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FOGSI FOCUS

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"Female Breast Surely A Savior Sometimes a Killer"

A FOGSI - Study on Female Breast Committee Publication

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PRESIDENT'S MESSAGE

Dr. P. K. Shah
FOGSI President

Dear Fogsian's,

It gives me immense pleasure to write for the FOGSI Focus on "Female Breast – Surely a Saviour; Sometimes a Killer". It has been written in a simple and easy to understand format on such a difficult & complicated subject.

I must congratulate Dr. Madhuri Patel, Dr. Surekha Tayade & team for making such a great effort. All the Chapters are carefully selected and written very methodically. There is clarity of thought and understanding of the subject which is evident in the writing of all the chapters.

This FOGSI Focus will immensely help medical practitioners and members of FOGSI.

I wish Dr. Madhuri Patel, Chairperson of Female Breast Committee & her team all the very best for their future endeavors. I will appreciate feedback & constructive criticism from readers.

Thanking you,

Yours sincerely,

Dr. P. K. Shah
President,
FOGSI

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Message from President Elect FIGO

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Breast related diseases in females have become very common in developing countries. We as Gynecologists and Obstetricians are usually the first to be consulted by female patients having problems related to breast. However, lack of knowledge about breast feeding and lack of awareness about breast related diseases, particularly, breast lump, has magnified this problem, both for doctors and the population at large. Hence, this aspect of women's health is very important and needs much more attention from us than is actually given.

FOGSI is doing its best to tackle this draconian issue by having a special committee "Study on Female Breast Committee" for the breast and breast related diseases. To highlight this issue Dr. Madhuri Patel and her team have made very sincere, comprehensive, dedicated efforts to bring this FOGSI Focus exclusively dedicated to the problems related to female breast. The topics, the contributors and the editors are all of top class and they all have collectively made a sincere effort to justify and explain this burning issue.

I am sure this issue of FOGSI Focus will be of great help to all the Obstetricians and Gynecologists, as said earlier, the first to be consulted, in diagnosis, treatment and further management. I am confident that the knowledge imparted through this issue will take us a step further in our primary goal of providing comprehensive care to our patients.

With best wishes

Dr C N Purandare

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Message from President, Maharashtra Medical Council

Prof. Dr. Kishor Taori

It gives me great pleasure to know that Study of Female Breast Committee of FOGSI is bringing out a Special issue of FOGSI Focus edited by Dr Madhuri Patel and Dr Surekha Tayade. The two subjects dealt in the book, breast feeding and breast carcinoma both, though diverse in nature are pertinent to women's health. The United Nations Children's Fund has voiced alarm at the decline of breastfeeding across East Asia, and stressed the need to ensure that mothers understand the long-term benefits of this important practice for the survival and development of their children. The health professionals as a whole and Obstetricians in particular have a great role to play in promotion of breast feeding. The common problems hindering exclusive breast feeding have to be addressed early and I am sure the learned authors of this book have been able to increase the knowledge and awareness in this regard.

Breast Carcinoma is on the rise in the developing world and we still lack the infrastructure and facilities for diagnosis and management of invasive breast disease. However the knowledge of proper screening and early diagnosis could win the battle over this killer disease. Health education programs and continuous update of knowledge of all the concerned health professionals is definitely the key for dealing with this entity. I am glad to note that Gynecologists have come forward to carry out this task of fighting mammary cancer which was considered a Surgeon's domain. Mass screening of 40 + women is being undertaken in future in India and as a Radiologist I suggest that Breast MR Spectroscopy should also be included in it.

I congratulate FOGSI, the editors and the contributors for their novel thinking on both these issues and hope this book will help to improve the knowledge and practice of effective breast feeding and cancer breast screening.

With Best Compliments

Dr Kishor Taori

Let the Life of Every Mother & Neonate Count

From The Editor's Desk

Dr Madhuri Patel

Vision is the art of seeing things invisible ….. Jonathan Swift

It gives me immense pleasure to bring to you this comprehensive FOGSI Focus on female breast. Surely the female breast is a source of life to the nursing infant and without its vital breast milk, human life could not have existed. Thus it is a "Savior" to the fullest extent. The symbolic meaning ascribed to the breast is associated with fertility and nourishment, both spiritual and physical, and in the wider sense – with life. However in later life this particular savior can itself suffer from the life threatening breast cancer and thus be a "Killer". Hence to highlight these two issues we have chosen the name "Female Breast Surely a Saviour; Sometimes a killer" for this FOGSI Focus. And it deals with the two subjects' breast feeding and breast carcinoma.

Obstetricians come across breast feeding related problems in their day to day practice and thus they have a great role to play in promotion of exclusive breast feeding. Many women and babies suffer with inappropriate breast feeding practices and if these problems are addressed during antenatal and immediate postnatal period, much suffering can be prevented and alleviated. The topics covered in this book deal with the ailments of the lactation period and suggest worthwhile solutions.

Breast cancer is the second leading cause of death in women after the lung /skin cancer in developed countries. In developing countries, it is second to cervical cancer. The ignorance, socio cultural taboos, cancer phobia and inadequate screening and treatment facilities contribute to cancer related morbidity and mortality. As responsible members of FOGSI we have an additional responsibility in early detection, screening and timely referral of all suspicious breast lesions for proper management and optimum outcome. The knowledge update in the second section of this book will surely serve as a ready reference for guiding us in this task.

So let's make our best effort in alleviating the suffering of all woman kind.

I sincerely thank Dr. C. N, Purandare, President Elect of FIGO and Dr. P. K. Shah, President FOGSI for their guidance and continuous support and all the authors for making this endeavor a success.

Wish you all FOGSI members, a very Happy New Year 2013.

M.A. Patel

Dr. Madhuri Patel

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From The Co-Editor's Desk

Dr Surekha Tayade

Knowledge is, indeed, that which, next to virtue, truly and essentially rises one man above another.

We are indeed happy to release this issue of FOGSI Focus on the eve of the 56th All India Congress of Obstetrics and Gynecology, Mumbai. FOGSI - Study of Female Breast Committee has chosen BREAST FEEDING AND BREAST CARCINOMA as theme subjects for this issue. Articles have been invited from learned authors on various topics of practical importance.

Breast feeding, an integral part of woman's reproductive life, a natural physiological process, often becomes a cause of anxiety and worry for the mother. She needs proper guidance and support during this unique phase of her life .Very often these women are referred to Pediatrician or nurses for the solution to their problems. Being the first contact person for their breast related issues, it is very essential that, we all update our knowledge on the subject.

The second section of this publication deals with Breast Carcinoma, the incidence of which is on the rise. In India .it has fallen in the domains of surgeons. Gynecologists are not primarily involved in the management of breast neoplasms. However they often get an opportunity of Breast examination during antenatal visits and during routine gynecological checkup. Thus screening for breast carcinoma is easily possible for them. Though Surgeons may be doing the opportunistic screening, Gynecologist have a major role to play in early detection of breast cancer. Over the decades the breast cancer mortality has decreased in the developed world because of improved screening programs and adjuvant therapy. However situation is still gloomy in developing countries including India. Let us take share of our responsibility to reduce the burden of breast cancer related morbidity and mortality.

I sincerely thank all authors, who have spared their valuable time for writing the articles for this issue of FOGSI focus. I also express my heartfelt gratitude towards Dr Madhuri Patel, for her constant Support, Guidance and Encouragement.

Tayade

Dr Surekha Tayade

I N D E X

Section – A : Breast Feeding

Section – B : Breast Carcinoma

Section – A : Breast Feeding

CHAPTER – 1

LACTATION – HOW AND WHY?

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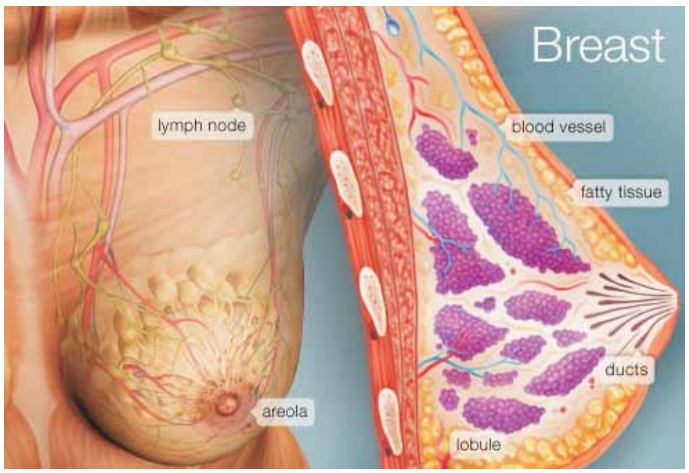
INTRODUCTION

BREAST milk is the most precious gift of a mother to her child. It is thought to be the best form of nutrition for neonates and infants. The properties of human milk facilitate the transition of life from in utero to outside. This dynamic fluid provides a diverse array of bioactive substances to the developing infant during critical periods of brain, immune system, and gut development. Besides contributing to baby's short-term and long-term well-being, breast milk also builds up bondage between mother and the baby, provides some degree of natural contraception as well as protects from certain future malignancies.

ANATOMY

Breast or the mammary gland is a modified sweat gland which is composed of about 20 lobes, each with an excretory lactiferous duct that opens at the nipple. The lobes, in turn, are composed of several lobules that contain secretory structures called alveoli and the terminal portions of the ducts. The epithelium of the alveoli and ducts is a simple one, except for the presence of a myoepithelial cell layer on the basal side of the epithelium. Myoepithelial cells are stellate, smooth muscle-like cells, and contraction of these cells in response to a stimulus expels milk from the lumens of the alveoli and ducts. Lobes and lobules are supported within a connective tissue matrix. The other major tissue component of the breast is adipose tissue. The lactiferous ducts empty at the nipple, which is a highly innervated, hairless protrusion of the breast designed for suckling by an infant (Fig. 1). The nipple is surrounded by a pigmented, hairless areola that is lubricated by sebaceous glands. Protrusion of the nipple, called erection, is mediated by sympathetic stimulation of smooth muscle fibers in response to suckling and other mechanical stimulation, erotic stimulation, and cold.



Though breast development begins at intrauterine life, its feminine modifications in shape and size occur at puberty. At puberty, estrogen increases ductal growth and branching. With onset of the luteal phase of the ovary, progesterone induces lobular growth and the formation of rudimentary alveoli. During non-pregnant cycles, the breasts develops somewhat and then regresses. Estrogen also increases the deposition of adipose tissue, which makes a major contribution to the size and overall form of the breasts. Adipose tissue expresses CYP19, so accumulation of which increases the local production of estrogens from circulating androgens.

WHY AND HOW?

Extensive breast development in pregnancy is because of enormous growth, branching and lobulo-alveolar development ,which is mainly brought about by a number of placental hormones like estrogen, progesterone, placental lactogen and a growth hormone variant (GH-V). Role of estrogen is to increase the size by increasing the number of the ducts whereas progesterone plays a role by increasing the number of alveoli. Human placental lactogen further stimulates alveolar development and may be involved in actual milk production (by making casein, lactalbumin and lactoglobulin) by the alveolar cells. Estrogen the key hormone for lactation acts on the breast both directly and indirectly through increasing maternal pituitary prolactin. Estrogen increases prolactin secretion from pituitary lactotropes. Estrogen also stimulates hypertrophy and proliferation of lactotropes, which accounts for the two fold increase in pituitary volume during pregnancy. Although epithelial cells express genes encoding milk protein and enzymes involved in milk production, progesterone inhibits the onset of milk production and secretion (galactopoiesis).

The principal lactogenic hormone, prolactin, secreted by the anterior pituitary is critical to the establishment of lactation. Prolactin stabilizes and promotes transcription of casein mRNA; may stimulate synthesis of alpha-lactalbumin, the regulatory protein of the lactose synthetase enzyme system; and increases lipoprotein lipase activity in the mammary gland. Prolactin levels decrease as lactation is established but nursing stimulates prolactin release from the pituitary which promotes continued milk production. Presence of normal levels of other hormones, including insulin, cortisol and thyroid hormone, parathyroid hormone, parathyroid hormone-related protein and human growth hormone is also necessary for galactopoiesis. Although the concentration of circulating prolactin increases during pregnancy so that by the end of gestation, levels are 10 to 20 times over normal amounts, prolactin is prevented from exerting its effect on milk secretion by elevated levels of progesterone. Following clearance of progesterone and estrogen at parturition, copious milk secretion begins. Although placental estrogen stimulates prolactin secretion and upregulation of prolactin receptor on alveolar epithelial receptor during

pregnancy, the stimulus for prolactin secretion during the nursing period is suckling by the infant. Levels of prolactin are directly correlated with the frequency and duration of suckling at the nipple. The link between suckling at the nipple and prolactin secretion involves a neuroendocrine reflex in which dopamine secretion at the median eminence is inhibited (the prolactin release inhibitory factor). It is also possible that suckling increases the secretion of unidentified prolactin -releasing hormones.

Fig. 2 Hormonal basis of milk synthesis and milk secretion

A recently described hormone, Fil (feedback inhibitor of lactation), seems to play an important role in regulation of milk supply. Fil acts locally within each breast. Fil is secreted into breast milk. When the breast is not emptied, Fil remains in contact with the alveolar cells. Fil appears to act on an apical receptor on the alveolar cell. This inhibits secretion of milk constituents. The complete mechanism is not yet understood, however this appears to be the mechanism of decreased milk production due to incomplete emptying of the breast.

The milk filling and distending the alveoli is not available to the nursing infant until the myoepithelial cells contract and squeeze out the milk in response to the milk "let down" reflex. This reflex is started by tactile stimulation by the suckling newborn and is made possible through the hypothalamus and posterior pituitary gland which releases oxytocin (a short chain protein hormone) into the bloodstream. This hormone causes contractions of cells within the breast and milk is ejected from the alveoli and small ducts to come to the mouth of the baby. Both negative and positive emotional factors affect this let down, so it is vital that a mother feels confident in her ability to breast feed, and should get very strong encouragement at this early stage.

Colostrum is thick, yellowish milk that is secreted by a woman's breast in the first several days after delivery. It has increased concentration of calcium, potassium, proteins, fat-soluble vitamins, minerals, antibodies and lymphocytes from the mother that help the baby resist infections. In absence of placental progesterone, early milk is subsequently modified by the ductal epithelium and produces mature milk almost after ten days post partum. Composition of mature human is as follows: Caloric value of human milk is 750 kcal / liter. The composition mentioned varies from woman to women, breast to breast, according to the phase of feeding e. g. fats and lipids are particularly high at the end of the feeding (hind milk). Its composition is optimum for baby's nutritional demand and digestive capacity. It is delivered at an optimum temperature which is acceptable to the baby.

Contraceptive effect of lactation is mainly because of inhibition of GnRH release by the action of high prolactin level which also antagonizes action of gonadotrophins on ovary. As a consequence, ovulation is prevented. But it is quite unreliable method of contraception as almost 5-10% woman become pregnant even in suckling period. Another important implication of breast feeding is that it is somehow protective against breast cancer. Nulliparity and absence of breast feeding ever are the risk factors for developing breast cancer. Along with all the health benefits , breast milk has certain demerits like poor supply of iron through breast milk, chances of infection like HIV, Hepatitis B , HTLV-1 via breast milk or passage of certain drugs e.g. alcohol, steroidal preparation etc from mother to baby .

Some exceptional conditions of galactorrhea may arise in non nursing women which may be due to some other reasons like pituitary chromophobe tumor, Chiary Frommel Syndrome etc. where there occurs high level of circulating prolactin. Genital atrophy, amenorrhea may be associated.

As no other alternative food can parallel the goodness of breast milk, it is highly commendable that every mother should nurse her newborn. Zeal of civilization should not deprive our future generations from such divine gift at any cost.

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CHAPTER 2

BREAST MILK - A VITAL FLUID

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INTRODUCTION:

Breast feeding is considered to be the ideal nutrition for all infants because of its proven health benefits. The World Health Organization (WHO), the American Academy of Pediatrics (AAP), the Indian Academy of Pediatrics (IAP) and the American College of Obstetricians and Gynecologists (ACOG) recommend exclusive breasting feeding for the first six months of life. Breast milk is the best source of nutrition for newborn babies, as it provides easily digestible nutrients in the right quantities. It's also packed with antibodies and helps to establish the baby's immune system. Those babies who are exclusively breastfed are reported to be at less risk of gastrointestinal, respiratory and urinary tract infections as compared to the babies who are bottle-fed. They are also less likely to become obese or experience constipation and vomiting. If there's a family history of allergies or diabetes, breastfed babies are less likely to develop these.

Breast milk contains substances that help the development of a baby's brain, retina, gut lining and protective sheath for the central nervous system. Breast milk also contains hormonal factors that help the baby's growth and development. It carries digestive enzymes, too, which help to digest the nutrients in milk, helping the baby's immature digestive tract. In addition to these direct short-term benefits, breastfeeding is associated with long-term benefits to the infant and mother, hence breastfeeding for all infants is strongly supported by both governmental and medical professional organizations. 1-2

COMPOSITION OF BREAST MILK :

The composition of human milk is both complex and remarkable for its variability and is ideally suited to the full-term infant.

1) ENERGY - The energy content of human milk is about 20 kcal/oz (0.67 kcal/ml).

2) NITROGEN - The nitrogen content of human milk is divided into protein and non protein nitrogen-containing compounds.

   a) Protein - The protein content for human milk is highest at birth and is approximately 2.3 gm/dL from mothers of full-term infants 3 and declines over the next two to four weeks to a steady level of approximately 1.8 gm/dL . This protein content provides about eight percent of the caloric needs of full-term infants and ensures an adequate protein status of the breastfed infant throughout the first year 4. Whey and casein are two fractions of protein defined by their solubility in acid. Approximately 70 percent of the proteins in human milk are in the soluble whey fraction and 30 percent in the insoluble casein fraction. In contrast, bovine milk protein contains 18 percent whey and 82 percent casein. The high proportion of whey protein in human milk is beneficial for infants for the following reasons. Compared to casein, whey is more easily digested and is associated with more rapid gastric emptying.-The whey protein fraction provides lower concentrations of potentially deleterious amino acids, phenylalanine, tyrosine, and methionine. In high levels, these amino acids may interfere with brain development. Infants fed human milk have lower levels of these amino acids than infants fed bovine milk. In addition, human milk has higher levels of cystine (needed to synthesize the antioxidant glutathione) and taurine (needed for bile conjugation and brain development) than bovine milk. The major human whey protein is lactalbumin. In bovine milk, the major whey protein is lactoglobulin, which may contribute to milk protein allergy and colic. Lactoferrin, lysozyme, and secretory immunoglobulin A are specific human whey proteins that improve host defense. Bovine milk only has trace amounts of these proteins.

   b) Non-protein nitrogen - In human milk, approximately 20 percent of the total nitrogen is in the form of nonprotein nitrogen-containing compounds such as nucleotides, free amino acids, and urea. In contrast, milk formula has <5 percent nonprotein nitrogen 5. Nucleotides represent 2 to 5 percent of the nonprotein nitrogen in human milk and are lacking in bovine milk. Nucleotides are important for gastrointestinal, immune, and metabolic functions.

3) LIPID - Lipid (fat) represents approximately 50 percent of the calories in human milk. The lipid and energy contents of human milk increase during lactation. Human milk facilitates lipid digestion and absorption by its organization of lipid into milk fat globule triglycerides. These globules are digested by bile salt-stimulated gastric lipase. Of the macronutrients in human milk, lipid is the most variable in concentration. The milk lipid content rises throughout lactation, varies over the course of one day, increases within feeds, and varies from mother to mother and perhaps with the degree of breast emptying. The total lipid content of human milk is not affected by maternal diet, although it may be correlated directly with maternal body fat stores. Despite the variability among women, human milk lipid content is adequate for the nutritional needs of the infant throughout lactation.

4) CARBOHYDRATES - Human milk carbohydrate is comprised principally of lactose, with a small proportion consisting of oligosaccharides. Studies in term infants demonstrate unabsorbed lactose in the feces of breast-fed infants, which is assumed to be a normal consequence of breastfeeding. A softer stool consistency, nonpathogenic bacterial fecal flora, and improved absorption of minerals have been attributed to the lactose in human milk 6. Oligosaccharides, found in carbohydrate polymers and glycoproteins, are important in the host defense of the infant as their structures mimic specific bacterial antigen receptors.

5) MINERAL AND TRACE ELEMENTS - The concentrations of calcium and phosphorus in human milk are relatively constant through lactation but are significantly lower than in formula. Despite lower mineral concentration and intake, bone mineral accretion and status of breastfed infants is similar to that of infants fed formula due to enhanced absorption (bioavailability) during the first year of life. In human milk, minerals are bound to digestible proteins and are also present in complex and ionized states making them more readily bioavailable than in bovine milk 7. Although concentrations of iron, zinc, and copper decline during lactation, the need for these nutrients is usually adequately met through the first six months of life.

6) VITAMINS - Maternal vitamin status affects the content of vitamins in human milk. For example, maternal vitamin deficiency can result in low vitamin concentrations in breast milk, which increase in response to maternal dietary supplementation. Potential vitamin deficiencies in breast-fed infants include:

   a) Mothers who are on a vegan diet may be deficient in the water-soluble vitamin B12 resulting in low breast milk levels. These mothers should receive vitamin B12 supplementation or should eat foods fortified with vitamin B12.

   b) Vitamin K deficiency is common in the newborn infant. This is due to the low vitamin K content of breast milk, inadequate production of vitamin K by an immature liver, absence of the bacterial flora that produce vitamin K, and poor placental transfer of vitamin K. In breast-fed infants, the plasma concentrations of all vitamin K dependent factors are about 20 percent of the adult values. Therefore, prophylactic administration of vitamin K1 oxide (phytonadione, 1 mg IM) is given to newborns shortly after birth to prevent vitamin K hemorrhagic disease of the newborn. The content of vitamin D in human milk is low. Vitamin D supplementation should be provided to exclusively breastfed infants and non-breastfed infants who do not ingest at an adequate amount of vitamin D-fortified milk daily.

BENEFITS OF BREAST FEEDING FOR INFANTS

Breastfeeding has direct clinical benefits as well as potential-long term benefits for the infant. The direct benefits of human milk include:

1) *Gastrointestinal function* - Several components of human milk stimulate gastrointestinal growth and motility, which enhance the maturity of the gastrointestinal tract. Other factors are protective and decrease the risk of necrotizing enterocolitis and other infection. These stimulatory and protective components include:

2) *Anti-microbial components* - Human milk contains a variety of heterogeneous agents that possess antimicrobial activity. Many of these factors have the following traits:
   - Persist through lactation
   - Resist the digestive enzymes in the infant's gastrointestinal tract
   - Act at the mucosal surfaces (eg, gastrointestinal, respiratory, and urinary tracts).

3) *Prevention of illnesses while breastfeeding* - In both developed and developing nations, human milk compared to formula decreases the risk of acute illnesses during the time period that the infant is fed. In developing countries, the overall morbidity and mortality is lower in breast-fed versus formula-fed infants. In addition, the incidence of gastroenteritis and respiratory disease is lower in breast-fed infants 8.

4) *Gastroenteritis* - Episodes of gastroenteritis and hospitalization for diarrhoea are decreased in infants who are breast-fed compared to formula-fed infants. The protective effect of human milk appears to be due to the presence of maternal antibodies.

5) *Respiratory disease* - Respiratory illnesses are reduced in frequency and/or duration in breast-fed compared to formula-fed infants 9. The protection from respiratory illnesses derived from breast milk compared to formula appears to attenuate by one year of age.

6) *Otitis media* - The incidence of otitis media and recurrent otitis media are reduced in breast-fed compared to formula-fed infants.

7) *Urinary tract infection* - Infants who were hospitalized for urinary tract infections were less likely to have been breast-fed compared to matched control patients. A mechanism for this protection has been suggested based on observations that breast-fed infants have greater content of oligosaccharides, lactoferrin, and sIgA in their urine compared with formula-fed infants.

8) *Sepsis* - The incidence of sepsis is reduced in premature infants receiving human milk.

LONG-TERM BENEFITS :

There is increasing evidence that breast milk has potential-long term benefits after the period of breastfeeding. These include possible reduction of acute illnesses, decreased risk of specific chronic diseases, and improved neurodevelopmental outcome compared to formula-fed infants.

- Acute illnesses – Exclusive breastfeeding compared to formula feeding has a protective effect in reducing acute illnesses even after breastfeeding is discontinued. Post-breastfeeding protection appears to increase with the duration of breastfeeding.
- Chronic disease – There are reported associations between the duration of breastfeeding and a reduction in incidence of :

  1) *Obesity* - Several studies have linked long-term reduction in obesity with breastfeeding in infancy 10. If breastfeeding reduces the risk of obesity, the mechanism is unknown. One theory is that breastfeeding, as opposed to bottle feeding, promotes less restrictive feeding styles that are more responsive to infant cues of hunger and satiety, allowing the infant greater self-regulation of energy intake, which prevents over feeding and excessive weight gain.

  2) *Cancer* - Breastfeeding has been associated with a reduction in the overall risk of childhood cancer as well as lymphoma and leukaemia 11.

  3) *Adult cardiovascular disease* - Breastfeeding is associated with decreases in cardiovascular disease (CVD) risk factors (dyslipidemia, obesity, and elevated C-reactive protein [CRP]). These findings indirectly link breastfeeding with a reduced risk of adult CVD.

  4) *Allergic conditions* - There are data that suggest breast feeding may be beneficial in reducing the risk of allergic disease.

  5) *Diabetes mellitus* - Breast-fed compared to formula-fed infants appear to have a decreased risk of developing Type 1 diabetes mellitus. This difference is thought to be due to a cell-mediated response to a specific cow's milk protein, beta-casein, which may be involved in the pathogenesis of type 1 diabetes mellitus. In addition, there are data suggesting that the incidence of type 2 diabetes mellitus is reduced in breast-fed infants than those who were formula-fed.

  6) *Neurodevelopmental outcome* - A number of studies have shown small neurodevelopmental advantages in children who were breast-fed compared to those who received formula feed.

7) *Cognitive development* — Although there have been several reports that breastfeeding improves cognitive development later in childhood and adolescence, this association remains uncertain. Improved long-term cognitive development in premature infants also has been reported with the receipt of human milk during hospitalization, including extremely low birth weight (ELBW) infants.

8) *Visual function* — Several studies have indicated that human milk-fed term and premature infants have improved visual function compared to formula-fed infants. This benefit has been attributed to docosahexaenoic acid (DHA), which is a component of phospholipids found in brain, retina, and red cell membranes. DHA is present in human milk but not in bovine milk. The severity and incidence of retinopathy of prematurity are decreased among breastfed compared to formula fed infants. This association may relate to the substantial antioxidant capacity of human milk compared with formula.

9) *Hearing function* — Auditory-evoked responses mature faster in breast-fed premature infants.

10) *Child behaviour* — Data from a survey suggested that breastfeeding for four months or longer was associated with a lower risk of behaviour problems in children at five years of age compared with a shorter duration of breastfeeding.

11) *Stress reduction* — There appears to be an analgesic effect of breastfeeding, which may be due to the enhanced maternal-infant bonding. Breastfed infants experience less stress during painful procedures than formula fed infants. The lactation hormones, oxytocin and prolactin, are important components of the stress axis and have a positive impact on social behaviours, including maternal-infant bonding. Another possible explanation for the analgesic effect of breastfeeding is a higher cortisol level in breast-fed compared to formula-fed infants. Improved bonding may reduce infant stress.

MATERNAL BENEFITS OF BREASTFEEDING :

As with infants, breastfeeding provides direct clinical benefits to mothers during lactation and long-term benefits beyond the breastfeeding period. The benefits to mothers while breastfeeding include the following

Good attachment -

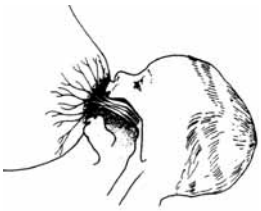

Figure 1 shows how a baby takes the breast into his or her mouth to suckle effectively. This baby is well attached to the breast.

The points to notice are: much of the areola and the tissues underneath it, including the larger ducts, are in the baby's mouth; the breast is stretched out to form a long 'teat', but the nipple only forms about one third of the 'teat'; the baby's tongue is forward over the lower gums, beneath the milk ducts (the baby's tongue is in fact cupped around the sides of the 'teat', but a drawing cannot show this); the baby is suckling from the breast, not from the nipple.

As the baby suckles, a wave passes along the tongue from front to back, pressing the teat against the hard palate, and pressing milk out of the sinuses into the baby's mouth from where he or she swallows it. The baby uses suction mainly to stretch out the breast tissue and to hold it in his or her mouth. The oxytocin reflex makes the breast milk flow along the ducts, and the action of the baby's tongue presses the milk from the ducts into the baby's mouth. When a baby is well attached his mouth and tongue do not rub or traumatize the skin of the nipple and areola. Suckling is comfortable, not painful and often pleasurable for the mother.

Poor attachment -

The points to notice are: only the nipple is in the baby's mouth, not the underlying breast tissue or ducts; - the baby's tongue is back inside his or her mouth, and cannot reach the ducts to press on them. Suckling with poor attachment may be uncomfortable or painful and may damage the skin of the nipple and areola, causing sore nipples and fissures (or "cracks"). Poor attachment is the commonest and most important cause of sore nipples, and may result in inefficient removal of milk and apparent low supply.

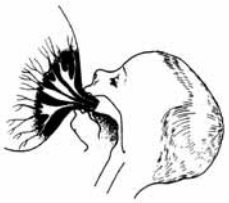

Figure 2 Shows what happens in the mouth when a baby is not well attached at the breast.

Signs of good and poor attachment

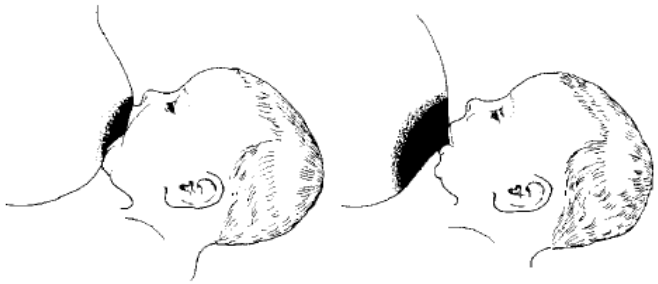

Figure 3 shows the four most important signs of good and poor attachment from the outside.

CAUSES OF POOR ATTACHMENT

Use of a feeding bottle before breastfeeding can cause poor attachment, because the mechanism of suckling with a bottle is different. Functional difficulties such as flat and inverted nipples, or a very small or weak infant, are also causes of poor attachment. However, the most important causes are inexperience of the mother and lack of skilled help from the health workers who attend her. Many mothers need skilled help in the early days to ensure that the baby attaches well and can suckle effectively. Health workers need to have the necessary skills to give this help.

EFFECTIVE SUCKLING

If a baby is well attached at the breast, then he or she can suckle effectively. Signs of effective suckling indicate that milk is flowing into the baby's mouth. The baby takes slow, deep suckles followed by a visible or audible swallow about once per second. Sometimes the baby pauses for a few seconds, allowing the ducts to fill up with milk again. When the baby starts suckling again, he or she may suckle quickly a few times, stimulating milk flow, and then the slow deep suckles begin. The baby's cheeks remain rounded during the feed. Towards the end of a feed, suckling usually slows down with fewer deep suckles and longer pauses between them. This is the time when the volume of milk is less, but as it is fat-rich hind milk, it is important for the feed to continue. When the baby is satisfied, he or she usually releases the breast spontaneously. The nipple may look stretched out for a second or two, but it quickly returns to its resting form.

INEFFECTIVE SUCKLING

A baby who is poorly attached is likely to suckle ineffectively. He or she may suckle quickly all the time, without swallowing, and the cheeks may be drawn in as he or she suckles showing that milk is not flowing well into the baby's mouth. When the baby stops feeding, the nipple may stay stretched out and look squashed from side to side, with a pressure line across the tip, showing that the nipple is being damaged by incorrect suction.

POSITIONING THE MOTHER AND BABY FOR GOOD ATTACHMENT

For successful breast-feeding, a baby and his or her mother need to be appropriately positioned. There are several different positions for them both but some key points need to be followed in any position.

Position of the mother

The mother can be sitting, lying down (Figure 4) or standing, if she wishes. However, she needs to be relaxed and comfortable, and without strain, particularly of her back. If she is sitting, her back needs to be supported, and she should be able to hold the baby at her breast without leaning forward.

Position of the baby

The babies can breastfeed in several different positions in relation to the mother across her chest and abdomen, under her arm (Figure 4) or alongside her body.

Whatever the position of the mother, and the baby's general position in relation to her, there are four key points about the position of the baby's body that are important to observe.

The baby's body should be straight, not bent or twisted. The baby's head can be slightly extended at the neck, which helps his or her chin

to be close in to the breast. He or she should be facing the breast. The nipples usually point slightly downwards, so the baby should not be flat against the mother's chest or abdomen, but turned slightly on his or her back able to see the mother's face. The baby's body should be close to the mother which enables the baby to be close to the breast, and to take a large mouthful. His or her whole body should be supported. The baby may be supported on the bed or a pillow, or the mother's lap or arm. She should not support only the baby's head and neck. She should not grasp the baby's bottom, as this can pull him or her too far out to the side, and make it difficult for the baby to get his or her chin and tongue under the areola.

BREAST FEEDING PATTERN

To ensure adequate milk production and flow for 6 months of exclusive breastfeeding, a baby needs to feed as often and for as long as he or she wants, both day and night 7. This is called demand feeding, unrestricted feeding, or baby-led feeding.

THE ROLE OF OBSTETRICIAN

Because the obstetrician often has the ?rst contact with the expectant mother, there is a unique and critical opportunity to in?uence her choice to breastfeed. It stands to reason that the approach of the obstetricians and their of?ce and clinic staff have an enormous in?uence on the mothers' ?nal choice. Accepting the premise that breastfeeding is the best choice, it follows that appropriate instruction, promotion, and support are needed to assure prospective mothers that this is the preferable and doable choice for them.

CURRENT TRENDS IN OBSTETRICS AFFECTING BREASTFEEDING

Obstetrics is a dynamic specialty with many social, ?nancial, and scienti?c factors affecting the discipline. Many social and ?nancial trends are resulting in negative effects. Therefore, the healthcare team must continually seek solutions to the changing landscape of practice.

Decreasing length of stay

Unlike in the past, when breastfeeding instruction, observation, and supervision were possible postpartum, today these measures are limited. Accordingly, much of the preparation and education must be provided during the antepartum period. The instruction and breastfeeding supervision require ef?cient and effective use of time in the hospital.

Rising Cesarean delivery rate

The pain and discomfort associated with Cesarean section will usually delay the initiation of breastfeeding and the neonate may be put on another milk. Thus operative interventions, such as caesarean section hampers breast feeding practices. Obstetricians have a major responsibility to reduce caesarean section rates and if done breast Feeding has to be strongly advocated and facilitated.

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CHAPTER 4

BREAST DISORDERS DURING PREGNANCY

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INTRODUCTION

Pregnancy causes unique physiological changes in the mammary glands in response to hormonal stimulation. Most of the benign lesions seen in breast during pregnancy are usually same as those in non-pregnant women. However, some breast disorders are unique to pregnancy. Although most disorders related to pregnancy are benign, pregnancy associated breast carcinoma (PABC) represents up to 3% of all breast malignancies.

PHYSIOLOGICAL CHANGES OF BREAST DURING FIRST TRIMESTER OF PREGNANCY

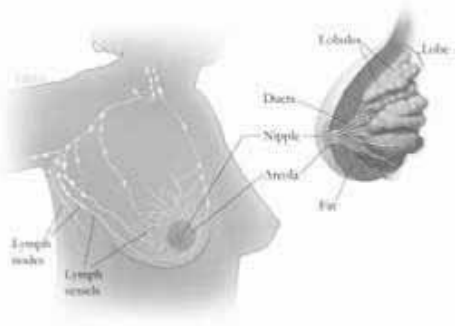


Fig. 1 Changes In Breast during Pregnancy

Early in the 2nd month of the pregnancy, increase in size of breasts begins due to increase in circulating hormones estrogen, progesterone and prolactin. This initial period of change occurs under estrogenic influence and is characterized by marked ductular sprouting with some branching and discrete lobular growth, simultaneous involution of the fibrofatty stroma and an increase in glandular vascularity, often accompanied by infiltration by mononuclear cells. (Fig1) Early in pregnancy, the colostrum is usually thick and yellow. As delivery approaches, it turns pale and nearly colourless.[1]

IMAGING OF BREAST IN PREGNANCY - ULTRASOUND

Ultrasound (US) is used before mammography to evaluate a palpable mass. Ultrasound can accurately diagnose a lump with cyst or a solid mass, but is much less accurate at distinguishing between benign or cancerous lesions.[2]

Mammograms

Mammography during pregnancy may be considered for women with signs or symptoms or US suspicious of a breast cancer. The gland appears very dense, heterogeneously coarse, nodular and confluent, with a marked decrease in adipose tissue and a prominent ductal pattern. Small studies have found that mammography poses little to no harm to the fetus during pregnancy if a lead shield is placed on the abdomen to block any possible radiation scatter.[3] The sensitivity of mammography in pregnant and lactating women is reduced due to increased parenchymal density. Instead, ultrasonography is the most appropriate radiologic method for evaluating breast masses.

MRI

MRI is indicated in pregnant women with breast lumps having a suspicion of cancer on mammography. Magnetic resonance imaging could play an important role in the differential diagnosis of pregnancy-related breast lumps, particularly during puerperium, thus avoiding unnecessary surgical biopsies. Until more data are available, the use of MRI during pregnancy should be carefully planned in selected case.[2,3,4]

EFFECT OF PREGNANCY ON DISEASES PRE-EXISTING IN BREAST

Most of the breast tumors diagnosed during pregnancy are pre-existing but are manifested during this time due to changes or growth of the tumour

Fibroadenoma

Fibroadenoma is one of the most common tumours of pregnancy and pregnancy may cause growth, infarction and secretory hyperplasia in these tumours.

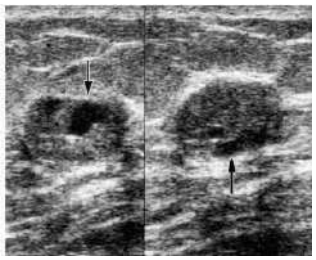


Fig. 2a Complex fibroadenoma Fig. 2b Cyst formation in fibroadenoma

The following changes are seen :

1. *Growth of Fibroadenoma :* Fibroadenoma is a hormone sensitive tumor most commonly found during pregnancy or lactation. The increased hormonal levels associated with pregnancy and lactation can induce tumor growth. Hence, existing or unknown fibroadenomas may be discovered during pregnancy. The benign radiologic appearance of the fibroadenoma during pregnancy is similar to its appearance in a nonpregnant women. However, in some of the pregnant women, US reveals a fibroadenoma with a prominent ductal pattern and proliferative changes under hormonal stimulation, leading to manifestations resembling those of complex fibroadenomas (Fig -2a) and cyst formation (Fig-2b). Cytologic analysis and results may be suspicious because of several normal physiologic changes in cellularity during pregnancy and lactation. Suspicious finding on cytology should be confirmed on core biopsy.
2. *Infarction in Fibroadenoma :* Fibroadenomas and lactating adenomas can develop foci of infarction during pregnancy. This phenomenon is usually detected in the 3rd trimester or after delivery, and is rare earlier. It can be clinically suspected if sudden pain occurs in a previously painless fibroadenoma. Intravascular thrombosis has been suggested as a causative factor. The radiological features of fibroadenomas with infarction show more lobulated margins, a heterogeneous echotexture and acoustic shadowing. If large infarcts occur, the tumor may show suspicious findings requiring histological analysis on core biopsy.
3. *Secretory hyperplasia or lactational change in fibroadenoma :* Secretory hyperplasia sometimes develops in fibroadenomas during pregnancy due to the epithelial hormone-sensitive component of the tumor responding to the gravid hormonal stimulation in a similar way as occurs in the mammary parenchyma. If the tumor is allowed to remain in the breast or is not detected until after delivery, it will be classified as a fibroadenoma with lactational change. Milk may be extracted at fine needle aspiration when fibroadenomas demonstrate lactational changes. These fibroadenomas with secretory hyperplasia may change in appearance on US, showing discrete heterogeneity in their echotexture with hyperechogenic areas, dilated ducts and cysts, thereby resembling complex fibroadenomas. Microcalcifications may be found at mammography, making fibroadenomas with secretory hyperplasia more conspicuous.[5,6,7]

BENIGN DISEASES CLOSELY RELATED TO PHYSIOLOGICAL CHANGES :

GESTATIONAL AND SECRETORY HYPERPLASIA

Usually gestational hyperplasia is related to pregnancy and secretory hyperplasia is related to lactation. Two different mammographic manifestations can coexist, Round punctate calcifications represent hyperplasia in the lobular acini, whereas linear calcifications correspond to ductal hyperplasia. Microcalcifications secondary to gestational or secretory hyperplasia must be distinguished clinically from a different entity known as pregnancy like hyperplasia or pseudolactational hyperplasia, which manifests with the same radiological and pathological findings in non-pregnant, non-lactating women. Malignant potentiality has not been described in secretory or lactational hyperplasia.

Spontaneous blood stained nipple discharge

Spontaneous bloody nipple discharge is an uncommon clinical condition during pregnancy and lactation. During the third trimester of pregnancy, proliferative changes within the ducts of the breasts may lead to bloody discharge from the nipple. This occurs when proliferative spurs of epithelium that extend into the ducts are traumatized, resulting in bleeding. Clinical follow-up is advised if no pathologic results are found and physical and US examinations are normal. Galactography is recommended if bloody secretion is limited to one duct because spontaneous blood stained secretion usually involves more than one duct. It must be remembered that blood stained nipple discharge represents an uncommon manifestation of Pregnancy Associated breast cancer (PABC).[5]

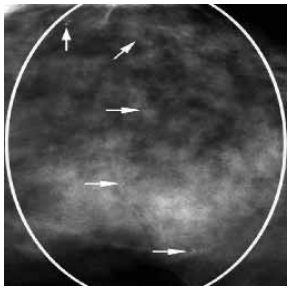


Fig. 3a Gestational Hyperplasia

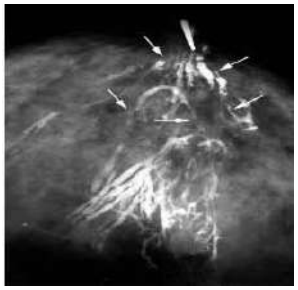


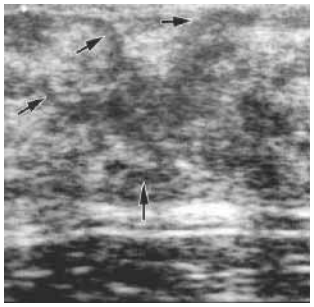
Fig. 3b Galactography

Gigantomastia

Gigantomastia is a very rare condition that complicates about one of every 100,000 pregnancies.1,5 It is characterized by massive enlargement of the breasts, resulting in tissue necrosis, ulceration, infection, haemorrhage and complications that can be life threatening in certain cases. Although, its etiology is unknown, gigantomastia is believed to represent an abnormal response to hormonal stimulation during pregnancy. Both glands grow dramatically, and weight of 4-6 kg per breast have been reported. The diagnosis of gigantomastia is based on clinical findings. Radiological and pathological studies are not required if no associated disorders are present. Treatment is based on bromocriptine administration, but surgical intervention (reduction mammoplasty or simple mastectomy with posterior reconstruction) is required if the disorder progresses.

Inflammatory disease

Granulomatous mastitis



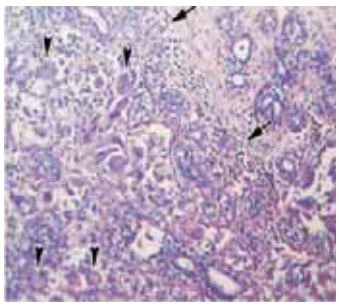


Fig. 4 Granulomatous Mastitis Fig. 4a Ultrasound 4b: Histopathological

Granulomatous mastitis is a very rare inflammatory disease of unknown cause that has been closely related to pregnancy, lactation and within 5 years of pregnancy. Inflammatory factors have been reported as a possible cause but a recent study isolated corynebacterium in up to 75% of cases. Generally, manifests as a distinct firm to hard mass that may involve any part of the breast but tends to spare the subareolar regions. The US appearance of multiple clustered, often contiguous tubular hypoechoic lesions has been considered suggestive of granulomatous mastitis. Unfortunately, this

is an uncommon manifestation whose imaging features most often resemble those of carcinoma (fig-4a).The diagnosis of granulomatous mastitis is based on exclusion, since it depends on the demonstration of a particular histologic pattern: a noncaseating, nonvasculitic granulomatous inflammatory reaction centered on lobules, combined with the exclusion of other granulomatous reactions, especially tuberculosis and fungal infections as well as sarcoidosis (fig-4b).The prognosis is often good, but local recurrence has been reported. Corticotherapy has proved effective. Primary treatment has classically been based on excisional biopsy, but close surveillance without surgery has also proved adequate in the management of cases involving spontaneous resolution. If corynebacterium is isolated with microbiologic or pathologic studies, antibiotic therapy based on the administration of penicillin should be effective.

BENIGN NEOPLASIA OF THE BREAST

Benign tumors of the breast include lactating adenoma and fibroadenoma. Fibroadenoma has already been discussed.

Lactating adenoma

Despite the name, lactating adenomas are more common during pregnancy than during lactation. Lactating adenomas typically present as painless palpable masses. The histology is characteristic, lobulated masses of acini or lobules, densely packed together with little intervening stroma and intact basement membrane. Despite abundant proliferative changes, there are no atypia. Pregnancy associated changes usually are noted, including intracytoplasmic or supranuclear vacuolation and secretions in gland lumens. The major task is to differentiate this benign mass from breast cancer. Diagnostic fine-needle aspiration cytology (FNAC) is an acceptable method of diagnosis. Large numbers of very similar cells are present, with some nuclear enlargement, prominent nucleoli, cellular dispersion against a background suggestive of necrosis, prominent cytoplasmic vacuoles, and a foamy/wispy appearance to the cytoplasm.[4,6]

Malignant tumors

Malignant diseases include PABC, and pregnancy-related Burkitt lymphoma of the breast

PREGNANCY ASSOCIATED BREAST CARCINOMA (PABC)

PABC is defined as breast cancer that occurs during pregnancy or within 1 year of delivery with the incidence of 0.3/1000 pregnancies.[2,3] It occurs between the age group of 32 to 38 years of age. With many women choosing to delay childbearing, it is likely that the incidence of breast cancer during pregnancy will increase. Most common presentation is a palpable mass. Swelling, erythema, and diffuse breast enlargement are less common. No damaging effects on the fetus from maternal breast cancer have been demonstrated, and there are no reported cases of maternal-fetal transfer of breast cancer cells.[8]

Diagnosis : The physiological changes of the breasts of pregnant and lactating women may hinder detection of small masses so early diagnosis of breast cancer may not occur. An average delay in diagnosis of 5 to 15 months from onset of symptoms is common and is a major factor responsible for the advanced stage and poor prognosis associated with PABC. Therefore, cancers are typically detected at a later stage than in a nonpregnant, age-matched population. To detect breast cancer, pregnant and lactating women should practice self-examination and undergo a breast examination as part of the routine prenatal examination by a doctor. If an abnormality is found, diagnostic approaches such as ultrasound and mammography may be used. (fig 5) Diagnosis may be safely accomplished with a fine-needle aspiration, core biopsy or excisional biopsy.[8,9] Core biopsy is the standard procedure for assessing breast masses during pregnancy. It is a safe, cost-effective, and easy method for making a precise diagnosis. The risk of bleeding is slightly increased due to the increased vascularity associated with pregnancy and lactation. The risk of infection and milk fistula formation are also increased. Obviously, these complications are more prone to develop with core biopsy than with fine-needle aspiration, but they occur infrequently.

Caution :

- Since 25% of mammograms in pregnancy may be negative in the presence of cancer, a biopsy is essential for the diagnosis
- of any palpable mass and, all masses found during pregnancy should be evaluated carefully.
- Several cellular changes normally occur in the epithelium of the breasts of pregnant women leading to a false-positive
- diagnosis of carcinoma with cytological analysis and must be interpreted with caution. Core biopsy is mandatory if malignancy is suspected.

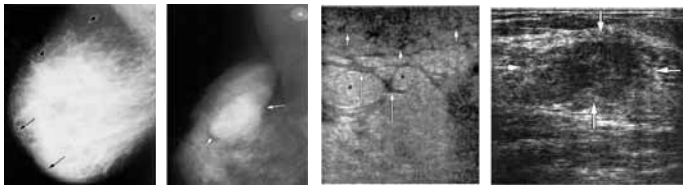


Fig. 5a Fig. 5b Fig. 5c Fig. 5d

Figures 5. Inflammatory carcinoma (a) Mammogram shows a marked diffuse increase in parenchymal density with skin thickening and thickened trabeculae due to dilated lymphatic vessel (b) US image shows skin thickening, a network of hypoechoic and anechoic tubular structures representing enlarged lymphatic vessels. PABC (c) Mammogram reveals a large lobular mass with obscured margins. (d) US image shows an irregular heterogeneous hypoechoic mass with indistinct margin.

- *Staging :* Nuclear scans cause fetal radiation exposure. If such scans are essential for evaluation, hydration and foley catheter drainage of the bladder can be used to prevent retention of radioactivity. Timing of the exposure to radiation relative to the gestational age of the fetus may be more critical than the actual dose of radiation delivered. Radiation exposure during the first trimester can lead to congenital malformations, especially microcephaly. A chest x-ray with abdominal shielding is relatively safe but it should be used only when it is essential for making treatment decisions. Evaluation of the liver can be performed with US, and brain metastases can be diagnosed with a MRI scan, both of which avoid fetal radiation exposure. However, no data evaluating the safety of MRI during pregnancy are available. For the diagnosis of bone metastases, a bone scan is preferable to a skeletal series because the bone scan delivers a smaller amount of radiation and is more sensitive. Hormone receptor assays are usually negative in pregnant breast cancer patients, because of receptor binding by high serum estrogen levels associated with pregnancy.[8,9]

Treatment Early stage cancer (stages I & II)

- *Surgery* (modified radical mastectomy) is the treatment of choice. Conservative surgery with postpartum radiation therapy has been

used for breast preservation. Data on the immediate and long-term effects of chemotherapy on the fetus are limited.8 Studies using adjuvant hormonal therapy alone or in combination with chemotherapy for breast cancer in pregnant women are also limited. Therefore, no conclusion has been reached regarding these options. However, if adjuvant chemotherapy is necessary, it should not be given during the first trimester to avoid the risk of teratogenicity and radiation therapy, if indicated, should be withheld until after delivery since it may be harmful to the fetus at any stage of development.

Late stage disease (stages III & IV)

First-trimester radiation therapy should be avoided. Chemotherapy may be given after the first trimester as discussed above. As the mother may have a limited life span and there is a risk of fetal damage with treatment during the first trimester, issues regarding continuation of the pregnancy should be discussed with the patient and her family. Termination of pregnancy may be considered based on the age of the fetus if maternal treatment options such as chemotherapy and radiation therapy are significantly limited by the continuation of the pregnancy.5

PABC in BRCA germline mutation carriers

BRCA 1 or BRCA 2 mutation carriers are at high risk for breast cancer, making strict surveillance mandatory. Therefore, before pregnancy and after delivery a complete clinical and radiologic evaluation is necessary to exclude any pathologic process.US and MR imaging evaluation are of great value.

PREGNANCY-RELATED BURKITT LYMPHOMA OF THE BREAST

Burkitt lymphoma is type of lymphoma arising from undifferentiated B cells. It has been classified into three categories :

1) The endemic type is seen in young Africans in close association with Epstein-Barr virus and malaria.
2) The sporadic type is seen in Europe and the United States.
3) Lymphoma associated with human immunodeficiency virus

Burkitt lymphoma of the breast affects pregnant or postpartum patients with massive enlargement of both breasts. Burkitt lymphoma of the breast is characterized by rapid spread and a poor prognosis. They are almost always bilateral. Mammography shows diffuse marked increase in parenchymal density. Massive bilateral involvement of the ovaries is common and tumors may develop in any of the abdominal organs, especially the liver, spleen, and kidneys and rarely in peripheral lymph node.

The majority of breast lesions encountered during pregnancy are benign. Physiological changes during pregnancy make evaluation of the breasts more difficult. Baseline and serial examinations are critical. Prompt and immediate biopsies of breast masses are important during pregnancy and benign-appearing or low-suspicion lesions should not be neglected.

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CHAPTER 5

CHALLENGES IN BREAST FEEDING

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INTRODUCTION

From time to time, mothers encounter problems with breastfeeding. Most problems are preventable with good breastfeeding practices. When problems do occur, early recognition and treatment enable a mother to begin or continue to enjoy breastfeeding and help reach the recommended goals of exclusive breastfeeding for six months and continued breastfeeding for 2 years and beyond.

FLAT AND INVERTED NIPPLES

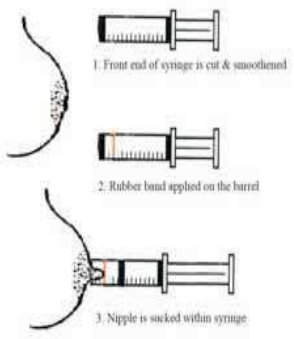

Fig. Preparing and using a syringe for treatment of inverted nipples.

Some women have nipples that turn inward instead of protruding, or that are flat and do not protrude. Nipples can also sometimes be flattened temporarily due to engorgement while breastfeeding. Antenatal treatment is probably not helpful. For example, stretching nipples, or wearing nipple shields does not help. Most nipples improve around the time of delivery without any treatment. Help is most important soon after delivery, when the baby starts breastfeeding: Build the mother's confidence; Explain that a baby suckles from the breast - not from the nipple; Encourage her to give plenty of skin-to-skin contact, and to let her baby explore her breasts; Help her to make her nipple stand out more before a feed; Sometimes making the nipple stand out before a feed helps a baby to attach. Stimulating her nipple may be all that a mother needs to do. Or she can use a hand breast pump, or a syringe to pull her nipple out; Express her milk and feed it to her baby with a cup.

BREAST ENGORGEMENT

Physiologic breast fullness is a normal process with lactogenesis as volume of breast increases with developing milk. Pathologic engorgement is when the breasts become firm, diffuse and painful due to overfilling that occurs due to ineffective or infrequent milk removal. It occurs around days 3-7. It involves congestion, accumulation of milk and edema secondary to obstruction of lymphatics. Primiparas are more affected.

Treatment

First reassure the mother that the engorgement is temporary and can be relieved. The principle of management is removal of milk. If milk is not removed, mastitis may develop, an abscess may form, and breast milk production may also decrease. So do not advise a mother "rest" the breast.

If the baby is able to suckle, he/she should feed frequently. This is the best way to remove milk. Help the mother to position her baby, so that he/she attaches well, suckles effectively and does not damage the nipple. If the baby is not able to suckle, help the mother to express milk.

She may be able to express by hand or she may need to use a breast pump, or a warm bottle to make the breast soft enough for the baby to suckle. Before feeding or expressing, stimulate the mother's oxytocin reflex by putting t a warm compress on her breasts. Massaging the breast lightly and gentle stimulation of breast is helpful. After a feed, put a cold compress on her breasts to reduce edema.

BLOCKED DUCT AND MASTITIS

Mastitis may develop in an engorged breast, or it may follow a condition called blocked duct.

Blocked duct occurs when the milk is not removed from part of a breast. The duct to that part of the breast is sometimes blocked by thickened milk. The symptoms are of lump which is tender, and sometimes redness of the skin over the lump is found. The woman has no fever and feels well. When milk stays in part of a breast, because of a blocked duct, or because of engorgement, it is called milk stasis. If the milk is not removed, it can cause inflammation of the breast tissue, which is called non-infective mastitis. Sometimes a breast becomes infected with bacteria, and this is called as infective mastitis. It is not possible to tell from the symptoms alone if mastitis is non-infective or infective. If the symptoms are all severe, the woman is more likely to need treatment with antibiotics.

Causes

The main cause of blocked duct and mastitis is poor drainage of all or part of a breast, may be due to: Infrequent breastfeeds; Ineffective suckling if the baby is poorly attached to the breast; Pressure from tight clothes, especially if she wears it at night; or from lying on the breast, which can block one of the ducts; If there is a nipple fissure, it provides a way for bacteria to enter the breast tissue. This is another way in which poor attachment can lead to mastitis.

Treatment

Look for a cause of poor drainage, and correct it. Ask the mother to breastfeed frequently. The breast should be gently massaged while her baby is suckling. Massage over the blocked area, and over the duct which leads from the blocked area, right down to the nipple. This helps to remove the block from the duct. She may notice that a plug of thickened milk comes out with her milk. (It is safe for the baby to

swallow the plug.) Apply warm compresses to her breast between feeds. Breastfeed the baby in different positions at different feeds. Usually, blocked duct or mastitis improves within a day when drainage to that part of the breast improves. If not improved, Treat her, or refer her for treatment with antibiotics, analgesics and rest.

SORE NIPPLES

Sore nipples and breast pain is one of the common factor causing mothers to abandon breast feeding. While managing such a case first look for a cause. Observe the baby breastfeeding, and check for signs of poor attachment. Examine the breasts. Look for signs of Candida infection, engorgement, fissures, red, shiny, or flaky skin of nipple & areola, itchiness or deep pain in areola and oral thrush in baby. Help the mother to improve her baby's attachment. Often this is all that is necessary. She can continue breastfeeding and need not rest the breast.

Ask the mother not to wash her breasts more than once a day and not to use soap, or rub hard with a towel. Washing removes natural oils from the skin and makes soreness more likely. Advise her not to use medicated lotions and ointments, because these can irritate the skin and there is no evidence that they are helpful. Rubbing a little expressed breast milk over the nipple and areola with finger promotes healing.

NEONATAL CONDITIONS

Baby may refuse to breastfeed due to :

- *Illness :* The baby may attach to the breast, but suckles less than before.
- *Blocked nose :* The baby suckles a few times, and then stops and cries.
- *Sedation :* Baby may be sleepy because of drugs that his/her mother was given during labor; drugs that she is taking for psychiatric treatment.

  Babies have strong feelings, and if they are upset they may refuse to breastfeed. They may not cry, but simply refuse to suckle. This is commonest when a baby is aged 3-12 months. Suddenly refuses several breastfeeds. This behavior is sometimes called a 'nursing strike'; due to separation from his/her mother, for example when she starts a job, or new career.
- *Rooting :* When a newborn baby `roots' for the breast, he/her moves his head from side to side as if he is saying `no'. However, this is normal behavior. Between 4 and 8 months of age, babies are easily distracted, for example when they hear a noise. They may suddenly stop suckling. It is a sign that they are alert. After the age of 1 year, a baby may wean himself/herself which is usually gradual.

MANAGEMENT OF REFUSAL TO BREASTFEED

Apparent refusal :

- *If it is rooting :* Explain that this is normal. She can hold her baby at her breast to explore her nipple. Help her to hold him/her closer, so that it is easier for him to attach.
- *If it is distraction :* Suggest that she try to feed him/her somewhere quieter for a while. If it is self-weaning: Suggest that she: makes sure that the child eats enough family food; gives him plenty of extra attention in other ways; continues to sleep with him because night feeds may continue. This is valuable at least up to the age of 2 years. Offer her breast whenever her baby is willing to suckle. She should not hurry to breastfeed again, but offer the breast if her baby does show an interest. He/she may be more willing to suckle when he/she is sleepy or after a cup feed, than when he/she is very hungry. She can offer her breast in different positions. If she feels her ejection reflex working, she can offer her breast then. Help her baby to breastfeed in these ways: Express a little milk into her baby's mouth. Position him/her well, so that it is easy for him to attach to the breast. She should avoid pressing the back of his head, or shaking her breast. Feed her baby by cup until he is breastfeeding again. She can express her breast milk and feed it to her baby from a cup (or cup and spoon). If necessary, use artificial feeds, and feed them by cup. She should avoid using bottles, teats and pacifiers (dummies) of any sort.

HOW OFTEN A MOTHER SHOULD EXPRESS MILK

- To establish lactation, to feed a low-birth-weight (LBW) or sick newborn: She should start to express milk on the first day, within six hours of delivery if possible. She may only express a few drops of colostrum at first, but it helps breast milk production to begin, in the same way that a baby suckling soon after delivery helps breast milk production to begin. She should express as much as she can as often as her baby would breastfeed. This should be at least every 3 hours, including during the night.
- To keep up her milk supply to feed a sick baby: She should express as much as she can as often as her baby would feed, at least every 3 hours.
- To build up her milk supply, if it seems to be decreasing after a few weeks: Express very often for a few days (every -1 hour), and at least every 3 hours during the night.
- To leave milk for a baby while she is out at work: Express as much as possible before she goes to work, to leave for the baby. It is also very important to express while at work to help keep up the supply
- To relieve symptoms, such as engorgement, or leaking at work: Express only as much as is necessary.
- To keep nipple skin healthy: Express a small drop to rub on the nipple after a bath or shower.

CHAPTER 6

BREAST FEEDING IN SPECIAL SITUATIONS

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INTRODUCTION

In 2002, WHO and UNICEF launched the Global Strategy for Infant and Young Child Feeding which calls upon all governments and others "to ensure that all health and other relevant sectors protect promote and support exclusive breastfeeding for six months, and continued breastfeeding up to two years of age or beyond, while providing women access to the support that they require – in the family, the community and the workplace – to achieve this goal". However certain special situations require special recommendations.

BREASTFEEDING AND HIV

Without preventive interventions, approximately one-third of infants born to HIV-positive mothers contract HIV through mother-to-child transmission, becoming infected during their mothers' pregnancy, childbirth or breastfeeding. In 2001, 800,000 children under the age of 15 contracted HIV, over 90 per cent of them through mother-to-child transmission of HIV (MTCT). Between 15 and 25% of children born to HIV-infected mothers get infected with HIV during pregnancy or delivery, while about 15% of the children get infected through breastfeeding.

Current WHO / UNAIDS / UNICEF infant feeding guidelines can be summarized as follows :

1. For women who are known not to be infected with HIV and for women whose infection status is unknown, protect, promote and support exclusive breastfeeding for 6 months, followed by continued breastfeeding, together with appropriate complementary feeding, for up to two years of age or beyond.
2. All HIV-infected mothers should receive counseling, which includes provision of general information about the risks and benefits of various infant feeding options, and specific guidance in selecting the option most likely to be suitable for their situation. Whatever a mother decides, she should be supported in her choice.
3. When replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breastfeeding by HIV-positive mothers is recommended; otherwise, exclusive breastfeeding is recommended during the first months of life.
4. HIV-infected mothers who breastfeed should be assisted to ensure that they use a good breastfeeding technique to prevent breast conditions like mastitis, breast abscesses and nipple fissures, which should be promptly treated if they occur.
5. To minimize HIV transmission risk, breastfeeding should be discontinued as soon as feasible, taking into account local circumstances, the individual woman's situation and the risks associated with replacement feeding (including infections other than HIV and malnutrition).
6. HIV-infected mothers who breastfeed should be provided with specific guidance and support when ceasing breastfeeding to avoid harmful nutritional and psychological consequences and to maintain breast health.
7. When HIV-infected mothers choose not to breastfeed from birth or stop breastfeeding later, they should be provided with specific guidance and support for at least the first 2 years of the child's life to ensure adequate replacement feeding. Programs' should strive to improve conditions that will make replacement feeding safer for HIV-infected mothers and families.
8. HIV-infected women should have access to information, follow-up clinical care, and support, including family planning services and nutritional support

Breastfeeding, which is essential for child survival has posed an enormous dilemma for mothers living with HIV. Now, WHO says mothers may safely breastfeed provided that they or their infants receive ARV drugs during the breastfeeding period. This has been shown to give infants the best chance to be protected from HIV transmission in settings where breastfeeding is the best option.

BREASTFEEDING WITH HEPATITIS B

WHO and UNICEF recommend that all infants be exclusively breastfed for at least 4 and if possible 6 months, and that they continue to breastfeed up to two years of age or beyond with the addition of adequate complementary foods from about 6 months of age. There is a considerable risk of morbidity and mortality among infants who are not breastfed. There is no evidence that breastfeeding from an HBV infected mother poses an additional risk of HBV infection to her infant, even without immunization. Thus, even where HBV infection is highly endemic and immunization against HBV is not available, breastfeeding remains the recommended method of infant feeding.

Even before the availability of hepatitis B vaccine, HBV transmission through breastfeeding was not reported. All infants born to HBV-infected mothers should receive hepatitis B immune globulin and the first dose of hepatitis B vaccine within 12 hours of birth. The second dose of vaccine should be given at aged 1–2 months, and the third dose at aged 6 months. The infant should be tested after completion of the vaccine series, at aged 9–18 months (generally at the next well-child visit), to determine if the vaccine worked and the infant is not infected with HBV through exposure to the mother's blood during the birth process. However, there is no need to delay breastfeeding until the infant is fully immunized. All mothers who breastfeed should take good care of their nipples to avoid cracking and bleeding.

BREASTFEEDING WITH NEONATAL JAUNDICE

Approximately 60% of full-term infants develop jaundice within several days of birth. Jaundice, or yellowing of the skin and eyes, occurs when a normal substance, bilirubin, builds up in the newborn's bloodstream faster than the liver can break it down and excrete it through the baby's stool. By breastfeeding more frequently or for longer periods of time, the infant's body can usually rid itself of the bilirubin excess. However, in some cases, the infant may need additional treatments to keep the condition from progressing into more severe hyperbilirubinemia, bilirubin encephalopathy or kernicterus. Breastfeeding jaundice may occur in the first week of life in more than 1 in 10 breastfed infants. The cause is thought to be inadequate milk intake, leading to dehydration or low caloric intake. It is a type of physiologic or exaggerated physiologic jaundice. Breast milk jaundice is far less common and occurs in about 1 in 200 babies. Here the jaundice isn't usually visible until the baby is a week old. It often reaches its peak during the second or third week. Breast milk jaundice can be caused by substances in mom's milk that decrease the infant's liver's ability to deal with bilirubin. Breast milk jaundice rarely causes any problems, whether it is treated or not. It is usually not a reason to stop nursing.

BREASTFEEDING AND SMOKING

A statement on the transfer of drugs and chemicals into human milk was first published in 19831with revisions in 1989 and 1994, the Committee on Drugs placed nicotine (smoking) in, "Drugs of Abuse-Contraindicated during Breastfeeding." The reasons for placing nicotine and, thus, smoking were documented decrease in milk production and weight gain in the infant of the smoking mother and exposure of the infant to environmental tobacco smoke as demonstrated by the presence of nicotine and its primary metabolite, cotinine, in human milk2 There is controversy regarding the effects of nicotine on infant size at 1 year of age3,4 There are hundreds of compounds in tobacco smoke; however, nicotine and its metabolite acotinine are most often used as markers of tobacco exposure. Nicotine is not necessarily the only component that might cause an increase in respiratory illnesses (including otitis media) in the nursing infant attributable to both transmammary secretion of compounds and environmental exposure. Nicotine is present in milk in concentrations between 1.5 and 3.0 times the simultaneous maternal plasma concentration5 and elimination half-life is similar—60 to 90 minutes in milk and plasma. There is no evidence to document whether this amount of nicotine presents a health risk to the nursing infant.

The Committee on Drugs wishes to support the emphasis of the American Academy of Pediatrics on increasing breastfeeding in the United States. Pregnancy and lactation are ideal occasions for physicians to urge cessation of smoking. It is recognized that there are women who are unable to stop smoking cigarettes. One study reported that, among women who continue to smoke throughout breastfeeding, the incidence of acute respiratory illness is decreased among their infants, compared with infants of smoking mothers who are bottle fed6. It may be that breastfeeding and smoking is less detrimental to the child than bottle feeding and smoking. The Committee on Drugs awaits more data on this issue. The Committee on Drugs therefore has not placed nicotine (and thus smoking) in any of the Tables but hopes that the interest in breastfeeding by a smoking woman will serve as a point of discussion about smoking cessation between the pediatrician and the prospective lactating woman or nursing mother. Alternate (oral, transcutaneous) sources of nicotine to assist with smoking cessation, however, have not been studied sufficiently for the Committee on Drugs to make a recommendation for or against them in breastfeeding women.

PSYCHOTROPIC DRUGS

Anti-anxiety drugs, antidepressants, and neuroleptic drugs have been placed in, "Drugs for Which the Effect on Nursing Infants is Unknown but May Be of Concern." These drugs appear in low concentrations (usually with a milk-to-plasma ratio of 0.5–1.0) in milk after maternal ingestion. Because of the long half-life of these compounds and some of their metabolites, nursing infants may have measurable amounts in their plasma and tissues, such as the brain. This is particularly important in infants during the first few months of life, with immature hepatic and renal function. Nursing mothers should be informed that if they take one of these drugs, the infant will be exposed to it. Because these drugs affect neurotransmitter function in the developing central nervous system, it may not be possible to predict long-term neurodevelopmental effects.

SILICONE BREAST IMPLANTS AND BREASTFEEDING

Approximately 800,000 to 1 million women in the United States have received breast implants containing silicone (elemental silicon with chemical bonds to oxygen) in the implant envelope or in the envelope and the interior gel. Concern has been raised about the possible effects to the nursing infant if mothers with implants breastfeed. This concern was initially raised in reports that described esophageal dysfunction in 11 children whose mothers had implants 7,8 . This finding has not been confirmed by other reports. Silicone chemistry is extremely complex; the polymer involved in the covering and the interior of the breast implant consists of a polymer of alternating silicon and oxygen atoms with methyl groups attached to the oxygen groups (methyl polydimethylsiloxane)9 . The length of the polymer determines whether it is a solid, gel, or liquid. There are only a few instances of the polymer being assayed in the milk of women with implants; the concentrations are not elevated over control samples10 There is no evidence at the present time that this polymer is directly toxic to human tissues; however, concern also exists that toxicity may be mediated through an immunologic mechanism. This has yet to be confirmed in humans. Except for the study cited above, there have been no other reports of clinical problems in infants of mothers with silicone breast implants11 . It is unlikely that elemental silicon causes difficulty, because silicon is present in higher concentrations in cow milk and formula than in milk of humans with implants12. The anticolic compound simethicone is a silicone and has a structure very similar to the methyl polydimethylsiloxane in breast implants. Simethicone has been used for decades in this country and Europe without any evidence of toxicity to infants. The Committee on Drugs does not feel that the evidence currently justifies classifying silicone implants as a contraindication to breastfeeding.

DRUG THERAPY OF THE LACTATING WOMAN

The following should be considered before prescribing drugs to lactating women :

1. Is drug therapy really necessary? If drugs are required, consultation between the pediatrician and the mother's physician can be most useful in determining what options to choose.
2. The safest drug should be chosen, for example, acetaminophen rather than aspirin for analgesia.
3. If there is a possibility that a drug may present a risk to the infant, consideration should be given to measurement of blood concentrations in the nursing infant.
4. Drug exposure to the nursing infant may be minimized by having the mother take the medication just after she has breastfed the infant or just before the infant is due to have a lengthy sleep period.

Data have been obtained from a search of the medical literature. Because methodologies used to quantitate drugs in milk continue to improve, this information will require frequent updating.

Physicians who encounter adverse effects in infants who have been receiving drug-contaminated human milk are urged to document these effects in a communication to the Food and Drug Administration and to the Committee on Drugs. This communication should include the generic and brand names of the drug, the maternal dose and mode of administration, the concentration of the drug in milk and maternal and infant blood in relation to the time of ingestion, the method used for laboratory identification, the age of the infant, and the adverse effects. Such reports may substantially increase the pediatric community's fund of knowledge regarding drug transfer into human milk and the potential or actual risk to the infant.

BREASTFEEDING IN PUBLIC

Breastfeeding in public is forbidden in some jurisdictions, not addressed by law in others, and a granted legal right in public and the workplace in yet others. Where it is a legal right, some mothers may nevertheless be reluctant to breastfeed[23, 24]and some people may object to the practice. The federal government and many states have laws that protect nursing women. These laws are based on the recognition of organizations such as the American Academy of Pediatrics, the American Congress of Obstetricians and Gynecologists, American Public Health Association, United Nations International Children's Emergency Fund (UNICEF), and the World Health Organization (WHO) that breastfeeding is the best choice for the health of a mother and her baby. Even with the growing awareness of the benefits of breastfeeding, women may find it difficult to do so in public. She should be asked to -

- Wear clothes that allow easy access to breasts, such as tops that pull up from the waist or button down.
- Use a special breastfeeding blanket around her shoulders.
- Breastfeed y baby in a sling. Slings or other soft infant carriers are especially helpful for traveling — it makes it easier to keep the baby comforted and close to the mother.
- Slip into a women's lounge or dressing room to breastfeed.
- Practice at home so that she can ensure that she is only being as revealing as she feels comfortable with.

"A hungry baby shouldn't be expected to wait. No mother can be forced to ignore the needs of her baby"

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CHAPTER 6

BREAST FEEDING AND CONTRACEPTION

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INTRODUCTION

For the nursing mother who wants to space her pregnancies, there are many birth control options to choose from. Each method offers advantages and disadvantages. Breast feeding itself has contraceptive benefits, however it is important to think about birth control options well before the time a mother becomes fertile again. What follows is a list of family planning options as they relate to breastfeeding women. It is important to emphasize that, hormonal methods containing estrogen should be avoided whenever possible.

LACTATIONAL AMENORRHOEA

LAM i.e. Lactational Amenorrhea is an effective contraceptive method. No contraception is required for 21 days after delivery[1]. After that also, breast feeding women have only 2% chance of conception if – and only if – all three LAM criteria continue to apply.

- Amenorrhea, since the lochia ceased.
- Exclusive breast feeding (at least four-hourly feeds) and night (at least six-hourly feeds)

If the interval between the feeds is larger or if night feeds are not given, the effectiveness decreases.

- Infant less than 6 months.

After 6 months even if exclusive breast feeding is continued it does not offer effective protection.

COUNSELLING REGARDING CONTRACEPTIVES

The counseling should start during the antenatal period itself and discussed after delivery in the labor room and first week postpartum[2], as women are more sensitive to contraceptive advice then. This is particularly important in a country like India where KAP gap is wide.

In India, 65% of women in the first year postpartum have an unmet need for family planning. Only 26% of women are using any method of family planning during the first year postpartum.

In order for a woman to make an informed choice about her contraceptive, following things must be asked while taking the history:

- Whether sexually active?
- Any ongoing sexual problems post- delivery?
- Early or late reversibility desired?
- Pattern of breast feeding? Any supplements given? Night feeds given or not?
- Past or present medical problems like hypertension, thrombo-embolism, trophoblastic disease etc.
- Any previous contraceptive used? Personal preference?

OPTIONS AVAILABLE TO THE BREAST FEEDING MOTHER

There is no such thing as IDEAL contraceptive and the option has to be tailor made for the woman in question. Today, there is a huge choice of contraceptives available in the market.

Options suitable for a breast feeding mother are -

Hormonal (progesterone only)	Non Hormonal
• Pills- POP • Injections • Implants • IUD • PVR (Progesterone Vaginal Ring)	• Natural - LAM • Barrier • Copper T • Sterilization (Tubal Ligation)

HOW SOON TO ADVICE CONTRACEPTION?

There is great variation in the return to fertility and sexual activity following childbirth but the earliest known time of ovulation is 27 days after delivery. Therefore, no contraception is needed until 21 days postpartum[1]. All women must be advised that they may become fertile ahead of the return of menstruation and should not delay the use of contraception. The timing of starting various contraceptive methods is discussed ahead.

If baby is being exclusively breast fed then Lactational Amenorrhoea can be a reliable method provided the criteria are fulfilled.

Combined OCPs or Progesterone only Pills

Estrogen decreases the quality and quantity of breast milk. A recent systematic review did not show an adverse effect on infant growth or development[4]. However, WHO recommends that COCPs should not be used in the first 6 weeks postpartum and should only be used between 6 weeks and 6 months if other, more appropriate methods, is unacceptable.[5]

Progesterones are secreted in breast milk (not in IUD) but small amounts of progesterones are not harmful to the new born and do not affect the quality and quantity of milk.

PROGESTERONE ONLY PILL (MINI PILL, POP)

Mechanism of action : Outside of lactation, fertile ovulation is prevented in at least 60% of cycles. Contraceptive effect is mainly due to progestogenic interference with mucus permeability, backed by some anti-nidatory activity at the endometrium.

Failure rate : Cerazette (75μg desogestrel) has Pearl Index failure rate of 0.17 per 100 women-years.

Starting routines for POP :

Condition before starting	*Start when?*	*Extra precautions?*
Post partum with lactation	Day 21, can be started. Later if LAM criteria fulfilled	No
Post partum non lactating	Day 21*	No
Post partum amenorrhea	Anytime	7 days

Starting routines for COC :

Condition before starting	*Start when?*	*Extra precautions?*
Post partum with lactation	Not recommended	No
Post partum non lactating	Day 21*(low risk of thrombosis)	No
After POP	First day of period	7 days
DMPA induced secondary amenorrhoea	Any day	Yes**

* Puerperal risk of thrombosis lasts longer if severe PIH or HELLP, COC use should be delayed till the return of normal B.P. and blood biochemistry.

** Prescriber should be confident that no blastocyst or sperm is already in upper genital tract, if necessary pregnancy test is done after at least 14 days of safe contraception or abstinence from intercourse

CHOICE OF CONTRACEPTION IN EARLY OR LATE RETURN OF FERTILITY

Early return of fertility	Late return of fertility
• Natural methods • Barrier (condoms) • POP (pills) • PVR (Progesterone Vaginal ring)	• Injections (DMPA) • Implant (Implanon) • Copper T • LNG IUD • Sterilization (if family complete)

DMPA

DMPA (Depot Medroxy Progesterone Acetate) 150 mg is given at interval of 12 weeks with extremely high effectiveness (0-1 failure per 100 women-years)

Timing of first dose

Condition before starting	*Start when?*	*Extra precautions?*
Post partum with lactation	6 weeks, POP preferable	No
Post partum non lactating	Day 21, if later with added precautions for 7 days	No
On POP	Any day	No

Overdue injections of DMPA with continuing sexual intercourse

Day 85 to 91 (13th week)	Injection + condoms / equivalent for 7 days
Day 92 to 98 (14th week)	Injection r/o pregnancy + Emergency Contraceptive + condoms / equivalent for 7days
Beyond day 98	Postpone injection r/o pregnancy + Emergency Contraceptive + condoms / equivalent for 7days

INTRAUTERINE CONTRACEPTIVE DEVICE

Post Partum IUCD - immediate post-placental, within 48 hours of delivery, and also during LSCS through uterine incision can be used. Interval IUCD can be inserted after 4 weeks.

NICE guideline suggests that both the IUD and IUS may be fitted from 4 weeks postpartum.6 The Mirena® IUS's product licensee however specifies fitting from 6 weeks postpartum.7

NEWER CONTRACEPTIVE OPTIONS

- *PVR8* - the Progesterone vaginal rings are inserted in the vagina for continuous use for up to three months and replaced with a new ring if breastfeeding is continued and extended contraception is desired. Women can use these rings continuously for up to one year. Although not recommended, the ring may be removed during sexual intercourse for a period of up to two hours. If the ring is removed for a longer period of time, an additional contraceptive method should be used for the following seven days. Upon weaning of the breastfeeding infant, progesterone rings should be replaced with another effective method if continued contraception is desired.
- *Injectables for future :*
  - Levonorgestrel Butanoate injection – 5 to 10 mg of LNG Butanoate, given 3 monthly; Advantages: less ovarian suppression, less amenorrhea and quicker return of fertility.
  - Injectable microspheres and microcapsules – biodegradable copolymer ; 3 monthly injection of 50 mg Norgestimate.

EMERGENCY CONTRACEPTIVES

Post coital contraceptive, LNG pills can be used but should not be used as primary method of contraception.Copper T can also be inserted for post-coital contraception. However LNG-IUS should not be used as post-coital intrauterine contraception; effective though it is in the long term use, it appears not to act as quickly as copper T.

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Section 2 : Breast Carcinoma

CHAPTER – 1

BREAST CARCINOMA- AN OVERVIEW

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INTRODUCTION

Blame modern lifestyle for it, but breast cancer has overtaken cervical cancer in India in numbers. According to Indian Council for Medical Research (ICMR), the incidence of breast cancer is on the rise, while cervical cancer is beginning to come down. Social taboos regarding breast cancer, prevent women from talking to friends and families, let alone doctors .This poses a big problem in early detection.[1]

BREAST CANCER BURDEN - GLOBAL AND INDIAN SCENARIO

Breast cancer is the most common cancer in women worldwide, comprising 16% of all female cancers. It is estimated that 519, 000 women died in 2004 due to breast cancer, and although breast cancer is thought to be a disease of the developed world, a majority (69%) of all breast cancer deaths occurs in developing countries (WHO Global Burden of Disease, 2004).[2] Incidence rates vary greatly worldwide, with age standardized rates as high as 99.4 per 100 000 in North America. Eastern Europe, South America, Southern Africa, and western Asia have moderate incidence rates, but these are increasing. The lowest incidence rates are found in most African countries but here breast cancer incidence rates are also increasing. Breast cancer is the most common of all cancers and is the leading cause of cancer deaths in women worldwide, accounting for >1.6% of deaths and case fatality rates are highest in low-resource countries. A recent study of breast cancer risk in India revealed that 1 in 28 women develop breast cancer during her lifetime. This is higher in urban areas being 1 in 22 in a lifetime compared to rural areas, where this risk is relatively much lower being 1 in 60. In India, almost 80 percent patients are in advanced stages when they come to hospitals.[3] The average age of the high risk group is 43-46 years unlike in the west, where women aged 53-57 years are more prone to breast cancer. Breast cancer is the most common cancer among women in the developed countries, other than skin cancer. It is the second leading cause of cancer death in women, after lung cancer. The chance of a woman having invasive breast cancer some time during her life is about 1 in 8. The chance of dying from breast cancer is about 1 in 36. Breast cancer death rates have been going down. This is probably the result of finding the cancer earlier and better treatment.

RISK FACTORS

The factors influencing breast cancer risk are broadly classified into modifiable and non –modifiable factors. The non-modifiable risk factors are age, gender, number of first degree relatives suffering from breast cancer, menstrual history, age at menarche and age at menopause. While the modifiable risk factors are BMI, age at first child birth, number of children, duration of breast feeding, alcohol, diet and number of unsuccessful pregnancies (abortions). Having a 1st-degree relative (mother, sister, and daughter) with breast cancer doubles or triples the risk of developing the cancer. About 5% of women with breast cancer carry a mutation in one of the 2 known breast cancer genes, BRCA1 or BRCA2. If relatives of such a woman also carry the gene, they have a 50 to 85% lifetime risk of developing breast cancer.

TYPES OF BREAST CANCERS

The most common types of breast cancer are: a) Infiltrating (invasive) ductal carcinoma. This cancer starts in the milk ducts of the breast. It then breaks through the wall of the duct and invades the surrounding tissue in the breast. This is the most common form of breast cancer, accounting for 80% of cases. b) Ductal carcinoma in situ is ductal carcinoma in its earliest stage (stage 0). In situ refers to the fact that the cancer hasn't spread beyond its point of origin. In this case, the disease is confined to the milk ducts and has not invaded nearby breast tissue. If untreated, ductal carcinoma in situ may become invasive cancer. It is almost always curable. c) Infiltrating (invasive) lobular carcinoma. This cancer begins in the lobules of the breast where breast milk is produced, but has spread to surrounding tissues or the rest of the body. It accounts for 10% to 15% of breast cancers. This cancer can be more difficult to diagnose with mammograms. Lobular carcinoma in situ is a marker for cancer that is only in the lobules of the breast. It isn't a true cancer, but serves as a marker for the increased risk of developing breast cancer later, possibly in both or either breasts. Thus, it is important for women with lobular carcinoma in situ to have regular clinical breast exams and mammograms. Cancers can also form in other parts of the breast but are less common.

WARNING SIGNS OF BREAST CANCER

A lump or thickening in or near the breast or in the underarm that persists through the menstrual cycle, a mass or lump, which may feel as small as a pea, a change in the size, shape, or contour of the breast, a blood-stained or clear fluid discharge from the nipple, a change in the look or feel of the skin on the breast or nipple (dimpled, puckered, scaly, or inflamed), redness of the skin on the breast or nipple, An area that is distinctly different from any other area on either breast ,a marble-like hardened area under the skin.

DIAGNOSTIC MODALITIES

a) Breast examination
b) Mammography
c) Digital mammography
d) Ultrasonography

Based on the results of these tests, a biopsy of the breast mass cells or tissue may be required. Laboratory tests, such as hormone receptor tests (estrogen and progesterone) and human epidermal growth factor receptor (HER2/neu), can show whether hormones or growth factors

are helping the cancer grow. If the test results show that they are (a positive test), the cancer is likely to respond to hormonal treatment or antibody treatment. These therapies deprive the cancer of the estrogen hormone or use a monoclonal antibody known as Herceptin to treat the cancer.

OTHER DIAGNOSTIC TESTS

e) Scinti-mammography : A technique in which radioactive contrast agents are injected into a vein in the arm. An image of the breast is taken with a special camera, which detects the radiation (gamma rays) emitted by the dye. Tumor cells, which contain more blood vessels than benign tissue, collect more of the dye and project a brighter image.

f) Positron emission tomography (PET) scanning : A technique that measures a signal from injected radioactive tracers that migrate to the rapidly dividing cancer cells. The PET scanner picks up the signal and creates an image.

g) Magnetic resonance imaging (MRI) : A test that produces very clear pictures, or images, of the human body without the use of X-rays. MRI uses a large magnet, radio waves, and a computer to produce these images.

h) Needle Biopsy / FNAC Confirmation of malignancy with cytology or histology is the minimum requirement for "indeterminate" or "high-risk" solid lesions. Fine-needle aspiration / Tru cut / core biopsy / surgical excision/ Incision biopsy / percutaneous breast biopsy for non-palpable disease are the various methods used to obtain tissue for pathological confirmation.

MANAGEMENT OPTIONS

Breast cancer can be treated using a multimodality approach of surgery, chemotherapy, radiotherapy and targeted therapy. The treatment options vary as per the stage of the tumor. The TNM staging is traditionally used to stage breast cancer. Patients are clinically grouped into one of the following categories -Operable Breast Cancer, Large Operable Breast Cancer, Locally Advanced Breast Cancer and Metastatic Breast Cancer. There are multiple ongoing clinical trials in breast cancer. The type of treatment recommended will depend on the size and location of the tumor in the breast, the results of laboratory tests done on the cancer cells, and the stage, or extent, of the disease. Breast cancer treatments are local or systemic. Local treatments are used to remove, destroy, or control the cancer cells in a specific area, such as the breast. Surgery and radiation treatment are local treatments. Systemic treatments are used to destroy or control cancer cells all over the body. Chemotherapy and hormone therapy are systemic treatments. A patient may have just one form of treatment or a combination, depending on her needs.

PREVENTION

Breast cancer is one of the curable cancers, if detected early. Any woman would dread getting cancer of the breast. Cancer subjects the family to unimaginable emotional stress.

Following steps are suggested for early detection :

1) Get a mammogram. The American Cancer Society recommends having a baseline mammogram at age 35, and a screening mammogram every year after age 40. Mammograms are an important part of health history. Recently, the US Preventive Services Task Force (USPTF) came out with new recommendations regarding when and how often one should have mammograms. These include starting at age 50 and having them every two years.[4]

2) Examine breasts each month after age 20. Breast self-examination should be performed at the same time each month, three to five days after your menstrual period ends. If one has stopped menstruating, it is adviced to perform the exam on the same day of each month. One gets familiar with the contours and feel of the breasts and will be more alert to changes.

3) Have breast examined by a healthcare provider at least once every three years after age 20, and every year after age 40. Clinical breast exams can detect lumps that may not be detected by mammogram.[5]

DEVELOPMENTS IN BREAST CANCER RESEARCH

Research into the causes, prevention, and treatment of breast cancer is being done in many medical centers throughout the world.

1) Causes of breast cancer : Some studies are looking at the effect of exercise, weight gain or loss, and diet on breast cancer risk. A large, long-term study is now going on to help find the causes of breast cancer. It is known as the Sister Study and it will follow 50,000 women whose sisters (not they themselves) have had breast cancer. Over 10 years, information will be gathered on many factors that might cause breast cancer.

2) Chemoprevention : Fenretinide, a drug related to vitamin A, is being studied as a way to reduce the risk of breast cancer. In a small study, this drug reduced breast cancer risk as much as tamoxifen. Other drugs are also being studied to reduce the risk of breast cancer.

3) New laboratory tests :

   a) *Gene studies* - In recent years, scientists have been able to link certain patterns of genes with more aggressive cancers — those that tend to come back and spread to distant sites. Some lab tests based on these findings are already available, but doctors are still trying to figure out the best way to use them.

   b) *Tumor cells in the blood* - Researchers have found that in many women with breast cancer, cells may break away from the tumor and enter the blood. These tumor cells can be found with sensitive lab tests.

4) Treatment :

   a) *Oncoplastic surgery* - Sometimes after breast surgery the breasts can be different sizes or shapes. Some doctors are trying to address this problem by combining cancer surgery and plastic surgery. This is called oncoplastic surgery. It involves reshaping the breast at the time of first surgery, and may mean operating on the other breast as well to make them look more alike. The main concern is whether or not oncoplastic surgery might be more likely to leave tumor tissue behind.

   b) *Breast reconstruction surgery* - Advances in re-attaching blood vessels (microvascular surgery) have led to improvements in breast reconstruction.

   c) *Radiation treatment* - For women who need radiation after breast-conserving surgery, newer methods such as hypofractionated radiation or accelerated partial breast irradiation are being studied to see if they work as well as standard treatment in keeping breast cancer from coming back. They can make it easier to get treatment since the treatment can be done on in a shorter time.

d) *New chemotherapy drugs* - Because advanced breast cancers are often hard to treat, researchers are looking for newer, better drugs. A drug class has been developed that targets cancers caused by BRCA mutations. This class of drugs is called PARP inhibitors and they have shown promise in clinical trials treating breast, ovarian, and prostate cancers that had spread and were resistant to other treatments. Further studies are being done to see if this drug can help patients without BRCA mutations.

5) Targeted therapies : Targeted therapies are a group of newer drugs that take advantage of gene changes in cells that cause cancer.

a) *Drugs that target HER2 :* Three drugs approved for use target excess HER2 protein: trastuzumab (Herceptin) and lapatinib (Tykerb), and pertuzumab (Perjeta). Researchers are also looking at using a vaccine to target the HER2 protein.

b) *Anti-angiogenesis drugs :* For cancers to grow, blood vessels must be made to feed the cancer cells. Some studies have found that breast cancers with many new, small blood vessels are likely to spread more quickly. Bevacizumab (Avastin) is an example of anti-angiogenesis drug. New drugs are being made that may be useful in stopping breast cancer growth by keeping new blood vessels from forming.

c) *Other targeted drugs :* Everolimus (Afinitor) is a targeted therapy drug that seems to help hormone therapy drugs work better. It is approved to be given with one certain hormone therapy drug to treat advanced hormone receptor-positive breast cancer in women who have gone through menopause. Other possible targets for new breast cancer drugs have been identified in recent years. Drugs based on these targets are now being studied, but most are still in the early stages of clinical trials- Bisphosphonates, Denosumab and Vitamin D.

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CHAPTER 2

BENIGN BREAST DISEASES (BBD)

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INTRODUCTION

The term Benign Breast Diseases (BBD) include many heterogeneous conditions from inflammatory to premalignant and many times the diagnosis is microscopic. In today's world malignant breast diseases is on the increasing trend; Benign Breast diseases are far common than malignant1 and the disorders go on increasing from the second to fourth decade and decline after menopause and beyond suggesting hormonal etiology in certain conditions. The presentation varies from pain, discharge, palpable masses to vague discomfort. .

Many of the patients present to gynecological outpatient with various symptoms and gynaecologists get the first opportunity to screen and manage them. Many BBD are self limiting and require only early diagnosis with clinicoradiological evaluation and biopsy for exclusion of cancer. Once benign, the treatment could be directed towards the symptoms and patient's education and counseling.

PATHOLOGY

The developmental pathology of benign breast diseases could be the abnormalities of the (1) Glandular breast parenchyma (2) Nipple-Areola complex and (3) Surrounding skin and various benign conditions are Hyperplasia, Cysts, Fibroadenomas, Intraductal papillomas, Sclerosing adenosis, Radial scars, Benign phyllodes tumors, Diabetic mastopathy (also called lymphocytic mastitis and sclerosing lymphocytic lobulitis) and many more.

SYMPTOMS

The symptoms of the BBD depend on the tissues of the breast involved. The symptoms could be of palpable lump, inflammatory mass, nipple discharge and non-palpable abnormality. A woman presenting with a mass or lump with symmetric or asymmetric nodularity with or without pain suggests the glandular and parenchymal involvement. Discharge, rash or retraction of the nipple suggests the involvement of Nipple – Areola complex.

WARNING SIGNS

Many a times women reports to a gynaecologist with mild or moderate symptoms. Though on the initial visit she may have the signs of the benign condition, one should explain how to look and perceive high risk symptoms and act immediately. The symptoms or warning signs could be blood stained nipple discharge, lump which is hard, swelling, warmth and any change in the breast color, dimpling or puckering of breast skin, change in the size and shape, and new onset pain at one or other site.

MASTALGIA

Pain in the breast has multiple characteristics. It could be extramammary, noncyclical and/or cyclical. Any disease of the breast can present with pain ranging be it benign or malignant and hence examination and thorough evaluation of mastalgia is essential. Age less than 30 yrs, diffuse pain and normal clinical examination will rule out cancerous disease in most of the situations but still follow up examination after 3 months is essential. Woman above 30 yrs, with localized pain and abnormal breast examination should be selected for Ultrasonography and mammographic evaluation1.

FIBROCYSTIC DISEASE

This is the most common BBD affecting women in their 2nd to 5th decade of life. These women could present with multifocal and bilateral lesions with symptoms of breast pain and tender nodules. Estrogen predominance seems to have a role in the etiology2. The management depends on the tissue biopsy and presence of atypical hyperplasia (AH). Absolute risk for invasive cancer with proliferative diseases with or without atypia is low. The disease with atypia has less than 20% risk to develop invasive cancer3.

FIBROADENOMA

Fibroadenomas are the second most common tumors of the breast and reported in 25% of the asymptomatic women. Most commonly seen in young adolescent girls but could be present in any age group. The exact etiology is unknown but there are numerous evidences and studies suggest that it could be because of the hormonal influence and some reports suggest the association with use of oral contraceptive pills before the age of 20 years3. They present as palpable, mobile, firm and nontender masses giving the 'mouse in the breast' feeling. The investigations include USG and fine needle aspiration cytology (FNAC) but excisional biopsy or core needle biopsy are preferred. They could be of any size but if more than 10 cms, excision is recommended. Restoration of the breast cosmosis is essential. In cases where they are of <3 cms Ultrasound guided cryoablation is the treatment of choice4.

PHYLLOIDES TUMOR

It is the fibroepithelial type of tumor and can have various clinical presentations. The rapid growth and local recurrence after inadequate excision differs them from the fibroadenomas which otherwise looks similar to the Phylloides tumor on ultrasound. Tissue diagnosis is mandatory in suspected cases and complete excision with clear margins should be the treatment of choice to avoid recurrence5.

LIPOMA

They present as soft, non tender and well circumscribed masses and are smooth and lobulated in consistency. The diagnosis is mostly clinical and no specialized investigation is required for the same. In suspicious cases USG and FNAC can be done. The tumor has no

potential to turn into cancer but in rapidly growing suspicious cases, excision could be the treatment of choice6.

ADENOMA

They could be the lactating adenomas occurring during pregnancy and lactation or tubular adenomas occurring during the reproductive years. Pathologically they are benign epithelial neoplasms; less stromal elements on histopathology differentiate them from fibroadenomas. They are lobulated and well defined and do not have risk of turning into cancer.

Obstetrician and gynaecologists should be aware of lactating adenomas as they are prevalent during pregnancy and puerperium. Clinically they are small, discreet, multiple, palpable and mobile masses of <3 cms. They may develop into ectopic lesions at vulva, axilla and chest wall. In most of the cases they are self limiting conditions but sometimes medical or surgical therapy is indicated7.

FAT NECROSIS

This disease occurs secondary to trauma either blunt or surgical. Women present with pain, skin thickening, erythema, retraction and ecchymosis mimicking malignancy on clinical examination. Clinical experience and radiological investigations can differentiate between fat necrosis and malignant disease. Hence complete evaluation is must8.

MANAGEMENT

Management of the BBD should have a comprehensive approach because an error in the diagnosis / management could result in lifelong suffering for the woman. An approach towards management should address the key issues in the order of History, Clinical Breast Examination, Investigation (Non invasive and invasive) and Therapy.

INVESTIGATIONS

A triple approach to work up which consists of clinical assessment, imaging and histopathology should be instituted. In clinical assessment age and clinical breast examination added by imaging will give satisfactory evaluation. Ultrasonography and Mammography should be supported by FNAC followed by biopsy and histopathology if required9.

TREATMENT

Many of the BBDs are self limiting and can be managed conservatively. In certain situations where histopathological diagnosis confirms benign disease without atypia, simple excision is helpful. In conditions associated with atypia more radical approach is advocated.

SUMMARY

BBD are common ailments in the women's life and no age is protected. When women present pain, lump or any other breast related symptom, work up, clinical examination, proper imaging and histopathology are imperative. Once the diagnosis is established, it itself indicates a way towards the treatment from conservative to excisional to radical. Patient's education and counseling should also be a part of holistic approach in management.

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CHAPTER 3

EARLY BREAST CANCER DETECTION BY CLINICAL BREAST EXAMINATION

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INTRODUCTION

The Incidence of breast cancer is on the rise in India especially in the urban population. This could be attributed to the early menarche, delayed child bearing and other aspects of lifestyle modifications .The literature is replete with comparisons between the many modalities of screening and early detection of breast cancer .Many controversies too exist about each modality and the cost effectiveness of these in various settings such as the right age groups the risk population and the ethnic groups .The new guidelines have also gone to suggest that women should be discouraged from examining their own breasts as experts say self- checks lead to more imaging procedures and biopsies without reducing cancer deaths proportionately. This advice is however being severely criticized by doctors and breast cancer survivors who detected their lumps through a self-check or by routine breast screening.

THE GYNECOLOGIST PERSPECTIVE

What is important is the fact that any gynecological examination should be used as an opportunity to examine the breasts and to teach the women self breast examination (SBE) correctly. Irrespective of the age groups and in the absence of any symptoms the clinical breast examination(CBE) should be an important component of the gynecological consultation .This needs to be systematic and this article highlights the correct technique and the nuances of clinical breast examination as to be practiced by a gynecologist.

AIMS OF CLINICAL BREAST EXAMINATION

The main goal of the clinical breast examination is to differentiate normal physiologic nodularity from a discrete breast mass. If a discrete mass is identified, evaluation is mandatory in all cases to exclude breast cancer. This evaluation is guided by the features of the clinical findings, the age of the woman, and her personal risk for breast cancer. Clinical breast examination is a skill and observation of the correct technique is essential, especially in the context of a mammogram without abnormalities.

CLINICAL BREAST EXAMINATION THE CORRECT TECHNIQUE

Adequate exposure of the breast and the forearms including the axillae is essential to allow proper inspection. The breasts should be inspected for asymmetry and skin changes such as dimpling and redness. Using the pads of the fingers, the breasts are gently felt, with special attention to shape, texture, presence of any lumps. In case lumps are felt,their location, their mobility and attachment to the skin or to deeper tissues should be assessed. The area under both arms should be thoroughly examined.

There are three specific components of the clinical breast examination that have been systematically evaluated and found to influence the accuracy of the examination[1, 2]. These are (1) amount of time spent on the examination, (2) the search pattern utilized, and (3) the finger technique in palpation[3, 4].

1. *Time spent on clinical breast examination :* This is one of the best predictors of sensitivity. Several studies have shown that spending two minutes on the breast examination improves sensitivity3,4. Although Baines et al reported that 5- to 10-minute examinations further improve sensitivity, this was conducted in the context of a research protocol[5]. This length of time could be potentially distressing to a patient and is not necessary or desirable. Even two minutes can seem like a long time for examination and the clinician has to be aware of this. It a good practice to describing the findings to patients and review the technique for self-breast examination while conducting the clinical breast examination. This can also be used as an opportunity to provide women with needed health education and feedback to understand what the clinician is evaluating during the length of the examination. This can help reduce anxiety and increase the woman's comfort level and help justify the need of such an examination. In addition, one of the most common reasons women express for failure to perform self-breast examination is their inability to interpret physiologic nodularity. Patient education during the clinical breast examination may improve adherence to the self-breast examination and help in involving the woman in the screening for breast pathologies.
2. *The exploration pattern for detection of abnormalities :* This is the most critical aspect of the clinical breast examination technique. Studies have documented that a systematic exploration pattern that ensures that all breast tissue is examined is essential for increasing the sensitivity of the clinical breast examination[3].The correct positioning of the patient is important .The woman is made to lie down in a supine position with her hands above her head. The area for examination should extend from the clavicle, medially to the midsternum, laterally to the midaxillary line, and to the inferior portion of the breast. In addition, the examination should include the axillary tail of breast tissue and the axilla to search for palpable lymphadenopathy[2]. One should be aware that the breast tissue is not evenly distributed across the chest. 50% of the breast tissue is located in the upper outer quadrant, and 20% is located under the nipple areolar complex[6].

Three such exploration patterns are commonly described for clinical breast examination :

1. *The radial spoke method :* wedges of tissue are examined beginning at the periphery toward the nipple in a radial pattern.

2. *The concentric circle method :* the breast is examined in larger or smaller concentric circles.
3. *The vertical strip pattern :* the breast tissue is examined in overlapping vertical strips across the chest wall. The vertical strip method is probably superior for ensuring that all breast tissue is examined, because the examiner is better able to track which areas have been examined, and the entire nipple-areolar complex is included.

   The first two methods (a and b) share similar limitations. Often the tissue under the nipple-areolar complex is omitted, thus as much as 20% of breast tissue goes unexamined5. Also, these two patterns are more likely to skip areas of tissue during the examination. The vertical strip examination pattern has been compared directly with the first two patterns in the examination of silicone breast models and has been shown to increase sensitivity of the examination.
4. *The finger technique :* This is another critical aspect of CBE. The pads of the 2nd, 3rd, and 4thfingers held together are used making little circles. The finger pads begin in each circle using light pressure, then repeat in the same area with medium and deep pressure before moving to the next area for examination. Observations of students indicate that failure to apply deep pressure limits the sensitivity of the examination in detecting deeper lesions. Systematic studies using both patients and silicone breast models have shown this to be a superior technique[3].

Many descriptions of the technique of breast examination are available which provide a detailed set of maneuvers with the patient in the sitting as well as lying position for inspection of visual abnormalities, such as skin puckering or dimpling, which would indicate a lesion affixed to other structures6. There is no systematic data to verify the added value of these procedures, which significantly extend the time of a screening examination[2, 7]. Such more detailed examination may be warranted for diagnostic evaluation when the patient presents with a breast complaint, and is not necessary for a standard screening examination. Given the limited time primary providers have to address so many facets of the patient's health, the time is best spent focused on the examination using the palpation techniques described above.

During palpation, visual inspection for skin abnormalities and nipple asymmetry should be conducted. Nipple expression for discharge is unnecessary and should not be performed. It has been demonstrated that while spontaneous discharge with hemorrhage is associated with benign and malignant lesions, expressed discharged is not[8].

PHYSIOLOGICAL VARIATIONS IN THE BREAST IN CONTEXT OF CBE

The normal physiology of breast tissue is one of nodularity. The variation in tissue is in part determined by menstrual phase of the cycle, with increased nodularity in the luteal phase of the cycle resulting from engorgement of vessels and stromal tissue[5]. However, the variation in nodularity of breast tissue among both premenopausal and postmenopausal women is considerable and must be recognized.

The most challenging aspect of the clinical breast examination is deciding whether to consider an area a part of the normal physiologic nodularity or a dominant mass. When conducting the clinical examination, one must first describe the overall texture of the breast tissue and specific areas of increased density or nodularity. After describing the underlying texture of the breast tissue, assess whether there is an area that would be described as discrete or dominant within the underlying nodularity. The discrete mass should be carefully described in terms of location, size, mobility, and texture. When it remains in doubt whether a palpable finding is discrete or part of physiologic nodularity, repeat examination during the follicular phase of the next menstrual cycle or second opinion from another colleague is reasonable.

RATIONALE OF CLINICAL BREAST EXAMINATION

Mammography and breast palpation remain important tools for detecting breast cancer, even for women under the age of 50, according to the results of a large analysis9.In a cohort of almost 6000 women with breast cancer, 65.5% of cancers were detected by mammography, 29.8% by palpation, and 4.7% by other methods. In women under the age of 50 years, approximately half of the tumors (48.3%) were detected by mammography, while a similar percentage of tumors (46.1%) were detected by palpation. Almost all of the breast cancers detected by palpitation were detected by the patient, as compared with those detected by a clinician. Of note, women with palpable tumors tended to have more advanced cancers, as compared with those whose tumors were detected by mammography, and this was applicable to women age 40 to 49 years and those over age 5010.It was also found that women with tumors detected by palpation were more likely to undergo mastectomy (46%) than those with tumors found via mammography (27%). Similarly, women with tumors detected by palpation were also more likely to undergo chemotherapy (22.7%) than those detected by mammography (15.7%)

Till date, mammographic screening is the most reliable method to detect breast cancer in asymptomatic patients. Although highly effective, it has significant limitations, so that the development of more accurate, convenient, and objective detection methods is needed. In the absence of microcalcifications, mammography often fails to detect tumors that are less than 5 mm in size, and also mammograms of women with dense breast tissue are difficult to interpret. For example, in a study of over 11,000 women with no clinical symptoms of breast cancer, the sensitivity of mammography was only 48% for the subset of women with extremely dense breasts, compared with 78% sensitivity for the entire sample of women in the study[11]. In addition, when an abnormality has been detected, further tests involving invasive steps must complement mammography to establish whether the detected abnormality is a cancer[12].

RECOMMENDATIONS FOR CBE

For average-risk asymptomatic women in their 20s and 30s, it is recommended that a breast exam be a part of a regular health examination, preferably at least every 3 years. For women 40 years of age and older, annual CBE can be an important complement to mammography, since a small percentage of cancers may be missed by mammography. Preferably, women should have their CBE shortly before their annual mammogram.

BREAST SELF EXAMINATION

All women should become familiar with both the appearance and feel of their breasts to detect any changes and report them promptly to their physician. Although the American Cancer Society no longer recommends that all women perform monthly breast self-exams (BSE), women should be informed about the potential benefits and limitations associated with BSE. Research has shown that self-awareness seems to be more effective for detecting breast cancer than structured BSE. Women who detect their own breast cancer usually find it outside of a

structured breast self-exam while bathing or getting dressed. A woman who wishes to perform periodic BSE should receive instruction from her health care provider and/or have her technique reviewed periodically.

The sensitivity of clinical breast examination has been evaluated in clinical trials in terms of the benefits in comparison to mammography. The sensitivity of clinical breast examination (48% to 69%)[2] is lower than that associated with mammography (75% to 90%)[13]. Of import, however is that clinical breast examination is able to identify the 10% to 25% of breast cancers that are missed by mammography[13,14]. The specificity of the clinical breast examination is 85% to 99%[2]. The predictive value of the clinical breast examination is the major limitation, because the examination alone cannot differentiate malignant from benign palpable lesions, and therefore all lesions must be considered and evaluated as malignant. Of the lesions detected by the clinical breast examination, only 6% to 46% are malignant, depending on the age of the patient[2].

The additional testing to exclude malignancy in women is a limitation of the clinical breast examination, as it is with all screening modalities currently available. The effects of false-positive results have been documented in terms of emotional distress and decreased plans for future screening[15]. However, given the low cost to women already being seen for other health issues and examinations, the clinical breast examination probably remains a cost-effective strategy.

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CHAPTER 4

IMAGING IN CARCINOMA BREAST

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INTRODUCTION

Breast cancer is taking a high toll in middle aged females in developed countries whereas in developing countries it is showing a rising trend. It is reported that 519, 000 deaths are caused by breast cancer and around 900, 000 women are diagnosed every year all over the world[1]. Before a female or her treating doctor can palpate, mammography demonstrates the abnormality of the breast cancer. Thorough and accurate evaluation can help diagnosing maximum breast cancer cases, hence reducing mortality and morbidity by providing proper management and treatment[2].

HISTORICAL ASPECTS

Breast cancer is known since the ancient times. The first ever recordings of breast tumor were seen in the Egyptian manuscript that dates back to 1600 B.C. The discovery of X-rays in 1895 by Wilhelm Conrad Roentgen was the breakthrough in the domain of breast imaging. In 1967, the center for Genomics Research, France introduced the first dedicated mammography machine. In early 1980s, the American Cancer Society, the National Cancer Institute and other organizations made mammography a routine screening procedure for asymptomatic women1. It was since 1960s that the ultrasonography has been put to use in clinical practice with continuous developments year after year 2. In 1977, the first human MRI scan was done and since then it become an important diagnostic modality for a variety of diseases including breast diseases[2].

MAMMOGRAPHY

Indications : (1) Screening asymptomatic women aged 50 years and over; (2) Screening asymptomatic women aged 35 years and over who have a high risk of developing breast cancer i.e. women who have one or more first degree relatives who have been diagnosed with premenopausal breast cancer/women with histological risk factors found at previous surgery, e.g. atypical ductal hyperplasia; (3) Investigation of symptomatic women aged 35 years and over with a breast lump or other clinical evidence of breast cancer; (4) Surveillance of the breast following local excision of breast carcinoma; (5) Evaluation of a breast lump in women following augmentation mammoplasty. Investigation of a suspicious breast lump in a man.

Normal mammographic appearance of breast[5] :

The amount of fat and glandular tissue in the breast, determine the mammographic appearance. Glandular tissue predominates in young women's breasts appearing as soft tissue density on mammograms whereas after involution of the glandular tissue as in old women most of the breast appears of fatty density. During involution, mixed soft tissue and fat density can be seen. A series of curved margins can be seen at the junction of subcutaneous tissue, retro mammary fat layers and the glandular tissue, the straightening or distortion of which indicates underlying glandular tissue pathology. Nipple, skin, blood vessels, ducts, Cooper's ligaments and axillary lymph nodes are the other normal structures also seen on mammograms.

Mammographic signs of Breast Carcinoma[4]

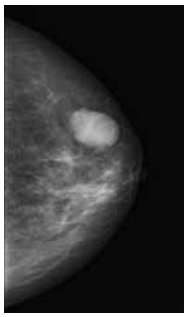
- Primary signs : Speculated mass / Lobulated mass
- Secondary signs : Architectural distortion / Clustered microcalcifications/ Asymmetric density/ Dilated duct /Skin thickening /Vascular asymmetry

Analyzing Masses :

- Locations : Although breast cancer can occur anywhere in the breast, it has also been described along the unresorbed mammary ridge. In the breast, it is most commonly seen in the upper outer quadrant. They are also mainly seen in the peripheral zone beneath the fat i.e. anterior to retromammary fat or just under the subcutaneous fat.
- Size : Though the size of the tumor does not help in segregating malignant from benign lesions, but it does indicate the prognosis. The metastasis spread is low for masses < 1cm in size 6.
- Shape : Five shapes of the mass are defined by ACR BIRADS i.e. round, oval, lobulated, irregular, architectural distortion. As the irregularity in the shape of the mass increases, the chances of malignancy increases. Spiculated architectural distortion without previous history of surgery and without any mass points to underlying malignancy 6.
- Margins : Five margins of the mass are defined by ACR BIRADS i.e. circumscribed, obscured, microlobulated, ill-defined and speculated. The breast cancer classically shows spiculated margins. Breast cancer may also present as obscured, microlobulated or ill-defined margins.
- Spiculated mass : It is a soft-tissue mass with radiating tentacles at the margin causing distortion of the surrounding breast tissue. These tentacles may be microscopic. Superficial or large tumors may involve the overlying skin thus causing skin retraction and skin thickening. Deep tumors may involve pectoralis muscle and thus cause its tethering. These masses may also be associated with irregular micro calcifications due to ductal carcinoma in situ or coarse calcifications due to tumor necrosis. Masses are easily visualized against a fatty breast due to high contrast difference between the mass and the breast tissue. However, the dense glandular breasts tend to obscure the masses. Hence, it is recommended to look for primary as well as secondary signs of carcinoma breast[4, 5].

- Architectural distortion : Multiple lines, 1-4 cm in length radiating towards a central scar is the mammographic appearance of architectural distortion of breast. It is not associated with soft tissue mass, however, it may be associated with microcalcifications.
- Asymmetric soft tissue density : It is a common finding and radiologically appears as low soft tissue density, lucency and curvilinear margins with no evidence of distortion.
- Calcifications : Calcifications that are punctate, pointed, irregularly shaped, variable in size and morphology within a mass or fine, linear, branching deposits strongly suggest breast cancer. Large tumor may show coarse calcifications due to tumor necrosis[6].

  Breast cancer usually presents as linear distribution, though it may also present as clustered or segmental distribution. Regional and diffusely scattered calcifications are almost always benign. However, while examining the pattern of distribution, the morphology also needs to be taken into account as rarely breast cancer can be extensive and may be seen in regional or diffusely scattered pattern.
- Skin and Nipple : Normal skin away from the areola measures 0.5-2 mm in thickness. Sizes of nipple and areolar skin vary from individual to individual. Skin thickening can be focal or diffuse, unilateral or bilateral. It can be due to tumour infiltration, post surgical scarring, infection, non specific inflammation, inflammatory breast cancer, primary skin conditions like psoriasis and lymphatic obstruction (local, regional, central), vascular obstruction (congestive heart failure, superior vena cava syndrome, anasarca), systemic diseases involving skin (e.g. scleroderma, dermatomyositis), breast irradiation. Skin and nipple retraction are seen in large advanced cases of breast cancers invading the skin and nipple. However, nipple retraction usually results from benign idiopathic process; postsurgical scar and fat necrosis also having their share 6.
- Dilated duct : Solitary dilated duct due to cancer but without other associated signs of cancer is extremely rare. Dilated duct due to cancer almost always shows symptoms like nipple discharge and other signs like soft tissue mass or calcifications[6].
- The Rule of Multiplicity : Most breast cancers are solitary and multiplicity of lesions generally points towards benignity with the exception of breast metastasis and rare multifocal cancer[6]. Metastases to breast from common primary sites are melanoma, ovary and lung[5].
- Axillary lymph nodes : Normal axillary lymph nodes are < 2 cm in size and have lucent center. Lymph nodes without central lucency and > 1.5 to 2 cm in size are abnormal. Mammography cannot differentiate benign from malignant adenopathy. Fine irregular calcifications in the axillary nodes especially similar to breast tumor calcifications should raise suspicion of metastasis[6].



BIRADS in Mammography :

BI-RADS is an acronym for Breast Imaging-Reporting and Data System, a quality assurance tool originally designed for use with mammography The system is a collaborative effort of many health groups but is published and trademarked by the American College of Radiology (ACR).The breast lesions are categorized as follows : 0 – Needs additional imaging evaluation; 1 - Negative; 2 – Benign finding; 3 – Probably benign finding (< 2% malignant) Initial short interval follow up; 4 – Suspicious abnormality (2-95 % malignant). Biopsy should be considered; 5 – Highly suggestive of malignancy (> 95 % malignant); 6 – Known biopsy proven malignancy

BREAST ULTRASOUND / SONOMAMMOGRAPHY

Indications : (1) Symptomatic breast lumps in women aged less than 35 years. (2) Breast lump developing during pregnancy or lactation. (3) Assessment of mammographic abnormality (+/- further mammographic views). (4) Assessment of MRI or scintimammography detected lesions. (5) Clinical breast mass with negative mammograms. (6) Breast inflammation. (7) The augmented breast (together with MRI). (8) Breast lump in a male (together with mammography). (9) Guidance of needle biopsy or localization. (10) Follow-up of breast cancer treated with adjuvant chemotherapy

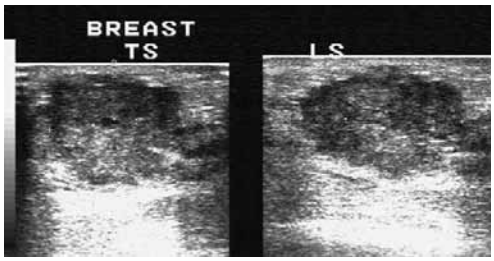


Figure 2 : A malignant nodule showing speculations and irregular margin

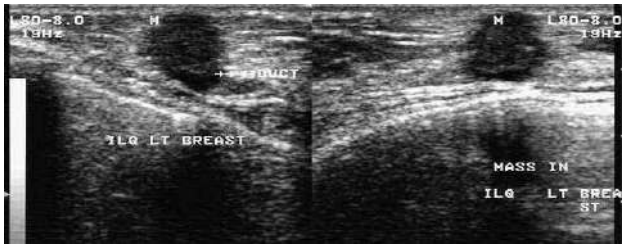


Figure 3 : A malignant nodule with irregular speculated margins, causing dilatation of adjacent duct. The nodule is taller than wide.

Figure 4: A benign nodule with sharply well defined margins (fibroadenoma)

Sonographic appearance of Breast cancer : Sonographically, invasive carcinoma may appear as stellate, circumscribed or diffuse masses. However, classic ultrasonographic findings of an invasive carcinoma are hypoechoic mass with in homogenous internal echoes, irregular margins and variable acoustic shadowing (7). Similar appearances can be seen in sclerosing fibro adenoma or radial scar thus creating confusion (5). Most spiculated carcinoma of or more than 1 cm diameter are detected on sonography (5). In a study, ratio of length of lesion to anteroposterior diameter was more than 1.4 in most fibroadenomas but not in carcinoma. Though exception to this rule may be seen (7).Sonography has limited role in detecting breast cancer and to differentiate benign from malignant lesions, so it should

always be used as an adjunct to mammography, never as a primary screening tool (7).The main role of ultrasound lies in differentiating solid from cystic masses(6).

MR MAMMOGRAPHY(6)

Indications : (1) Detect or exclude primary carcinoma in mammographically dense breast (as a supplement to mammography). (2) Detect recurrence after reconstructive surgery especially those with impants and extensive scarring. (3) Lymph node metastasis in the axilla when the primary tumor is unclear. (4) Clinical monitoring of breast carcinoma during neoadjuvant chemotherapy. (5) Unclear diagnostic findings from mammography and/or sonography. (6) Non-contrast MRI to verify or exclude defects in breast implants

Contraindications : Cardiac pacemakers; Heart valves and surgical clips (in heart or brain); Adverse reaction to gadolinium in previous MR examination

When to do MR Mammography? In premenopausal patients the procedure should be done in 2nd or 3rd week of menstrual cycle. This is because in 1st or 4th week, increased contrast enhancement is observed due to increased vascularity.

MR Anatomy of diseased breast : On unenhanced T1W GRE, dysplasia, cysts, benign & malignant tumors appear hypointense. Irregular circumscribed rapid enhancement after contrast with or without washout and rim enhancement is suspicious for malignancy. Diffuse enhancement usually in benign changes of glandular tissue but malignancy cannot be excluded. In absence of enhancement, an invasive carcinoma can be excluded with high degree of certainty. It should not be used as a primary modality for breast cancer but as an adjunct to mammography or ultrasonography.

Dynamic contrast enhancement : After administration of contrast, breast is scanned every 1-2 minutes. The signal intensity of breast tissues and breast lesions can be compared from one scan to the other. The dynamics of contrast enhancement over time is plotted against the region of interest in the breast. This helps in evaluating a breast lesion. Fibroadenomas enhance rapidly and remain so for several minutes. Breast carcinomas enhance immediately, reach a plateau and then wash off fast. Normal breast tissue enhances mildly slowly.

MR SPECTROSCOPY

MR Spectroscopy shows promising results in differentiating benign from malignant lesions. High levels of choline are seen in malignant lesions, whereas low levels are seen in benign lesions and normal breast tissue. High levels of glycerophosphocholine and lactate are seen in metastatic axillary lymph nodes.

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CHAPTER 5

MANAGEMENT OF BREAST CARCINOMA

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INTRODUCTION

Breast cancer remains the most common cancer among women worldwide especially in urban population. Since the era of Sir William Halsted; breast cancer management has changed from radical mastectomy & axillary dissection to conservation of breast. Concept that Breast cancer is a systemic disease at its presentation has shifted breast cancer treatment into a multidisciplinary science. Conservative and selective surgical approaches to the breast and to the axilla, once viewed with skepticism, have now become standard of therapy for most patients with early breast cancer. However, as the current goal for breast cancer patients is "conservation" instead "the more radical excision the better", the impact of local recurrence on survival remains a relevant issue, and is presently a subject of research and debate. Lot of importance is being given to the early detection of breast cancer.

STAGING OF BREAST CANCER

Accurate staging of patients with breast cancer has two main objectives: it allows appropriate treatment and it determines prognosis. In Most of patients TNM staging is done.

Stage I	T1 N0 M0
Stage IIA	T0, T1 N1 M0 T2 N0 M0
Stage IIB	T2 N1 M0 T3 N0 M0
Stage IIIA	T0, T1, T2 N2 M0 T3 N1, N2 M0
Stage IIIB	T4 Any N M0 Any T N3 M0
Stage IV	Any T Any N M1

SURGERY FOR OPERABLE BREAST CANCER

The treatment options for patients with early-stage (Stage I and II) invasive breast cancer today are breast-conservation therapy (BCT) with adjuvant radiation therapy and modified radical mastectomy (MRM) with or without breast reconstruction with adjuvant chemotherapy. Conservative breast surgery was introduced for small breast cancers in the 1970s. There was a gradual trend towards earlier stage at diagnosis and the logical extension of both was to reduce the magnitude of the local surgery and attempt to preserve the organ. So that psychological upsets are less. Some of the problems of BCT are:

- Risk of Recurrence - After BCT or mastectomy, there is a risk of breast cancer recurrence. Trials of partial mastectomy have shown an incidence of breast recurrence of between 1% and 4% per year
- Adjuvant Radiation Therapy - Adjuvant radiation therapy reduces the incidence of local recurrence and is an essential part of BCT. Addition of Radiation therapy may sometimes compromise the cosmoses.
- Axillary Surgery - Axillary dissection (AD) has been integral part of breast cancer surgery from the era of Halsted. The status of the axillary nodes remains the most powerful prognostic indicator in the treatment of invasive breast cancer. Concept of sentinel node biopsy has a definite impact on axillary surgery in breast cancer and to a larger extent reduced the incidence of morbidity of unnecessary Axillary dissection in clinically node negative axilla.

SURGERY FOR LOCALLY ADVANCED BREAST CANCER

Surgery plays a less important role in Stage III breast cancer because a large majority of patients with Stage III breast cancer will have axillary lymph node involvement, and a significant proportion will have distant metastases present at the time of diagnosis. Surgery alone has a high failure rate for locally advanced breast cancer, and the long-term survival rate is dismal. The primary aim in this setting is to achieve local control, down stage the disease by neoadjuvant modalities and then surgery. Currently, after the diagnosis on core biopsy or incisional biopsy the usual treatment involves the use of induction chemotherapy with an Adriamycin based regime, followed by surgery. Evidence suggests that the primary chemotherapy has definite advantages, that the response to treatment can be monitored. In addition, BCT may become possible after tumor down staging. Further chemotherapy is used following the surgery if there was good response to the chemotherapy, and once the chemotherapy is complete, adjuvant radiation therapy may be used. The best local control rates are seen with surgery and radiation therapy following induction chemotherapy.

DISTANT METASTATIC DISEASE

Surgery has a negligible role in the management of distant recurrences. Evidence based medicine suggest that if visceral or bony metastasis if present, then there is always a multi organ involvement. Surgery is occasionally required for the palliation of recurrences. The most common situation is in the management of bony metastases, where internal fixation of long bones can prevent pathologic fractures, or may be needed in their treatment.

TAMOXIFEN FOR ADJUVANT THERAPY

The benefits of tamoxifen were most significant in women with the highest estrogen-receptor expression. This was seen for women who were randomized to tamoxifen for a median duration of 1, 2 or 5 years.

CHEMOTHERAPY IN THE ADJUVANT SETTING

The chemotherapy regimen used in the majority of trials was CMF (cyclophosphamide, methotrexate and 5-fluorouracil [5-FU]).Chemotherapy has a proportional reduction in the risk of recurrence and death among women with lymph-node positive and node-negative disease similar to that seen with tamoxifen.

NEW APPROACHES FOR ADJUVANT THERAPY

Recently, the use of full-dose single agents administered in a sequential fashion (e.g., doxorubicin for 4 cycles, followed by paclitaxel for 4 cycles, followed by cyclophosphamide for 4 cycles) A new approach to therapy that has been investigated in patients with metastatic disease is the use of trastuzumab (Herceptin®), a monoclonal antibody that is directed against the HER-2/neu receptor. When added to chemotherapy, trastuzumab has been shown to increase the efficacy of chemotherapy,

RADIATION THERAPY FOR EARLY-STAGE BREAST CANCER

Six randomized trials, both in the United States and Europe, demonstrated conclusively that lumpectomy followed by radiation therapy to the conserved breast tissue was as effective as modified radical mastectomy in controlling breast cancer and in achieving commensurate survival. The ideal candidate for breast-conservation therapy is a patient who has a unifocal tumor 5 cms or smaller in size that is excised with a negative margin. Ideal candidates for breast-conservation therapy are the ability to follow the patient mammographically. Those patients who have tumors detected mammographically, particularly by virtue of microcalcifications, must undergo post excision mammography to assess the status of the breast tissue in the region of excision.

RADIATION THERAPY FOR LOCALLY ADVANCED BREAST CANCER

All patients with locally advanced breast cancer have a high local tumor burden and a high likelihood of systemic metastases. Therefore, aggressive systemic chemotherapy plays a central role in their management. Both local-regional radiation therapy and mastectomy, when possible, are useful in securing local control. Most patients with Stage III breast cancer will receive chemotherapy as their first therapeutic maneuver. This permits the earliest treatment of micrometastatic disease, assessment of response to therapy and, in many cases, conversion of inoperable or nearly inoperable disease to operable disease. Comprehensive chest-wall radiation is indicated for all patients with this stage breast cancer.

ENDOCRINE THERAPY

Is sometimes used after surgery in women who have hormone receptor-positive cancer (tumors whose growth seems dependant on estrogen).These drugs include tamoxifen for premenopausal women and the aromatase inhibitors Arimidex, Femara and Aromasin for postmenopausal women. It is to be given for 5 years.

BIOLOGICAL THERAPY

In about 25% of women with breast cancer, an excess of a protein known as HER2 makes the cancer spread quickly. Herceptin is a drug that's been approved to treat women with metastatic breast cancer that is HER2-positive. It stops this protein from making the cancer grow and makes chemotherapy more effective. It is most often used in combination with chemotherapy. Multiple clinical trials have shown an improved outcome, when Herceptin is added to chemotherapy, and then continued for a total of one year, in the adjuvant setting of breast cancers, even those of small sizes.

CONCLUSION

Breast cancer is one of the most prevalent malignancies among women in the western world. Well-designed scientific trials in the diagnosis and management of this disease remain paradigms for investigators in all fields. The value of a multimodality approach to each patient's care cannot be overemphasized. Radiologists, pathologists, surgeons, medical and radiation oncologists have all contributed to the improvements that have been achieved in the rates of survival from this disease. Their continued collaboration will assure further advances and, ultimately, the conquest of breast cancer. Though the treatment of breast cancer has modified from the era of Sir William Halsted, Radical Mastectomy to Breast conservation, but in many parts of the modern world ,the surgical treatment of breast cancer in a given community is modified radical mastectomy with or without reconstruction and adjuvant therapy. It may be concluded that treatment has to be individualized as per the stage, site, size of breast, histological type, availability of adjuvant treatment centers.

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CHAPTER 6

THE CARE OF THE UTERUS WHILE PRESCRIBING TAMOXIFEN IN BREAST CARCINOMA

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BACKGROUND

Tamoxifen a, nonsteroidal antiestrogen agent act as an antagonist of the estrogen receptor in breast tissue via its active metabolite, hydroxytamoxifen, while in other tissues such as the endometrium, it behaves as agonist. Tamoxifen is widely used as an adjunctive therapy for women with breast cancer.

Tamoxifen belongs to a class of agents known as selective estrogen receptor modulators (SERMs). Although the primary therapeutic effect of tamoxifen is derived from its antiestrogenic properties, this agent also has modest estrogenic activity. In standard dosages, tamoxifen may be associated with endometrial proliferation, hyperplasia, polyp formation, invasive carcinoma, and uterine sarcoma. Any symptoms of endometrial hyperplasia or cancer reported by a postmenopausal woman taking tamoxifen should be evaluated. Premenopausal women treated with tamoxifen have no known increased risk of uterine cancer and as such require no additional monitoring beyond routine gynecologic care. If atypical endometrial hyperplasia develops, appropriate gynecologic management should be instituted, and the use of tamoxifen should be reassessed.

TAMOXIFEN INDICATIONS

It is currently approved by the FDA for the following indications :

1. Adjuvant treatment of breast cancer (treatment of both early and advanced ER+ (estrogen receptor positive) breast cancer in pre- and post-menopausal women)
2. Metastatic breast cancer
3. Reduction of contralateral breast cancer & breast cancer incidence in high-risk women

REVIEW OF LITERATURE

Most studies have found that the relative risk of developing endometrial cancer for women taking tamoxifen is two to three times higher than that of an age-matched population. The level of risk of endometrial cancer in women treated with tamoxifen is dose and time dependent. Studies suggest that the stage, grade, histology, and biology of tumors that develop in individuals treated with tamoxifen (20 mg/d) are no different from those that arise in the general population. However, some reports have indicated that women treated with a higher dosage of tamoxifen (40 mg/d) are more prone to develop more biologically aggressive tumors. In one early study (1994) of the National Surgical Adjuvant Breast and Bowel Project (NSABP), the rate of endometrial cancer occurrence among tamoxifen users, who were administered 20 mg/d was 1.6 per 1,000 patient years, compared with 0.2 per 1,000 patient years among control patients taking a placebo. In this study, the 5-year disease-free survival rate from breast cancer was 38% higher in the tamoxifen group than in the placebo group, suggesting that the small risk of developing endometrial cancer is outweighed by the significant survival benefit provided by tamoxifen therapy for women with breast cancer. The survival advantage with 5 years of tamoxifen therapy continued with long-term follow-up, but extending the duration of tamoxifen use to 10 years failed to improve the survival benefit gained from 5 years of tamoxifen use. In a more recent update of all NSABP trials in 2004 of patients with breast cancer, the rate of endometrial cancer was 1.26 per 1,000 patient years in women treated with tamoxifen versus 0.58 per 1,000 patient years in the placebo group.

Uterine sarcomas consisting of malignant mixed müllerian tumors, leiomyosarcoma, and stroma cell sarcomas are a rare form of uterine malignancy occurring in 2–5% of all patients with uterine malignancies. In a review of all NSABP breast cancer treatment trials, the rate of sarcoma in women treated with tamoxifen was 17 per 100,000 patient years versus none in the placebo group. This is compared with the incidence of one to two per 100,000 patient years in the general population.

The NSABP prevention trial (P-1) data suggest that the risk for both invasive and noninvasive breast cancer is reduced markedly with tamoxifen prophylaxis. The risk ratio for developing endometrial cancer was 2.53 in women using tamoxifen compared with women receiving a placebo. In addition, the ability of tamoxifen to induce endometrial malignancy as well as other histopathologic conditions appears to differ between premenopausal and postmenopausal women. In the prevention trial of high-risk women, there was no statistically significant difference in endometrial cancer rates between women treated with tamoxifen and those in the placebo group in the women aged 49 years and younger; however, in women aged 50 years and older, the risk ratio was 4.01 (95% confidence interval, 1.70–10.90) for those treated with tamoxifen versus those receiving placebo. The annual rate was 3.05 malignancies per 1,000 women treated with tamoxifen versus 0.76 malignancies per 1,000 women receiving placebo. Another study of women with breast cancer found that premenopausal women, treated or untreated, had no differences in endometrial thickness on ultrasound examination, uterine volume, or histopathologic findings, whereas postmenopausal women treated with tamoxifen had significantly more abnormalities.

SCREENING FOR WOMEN ON TAMOXIFEN

Several approaches have been explored for screening asymptomatic women using tamoxifen for abnormal endometrial proliferation or endometrial cancer. Correlation is poor between ultrasonographic measurements of endometrial thickness and abnormal pathology in

asymptomatic tamoxifen users because of tamoxifen-induced subepithelial stromal hypertrophy. In asymptomatic women using tamoxifen, screening for endometrial cancer with routine transvaginal ultrasonography, endometrial biopsy, or both has not been shown to be effective. Although asymptomatic postmenopausal tamoxifen-treated women should not have routine testing to diagnose endometrial pathology, sonohysterography has improved the accuracy of ultrasonography in excluding or detecting anatomical changes, when necessary.

Other data suggest that low- and high-risk groups of postmenopausal patients may be identified before the initiation of tamoxifen therapy for breast cancer. Pretreatment screening identified 85 asymptomatic patients with benign polyps in 510 postmenopausal patients with newly diagnosed breast cancer (16.7%). All polyps were removed. At the time of polypectomy, two patients had atypical hyperplasias and subsequently underwent hysterectomies. The rest were treated with tamoxifen, 20 mg/d, for up to 5 years. The incidence of atypical hyperplasia was 11.7% in the group with initial lesions versus 0.7% in the group without lesions ($P < .0001$), an 18-fold increase in risk. In addition, polyps developed in 17.6% of the group with initial lesions versus 12.9% in the group without.

USE OF PROGESTINS

Although the concurrent use of progestin reduces the risk of endometrial hyperplasia and cancer in patients receiving unopposed estrogen, the effect of progestin on the course of breast cancer and on the endometrium of women receiving tamoxifen is not known. Therefore, such use cannot be advocated as a means of lowering risk in women taking tamoxifen.

RECOMMENDATIONS

The American Congress of Obstetricians & Gynecologist (ACOG) recommends the following :

- Postmenopausal women taking tamoxifen should be monitored closely for symptoms of endometrial hyperplasia or cancer.
- Premenopausal women treated with tamoxifen have no known increased risk of uterine cancer and as such require no additional monitoring beyond routine gynecologic care.
- Women taking tamoxifen should be informed about the risks of endometrial proliferation, endometrial hyperplasia, endometrial cancer, and uterine sarcomas. Women should be encouraged to promptly report any abnormal vaginal symptoms, including bloody discharge, spotting, staining, or leucorrhea.
- Any abnormal vaginal bleeding, bloody vaginal discharge, staining, or spotting should be investigated.
- Emerging evidence suggests the presence of high- and low-risk groups for development of atypical hyperplasias with tamoxifen treatment in postmenopausal women based on the presence or absence of benign endometrial polyps before therapy. Thus, there may be a role for pretreatment screening of postmenopausal women with transvaginal ultrasonography, and sonohysterography when needed, or office hysteroscopy before initiation of tamoxifen therapy.
- Unless the patient has been identified to be at high risk for endometrial cancer, routine endometrial surveillance has not been effective in increasing the early detection of endometrial cancer in women using tamoxifen. Such surveillance may lead to more invasive and costly diagnostic procedures and, therefore, is not recommended.
- Tamoxifen use should be limited to 5 years duration because a benefit beyond this time has not been documented.
- If atypical endometrial hyperplasia develops, appropriate gynecologic management should be instituted, and the use of tamoxifen should be reassessed. If tamoxifen therapy must be continued, hysterectomy should be considered in women with atypical endometrial hyperplasia. Tamoxifen use may be reinstituted following hysterectomy for endometrial carcinoma in consultation with the physician responsible for the woman's breast care.

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CHAPTER 7

BREAST CANCER AND FERTILITY PRESERVATION MODALITIES

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INTRODUCTION

Over past 25 years, breast cancer incidence has risen globally, with the highest rates reported in westernized countries. Reasons for this trend include change in reproductive patterns, increased screening facilities and dietary changes. In Asian and Pacific Islander women the incidence has continued to increase at 1.5% per year, they are still significantly lower than the rates in white women. In a recent study conducted at All India Institute of Medical Sciences (AIIMS) has found that nearly one in 10 women, who visited the hospital between 2000 and 2011 afflicted with the disease, was younger than 35 years1.Reductions in death rates from breast cancer largely reflect the early detection with the use of screening mammography and more effective multiagent adjuvant chemotherapy regimens[1]. Unfortunately, a considerable number of patients feel that their cancer physicians do not sufficiently inform them about the impact of the cancer therapy on fertility and the options to preserve it[2]. It is important to provide the most up-to-date and accurate information on the adverse effects of cancer treatments on fertility to young cancer patients whose concerns about their future fertility may shape their treatments.

EFFECTS OF CHEMOTHERAPY ONOVARIAN FUNCTIONS

Any toxic insult that targets the primordial follicles will result in a diminishment or total exhaustion of the ovarian reserve. Gonadal toxicity associated with the use of chemotherapy agents varies depending on the age of the patient and the type and cumulative dose of the cancer drugs. Chemotherapy agents particularly of the alkylating category (e.g., cyclophosphamide) are more cytotoxic and appear to exert their gonadotoxic effects via follicular loss in the human ovary by activating apoptotic machinery in both oocyte and enclosing granulosa cells as revealed by a human ovarian xenograft model.3Younger patients (<35 years of age) have higher primordial follicle counts in their ovaries, and therefore they are more likely to retain some residual ovarian function post exposure to toxic insult than do older patients (>35 years of age). Because alkylating agents are not cell cycle specific, they are able to damage cells at different stages of the cell cycle including resting primordial follicles, resulting in a more widespread effect. Resting primordial follicles appear to be more sensitive to cyclophosphamide-induced gonadotoxicity than growing follicles at the primary stage and beyond 3. By contrast, chemotherapy agents that act in a cell cycle–specific manner, such as 5-fluorouracil and methotrexate, are less harmful for primordial follicles. Most of the published clinical studies used amenorrhea as a surrogate marker of infertility occurring during and after chemotherapy administration 4. Anthracycline-based regimens are less toxic than combinations containing an alkylating agent; therefore they are associated with a lower risk of permanent ovarian failure.

GONADOTROPIN-RELEASING HORMONE AGONISTS AS AN ADJUVANT HORMONAL THERAPY IN BREAST CANCER TREATMENT

Hormonal manipulation has been used for over 100 years to treat breast cancer. Ovarian ablation/suppression and tamoxifen are currently accepted adjuvant endocrine therapies for premenopausal breast cancer. Methods of permanently ablating ovarian function include surgical oophorectomy and radiation-induced ovarian failure; medical castration with luteinizing hormone-releasing hormone analogues is a reversible approach. Adjuvant chemotherapy frequently results in permanent amenorrhea and thus represents an indirect form of ovarian ablation. These agents include LHRH agonists and antagonists, both of which decrease ovarian estradiol production indirectly by impinging on the hypothalamic-pituitary-ovarian axis which causes infertility by ovarian failure5.Ultimately all these chemotherapy drugs impair ovarian function and which further impairs fertility.

EFFECT OF RADIOTHERAPY ON FERTILITY

Ovarian follicles are sensitive to damage from ionizing radiation, which may result in atrophy of the organ and reduced primordial follicle reserve . Pelvic radiation also exerts an effect on the uterus, causing changes in both the musculature and blood flow, which can lead to endometrial damage and a higher rate of obstetrical complications .

FERTILITY PRESERVATION OPTIONS IN BREAST CANCER PATIENTS

The reduction of ovarian reserve in breast cancer patients with the use of adjuvant/neoadjuvant chemotherapy is compounded by the need to delay pregnancy while undergoing hormonal treatment (tamoxifen with or without GnRH agonists) for =5 years in ER-positive diseases. The 5-year survival in all stages of breast cancer has reached 89%in the United States. 6 As a result of the high survival rates and the increased emphasis on the quality of the life of the survivor, fertility preservation is gaining importance. As stressed in the recent clinical guidelines by the American Society of Clinical Oncology, all cancer patients with interest in future fertility should be referred for consideration of fertility preservation.7 Current fertility preservation options vary from well-established embryo freezing to experimental ovarian tissue and oocyte freezing. Embryo cryopreservation has been a proven method to preserve fertility. However, in nearly all cancers, with the possible exception of breast cancer, chemotherapy is initiated soon after diagnosis. Because preparation and stimulation for oocyte retrieval usually requires 2 to 3 weeks or longer, it is generally not feasible to freeze embryos from an adult female cancer patient for potential future use. Even in breast cancer patients, most would not be candidates for oocyte or embryo freezing due to concerns that

high oestrogen levels might have detrimental effects on the primary tumour.

1. *Embryo Freezing :* IVF and embryo cryopreservation is the most established fertility preservation technique for patients with partners and a sufficient amount of time before cancer treatment. It is not technically challenging and has been used for nearly two decades to store unused embryos from IVF and embryo transfer cycles. Although isolated pregnancies from egg freezing have been reported for many years, it is only recently that egg freezing can be performed with reproducible success resulting in reasonable survival rates (50-70%), fertilization rates (50-60%) and pregnancy rates approaching those obtained with fresh eggs. Embryo freezing is a well established procedure in most IVF laboratories, and generally results in reasonable success rates. The national average live birth rates for women under 38 years of age is 21% (ASRM/SART Report, 2000)

2. *Oocyte Freezing :* Cryopreservation of oocytes is an emerging option suitable for young adolescents, women without partners, or women who do not wish to have their oocytes fertilized by sperm from a partner or anonymous donor. The first live birth after successful oocyte cryopreservation in a human was reported in 1986.8 Unfortunately, it is still associated with lower pregnancy rates in contrast with more encouraging results with IVF and embryo freezing due to some technical challenges encountered during the freeze-thaw process and the in vitro maturation of immature oocytes .Even though oocyte cryopreservation is still considered experimental, the technology is improving, and our recent meta-analysis showed that live-birth rates per oocyte thawed were 1.9% and 2.0% for slow freezing and vitrification, respectively, before June 2005. Live-birth rates per injected oocyte and ET, respectively, were 3.4% and 21.6% for slow freezing and were 6.6% and 60.4% for IVF with unfrozen oocytes. These success rates appear to be even higher with a more recent oocyte freezing technique, vitrification, but the data are limited on the latter live-birth rate for per injected oocyte is 3.4% for slow frozen oocytes.9 It is thought that mature oocytes are arrested at metaphase II and therefore more prone to cryo damage because the spindle apparatus is fully extended at metaphase II and prone to disassembly at lower temperature, with subsequent chromosome dispersion and aneuploidy.

3. *Ovarian Tissue Freezing :* Ovarian tissue cryopreservation remains a promising clinical technique because it avoids ovarian stimulation and provides the opportunity for preserving gonadal function in prepubertal, as well as adult patients. Ovarian cryopreservation may be the only option for fertility preservation in breast cancer patients who do not want or do not have time to undergo ovarian stimulation for oocyte or embryo cryopreservation. Ovarian tissue cryopreservation does not require ovarian stimulation, and ovarian tissue can be harvested laparoscopically without any preparation. The ovarian cortex contains primordial follicles with oocytes arrested in the diplotene of prophase of the first meiotic division. It has been suggested that the relatively high surface-to-volume ratio, low metabolic rate, and the absence of zona pellucida make primordial follicles less susceptible to damage from freezing.10 One of the major concerns in transplanting ovarian tissue from cancer patients is the risk for reseeding cancer cells. Previous studies showed that most of the occult metastases belong to the infiltrating lobular histological subtype, which constitutes <15% of all breast cancers and more commonly occurs in postmenopausal women.11 It should also be remembered that patients with BRCA-1 and BRCA-2genes are at a higher risk for harbouring occult ovarian cancer. To date no cancer recurrence in ovarian grafts has been reported in the medical literature.

CONCLUSION

Several options are available to preserve fertility in breast cancer patients undergoing chemotherapy. The most appropriate option should be determined considering several factors, including the patient's age, the type of adjuvant treatment, the time available before chemotherapy, and the length of delay to childbearing post chemotherapy. Embryo cryopreservation is the method of choice with the highest success rate. Oocyte cryopreservation is considered in single women who do not wish to use donor sperm. Both approaches require 2 weeks of ovarian stimulation beginning with the onset of the patient's menstrual cycle. Recently developed ovarian stimulation protocol with aromatase inhibitor letrozole appears to provide a safe ovarian stimulation. When a breast cancer patient does not have sufficient time to undergo ovarian stimulation, ovarian cryopreservation can be offered as the last resort. The benefit of ovarian protection by GnRH agonist treatment is unproven.

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CHAPTER 8

BREAST CANCER AND THE PINK RIBBON CAMPAIGN

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INTRODUCTION

Breast cancer is a one of the leading cause of death in women especially in the western countries where it is the number one killer in women. We are not lagging far behind but still it is the second common cause of cancer related in women in our country; the first being cervical cancer. In India 100,000 women are newly diagnosed with breast cancer every year. This figure is expected to increase to 130,000 by 2020. Around 50,000 women die from breast cancer every year in India and it has become the leading cause for death among women in metropolitan cities. More than one million women worldwide are diagnosed with breast cancer annually.

The pink ribbon is an international symbol of breast cancer awareness. Pink ribbons and the colour pink in general is used for promotion of awareness of breast cancer. It also expresses moral support for women with breast cancer.

HOW IT BEGAN?

The first known use of a pink ribbon in connection with breast cancer awareness was in the fall of 1991, when the Susan G. Komen Foundation handed out pink ribbons to participants in its New York City race for breast cancer survivors. The pink ribbon was adopted as the official symbol of National Breast Cancer Awareness Month the next year, in 1992. The pink ribbon was derived from the popular red ribbon for AIDS awareness.

The initiative was a brainchild of Alexandra Penney, the editor-in-chief of the women's health magazine Self, and breast cancer survivor. Evelyn Lauder, the senior corporate vice president at the cosmetics company Estée Lauder created a ribbon for the cosmetics giant to distribute in stores in New York City.

WHY PINK?

The colour pink is considered feminine in modern Western countries. It evokes traditional feminine gender roles, caring for other people, being beautiful, being good, and being cooperative. The pink ribbon represents fear of breast cancer, hope for the future, and the charitable goodness of people and businesses that publicly support the breast cancer movement. The intention is to evoke solidarity with women who currently have breast cancer.

Some breast cancer-related organizations, such as Pink Ribbon International uses the pink ribbon as their primary symbol. Susan G. Komen for the Cure uses a stylized "running ribbon" as their logo. While specifically representing breast cancer awareness, the pink ribbon is also a symbol and a proxy of goodwill towards women in general. Buying, wearing, displaying, or sponsoring pink ribbons signals that the person or business cares about women. The pink ribbon is a marketing brand for businesses that allows them to promote themselves with women and identify them as being socially aware.

GROWING TOWARDS AN INTERNATIONAL MOVEMENT

Breast cancer awareness started to grow, more and more organizations started to incorporate the pink ribbon as the symbol for breast cancer. In October 6th, 1997 American citizen Paul Davidson registered pinkribbon.com and launched a website directed to and available for all people in the world engaged with breast cancer. The website was dedicated to raising awareness and funding for breast cancer.

In 2008, the initiative was extended & expanded creating the nonprofit network Pink Ribbon Inc. in New York, USA. The idea launched of an international charity platform for breast cancer awareness and funding with clear cut objectives viz. awareness, advocacy, alliances, alignment and accreditation.

Throughout the years this initiative has grown into the international platform covering more than 30 countries over 5 continents.

HOW IT HAS BEEN DONE?

Each October, hundreds of products are emblazoned with pink ribbons, coloured pink, or otherwise sold with a promise of a small portion of the total cost being donated to support breast cancer awareness or research.

In Canada, the Royal Canadian Mint produced a silver commemorative breast cancer coin. 15,000 coins were produced during 2006. On one side of the coin, a portrait of Her Majesty Queen Elizabeth is illustrated, while on the other side a pink ribbon has been enamelled. Additionally, 30 million 25-cent coins were produced with pink ribbons during 2006 for normal circulation. It was designed by the mint's director of engraving, Cosme Saffioti. This coloured coin is the second in history to be put into regular circulation.

RECOMMENDATIONS FOR BREAST CANCER AWARENESS

- PRIORITY ONE – HAVE A REGULAR SCREENING MAMMOGRAM FROM 40

  A screening mammogram is the best method for the early detection of unsuspected breast cancer in women who have no signs or symptoms of breast cancer, in other words, 'well' women. The Foundation recommends a screening mammogram as follows :

- Yearly breast screening mammograms for women 40-49 years of age)
- Every two years for women from the age of 50 onwards. This may not be practical in a country like ours.

PRIORITY TWO - KNOW YOUR BREASTS

From the age of 20, the Foundation recommends women become aware of how their breasts look and feel:

– Know what is normal for you

– Know what changes to look and feel for

Breast changes to see your family doctor about are :

- A new lump or thickening, especially if it is only in one breast
- A breast pain that is unusual
- A change in breast shape or size
- A change in the skin of the breast such as: Puckering or dimpling or Reddening or a rash
- Any change in a nipple, such as: A turned-in nipple, A discharge that occurs without squeezing or Crusting, ulcer or redness

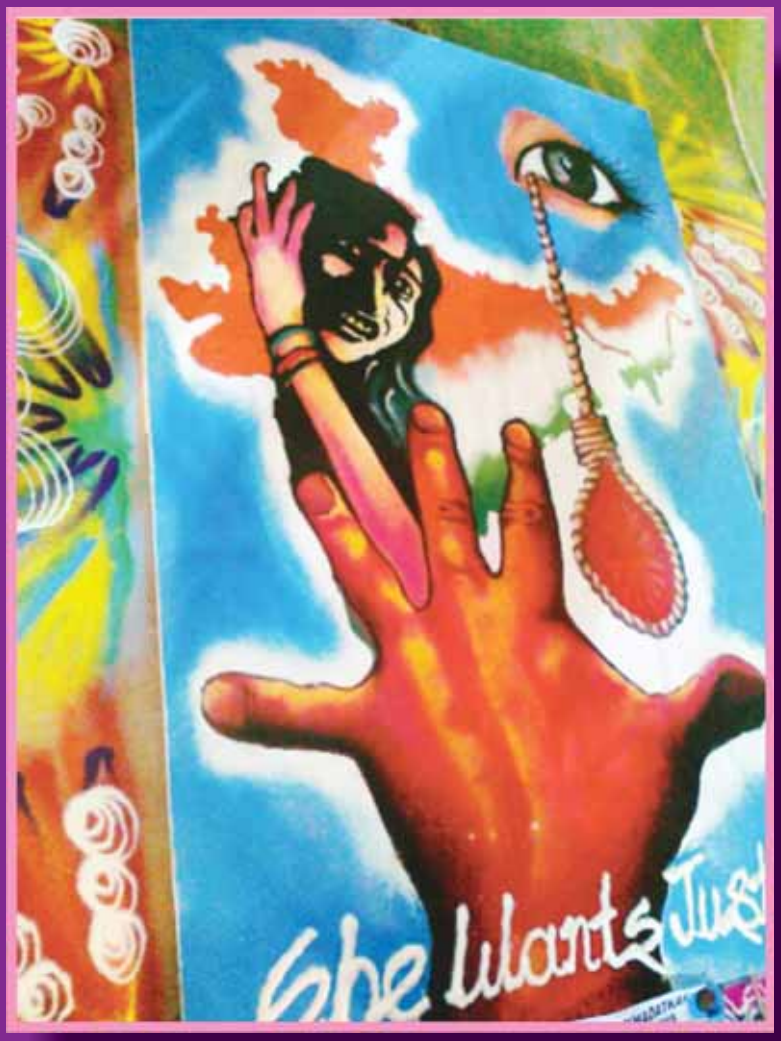
PINK RIBBON ACTIVITIES IN INDIA

Pink ribbon activities were initiated in our country about 4 years ago. Various activities are planned in the month of October which is for breast awareness month. Different celebrities are roped in to promote importance of awareness. These include arranging walks, painting the city pink & training of health workers in examination of breast for early.

Academic Activities of Study of Female Breast Committee, FOGSI

This issue of FOGSI FOCUS is dedicated to "Damini"

LET JUSTICE BE DONE



Save Women, Save Humanity, Save Human Existence