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**VARIOUS TYPES AND MANAGEMENT OF BREAST CANCER: AN OVERVIEW****Ganesh N. Sharma\*<sup>1</sup>, Rahul Dave<sup>1</sup>, Jyotsana Sanadya<sup>2</sup>, Piush Sharma<sup>2</sup>, K.K.Sharma<sup>3</sup>**

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**ABSTRACT**

Now days, breast cancer is the most frequently diagnosed life-threatening cancer in women and the leading cause of cancer death among women. Since last two decades, researches related to the breast cancer has lead to extraordinary progress in our understanding of the disease, resulting in more efficient and less toxic treatments. Increased public awareness and improved screening have led to earlier diagnosis at stages amenable to complete surgical resection and curative therapies. Consequently, survival rates for breast cancer have improved significantly, particularly in younger women. This article addresses the types, causes, clinical symptoms and various approach both non- drug (such as surgery and radiation) and drug treatment (including chemotherapy, gene therapy etc.) of breast cancer.

Key Words: Breast Cancer, Tumor, Chemotherapy, Gene Therapy.

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**INTRODUCTION**

Breast cancer is the most common cause of cancer in women and the second most common cause of cancer death in women in the U.S.

Breast cancer refers to cancers originating from breast tissue, most commonly from the inner lining of milk ducts or the lobules that supply the ducts with milk.

Worldwide, breast cancer comprises 10.4% of all cancer incidences among women, making it the second most common type of non-skin cancer (after lung cancer) and the fifth most common cause of cancer death. In 2004, breast cancer caused 519,000 deaths worldwide (7% of cancer deaths; almost 1% of all deaths). Breast cancer is about 100 times more common in women than in men, although males tend to have

poorer outcomes due to delays in diagnosis.

Cancer cells are very similar to cells of the organism from which they originated and have similar (but not identical) DNA and RNA. This is the reason why they are not very often detected by the immune system, in particular, if it is weakened [1].

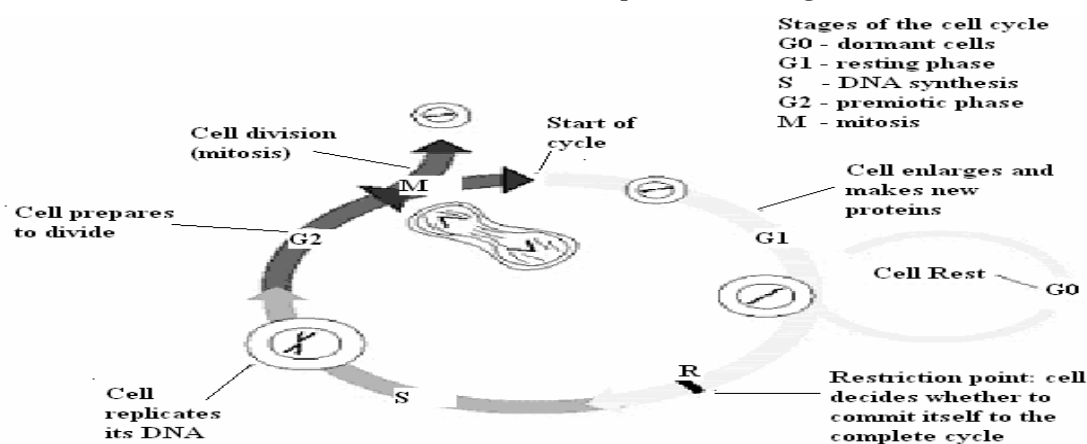
Cancer cells are formed from normal cells due to a modification / mutation of DNA and / or RNA. These modifications / mutations can occur spontaneously (II Law of Thermodynamics - increase of entropy) or they may be induced by other factors such as: nuclear radiation, electromagnetic radiation (microwaves, X-rays, Gamma-rays, Ultraviolet-rays etc.), viruses, bacteria and fungi, parasites (due to tissue inflammation / irritation), heat, chemicals in the air, water and food, mechanical cell-level injury, free radicals, evolution and ageing of DNA and RNA, etc. All these can produce mutations that may start cancer. Cancer can be called therefore

"Entropic Disease" since it is associated with the increase of entropy of the organism to the point where the organism cannot correct this itself. External intervention is required to allow the organism to return to a stable entropic state [2].

Cancer develops if the immune system is not working properly and / or the amount of cells produced is too great for the immune system to eliminate [3]. The rate of DNA and RNA mutations can be too high under some conditions such as: unhealthy environment (due to radiation, chemicals, etc.) [4], poor diet (unhealthy cell environment) [5], people with genetic predispositions to mutations [6] and people of advanced age (above 80) [7].

**The cell cycle**

In cancerous cells, the process of cell division is disrupted and unregulated, resulting in cell proliferation and tumor growth. The normal cell cycle is as represented in figure 1.



**Fig. 1: Stages of normal cell cycle [8]**

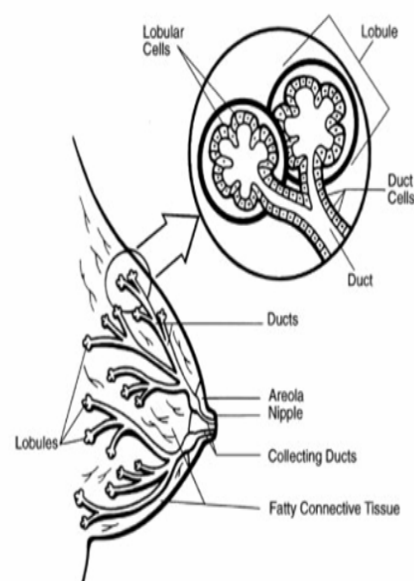
## BREAST CANCER

Usually, cancer is named after the body part in which it originated; thus, breast cancer refers to the erratic growth and proliferation of cells that originate in the breast tissue [9].

The breast is composed of two main types of tissues i.e., glandular tissues and stromal (supporting) tissues. Glandular tissues house the milk-producing glands (lobules) and the ducts (the milk passages) while stromal tissues include fatty and fibrous connective tissues of the breast. The breast is also made up of lymphatic tissue-immune system tissue that removes cellular fluids and waste [10].

There are several types of tumors that may develop within different areas of the breast. Most tumors are the result of benign (non-cancerous) changes within the breast. For example, fibrocystic change is a non-cancerous condition in which women develop cysts (accumulated packets of fluid), fibrosis (formation of scar-like connective tissue), lumpiness, and areas of thickening, tenderness, or breast pain [11].

Most breast cancers begin in the cells that line the ducts (ductal cancers). Some begin in the cells that line the lobules (lobular cancers), while a small number start in the other tissues [12].



**Fig. 2: Structure of breast**

## TYPES OF BREAST CANCER

### According to site

**Non-Invasive Breast Cancer** cells that are confined to the ducts and do not invade surrounding fatty and connective tissues of the breast. Ductal carcinoma in situ (DCIS) is the most common form of non-invasive breast cancer (90%). Lobular carcinoma in situ (LCIS) is less common and considered a marker for increased breast cancer risk.

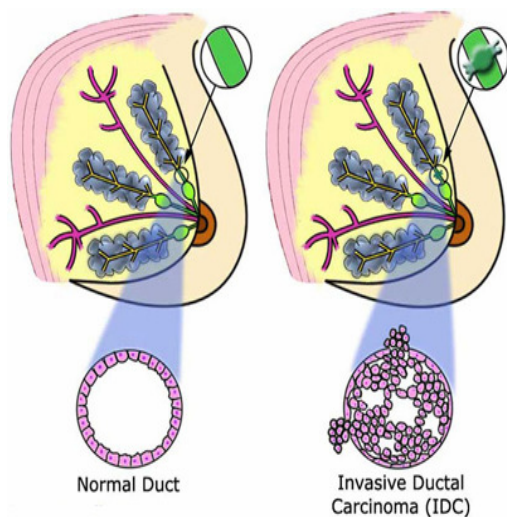
**Invasive Breast Cancer** cells that break through the duct and lobular wall and invade the surrounding fatty and connective tissues of the breast. Cancer can be invasive without being

metastatic (spreading) to the lymph nodes or other organs [13].

### Frequently occurring Breast cancer

**Lobular carcinoma in situ (LCIS)** (LCIS, lobular neoplasia): The term, "in situ," refers to cancer that has not spread past the area where it initially developed. LCIS is a sharp increase in the number of cells within the milk glands (lobules) of the breast.

**Ductal carcinoma in situ (DCIS)**: DCIS, the most common type of non-invasive breast cancer, is confined to the ducts of the breast. For example, ductal comedocarcinoma.



**Fig. 3: Typical Structure associated with ductal carcinoma**

### Infiltrating lobular carcinoma (ILC)

ILC is also known as invasive lobular carcinoma. ILC begins in the milk

glands (lobules) of the breast, but often spreads (metastatizes) to other regions of the body. ILC accounts for 10% to 15% of breast cancers.

**Infiltrating ductal carcinoma (IDC)**: IDC is also known as invasive ductal carcinoma. IDC begins in the milk ducts of the breast and penetrates the wall of the duct, invading the fatty tissue of the breast and possibly other regions of the body. IDC is the most common type of breast cancer, accounting for 80% of breast cancer diagnoses [14, 15].

### Less commonly occurring Breast cancer

**Medullary carcinoma**: Medullary carcinoma is an invasive breast cancer that forms a distinct boundary between tumor tissue and normal tissue. Only 5% of breast cancers are medullary carcinoma.

**Mucinous carcinoma**: Also called *colloid carcinoma*, mucinous carcinoma is a rare breast cancer formed by the mucus-producing cancer cells. Women with mucinous carcinoma generally have a better prognosis than women with more common types of invasive carcinoma.

**Tubular carcinoma**: Tubular carcinomas are a special type of infiltrating (invasive) breast carcinoma.

Women with tubular carcinoma generally have a better prognosis than women with more common types of invasive carcinoma. Tubular carcinomas account for around 2% of breast cancer diagnoses.

#### **Inflammatory breast cancer**

Inflammatory breast cancer is the appearance of inflamed breasts (red and warm) with dimples and/or thick ridges caused by cancer cells blocking lymph vessels or channels in the skin over the breast. Though inflammatory breast cancer is rare (accounting for only 1% of breast cancers), it is extremely fast-growing.

#### **Paget's disease of the nipple**

A rare form of breast cancer that begins in the milk ducts and spreads to the skin of the nipple and areola, Paget's disease of the nipple only accounts for about 1% of breast cancers.

#### **Phylloides tumor**

Phylloides tumors (also spelled "phylloides") are can be either benign (non-cancerous) or malignant (cancerous). Phylloides tumors develop in the connective tissues of the breast and may be treated by surgical removal. Phylloides tumors are very rare; less than 10 women die of this type of breast cancer each year in the United States [16, 17, 18].

## **CAUSES OF BREAST CANCER**

### **A previous history of breast cancer**

A woman who has had breast cancer has an increased risk of getting breast cancer in the other breast [19].

### **Significant family history**

If several members of patient's family have had particular types of cancer, patient may have an increased risk of developing breast cancer [19, 20].

### **Genetic causes**

Family history has long been known to be a risk factor for breast cancer. Both maternal and paternal relatives are important. The risk is highest if the affected relative developed breast cancer at a young age, had cancer in both breasts, or if she is a close relative. First-degree relatives, (mother, sister, daughter) are most important in estimating risk. Several second-degree relatives (grandmother, aunt) with breast cancer may also increase risk. Breast cancer in a male increases the risk for all his close female relatives. *BRCA1* and *BRCA2* are abnormal genes that, when inherited, markedly increase the risk of breast cancer to a lifetime risk estimated between 40 and 85%. Women who have the *BRCA1* gene tend to develop breast cancer at an early age [21].

**Hormonal causes**

Alteration in hormonal level may precipitate breast cancer. It could be attended by starting and stopping of periods (Menstrual Cycle), Pregnancy in early age, Hormonal replacement therapy, Use of oral pills etc [22].

**Life style and dietary cause**

Sedentary life style, high dietary intake of fat obesity particularly in postmenopausal women may cause breast cancer. The use of alcohol is also another one cause of breast cancer. The risk increases with the amount of alcohol consumed. Women who consume two to five alcoholic beverages per day have a risk about one and a half times that of nondrinkers for the development of breast cancer [23, 24].

**Environmental cause**

There is known to be a slight increase in risk in ladies who work with low doses of radiation over a long period of time- for example, X-ray technicians [23, 24].

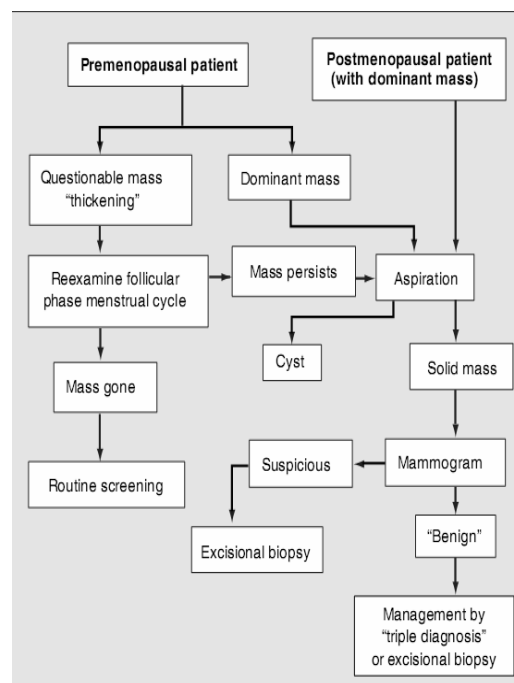
**Sign and symptoms**

The classic symptom for breast cancer is a lump found in the breast or armpit. Doing monthly breast self-exam (BSE) is a great way to be familiar with the breasts' texture, cyclical changes, size, and skin condition. The general alerting features of breast cancer are such as swelling or lump (mass) in the breast,

swelling in the armpit (lymph nodes), nipple discharge (clear or bloody), pain in the nipple, inverted (retracted) nipple, scaly or pitted skin on nipple, persistent tenderness of the breast, and unusual breast pain or discomfort. In Advanced stage (Metastatic) of disease underarm lymph nodes are present with other symptoms such as bone pain (bone metastases), shortness of breath (lung metastases), drop in appetite (liver metastases), unintentional weight loss (liver metastases), headaches, neurological pain or weakness [25].

**Screening/diagnosis of breast cancer**

Breast cancer is usually diagnosed by biopsy of nodule detected by mammogram or by palpitation [26].



**Fig. 4: Various approaches for diagnosis of breast cancer [27]**

### Stages of Breast Cancer

When cancer is diagnosed, a stage is assigned to it, based on how advanced it is. The stage helps doctors determine the most appropriate treatment and the

prognosis. Stages of breast cancer may be described generally as in situ (not invasive) or invasive. Stages may be described in detail and designated by a number (0 through IV).

**Table 1: Stages of Breast Cancer [28]**

Stage	Description
<b>In situ carcinoma</b>	
0	The tumor is confined, usually to a milk duct or milk-producing gland, and has not invaded surrounding breast tissue.
<b>Localized and regional invasive cancer</b>	
I	The tumor is less than $\frac{3}{4}$ inch (2 centimeters) in diameter and has not spread beyond the breast.
IIA	The tumor is $\frac{3}{4}$ inch or less in diameter and it has spread to one to three lymph nodes in the armpit, microscopic amounts have spread to lymph nodes near the breastbone on the same side as the tumor, or both <i>or</i> The tumor is larger than $\frac{3}{4}$ inch but smaller than 2 inches (5 centimeters) in diameter but has not spread beyond the breast.
IIB	The tumor is larger than $\frac{3}{4}$ inch but smaller than 2 inches in diameter, and it has spread to one to three lymph nodes in the armpit, microscopic amounts have spread to lymph nodes near the breastbone on the same side as the tumor, or both <i>or</i> The tumor is larger than 2 inches in diameter but has not spread beyond the breast.
IIIA	The tumor is 2 inches or less in diameter and has spread to four to nine lymph nodes in the armpit or has enlarged at least one lymph node near the breastbone on the same side as the tumor <i>or</i> The tumor is larger than 2 inches in diameter and has spread to up to nine lymph nodes in the armpit or to lymph nodes near the breastbone.
IIIB	The tumor has spread to the chest wall or skin or has caused breast inflammation (inflammatory breast cancer). The tumor can be any size plus at least one of the following: It has spread to 10 or more lymph nodes in the armpit. It has spread to lymph nodes under or above the collar bone.
IIIC	It has spread to lymph nodes in the armpit and has enlarged at least one lymph node near the breastbone on the same side as the tumor. It has spread to four or more lymph nodes in the armpit, and microscopic amounts have spread to lymph nodes near the breastbone on the same side as the tumor.
<b>Metastatic cancer</b>	
IV	The tumor, regardless of size, has spread to distant organs or tissues, such as the lungs or bones, or to lymph nodes distant from the breast.

### Management of Breast Cancer

Following approaches are to be made for the management of breast cancer. They are as follows;

#### Surgery

Depending on the stage and type of the tumor, lumpectomy (removal of the lump only), or surgical removal of the entire breast (mastectomy) is performed. Standard practice requires the surgeon to establish that the tissue removed in the operation has margins clear of cancer, indicating that the cancer has been completely excised. If the removed tissue does not have clear margins, further operations to remove more tissue may be necessary. This may sometimes require removal of part of the pectoralis major muscle, which is the main muscle of the anterior chest wall. More recently, the technique of sentinel lymph node (SLN) dissection has become popular, as it requires the removal of far fewer lymph nodes, resulting in fewer side effects. Advances in sentinel lymph node mapping over the past decade have increased the accuracy of detecting sentinel lymph node from 80% using blue dye alone to between 92% and 98% using combined modalities [29, 30].

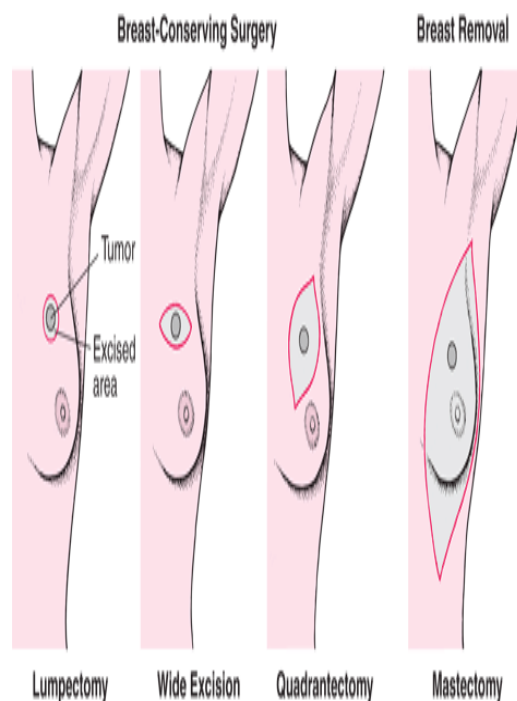
Surgery for breast cancer consists of two main options.

In **breast-conserving surgery**, only the tumor and an area of normal tissue surrounding it are removed. Breast-conserving surgery includes the following:

**Lumpectomy:** A small amount of surrounding normal tissue is removed.

**Wide excision:** Also called as partial mastectomy in which somewhat larger amount of the surrounding normal tissue is removed

**Quadrantectomy:** About one fourth of the breast is removed.



**Fig. 5: various types of surgery applied for breast cancer**



In **mastectomy**, all breast tissue is removed.

### **Radiation Therapy**

Radiation therapy involves using high-energy X-rays or gamma rays that target a tumor or post surgery tumor site. These radiations are very effective in killing cancer cells that may remain after surgery or recur where the tumor was removed. In addition to this treatment implanted radioactive catheters (brachytherapy), similar to those used in prostate cancer treatment, can be used. However this treatment option has been superseded by electron beam radiotherapy to the breast scar. Radiation therapy for breast cancer is usually performed after surgery and is an integral component of breast-conserving therapy. The dose of radiation must be strong enough to ensure the elimination of cancer cells. Treatments are typically given over a period of five to seven weeks, performed five days a week. Each treatment takes about 15 minutes [31, 32].

### **CHEMOTHERAPY**

Chemotherapy is the use of anti-cancer drugs to treat cancerous cells. Specific treatment for the breast cancer will be based on; overall health, medical history, age (whether menstruation is there or not), type and stage of the cancer, tolerance for specific medications and procedures etc. Chemotherapy treatments are often

given in cycles; a treatment for a period of time, followed by a recovery period, then another treatment. Chemotherapy can be given before surgery to shrink the tumor and sometimes make breast conserving surgery possible rather than a mastectomy. Many times, it is given after surgery and may be given every three weeks or every two weeks in a “dose dense” fashion [33, 34]. Commonly used agents in breast cancer chemotherapy are [35];

### **Nanotechnology in breast cancer**

The field of nanotechnology has rapidly evolved as evidenced by the fact that there are more than 150 ongoing clinical trials investigating the efficacy of nanotechnology based drug delivery carriers targeting cancer. Various liposomal doxorubicin formulations were developed in an effort to improve the therapeutic index of the conventional doxorubicin chemotherapy while maintaining its anti-tumor activity. For example, the efficacy of three liposomal doxorubicins are currently being used: liposomal daunorubicin (DaunoXome®), liposomal doxorubicin (D-99, Myocet™J), and pegylated liposomal doxorubicin (Doxil® marketed and distributed in the U.S. and Caelyx® distributed outside the U.S.). Generally, these agents exhibit efficacies comparable to those of conventional doxorubicin, except with better safety profiles and less cardio

toxicity. In addition to liposomal doxorubicin, albumin-bound paclitaxel (Abraxane ®) is another example of an EPR based nanovector application for breast cancer chemotherapy. Paclitaxel is highly hydrophobic and dissolved in cremophor to prevent paclitaxel

precipitation. However, cremophor-associated toxicities are severe (hypersensitivity reaction and neurotoxicity) and challenge the application of paclitaxel. Albumin-bound paclitaxel was developed to improve the solubility of paclitaxel [36].

**Table 2: Chemotherapeutic agents used in management of breast cancer**

S. No.	Abbreviations	Component
1	AC	Doxorubicin (Adriamycin) 60 mg/m <sup>2</sup> IV, day 1 Cyclophosphamide 400-600 mg/m <sup>2</sup> IV, day 1 (Repeat cycle every 21 days) Cyclophosphamide 100 mg/m <sup>2</sup> PO, days 1-14
2	CAF (FAC)	Doxorubicin 25 mg/m <sup>2</sup> IV, days 1, 8, or 60 Fluorouracil 500-600 mg/m <sup>2</sup> IV, days 1, 8 (Repeat cycle every 28 days) Cyclophosphamide 500-600 mg/m <sup>2</sup> IV, day 1
3	CMF(CNF,FNC)	Fluorouracil 500-600 mg/m <sup>2</sup> IV, day 1 Mitoxantone 10-12 mg/m <sup>2</sup> IV, day 1 (Repeat cycle every 21 days) Cyclophosphamide 100 mg/m <sup>2</sup> PO, days 1-14
4	CMF	Methotrexate 40 mg/m <sup>2</sup> IV, day 1, 8 Fluorouracil 600 mg/m <sup>2</sup> IV, days 1, 8 (Repeat cycle every 28 days) Mitoxantone 12 mg/m <sup>2</sup> IV, day 1
5	NFL	Fluorouracil 350 mg/m <sup>2</sup> IV, days 1-3, given after leucovorin Leucovorin 300 mg IV over 1 h, days 1-3 (Repeat cycle every 21 days)
6	Sequential DOX-CMF	Doxorubicin 75 mg/m <sup>2</sup> IV, every 21 days for 4 cycles, Followed by CMF for 8 cycles Vinblastin 4.5 mg/m <sup>2</sup> IV, day 1
7	VATH	Doxorubicin 45 mg/m <sup>2</sup> IV, day 1 Thiotepa 12 mg/m <sup>2</sup> IV, day 1 Fluoxymesterone 10 mg PO tid (Repeat cycle every 21 days)
8	Vinorelbine & Doxorubicin	Vinorelbine 25 mg/m <sup>2</sup> IV, days 1, 8 Doxorubicin 50 mg/m <sup>2</sup> IV, day 1 Repeat cycle every 21 days Docetaxel 60-100 mg/m <sup>2</sup> IV, over 1h, every 21 days, and dexamethasone 8 mg PO bid for 5 days, begin 1 day before docetaxel
9	Single-Agent Regimens	Gemcitabine 725 mg/m <sup>2</sup> IV, over 20 min, weekly for 3 wk, followed by 1-wk rest Repeat cycle every 28 days Paclitaxel 250 mg/m <sup>2</sup> IV, over 3 or 24 h, or 175 mg/m <sup>2</sup> IV, over 3 h, every 21 days Vinorelbine 30 mg/m <sup>2</sup> IV, every 7 days

**Table 3: Age related approaches to chemotherapy for management of breast cancer**

Age Group	Lymph Node Status	Endocrine Receptor (ER) Status	Tumor	Recommendation
Premenopausal	Positive	Any	Any	Multi drug chemotherapy + tamoxifen if ER-positive + trastuzumab in HER-2/neu positive tumors
Premenopausal	Negative	Any	>2 cm, or 1-2 cm with other poor prognostic variables	Multidrug chemotherapy + tamoxifen if ER-positive + trastuzumab in HER-2/neu positive tumors
Postmenopausal	Positive	Negative	Any	Multidrug chemotherapy + trastuzumab in HER-2/neu positive tumors
Postmenopausal	Positive	Positive	Any	Aromatase inhibitors and tamoxifen with or without chemotherapy + trastuzumab in HER-2/neu positive tumors
Postmenopausal	Negative	Positive	>2 cm, or 1-2 cm with other poor prognostic variables	Aromatase inhibitors and tamoxifen + trastuzumab in HER-2/neu positive tumors
Postmenopausal	Negative	Negative	>2 cm, or 1-2 cm with other poor prognostic variables	Consider multi drug chemotherapy +

**Recent approaches in management of breast cancer**

**Gene Therapy**

It is generally accepted that cancer arises because of an accumulation of multiple molecular genetic defects that culminate in a cellular phenotype characterized by unregulated growth. Based on the knowledge, a variety of gene therapy strategies have been

developed as potential new therapies for cancer. Current knowledge of proto-oncogene and tumor suppressor genes in the genesis of malignancy has stimulated the development of gene therapy tactics directed at ablating or restoring such genes, respectively. In other strategies, cancer cells are endowed with the ability to convert a systemically delivered prodrug to a toxic metabolite, or a target for destruction

by replicating viral vectors conversely transfer of drug resistance genes into normal cells may provide chemoprotection during high dose antineoplastic treatment. Finally, immune system modulation can activate anticancer drug defense mechanisms [39].

### **Oncogenes Inactivation**

Several oncogenic proteins have been identified and associated with various malignancies. The most commonly applied approach in clinical trials to date has been use of antisense strategies. Transcription of oncogenes also can be inhibited by using adenoviral gene E1A, which interfere with the transcription of erbB-2, a strategy useful in treating cancer that over express this oncogenic protein, such as breast and ovarian cancer [39].

### **Augmentation of Tumor Suppressor Genes**

More than 24 tumor suppressor genes have been identified, and mutations in these genes have been associated with a variety of neoplastic conditions. Several clinical trials are under way to deliver p53 using adenoviral vectors to a variety of cancers. Similarly, viral vectors have been utilized to introduce a retinoblastoma gene and breast cancer gene BRCA1 into bladder and ovarian cancer, respectively. In some situations,

this approach will fail, because the mutant gene exhibits dominant negative effects on the normal gene. To circumvent this problem for p53 gene therapy, a genetic repair strategy rather than a gene augmentation approach could be more effective.

### **Cell-Target Suicide**

A conversion of a pro drug to a toxic metabolite by genetically engineering tumor cells is an attractive way to create an artificial difference between normal and neoplastic tissue. This can be achieved by the expression of a gene that confers a dominant, negatively selectable phenotype to the cancer cells, such as cell death imparted by expression of a prodrug – metabolism enzyme. Greater selectivity in killing malignant cells will be obtained by transferring a gene that is not normally found in human beings (e.g. HSV-thymidine kinase), rather than by overexpression an endogenous gene. The prototype for this approach utilizes the HSV-1 Thymidine kinase gene given to combination with prodrug ganciclovir in a manner distant from mammalian thymidine kinase. Phosphorylated ganciclovir is ultimately incorporated into DNA and inhibits DNA synthesis and transcription. The efficacy and safety on this approach is being tested in several clinical trials involving multiple malignancies [40].

**Chemoprotection Approach**

The MDR-1 gene encoding the multidrug therapy transporter protein (also known as P-glycoprotein) has received much attention in this regard. This transmembrane protein transports a wide variety of chemotherapeutic agents (e.g. doxorubicin, vinca alkaloids, epipodophyllotoxins and paclitaxel) and other drugs out of cells, thus protecting them from the agents' toxic effects.

**Virus-mediated oncolysis**

Certain viruses, including adenovirus, and HSV-1 can infect and lyse tumor cells. The use of oncolytic virus in combination with other gene based antineoplastic strategies has emerged as a promising addition to the multidimensional treatment of cancers. Selective replication of virus in tumor cells leads to the cell lysis and to local dissemination of infective viral progeny to neighboring cancer cells. Most investigational uses of this strategy have utilized replication-competent adenovirus and HSV-1.

**Immunomodulation**

Various cytokines can enhance immunity against cancer cells, and this observation has stimulated the development of gene-based approaches to modulate the immune reaction in malignancy.

**Ectopic Cytokine Expression:** A variety of cytokines have been shown to decrease tumor growth when ectopically expressed in tumor cells or in their microenvironment. Some

immunostimulatory agents do not alter the growth rate of the tumor initially, but lead to immunity against tumor growth if the animal is later challenged with wild type tumor cells.

**Immune enhancement:** One such approach is to express on the surface of cancer cells highly immunogenic molecules, such as allotype MHC antigens. It has been long known that those additional "costimulatory" pathways distinct from the T-cell are needed to achieve T cell activation. The molecules B7-1 (CD 80) and B7-2 (CD 86) stimulate one such pathway. The B7s, whose expression normally is limited to antigen presenting cells and other specialized immune effector cells, engage specific receptors on the T cells surface in concert with antigen binding to the T-cell receptor [41].

**CURRENT RESEARCHES****Human Antimicrobial Protein hCAP18/LL-37 Promotes a Metastatic Phenotype in Breast Cancer**

Human cathelicidin antimicrobial protein, hCAP18, and its C-terminal peptide LL-37 is a multifunctional protein. In addition to being important

in antimicrobial defense, it induces chemotaxis, stimulates angiogenesis and promotes tissue repair. We previously showed that human breast cancer cells express high amounts of hCAP18, and hypothesised that hCAP18/LL-37 may be involved in tumor progression [42].

#### **Genetic variation in stromal proteins decorin and lumican with breast cancer: investigations in two case-control studies**

The stroma is the supportive framework of biologic tissue in the breast, consisting of various proteins such as the proteoglycans, decorin and lumican. Altered expression of decorin and lumican is associated with breast tumors. We hypothesized that genetic variation in the decorin (*DCM*) and lumican (*LUM*) genes may contribute to breast cancer [43].

#### **Prognostic impact of tumor-specific HMG-CoA reductase expression in primary breast cancer**

It has been previously reported that tumor-specific expression of the rate-limiting enzyme, 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoAR), in the mevalonate pathway is associated with more favorable tumor parameters in breast cancer. In the present study, it is examined the prognostic value of HMG-CoAR expression in a large cohort of

primary breast cancer patients with long-term follow up [44].

#### **Monoclonal antibodies in human cancer**

Mouse, chimeric, humanized and human monoclonal antibodies (MABs) are all in use for treatment of human cancer. Antibodies can activate the immune system (antibody-dependent cellular cytotoxicity [ADCC], complement-dependent cytotoxicity [CDC], induction of tumor immunity [idiotype network]). The best therapeutic effect may be obtained if MABs are used early in the course of the disease [45].

#### **CONCLUSION**

The occurrence of breast cancer in female can be observed in only 5% cases with a malignant mass present with breast pain. Other symptoms such as immobility, skin changes (i. e, thickening, swelling, and redness) or nipple abnormalities (i.e., ulceration, retraction, spontaneous bloody discharge) may also be present at the same time. Today there are so many approaches, which can be made for the treatment of the cancer of breast such as surgery, radiation therapy chemotherapy, hormonal therapy and recently nanotechnology and gene therapy. With advances in screening, diagnosis, and treatment, the death rate for breast cancer has declined. In fact, about 90% of women newly diagnosed

with breast cancer will survive for at least five years. Research is ongoing to develop even more effective screening and treatment programs.

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