Editorial

›› **Robert L. Barbieri, MD** Editor in Chief

We must take the lead in the battle against breast cancer

ObGyns have done so much to stop cervical cancer. Can't we do more to reduce the risk of death from breast malignancy?

- Cancer of the cervix is the cause of death in **2.3 of every 100,000** white women annually in the United States.
- For breast cancer, the death rate in the same population is, comparatively, more than 10-fold: **24.4 of every 100,000** women.

Those numbers, from the American Cancer Society, immediately raise a question for me: Why is the rate of death from cervical cancer so low in comparison to what's been reported for breast cancer?

The answer, in part, is that ObGyns and other clinicians have worked hard to implement effective cervical cancer prevention and screening programs and have treated preinvasive precursor lesions aggressively. ObGyns have led the way in reducing death from cervical cancer.

My second question, then, is: As guardians of women's health, can't ObGyns be doing more than we are to reduce the rate of death from breast cancer?

Here are some observations, gathered from a look at the scientific literature, on what we can do to make a difference, and where we remain stymied, in the battle against breast cancer.

Is the Gail risk calculator part of your practice? Is chemoprevention?

Instant Poll

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A lack of "molecular intelligence" puts us at a disadvantage

Harald zur Hausen was co-awarded the Nobel Prize in Physiology or Medicine in 2008 for discovering the role of human papillomavirus (HPV) in cervical cancer. Thanks to his work, and that of his colleagues and other researchers, the molecular mechanisms that give rise to cervical cancer are reasonably well understood: When oncogenic types of HPV integrate into the genome of cervical cells, that integration prompts expression of two viral proteins: E6, which binds to p53, and E7, which binds to retinoblastoma protein (Rb)—leading to an increase in cell proliferation and oncogenesis.

Understanding the basic biology of cervical cancer has helped us design prevention, screening, and treatment strategies that work.

In contrast, the molecular mechanisms that cause breast cancer aren't understood. Men rarely get breast cancer, however, so we can deduce that female reproductive hormones, including estradiol and progesterone, probably play an important role in the pathogenesis of breast cancer.

Reproductive risk factors are well-established

Epidemiologic studies show that the risk of breast cancer is increased by:

- early menarche
- late menopause
- late age at first birth
- obesity in postmenopausal women.

Conversely, breastfeeding and exercise reduce the risk of breast cancer.

The evidence suggests, therefore, that you should counsel your patients to:

- exercise regularly
- breastfeed their newborn
- maintain normal body mass.

The value of examination

Mammography and the clinical breast exam detect about 90% and 50% of breast cancers, respectively, in screening programs. In a prospective trial of more than 39,000 women who were 50 to 59 years old and followed for as long as 13 years, a standardized and thorough clinical breast exam was as effective as a breast exam plus mammography for detecting invasive breast cancer that caused death.[1]

Clinical breast exam. According to some experts, a thorough clinical breast exam requires at least 6 minutes of examination time. One recommended technique includes the following steps:

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TABLE Questions in the NCI's breast cancer risk calculator

Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS)?
What is the woman's age?*
What was the woman's age at the time of her first menstrual period?
What was the woman's age at the time of her first live birth of a child?
How many of the woman's first-degree relatives—mother, sisters, daughters—have had breast cancer?
Has the woman ever had a breast biopsy? • How many breast biopsies (positive or negative) has the woman had? • Has the woman had at least one breast biopsy with atypical hyperplasia?
What is the woman's race/ethnicity?

*This tool only calculates risk for women 35 years of age or older.

- flatten breast tissue against the chest
- examine the breast in vertical strips
- use three different degrees of pressure to examine the breast
- examine each breast for at least 3 minutes.[2]

Breast self-exam hasn't been demonstrated to effectively detect breast cancer, but it does increase the rate at which women detect benign breast lesions.[3] It may be that breast self-examination, as taught today, is insufficiently thorough to detect breast cancer.

Screening technology: Use it properly

Mammography. For women older than 50 years, annual mammography reduces mortality from breast cancer by approximately 35%.[4] For women who are 40 to 50 years old, annual or semiannual mammography reduces mortality from breast cancer by about 15%.[5] In my practice, I recommend that all women older than 40 years have a mammogram annually.

Magnetic resonance imaging of the breast is much more expensive than mammography. It requires a contrast agent, such as gadolinium, which can cause nephrogenic systemic fibrosis.

MRI of the breast is more sensitive, but less specific, than mammography.

The American Cancer Society cautions against using MRI as part of a screening algorithm for breast cancer unless the woman's lifetime risk of breast cancer is greater than 20% to 25%.[6] This level of risk is found most often in women who have a BRCA mutation; who have had chest irradiation (for example, for lymphoma); and who have a strong family history of breast cancer.

Some women benefit from chemoprevention

The Gail model. Women who are at high risk of breast cancer may benefit from hormonal chemoprevention with a selective estrogen receptor modulator (SERM). The Gail model is the most widely used tool for assessing such risk.

A Web version of the Gail model risk calculator that accounts for different risk factors among women of various racial backgrounds is available at www.cancer.gov/bcrisktool/default.aspx. The factors that contribute to calculating the 5-year risk estimate are listed in the **TABLE**.

But the Gail model has a major weakness: It performs better when applied to populations of women, rather than to individuals—and prevention decisions are, of course, made indi-

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Instant Poll

QUESTION 1

Using the Gail risk calculator

In the past year, I have recommended that postmenopausal women in my practice calculate their 5-year risk of breast cancer using the Gail model calculator.

- YES
- NO

QUESTION 2

Rx: chemoprevention

Over the past year, I have prescribed raloxifene or tamoxifen more often than in the past to prevent breast cancer in postmenopausal women at increased risk.

- YES
- NO

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vidually. When the Gail model calculates that a given postmenopausal woman has a 5-year risk of breast cancer ≥1.66%, she may benefit from treatment with a SERM. It's likely that more women could be formally assessed for their risk of breast cancer if their physician used a risk-prediction model.

Which SERM? As Dr. Steven Goldstein says in his review of breast cancer chemoprevention on page 44, raloxifene, 60 mg/d, taken for 5 years, significantly reduces the risk of invasive breast cancer in a postmenopausal woman at increased risk of breast cancer. In the STAR trial, both raloxifene and tamoxifen similarly reduced the risk of breast cancer; when raloxifene was compared with tamoxifen, however, raloxifene was associated with a lower risk of thromboembolic events and cataracts.[7]

In postmenopausal women at increased risk of breast cancer, it's likely that SERMs are underutilized for their preventive ability.

Close care for survivors

More and more, women survive breast cancer because of early detection by mammography and aggressive adjuvant treatment. Experts now recommend that survivors be evaluated for chemotherapy-induced cognitive dysfunction, fatigue, osteoporosis, and sexual dysfunction, and that they be offered weight-management tools and psychosocial support.

In addition, these women should continue to have mammography, annually; breast self-exam should be emphasized to them; and they should be provided with regular gyn care. Breast cancer survivors need the care of clinicians who are sufficiently aware of the myriad of issues that affect their quality of life.

Past success offers a model for what's next

We are clearly being challenged here, as leaders in advancing women's health. We must play a central role in reducing the health impact of breast cancer by being actively involved in counseling, prevention, and screening, and in caring for survivors.

To return to my opening comparison, the lifetime risk of cervical cancer is about 1 in 145; for breast cancer, that risk is 1 in 8. My hope? That we will, some day soon, celebrate how much we've reduced the rate of breast cancer—echoing the success we've had reducing the rate of cervical cancer and the number of women who die from that disease.

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