Staying abreast: Learn the facts about Breast Cancer Risk

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DNA damage leads to Cancer

- Is fundamentally a disease caused by **damage to the DNA**
- These mutations can be inherited from
  1. Your parents
  2. Increasing age

Source: NASA.gov
Normal Cells vs. Cancer Cells

Normally, cells grow and divide to form new cells as needed. When cells grow old, they die and new cells replace them.

Sometimes, this process goes wrong.
CARCINOGENESIS

INITIATION

PROMOTION

TRANSFORMATION

PROGRESSION

Carcinogen

Geneic Change

Cell Multiplication

Malignant Cell

Malignant Tumor

Adapted from: http://hepatitiscnewdrugs.blogspot.com
Cancer Tends to Corrupt Surrounding Environment

Source: National Cancer Institute
Breast Cancer

- **In situ breast cancer**
  - “Stage 0”

- **Invasive breast cancer**
  - Stage I-IV

- **Local**: still confined to the primary site

- **Regional**: spread to regional lymph nodes or directly beyond the primary site

- **Distant**: metastasized

http://www.cancerhelp.org.uk
Mammogram and corresponding gross specimen demonstrating a dense discrete mass within the breast.
Tumor Types

Normal Ductal Lumen
Benign Proliferative Changes
Atypical Hyperplasia
Ductal Carcinoma In Situ
Invasive Carcinoma

Accumulation of genetic and epigenetic changes
What Causes Cancer?

1. Genetics
2. Things You’re Exposed To
3. Things You Do and Don’t Do
Risk Factors

What are risk factors?

- A risk factor is anything that affects your chance of getting the disease

Examples:
- Sun exposure increases likelihood of skin cancer
- Smoking increases likelihood of lung cancer

www.katiethornernutrition.com
www.acneinstein.com
Cancer Risk and Aging

Source: National Cancer Institute
# Probability of Developing Breast Cancer

## Table 4. Age-Specific Probabilities of Developing Invasive Breast Cancer*

<table>
<thead>
<tr>
<th>If current age is:</th>
<th>The probability of developing breast cancer in the next 10 years is:</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>0.05%</td>
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<tr>
<td>30</td>
<td>0.43%</td>
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<tr>
<td>40</td>
<td>1.43%</td>
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<tr>
<td>50</td>
<td>2.51%</td>
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<tr>
<td>60</td>
<td>3.51%</td>
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<tr>
<td>70</td>
<td>3.88%</td>
</tr>
<tr>
<td>Lifetime risk</td>
<td>12.28%</td>
</tr>
</tbody>
</table>

*American Cancer Society, Surveillance Research, 2007*
# Risk Factors

## Table 3. Factors That Increase the Relative Risk for Breast Cancer in Women

<table>
<thead>
<tr>
<th>Relative Risk</th>
<th>Factor</th>
</tr>
</thead>
</table>
| > 4.0         | • Female  
                • Age (65+ versus <65 years, although risk increases across all ages until age 80)  
                • Certain inherited genetic mutations for breast cancer (BRCA1 and/or BRCA2)  
                • Two or more first-degree relatives with breast cancer diagnosed at an early age  
                • Personal history of breast cancer  
                • High breast tissue density  
                • Biopsy-confirmed atypical hyperplasia |
| 2.1–4.0       | • One first-degree relative with breast cancer  
                • High-dose radiation to chest  
                • High bone density (postmenopausal) |
| 1.1–2.0       | Factors that affect circulating hormones  
                • Late age at first full-term pregnancy (>30 years)  
                • Early menarche (<12 years)  
                • Late menopause (>55 years)  
                • No full-term pregnancies  
                • Never breastfed a child  
                • Recent oral contraceptive use  
                • Recent and long-term use of hormone replacement therapy  
                • Obesity (postmenopausal) |
|               | Other factors  
                • Personal history of endometrium, ovary, or colon cancer  
                • Alcohol consumption  
                • Height (tall)  
                • High socioeconomic status  
                • Jewish heritage |

Adapted with permission from Hulka et al, 2001.
Who is at high risk for breast cancer?
All Cancers Arise from Gene Mutations

Germline mutations
- Present in egg or sperm
- Are heritable
- Cause cancer family syndromes

Somatic mutations
- Occur in tumor only
- Are not heritable
- Are more common
Inherited Cancers

Knudson’s 2 Hit Hypothesis

Sporadic Cancer: 2 acquired mutations

Hereditary Cancer: 1 inherited and 1 acquired mutation
Natural History of Breast and Ovarian Cancer in BRCA1/BRCA2 Mutation Carriers

Chen et al. JCO Feb 20, 2006
General Indications for Referral to Genetic Counseling

- Unusually early age of onset for a specific cancer
- Multiple primary cancers in a single individual
- Bilateral cancer in paired organs or multifocal disease
- Clustering of the same type of cancer in close relatives
- Cancers occurring in multiple generations of a family
- Occurrence of rare tumors (e.g., retinoblastoma, adrenocortical carcinoma, ocular melanoma, paraganglioma, or duodenal cancer)
- Unusual presentation of cancer (e.g., male breast cancer)
- Uncommon tumor histology (e.g., medullary thyroid carcinoma, type 2 papillary kidney cancer)
Breast Density

- The relative risk of women with 75% or more percent mammographic density (PMD) compared to 10% or less is between 4-6 fold
- PMD is associated inversely with greater age, parity and weight, menopause, and tamoxifen
- PMD is positively associated with greater height, family history of breast cancer and HT
- 16% of all breast cancers have been attributed to a density of 50% or more
- Although can mask the diagnosis of breast cancer from longitudinal study, believed to be an independent risk factor
Breast Density

Figure 1. Examples of mammographic density. (a) 0% mammographic density, (b) less than 10%, (c) less than 25%, (d) less than 50%, (e) less than 75%, and (f) greater than 75%. On the right is an illustration of Cumulus in the measurement of mammographic density. The red line outlines the breast, and the green line outlines the area of density. Republished with permission from [2].
Tools to Assess Breast Cancer Risk

IBIS Assessment Tool
(http://www.ems-trials.org/riskevaluator/)

Breast Cancer Risk Assessment Tool
(http://www.ems-trials.org/riskevaluator/)

Risk Calculator

1. Does the woman have a medical history of any breast cancer or ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)?

2. What is the woman's age? This tool only calculates risk for women 35 years of age or older.

3. What was the woman's age at the first menstrual period?

4. What was the woman's age at the time of her first live birth of a child?

5. How many of the woman's first-degree relatives - mother, sisters, daughters - have had breast cancer?

6. Has the woman ever had a breast biopsy?

6a. How many breast biopsies (positive or negative) has the woman had?

6b. Has the woman had at least one breast biopsy with abnormal findings?

7. What is the woman's race/ethnicity?

7a. What is the sub race/ethnicity?
Lifestyle Approaches to Reducing Breast Risk Cancer
Causes of Overweight

- Family History and Genetics
- Metabolism
- Environment
- Behavior and Habits
Energy Balance

- Important to maintain a healthy weight
- Amount you take in needs to include what your body uses
- If overweight, reduce caloric intake to lose weight

originalstrength.net
**Healthy Weight**

**Body Mass Index**
- Measurement of body fat based on height and weight

**BMI Categories:**
- Underweight = <18.5
- Normal weight = 18.5–24.9
- Overweight = 25–29.9
- Obesity = BMI of 30 or greater

**The BMI Tables**

**Aim for a Healthy Weight:**
- Limitations of the BMI
- Assessing Your Risk
- Controlling Your Weight
- Recipes

[Download the BMI Calculator iPhone App](http://www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm)
Sustained weight loss and breast cancer risk in postmenopausal women who never used postmenopausal hormones

Hormones

Combination of Hormones

Estrogen only

Source: drugs.com
Making the case for breast cancer prevention

- Since 1998 8 phase III breast cancer prevention trials have been conducted and ALL of them have demonstrated a reduction in breast cancer incidence.

- Four national guidelines ASCO, USPTF, NCCN and the UK Nice guidelines are all in support of the use of chemoprevention for women at higher risk.

- Tamoxifen, Raloxifene, Aromatase Inhibitors

Visvanathan K ASCO risk reduction guidelines JCO 2013


www.nice.org.uk/
Comparison of NNT in primary prevention trials in oncology and cardiology

Abbreviations: CVD, cardiovascular; IBC, invasive breast cancer; JUPITER, Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin.
Study of Tamoxifen and Raloxifene
NSABP Protocol P-2 Schema

- Risk Eligible 5yr Gail risk ≥ 1.66
- Postmenopausal Women

Stratification
- Age
- Relative Risk
- Race
- History of LCIS

- Tamoxifen
  20 mg/day for 5 years

- Raloxifene
  60 mg/day for 5 years
Trial Schema

Postmenopausal women:
• Ages 40-70
• Increased risk of breast cancer:
  • Family history
  • Atypia / LCIS
  • Breast density
• No HRT

Anastrozole 1 mg/day (N=1920)

Placebo (N=1944)

N=3864

5 years

Exclusion
On HRT
Severe osteoporosis T score < 4
2 vertebral fracture
Life expectancy 10 yrs

<table>
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<tr>
<th></th>
<th>Baseline</th>
<th>6 M</th>
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Summary of Recommendations

1. Chemoprevention should be discussed in women at increased risk for breast cancer. There are now many options. In conjunction with discussion of risks and benefits

2. Particularly women with ADH, LCIS, higher risk women

3. Need to factor in age, race and presence of uterus in decision with respect to SERMs

4. In terms of toxicity younger women have less toxicity but also often less risk.

5. AI (not FDA approved yet) but clearly have a role in chemoprevention.
Overall Cancer Prevention

1. Stop using tobacco
2. Maintain a reasonable weight
3. Increase physical activity
4. Eat 5-9 fruits and vegetables daily
5. Increase fiber and reduce saturated fat
6. Limit alcohol consumption
7. Limit exposure to the sun
8. Get immunized (younger)
9. Avoid risky behaviors
10. Treat precursor lesions

* Become aware of your cancer risk
Take Home Messages

1. Be aware of your risk factors for breast cancer
2. Be aware of your breast cancer risk
3. Optimize lifestyle factors to minimize risk
4. If you have a strong family history consider a referral to a genetics clinic
5. If you are at moderately increased risk discuss chemoprevention with your doctors
6. Screen
7. Inform other women so they can also optimize their breast health
Thank you!