

# Breast Cancer Risk Factors & Treatment



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# Epidemiology

- American Cancer Society estimates:
- 211,240 new cases of breast cancer in US women and 40,410 deaths in 2005
- 1690 new cases of breast cancer in US men and 460 deaths in 2005
- 32% of all cancers in American women
- 15% of all cancer deaths in American women



# Epidemiology

- Second leading cause of cancer deaths among all US women (after lung cancer)
- Leading cause of cancer deaths among women ages 20 to 59



# Improved 5 Year Survival Rates

	1960	1998
White women	63%	88%
Black women	46%	73%

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# Risk Factors for Breast Cancer

- Genetic
- Hormonal
- Environmental
- Dietary

5/3/2005



# Genetic Risk Factors for Breast Cancer

- Female sex—women have more breast tissue than men, consequently a higher risk of breast cancer than men, roughly 100:1



# Genetic Risk Factors for Breast Cancer

- BRCA1 or BRCA 2 mutation increases risk of breast cancer by 6.0-14.0 fold
- BRCA 1 and BRCA 2 are tumor suppressor genes that play a role in cellular DNA repair
- Approximately 10% of breast cancer is familial and related to BRCA1 or BRCA2



# BRCA1 and BRCA2

- Associated cancers tend to be more aggressive, of a higher grade, and hormone receptor negative
- Confer 50 to 87% lifetime risk of breast cancer
- Also increase risk of ovarian cancer
- Genetic testing is available for women with appropriate family history



# Genetic Risk Factors

- Li-Fraumeni Syndrome, abnormal TP53 gene on chromosome 17p, associated with premenopausal breast cancer, childhood sarcomas, brain tumors, leukemia, and adrenocortical adenomas



# Genetic Risk Factors

- Cowden's Syndrome, abnormal PTEN tumor suppressor gene on chromosome 10 associated with premenopausal breast cancers, gastrointestinal malignancies, and benign and malignant thyroid disease



# Genetic Risk Factors

- Peutz-Jegher's Syndrome, abnormal STK11 tumor suppressor gene on chromosome 19, associated with cancers of the stomach, colon, pancreas, small intestine, thyroid, breast, lung, and uterus



# Hormonal Factors

- Menarche < age 12 increases risk
- Menopause > age 55 increases risk
- 1<sup>st</sup> child after age 30 or nulliparous
- Greater than 5 years on oral contraceptives
- Prolonged combined estrogen-progesterone replacement therapy



# Benign Breast Disease

- Atypical Hyperplasia
- Hyperplasia
- Breast Biopsy

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# Environmental Factors

- Exposure to ionizing radiation

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# Dietary Factors

- Alcohol consumption, greater than 1 drink/day
- Obesity, especial postmenopausal



# Prevention

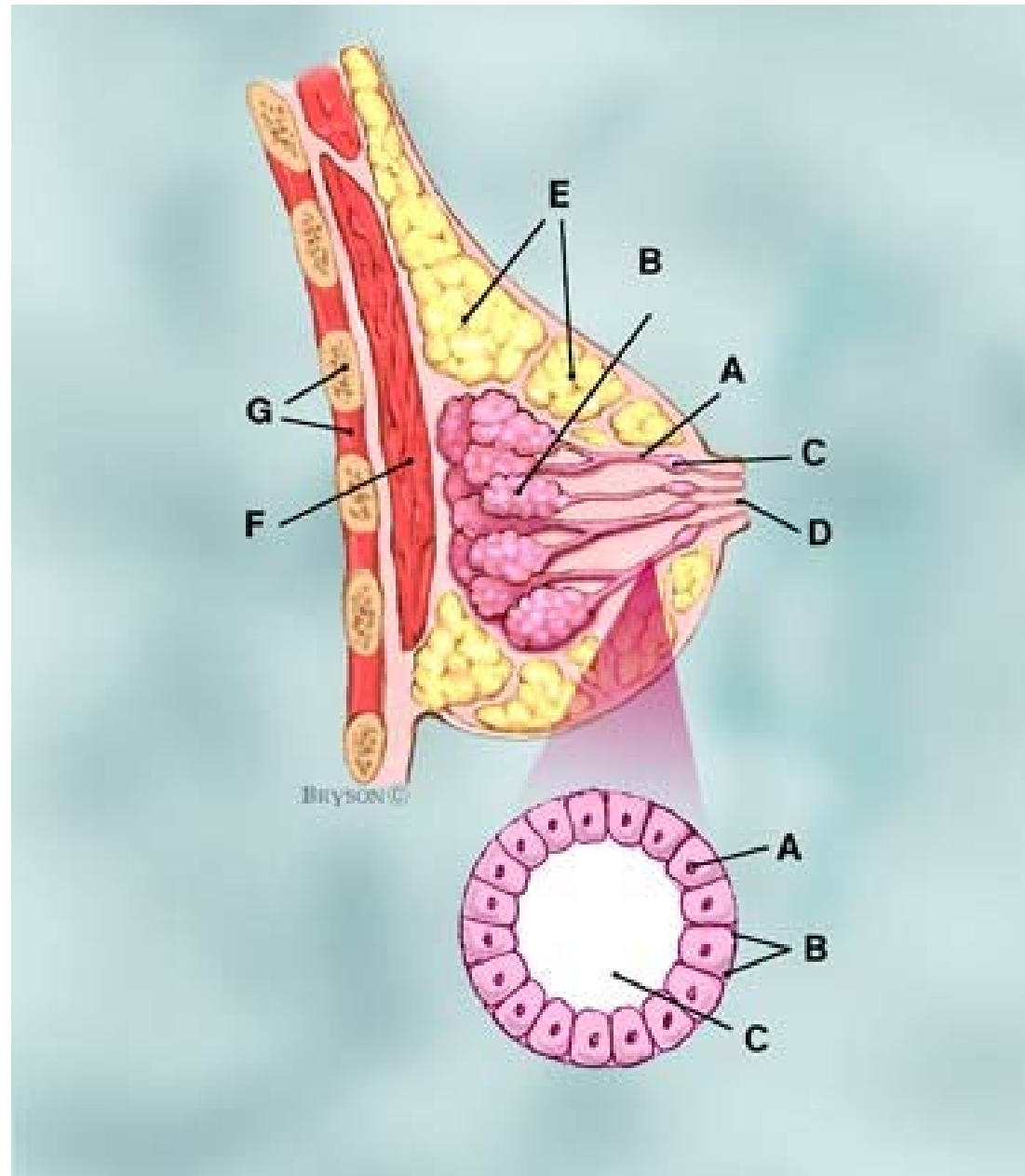
- Tamoxifen for high risk women
- For consideration:
  - Early childbearing
  - Prolonged lactation
  - Weight reduction
  - Regular exercise, especially during adolescence
  - Prophylactic mastectomy



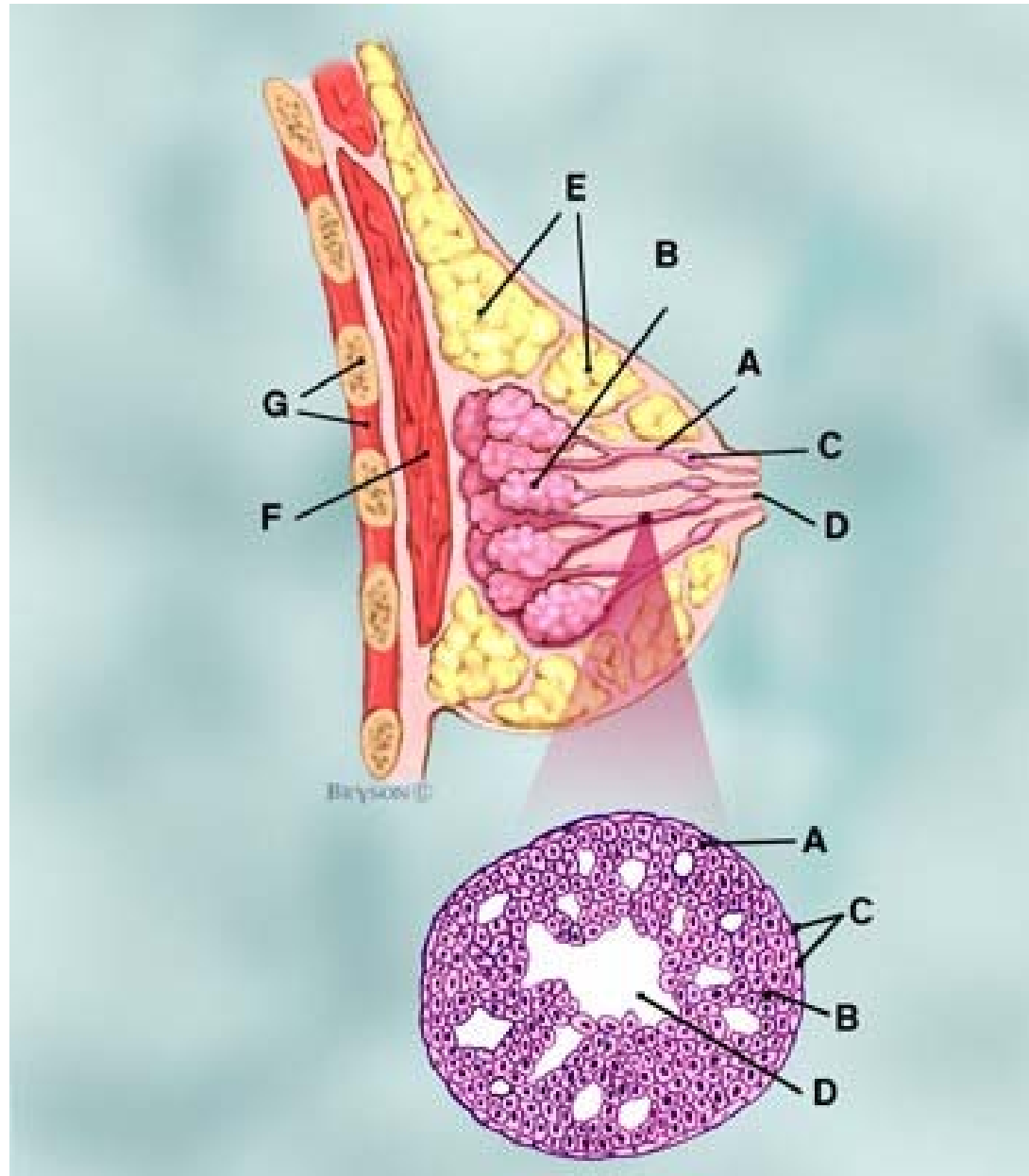
# Diagnosis and Treatment

- Patient feels a breast mass or has an abnormal radiologic screening exam
- Surgical biopsy or aspiration
- Observation (LCIS), lumpectomy or mastectomy
- Staging
- Delivery of adjuvant therapies—radiation and/or chemotherapy, hormonal therapies

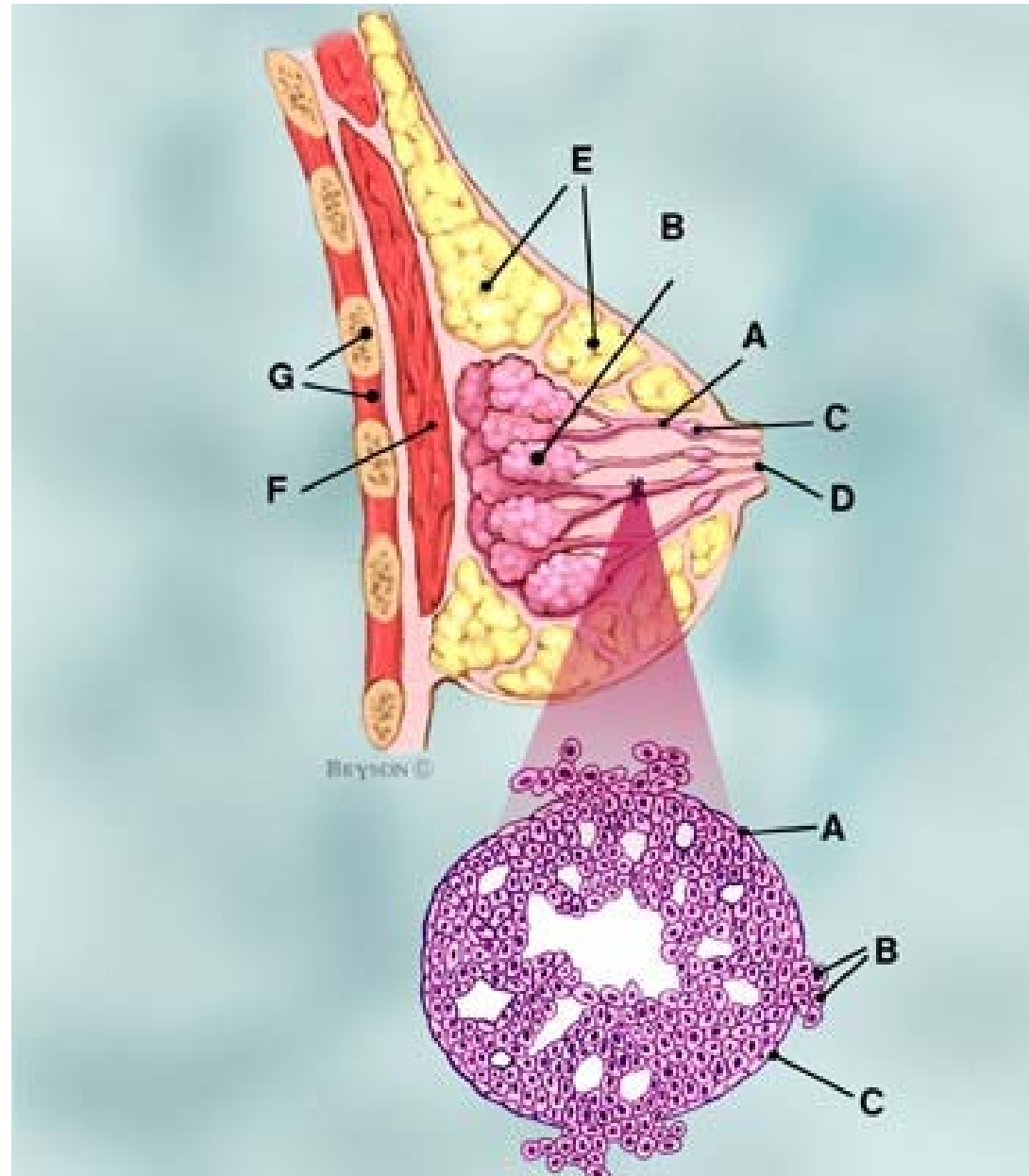
# Normal Breast



# DCIS (Ductal Carcinoma in Situ)



# Invasive Cancer





# Pathology Report

- Invasive vs. Non-invasive
- Histologic Type- Ductal (85%) vs. Lobular
- Grade (estimate of the aggressiveness under microscope)
- Size
- Margins
- Lymph Nodes
- Estrogen/ Progesterone Receptor (2/3 positive)
- Her-2/ neu

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# Stages

- Stage 0 -- carcinoma in situ
- Stage I – tumor < 2 cm, no nodes
- Stage II – tumor 2 to 5 cm, +/- nodes
- Stage III – locally advanced disease, fixed or matted lymph nodes and variable tumor size
- Stage IV – distant metastases (bone, liver, lung, brain)

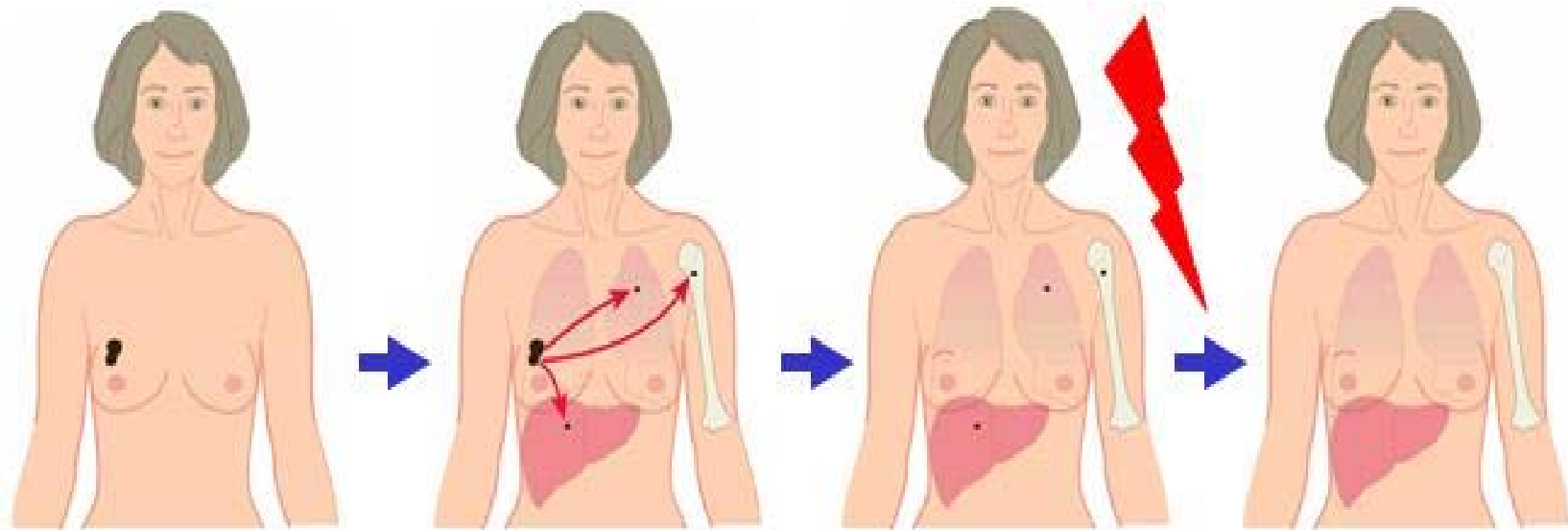


# What now?

## ■ Stage 0-III

- Risk of recurrence is individual
- What can we do to reduce the risk of recurrence in the breast, and systemically ?
- Meet with Radiation Oncologist and Medical Oncologist

# Principle of Adjuvant Treatment





# Adjuvant Therapy

- Radiation Therapy (local)
  - Chemotherapy (systemic)
  - Hormonal agents (systemic)
- 
- Each therapy adds to reduction of recurrent disease.
  - Therapy is individualized, discussion with health care provider.



# Chemotherapy Drugs

- Adriamycin, Epirubicin
- Cytosan
- Methotrexate, 5-fluorouracil
- Taxol, Taxotere
- Navelbine
- Intravenous
- Nausea, hair loss, low blood counts, cardiac toxicity, bladder toxicity, nerve damage
- Given for adjuvant or recurrent disease.00



# Hormonal agents

- Tamoxifen
- Can be given to pre or post menopausal women
- Works by blocking estrogen receptors in breast cells, inhibiting their growth
- Side effects include hot flashes, depression, increased risk of uterine cancer and blood clots
- Taken daily by mouth for 5 years



# Aromatase Inhibitors

- Aromatase is the enzyme that converts androgens to estrogen
- AIs are only given to postmenopausal women
- “May” be more effective than Tamoxifen
- Examples: Anastrozole/Arimidex, Letrozole/Femara, Exemestane/Aromasin
- Side effects include hot flashes, depression, osteoporosis, joint pains
- Taken daily by mouth for variable periods of time



## Post-menopausal Hormonal Therapy

- Post-menopausal women with ER/PR positive disease have the choice of Tamoxifen or Aromatase Inhibitors.
- Discuss with your physician the benefits and risks of each drug in your specific case.
- The choice can be different depending on several factors.
- Several ongoing clinical trials will determine which therapy is best.



## What now?

- Stage IV (spread outside the breast and regional lymph nodes)
  - Common locations of metastatic disease (bone, liver, lung)
  - Meet with Medical Oncologist and perhaps a Radiation Oncologist
  - Considered treatable, but not curable
  - Treatment options- Hormonal, Herceptin, Chemotherapy, Radiation Therapy



# Monoclonal antibodies

- Trastuzumab/Herceptin
- Given to patients whose cancer cells overexpress Her-2-neu as measured by IHC or FISH (25 to 30% of patients)



# Bisphosphonates

- Bone strengtheners
- Given for therapy-induced osteoporosis or for cancer that has spread to bone
- Zometa (Zoledronic acid)
- Aredia (Pamidronate)
- Each lowers calcium and has been shown to reduce the risk of fracture in pts with cancers metastatic to bone.

