Breast Cancer

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Abstract:
- Breast cancer is currently the most common cancer of women in India.
- Chronic endogenous or exogenous exposure to estrogens is proven to increase the risk of breast cancer in women. The other modifiable risk factors are obesity, lack of physical exercise, decreased fat and increased fruit and vegetable intake in diet.
- Screening mammography is cost effective and useful when used for high risk women in India rather than subjecting all women to it.
- Triple assessment includes clinical, imaging and pathological assessment to diagnose a breast lump as malignant. The fourth assessment is follow-up if the lesion was not proven malignant.
- Pathologically, breast cancers are divided into four prognostic subtypes based on estrogen, progesterone and HER2 neu receptors.
- Breast cancer requires both systemic and local treatment. Local treatments are surgery and radiation therapy. Systemic treatment involves chemotherapy, biological and hormonal therapy. Stage I and Stage II can be considered as ‘early breast cancer’ while stage III is locally advanced and stage IV is metastatic. The prognosis depends upon the stage and the systemic disease determines survival. Therefore the dictum for modern treatment is less local and more systemic treatment to improve the outcome for the patient.
- Breast conservation surgery, sentinel lymph node biopsy, partial breast irradiation are examples of local treatment.
- Systemic therapy options now include various hormone therapies along with chemotherapeutic agents. The most common side effects encountered in local therapies are seroma collection and lymphedema.
- Metastatic breast cancer is primarily managed using palliative systemic chemotherapy, though surgical excision and or radiotherapy have been used in selected cases of isolated metastasis successfully.

Introduction

How common is breast cancer and what is the burden in our society?
Breast cancer has overtaken cervical cancer recently and is currently the most common cancer of women in India (Fig 1). According to GLOBOCAN 2012, there are 1,45,000 new cases for the year in India and 70,000 breast cancer deaths and the 5-year prevalence is 3,97,000. Breast cancer constitutes 25% of all cancers.¹ Approximately 1.17 per 10,000 population gets diagnosed of breast cancer and every 8 minutes, there is a death due to breast cancer in our country and the burden is increasing. Figure 1: Changing incidence of cancers in women in India¹
Box 1: Risk factors for breast cancer

**Strong risk factors**
1. Older age group
2. Early menarche
3. Late first live birth,
4. Late menopause,
5. Nulliparity and
6. Proliferative breast disease

**Other risk factors**
1. Obesity
2. Hormone replacement therapy
3. Alcohol and smoking
4. Increased fat and red meat intake, 
   less vegetables (not well proven)
5. NSAIDs, calcium, Vitamin D 
   supplements (equivocal evidence)

### Etiology of breast cancer

The etiology of breast cancer is multifactorial.

Fifty percent of breast cancers could be attributed to one of factors such as older age, early menarche, late first live birth, late menopause, nulliparity and proliferative breast disease (hyperplasia on biopsy). Age is the strongest risk factor and the risk of breast cancer is higher with increase in age. Less than 10% of the patients have an inherited genetic cause as etiology for their breast cancer and only a minority can be detected on testing.

The other factors such as lifestyle and environmental factors could increase the risk of developing breast cancer such as obesity, sedentary lifestyle, and exogenous hormones.

Obesity and weight gain in adulthood is associated with a higher risk of breast cancer. Reduced physical exercise and activity increases the risk of breast cancer. Insulin growth factor-1 and hence diabetes seems to be another risk factor although not completely proven. Hormone replacement therapy increases estrogen stimulation of the breast tissue in the body and hence increases the risk. There is weak evidence that increased fat and red meat intake and decreased fruits and vegetables can increase the risk of breast cancer. Alcohol and smoking habits increase the risk.

There is equivocal evidence that NSAIDs, calcium and vitamin D supplements could protect against breast cancer.

### Breast cancer screening

**Is screening helpful for breast cancer?**

‘Screening’ involves testing of normal individuals at increased risk to detect cancer early. There are 3 components- breast self-examination, clinical breast examination by a physician and screening mammography. Of these, screening mammography has been shown to improve survival. The role of the other two components is doubtful although they are tools to increase awareness and may benefit indirectly.

**What are the modalities to screen?**

Mammography has been proven to be the best tool for breast cancer screening. Ultrasound of the breasts is an alternative in women aged less than 35 and in women with dense breasts on mammography. MRI of the breasts is cumbersome, needs expertise and requires a breast MRI coil. It is useful only as an adjunct to evaluate suspicious lesions detected on mammography.

Countries with a high incidence of breast cancer such as in Northern Europe and America have implemented age

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**Table 1: Worldwide statistics on breast cancer**

<table>
<thead>
<tr>
<th>Estimated numbers (thousands)</th>
<th>Cases</th>
<th>Deaths</th>
<th>5-year Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>World</td>
<td>1671</td>
<td>522</td>
<td>6232</td>
</tr>
<tr>
<td>More developed regions</td>
<td>788</td>
<td>198</td>
<td>3201</td>
</tr>
<tr>
<td>Less developed regions</td>
<td>883</td>
<td>324</td>
<td>3032</td>
</tr>
<tr>
<td>WHO Africa region</td>
<td>100</td>
<td>49</td>
<td>318</td>
</tr>
<tr>
<td>WHO Americas region</td>
<td>408</td>
<td>92</td>
<td>1618</td>
</tr>
<tr>
<td>WHO East Mediterranean region</td>
<td>99</td>
<td>42</td>
<td>348</td>
</tr>
<tr>
<td>WHO Europe region</td>
<td>494</td>
<td>143</td>
<td>1936</td>
</tr>
<tr>
<td>WHO South-East Asia region</td>
<td>240</td>
<td>110</td>
<td>735</td>
</tr>
<tr>
<td>WHO Western Pacific region</td>
<td>330</td>
<td>86</td>
<td>1276</td>
</tr>
<tr>
<td>IARC membership (24 countries)</td>
<td>935</td>
<td>257</td>
<td>3591</td>
</tr>
<tr>
<td>United States of America</td>
<td>233</td>
<td>44</td>
<td>971</td>
</tr>
<tr>
<td>China</td>
<td>187</td>
<td>48</td>
<td>697</td>
</tr>
<tr>
<td><strong>India</strong></td>
<td><strong>145</strong></td>
<td><strong>70</strong></td>
<td><strong>397</strong></td>
</tr>
<tr>
<td>European Union</td>
<td>362</td>
<td>92</td>
<td>1444</td>
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</tbody>
</table>
based mammography screening programmes. The age group that benefits from screening for breast cancer is 41-69. There can be nearly 17% reduction in mortality when screening detects breast cancer in the age group 41-50 and 25-30% reduction in mortality when detected by screening in the age group 51-69. ACS (American cancer society) recommends starting screening mammography at age 45 and then an annual mammography till age 54, then every 2 years till age 70, continuing beyond 70 only if expected life expectancy is more than 10 years.\textsuperscript{8}

**Screening in the Indian context:**
India has a large population with a relatively low risk and the cost of screening is high, further leading to negative biopsies and attendant fear and emotional impact. Taking these factors into consideration, there is general consensus that it would be prudent to recommend screening to only high risk women.\textsuperscript{9,10}

One would of course, order mammographic screening for any woman above 35 years who requests screening based on her own perception of risk. Additionally, there is scope for ‘opportunistic screening’ where we can advise relatives of cancer patients or those with known hyperplastic breast disease to undergo mammographic screening as they would be at increased risk and coming to hospital, anyway.

Who are the high risk women? There are models to characterize women into high risk such as “Gail model risk calculator”, University of Pennsylvania calculator for risk of genetic mutation (BRCA1&2). These are available for online use and can be applied to patients in the practice.\textsuperscript{11}

<table>
<thead>
<tr>
<th>Table 2: Risk factors and protective factors for breast cancer\textsuperscript{12}</th>
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<tbody>
<tr>
<td><strong>Risk factors</strong></td>
</tr>
<tr>
<td>Deleterious BRCA1/BRCA2 genes</td>
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<tr>
<td>Mother or sister with breast cancer</td>
</tr>
<tr>
<td>Age</td>
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<tr>
<td>Age at menarche</td>
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<tr>
<td>Age at first birth</td>
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<tr>
<td>Age at menopause</td>
</tr>
<tr>
<td>Use of contraceptive pills</td>
</tr>
<tr>
<td>HRT (estrogen + progestin)</td>
</tr>
<tr>
<td>Alcohol</td>
</tr>
<tr>
<td>Breast density on mammography</td>
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<tr>
<td>Bone density</td>
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<tr>
<td>History of a benign breast biopsy</td>
</tr>
<tr>
<td>History of atypical hyperplasia on biopsy</td>
</tr>
<tr>
<td><strong>Protective factors</strong></td>
</tr>
<tr>
<td>Breast feeding (months)</td>
</tr>
<tr>
<td>Parity</td>
</tr>
<tr>
<td>Recreational exercise</td>
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<tr>
<td>Postmenopause body mass index (kg/m2)</td>
</tr>
<tr>
<td>Oophorectomy before age 35 years</td>
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<tr>
<td>Aspirin</td>
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</tbody>
</table>
Box 2: What are the symptoms and signs of breast cancer?

1. **Painless lump**: Most common presentation is a painless lump in the breast or axilla that could feel rounded, irregular or just a hard shapeless knot, particularly if it does not shrink or lessen after the next menstrual cycle. Pain usually signifies a benign etiology; however, about 10% of breast cancers may have associated pain usually a dull ache.

   Clinically, a cancerous breast lump would be a hard, immovable, single dominant lesion with irregular borders. Advanced lesions would include axillary lymph nodes and skin changes such as erythema, thickening, ulceration or dimpling of the overlying skin (peau d’orange).

2. **Change in size, shape or symmetry of the breast**,  
3. **Dimpling, puckering or indentation in the skin of the breast**  
4. **Nipple retraction**,  
5. **Nipple-areolar skin changes** - like scaling or ulceration (Paget’s disease)  
6. **Blood stained fluid discharge** - from the nipple.
7. **Symptoms of metastatic breast cancer** depend on the organs involved, with the most common sites of involvement being the bone (e.g., back or leg pain), liver (abdominal pain, nausea, jaundice), and lungs (e.g., shortness of breath or cough).

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Figure 2: Signs of breast cancer

a) Painless breast lump, b) Puckering/indentation of breast c) Nipple-areolar skin changes, d) Blood-stained discharge. (Image source: http://evaigeren.blogspot.in )

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Figure 3:

a) Nipple retraction and lifting of the right breast,  
   b) Pagets disease of nipple

Diagnostic evaluation

**Triple assessment:** The ‘Triple assessment’ diagnostic evaluation for breast cancer in a patient includes three modalities – Clinical examination, Imaging and Pathological examination. The triple assessment is 95-98% accurate in diagnosing breast cancer.

**Figure 4: Triple assessment**

### Box 3: Diagnostic evaluation - Do’s and Don’ts

- **Watch out!** If the lump has no definitive diagnosis and there is a chance of misdiagnosis, the 4th assessment is FOLLOWUP. The triple assessment is 95-98% accurate- “Always is always wrong, never is never right”. The approach to a breast lump is to prove it is not a cancer than to prove it is a cancer. **If a lump is not proven to be a cancer on triple assessment and the woman is at risk, it should be excised or followed up closely to prove it is not a cancer.**

- If there is a high index of suspicion mainly because age is over 30, even when triple assessment is negative, advise excision biopsy. Excisional biopsy should be performed in women with clinically suspicious lesions that are equivocal on imaging, FNA (fine needle aspiration), or CNB (core needle biopsy). Lumpectomy without a needle biopsy sometimes leads to an unprepared cancer diagnosis and makes further optimal cancer management difficult.

- Cystic lesions that resolve after FNA do not require further evaluation unless they recur. If CBE (clinical breast examination), FNA, and imaging indicate benign disease, the CBE should be repeated in four to six weeks.
Mammography

Mammography is a breast imaging modality that uses low dose X-rays to detect early breast carcinoma. A typical benign lesion is seen as an oval, well circumscribed, low density lesion with scattered benign appearing calcification and no architectural distortion. (Fig. 6,7)

A malignant lesion, on the other hand, has an irregular shape with spiculated margins, is usually of high density with malignant appearing calcifications and surrounding architectural distortion (Fig. 8,9,10). In addition, malignant lesions may have other associated findings such as focal skin thickening, skin and nipple retraction and axillary lymphadenopathy.

Benign calcifications typically include track-like vascular calcification, egg shell/rim calcification, popcorn calcification, rod like calcification along the axis of the duct, scattered punctuate calcifications (Fig. 5,8) and skin/dermal calcification. Calcification that raises suspicion of malignancy include amorphous calcification (without a definite shape), fine pleomorphic calcification typically in a segmental distribution and fine linear branching calcification.

### Table 3: Characteristics of benign and malignant lesions in a mammograph

<table>
<thead>
<tr>
<th>BENIGN</th>
<th>MALIGNANT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well circumscribed, smooth margins</td>
<td>Spiculated, ill defined margins</td>
</tr>
<tr>
<td>Macrolcalcifications are large, coarse</td>
<td>Microcalcifications are linear, branching or pleomorphic</td>
</tr>
<tr>
<td>Scattered calcifications</td>
<td>Tightly clustered calcifications</td>
</tr>
<tr>
<td>Long axis of the lesion may be along the normal tissue plane</td>
<td>May not be so</td>
</tr>
<tr>
<td>Contains fat</td>
<td>Not commonly seen</td>
</tr>
<tr>
<td>No architectural distortion</td>
<td>Architectural distortion commonly seen</td>
</tr>
</tbody>
</table>

Pathology

The most common histopathological type is infiltrating ductal carcinoma of no special type. Special histological types are mucinous, tubular, papillary and medullary often indicating a better prognosis. The infiltrating lobular type is rarer and treatment is same as for infiltrating ductal carcinoma. Other rare breast malignancies include malignant phyllodes tumor, sarcoma and lymphoma.

Post diagnosis evaluation is needed to know the type of breast carcinoma. The four prognostic subtypes based on receptors ER (estrogen receptor), PR (progesterone receptor), HER2/neu are

a) ER positive, PR positive, HER2/neu negative
b) ER positive, PR positive, HER2/neu positive (triple positive)
c) ER negative, PR negative, HER2/neu positive
d) ER negative, PR negative, HER2/neu negative (triple negative)

Recently, the following molecular subtypes based on gene expression profiles have been identified -

a) Luminal A (best prognosis)  b) Luminal B  c) Her2/neu enriched d) Basaloid (worst prognosis)

These gene mutation typified cancer types closely resemble the preceding receptor based classification which can be used as a simpler, cost effective surrogate for treatment planning and prognostication.15
Figure 5 - scattered popcorn calcifications in the right breast – typical of benign calcification, Figure 6 - Oval, well circumscribed mass in the upper outer quadrant of the right breast measuring ~ 15.5 x 9 mm, No obvious calcification. - suggestive of a benign lesion such as fibroadenoma. Figure 7 shows a 5.5 x 4.5 cm, well defined homogenous mass in the upper outer quadrant of the left breast – suggestive of a benign lesion (biopsy proven hamartoma).

Figure 8 shows typical pleomorphic and branching tubular clustered calcifications (arrow) with associated underlying focal asymmetry in the left breast – characteristic of malignant calcification (biopsy proven invasive ductal carcinoma). Figure 9 shows an ill defined, spiculated mass (arrow) in the left lower quadrant with surrounding architectural distortion highly suggestive of malignancy (biopsy proven invasive ductal carcinoma). Figure 10 shows a 26 x 18 mm speculated mass with a few microcalcifications in the right upper outer quadrant (black arrow) with overlying focal skin thickening and nipple retraction (white arrow) – characteristic of malignancy (biopsy proven invasive ductal carcinoma). There is another 15 mm irregular mass in the upper inner quadrant, also suspicious for malignancy.
Management of Breast Cancer

What is the current management of breast cancer?

Breast cancer has a systemic and a local component. It therefore requires both systemic and local treatment. Local treatments are surgery and radiation therapy. Systemic treatment involves chemotherapy, biological and hormonal therapy.

- Stage I and Stage II can be considered as ‘early-stage breast cancer’
- Stage III is locally advanced breast cancer
- Stage IV is metastatic breast cancer (spread to the body systems)

The prognosis depends upon the stage and the systemic disease determines survival. Therefore the dictum for modern treatment is less local and more systemic treatment to improve the outcome for the patient.

In general, management of ‘early-stage breast cancer’ involves surgery (mastectomy or breast conservation surgery) followed by adjuvant therapy which includes adjuvant chemotherapy, radiotherapy and endocrine therapy based on the histopathological report.

The management of locally advanced breast cancer management includes neoadjuvant (upfront) chemotherapy to reduce the size of disease and make it amenable to surgery. Following surgery, the patient receives adjuvant (additional) chemotherapy, radiotherapy and endocrine therapy if hormone receptor (ER = estrogen receptor) positive.

<table>
<thead>
<tr>
<th>Stage Grouping</th>
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</thead>
<tbody>
<tr>
<td>Stage 0</td>
</tr>
<tr>
<td>Stage I</td>
</tr>
<tr>
<td>Stage IIA</td>
</tr>
<tr>
<td>Stage IIB</td>
</tr>
<tr>
<td>Stage IIIA</td>
</tr>
<tr>
<td>Stage IIIIB</td>
</tr>
<tr>
<td>Stage IV</td>
</tr>
</tbody>
</table>

*Note: Stage designation may be changed if postsurgical imaging studies reveal the presence of distant metastases, provided that the studies are carried out within 4 months of diagnosis in the absence of disease progression and provided that the patient has not received neoadjuvant therapy.*

Staging:

TNM classification is widely used according to American Joint Committee on Cancer and the International Union for Cancer Control (AJCC-UICC)

**T-TUMOR**

- T0: No evidence of primary tumor
- T1: Up to 2 cm in size
- T2: >2 up to 5 cm in size
- T3: More than 5 cm in size
- T4: Tumor of any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)
  - T4a: Extension to the chest wall, not including only pectoralis muscle adherence/invasion
  - T4b: Ulceration and/or ipsilateral satellite nodules and/or edema (including peau d'orange) of the skin, which do not meet the criteria for inflammatory
  - T4c: Both T4a and T4b
  - T4d: Inflammatory carcinoma

**N-NODE**

- N0: No nodes
- N1: Metastases to movable ipsilateral level I, II axillary lymph node(s)
- N2: Metastases in ipsilateral level I, II axillary lymph nodes that are clinically fixed or matted; or in clinically detected ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastases
- N3: Metastases in ipsilateral infraclavicular (level III axillary) lymph node(s) with or without level I, II axillary lymph node involvement; or in clinically detected ipsilateral internal mammary lymph node(s) with clinically evident level I, II axillary lymph node metastases; or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement

**M-METASTASIS**

- M0: No clinical or radiographic evidence of distant metastases
- M1: Distant detectable metastases as determined by classic clinical and radiographic means and/or histologically proven larger than 0.2 mm
Local therapy

**Principles of Surgery**

In early stages of breast cancer, surgery is the principal modality of treatment. It can be either breast conservation surgery or modified radical mastectomy. Breast conservation surgery (See box 4) involves removal of only the involved breast tissue with adequate margins along with axillary lymph node biopsy or dissection. Modified radical mastectomy involves removal of the entire breast tissue and axillary lymph nodal biopsy or dissection.

Sentinel lymph node biopsy is indicated in selected patients such as clinically node-negative, invasive breast cancer and may also be considered for ductal carcinoma in situ (DCIS). It involves the use of an isotopic tracer like Technetium sulfur colloid and/or blue dyes like isosulfan blue and methylene blue to identify the first draining nodes in the axilla at the time of surgery. It is recommended to remove up to 4 nodes for an accurate prediction that there is no lymph nodal metastasis.\(^\text{16}\)

**Box 4: Breast conservation surgery**

Breast conservation surgery involves removal of only the involved breast tissue with adequate margins along with axillary lymph node biopsy or dissection. Breast tissue that is not involved by tumour is conserved. Breast conservation surgery will require adjuvant radiotherapy irrespective of the stage.

**Indications:** The decision to do breast conservation surgery in early breast cancer depends upon

1. Patient choice
2. The tumor: breast ratio
3. When adequate cosmesis can be achieved with adequate tumour-free margins in a compliant patient.

**Absolute contraindications:**

1. Multicentric breast cancer (tumors in more than one quadrant) or
2. Diffuse malignant appearing microcalcifications
3. Prior therapeutic radiation to the breast region, such as mantle radiation for Hodgkin’s lymphoma, is considered an absolute contraindication.\(^\text{16}\)

**Principles of radiotherapy**

Radiotherapy is an integral part of breast cancer treatment. It involves the use of megavoltage X-rays or Gamma rays to irradiate the whole breast or the chest wall and the supraclavicular region. Radiation therapy is usually given after the completion of adjuvant chemotherapy.

- Following breast conservation surgery, all patients should receive adjuvant radiotherapy to the breast.
- Following mastectomy, radiotherapy is indicated in locally advanced disease and in cases of node positive disease.

In the conventional technique, radiation is delivered using two opposing beams tangential to the chest wall up to a dose of 50 Gy in 25 fractions. The similar dose and beams are used for conserved whole breast followed by a boost of extra radiation dose to the tumor bed. The supraclavicular region is included in radiation portal in cases of node positive axilla and in advanced T stages. The axilla is not usually included in the portals unless until there is gross residual disease in axilla or extra-nodal extension.\(^\text{18}\)

Presently newer hypo-fractionation schedules have come up in which fewer fractions of higher doses (eg: 40 Gy in 15 fractions) are used which implies, treatment will be completed in a shorter time interval with similar cosmetic outcome.\(^\text{19}\)

**Complications associated with local treatment and their management**

- **Minor complications:** observed post mastectomy include wound dehiscence, flap necrosis and seroma (accumulation of clear interstitial fluid in the wound) formation, axillary pain syndromes and shoulder stiffness. It is advisable to keep closed suction drains with waterproof dressing until there is a stable low output of serous fluid (<50 ml) in the drain to reduce the incidence of seroma formation. Poor cosmetic outcome of conserving surgery is usually due to improper patient selection or surgical technique.
- **Post radiotherapy long term side effects:** include skin changes like fibrosis and pigmentation, and rarely cardiac toxicity (in left sided breast cancers) and pulmonary toxicity.
• **Lymphedema**: in the upper limb is a common long term sequel of both surgery and radiotherapy. A CMC study (unpublished) found an incidence of 25.2% at one year follow up. Management involves the expertise of doctor, nurse and physiotherapist. Prevention strategies include avoidance of trauma and infection in the arm. The patient should return to all normal non-strenuous household or employment activity after 6 weeks to encourage lymphatic drainage in the limb. Early detection of lymphedema by measuring girth is important and treatment includes upper limb and shoulder exercises, manual lymphatic drainage (massage) and bandaging in more advanced cases.  

**Systemic Therapy**

**Principles of chemotherapy**

Almost all patients benefit from chemotherapy. The exceptions are very early cancers with low risk of metastasis, certain low risk tumours responsive to hormonal therapy and patients with co-morbidities at higher risk of serious side effects. In patients with early breast cancer, prognostic features such as size, lymph node status, biologic features including ER status, HER2/neu status, and pathologic grade determines the need for adjuvant chemotherapy. Also in the present era, genomic analysis like Oncotype Dx and MammaPrint may be of use in deciding the need for chemotherapy in low risk ER positive cancers.  

In the initial era of chemotherapy, first generation drugs including cyclophosphamide, methotrexate, 5-fluorouracil (CMF) were used. After the introduction of anthracyclines, they have become an integral part of combination chemotherapy regimens like CAF (Triple drug) and AC (Two drugs). The ‘taxanes’ are also added especially in node positive and receptor negative tumours. Traditionally, a 3 week recovery period from bone marrow suppression has been advised between chemotherapy doses; however, ‘dose dense’ schedules with shortened intervals are used in the younger age group.

**Principles of hormonal therapy**

Hormonal therapy is advocated in patients with either ER/PR positive population. Tamoxifen (a selective estrogen receptor modulator) is used preferably in premenopausal women. Aromatase inhibitors (AIs) like letrozole or anastrazole are used in postmenopausal setting. Other hormonal agents like exemestane and fulvestrant are used in a second line setting. Patients taking tamoxifen should continue taking the drug for atleast 5 - 10 years or switch over to another agent if menopausal status achieved.

**Targeted therapy with monoclonal antibodies against Tyrosine Kinase receptor HER-2**: Patients with amplified HER2/neu status can be offered monoclonal antibody treatment with trastuzumab for a period of at least one year in either neoadjuvant or adjuvant setting based on the stage of the disease.

**Management of Recurrent and Metastatic breast cancer**

Locally recurrent breast cancer may be considered for re-excision if feasible followed by reconstruction of the defect. Metastatic breast cancer is primarily managed using palliative systemic chemotherapy, though surgical excision has been used in selected cases of isolated metastasis successfully. The most active classes of drugs include anthracyclines, taxanes, vinca alkaloids, alkylating agents, and antimetabolites. Endocrine therapy is the preferred option for women with hormone receptor–positive tumors who do not have significant systemic involvement. In contrast, systemic chemotherapy is typically reserved for women with hormone-refractory disease, hormone receptor–negative disease, and selected women with rapidly progressive or symptomatic visceral metastases. Patients with osseous metastases should receive bisphosphonates. Palliative radiotherapy may be employed in case of brain secondaries, painful metastases, impending spinal cord compression or if significant risk of pathological fracture is present. Palliative mastectomy can be considered for fungating or painful breast cancer primary lesions.

**References:**


