BREAST CANCER

EPIDEMIOLOGY

- Collectively, US, India and China account for almost one third of the global breast cancer burden.
- India has a long way to go!
- See the images below and listen to the discussion and you will understand why.

SOURCE: HTTP://GLOBOCAN.IARC.FR

Breast Cancer

Estimated Incidence, Mortality and Prevalence Worldwide in 2012

Estimated numbers (thousands)	Cases	Deaths	5-year prev.
World	1677	522	6255
More developed regions	794	198	3224
Less developed regions	883	324	3032
WHO Africa region (AFRO)	100	49	318
WHO Americas region (PAHO)	408	92	1618
WHO East Mediterranean region (EMRO)	99	42	348
WHO Europe region (EURO)	500	143	1960
WHO South-East Asia region (SEARO)	240	110	735
WHO Western Pacific region (WPRO)	330	86	1276
IARC membership (24 countries)	940	257	3614
United States of America	233	44	971
China	187	48	697
India	145	70	397
European Union (EU-28)	387	91	1467

SOURCE: HTTP://GLOBOCAN.IARC.FR

International Agency for Research on Cancer

World Health Organization

- / +

Year: 2012

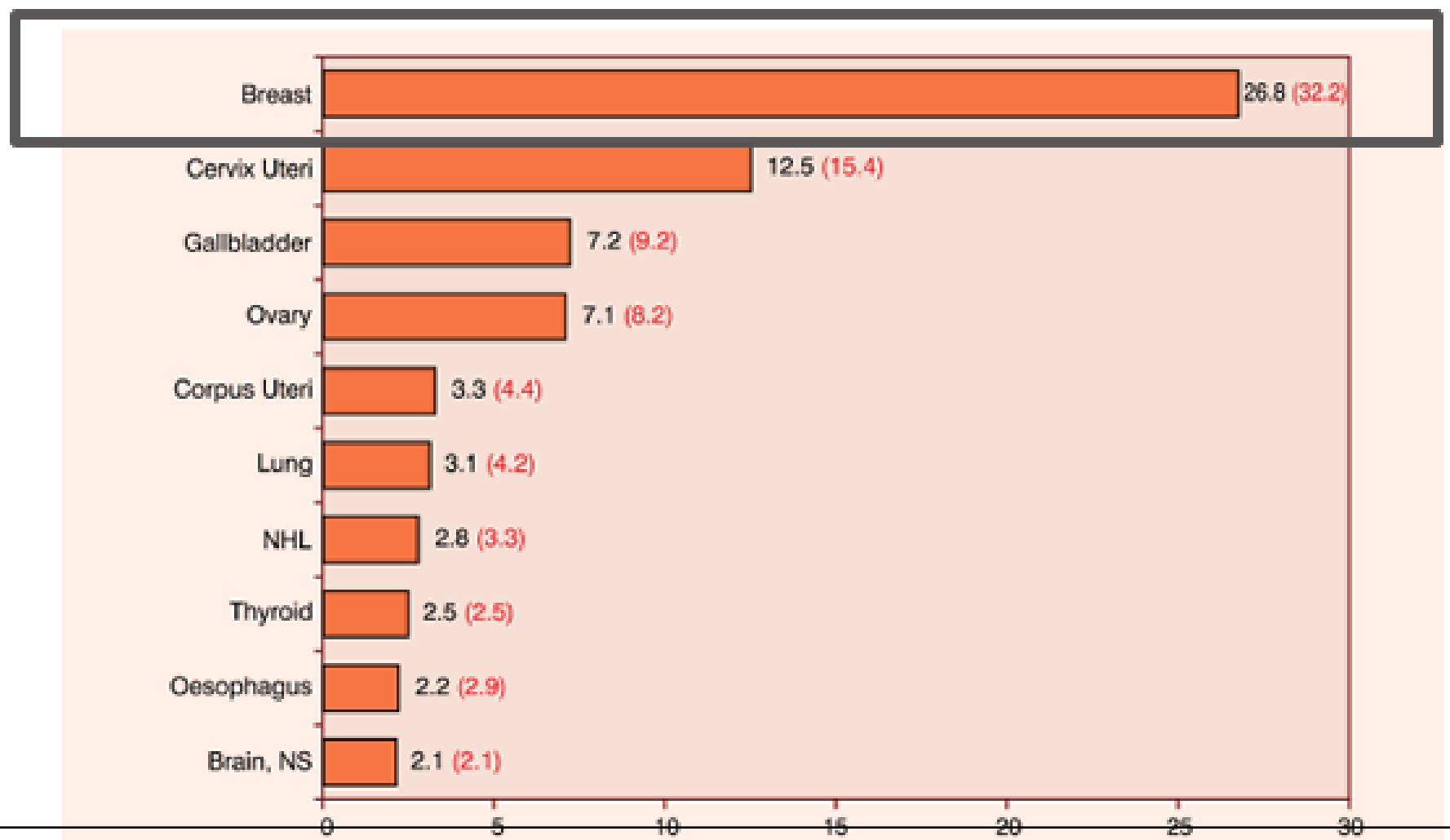
Metric	Country	Count	ASR/P
C50 : Breast			
Incidence - Female	India	144,937	25.8
	United States of America	232,714	92.9
	China	187,213	22.1
Mortality - Female	India	70,218	12.7
	United States of America	43,909	14.9
	China	47,984	5.4
Prevalence (5yr) - Female	India	396,991	92.6
	United States of America	970,693	753.7
	China	697,327	129.3

Three-Year Report of the PBCRs: 2009-2011 Leading Sites of Cancer

Fig. 2.6: Ten Leading Sites of Cancer - Delhi (2008-2009)

Age Adjusted Incidence Rates given in parentheses

Females



SOURCE : THREE YEAR REPORT OF THE PBCR'S : 2009 - 2011. NCRP. ICMR. GOVT. OF INDIA

?

- Why is the mortality so high?
- more patients turn up in later stages.

- What are the reasons for late presentations?
- lack of awareness,
- shyness on part of patients,
- social stigma,
- ignorance of doctors

So what do we learn today?

WHO prediction for breast cancer in India

- For the years 2015, there will be an estimated 1,55,000 new cases of breast cancer and about 76000 women in India are expected to die of the disease. The gap only seems to be widening, which means, we need to work aggressively on early detection.

RISK FACTORS

- Three main groups:
- Major
- Intermediate and
- Minor

Major risk factors

- **Gender**

❖100 times more common in women than in men.

- **Age**

❖Very rare before the age of 20 and rare below 30 years.

❖The incidence of breast cancer doubles every 10 years until the menopause.

- **Previous breast cancer**
- **Family history and genetic predisposition**

Intermediate risk factors

- **Diet and alcohol intake**
- **Endocrine factors**

➢Increased duration of exposure to endogenous estrogens.

➢Early age of menarche (age< 12), late age of menopause (> 55), and late age at first pregnancy (> 30),nulliparity,HRT,OCPs.

➢Lifetime number of menstrual cycles.

- **Irradiation**

Minor and controversial risk factors

- **Body size**
- **Stress**

Genetics of breast cancer

BRCA 1

BRCA 2

- BRCA-1 is located on chromosome 17q.
- BRCA-1–associated breast cancers are invasive ductal carcinomas, are poorly differentiated, and are hormone receptor–negative.
- BRCA-2 is located on chromosome 13q .
- BRCA-2–associated breast cancers are invasive ductal carcinomas, are well differentiated and express hormone receptors.

PATHOLOGY

Why?

- Paramount importance in establishing the diagnosis of the tumour.
- It also helps determine the patient's prognosis
- There are many methods of pathologically classifying breast cancer; most are based on whether the tumour is **invasive or non-invasive** and whether it is derived from the **duct** system or the **lobule.**

Ductal carcinoma of the breast

Most common form of breast cancer accounting for 85 to 90 per cent of all cases.

Lobular carcinoma of the breast

subdivided into *in situ and invasive forms*

Clinical scenarios

- A 38 years old lady (with a history of breast cancer in her sister) presented with a 4 cm lump in her right breast which turned out to be a cancer and had a few enlarged axillary nodes. She had noticed the lump only a few months back. However, on evaluating all past records, doctor found one mammogram done 2 years back (was advised by her gynecologist), just for screening; she did not have any lump or other symptom then. In that mammogram, there was a small area of stippled microcalcification, which was very suspicious (Stippled microcalcifications are pathognomonic for cancer) . The radiologist had also mentioned it in the report. But since there was no palpable lump, her gynecologist told her, not to worry. She didn't do anything for that for the next 2 years, and finally, was detected with cancer in the same site, in a minimum of clinical stage 2B. Finally after surgery, 5 (out of 27) nodes were positive for cancer and this placed her in stage **3A.** So please understand here, the gynecologist advised the mammogram, but did not not know how to interpret or act, and the lady, who would have otherwise been detected with cancer of stage 1 and would have had more than 90% chance of 10 years survival, now ended up with stage 3A and will have about 60% chance of 5 year survival. So two years of wait have definitely decreased her life by 5 years.

- A 32 years old lady presented with a history of heaviness in breast before the periods as well as pain in the breast for a few days before the periods. On clinical examination, breasts were normal, except for slightly engorged. Again here, her family doctor had advised her mammography (I wouldn't have advised her mammography, if at all needed, I would have gone for an ultrasound of the breast first). On the ultrasound which was done with the mammogram, there were multiple cysts of varying sizes in both the breasts, from few millimetres to 8 to 9 millimetres. She was overtly worried about cancer, and had already taken opinion from one surgeon and one gynecologist. One had advised surgery (!!) and the other had given some non specific medications. All the doctor did was to reassure her, that this was nothing to worry about (She was visibly more worried about the cancer than the symptoms of pain and heaviness she had). The doctor assured her that this was not cancer, this did not require surgery, this occurs in many women of her age - some have more symptoms while some have less symptoms, and that over a period of time, it will all settle. Gave her some symptomatic medications and some vitamin supplements and believe me, after three months, she was almost settled of symptoms and was very happy. Not that medications worked or something, but it was the re assurance that worked.

CLINICAL FEATURES

- A lump
- Changes in the skin may be the sole presenting symptom.
- Puckering .
- Peu d'orange .
- Ulceration .
- Nipple distortion and inversion .
- A unifocal or bloodstained nipple discharge.

Diagnosis

- ***Fine-needle aspiration cytology***
- ***Core biopsy***
- **Mammography**

TNM definitions

Primary Tumour

- Tx – Primary tumour cannot be assessed
- To – No evidence of primary tumor
- Tis – Carcinoma in situ
- T1 – Tumor 2 cm or less
- T2 – 2 – 5 cm tumor
- T3 – Tumor 5 cm and above
- T4 – Extn. to chest wall / skin

Regional lymph node involvement - clinical

NX – Regional lymph nodes cannot be assessed.

No – No regional lymph nodes.

N1 – Movable ipsilateral axillary nodes.

N2 – Fixed ipsilateral axillary nodes.s

N3 – Ipsilateral internal mammary nodes

Regional lymph node involvement - pathological

- pNX – Regional lymph nodes cannot be assessed.
- pNo – No regional lymph node metastasis.
- pN1 – Movable ipsilateral axillary node metastasis.
  - pN1a – Micrometastases (< 0.2 cm)
  - pN1b – Metastases (> 0.2 cm)
    - i) 1 – 3 nodes
    - ii) 4 or more nodes
    - iii) extending beyond the capsule (< 2 cm)
    - iv)Metastases to nodes (> 2 cm)
- pN2 - Fixed ipsilateral axillary nodes
- pN3 – Ipsilateral internal mammary nodes

Distant Metastases

- Mx – Distant metastases cannot be assessed.
- Mo – No distant metastases.
- M1 – Distant metastases (ipsilateral supraclavicular lymph nodes)

AJCC / UICC Stage grouping

• St 0 -	Tis	No	Mo
• St 1 –	T1	No	Mo
• St 2a			
	To	N1	Mo
	T1	N1	Mo
	T2	No	Mo
• St 2b			
	T2	N1	Mo
	T3	No	Mo

AJCC / UICC Stage grouping

- St 3a

To	N2	Mo
T1	N2	Mo
T2	N2	Mo
T3	N1	Mo
T3	N2	Mo

- St 3b

T4	any N	Mo
any T	N3	Mo

- St 4

any T	any N	M1

STAGING

- **The Manchester system (1940)**
- **Stage I**. Tumour confined to breast. Any skin involvement covers an area less than the size of the tumour.
- **Stage II**. Tumour confined to breast. Palpable, mobile axillary nodes.
- **Stage III**. Tumour extends beyond the breast tissue because of skin fixation in an area greater than the size of the tumour or because of ulceration. Tumour fixity underlying fascia.
- **Stage IV**. Fixed axillary nodes, supraclavicular nodal involvement, satellite nodules or distant metastases.

MANAGEMENT

Management of non-invasive breast cancer

Stage 0

LCIS

- Because LCIS is considered a marker for increased risk rather than an inevitable precursor of invasive disease, the current treatment of LCIS is **observation with or without tamoxifen.**
- The goal of treatment is to prevent or detect at an early stage the invasive cancer.
- There is no benefit to excising LCIS, as the disease diffusely involves both breasts and the risk of invasive cancer is equal for both breasts. The use of **tamoxifen as a risk-reduction strategy** should be considered in women with a diagnosis of LCIS.

DCIS

- Women with DCIS and evidence of widespread disease (two or more quadrants) require mastectomy.
- For women with limited disease, lumpectomy and radiation therapy are recommended.
- Low-grade DCIS of the solid, cribriform, or papillary subtype, which is less than 0.5 cm in diameter, may be managed by lumpectomy alone.
- Adjuvant tamoxifen therapy is considered for all DCIS patients.

- **Simple mastectomy**
- 95% cure rate
- Rarely relapse, due to micro-invasive cancer
- No need for axillary dissection
- **Wide excision alone**—30% recurrence at 5 years
- **Wide excision + radiotherapy**—15% recurrence at 5 years

Early Invasive Breast Cancer

Stage I, IIa, or IIb

T1–3, N0–1 tumors.

- Treatment of the breast and axilla
- Pathological staging to direct adjuvant therapy
- Adjuvant therapy—endocrine, chemotherapy, radiotherapy
- Follow-up

Breast surgery

- **Quadrantectomy** removes the primary cancer with a margin of 2.0 cm of normal breast tissue.
- **Lumpectomy** is the removal of the tumour mass with a limited portion of normal tissue (1 cm).
- **MRM**

INDICATIONS OF BCS

- T1,T2lesions, N0/N1,M0 disease.
- Tumor>4cm in a large breast.
- Single clinical and mammographic lesion.
- Patient should be willing tomaccept the chances of recurrence.

CONTRA INDICATIONS OF BCS

- T4,N2 Lesions
- Patients choice
- Multifocal/Multicentric disease
- Tumor size high as compared to breast size.
- Extensive calcification on mammography
- Pregnancy
- Persistent positive margins
- Patient’s contraindication to radiotherapy.

Treatment of the axilla

- Surgery
- —sentinel node biopsy:
- —removal of first node which contains secondary deposit
- —use either blue dye or 99MTc colloid
- —negative sentinel node avoids clearance

Loco-regional radiotherapy

- Reduce the risk of local recurrence after BCS
- Irradiation of axilla—not required if clearance performed
- Radiation to axilla may cause lymphodema and brachial neuropathy

Adjuvant endocrine therapy

- 60% of breast cancers are oestrogen receptor positive
- **Ovarian ablation**
- Side-effects of tamoxifen—menopausal symptoms
- —endometrial cancer, 4-fold increase in risk
- **LHRH agonists**

Adjuvant chemotherapy

- CMF (cyclophosphamide, methotrexate, 5FU)
- Anthracycline regimes may be better
- Taxanes based regimes

Management of locally advanced breast cancer

Stage IIIa or IIIb

- The probability of metastatic disease is high (>70%).
- A combination of neoadjuvant chemotherapy, surgery and radiotherapy is commonly used.

Management of metastatic breast cancer

- Aim is palliation
- If hormone-sensitive, bony disease—may survive years .
- Visceral, ER-negative disease has bad prognosis
- Usual sites—lung, liver, bone, brain
- Rare sites—choroid, pituitary
- Combination of endocrine therapy, chemotherapy, radiotherapy and symptomatic tt is given.

SENTINAL LYMPH NODE BIOPSY

SENTINEL NODE CONCEPT

Based on the hypothesis lymph flow is orderly, predictable & tumor cells spread sequentially

Sentinel node is the first node encountered by the tumour cells

The sentinel node is in the direct pathway of the primary tumour

Advantages of sentinel node biopsy

- Minimally Invasive
- Low Cost
- low morbidity
- Nodal metastasis outside axilla detected
- obviates the need for ALND without compromising staging & local control

Disadvantages of Sentinel node Biopsy

- Has a False negative rate of 6% (ALND3%)
- Not useful in clinically involved axilla
- Not useful in pregnancy & lactation
- Cannot be done in multifocal / multicentric breast carcinomas
- Cannot be done in patients with previous breast surgery on the same side

Technique

Blue dye isosulfan blue (or)
technitium labelled colloidal albumin with gamma camera and probe can be used

Sub dermal injection

A single dose of 0.2 ml of the dye is injected at the tumour site sub-dermally one day prior to surgery

Peri tumour injection

Dye injected at four sites.
Larger volumes are given
Removal of dye or tracer is slower due to scanty lymph supply of breast parenchyma
imaged 1 to 2 hrs after injection

SENTINEL LYMPH NODE DISSECTION WITH DYE TECHNIQUE

Blue lymphatics leading to SLN are traced

Discolouration of breast and blue urine

ISOTOPE TECHNIQUE

Probe guided surgery is superior
Useful for intra-operative localisation
After removal of SLN probe is reapplied to site and radioactivity measured for confirmation

PIT FALLS IN SENTINEL NODE DISSECTION

- 6% FALSE NEGATIVE
- SKIP PHENOMENON & CHANGED FLOW DIRECTION
- INFILTRATION BY CARCINOMA
- FATTY DEGENERATION
- UPPER OUTER QUADRANT -CLOSE PROXIMITY TO SENTINEL NODE. SHINE THROUGH PHENOMENON-Breast to be retracted when probing

Special problems

SPECIAL PROBLEMS IN BREAST CANCER – PAGETS DISEASE

Rare before 30 years, peak between 50 & 60
Can occur in the male
Erythematous exudative or scaly lesion appears first on the nipple spreads to areola
Does not involve surrounding skin
Nipple retraction & nipple pigmentation & mass

D D for Pagets disease

Chronic Eczema
Malignant melanoma
Syphilitic chancre
Bowens disease
Mammary ductectasia

Mammography

Mass , sub areolar micro calcification or only thickening of nipple areola complex

Biopsy

Full thickness nipple biopsy or exfoliative scrape cytology

PAGETS TREATMENT

1) with palpable mass-
segmentectomy with 1.5 cm margin
with ALND with PO-RT
2)if resection margins positive or muticentric or solid or comedo type or high grade with necrosis
completion mastectomy is done

Pagets without palpable mass

Biopsy of nipple areola complex positive
first step: On mammo no occult mass.no microcalcification—do segmentectomy of nipple areola complex +RT without axillary dissection
Mammography + ve
Stereotactic needle localisation of occult mass or microcalcification with frozen section biopsy and proceed
Tamoxifen

BREAST CANCER IN PREGNANCY& LACTATION

DELAY IN DIAGNOSIS

1) firm ,nodular &hypertrophied breast
2) small tumours can be missed
3) present at advanced stage
4) high proportion of ER-ve
5) bad prognosis

BREAST CANCER IN PREGNANCY

Mammography

FALSE NEGATIVE rate is high due to high radiographic density of pregnant breast

BREAST CANCER IN PREGNANCY

Alkaline phosphatase is elevated in pregnancy

Chest X-ray is allowed with proper shielding

Bone scan

A) Stage 1 & 2-Bone mets uncommon scan not done

B)Stage 3 Especially with bone pain

Bone scan done in later stages of pregnancy or after pregnancy

BREAST CANCER IN PREGNANCY

Treatment

Modified Radical Mastectomy is the choice irrespective of the trimester

In the first & second trimester breast conservation with radiotherapy should not be done due to radiation induced anomalies in foetus

Study questions

- A 57-year-old woman undergoes core-needle biopsy of a breast mass. The pathologic diagnosis is infiltrating ductal carcinoma of the breast.
- **How will you stage this cancer?**
- **What are the important prognostic factors?**

A 49-year-old woman presents with a breast mass. You are examining the affected breast.

◆ **How would the following clinical findings affect the woman's prognosis?**

1. ***Red edematous breast with an underlying mass***
2. ***Edema of the skin overlying the mass***
3. ***Puckering of the skin overlying the mass***
4. ***Retraction of the nipple***
5. ***A 1.5-cm mass fi xed to the deeper tissues***
6. ***A lymph node palpable in the supraclavicular area***
7. ***A hard, fi xed lymph node in the ipsilateral axilla***
8. ***Arm edema***

- A 60-year-old woman has breast cancer and undergoes preliminary staging. The lesion is 1.5 cm in diameter, and no axillary nodes are palpable. A metastatic workup is negative.
- **What stage is this woman's cancer?**
- **What are this woman's surgical options, both for sampling the lymph nodes and treating the primary tumor?**

- A 38-year-old woman is scheduled for a mastectomy and sentinel node biopsy. She is concerned about her appearance and would like to know her options for breast reconstruction.
- **What options should you offer?**

- A 38-year-old woman presents with a 3-month history of a progressively enlarging breast mass. At the time she sees you, she has a 6- 7-cm fi xed mass, with erythema and edema on the upper, outer aspect of her right breast. Clinically, her axilla is positive with enlarged, firm lymph nodes.
- **What is the suspected diagnosis?**
- **What histologic features are typical of this condition?**
- The surgeon confirms the physical findings and obtains a punch biopsy of the mass. Pathology reveals inflammatory carcinoma. Estrogen and progesterone receptors are negative.
- **What is the recommended treatment?**

- A 55-year-old woman has a modified radical mastectomy for a stage II carcinoma of the breast.
- ***A small, 0.5-cm nodule in the suture line 5 years after surgery.***
- ***A mammographic abnormality in the opposite breast***
- ***Elevated liver function studies***
- ***A fracture of the femur***