

CANCER ADVANCES IN FOCUS

Breast Cancer

Yesterday

- In 1975, the incidence rate for female breast cancer in the United States was 105 new cases diagnosed for every 100,000 women in the population; the mortality rate was 31 deaths for every 100,000 women.
- Among women diagnosed with breast cancer during the period from 1975 through 1977, about 75% survived their disease at least 5 years. Among white women, the 5-year relative survival rate was 76%; among African American women, it was 62%.
- Mastectomy was the only accepted surgical option for breast cancer treatment.
- Only one randomized trial of mammography for breast cancer screening had been completed. Several other trials and the joint National Institutes of Health (NIH) and American Cancer Society (ACS) Breast Cancer Detection Demonstration Projects were just beginning.
- Clinical investigation of combination chemotherapy, using multiple drugs with different mechanisms of action, and of hormonal therapy as postsurgical (adjuvant) treatment for breast cancer was in its earliest stages.
- In the mid-1970s, clinical evaluation of the drug tamoxifen, a selective estrogen receptor modulator (SERM), as a hormonal treatment for breast cancer was just beginning.
- No gene associated with an increased risk of breast cancer had yet been identified.

Today

- In 2007, the latest year for which we have updated statistics, the U.S. incidence rate for female breast cancer was approximately 125 new cases diagnosed for every 100,000

women in the population; the mortality rate was approximately 23 deaths for every 100,000 women. Although the incidence rate in 2007 was higher than that in 1975, this rate has been declining since 1998-1999, when it peaked at a rate of 141 new cases for every 100,000 women in the population. The breast cancer death rate in the United States has been declining steadily since 1989-1990, when it peaked at a rate of 33 deaths for every 100,000 women.

- Among women diagnosed with breast cancer during the period from 1999 through 2006, 90% were expected to survive their disease at least 5 years. Among white women, the 5-year relative survival rate was 91%; among African American women, it was 78%. The increase in breast cancer survival seen since the mid-1970s has been attributed to both screening and improved treatment.
- Breast-conserving surgery (lumpectomy) followed by local radiation therapy has replaced mastectomy as the preferred surgical approach for treating early-stage breast cancer.
- Routine mammographic screening is an accepted standard for the early detection of breast cancer. The results of eight randomized trials, the NIH-ACS Breast Cancer Detection Demonstration Projects, and other research studies showed that mammographic screening can reduce the mortality from breast cancer.
- Combination chemotherapy is a standard of care in the adjuvant treatment of operable breast cancer. The goal of this systemic therapy is to eradicate cancer cells that may have spread beyond the breast. Neoadjuvant chemotherapy, or chemotherapy given before surgery to reduce the size of the tumor and to increase the chance of breast-conserving surgery, is also an option.
- Hormonal therapy with SERMs (such as tamoxifen) and aromatase inhibitors is now standard in the treatment of women with estrogen receptor-positive breast cancer, both



as adjuvant therapy and in the treatment of advanced disease. Estrogen receptor-positive breast cancer cells can be stimulated to grow by the hormone estrogen. SERMs interfere with this growth stimulation by preventing estrogen from binding to the estrogen receptor. In contrast, aromatase inhibitors block estrogen production by the body. Food and Drug Administration (FDA)-approved aromatase inhibitors include anastrozole, exemestane, and letrozole.

- Tamoxifen and another SERM, raloxifene, have been approved by the FDA as treatments to reduce the risk of breast cancer in women who have an increased risk of developing the disease.
- The monoclonal antibody trastuzumab is an accepted treatment for breast cancers that overproduce a protein called human epidermal growth factor receptor 2, or HER2. This protein is produced in abnormally high amounts by about 20% of breast tumors. Breast cancers that overproduce HER2 tend to be more aggressive and are more likely to recur. Trastuzumab targets the HER2 protein specifically, and this antibody, in conjunction with adjuvant chemotherapy, can lower the risk of recurrence of HER2-overproducing breast cancers by about 50% in comparison with chemotherapy alone.
- Several breast cancer susceptibility genes have now been identified, including *BRCA1*, *BRCA2*, *TP53*, and *PTEN/MMAC1*. Approximately 60% of women with an inherited mutation in *BRCA1* or *BRCA2* will develop breast cancer sometime during their lives, compared with about 12% of women in the general population. Women with inherited *BRCA1* or *BRCA2* gene mutations also have an increased risk of ovarian cancer.

Tomorrow

- We will use our rapidly increasing knowledge in the fields of cancer genomics and cell biology to develop more effective and less toxic treatments for breast cancer and to improve our ability to identify cancers that are more likely to recur. Moreover, we will use this knowledge to tailor breast cancer therapy to the individual patient. For example, gene expression analysis has led to the identification of five subtypes of breast cancer that have distinct biological features, clinical outcomes, and responses to chemotherapy. This knowledge can be

exploited in the development of treatment strategies based on the specific characteristics of a woman's tumor. Furthermore, a patient's response to chemotherapy is influenced not only by the genetic characteristics of their tumor but also by inherited variations in genes that affect the body's ability to absorb, metabolize, and eliminate drugs. Our growing knowledge should enable prediction of tumor responses to individual chemotherapy drugs or classes of drugs, as well as the likelihood of severe adverse effects from them. This knowledge should also aid in the development of more individualized treatments and permit the design of more effective and less toxic chemotherapy agents.

- We will use our increasing knowledge of the immune system to enhance the body's ability to recognize and destroy cancer cells. The knowledge we have acquired thus far has facilitated the development of several promising breast cancer treatment vaccines that are currently under clinical evaluation.
- We will use advanced technologies, including genomic technologies, to improve our ability to detect breast cancer at its earliest stages, when it is most treatable, and to better define individual risk for this disease.
- We will strive to understand, address, and eliminate factors that contribute to the higher mortality from breast cancer experienced by African American women compared with women of other racial and ethnic groups.

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