Women's health and Cancer

- Cancer Overview (from the WHO)

Cancer Death Rates* Among Women, U.S., 1930-2004

*Age-adjusted to the 2000 US standard population.

Estimated Cancer Deaths in Women – 2012 (ACS)

- 29% Lung & bronchus = 72,590
- 14% Breast = 39,510
- 9% Colorectal = 25,700
- 7% Pancreas = 18,540
- 6% Ovary = 15,500
- 4% Leukemia = 10,040
- 3% Non-Hodgkin Lymphoma = 8,620
- 2% Liver/Bile duct = 6,570
- 2% Brain & CNS = 5,890
Trends - Cancer Incidence among Women by Race/Ethnicity, 1999-2008

- **All Women**
  - Significant decreases in:
    - Breast cancer: 1.2% per year
    - Cervical cancer: 2.3% per year
    - Ovarian cancer: 1.7% per year
  - Significant increases in:
    - Melanoma of the skin: 2.5% per year
  - Remained unchanged: Lung cancer

- **Black Women**
  - Significant decreases in:
    - Cervical cancer: 3.6% per year
  - Remained unchanged:
    - Lung cancer, Ovarian cancer, Melanoma, Breast cancer

- **Hispanic Women**
  - Significant decreases in:
    - Cervical cancer: 3.3% per year
  - Remained unchanged:
    - All others

- **Asian/Pacific Islander Women**
  - Significant decreases in:
    - Cervical cancer: 3.0% per year
  - Remained unchanged:
    - All others

Good news: death rates are declining
Bad news: "rates for the least educated are 2 ½ times higher than for the most educated" ACS

Trends in the Number of Cancer Deaths Among Men and Women, US, 1930-2005

Death rates higher for men due to differences in tumor behavior, late detection, and presence of other illnesses. (AACR)

2012 Estimated US New Cancer Cases

Men: 848,170

- Lung & bronchus: 14%
- Prostate: 29%
- Colon & rectum: 9%
- Pancreas: 3%
- Oral cavity & pharynx: 3%
- Leukemia: 3%
- Melanoma: 5%
- Urinary bladder: 7%
- Non-Hodgkin lymphoma: 4%
- Kidney & renal pelvis: 5%
- All other sites: 18%

Women: 790,740

- Lung & bronchus: 14%
- Breast: 29%
- Colon & rectum: 9%
- Thyroid: 5%
- Ovary: 3%
- Non-Hodgkin lymphoma: 4%
- Kidney & renal pelvis: 3%
- Uterine corpus: 6%
- Pancreas: 3%
- Melanoma: 4%
- All other sites: 29%

Source: American Cancer Society, 2013.
Cancer basics:
- Abnormal cell division
- Due to mutations in DNA

Breast Cancer Overview

II. Breast Cancer Statistics

Breast cancer is the second leading cause of cancer-related deaths in women today.
- 39,620 women were expected to die of BC in 2013.
- Death rates have steadily decreased since 1990, due to earlier detection.

Most commonly diagnosed cancer among women worldwide (excluding nonmelanoma skin cancers):
- 296,980 women new cases in 2013.
- 1/8 chance during your lifetime of developing breast cancer (if you live to age 80).
- The incidence has decreased over the past decade – due to a reduction in the use of hormone replacement therapy for menopausal symptoms.

Male breast cancers account for approximately 1% of all breast cancer cases.
- 2,240 men will be diagnosed with breast cancer this year.
A. Life-time risks of developing BC

<table>
<thead>
<tr>
<th>Age</th>
<th>Probability of Developing Breast Cancer Within 10 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>0.44%</td>
</tr>
<tr>
<td>40</td>
<td>1.47%</td>
</tr>
<tr>
<td>50</td>
<td>2.38%</td>
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<tr>
<td>60</td>
<td>3.56%</td>
</tr>
<tr>
<td>70</td>
<td>3.82%</td>
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</tbody>
</table>

**Age is a factor!**


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B. Ethnic Profile

- White and African-American women have the highest incidence of invasive breast cancer in the US.
- African-American women are more likely to develop premenopausal breast cancer; 79% 5 year survival rate compared to 92% survival rate.
- African-American have the highest death rate from breast cancer and are more likely to be diagnosed with a later stage of breast cancer than White women.

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C. Cases of BC Worldwide

- Top 4 countries - Belgium, Denmark, France, Netherlands (US ranks #9)
- The risk of getting breast cancer worldwide is lowest in western Africa and eastern Asia.
- But studies show women can take on the breast cancer risk of the country they move to within as little as one generation.

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What factors increase a woman’s risk of BC?

- Genetic mutations in certain genes: BRCA1, BRCA2, and others (HIGH)
- Family history (HIGH), two or more 1st degree relatives
- Radiation Therapy between age 10-30 (HIGH)
- Mammographic breast density (extremely dense or unevenly dense) Moderate
- Family history (Moderate) one 1st degree relative
- Reproductive and menstrual history (Moderate)
- Alcohol consumption – 2 drinks per day (Low)
- Long-term use of hormone replacement therapy (Low)
- Post-menopausal Obesity (Low)
- Race & Socioeconomic status (Low)

Inherited BC

A. BRCA1 and BRCA2 most common genes related to hereditary BC
   - Autosomal dominant pattern
   - 5-10% of all breast cancers are inherited
   - Multifactorial!!!
   
   **It is estimated that 86% of the women with a mutation in the BRCA-1 gene will develop breast cancer by age 70.**


B. Other Genetic Factors

- Other genes whose products normally interact with the BRCA1 or BRCA2 proteins, and contribute to their normal function, may be more frequently altered in sporadic forms of breast cancer
- Variations of the EMSY, ATM, CHEK2, and RAD51 genes increase the risk of developing breast cancer.
C. Spontaneous BC

**STUCK ACCELERATOR and/or BRAKE FAILURE**
- p53
- HER2/cerbB-2/neu
- ERα/ERβ

III. Types of Breast Cancer

- Majority (over 80%) begins in either the milk ducts (DUCTILE cancer) or the lobular (milk-producing) tissue (LOBULAR cancer)
- Either type, if diagnosed early enough, may be called “in situ”
- Invasive: cancers started in the lobules or ducts of the breast but have broken through the duct or glandular walls to invade the surrounding tissue of the breast
  - Regional v. Distant

1. **Lobular carcinoma in situ (LCIS):** It is a lesion found in the milk-glands that has not spread. Although not a true cancer, it may increase the risk of developing into cancer later - increases the risk (10%-20%)
2. **Ductal carcinoma in situ (DCIS):** This is breast cancer at its earliest stage that has not spread. Detected by mammography. Nearly 100% of women with cancer at this stage can be cured.
3. **Invasive lobular carcinoma (ILC):** This cancer starts in the milk glands (lobules), breaks through the wall of the gland and invades the fatty tissue of the breast. Accounts for 15-20% of all breast cancers.
4. **Invasive ductal carcinoma (IDC):** This cancer starts in the milk ducts, breaks through the wall of the duct, and invades the fatty tissue of the breast. IDC is the most common type of breast cancer, as it accounts for nearly 80% of breast cancer.
Stages of Breast Cancer

Stage 0 (called carcinoma in situ) refers to abnormal cells lining a gland in the breast (Lobular carcinoma in situ or LCIS) or abnormal cells lining a duct (Ductal carcinoma in situ or DCIS).

Stage I early stage breast cancer where the tumor is less than 2 cm across and hasn’t spread beyond the breast.

Stage II early stage breast cancer where the tumor is either less than 2 cm across and has spread to the lymph nodes under the arm; or the tumor is between 2 and 5 cm; or the tumor is greater than 5 cm and hasn’t spread outside the breast.

Stage III locally advanced breast cancer where the tumor is greater than 5 cm across and has spread to the lymph nodes under the arm; or the cancer is extensive in the underarm lymph nodes; or the cancer has spread to lymph nodes near the breastbone or to other tissues near the breast.

Stage IV metastatic breast cancer where the cancer has spread outside the breast to other organs in the body.

IV. Detection of BC

Symptoms: early stage - none, as it progresses the most common sign is a painless mass
- Breast pain, persistent changes to the breast (thickening, swelling, distortion), nipple abnormalities, or tenderness.
- Critical - become familiar with the appearance and feel of your breasts so you can promptly report any changes!

Self-awareness is thought to be more effective for detecting breast cancer than a monthly breast self-exam

1) CBE – every 3 years for 20s-30s, annually >40
2) Mammogram
3) Ultrasound: best test for distinguishing a cyst from a solid tumor
4) MRI – high false +, useful in determining if cancer has spread to lymph
5) Ductile lavage & Ductoscopy

ACS recommendations:

- A clinical breast exam should be part of a periodic health exam, about every 3 years for women in their 20s and 30s, and every year for women 40 and older.
- Yearly mammograms are recommended starting at age 40.
- Women should know how their breasts normally feel and report any breast changes promptly to their health care providers.
- Annual screening MRI is recommended for women with an approximately 20%-25% or greater lifetime risk of breast cancer, including women with a strong family history of breast or ovarian cancer; BRCA mutation +.
- If lifetime risk is <15%, ACS is against MRI Screening.

Overdiagnosis and overtreatment as a result of cancer screening are a major concern. It is estimated that for every 100 women who are told they have breast cancer, as many as 30 have cancers that are so slow-growing they are unlikely even to be life-threatening.” Parker-Pope, 2009
Continued declines in mammography use might result in increased breast cancer mortality.

Computer-aided detection (CAD) mammogram

85% of breast cancers begin in the duct

Ductoscopy:
(A) Normal mammary ducts,
(B) Intraductal papilloma
(C) DCIS.

Al Sarakbi et al. International Seminars in Surgical Oncology 2006 3:16

Diagnostic Surgery:
• Fine Needle Aspiration
• Core Needle Biopsy
• Excisional or Incisional Biopsy

Treatment: Hormone Therapies

- SERMS - selective estrogen-receptor modulators
  - (Tamoxifen)
  - Increases the risk of uterine & endometrial cancer
- Aromatase Inhibitors
  - Works in post-menopausal women; side effect = bone density loss
  - (Aromasin)
VI. BC Treatments & Therapies

Treatment regimes work best if they can be individualized for each woman!

Tests to determine treatment options:
- Estrogen & Progesterone receptor test
- Human epidermal growth factor type 2 receptor test
- Multigene tests
  - Oncotype DX
  - MammaPrint

Treatment – depends on type of cancer, the stage, sensitivity to hormones, overexpresses HER2/neu

- Treatment of ductal carcinoma in situ (DCIS) may include the following:
  - Breast-conserving surgery and radiation therapy with or without tamoxifen.
  - Total mastectomy with or without tamoxifen.
  - Breast-conserving surgery without radiation therapy.
  - (treatments for DCIS still based on an invasive cancer model)
Treatment of lobular carcinoma \textit{in situ} (LCIS) may include the following:
  
  - Biopsy to diagnose the LCIS followed by regular examinations and regular mammograms to find any changes as early as possible. This is called observation.
  - Tamoxifen to reduce the risk of developing breast cancer.
  - Bilateral prophylactic mastectomy. This treatment choice is sometimes used in women who have a high risk of getting breast cancer. Most surgeons believe that this is a more aggressive treatment than is needed.

Treatment of stage I, stage II, stage IIIA, and operable stage IIIC breast cancer may include the following:
  
  - Breast-conserving surgery to remove only the cancer and some surrounding breast tissue, followed by lymph node dissection and radiation therapy.
  - Modified radical mastectomy with or without breast reconstruction surgery.
  - Sentinel lymph node biopsy followed by surgery.

5 Year Survival Rates:
- Stage 0 = 93%.
- Stage I = 91%, Stage IIA = 81%, Stage IIB = 74%, Stage IIIA = 67%
- Stage IIB = 41%, Stage IIIC = 49%, Stage IV = 15%

Social Impact of BC

- Alters the woman’s self image
- Impacts the woman’s sexuality
- Impacts her relationships
- Isolates her from her peers
- Imposes financial burdens
- Causes changes in lifestyle

References:
Useful sites:

- http://www.cancer.org/cancer/breastcancer/index
- http://www.breastcancer.org/treatment
- http://www.physio-pedia.com/Breast_Cancer