulation.[1] They are a part of a woman's internalized body image that she develops during her adolescence and carries with her for the rest of her life. Any change in her breasts due to surgery, illness, or infection threatens this feminine internal view of self-giving rise to state of disequilibrium. It can be a "double whammy"—both her femininity and her ability to breastfeed can be threatened.[2] Proponents of breastfeeding have accepted even before the upsurge of interest and research in attachment, that the major reason to breastfeed is to provide the special relationship and closeness that accompanies nursing.[3]

Breastfeeding is an essential part of woman's reproductive cycle. Exclusive breastfeeding for 6 months as recommended by the American Academy of Pediatrics (AAP) followed by timely, adequate, safe, and appropriate complementary feeding practices, with continued breastfeeding for up to 2 years or beyond, provides the key building block for child survival, growth, and healthy development.

TROUBLES DURING BREASTFEEDING

Lactating breasts can come across number of adverse situations.

Pregnancy, Labor, and Birth Complications[4]

While pregnancy, labor, and birth are assumed as natural physiological processes, there can be adverse situations from point of view of breastfeeding.

- Hypertensive disorders of pregnancy: To reduce the stress and other noxious stimuli that could provoke a seizure, breastfeeding with mother and baby in skin-to-skin contact might actually be therapeutic due to calming and sedating effects of prolactin and oxytocin
- Cesarean delivery: Baby can be put to breast even in operation theatre with the help of the staff. The first touch with the mother plays a major role in the initiation of breastfeeding. Postoperative antibiotics most commonly used are "usually compatible with breastfeeding"
- Postpartum hemorrhage: Due to pituitary infarction and necrosis (Sheehan syndrome) secondary to postpartum hemorrhage leading to hypotension, the alveoli can get involuted, there will be no prolactin secretion and lactation might get suppressed. Prolactin stimulating drugs such as metoclopramide have been used to treat this
- Episiotomy: The relatively minor obstetric procedure can be extremely painful and can interfere with milk ejection reflex. Mother should be encouraged to initiate breastfeeding as early as possible
- Assisted birth or operative vaginal deliveries: The babies who get delivered vaginally by assisted technique, may get mark bleeding of the scalp and face with associated increased bilirubin levels and poor feeding
- Retained placenta: Lactogenesis II is inhibited by placental retention, should start after manual removal of placenta
- Venous thrombosis: Serious event requiring anticoagulant therapy with heparin, warfarin or a newer lower molecular fraction of heparin and they are considered compatible with breastfeeding
- Postpartum infection: The perineal, vaginal, and cesarean incision infections are usually easily treated with antibiotics that are compatible with breastfeeding
- Side effects of labor medications that can affect breastfeeding: In standard settings, mothers are encouraged to have uninterrupted skin-to-skin contact to minimize the effects of labor medications on lactation success.

Problems Related to the Lactating Breast Itself

Not Enough Milk

This is the most common complaint.

Management:[5] The capacity of newborn stomach at birth is around 5–7 mL, for which the quantity of colostrum secreted (35–40 mL/first 24 hours) is more than enough and for that matter frequent feeding (8–10 times/24 hours) satisfies the requirement of the newborn. Frequent breastfeeding also stimulates breakdown of liver glycogen in to glucose that together with calories in colostrum satisfy the energy requirement of the newborn. There is no danger of baby becoming hypoglycemic.

Cracked/Sore/Damaged Nipple

The causes are:[5]

- Improper latch on
- Frequent washing of areola and nipple with soap and water
- Fungal infection
- Tight frenulum that restricts the movement of tongue
- Nipple may get cracked at the base if the child is taken away abruptly from the breast while feeding.

Prevention and management:[5]

- Correct attachment and application of fat rich hind milk
- Routine once a day cleaning of the breasts during bath is all that is required
- Treat fungal infection in mother as well as baby
- Tongue tie can be corrected surgically
- If the baby has to be removed from the breast, first release the vacuum.

Retracted and Inverted Nipple

The pulling back of the nipple may be either harmless (the majority of retractions) or malignant (occasionally associated with breast cancer). Make sure not to confuse retracted nipples with inverted nipples. A retracted nipple appears flat and broad. An Inverted nipple can be pulled out. Retracted nipple cannot be pulled outward. It does not protrude or becomes erect when stimulated or cold.[7] During antenatal care visits, these mothers should be just identified and follow up given after delivery. Latching on may be difficult in few mothers and they should be given proper guidance, help, and support. Mother's confidence should be built up. No evidence to support use of nipple shield but if mother knows about that and wants to use that its use will help her to increase her confidence and satisfaction that she is on some treatment. Syringe method can be tried in few mothers with inverted nipple.[6] If a baby cannot suckle effectively in the first week or two, help his mother to feed with expressed milk.

Engorged Breasts[8]

Excessive production or incomplete emptying of breast (infrequent suckling or poor attachment) will cause heaviness, hardening, and pain in the breast (engorgement).

Prevention and management: Engorgement can be prevented by timely expression of milk. Unattended engorgement can lead to decreased milk production due to action of local feedback inhibitor of lactation.

Mastitis in the Breast[8]

It is a preventable but common lactation problem. It occurs due to:

- Milk stasis
- Insufficient milk removal
- Hyperlactation
- Cracked nipples
- Maternal stress
- Use of nipple creams.

Prevention and treatment: It begins with breastfeeding information and education. Adequate rest, good nutrition, psychological support, and proper hand washing are

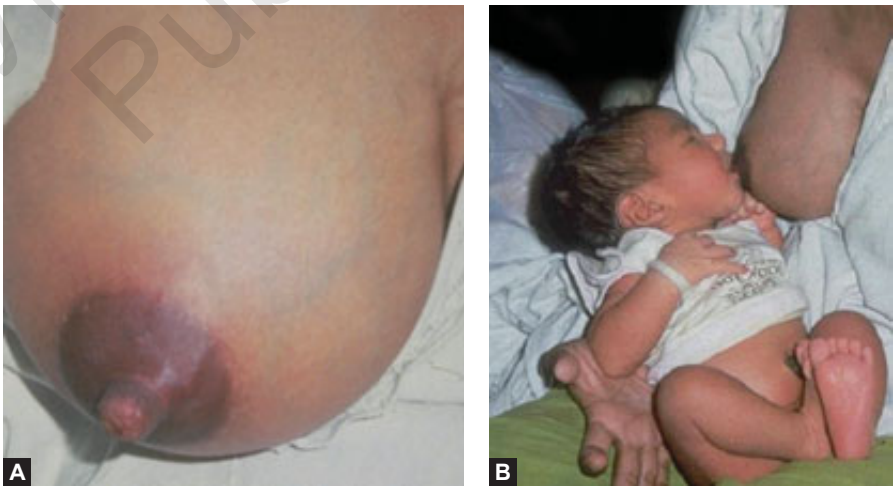

Figure 1: A, Sore nipple; **B,** Improper breastfeeding position.[6]

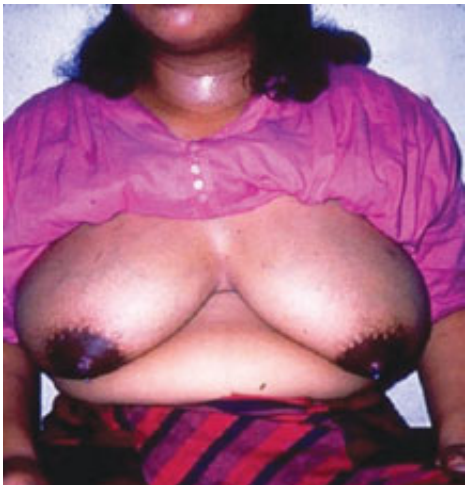

Figure 2: Full breasts.[8]

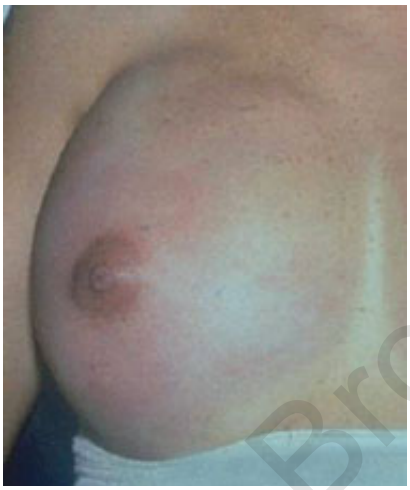

Figure 3: Engorged breasts.[8]

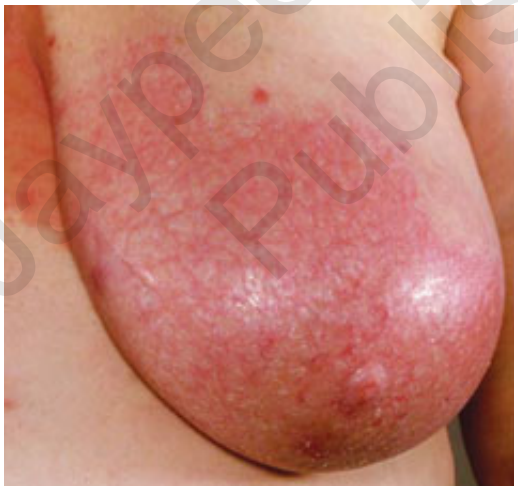

Figure 4: Mastitis.

common guidelines. Treatment of the underlying cause and antibiotic therapy is required. Warm moist packs or cold/cabbage compresses between feeds whichever gives greatest comfort to the mother should be used (WHO, 2000).

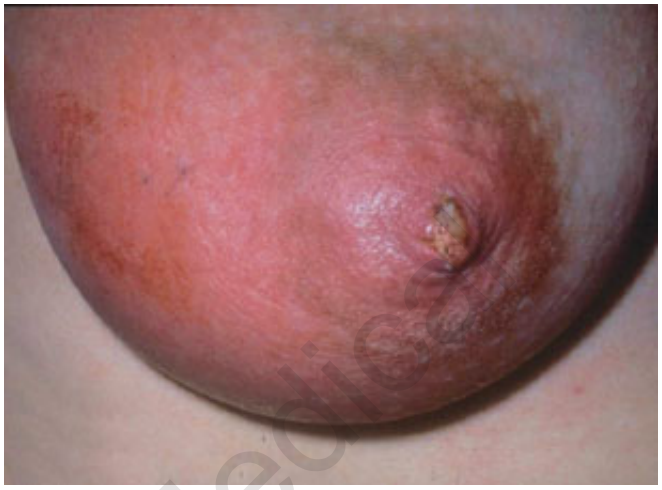

Figure 5: Abscess (pus) formation due to localization of infection.

Breast Abscess[8]

Mastitis if remains neglected and untreated may progress to breast abscess. The baby should be allowed to continue breastfeed. The abscess can be preferably treated with aspiration technique.

Galactocele

A benign cyst, often called a milk retention cyst. Presence of a galactocele should not interrupt breastfeeding.

Duct Ectasia

It is also known as comedo mastitis, varicocele tumor, or granulomatous mastitis. Lactation can aggravate the condition but is not a contraindicated.

Fibrocystic Disease[8]

It is a benign condition of the breast. The condition does not contraindicate breastfeeding.

Breast Cancer[9]

Approximately 1–3% of masses diagnosed during pregnancy and lactation are malignant. Infants are generally weaned from the breast if chemotherapy is necessary or the breast-milk is fed to the baby depending upon the half-lives of the various chemotherapeutic agents.

Augmentation Mammoplasty[7]

Lactation success depends upon the functional breast tissue. Women who have periareolar incision are at the highest risk for milk insufficiency.

Reduction Mammoplasty

Full breastfeeding is a possibility with the pedicle technique but not with the free nipple technique.

Dermatitis Involving the Breast, Nipple, and Areola

Herpes simplex with active oozing lesions on the nipple or areola requires interrupted breastfeeding till the lesions heal.

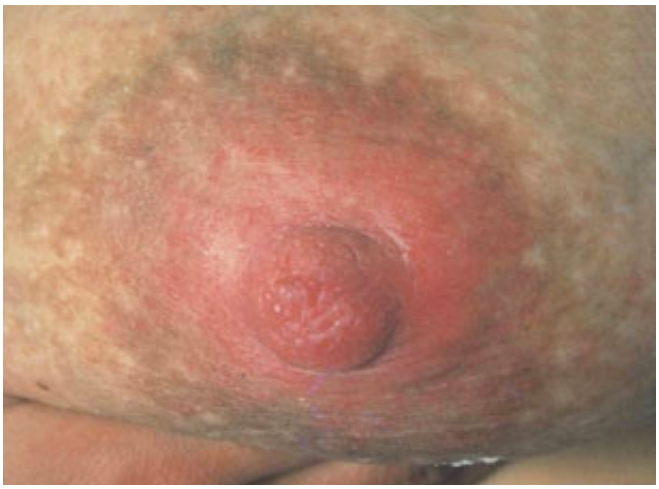

Figure 6: Candidiasis.

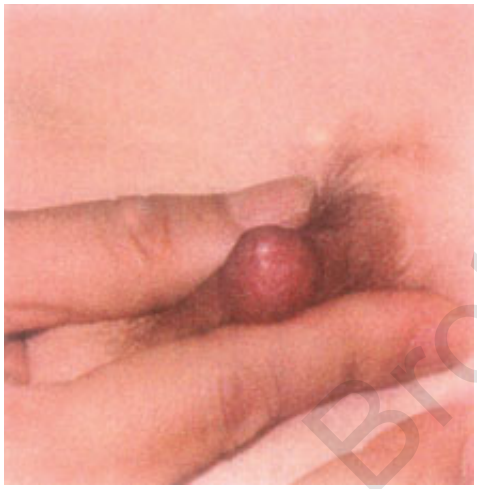

Figure 7: Vasospasm.

Mammary Candidiasis (Thrush)[9]

It is also known as thrush or monilia. Both mother and the baby should be treated simultaneously.

Abnormal Nipple Tenderness (Sore) and Damage

In late pregnancy and early breastfeeding period, there is normal tenderness due to increased sensitivity of the nipple. It is relieved as the milk volume increases.

Vasospasm of the Nipple (Raynaud's Phenomenon Like Condition)[9]

It causes extreme pain, stinging, and burning of the nipple. Management includes:

- Initiate the milk ejection reflex or express drops of colostrum before putting baby to the breast
- Feeding on the less tender side first
- Review and/or correct positioning
- Warm compresses
- Avoid cold air
- Reduction of nicotine and caffeine intake
- Use of safe analgesics
- Vitamin 6, calcium, and magnesium supplementation
- Nifedipine
- Breast milk can be applied to nipples.

Unsubstantiated Low Milk Supply (Perceived Insufficiency)[10]

The vast majority of insufficient milk supply is perceived rather than real.

Management:

- Mothers should be taught about normal physiologic breastfeeding. Successful nursing mothers generally breastfeed 8–12 or more times in 24 hours, feed at night, not to decrease the frequency of breastfeeding to let the breasts fill.
- The baby should drain the first breast fully before being offered the second.
- Mothers should get support and encouragement
- Mother may be on certain medications and foods that may reduce milk supply, e.g., pseudoephedrine, bromocriptine, oral contraceptive pills, methyldopa, etc.

Pathophysiologic Lactation Failure

The reasons of failure include:

- Delayed lactogenesis II
- Maternal nipple anomalies
- Insufficient glandular tissue due to asymmetric size and/or shape, maternal issues (illness of mother, infection, anemia, chronic conditions).

BASIC MANAGEMENT OF MILK INSUFFICIENCY

Can be managed by providing as close to a breastfeeding relationship as possible by supplementing at the breast, alternative feeding while holding baby on the bare breast, use of galactogogues, e.g., metoclopramide, domperidone.

CONCLUSION

The breastfeeding mother needs proper counseling, guidance, education, information, and support at all levels to overcome the troubles. "Mother's joy begins when new life is stirring inside. When a tiny heartbeat is heard for the very first time, and a playful kick reminds her that she is not alone." So let the mother enjoy the motherhood by empowering, enabling her to breastfeed successfully even if she faces troubles during breastfeeding.

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12

CHAPTER

Breast Abscess

Parimala Devi

INTRODUCTION

The breast is an appendage of skin and is a modified sweat gland, the shape of the female breast is due to the fat contained within fibrous septa. In the adolescent and young adults the breast is firm and prominent, with age the glandular and fibrous element atrophies, the skin stretches and breasts sag. The breast lies between the skin and pectoral fascia to which it is loosely attached. It extends from the second to the sixth rib and from the lateral border of the sternum to the mid-axillary line. Breast abscesses can be classified into: Lactational and nonlactational. Nonlactating breast abscesses can be further divided into–central (periareolar) infection and peripheral infection.

LACTATING INFECTION

When infection does occur, it usually develops within the first 6 weeks of breastfeeding or occasionally, during weaning. Presenting features are pain, swelling, tenderness, and a cracked nipple or skin abrasion. *Staphylococcus aureus* is the most common organism but occasionally *Staphylococcus epidermidis* and streptococci are also implicated. Drainage of milk from the affected segment is often reduced, causing stagnant milk to become infected.

NONLACTATING INFECTION

Central or Periareolar Infections

This is most commonly seen in young women (mean age 32 years). The underlying cause is periductal mastitis. Current evidence suggests that smoking is important in the etiology of nonlactational infection. Substances in cigarette smoke either directly or indirectly damage the subareolar breast ducts and the damaged tissue becomes infected by either aerobic or anaerobic organisms.

Clinical Features

Include breast pain, erythema, periareolar swelling and tenderness, and/or nipple retraction and these occur in relation to the affected duct.

Peripheral Nonlactating Abscess

These are less common than periareolar abscesses and are sometimes associated with an underlying condition, such as diabetes, rheumatoid arthritis, steroid treatment, or trauma.

INVESTIGATIONS

Breast Ultrasound

For an erythematous area, ultrasonography helps to identify an underlying abscess Abscesses usually form a hypoechoic lesion. This is the preferred imaging modality in adolescents, and is applicable in neonates with suspected breast infection. The hypoechoic lesion (abscess) may be well circumscribed, macrolobulated, irregular, or ill-defined with possible septae.

Diagnostic Needle Aspiration Drainage

A breast abscess can be drained by needle aspiration for therapeutic and diagnostic purposes. Purulent fluid indicates a breast abscess.

MANAGEMENT OF LACTATING ABSCESS

Treated with flucloxacillin 500 mg 6 hourly or co-amoxiclav 375 mg 8 hourly. If allergic to penicillin then clarithromycin 500 mg 12 hourly. Established abscess treated by recurrent aspiration or incision and drainage. Encourage women to breastfeed to promote milk drainage.

MANAGEMENT OF NONLACTATING ABSCESS

Treatment is with appropriate antibiotics. Co-amoxiclav 375 mg 8 hourly or combination of clarithromycin and metronidazole. Abscess is aspirated or incised and drained. Recurrent infection because the treatment does not remove the damaged sub areolar duct which requires total duct excision.

PREVENTION

Primary Prevention

Good breastfeeding habits (e.g., emptying breasts fully and proper latching) and proper nipple hygiene may help to minimize the risk of developing lactational mastitis. Sterile equipment and techniques should be used for nipple piercing.

Secondary Prevention

- Breastfeeding should be encouraged if feasible during lactation
- Smoking cessation should also be encouraged, to minimize the risk of recurrence
- Mastitis may increase the risk of transmission of HIV through breastfeeding. Therefore, if an HIV-positive woman develops mastitis or an abscess, she should avoid breastfeeding from the affected side while the condition persist.

13

CHAPTER

Mastalgia

Sujata A Dalvi

INTRODUCTION

Mastalgia or breast pain is a medical condition most often associated with developing condition or disease of breast. It is usually benign. It is usually breast tenderness that is felt. Other names for mastalgia are "Mammalgia" or "Mastodynia".[1] Breast cancer foundation has defined breast pain/mastalgia as any pain, tenderness, or discomfort in breast or underarm region. It has also added that in most cases, breast pain is not a sign of breast cancer. In the United States, CA Pacific Medical has stated that approximately 50–70% of women have mastalgia. United Kingdom (UK) Health Authorities have mentioned that 66% of women in age group of 30–50 years have mastalgia.[2]

Mastalgia can range from minor to severely incapacitating. This pain can be felt as dull ache, heaviness, tightness, burning sensation, pinching, sharp, stabbing, or shooting pain in the breast. This does not include pain during lactation or weaning due to mastitis or breast engorgement.[3]

TYPES

- Cyclic: The pain intensity changes with menstrual cycle. It is usually more in luteal phase and becomes less with onset of menstruation
- Noncyclic: The pain remains unchanged throughout the menstrual cycle. It can be less frequent and often difficult to make diagnosis
- Extramammary (nonbreast pain): It is pain that feels as if source is within the breast. It is also known as referred pain.[4]

CYCLIC MASTALGIA

Some degree of it is felt during menstrual cycle and is taken as normal. It can occur in women with premenstrual syndrome (PMS) and fibrocystic breast changes. It is also present in young women who are on oral contraceptive pills or postmenopausal women on hormone replacement therapy.

Etiology

This pain occurs due to cyclic hormonal effects, associated with ovulation or pharmacologic agents. Estrogen stimulates ductal elements, progesterone stimulates stroma with extracellular proliferation, and prolactin stimulates ductal secretion leading to pain.

In most cases, pain affects upper, outer area of both the breasts, can spread to arms and can cause swelling of breasts. It starts 2–3 days before menstruation and gets better by onset or end. In some, pain starts many more days before the start of menstruation.

National Health Service UK has mentioned that "cyclical breast pain is not linked to high-risk of developing breast cancer."

Cyclic mastalgia is not significantly associated with PMS.[5] Although, it is associated with menstrual cycle, 82% do not have PMS. If associated with PMS, it merits further investigations as a recurrent pain disorder whose presentation, etiology, and effective treatment are likely to differ from those of PMS.

NONCYCLIC MASTALGIA

It occurs during puberty, menopause, or pregnancy when physiological hormonal changes occur. This pain is felt during breast trauma, mastitis, inflammatory breast cancer, or with breast lump like fibroadenomas. Large pendulous breasts cause mastalgia due to weakening of Cooper's suspensory ligaments causing ptosis especially after lactation and menopause. Postmenopause breasts become less dense, soft and there is fatty replacement of breast parenchyma leading to pain.

It is felt in one breast or one quadrant of breast and can spread across the chest. It can be continuous or sporadic.

Localized signs in case of breast trauma or mastitis may be present.

EXTRAMAMMARY MASTALGIA

It can be due to cardiac problems like angina or pulmonary like pneumonia or gastrointestinal due to esophagitis. Inflammation of costochondral junction, severe liver damage, shingles or herpes zoster can also give rise to pain that can mimic mastalgia. Those who are on digitalis, methyldopa, spironolactone, anabolic steroids, oxy-metholone or chlorpromazine can also experience similar type of pain.

EVALUATION

Detailed history should include age, unilateral or bilateral, cyclical or noncyclical, related to menstrual cycle (luteal phase) with relief with onset of menstruation, breast trauma, previous breast surgery, vigorous exercise, medications like digitalis, methyldopa, spironolactone, chlorpromazine, breast feeding, nipple discharge, local redness, lump, or fever.

Clinical breast examination should be done to rule out evidence of any lump, skin changes, tenderness, and discharge from nipples. It should include thorough examination of axillae.

BREAST PAIN ASSESSMENT

Daily breast pain chart should be maintained for documentation. Quantifying breast pain may be difficult because of its variability. Before starting any therapy for breast pain, patients should be asked to document the frequency and severity of their pain on daily basis for at least one menstrual cycle using a visual linear analog scale.[6] The pain score ranges from 0 to 10. The pain scale is also helpful in assessing treatment response in mastalgia, which is characterized by waxing and waning of symptoms and a high spontaneous remission rate. The scores of a full month can be summated and its mean, median, standard deviation, or 95% confidence interval can be computed. This objective recording and mensuration of breast pain with separate explicit recording of menstruation before and after therapy with a drug is beneficial for those on therapy of mastalgia. It also allows exact record of "alteration of menses" with hormonal agents viz. centchroman, tamoxifen, danazol, and luteinizing hormone-releasing hormone analogues.

These measures are particularly important for cyclic mastalgia as the diagnosis based on recall of symptoms is only 65% sensitive and that on prospective breast pain diary is 69% specific.

Research criteria for the diagnosis of cyclic mastalgia are—(1) pain severity greater than 4.0 cm measured on 10.0 cm visual analog scale and (2) pain duration of at least 7 days per month.

Investigations like sonomammography and mammogram are needed to detect any pathology in breast. Core needle biopsy needs to be done, if breast lump is suspicious.

MANAGEMENT

Reassurance is the most important part of management. Some may decline treatment especially with cyclical mastalgia.

Nutritional supplements like flaxseed–25 g daily (Society of Obstetricians and Gynaecologists of Canada)[7] or vitamin E (600 mg) daily is recommended. Nonsteroidal anti-inflammatory drugs can be used to relieve pain in patients with moderate to severe pain.

Lifestyle modification like avoid excess caffeine, low fat diet, and avoidance or decreased smoking should be implemented. Supportive garments, like during day time–well-fitting; sleep time–soft and supportive; and exercise time–good sports bra should be used.

In case of extramammary cause of pain, it should be treated first.

MEDICATIONS

- Oral contraceptives: Show improvement in 50% of patients, but side effects preclude their use, unless symptoms are severe
- Bromocriptine: It suppresses prolactin secretion and hence is effective in 20% noncyclical and 47% cyclical mastalgia. It can have side effects like headache, seizures, or stroke
- Tamoxifen: It relieves 90% cyclical and 56% of noncyclical pain. However, patient may suffer from adverse effects like hot flashes, vaginal discharge, thromboembolic phenomenon and possibility of uterine cancer
- Danazol: It is a testosterone derivative. It relieves 70% of cyclical and 31% noncyclical pain. However, it is not recommended for longer durations due to adverse effects like irregular menstruation, hirsutism, muscle cramps, depression, dyspareunia, acne, voice changes, and weight gain. It is also contraindicated in pregnancy and in patients with thromboembolic disease
- Luteinizing hormone releasing agonist like leuprolide acetate/gosereline: They can be used in acute severe mastalgia with an 80% response rate. It affects bone density if used for more than 3 months and is expensive.
- Evening primrose oil: It is labelled as a nutritional supplement. It contains gamma linolenic acid which is a precursor of prostaglandin E1. It is effective in 45% of cyclic and 30% of noncyclic mastalgia. It can be used as first-line therapy as it has minimal adverse effects (mild gastrointestinal discomfort) and is cost-effective. The onset of action takes about 4–6 weeks. The dosage is 3 g/day for minimum of 3–6 months
- Selective estrogen receptor modulators (SERMs): They help in relieving mastalgia. The dosage is 30–60 mg once

a day for 3 months. Less dosage of SERMs can be used along with evening primrose oil in select cases.

CONCLUSION

Many women have mastalgia at some time in their life. Breast pain is usually associated with benign breast condition. Rarely, it is a sign of breast cancer. Symptomatic patients need to consult the medical personnel, get examined and investigated, if required.

Reassurance is the main pillar of management. Nutritional and supportive therapy is the first line of treatment for cyclic pain. Prescription drugs and therapies can be used in patients with severe symptoms but they cannot be given for longer time and hence are not very useful in relieving symptoms. Evening primrose oil is recommended for treatment of mastalgia. It is safe, effective and does not have any adverse reaction.

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14

CHAPTER

Abnormal Nipple Discharge

Charulata A Bapaye

INTRODUCTION

Breast disorders are one of the most common gynecological problems and nipple discharge is an important presenting symptom. As many as 80% women will experience at least one episode of nipple discharge during their reproductive years.[1] Nipple discharge maybe physiological, pathological, unilateral, or bilateral. A careful assessment is required in all cases as the causes for nipple discharge range from benign lactation to underlying malignancy.[2]

CAUSES OF NIPPLE DISCHARGE[3]

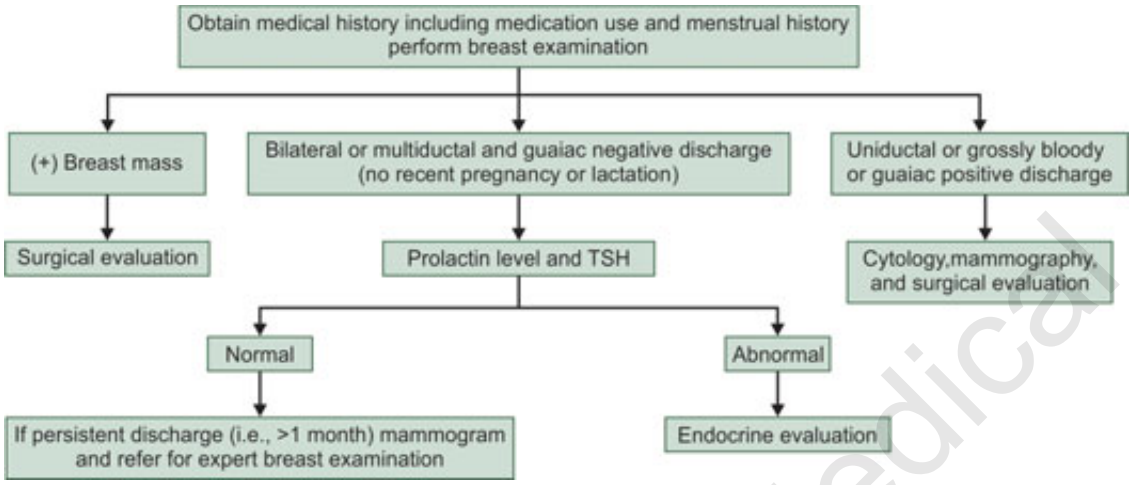
- Discharges from a single duct:
  - Blood stained: Intraductal papilloma (most common cause), intraductal carcinoma, and duct ectasia
  - Serous (any color): Fibrocystic disease, duct ectasia, carcinoma
- Discharges from more than one duct:
  - Blood stained: Carcinoma, ectasia (most common cause), and fibrocystic disease
  - Black or green: Duct ectasia (highly specific)
  - Purulent: Infection, retroareolar abscess, and tuberculosis
  - Serous: Fibrocystic disease, duct ectasia, and carcinoma
  - Milk (maybe white, grey, and brown): Lactation (overall most common cause), Post lactation period, nipple stimulation, early pregnancy, hypothyroidism, pituitary adenoma, antipsychotic medication side effect, etc.
- Discharge from the surface:
  - Paget's disease
  - Eczema, psoriasis
  - Chancre.

Risk of malignancy is higher if discharge is from a single duct and even higher if the discharge is bloody.

Therefore, the first step in management of a case with any nipple discharge is to exclude malignancy.

CLINICAL APPROACH TO A CASE OF NIPPLE DISCHARGE (FLOWCHART 1)

1. First step is always a detailed history and physical examination. Points during examination include:
   - Pregnancy status—If pregnant and discharge is bilateral then its most likely galactorrhea with a benign outcome
   - Unilateral/bilateral
   - Color of discharge
   - Number of ducts involved
   - Presence or absence of lump
2. Red flags in a case of nipple discharge which warrant radiological investigation:
   - Unilateral discharge
   - Bloody/serous discharge
   - Skin/nipple changes
   - Lump
3. No red flags:
   - If discharge is bilateral, milky/nonbloody, without any red flags then perform:
     - Pregnancy test
     - Guaiac test to rule out blood in discharge
     - Tests to check serum thyroid stimulating hormone and prolactin
4. If none of these investigations yield a diagnosis, then perform a pituitary magnetic resonance imaging to look for an adenoma.
5. Treatment is cause specific.
   - Red flags present: If a lump is evident then proceed with triple assessment algorithm
     - Clinical assessment
     - Radiology (ultrasonography, mammography)



Flowchart 1: Algorithm for management of nipple discharge.

- Histology (fine-needle aspiration cytology, core needle biopsy).[4]

6. A negative cytology report doesn't rule out malignancy. *In-situ* disease will also not show up on cytology. If lump is not clinically evident, it still is ruled out with help of radiology
7. Magnetic resonance imaging for evaluation of nipple discharge is controversial (94.7% sensitive and 78.9% specific in diagnosing malignancy)[5]
8. Next step depends upon number of ducts involved:
   - Ductography is performed in cases of nipple discharge especially if it is bloody
   - Cannulating the duct is technically challenging
   - Radiopaque contrast is injected into one or more ducts and mammography is performed. It has a sensitivity of 76% for detecting malignancy, specificity of 11%:[6]
     - Intraductal papilloma seen as small filling defects surrounded by contrast media
     - Cancers are visualized as irregular masses or as multiple intraluminal filling defects
     - Duct ectasia shows a dilated cystic structure.
9. In single duct discharge, microdochectomy is performed and biopsied. It serves diagnostic as well as therapeutic purpose. If dysplasia/malignancy is found on biopsy, further management needs to be planned.

Microdochectomy

Do not express discharge before performing the procedure. It makes it difficult to identify the affected duct. A lacrimal probe or a stiff nylon suture is inserted into the duct from which the discharge is emerging. A tennis racquet incision is made to encompass the entire duct or a periareolar incision is used and the nipple flap dissected to reach the duct. The duct is then excised.

In multiple duct discharge, if patient is in symptomatic distress then radical duct excision with biopsy is done.

Hadfield's Cone Excision[3]

The entire major duct system is removed without sacrifice of the breast form. A periareolar incision is made and a cone of tissue is removed with its apex just deep to the surface of the nipple and its base on the pectoral fascia. The resulting defect may be obliterated by a series of purse-string sutures; although, a temporary suction drain will reduce the chance of long term deformity.

Patient must be warned preoperatively that she won't be able to breast feed after the procedure and may experience altered nipple sensation. It is currently a less preferred procedure.

If patient is not in distress, then a cytology with ductoscopy or ductal lavage is performed and patient is observed with regular follow-ups if no malignancy found.

Ductoscopy using microendoscopes is feasible but is generally not revealing.

MAMMARY DUCT ECTASIA

- It is the dilatation of breast ducts with periductal inflammation. Patient generally presents with:
  - Nipple discharge of any color (serous discharge is most common, cheesy/green/black is most specific), frequently bilateral
  - Subareolar mass
  - Abscess
  - Mammary duct fistula
  - Nipple retraction
- Duct ectasia is diagnosed with the help of ultrasonography or ductography
- If mass/nipple retraction is present, a carcinoma must be excluded with mammography and negative cytology. In case of persisting suspicion mass should be excised
- Duct ectasia can be treated conservatively when asymptomatic[2]

- Otherwise, Hadfield's operation is done. Care must be taken to shave the back of the nipple to ensure all terminal ducts have been removed otherwise the condition will recur.

INTRADUCTAL PAPILLOMA

They are true polyps of epithelium lined breast ducts. They are benign lesions with no increased risk of malignancy. Mostly solitary[2] within 4–5 cm of the nipple orifice. Generally less than 1 cm but can grow up to 4–5 cm.
Common among women aged 30–50 years[2]

Clinical Features

- Bloody nipple discharge
- Diagnosis by ductography.

Treatment

Microdochectomy—Complete excision of the duct with the tumor.

CONCLUSION

Nipple discharge is common during a woman's reproductive years even in nonpregnant or nonlactating women. It is usually not serious but it may be the first symptom of an underlying malignancy. Therefore, it does warrant a thorough medical checkup.

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CHAPTER

Breast Augmentation and Reduction

Pratibha Singh

INTRODUCTION

Breast augmentation today is one of the most frequently performed plastic surgical procedures. As breast aesthetic surgery becomes more common, past stereotypes and stigmas are changing. In a Healthy Women survey, 53% of women said they were more accepting of breast augmentation than they used to be. Women who have undergone breast augmentation surgery are confident and feminine.[1]

On the opposite end of the spectrum of breast aesthetic surgery is breast reduction. This procedure, which may be considered a cosmetic surgical procedure, is often performed to relieve significant physical and emotional problems resulting from overly large and heavy breasts that can cause numerous problems like neck, back and shoulder pain, chafing or rash, significant limitation in daily activities, which may lead to unhappiness and potential dissatisfaction with their appearance. The result is psychological issues like depression, stigmatization, poor self-esteem, and anxiety, especially in adolescents. This surgery is considered one of the most rewarding breast surgeries, with profound positive effects on physical and mental health.

BREAST AUGMENTATION

The decision to have breast augmentation is a personal one. While about 91% of women cited the desire to reshape their breasts following a major physical change,[1] like weight loss or childbirth, some women who have very small breasts (micromastia) undergo breast augmentation which can significantly restore and reshape along with improving their overall self-confidence, self-perception, and sense of attractiveness.[2]

BREAST REDUCTION

The procedure is performed on women of all ages, including adolescents whose psychological health is threatened because they are teased about their breast size or are unable to wear typical teenage clothing. For obese females it is recommended to lose weight prior to surgery, so that surgery will become easy and risk will be less and sometimes additionally excess weight may reduce which may be contributing to the size of the breasts.

DIAGNOSIS

Most women opting for any of these procedures are young and healthy; however, a full medical evaluation is still required which includes:

- History of smoking or obesity: It should be dealt by quitting smoking and losing weight, to reduce the risk of complications from surgery
- Other surgeries on breast or chest wall
- Medication including over-the-counter drugs, herbal and nutritional supplements, and vitamins
- Any family history of breast cancer. While it is safe and recommended to have a mammogram with breast implants
- Additionally, with breast reduction surgery it is ideal to have the breast tissue evaluated by a pathologist. This evaluation could pick up early signs of breast cancer or cellular changes.

TREATMENT

Breast augmentation (augmentation mammoplasty) can be done through two techniques.[3]

Autologous Fat Transfer

It is a procedure where fat cells extracted through liposuction from body areas like abdomen, thighs, and hip are prepared and injected into the breasts. Fat transfer for breast augmentation is preferred by women who do not wish to add a foreign object in their body. The women should, however,

have enough fat in the body for autologous fat transfer to breasts. It is simple and completely safe.[3,4]

Breast Implants

There are different types of breast implants used for breast augmentation. Implants differ in shape, size, texture, and the material used in them. Saline and silicone filled implants are two main types. Both have their own advantages and disadvantages. After the Food and Drug Administration clearance to use silicone implants for cosmetic surgery, silicone implants are most popular because of their natural feel, texture and are less likely to cause rippling than saline implants. Whereas advantage of saline implants is that the size of some implants can be adjusted during or after surgery by adding saline to the implant. But today's silicone gel-filled breast implants benefit from improved manufacturing technology and more stringent tolerance specifications. Major changes include thicker shells and more cohesive gel to reduce the risk of rupture and are completely safe even after they burst, which is why they are preferred over saline implants all across the world. Round shaped cohesive silicone gel implants are the most popular implant.[3,5]

Candidates are those who are:

- Physically and mentally healthy
- Above 18 years of age
- Not currently pregnant or nursing
- Have realistic expectations from breast implants plastic surgery.

Procedure

Incisions

It involves the incisions that minimize scarring and are discreet in their location:

- Inframammary: Is ideal for women whose breasts sag a bit since the natural droop of the breast hides the incision
- Transaxillary: Is more commonly used in young nulliparous with small areolas

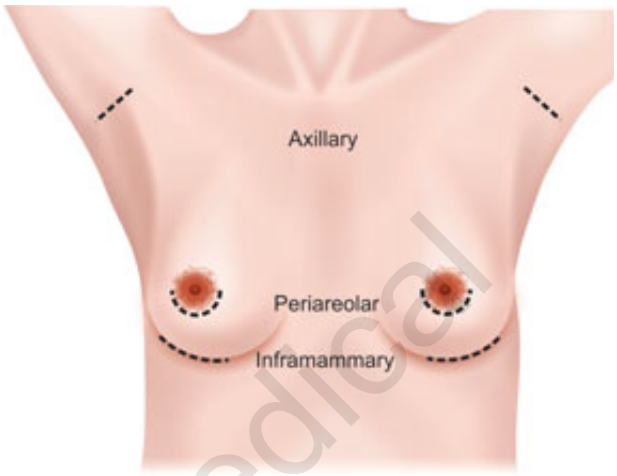

Figure 1 : Types of incisions for augmentation mammoplasty.[6]

- Periareolar: The implant is inserted through an incision around the nipple. However, may interfere with breast-feeding.

Placement of implant

A pocket is created for the implant to be placed in two ways:

1. Subglandular: Where there is enough breast tissue to cover the implant
2. Submuscular or subpectoral: In women with smaller breasts.

TRANSUMBILICAL BREAST AUGMENTATION

Another technique of placing the deflated implant through the belly button and taking it up to the breast thereby resulting in no incision and scar on the breast. Here, the surgeon "tunnels" up through chest area to a pocket under the breast or chest muscle. Once the implant is placed, it is inflated with the saline solution. This procedure has a

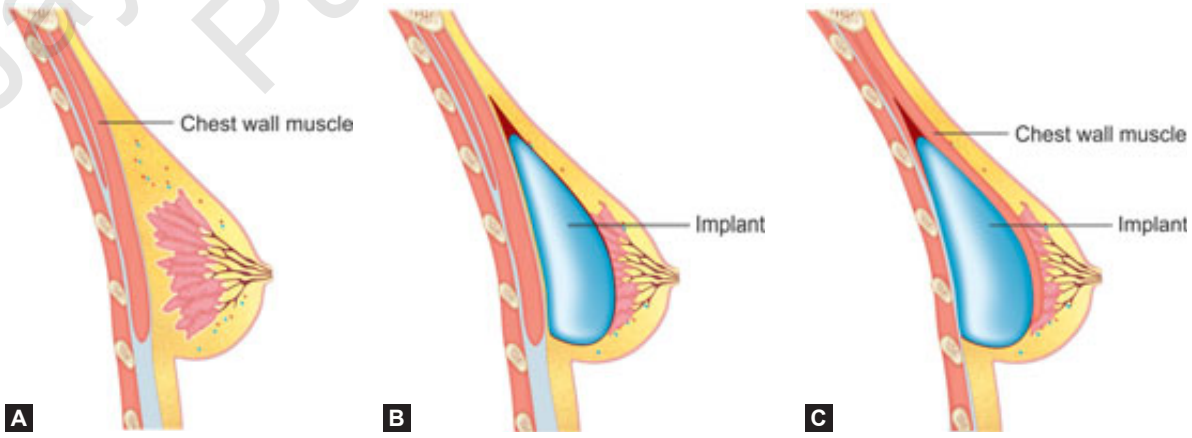

Figure 2 : Types of placement of implants. **A,** Before implant; **B,** Subglandular implant; **C,** Submuscular implant.[7]

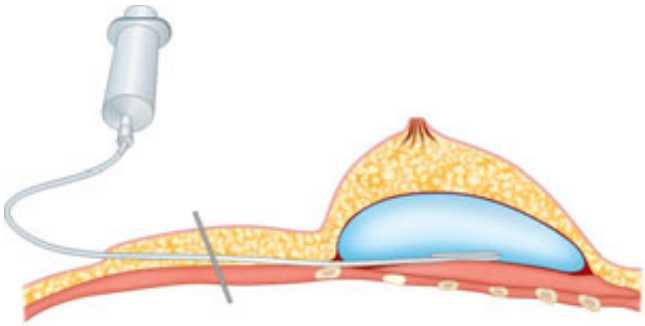

Figure 3: Transumbilical breast augmentation.[8]

faster recovery time and less scarring. But, here only saline implants can be used and silicone implants which are much superior cannot be used.

Complications

Complication are rare and around 10%. They include:

- Capsular contracture: Is when scar tissues around the implant thicken and contract. However, its chances are less when implant is placed in the submuscular position
- Deflation: Especially with saline implants
- Rupture
- Infection
- Changes in nipple/breast sensation
- Breast pain
- Hematoma
- Displacement or migration of implant.

Many of these complications can be prevented by using proper technique of insertion and by using antibiotics.

Despite the risk of complications and additional surgeries, most women are happy with the outcome.

The 2013 study published in Plastic and Reconstructive Surgery found that 98% of women who had undergone breast augmentation surgery were satisfied.[9]

Recovery

A recovery period of about 24–48 hours is required with few days of reduced activity. Patients can resume normal activities within a month to 6 weeks and are advised to wear a special bra to prevent the breast implants from moving.

BREAST REDUCTION SURGERY (REDUCTION MAMMOPLASTY)

Surgery depends on several factors like medical history, size, and shape of breasts, desire to breastfeed, and surgeon's skill.

- The most common procedure, according to the American Society for Aesthetic Plastic Surgery, is one where an anchor-shaped incision around the areola downward, following the natural curve of the crease beneath the breast.[1] Excess fat and tissues is removed and the nipple and areola repositioned higher and the breast is reshaped. The major disadvantage of this procedure is scarring
- For moderate reduction, a vertical or short scar technique may be used. The scars are located only around the areola and down the vertical midline
- For only a small reduction or a redo of a breast reduction, liposuction may be considered.

Complications

- Bleeding: Can be managed by insertion of drain for a couple of days
- Infection: Can be managed with adequate antibiotics cover
- Changes in the sensitivity of their breasts and nipples
- If the blood supply is reduced, the nipple area or other areas of skin may slough off
- Other complications include:
  - Fat necrosis or lumpiness in the breast
  - Inability to breastfeed—because some of the ducts leading to the nipple may be cut during the operation

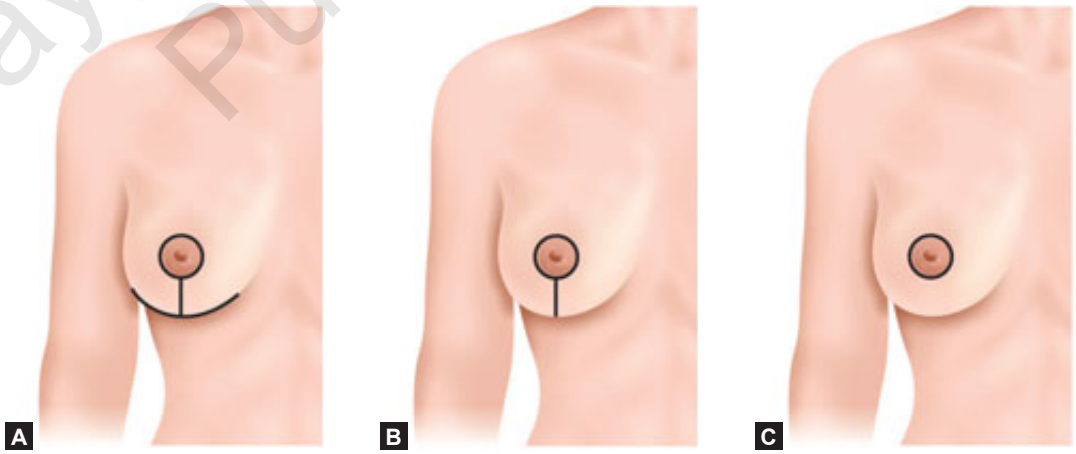

Figure 4: Incisions for breast reduction. **A,** Anchor; **B,** Lollipop; **C,** Donut.

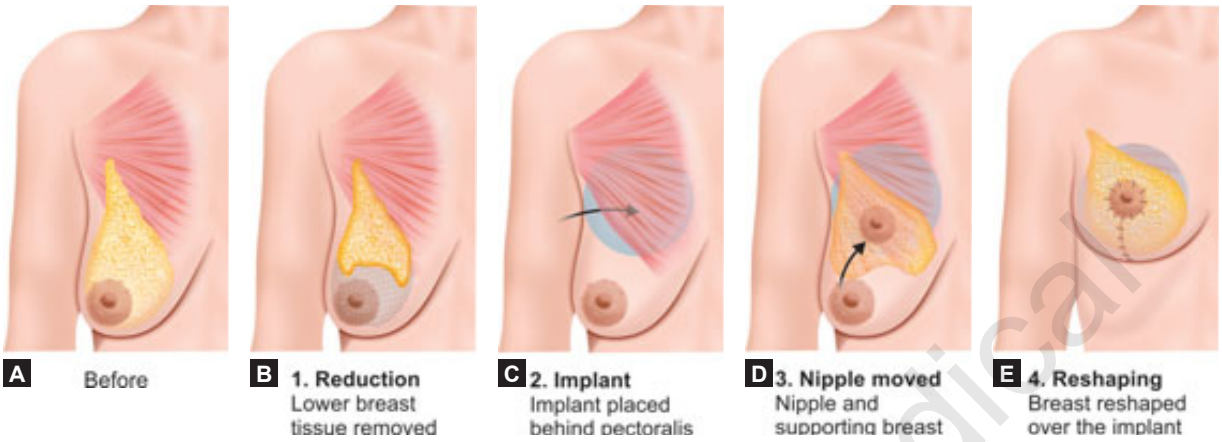

Figure 5: Breast augmentation and reduction.[10]

- Delayed healing
- Minor differences between breasts following the operation.

One way to reduce risk of complications is by quitting smoking. A study found the risk of complications after breast reduction surgery was 3 times higher in smokers than nonsmokers.

Although revisions are uncommon, they may be necessary in some women following breast reduction surgery.

Recovery

After surgery, it is advised to wear a postsurgical bra over gauze dressings for 4 weeks. It may take up to 6 months for breasts to return to normal, and patient will be able to resume normal activities within 6 weeks.

BREAST AUGMENTATION AND REDUCTION

It is a novel concept in breast enhancement and only recently has it been described in the plastic surgery literature. The breast augmentation and reduction (BAR) procedure combines the best of these two procedures that is BAR surgery, removing saggy breast tissue at the bottom of the breast and adding volume to the upper breast with the implant. The nipple-areola complex is moved to the ideal place on the face of the new breast. Compared to a breast reduction, the BAR procedure offers great benefits in terms of breast shape and location on the chest.[1]

BREAST LIFT (MASTOPEXY)

It does not require removal of breast tissue, but instead, reshapes the tissue and moves the nipple-areola complex to an improved location. This "lifting" procedure results in an improved shape but, again, the shape may not remain same and over a time the breast may sag again. Although an easy procedure, but without an implant its value is not superior.

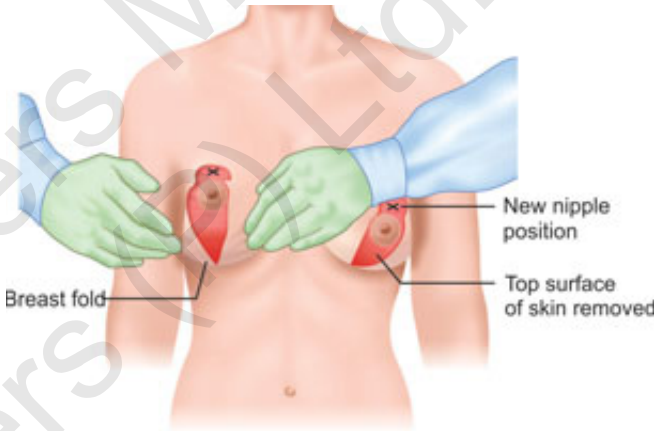

Figure 6: Breast lift procedure.[11]

CONCLUSION

Beautiful and sumptuous breasts are every woman's desire. Shape, size, and firmness of breasts dictate their attractiveness, and therefore a lack of them is a hindrance to a woman's self-esteem. Breast implants offer permanent and best solution to women with underdeveloped breasts. The breast augmentation surgery has a gratifying outcome giving women fuller proportionate breasts and boosting their self-confidence. Special supportive bras help reshaping the breasts and the scars heal uneventfully and are hidden discreetly.

Breast look beautiful and there is no two way about it. Women with fuller breasts can cast a mesmerizing effect but when the breasts are bigger, then they come with their share of drawbacks and looks ugly. When breast size limits life, breast reduction surgery is the best option to decrease and shape them to look beautiful.

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16

CHAPTER

The Aging Breast: Clinician's View

Archana M Dwivedi

INTRODUCTION

The breast is an important secondary sexual organ. It is an erogenous zone and its stimulation leads to orgasm, but more importantly it gives a woman her female identity. Hence, the aging of breast tissue has great psychosocial impact for women. In humans, aging represents the accumulation of change in a woman over time encompassing physical, psychological, and social changes. This chapter will outline these changes in brief with clinical perspective.

DEVELOPMENT OF BREASTS

The changes from birth to menopause are a sequelae of changes in hormonal levels in female body—importantly estrogen, progesterone, prolactin, and human growth hormone.

- At birth, the breast histologically consists of a simple system of ducts without alveoli (however, exaggerated development is occasionally seen, under the influence of maternal estrogens)
- Involution changes occur in breasts within 1–2 weeks, but these are typically more complete in males than female neonates
- By the age of 9–10 years, thelarche (pubertal breast development) has usually commenced

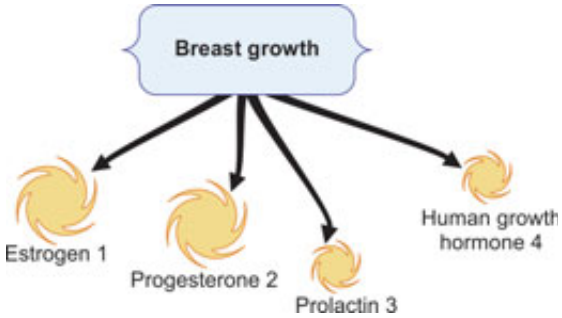

Figure 1: Hormones influencing breast.

- Over the next 3–4 years, the breasts enlarge, the areola grows and then the mamillary ducts and finally alveoli mature
- Throughout menarche, fat deposition occurs to make the breasts more prominent and round
- In reproductive phase and especially during pregnancy, breast parenchyma enlarges under the influence of estrogen, progesterone, and prolactin
- Perimenopause and menopause causes the actual aging of skin and parenchymal components of breasts with decrease in estrogen hormone
- The rate at which a woman's breasts droop and the degree of ptosis depends on many other factors too (discussed further).

As one ages, the tissue and structure of breasts begin to change. This is due to differences in reproductive hormone levels caused by the natural process of aging. Through these changes, the breasts begin to lose their firmness and fullness. Female breast ptosis or sagging is a natural consequence of aging.

In addition to the above physiological changes, with age comes an increased risk of developing growths in the breast, such as fibroids, cysts, and cancer. However, it's important to keep in mind that women of any age can develop these conditions.

CAUSES OF BREAST AGING

As mentioned previously, aging starts around menopause with:

- Natural decline of estrogen: One of the main culprits of breast aging is a natural decline of the female reproductive hormone estrogen. This reduced amount of estrogen causes the skin and connective tissue of the breast to become less hydrated, thus making it less elastic. With less elasticity, the breasts lose firmness and fullness, and can develop a stretched and loose appearance. Furthermore, dense breast tissue is replaced by fatty

tissue as the aging process continues. It is not uncommon for an older woman to change her cup size

- Menopause: Most age-related changes in the breast occur around the time of menopause. Menopause is a natural process during which a woman ceases ovulation and menstruation, and after which she can no longer have children. This transition normally occurs between the ages of 45 and 55. A woman is in menopause once she has not had a period for 12 consecutive months
- Other causes:
  - Women who have had their ovaries surgically removed can have changes in their breasts at any time due to the loss of hormones
  - People with collagen deficiencies (such as in Ehlers-Danlos syndrome) may experience increased ptosis due to a loss of skin elasticity.

Key factors influencing breast ptosis over a woman's lifetime are:

- Cigarette smoking
- Her number of pregnancies
- Higher body mass index
- Larger bra cup size
- Significant weight gain and loss
- Exposure to sun.

COMMON CLINICAL FINDINGS OF THE AGING BREAST

Aging changes in the breasts are visible upon physical examination. Common changes that occur in the breast due to age include:

- Stretch marks
- Downward pointing nipples
- An elongated, stretched, or flattened appearance
- Drooping breasts or ptosis
- Wider space between the breasts
- Lumpiness, which may be due to benign fibrocystic changes in the breast or serious conditions such as breast cancer.

Puckering, redness, or thickening of breast skin, a pulled in nipple, nipple discharge, breast pain, or hard lumps are not considered normal aging changes (regular self breast examination; clinical examination; mammo-sonography and/or mammography may help to differentiate normal from abnormal).

PREVENTION AND TREATMENT OF AGING BREASTS AND CONSEQUENCES

- Many breast changes are a normal part of the aging process
- There's no sure way to prevent your breasts from being affected by changes due to natural aging
- However, the effects of aging can be avoided
- Generally, being as kind to your body as possible, throughout your life, is important.

If the woman is significantly distressed by changes in breast tissue, it is helpful to consider cosmetic surgery. Cosmetic surgery can replace the fullness of the breasts as well as the position of the nipples.

When it comes to stretch marks, there is no definitive treatment. Some topical products may be useful in minimizing their appearance though. In some studies, the herb *Centella asiatica*[1] along with the prescription medication tretinoin[2,3] has been effective in reducing the appearance of stretch marks.

Alternatively, laser treatments are also available.

Myth: Many women and medical professionals mistakenly believe that breastfeeding increases sagging. It is also commonly believed that the breast itself offers insufficient support and that wearing a bra prevents sagging. This has not been found to be true. Breastfeeding has its own merits too.

Simple lifestyle measures to slow aging can be done. According to the American Institute for Cancer Research these include:

- Getting adequate and regular sleep
- Participating in regular exercise, can do best to promote a gentle aging process
- Maintaining a healthy weight—obesity raises your breast cancer risk
- Get regular exercise. Four or more hours a week of moderate to vigorous activity lowers your breast cancer risk
- Not smoking or smoking cessation are important for good skin and tissue health
- Limit alcohol intake—Swallowing two or more alcoholic drinks a day raises your cancer risk
- Eat a healthy diet. A diet rich in vegetables and fruits can help stave off weight gain and may minimize cancer risk.

Practicing relaxation and breathing techniques can be helpful as alternate therapy:

- Yoga
- Box breathing
- Meditation.

CONCLUSION

To summarize, "the breast is an amazing organ." It is the only organ that we are not born with, and it changes along with the stages of your life—puberty, pregnancy, and then involution, perimenopause, and menopause. To accept the changes and act toward healthy lifestyle is the answer.

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17

CHAPTER

Breast Imaging and Risk Assessment

Amrit Gupta

INTRODUCTION

Breast cancer ranks number one cancer amongst Indian females with age adjusted rate as high as 25.8 per 100,000 women and mortality 12.7 per 10,000 women. Age adjusted incidence is found to be as high as 41 per 10,000 women for Delhi followed by Chennai (37.9), Bangalore (34.4), and Thiruvanthipuram (33.7). A statistically significant increase in age adjusted rate over time (1982–2014) was observed. Breast cancer projection for India during time periods 2020 suggests that number to go as high as 1,797,900 new cases. Better health awareness and availability of breast cancer screening programs and treatment facilities would cause a favorable and positive clinical picture in the country.[1]

BREAST IMAGING

Mammography is currently the best radiographic screening tool available for the early detection of breast cancer and the reduction of breast cancer mortality.

Mammography is a special type of X-ray imaging used to create detailed images of the breast. Mammography uses low dose X-rays, achieved by using targets made of low atomic weight alloys (e.g., molybdenum and rhodium). Filters made of aluminum, molybdenum, beryllium, rhodium, or palladium are used to eliminate photons that do not contribute to the image, thereby minimizing the radiation dose to the patient.

There are two types of mammography examinations: Screening and diagnostic. Screening mammography is done in asymptomatic women. A screening examination consists of two images of each breast in the cranial-caudal and medio-lateral-oblique projections that are viewed together.

Ultrasonography (USG) is relatively an accepted method, but its role in screening is widely debated. It is used for diagnostic differentiation of cysts from solid masses, and for guidance in interventional procedures. Current practice and recommendations from American College of Radiology suggests that mammography is the first choice for screening of all women. Ultrasonography should be considered in high-risk patients who cannot tolerate magnetic resonance imaging (MRI) and intermediate-risk patients with category C and D breast density.

The MRI and computed tomography (CT) may have adjuvant roles in the diagnosis of breast cancer. The MRI may prove useful in screening younger women with dense breasts who are at a special high risk of developing breast cancer (e.g., strong family history). Computed tomography may be used as an adjuvant for monitoring spread. Although CT imaging involves some exposure to radiation, it should be considered in patients in whom MRI is contraindicated.[2]

Breast Imaging, Reporting and Data System

Breast Imaging, Reporting and Data System (BI-RADS) is a classification system proposed by American College of Radiologists in 1986 with original report released in 1993. This was deemed imperative due to exponential increase in mammography in 1980, when yearly mammograms were implemented in screening protocols. To add to this was overwhelming variation amongst radiology reports. Hence, BI-RADS was developed to standardize the risk assessment and provide uniformity of reports. Lexicon descriptors were designed to predict both benign and malignant disease, eliminate ambiguity, allow automated data collection, and facilitate communication with referring physicians. Structured reports were organized into several categories, including breast density, description of findings, and a final decision-oriented assessment. Although it was started out for use with breast screening mammography, it was later adopted for use with MRI and USG. Revisions were made in 1995, 1998, and 2003. The BI-RADS fifth edition consolidates, improves, and expands the lexicon for mammography, breast USG, and breast MRI.[3]

Various categories for reporting include:

- Category 0:
  Mammography: Incomplete–need additional imaging evaluation and/or prior mammograms for comparison
  Ultrasound and MRI: Incomplete–need additional imaging evaluation
- Category 1: Negative
- Category 2: Benign
- Category 3: Probably benign
- Category 4: Suspicious mammography and ultrasound
  i. Category 4A: Low suspicion for malignancy
  ii. Category 4B: Moderate suspicion for malignancy
  iii. Category4C: High suspicion for malignancy
- Category 5: Highly suggestive of malignancy
- Category 6: Known biopsy–proven malignancy

RISK ASSESSMENT

Several statistical models have been developed for assigning absolute risk of developing breast cancer. Some models are based solely on family history, such as the Claus model,[4] some are based on family history, *BRCA1/2* carrier status, and polygenes such as the *BOADICEA* model,[5] whereas others incorporate non-genetic risk factors, such as the BCRAT model[6] and the International Breast Cancer Intervention Study model (IBIS, also called the Tyrer Cuzick model).[7]

The most common means of estimating an individual woman's risk of developing breast cancer is by application of a statistical tool known as the Gail model also known as BCRAT model. The Gail model was derived from the data from an American Cancer Society study regarding feasibility of mammographic screening of the American female population, the Breast Cancer Detection and Demonstration Project (BCDDP). Breast cancer risk factors generated from a case control subset of BCDDP participants are combined with estimates of baseline risk generated from the surveillance, epidemiology, and end results (SEER) program incidence data to compute individualized, absolute estimates of breast cancer risk.[3]

Risk factor components of the Gail model include age at time of counseling, age at menarche, age at first live birth, history of prior breast biopsies, and first-degree relatives who have breast cancer. The Gail model was modified for determination of eligibility to participate in the National Surgical Adjuvant Breast Project (NSABP) chemoprevention trials, and the modified version was made available as a Web-based program (http://www.nci.nih.gov/bcrisktool/).

However, it does not include information on *BRCA1/2* mutation status or extended family history (meaning breast cancers in male relatives, number and breast cancer status/ovarian cancer status of second-degree relatives, and age of onset of all affected relatives).

In contrast, the IBIS model includes extended family history, *BRCA1/2* genetic status with nongenetic risk factors such as age, age at menarche, parity, age at first live birth, age at menopause, history of hormone replacement therapy use, history of hyperplasia/atypical hyperplasia, history of lobular carcinoma *in situ*, height and body mass index.

TABLE 1: Interpretation of responses to risk assessment questions

Risk level	*Responses*
Increased risk based on personal history	Yes to any: 1, 2, 3, 4, 5, 6 (#3 applies only to women 50 years or older)
Increased risk based on family history	Yes to any: 7, 8
Average risk	No to all

The following questions are used to identify women at increased risk for breast cancer (Table 1 for definitions of risk levels). The results can help identify which women should be offered a referral to genetics or oncology for counseling about genetic testing and eligibility for chemoprevention, surgical prevention, and/or MRI screening. The results can also be used to guide screening decisions, including screening interval, age to begin screening, and screening method(s). Because risks may change over time, these risk assessment questions should be asked of women at regular intervals, starting at age of 18 years and continuing through age of 74 years. The questions are incorporated into the online health profile and the well visit questionnaire and are also asked at each visit for a screening mammogram with the Breast Cancer Risk Questionnaire. The algorithm for screening for breast cancer is a very useful tool for clinical practice (*see* Appendix 1).[8]

QUESTIONS

Personal History

1. Breast biopsy
2. Radiation therapy to the chest between the ages of 10 and 30 years for Hodgkin's disease
3. Breast cancer at age 50 or older
4. Breast cancer before age of 50 years
5. Ovarian cancer at any age
6. Known *BRCA1* or *BRCA2* gene mutation or Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome.

Family History

7. Patient has had a mother, sister, or daughter with:
   - Breast cancer before age of 50 years, or
   - Breast cancer in both breasts, or
   - Breast and ovarian cancer
   - Known *BRCA1* or *BRCA2* gene mutation or Li-Fraumeni syndrome, Cowden syndrome, or Bannayan-Riley-Ruvalcaba syndrome.

8. Patient has had:
   - At least three female family members (mother, grandmother, sister, daughter, or aunt) with breast cancer, regardless of age at onset
   - At least two female family members on same side with ovarian cancer, regardless of age at onset
   - One female family member with breast cancer and another female family member with ovarian cancer on same side, regardless of age at onset
   - At least two female family members on the same side with breast cancer before age of 50 years
   - At least one female family member of Ashkenazi ancestry with breast or ovarian cancer, regardless of age at onset
9. At least one male family member with breast cancer.

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CHAPTER

BRCA1 and *BRCA2*: Time to Clarify Doubts!

Beenu K Singh

INTRODUCTION

As per recent statistics, published by Indian Council of Medical Research in 2016, breast cancer topped the list of the most common cancers in India with over 144,000 cases being reported every year. Approximately 5–10% of the breast cancers have an underlying genetic predisposition. Women with genetic susceptibility have a much higher risk, almost 50–80%, of developing cancers as compared to the general population with a much earlier age of presentation and with higher mortality rates; therefore early screening has become extremely important. It was in the early nineties when the breast cancer gene 1 and 2 (*BRCA1*, *BRCA2*) were identified as the cause for genetic predisposition in hereditary breast and ovarian cancers (HBOC), both of which can be detected by genetic testing. The HBOC accounts for 60–75% of inherited cases of breast cancer. *BRCA1* and *BRCA2* associated HBOC is characterized by increased risk of female and male breast cancers, ovarian cancers, and other malignancies including fallopian tube cancer, primary peritoneal cancer, prostate cancer, pancreatic cancer, and melanomas. Less commonly, breast cancer is due to other hereditary syndromes, such as Li-Fraumeni and Cowden syndromes, which are associated with mutations in the *TP53* and *PTEN* genes, respectively. Due to the scarce availability of genetic testing, high cost and unawareness regarding implementation of the result in clinical practice, for last many years utility of it has been questioned by many scientists and clinicians, but within last one decade there has been lot of understanding made in this field. In this section, some of the common questions which a gynecologist may come up with are discussed.

WHAT IS *BRCA1* AND *BRCA2* MUTATION AND WHAT IS THE RELEVANCE OF TESTING THEM?

Germline *BRCA1* or *BRCA2* mutations account for approximately 10% of all ovarian cancers, 20–40% of breast cancers that runs in families and about 5–10% of all breast cancer patients. *BRCA1* and *BRCA2* are tumor suppressor genes. *BRCA1* is located on chromosome 17 and is involved in both deoxyribonucleic acid (DNA) repair and regulation. *BRCA2* is located on chromosome 13 and is involved in repair of replication mediated double-strand DNA breaks. *BRCA1* and *BRCA2* mutations are inherited in an autosomal dominant manner. Majority of the patients inherit the mutated copy from either of their parent, this is referred to as the germline mutation and, i.e., either the egg or the sperm harbors the mutated copy which may be passed on to the offspring. As a result, all the cells of the body carry the variation in the gene. Although mutations in these genes are highly penetrant, not all individuals develop the cancers; this could be due to incomplete penetrance. Offspring and siblings of carrier individuals are at a 50% risk of inheriting the mutation. Once a cancer predisposing *BRCA1* or *BRCA2* germ-line pathogenic variant has been identified in a family, testing of at-risk relatives can be performed to identify mutation carriers.

Identifying pathogenic variants in the women in these two genes, understand their lifetime risks for breast and ovarian cancers, therefore helps them make an informed decision regarding management of cancer risks and to make subsequent lifestyle decisions such as child bearing and taking decisions to undergo risk reducing surgeries.

WHO ARE THE CANDIDATES TO UNDERGO *BRCA1* AND *BRCA2* GENETIC TESTING?

Guidelines from the National Comprehensive Cancer Network and the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors provide detailed criteria for identifying candidates for genetic counseling and possible testing for HBOC.[1] Key criteria for hereditary cancer risk evaluation and possible testing are:

- Females with:
  - Breast cancer diagnosed at less than equal to 50 years of age

- Triple-negative breast cancer-(estrogen receptor-negative, progesterone receptor-negative, and human epidermal growth factor receptor 2–negative diagnosed at less than equal to 60 years of age
- Two or more primary breast cancers
- Invasive ovarian or fallopian tube cancer, or primary peritoneal cancer
- Male breast cancer in family
- Any HBOC associated cancers, regardless of age at diagnosis, and of Ashkenazi (central or eastern European) Jewish ancestry

- Patients with breast cancer and first-, second-, or third-degree relatives with:
  - Breast cancer diagnosed at less than equal to 50 years of age in one or more relatives
  - Invasive ovarian, fallopian tube, or primary peritoneal cancer in one or more relatives
  - Breast, prostate, and/or pancreatic cancer, diagnosed at any age in two or more relatives.

WHAT GENETIC TESTING TO BE USED?

Several genetic tests are available to detect mutations in *BRCA1* and *BRCA2*. These include:

Targeted Mutation Analysis

BRCA1 and *BRCA2* testing is commercially available and utilizes blood, saliva, or buccal mucosa samples for analyses. The *BRCA* genes are large, and hundreds of different mutations have been identified. As a result, complete analysis of the *BRCA1* and *BRCA2* genes to exclude both known (i.e., relatively common) and novel (or rare) mutations is often desired, but as this testing is expensive, if patients have a relative who has tested positive for a deleterious mutation, targeted (single-site) mutational analysis can be performed, which is much less expensive compared with comprehensive testing.

BRCA Analysis with Large Genomic Rearrangements Testing (BART)[2]

For individuals from a family without a known *BRCA1/2* mutation (and who meet the testing criteria) should be offered with comprehensive genetic testing, including full gene sequencing of *BRCA1/2* and testing for large genomic rearrangements (deletion duplication testing). At present, analysis of the *BRCA* genes routinely includes evaluation of large rearrangement (LR), called as BART. Patients who previously underwent *BRCA1/BRCA2* testing without analysis for LR should be counseled regarding the chance that they may harbor one of these mutations.[3,4]

Next Generation Panel Testing[5-7]

Although mutations in *BRCA1* and *BRCA2* are the most commonly implicated in women with hereditary breast/ovarian cancer, in clinical practice, some women who undergo such testing will test negative. In families where more than one gene can explain an inherited cancer syndrome, multigene panels may be considered. Next generation sequencing allows for multiple genes to be sequenced simultaneously. These panels include both high and moderate penetrance genes responsible for causing HBOC. For example, ovarian cancer is mainly associated with *BRCA1/2* mutations, but it may also be associated with mutations in *BARD1*, *BRIP1*, *CHEK2*, *MRE11A*, *MSH6*, *NBN*, *PALB2*, *RAD50*, *RAD51C,* and *TP535*. Likewise, in addition to *BRCA1/2*, hereditary breast cancers may also be caused due to pathogenic variants[8] in *PALB2*, *TP53*, *PTEN*, *STK11,* and *CDH15*.

IF A PERSON QUALIFIES FOR *BRCA1* AND *BRCA2* GENETIC TESTING, WHAT NEXT?

Whenever possible, all patients who are candidates for genetic testing should be referred to a qualified genetic counselor. Given the complexity of genetic testing options and their interpretation, pretest and post-test genetic counseling is critical. An important component of pretest counseling is a detailed review of the patient's past medical history and family history, which should include information on maternal and paternal relatives, preferably covering at least three generations. This process is key to determining not only which individuals should undergo genetic counseling, but also in ordering the right test and counseling the patient about the rationale for testing and the likelihood of obtaining a positive result. It also provides them with information needed to understand the potential impact, the test results may have for themselves and their relatives. Particularly with the advent of next generation multigene panel testing, which is an expensive test, appropriate pretest genetic counseling is critical.[9,10]

High-risk individuals who decline genetic testing should be offered for an ongoing genetic counseling and psychological support, if they are anxious or distressed. These individuals should receive individualized guidelines for cancer surveillance and risk reduction based on their personal and family history.

WHO ALL TO BE TESTED IN THE FAMILY?

Whenever possible, the first genetic testing should be performed on the affected members in the family to determine the underlying mutation. If more than one family member is affected, members with the youngest age of onset/multiple primaries/having other associated cancers/most closely related to the individual seeking consultation, should be considered. Testing unaffected individuals should only be considered when the affected family member is not available for testing, as the test being expensive; yield may not be good if done on unaffected individual, once exact mutation is known other members may undergo only targeted analysis instead of multipanel testing.

HOW TO INTERPRET RESULTS?

Results of genetic testing may come out as positive, negative, or uninformative:

- Positive results: A positive result means that a deleterious mutation is identified in a gene such as *BRCA1* or *BRCA2* and therefore has an increased risk of developing certain cancers. However, it cannot tell whether or when an individual will develop the cancer. Additionally, a positive test result has implications for the family members and future generations too, hence should be counseled accordingly
- True negative results: A true negative result means that a familial mutation has been ruled out in the tested individual. For women with a true negative *BRCA1/BRCA2* test result, the risks of breast and ovarian cancer are usually similar to general population risks, provided that, if there is a same mutation within the family, there is no significant family history of cancer on the noncarrier side of the family and no other major risk factors for these cancers (environmental and reproductive)
- Uninformative (negative) result: There are two types of uninformative results. The first occurs when genetic testing results do not indicate the presence of a deleterious or pathogenic mutation, and there is no known cancer susceptibility mutation in the family. The second is known as a variant of uncertain significance.[11] An uninformative negative result may be due to a number of possibilities that may depend in part on what testing was performed. The possibilities include:
    - A deleterious mutation could be present in *BRCA1* or *BRCA2* that cannot be detected by available methods
    - A deleterious mutation could be present in *BRCA1* or *BRCA2* that was not detected by previous methods that did not screen for LR
    - A deleterious mutation could be present in *BRCA1* or *BRCA2* that would be detected by performing comprehensive testing
    - A deleterious mutation may be present in a gene for which testing was not performed, such as on a multigene panel
    - The affected individual being tested has sporadic rather than hereditary cancer
    - A *BRCA1* or *BRCA2* or other gene alteration is identified but its significance is unclear, also termed a variant of uncertain significance. In this instance, it is unclear if the variant is an undefined deleterious mutation, a benign polymorphism, or variant with an intermediate risk of cancer.[12]

WHAT IF TEST COMES OUT TO BE POSITIVE?

First of all, clinicians should document that patients are informed about who in their family is at risk for hereditary cancer and what the potential implications are. Post-test counseling is also critical as it provides an opportunity to review information about hereditary breast and ovarian cancer syndromes and provides an opportunity for patients to understand and assimilate their results, and to consider next steps if needed.

CONCLUSION

To conclude, breast cancer being the most common cancer amongst the females requires urgent attention from health providers and policy makers both. Identification of BRCA mutations in breast cancer patients influences treatment and survival and may also be of importance for their relatives. As most of the times gynecologists are the first doctors to whom these patients contact, it is our utmost responsibility to learn about exact role of *BRCA 1* and *BRCA 2* testing in order to implement it wisely in day to day practice.

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CHAPTER

Breast Cancer

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INTRODUCTION

Breast cancer is the most common invasive cancer in women, and the second main cause of cancer death in women, after lung cancer. Advances in screening and treatment have improved survival rates dramatically since 1989. There are around 3.1 million breast cancer survivors in the United States (U.S.). The chance of any woman dying from breast cancer is around 1 in 37, or 2.7%.

In 2017, around 252,710 new diagnoses of breast cancer are expected in women, and around 40,610 women are likely to die from the disease. Awareness of the symptoms and the need for screening are important ways of reducing the risk.

Breast cancer can affect men too, but this article will focus on breast cancer in women.

FAST FACTS ON BREAST CANCER

Here are some key points about breast cancer.

- Breast cancer is the most common cancer among women
- Symptoms include a lump or thickening of the breast, and changes to the skin or the nipple
- Risk factors can be genetic, but some lifestyle factors, such as alcohol intake, make it more likely to happen
- A range of treatments is available, including surgery, radiation therapy, and chemotherapy.

Many breast lumps are not cancerous, but any woman who is concerned about a lump or change should see a doctor.

SYMPTOMS

The first symptoms of breast cancer are usually an area of thickened tissue in the breast, or a lump in the breast or in an armpit. An early diagnosis of breast cancer increases the chance of recovery. Other symptoms include:

- Pain in the armpits or breast that does not change with the monthly cycle
- Pitting or redness of the skin of the breast, like the skin of an orange
- A rash around or on one of the nipples
- A discharge from the nipple, possibly containing blood
- A sunken or inverted nipple
- A change in the size or shape of the breast
- Peeling, flaking, or scaling of the skin on the breast or nipple

Most lumps are not cancerous, but women should have them checked by a health care professional.

STAGES

Cancer is staged according to the size of the tumor and whether it has spread to lymph nodes or other parts of the body.

There are different ways of staging breast cancer. One way is from stage 0–4, but these may be broken down into smaller stages.

- Stage 0: Known as ductal carcinoma *in situ* (DCIS), the cells are limited to within a duct and have not invaded surrounding tissues
- Stage 1: At the beginning of this stage, the tumor is up to 2 cm across and it has not affected any lymph nodes
- Stage 2: The tumor is 2 cm across and it has started to spread to nearby nodes
- Stage 3: The tumor is up to 5 cm across and it may have spread to some lymph nodes
- Stage 4: The cancer has spread to distant organs, especially the bones, liver, brain, or lungs.

CAUSES

After puberty, a woman's breast consists of fat, connective tissue, and thousands of lobules, and tiny glands that produce milk for breast-feeding. Tiny tubes, or ducts, carry milk toward the nipple.

In cancer, the body's cells multiply uncontrollably. Breast cancer usually starts in the inner lining of milk ducts or the lobules that supply them with milk. From there, it can spread to other parts of the body.

RISK FACTORS

The exact cause remains unclear, but some risk factors make it more likely. Some of these are preventable.

Age

The risk increases with age. At 20 years, the chance of developing breast cancer in the next decade is 0.6%. By the age of 70 years, this figure goes up to 3.84%.

Genetics

If a close relative has or has had, breast cancer, the risk is higher.

Women who carry the *BRCA1* and *BRCA2* genes have a higher risk of developing breast cancer, ovarian cancer or both. These genes can be inherited, *TP53* is another gene that is linked to a greater breast cancer risk.

A History of Breast Cancer or Breast Lumps

Women who have had breast cancer before are more likely to have it again, compared with those who have no history of the disease.

Having some types of benign, or noncancerous breast lumps increases the chance of developing cancer later on. Examples include atypical ductal hyperplasia or lobular carcinoma *in situ*.

Dense Breast Tissue

Breast cancer is more likely to develop in higher density breast tissue.

Estrogen Exposure and Breast-feeding

Being exposed to estrogen for a longer period appears to increase the risk of breast cancer.

This could be due to starting periods earlier or entering menopause later than average. Between these times, estrogen levels are higher.

Breast-feeding, especially for over 1 year, appears to reduce the chance of developing breast cancer, possibly because pregnancy followed by breastfeeding reduces exposure to estrogen.

Body Weight

Women who are overweight or have obesity after menopause may have a higher risk of developing breast cancer, possibly due to higher levels of estrogen. High sugar intake may also be a factor.

Alcohol Consumption

A higher rate of regular alcohol consumption appears to play a role. Studies have shown that women who consume more than three drinks a day have a 1.5 times higher risk.

Radiation exposure

Undergoing radiation treatment for a cancer that is not breast cancer increases the risk of breast cancer later in life.

Hormone treatments

The use of hormone replacement therapy (HRT) and oral birth control pills have been linked to breast cancer, due to increased levels of estrogen.

Occupational hazards

In 2012, researchers concluded that exposure to certain carcinogens and endocrine disruptors, for example in the workplace, could be linked to breast cancer.

In 2007, scientists suggested that working night shifts could increase the risk of breast cancer, but more recent research concludes this is unlikely.

COSMETIC IMPLANTS AND BREAST CANCER SURVIVAL

Women with cosmetic breast implants who are diagnosed with breast cancer have a higher risk of dying from the disease and a 25% higher chance of being diagnosed at a later stage, compared with women without implants.

This could be due to the implants masking cancer during screening, or because the implants bring about changes in breast tissue. More research is needed.

TYPES

Breast cancer can be:

- Ductal carcinoma: This begins in the milk duct and is the most common type
  Lobular carcinoma: This starts in the lobules
- Invasive breast cancer is when the cancer cells break out from inside the lobules or ducts and invade nearby tissue, increasing the chance of spreading to other parts of the body
- Noninvasive breast cancer is when the cancer is still inside its place of origin and has not broken out. However, these cells can eventually develop into invasive breast cancer.

Breast cancer can also affect men, but it is less common in men than in women.

DIAGNOSIS

A diagnosis is often made as the result of routine screening, or when a woman approaches to the doctor after detecting symptoms.

Some diagnostic tests and procedures help to confirm a diagnosis.

Breast Exam

The physician will check the patient's breasts for lumps and other symptoms. The patient will be asked to sit or stand with her arms in different positions, such as above her head and by her sides.

Imaging tests:

- A mammogram is a type of X-ray commonly used for initial breast cancer screening. It produces images that can help detect any lumps or abnormalities. A suspicious result can be followed up by further diagnosis. However, mammography sometimes shows up a suspicious area that is not cancer. This can lead to unnecessary stress and sometimes interventions
- An ultrasound scan can help differentiate between a solid mass and a fluid-filled cyst
- A magnetic resonance imaging scan involves injecting a dye into the patient, to find out how far the cancer has spread.

Biopsy

A sample of tissue is surgically removed for laboratory analysis. This can show whether the cells are cancerous, and, if so, which type of cancer it is, including whether or not the cancer is hormone-sensitive.

Diagnosis also involves staging the cancer, to establish:

- The size of tumor
- How far it has spread
- Whether it is invasive or noninvasive
- Whether it has metastasized, or spread to other parts of the body

Staging will affect the chances of recovery and will help decide on the best treatment options.

TREATMENT

Treatment will depend on:

- The type of breast cancer
- The stage of the cancer
- Sensitivity to hormones
- The patient's age, overall health, and preferences.

The main options include:

- Radiation therapy
- Surgery
- Biological therapy, or targeted drug therapy
- Hormone therapy
- Chemotherapy

Factors affecting the choice will include the stage of the cancer, other medical conditions, and individual preference.

Surgery

If surgery is needed, the choice will depend on the diagnosis and the individual.

Lumpectomy

Removing the tumor and a small margin of healthy tissue around it can help prevent the spread of the cancer. This may be an option if the tumor is small and likely to be easy to separate from the surrounding tissue.

Mastectomy

Simple mastectomy involves removing the lobules, ducts, fatty tissue, nipple, areola, and some skin. Radical mastectomy removes muscle from the chest wall and the lymph nodes in the armpit as well.

Sentinel Node Biopsy

Removing one lymph node can stop the cancer spreading, because if breast cancer reaches a lymph node, it can spread further through the lymphatic system into other parts of the body.

Axillary Lymph Node Dissection

If there are cancer cells on a node called the sentinel node, the surgeon may recommend removing several lymph nodes in the armpit to prevent the spread of disease.

Reconstruction

Following breast surgery, reconstruction can recreate the breast so that it looks similar to the other breast. This can be done at the same time as a mastectomy, or at a later date. The surgeon may use a breast implant, or tissue from another part of the patient's body.

Radiation Therapy

Controlled doses of radiation are targeted at the tumor to destroy the cancer cells. Used from around a month after surgery, along with chemotherapy, it can kill any remaining cancer cells.

Each session lasts a few minutes, and the patient may need 3–5 sessions per week for 3–6 weeks, depending on the aim and the extent of the cancer.

The type of breast cancer will dictate what type of radiation therapy, if any, is most suitable.

Adverse effects include fatigue, lymphedema, darkening of the breast skin, and irritation of the breast skin.

Chemotherapy

Medications known as cytotoxic drugs may be used to kill cancer cells, if there is a high-risk of recurrence or spread. This is called adjuvant chemotherapy.

If the tumor is large, chemotherapy may be administered before surgery to shrink the tumor and make its removal easier. This is called neo-adjuvant chemotherapy.

Chemotherapy can also treat cancer that has metastasized, or spread to other parts of the body, and it can reduce some symptoms, especially in the later stages.

It may be used to reduce estrogen production, as estrogen can encourage the growth of some breast cancers. Adverse effects include nausea, vomiting, loss of appetite, fatigue, sore mouth, hair loss, and a slightly higher susceptibility to infections. Medications can help control many of these.

Hormone Blocking Therapy

Hormone blocking therapy is used to prevent recurrence in hormone-sensitive breast cancers. These are often referred to as estrogen receptor positive and progesterone receptor positive cancers. Hormone blocking therapy is normally used after surgery, but it may sometimes be used beforehand to shrink the tumor.

It may be the only option for patients who cannot undergo surgery, chemotherapy, or radiotherapy.

The effects normally last for up to 5 years after surgery. The treatment will have no effect on cancers that are not sensitive to hormones.

Examples include:

- Tamoxifen
- Aromatase inhibitors
- Ovarian ablation or suppression
- A luteinising hormone-releasing hormone agonist drug called goserelin, to suppress the ovaries. Hormone treatment may affect a woman's future fertility.

Biological Treatment

Targeted drugs destroy specific types of breast cancer. Examples include trastuzumab (Herceptin), lapatinib (Tykerb), and bevacizumab (Avastin). These drugs are all used for different purposes.

Treatments for breast and other cancers can have severe adverse effects.

The patient should discuss with a doctor the risks involved and ways to minimize the negative effects, when deciding on treatment.

OUTLOOK

With treatment, a woman who receives a diagnosis of stage 0 or stage 1 breast cancer has an almost 100% chance of surviving for at least 5 years.

If the diagnosis is made at stage 4, the chance of surviving another 5 years is around 22%.

Regular checks and screening can help detect symptoms early.

PREVENTION

There is no sure way to prevent breast cancer, but some lifestyle decisions can significantly reduce the risk of breast and other types of cancer.

These include:

- Avoiding excess alcohol consumption
- Following a healthy diet with plenty of fresh fruits and vegetables
- Getting enough exercise
- Maintaining a healthy body mass index.

Women should think carefully about their options for breast-feeding and the use of HRT following menopause, as these can affect the risk.

Preventive surgery is an option for women at high-risk.

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CHAPTER

Chemotherapy for Breast Cancer

Revathy Janakiram

INTRODUCTION

Breast cancer is the second leading cause of mortality in women. Combination of chemotherapy and hormonal therapy would be expected to halve the mortality in patients with estrogen receptor (ER) positive disease during the first 15 years of diagnosis.[1] Similarly, poly chemotherapy significantly improves the outcomes in patients with ER poor breast carcinoma.[2] The stage of breast cancer is an important factor in making decisions about the treatment options. Other factors of importance are: If the cancer cells contain hormone receptors, [that is, if the cancer is ER-positive or progesterone receptors (PR)-positive], if the cancer cells have large amounts of human epidermal growth factor receptor 2 (HER2) protein, (i.e., if the cancer is HER2-positive), menopause status, and grade of the tumor.

WHEN IS CHEMOTHERAPY USED?

- Not all women with breast cancer will need chemotherapy, but there are several situations in which it may be recommended:
  - After surgery (adjuvant chemotherapy): Adjuvant chemotherapy is used to kill cancer cells that might have been left behind or have spread but can't be seen, even on imaging tests (micrometastasis). If these cells were allowed to grow, they could form new tumors at other places in the body
  - Before surgery (neoadjuvant chemotherapy): Neo-adjuvant chemotherapy can be used to shrink the tumor so it can be removed with less extensive surgery. Therefore, it is often used to treat cancers that are too big to be removed by surgery at the time of diagnosis (called locally advanced cancers)
  - For advanced breast cancer: Chemotherapy can be used as the main treatment for women whose cancer has spread outside the breast either when it is diagnosed or after initial treatment
- There are tests available, such as Oncotype DX and MammaPrint that can help determine which women will most likely benefit from chemotherapy after breast surgery. In most cases (especially in adjuvant or neo-adjuvant treatment), chemotherapy is most effective when combinations of drugs are used. The length of treatment depends on how well the chemotherapy is working and how well it is tolerated.

ADJUVANT SYSTEMIC CHEMOTHERAPY

Various trials confirmed that micrometastasis are present in many patients at the time of diagnosis and that systemic therapy to eradicate them markedly improves disease free and overall survival of patients. Mortality rates have declined 2% per year for the past 20 years. The first trial of adjuvant chemotherapy was performed by the National Breast Cancer Bowel and Breast Project in 1958.[3]

The most common drugs used for adjuvant and neoadjuvant chemotherapy include:

- Anthracyclines, such as doxorubicin (adriamycin) and epirubicin (ellence) introduced in 1980s
- Taxanes, such as paclitaxel (taxol) and docetaxel (taxotere)
- 5-fluorouracil (5-FU)
- Cyclophosphamide (cytoxan)
- Carboplatin (paraplatin).

Most often, combinations of 2 or 3 of these drugs are used.

Dose Intensity

Another way to improve the benefit of adjuvant chemo therapy is to increase the dose intensity formulated as body size adjusted dose (mg/m^2) divided by time (per week). One

method of increasing dose intensity is dose escalation, which was found to improve the outcomes.[4]

Dose Density

The Norton Simon model predicts that the optimal treatment of a heterogeneous mix of cells (in terms of chemotherapy sensitivity) is to eradicate the numerically dominant, faster-growing cells first, followed by eradication of the more slowly growing resistant cells. This is termed sequential therapy and was found to be superior to alternating therapy.[5]

NEOADJUVANT CHEMOTHERAPY

Preoperative chemotherapy is the preferred therapeutic modality for locally advanced (T3 or T4) and inflammatory breast cancer. Preoperative chemotherapy can be used to downstage tumors and facilitate breast conservation in women who otherwise needed mastectomy. A standard preoperative regimen include taxane. In addition anthracyclines should be considered. For HER2 positive tumors, incorporation of trastuzumab is strongly recommended. Even among patients who have complete clinical response to preoperative chemotherapy, definitive breast surgery is recommended as there could be microscopic residual disease. The absence of any residual invasive tumor in surgical specimen is referred to as pathological complete remission and is associated good prognosis.

New Chemotherapy Agents

With incremental benefits observed from the use of anthracyclines and taxanes, new drugs were added to see if small additional gains could be attained. Gemcitabine has been tested in the tAnGO trial.[6]

Addition of bevacizumab to standard chemotherapy compared to chemotherapy alone in patients with triple negative breast cancer was found to have no benefit.

The absence of PR and/or the over expression of the HER2 or high recurrence score may indicate a relative endocrine resistance and drive a decision to chemotherapy.

CHEMOTHERAPY FOR ADVANCED BREAST CANCER

Chemotherapy drugs useful in treating women with breast cancer that has spread include:

- Taxanes, such as paclitaxel (taxol), docetaxel (taxotere), and albumin-bound paclitaxel (abraxane)
- Anthracyclines (doxorubicin, pegylated liposomal doxorubicin, and epirubicin)
- Platinum agents (cisplatin, carboplatin)
- Vinorelbine (navelbine)
- Capecitabine (xeloda)
- Gemcitabine (gemzar)
- Ixabepilone (ixempra) albumin-bound paclitaxel (nab-paclitaxel or abraxane)
- Eribulin (halaven).

Although, drug combinations are often used to treat early breast cancer, advanced breast cancer more often is treated with single chemotherapeutic drug. Still, some combinations, such as paclitaxel plus carboplatin, are commonly used to treat advanced breast cancer. For cancers that are HER2-positive, one or more drugs that target HER2 may be used with chemotherapy. Moderate to high risk HER2 positive cases should receive chemotherapy (anthracycline/taxanes and trastuzumab). Patients receiving trastuzumab based therapy should have left ventricular ejection fraction evaluated prior to initiating therapy and then at regular intervals during therapy.

POSSIBLE SIDE EFFECTS OF CHEMOTHERAPY FOR BREAST CANCER

These depend on the type and dose of drugs given, and the length of treatment. Some of the most common possible side effects include: Hair loss, nail changes, mouth sores, loss of appetite or weight changes, nausea and vomiting, diarrhea, fatigue etc. Doxorubicin, epirubicin, and some other chemotherapy drugs rarely can cause cardiomyopathy. The risk is highest if the drug is used for a long time or in high doses.

Many drugs used to treat breast cancer, including the taxanes (docetaxel and paclitaxel), platinum agents (carboplatin, cisplatin), vinorelbine, eribulin, and ixabepilone, can damage nerves outside of the brain and spinal cord. This can sometimes lead to symptoms (mainly in the hands and feet) like numbness, pain, burning or tingling sensations, sensitivity to cold or heat, or weakness. In most cases this goes away once treatment is stopped, but it might last a long time in some women or may become permanent.

Certain drugs, such as capecitabine and liposomal doxorubicin, can irritate the palms of the hands and the soles of the feet. This is called hand-foot syndrome. Therapy related myeloid neoplasms such as treatment related myelogenous leukemia has been described.

CONCLUSION

The use of cytotoxic chemotherapy in both advanced and early stage breast cancer has made significant progress in the last 10 years with several landmark studies identifying clear survival benefits for newer therapies. In spite of these developments the optimal approach for any specific patient cannot be determined from a literature review or decision-making algorithm alone. Treatment choices are predominantly based on practice determined by individual or collective experience and the historical development of treatment within a locality. The improvement in the understanding of molecular biological basis of breast cancer provides possible targets for novel therapies. Chemotherapy is the only option for patients with triple negative breast cancer. The decision regarding type and duration of chemotherapy should be independent of the hormone

receptor status. Data today suggest that poly chemotherapy with anthracyclines and taxane based regimen is superior. When chemoendocrine therapy is recommended, sequential rather than concurrent administration appears to be the most prudent strategy.[7]

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21

CHAPTER

Principles of Mastectomy

Sneha S Bhuyar, Surendra Bhuyar

DEFINITION

Removal of breast tissue completely or partially is called as mastectomy.

HISTORY

- 549 A.D: Court physician Aetius of Amida proposed to Theodora
- 1882: Sir William Stewart Halsted proposed radical mastectomy
- 1945:Patey and Dyson proposed modified radical mastectomy
- 1981: Breast conservative surgery
- In past era, a radical mastectomy, i.e., complete removal of breast along with axillary lymph node dissection was the standard treatment for breast cancer. However, surgical breakthroughs over the past two decades have given women more options than ever before. Nowadays less invasive breast conserving treatments are available to many women.

TYPES OF MASTECTOMY

- Classical Halsted radical mastectomy
- Extended radical mastectomy
- Modified radical mastectomy:
  - Patey's modified radical mastectomy
  - Scansion's modified radical mastectomy
  - Madden's modified radical mastectomy
  - Auchincloss modified radical mastectomy
- Simple/total mastectomy
- Skin sparing mastectomy
- Conservative mastectomy
- Prophylactic mastectomy
- Toilet mastectomy.

GENERAL INDICATIONS OF MASTECTOMY

- Woman with carcinoma breast
- Men with carcinoma breast
- No or minimal response to systemic therapy for carcinoma breast
- Extensive benign disease of breast
- Prophylactic.

Which Procedure is Suitable for the Given Patient?

The biology and behavior of breast cancer affects the treatment plan. Some tumors are smaller but grow fast, while others are larger and grow slowly. Treatment options and recommendations are very personalized and depend on several factors including:

- Age and menstrual status
- Size of the tumor
- Size of the breast
- Stage of malignancy
- Axillary lymph nodes status
- Biological aggressiveness of the tumor
- Receptive status of the tumor (estrogen receptor, progesterone receptor)
- Receptor gene *BRCA1* and *BRCA2* status
- Availability of radiotherapy
- Multicentricity or multifocality of origin
- Patient's choice
- Prophylactic/therapeutic/conservative.

Which Procedure is the Best?

When the tumor size is more than 1 cm it usually becomes systemic. No single method is considered better in terms of disease-free survival or mortality. Suitable local therapy along with systemic therapy is the most appropriate approach.

Loco-regional therapy includes:
- Surgery
- Radiotherapy.

Systemic therapy includes:
- Chemotherapy
- Hormonal therapy
- Monoclonal antibodies.

PREOPERATIVE MANAGEMENT

- Triple assessment
- Metastatic workup
- Routine blood investigation
- Preanesthetic evaluation
- Control of medical conditions like diabetes mellitus and hypertension
- Counseling and written informed consent
- Part preparation: Neck to mid-thigh including axilla, arm, and pelvis.

OPERATIVE PROCEDURES

Simple/Total Mastectomy

Indications

- Stage I and IIA carcinoma
- Large cancers that persist after adjuvant therapy
- Multifocal/multicentric.

Procedure

- Removal of entire breast tissue without dissection of axillary contents. Sometimes the sentinel lymph node, i.e., the first axillary lymph node to metastasize cancer cells is removed.

Modified Radical Mastectomy

Indications

- Locally advanced breast cancer

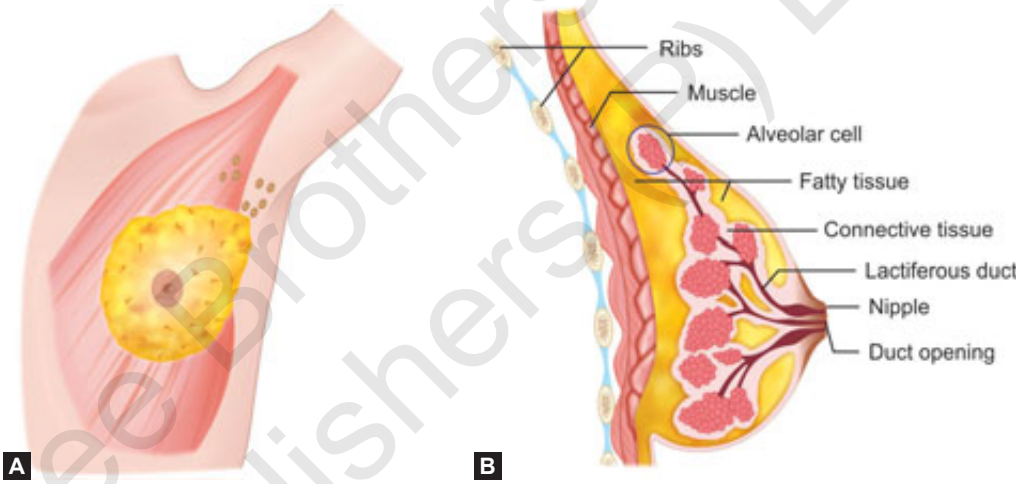

Figure 1: Anatomy of breast.

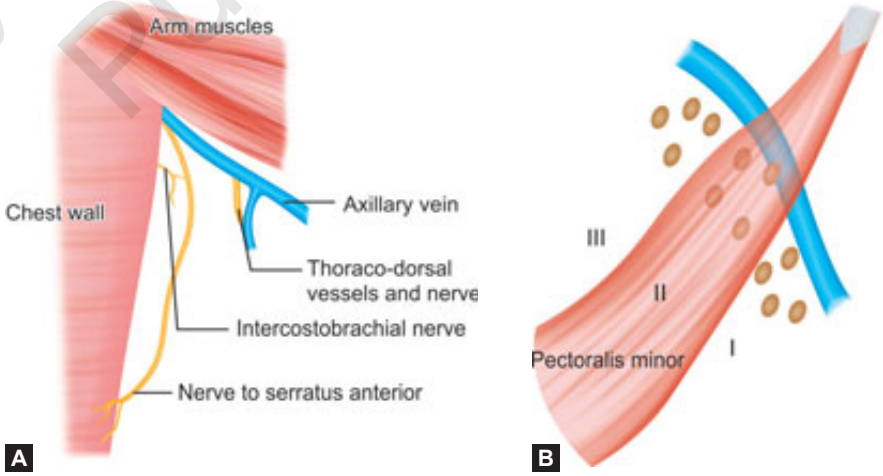

Figure 2: Anatomy of axilla.

- Residual large cancers that persist after adjuvant therapy
- Multifocal/Multicentric disease

Procedure

- Removal of entire breast tissue along with axillary contents (lymph nodes and fatty tissue) en bloc
- In contrast to classical radical mastectomy, both pectoralis major and minor muscles are spared
- This type of mastectomy is used to examine the axillary lymph node status and helps to identify whether the malignancy has spread beyond the breast.

Modifications

- Patey's
- Scanlon's
- Madden's
- Auchincloss
  - Patey was the first surgeon to modify classical Halsted's radical mastectomy. He used to remove pectoralis minor muscle for removal of interpectoral metastatic lymph nodes and hence achieve completeness of radical surgery but spare pectoralis major, as it would help in prosthetic breast implant reconstruction
  - Madden and Auchincloss further modified the procedure and started removing entire breast tissue with axillary content and sparing pectoral muscles. According to them, results of these procedure were comparable with Patey's method. Hence, nowadays these methods are more popular and widely accepted.

Halsted's Radical Mastectomy

- First performed in 1882 by Sir William Stewart Halsted
- It is the most extensive procedure.

Procedure

- In this procedure, entire breast, axillary lymph nodes, Fat, fascia, and pectoral muscles are removed
- This procedure is more disfiguring than modified radical mastectomy and nowadays it is reserved for tumors involving pectoral muscles or recurrent breast cancers.

Disadvantages

- Bad scars and unacceptable deformity
- Reduced range of mobility of shoulder
- Lymphoedema of upper extremity on same side.

Skin Sparing Mastectomy

- In this procedure, the breast tissue is removed through a conservative incision made around the areola
- Increased amount of skin is preserved as compared to traditional mastectomy to facilitate breast reconstruction
- Patients with cancers that involve the skin like inflammatory breast carcinoma cannot be subjected to this procedure
- Local recurrence is acceptable: 0–3%.

Breast Conservation Surgery

Indications

- Carcinoma *in-situ*
- Stage I breast malignancy
- Stage II breast malignancy without lymph node involvement
- Clinically down stage malignancy.

Procedure

- Wide local excision/lumpectomy: Complete removal of tumor with tumor-free margins of breast
- Quandrantectomy: Removal of complete quadrant of breast where the lump is present
- After breast conservative surgery, local radiotherapy is essential or else the local recurrence rate is very high, i.e., up to 40%.

Follow-up After Breast Conservation Surgery

- Mammogram after 6 months of radiotherapy is compulsory
- Clinical evaluation and mammogram every year afterwards
- If focal recurrence is detected, mastectomy must be performed.

Subcutaneous Mastectomy

- In subcutaneous mastectomy, breast tissue is removed but the nipple-areola complex is preserved
- It was historically performed only prophylactically or for extensive benign disease like cystosarcoma phylloid
- Rarely performed as large amount of breast tissue is left *in-situ.*

Extended Radical Mastectomy

- Radical mastectomy with intrapleural en bloc resection of internal mammary lymph nodes by sternal splitting and supraclavicular lymph nodes
- This procedure is obsolete.

Toilet Mastectomy

- Done in fungating or ulcerative growths
- Palliative simple mastectomy.

Prophylactic Mastectomy

- This procedure is used as a preventive measure against breast cancer
- The aim of this surgery is to remove whole breast tissue that could potentially develop malignancy
- The surgery is generally considered when the patient has mutation in *BRCA1* and *BRCA2* which are tumor suppressor genes. Harmful mutation in these genes may produce a hereditary breast ovarian cancer syndrome.

SURVIVAL AFTER BREAST CONSERVATIVE SURGERY AND MASTECTOMY

Many institutions and organizations have perform a comparative study between breast conservative surgery with local radiotherapy and mastectomy to know the overall survival rate and disease free survival rate after 5 years, 8 years, 10 years, 15 years, and 18 years.

After the studies it has been found that the results are almost equal and comparable in both the methods. The survival as well as disease free survival is highest after six year and lowest after eighteen years.

The survival rate after 6 years is in between 78 and 82%. Whereas disease free survival rate after 6 years is in between 66 and 70%. The survival rate after 18 years is in between 62 and 65%.

POSTOPERATIVE CARE

- Apart from routine postoperative care, examination of wound on day 3
- Drain is removed when it is less than 30 mL
- Any collection can be aspirated with aseptic precautions
- Staples can be removed after 10 days
- Arm movement is started within 1st week
- Active shoulder and upper limb exercise start after 2 weeks.

COMPLICATIONS

More Common

- Reduced movement of shoulder
- Numbness
- Lymphedema
- Pain.

Less Common

- Hematoma
- Skin flap necrosis
- Fibrosis
- Ringing of scapula
- Psychological implications
- Chronic/phantom pain.

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22

CHAPTER

Ultrasound Guided Breast Biopsy

Charu Modi

INTRODUCTION

Any lump, swelling, or abnormality in the breast is often detected by physical examination, mammography, or imaging studies. However to differentiate between benign or cancerous lesion one has to resort to biopsy from the tissue.

A breast biopsy is the removal of breast tissue to examine it for signs of breast cancer or other disorder. It is performed when a breast ultrasound shows an abnormality such as a suspicious solid mass, a distortion in the normal architecture of breast tissue, an area of abnormal tissue change, etc. There are several types of breast biopsies like stereotactic, ultrasound guided, magnetic resonance imaging guided, and excisional breast biopsy.

A ultrasound guided breast biopsy uses sound waves to help locate such lesions and remove a tissue sample for examination under microscope. It is less invasive, leaves little or no scarring and does not involve any radiation exposure.

TYPES OF BIOPSY PROCEDURES

- Fine needle aspiration: It uses a very small needle to take out fluid or cells from the suspected area
- Core needle: Uses a large hollow needle to remove a sample of breast tissue
- Vacuum assisted device: Uses a vacuum powered instrument to collect multiple tissue samples during single insertion
- Wire location: A guide wire is placed in the suspicious area to help locate the lesion for surgical biopsy.

The procedure involves a transducer that is used to do the scanning which sends out high frequency sound waves and the images are transmitted to the computer screen. Other sterile equipments involved are syringes, sponges, forceps, scalpel, and a specimen cup, or a microscope slide. Female has to stop aspirin, blood thinners, and other herbal medications 3–5 days prior to the procedure. At times local anesthesia is required for the same.

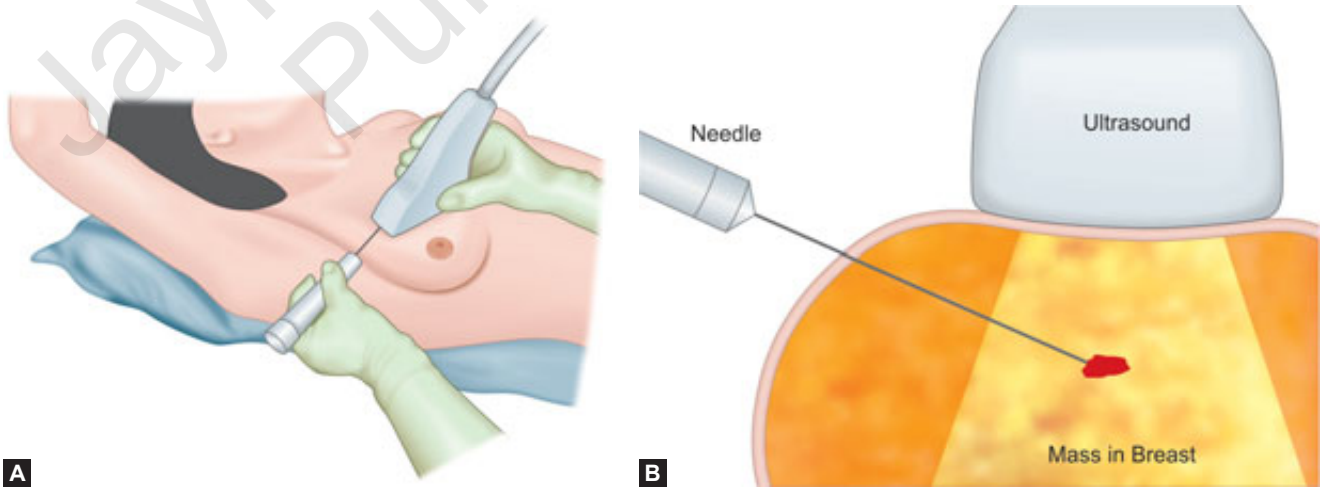

Figure 1: Ultrasound guided breast biopsy.

Procedure involves the following steps:

- Patient lies on her back
- Cleaning of the breast area is done
- Doctor makes a very small cut on the breast area that needs to be biopsied
- Ultrasound machine is used to guide the needle to the abnormal area (Fig. 1)
- Several small pieces of tissue are taken
- A small metal clip may be placed into the breast in the area of the biopsy to mark, if needed.

The preferred biopsy technique is the "freehand" technique based on the description by Parker et al.[1] and by other authors,[2-5] where the radiologist manipulates the transducer with one hand and the core biopsy (CB) device with the other. As regards technical standards, there are small regional variations. In box 1, a checklist is suggested.

Figure 2 shows the main steps at ultrasound-guided breast CB. Initially, the antisepsis of the exposed area is performed by means of sterile gauze pad and antiseptic solution (chlorhexidine, povidone iodine, or alcohol). The lesion to be biopsied is identified with the transducer and, it is recommended that with the palm of the same hand, the fourth and fifth fingers resting on the field without exerting pressure on the breast the physician avoids the motion of the breast. By keeping the area of interest farther from the needle insertion point, it is possible to observe its entire trajectory, from the skin surface up to the lesion.

The recommended access area is the peripheral curvature of the breast, positioning the needle at 2–3 cm away from the edge of the transducer, in parallel to the chest wall and perpendicularly to the transducer, allowing a better ultrasound visualization of the needle and reducing the risk for pneumothorax (Fig. 3A). The access through the nipple-areolar complex should be avoided. In cases of very deep or centrally and superficially located lesions, the oblique needle access may be necessary, which may impair its visualization on ultrasound. In such cases, the transducer should be angled at approximately 90° (Fig. 3B).

BOX 1 Checklist for ultrasound-guided core biopsy of breast

1. Review previous imaging studies and perform a well-documented targeted ultrasonography scan
2. Evaluate whether the biopsy is appropriately indicated
3. Obtain the term of free and informed consent from the patient after having explained its entire contents
4. Define the pathway to approach the lesion, as well as which of the physician's hands will be used for each function
5. Carry out the antisepsis of the transducer and prepare the materials on a portable table
6. Don the sterile gloves and couple the core biopsy needle (14G) to the device. Perform a triggering test, checking out the needle travel, as well as the triggering sound from the device
7. Aspirate the anesthetic agent (1–2% lidocaine without vasoconstrictor)
8. Positioning the patient (usually in dorsal or anterior oblique decubitus)
9. Perform the antisepsis over a wide area around the lesion, over which a sterile fenestrated drape should be placed. The antiseptic or sterile gel will serve as an ultrasound conductive agent
10. Sonographically identify the lesion. The palm of the hand holding the transducer and the fourth and fifth fingers exert some pressure on the breast to avoid its motion
11. Remember the access and entry point defined on item 4. Under ultrasound guidance, inject the anesthetic agent through the entire pathway up to the lesion
12. Make a 2–3 mm incision on the skin over needle entry point
13. Insert the biopsy needle through the incision, attempting to follow the same pathway of the anesthetic needle towards the lesion border. At this point, the needle is to be directed to a position parallel to the nodule
14. Tell the patient that a sample is about to be obtained, and trigger the device action
15. Cross-sectionally and longitudinally slide the transducer aiming at verifying whether the needle penetrated the nodule and that no injury occurred to the chest wall
16. Retrieve the sample from the needle with the scalpel blade or sterile needle, placing it in the vial with formaldehyde, briefly evaluating its characteristics
17. Repeat steps 13–16 until a minimum of five good samples are obtained, preferably from different areas of the lesion (center, 3, 6, 9, and 12 o'clock positions). In cases of microcalcifications, at least 10 samples should be collected and submitted to radiography, identifying, and separating those without calcifications from the ones with calcium
18. Compress the lesion and incision areas for at least 5 min and apply ice locally
19. Perform asepsis and apply compressive dressings which should be left in place for 24–48 h
20. Instruct the patient to avoid intense physical exertion and prescribe pain relievers and nonsteroid anti-inflammatory medication, as necessary
21. Clarify doubts and schedule return as soon as the histopathological results are available

Note: The presence of an assistant is valuable during the procedure. Such an assistant can perform the functions described on items 5, 8, 9, 16, 18, and 19. This will make the procedure swifter and the physician will be able to exert compression on the breast after triggering the CB device, thus decreasing the risk for development of hematoma.

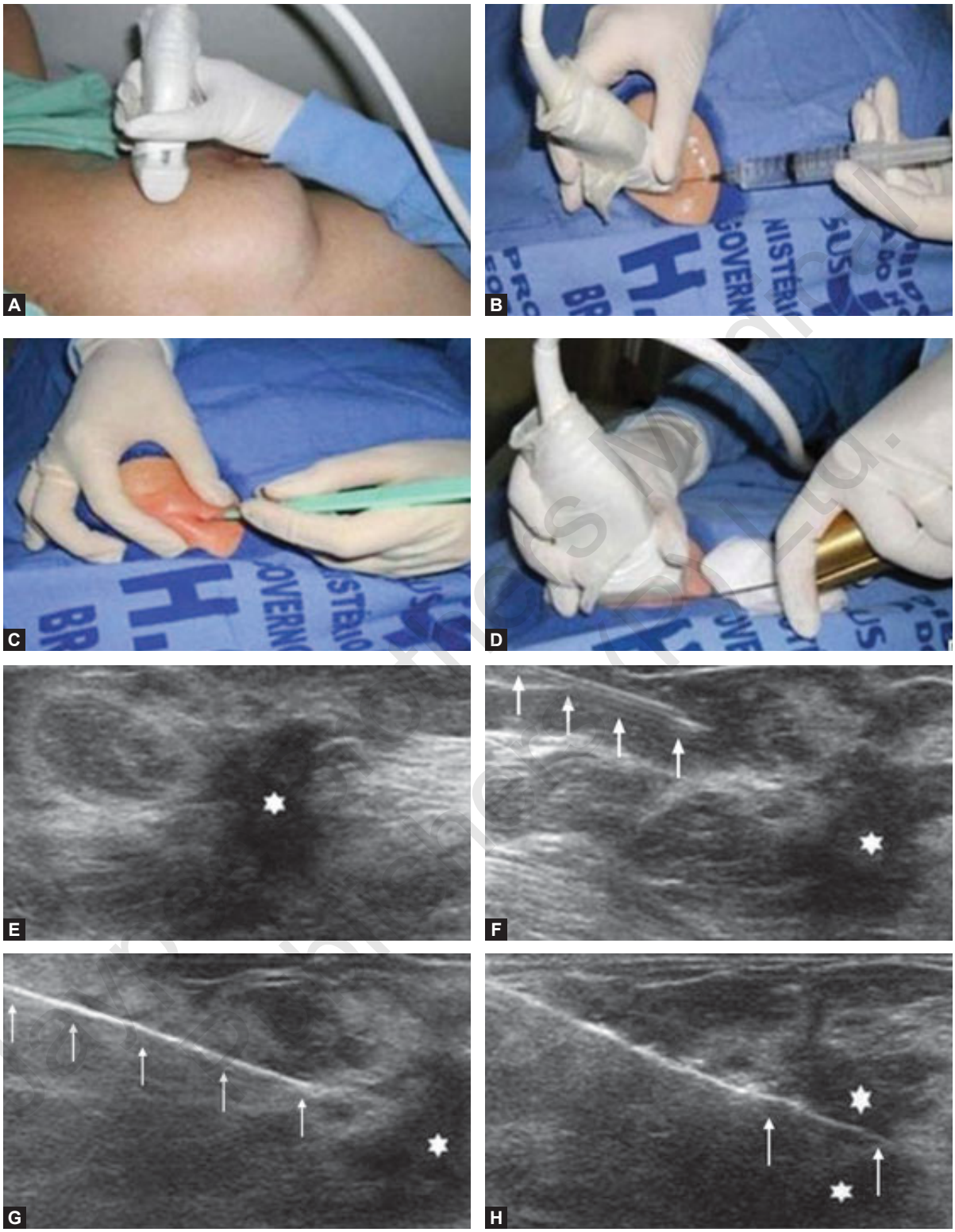

Figure 2: Main steps of ultrasonography-guided core biopsy of breast. **A** and **E,** Identification of the suspicious lesion (asterisk); **B** and **F,** Infiltration of the anesthetic though the pathway up to the lesion. The anesthetic needle is visualized as a fine hyperechogenic line (wide arrows); **C,** 2–3 mm incision on the numbed area; **D** and **G,** Through the incision, the same pathway utilized for anesthesia is utilized for insertion of the core needle (thin arrows) up to the lesion border; **H**, Once the core biopsy device is triggered, one must check whether the needle penetrated the lesion (asterisks). It is possible to observe the segment of the needle which advanced over the nodule (space between arrows).

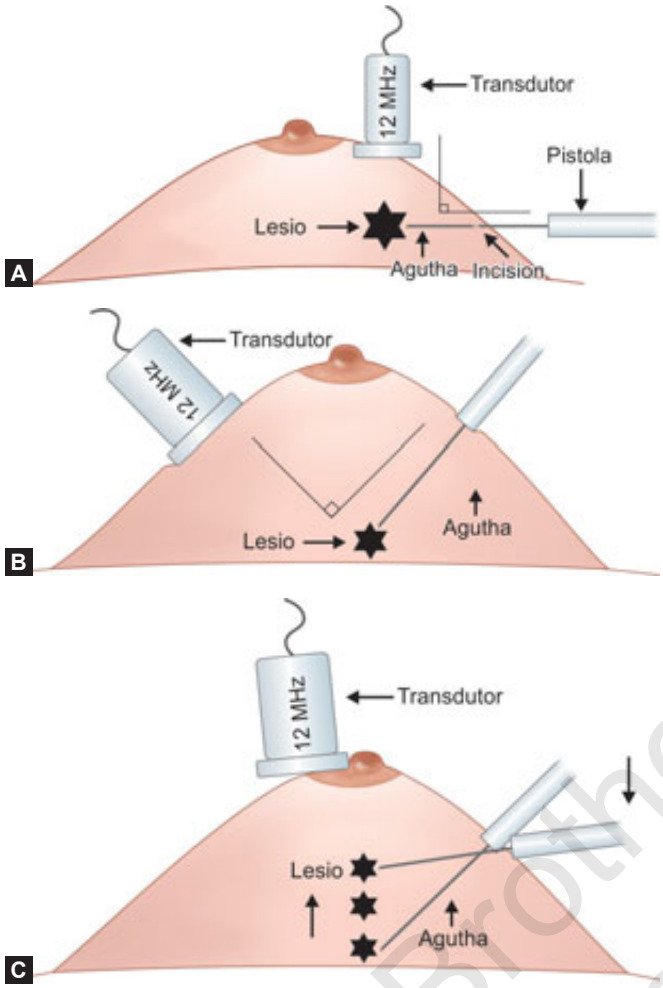

Figure 3: Commonly utilized approaches at ultrasound-guided core biopsy of breast. **A,** Needle parallel to the chest wall, perpendicular to the transducer. Better sonographic visualization of the needle and lower risk for pneumothorax; **B**, Needle angulated in relation to the chest wall. The transducer is guided in an attempt to maintain a perpendicular angle. Useful in very deep or superficial central lesions; **C**, The inferior movement of the core biopsy device may help to move the lesion away as much as possible from the chest wall.

After the procedure, needle is removed and ice as well as pressure is applied to the site to stop bleeding. The tissue is then sent to the laboratory for examination.

BENEFITS

- It is an outpatient procedure
- The procedure is less invasive than surgical biopsy, does not produce any scar mark and is less time consuming
- Ultrasound imaging does not use any ionizing radiation
- It reliably provides tissue samples needed for examination
- Compared with stereotactic biopsy, this is faster and avoids the need for ionizing radiation exposure
- It is possible to follow the motion of biopsy needle as it moves through the breast tissue
- Less expensive than other biopsy methods
- Short recovery time
- Patient can go home the same day or can resume her daily activities soon.

RISKS

- Risk of bleeding and hematoma formation
- Occasional patient discomfort which can be readily controlled by pain relieving medication
- Risk of infection
- There is a small chance of non-recovery of tissue
- Very small lesions may be missed out if the breast is quite dense and there is presence of clustered calcification.

CONCLUSION

The number of patients who require breast biopsy has increased over the past years, mainly because of wider access of the population to breast cancer screening allowing earlier diagnosis. Thus, a proportional or greater increase in the number of professionals who perform histological diagnoses is necessary in order to reduce the wait for a definitive diagnosis and increase the patients' survival. Ultrasonography-guided core biopsy of breast has become the method of choice for all alterations visualized at the method, with sensitivity rates which are very close to those of surgical biopsy. A multidisciplinary approach involving the tripod clinical practice-radiology-pathology is responsible for the highest rate of accuracy of the technique and must always be adopted. Finally, the radiologist also plays an important role in the follow-up of such patients, with whom a sound relationship must be maintained in order to guarantee the patients' return and appropriate follow-up.

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CHAPTER

Fibroadenomas

Piyush Malhotra

INTRODUCTION

Fibroadenoma is a term used to describe a broad range of solid, benign breast lesions that commonly effect premenopausal women. Fibroadenomas are often discovered as a palpable mass, which might feel firm, smooth, rubbery, or hard, perhaps like a pea or a grape. They are usually painless and will often move easily when touched. Fibroadenomas are affected by hormones and tend to fluctuate (or increase) in size during menstrual cycle, pregnancy, and breast feeding or if using hormone replacement therapy and oral contraceptives. Fibroadenomas remain unique of the utmost common benevolent tumors of the breast in females under 30 years of age. In young people, the overall occurrence of fibroadenoma is 2.2%. They account for 68% of all breast masses and 44–94% of biopsied breast abrasions. Fibroadenomas are sometimes called breast mice or a breast mouse owing to their high mobility in the breast.[1]

Histologically, fibroadenoma is a benevolent biphasic tumor with epithelial and stromal components. Furthermore, a palpable mass in the adolescent breast incurs anxiety for both the patient and family. Fibroadenomas were earlier acknowledged as benign tumors of breast but are now deliberated to be abnormalities of normal development rather than neoplasms. The purpose is that fibroadenomas mature from an entire breast lobule, which is conflicting to the origin of neoplasm from a lone cell by way of indication of propagation of both connective tissue and lobular epithelium. Histologically, fibroadenomas resemble a hyperplastic breast lobule and they respond to same hormonal stimuli as the normal breast tissue.[2] The biological conduct of fibroadenoma is capricious; they may degenerate, remain static, or grow gradually. Traditionally, all fibroadenomas were treated by surgical excision just to exclude malignancy. The doctrine that all discrete breast lumps should be excised has recently been challenged because if confident diagnosis and exclusion of malignancy is possible with preoperative investigations than the need for excision biopsy can be obviated. The current view that fibroadenomas are hyperplastic rather than neoplastic lesions and proposed hormonal influences, it is appealing to consider fibroadenomas as an aberration of normal lobular hypertrophy during the period of maximal estrogen exposure.[3] This concept gives support to a policy of nonsurgical management.

TYPES OF FIBROADENOMA

Subclasses of fibroadenomas consist of simple fibroadenoma, giant juvenile fibroadenoma, and multicentric fibroadenoma. Approximately 70–90% of fibroadenomas remain simple fibroadenomas, the utmost collective kind of fibroadenoma. Giant juvenile fibroadenomas exist as exceptional variant of fibroadenoma. They are demarcated as one promptly broadening encapsulated fibroadenoma with a span greater than 5 cm, deliberating over 500 g, or transferring at least four-fifths of the breast. Giant fibroadenomas are concomitant by means of skin ulcerations and venous enlargement.[4,5] The occurrence of giant fibroadenomas is just about 0.5–2% of all fibroadenomas. Populations liable to giant fibroadenomas remain women aged 10–18 years and African-American women. Giant fibroadenoma is the ultimate collective origin of autonomous macromastia in adolescent women. Multicentric fibroadenomas are numerous fibroadenomas arising in different quadrants of the breast. The occurrence of multicentric fibroadenoma is approximately 10–25% of all fibroadenomas. Although, fibroadenomas are benign breast masses, women with fibroadenomas are at a 2.17 times increased risk for breast cancer. The incidence of malignancy arising from a fibroadenoma specimen is rare, and ranges from 0.002 to 0.125%.[6]

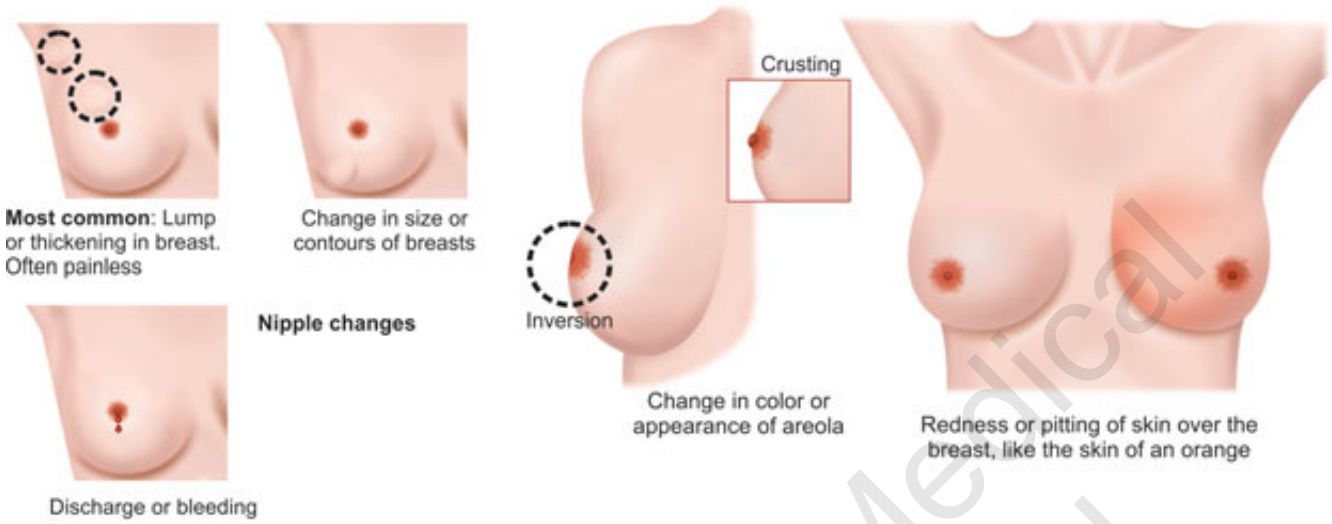

Figure 1: Signs and symptoms of fibroadenomas.

CAUSES AND SIGNS

More than 70% of fibroadenomas present as a single mass, and 10–25% of fibroadenomas present as multiple masses. Typically, fibroadenoma presents as a painless, smooth, mobile, rubbery mass with distinct borders usually ranging from 1 to 3 cm in size on the upper outer quadrant of the breast (Fig. 1). It can also be small enough that it is only seen on microscopic examination or it can be larger than 10 cm and cause breast asymmetry and significant esthetic deformation of the breast.[5,6] The size of the fibroadenoma can shrink or expand spontaneously, or it can be hormonally responsive and vary in size in conjunction with the menstrual cycle. Fibroadenomas can also vary in clinical presentation, ranging from being asymptomatic to causing debilitating pain.

The exact etiology of fibroadenoma is unknown. However, several studies show that estrogen influences the development of fibroadenomas. In a large population study of 265,402 women, risk factors for development of fibroadenoma include young age (<35 years), self-breast examination, and prior history of benign breast disease. Exposure to an estrogen-progesterone oral contraceptive before menopause and increasing number of live births decreases the risk of fibroadenoma.[7,9] There is also a correlation between body mass index and incidence of fibroadenoma. In a study of 1,717 patients, the incidence of fibroadenoma peaked in the body mass index group of 25–29.9 kg/m^2. Fibroadenomas can also be associated with syndromes such as Beckwith-Wiedemann syndrome, Maffucci syndrome, and Cowden syndrome.

The natural history of fibroadenoma varies from individual to individual. Some fibroadenomas may remain dormant without any change in size. Others may grow slowly in size. Overall, most fibroadenomas decrease in size as they lose cellularity, infarct with resultant calcification and hyalinization. In the adolescent population, 10–40% of fibroadenomas spontaneously regress.[9,10]

DIAGNOSIS

Tests to Evaluate the Breast Lump

Diagnostic Mammography

Mammography uses X-rays to produce an image (mammogram) of suspicious areas in the breast tissue. A fibroadenoma might appear as a breast mass with smooth, round edges, distinct from surrounding breast tissue.

Breast Ultrasound

This technology uses sound waves to produce pictures of the inside of the breast. Your doctor might recommend a breast ultrasound in addition to a mammogram to evaluate a breast lump if you have dense breast tissue.

For women younger than 30 years of age who have a breast lump, the doctor likely will order a breast ultrasound first to evaluate the lump.[11]

If a mammogram indicates that you have a breast lump or other abnormality, a breast ultrasound might be used to further assess the lump. A breast ultrasound can help the doctor determine whether a breast lump is solid or filled with fluid. A solid mass is more likely a fibroadenoma; however, a fluid-filled mass is more likely a cyst.

Procedures to Evaluate the Breast Lump

Fine-needle Aspiration

Through a thin needle inserted into your breast, the doctor attempts to withdraw the contents of the breast lump. If fluid comes out, the lump is likely a cyst (Fig. 2).

Core Needle Biopsy

A radiologist with guidance from an ultrasound usually performs this procedure. The doctor uses a needle to collect tissue samples from the lump, which go to a laboratory for analysis.[9,12]

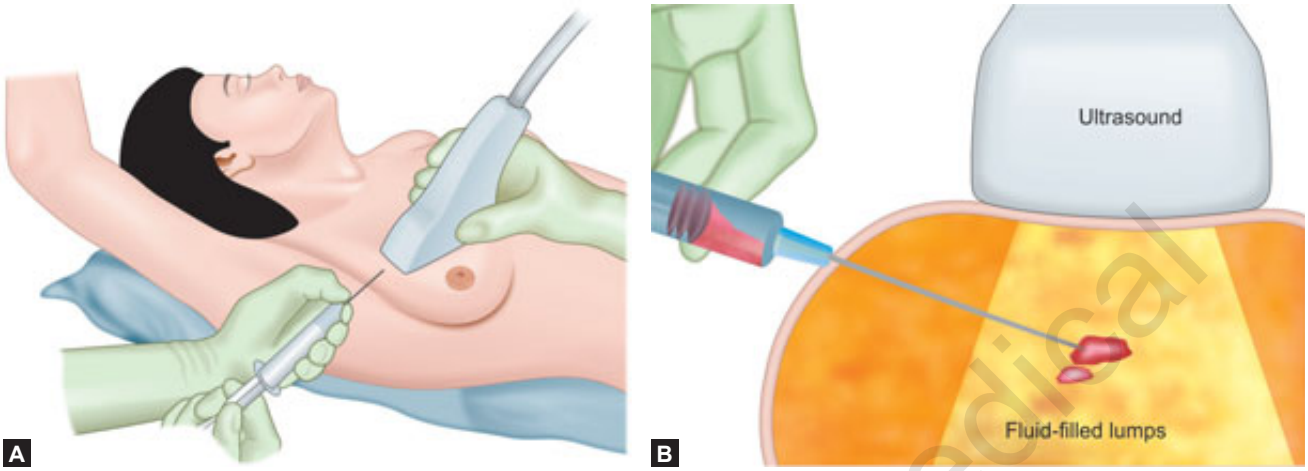

Figure 2: Fine-needle aspiration. **A,** Fine needle aspiration; **B,** Core needle biopsy.

TREATMENT

In many cases, fibroadenomas require no treatment. However, some women choose surgical removal for their peace of mind.

Nonsurgical Management

If the doctor is reasonably certain that your breast lump is a fibroadenoma—based on the results of the clinical breast exam, imaging tests, and biopsy, you might not need surgery.[13]

The patient might decide against surgery because:

- Surgery can distort the shape and texture of the breast
- Fibroadenomas sometimes shrink or disappear on their own
- The breast has multiple fibroadenomas that appear to be stable—no changes in size on an ultrasound compared to an earlier ultrasound

If you choose not to have surgery, it is important to monitor the fibroadenoma with follow-up visits to your doctor for breast ultrasounds to detect changes in the appearance or size of the lump. If you later become worried about the fibroadenoma, you can reconsider surgery to remove it.

Surgery

The doctor might recommend surgery to remove the fibroadenoma if one of your tests—the clinical breast exam, an imaging test, or a biopsy—is abnormal or if the fibroadenoma is extremely large, gets bigger, or is symptomatic.[12]

Procedures to remove a fibroadenoma include:

- Lumpectomy or excisional biopsy: In this procedure, a surgeon removes breast tissue and sends it to a laboratory to check for cancer
- Cryoablation: The doctor inserts a thin, wand-like device (cryoprobe) through your skin to the fibroadenoma. A gas is used to freeze and destroy the tissue.

After a fibroadenoma is removed, it's possible for one or more new fibroadenomas to develop. New breast lumps need to be assessed with a mammogram, ultrasound, and possibly biopsy—to determine if the lump is a fibroadenoma or might become cancerous.[5,14]

CONCLUSION

Fibroadenomas are benign, which means they are not cancerous, and do not turn into cancer. Any breast mass can evoke anxiety in the patient. This is especially true in the adolescent population. Hence, as fibroadenomas are completely benign and do not carry a risk of malignancy especially in women less than 30 years of age, the non-operative management seems a viable option. A complex fibroadenoma is associated with a modest increase in long-term risk of breast cancer. A woman with this mass is 1.5–2 times more likely to develop breast cancer in her lifetime than women in general.

To give some perspective, some BRCA1 and BRCA2 genetic mutations increase the risk of breast cancer by a factor of 7–11 times. The treatment of a complex fibroadenoma is complete surgical removal followed by enhanced surveillance or enhanced screening for breast cancer.

For routine surveillance, must encourage women at normal risk, under the age of 40 years, to practice breast awareness and get routine clinical breast examinations.

Breast awareness is the concept that women should know how their breasts normally look and feel and seek assessment of any breast change promptly from their health care provider.

However, it is emphasized that further clinical research is required to assess the safety and to evaluate the potential economic gain as well as the benefit of decreased physical and emotional trauma to the patient.

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CHAPTER

Guidelines for Breast Cancer Screening

Rachna Dubey

INTRODUCTION

Breast cancer is the most common invasive cancer in women worldwide. It comprises 22.9% of invasive cancers in women and 16% of all female cancers. Breast cancer is the second most common cause of cancer related mortality after lung cancer. Breast cancer is strongly related to age, with only 5% of breast cancers occurring in women under 40 years of age. The incidence of breast cancer varies greatly around the world. It is lowest in less developed countries and greatest in more developed countries.

BREAST CANCER RISK FACTORS

- Family history of breast cancer, ovarian cancer, or other hereditary breast and ovarian syndrome associated cancer (e.g., prostate cancer, pancreatic cancer)
- Known deleterious gene mutation (*BRCA1, BRCA2, P53, HER2/neu, C-erB2, C-myc*, etc.)
- Prior breast biopsy with specific pathology
- Atypical hyperplasia (lobular or ductal)
- Lobular carcinoma *in situ*
- Early menarche (<12 years)
- Late menopause (>55 years)
- Nulliparity
- Prolonged interval between menarche and first pregnancy
- Menopausal hormone therapy with estrogen and progestin (decreased risk with estrogen alone)
- Not breastfeeding
- Increasing age
- Certain ethnicities (e.g., increased risk of *BRCA* mutation in Ashkenazi Jewish women)
- Higher body mass index
- Alcohol consumption
- Smoking
- Dense breast on mammography
- Prior exposure to high dose therapeutic chest radiation in young women (10–30-year-old).

PREVENTION

Nobody knows exactly what causes breast cancer and there are no sure ways to prevent breast carcinoma; however, still maintaining a healthy weight, regular exercise, nutritious diet, and regular breastfeeding after delivery can prevent breast cancer.

SCREENING OF BREAST CANCER

Getting regular screening test is the most reliable way to get breast cancer detected early. The goal of screening for cancer is to detect preclinical disease in healthy, asymptomatic patient to prevent adverse outcome, improved survival and avoid the need for more intensive treatment.

American Cancer Society Screening Recommendations

Screening differs in average and high-risk woman. Breast cancer risk assessment is very important for identifying woman who may benefit from more intensive breast cancer surveillance. Risk assessment and identification of woman at high-risk allows for referral to health care provider with expertise in cancer genetics counseling and testing for breast cancer related germ line mutation (e.g., *BRCA*) (Table 1).

Screening Methods

Breast Self-examination

American Cancer Society states that women should be counseled, regarding the importance of being alert to breast changes (breast self-awareness). Unlike breast self-

TABLE 1: Risk assessment in women

Average risk woman	*High-risk woman*
Does not have personal history of breast cancer	Life time risk of breast cancer is 20–25% or greater
No genetic mutation of *BRCA* gene	Have a known *BRCA1* and *BRCA2* gene mutation
Do not have family history of cancer	First degree relative with *BRCA1* and *BRCA2* gene mutation and home not had genetic testing themselves
Did not have exposure to radiation	Had radiation therapy of chest between 10 and 30 years of age

examination (BSE), breast self-awareness does not include the recommendation for women to examine their breast on routine basis.

Clinical Breast Examination

It may be offered to asymptomatic average risk women. If performed for screening, should be done at intervals of every 1–3 years for woman aged 25–39 years and annually for women 40 years and older. American Cancer Society however, does not recommend clinical breast examination (CBE).

Mammography

It remains the gold standard for screening for most woman, while woman with dense breast experience reduced sensitivity.

TABLE 2: Recommendations for breast cancer screening in average-risk women

	American College of Obstetricians and Gynecologists	*US Preventive Services Task Force*	*American Cancer Society*	*National Comprehensive Cancer Network*
Clinical breast examination	May be offered* every 1–3 years for women aged 25–39 years and annually for women 40 years and older	Insufficient evidence to recommend for or against[†]	Does not recommend[‡]	Recommends every 1–3 years for women aged 25–39 years. Recommends annually for women aged 40 years or older
Mammography initiation age	Offer starting at the age of 40 years[§] Initiate at ages 40–49 years after counseling, if patient desires Recommend by no later than age 50 years if patient has not already initiated	Recommend at age 50 years[‖] Age 40–49 years: The decision to start screening mammography in women before the age of 50 years should be an individual one[¶]	Offer at ages 40–45 years[¶] Recommend at age 45 years[#]	Recommend at age 40 years
Mammography screening interval	Annual or biennial[§]	Biennial[‖]	Annual for women aged 40–54 years[‡] Biennial for the option to continue annual screening for women 55 years or older[‡]	Annual
Mammography stop age	Continue until age 75 years Beyond 75 years, the decision to discontinue should be based on a shared decision making process that includes a discussion of the woman's health status and longevity	The current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women 75 years and older[†]	When life expectancy is less than 10 years[‡]	When severe comorbidities limit life expectancy to 10 years or less

*Offered in the context of shared, informed decision-making approach that recognizes the uncertainty of additional benefits and harms of clinical breast examination beyond screening mammography.

[†]Category I recommendation.

[‡]Qualified recommendation.

[§]Decision between options to be made through shared decision-making after appropriate counseling.

[‖]Category B recommendation.

[¶]Category C recommendation. The Task Force notes that "Women who place a higher value on the potential benefit than the potential harms may choose to begin screening between the ages of 40 and 49 years."

[#]Strong recommendation.

Source: The American College of Obstetricians and Gynecologists-Practice Bulletin. Clinical management guide lines for Obstetrician-Gynecologists. Number 179 July 2017.

Mammogram should be done in first 14 days of menstruation. Avoid mammogram a week before menstruation.
Advantages:

- Mammography screening could potentially identify a nonpalpable mass measuring approximately 1 mm–1 cm during its preclinical phase, 3 years before it becomes palpable
- A negative mammogram does not deter further intervention if there is clinical suspicion of malignancy. Mammogram and clinical examination have 94.6% sensitivity in detection of breast cancer.

Disadvantages:

- False positive test results
- Anxiety and distress
- Discomfort during procedure
- Overdiagnosis and overtreatment.

Digital Breast Tomosynthesis

It is also known as three dimensional mammography. It helps in increased cancer detection, decreased biopsy rates and less recalls for that patient.

Magnetic Resonance Imaging

Around 80% of invasive cancers are detected by MRI compared to 33% by mammography.

Recommendations:

- Recommended in woman with known *BRCA1* or *BRCA2* gene mutation
- Have first degree relative with a *BRCA1* and *BRCA2* gene mutation but untested
- History of chest radiation between 10 and 30 years of age
- Association with other genetic syndromes (Li-Fraumeni and Cowden syndrome)
- A lifetime risk of breast cancer of 20% or greater, according to risk assessment tools that are based mainly on family history.

The American Cancer Society recommends against MRI screening for women whose lifetime risk of breast cancer is less than 15%. Approximately 80% of invasive cancers were detected by MRI compared to 33% by mammography.

If MRI is used, it should be in addition to, not instead of, a screening mammogram. This is because although an MRI is more likely to detect cancer than a mammogram, it may still miss some cancers that a mammogram can detect.

RECOMMENDATIONS OF AMERICAN CANCER SOCIETY IN DETAIL

I. Breast examination (BSE or CBE) are no longer recommended by American Cancer Society, but it says all woman should be familiar with how their breast normally looks and feels and report any changes.

IIa. Woman with an average risk of breast cancer should begin yearly mammogram at the age of 45 years (strong recommendation).

IIb. Woman aged 55 years or more should have mammogram every other year (recommendation) or have the opportunity to continue screening annually.

IIc. Woman should have opportunity to begin annual screening between the ages of 40 and 44 years (qualified recommendation)

III. Regular mammogram should continue for as long as a woman is in good health and life expectancy of 10 years or longer

IV. Woman at high-risk need to begin screening earlier and/or more often. Yearly mammogram along with MRI is recommended as early as 30 years of age.

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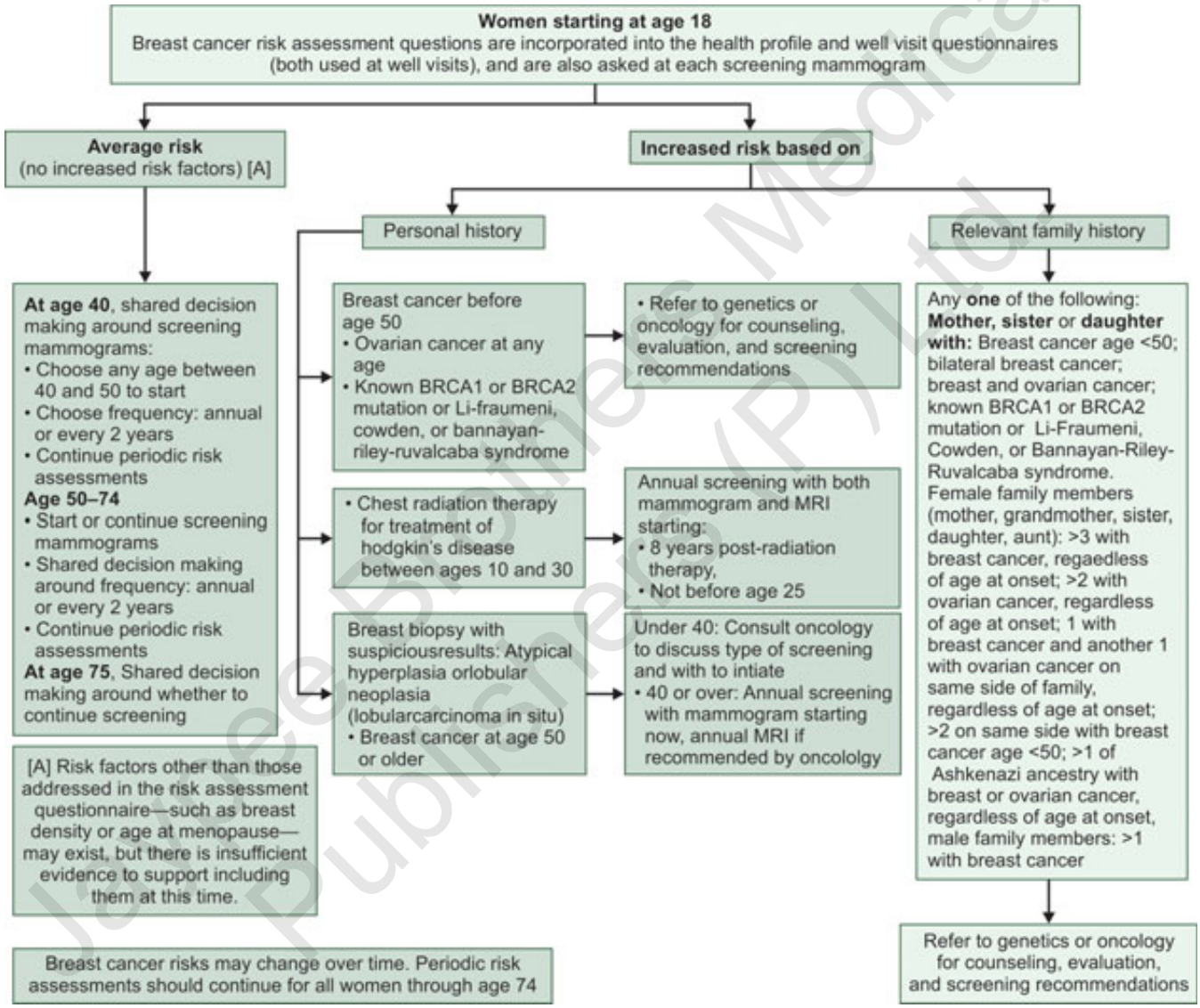
APPENDIX 1

Screening Recommendations for Breast Cancer Based on Risk Assessment

Amrit Gupta



Source: This evidence-based guideline was developed by Kaiser Parmanente Washington (KPWA). It was adapted from the 2016. US Preventive Service Task Force guideline and the 2015 American Society Cancer guideline.

Breast cancer still has a very silent course in our country due to various factors such as lack of awareness, shyness on part of the women themselves, and lack of promptness in management strategies. This results in detection at advanced stages where morbidity is high and cure suboptimal. Better cancer screening programmes with awareness will definitely bring a change in the women's health and outcomes.