

## HRT After Breast Cancer: Recurrence and Mortality

**F**indings from a data analysis (O'Meara ES, Rossing MA, Daling JR, et al. Hormone replacement therapy after a diagnosis of breast cancer in relation to recurrence and mortality. *J Natl Cancer Inst* 2001;93:754-61) suggest that hormone replacement therapy (HRT) in women previously diagnosed with invasive breast cancer does not appear to increase the risk of recurrence or mortality, and might even have a protective effect.

The investigators collected data on 2,755 women (ages 35-74 years) who had been diagnosed with incident invasive breast cancer while enrolled in a large health maintenance organization from 1977 through 1994. Pharmacy data were used to identify 174 women who were HRT users after the cancer diagnosis, and each of these women was matched (similar age, disease stage and year of diagnosis) to four randomly selected non-users of HRT (n = 695). The women in the analysis were recurrence-free upon HRT initiation or, in the case of nonusers, at the equivalent time since diagnosis. Recurrence and mortality rates through 1996 were calculated, and adjusted relative risks were estimated.

The analyses revealed a rate of recurrence of 17 per 1,000 person-years among the HRT users, and 30 per 1,000 person-years among the nonusers. After adjustment for bilateral oophorectomy, hysterectomy, mastectomy and tamoxifen use, the risk of recurrence was 0.50 for the HRT group, relative to nonusers. Median follow-up for mortality was 4.6 years. The relative risk of dying of breast cancer was 0.34 for the HRT users, compared to the nonusers; the relative risk for all-cause mortality was 0.48.

The investigators suggest that the findings be "interpreted with caution," noting that certain findings from the study "argue against a causal influence of HRT after breast cancer on recurrence and



mortality." Disease-free and overall survival were, for example, unaffected by cumulative use of HRT or by the form of HRT used (oral or vaginal).

## PTH and Postmenopausal Osteoporosis

**I**n a phase III clinical trial (Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone (1-34) on fractures and bone mineral density in postmenopausal women. *N Engl J Med* 2001;344:1434-41), recombinant human parathyroid hormone (PTH) (1-34), which helps to stimulate osteoblasts to form new bone, significantly increased bone density and reduced the risk of new fractures in postmenopausal women with prior osteoporotic fractures.

A total of 1,637 postmenopausal women with prior vertebral fractures were randomized to receive daily subcutaneous PTH (1-34) 20 or 40 µg, or placebo. All patients took daily calcium and vitamin D supplements. The PTH was well tolerated and, compared to placebo, was associated with a reduction in the risk of new spinal fractures of approximately two-thirds and a reduction in the risk of new nonspinal fractures of slightly greater than one-half. The researchers note that there was roughly a 90% reduction in the risk of the most severe fractures.

PTH-treated patients also experienced significant increases in vertebral, femoral

and total-body bone mineral density (BMD). Greater BMD increases were observed with the 40- than with the 20-µg dose, but both doses had similar effects on fracture risk, and patients taking the higher dose were more likely to experience side effects.

The researchers report that none of the patients in the study developed bone tumors (as had been seen in rats treated with long-term PTH). They go on to note that, because patients would likely be treated with PTH for relatively short durations, the findings from the rat studies "do not represent a risk for patients."

Eli Lilly and Company filed a new drug application for the PTH formulation at the end of 2000, and FDA approval for Forteo, the proposed brand name for the product, is anticipated before the end of 2001.

## Participants Sought for POF/ Testosterone Replacement Study

**R**esearchers at the National Institute of Child Health and Human Development (NICHD) are recruiting women for a study that will compare physiologic estrogen replacement with physiologic estrogen-plus-androgen replacement in young women with premature ovarian failure (POF). The study is designed to determine which regimen is more beneficial for bone mineral density (BMD) and other metabolic parameters related to the risk for cardiovascular disease.

Women with POF will be randomized to receive transdermal (patches) estradiol plus placebo or estradiol plus testosterone; both groups will receive cyclic progestin. A group of age-matched women with normal ovarian function will serve as contemporaneous controls for bone density and other study measures. The primary outcome parameter is femoral neck BMD, to be assessed at baseline and after 1, 2 and 3 years of treatment. Other outcome parameters include lumbar spine BMD, markers of bone turn-

over, cardiovascular disease risk factors and cognitive function.

The research is being conducted by the Gynecologic Endocrinology Unit at the National Institutes of Health in Bethesda, Maryland, under a Collaborative Research and Development Agreement between the National Institutes of Health and Procter and Gamble Pharmaceuticals.

For enrollment information, contact Vien Vanderhoof at 877/206-0911 (toll-free) or 301/435-7926.

### Daily Aspirin and CVD Primary Prevention

**P**rimarily Prevention Project investigators (Collaborative Group of the Primary Prevention Project. Low-dose aspirin and vitamin E in people at cardiovascular risk: A randomised trial in general practice. *Lancet* 2001;357:89-95) report that daily low-dose aspirin reduced the frequency of all cardiovascular endpoints measured in their randomized, placebo-controlled trial.

The researchers recruited 4,573 patients (2,583 women) from 1994 to 1998. Most of the patients (94.7%) had at least one major cardiovascular risk factor at baseline (high cholesterol levels, diabetes, obesity, family history of premature heart attack or age >65 years). Mean follow-up was 3.6 years.

Use of aspirin 100 mg/day reduced the frequency of all endpoints (cardiovascular disease mortality, nonfatal myocardial infarction and nonfatal stroke), with a significant reduction in the relative risk of mortality (from 1.4% to 0.8%). Severe bleeding events were significantly more frequent in the aspirin group (1.1%) than in the nonaspirin users (0.3%); one bleeding complication resulted in death. The investigators report that during the approximately 8,000 person-years of aspirin treatment, there was no indication that continuous aspirin use created an excess hemorrhagic cardiovascular event risk. Vitamin E (300 mg/day), taken con-

currently with the aspirin therapy, did not affect the endpoints. The trial was halted prematurely when its findings were shown to corroborate those of two other large trials providing evidence of aspirin's benefit for primary prevention of cardiovascular disease.

### Raloxifene and Cognitive Function

**L**ong-term raloxifene use does not appear to affect cognitive function in postmenopausal women with osteoporosis, according to a recently published report (Yaffe K, Krueger K, Sarkar S, et al. Cognitive function in postmenopausal women treated with raloxifene. *N Engl J Med* 2001;344:1207-13).

The investigators collected cognitive function data on 7,478 postmenopausal women with osteoporosis who participated in the Multiple Outcomes of Raloxifene Evaluation trial. The women were randomly assigned to receive raloxifene 60 mg/day, raloxifene 120 mg/day or placebo for 3 years. Six cognitive function tests were conducted at baseline, and again at 6 months and at 1, 2 and 3 years.

Test scores improved slightly in all three groups over the course of the 3 years. In the two raloxifene groups combined, the risk of cognitive decline (as measured by four of the tests) did not vary significantly when compared to that of the placebo group; in fact, a trend toward less decline in verbal memory and attention was observed in the raloxifene groups. The investigators note that, in general, cognitive function was neither helped nor harmed by treatment with raloxifene.

### Cervical Smears After Normal Smears in Postmenopausal Women

**F**indings from a prospective study (Sawaya GF, Grady D, Kerlikowske K, et al. The positive predictive value of cervical smears in previously screened women: The Heart and Estrogen/progestin Replacement Study (HERS). *Ann Intern Med* 2000;133:942-50) suggest that

cervical smears within 2 years of a normal smear are not needed in low-risk postmenopausal women. Investigators followed 2,561 women (mean age, 66.7 years) for 2 years after normal baseline cervical smears. New cytologic abnormalities were found in the smears of 110 women during the 2-year follow-up, and 231 interventions were subsequently performed. Histologic diagnoses were obtained for 103 of the women; 94 final diagnoses were normal, and the most serious diagnosis was a single case of mild to moderate cervical intraepithelial neoplasia. The positive predictive value of abnormalities found during the 2 years was 0.9%.

Concluding that the risk of unnecessary diagnostic procedures exceeds the likelihood of detecting clinically important cervical disease in these low-risk postmenopausal women, the investigators urge practitioners to be "cautious about applying tests that have a high likelihood of yielding false-positive results..."

### Timing of Increase in Menopause-Related Symptoms

**F**indings from a prospective, population-based study (Dennerstein L, Dudley EC, Hopper JL, et al. A prospective population-based study of menopausal symptoms. *Obstet Gynecol* 2000;96:351-8) point to the transition between early and late perimenopause as a time of increase in menopause-related symptoms. The 438 Australian-born women in the study, ages 45-55 years at baseline, were followed with annual assessments conducted for menopause-related symptoms over 7 years. The authors report that the women experienced the greatest change in severity of menopause-related symptoms—primarily hot flashes, night sweats and vaginal dryness—during the transition between early and late perimenopause; the number of women reporting five or more such symptoms during this period increased by 14%. During late perimenopause, the greatest increases in symptom severity were noted

for troublesleeping, vaginal dryness, night sweats and hot flashes. Variables significantly related to the onset of hot flashes were decreased levels of serum estrogen, a history of more than 10 pack-years of smoking, and having an unskilled or no occupation.

### Clinical Proceedings on Mature Sexuality

The Association of Reproductive Health Professionals (ARHP) has announced the availability of their monograph, *Clinical Proceedings on Mature Sexuality*, the objective of which is to “raise the awareness of sexuality as an important issue in the lives of patients among healthcare providers....” The monograph is funded by an unrestricted

educational grant from Solvay Pharmaceuticals, Inc.

ARHP notes that the *Proceedings* incorporates all literature on the subject of mature sexuality published during the past 5 years, providing clinicians with a reference tool for use in speaking to older patients about their sex lives. The monograph includes findings from several surveys of older Americans, including one designed to ascertain older adults’ views on sexual behavior. An extensive assessment of the problem of sexual dysfunction in older adults, with suggestions related to identification and treatment, is also included. A section on patient-provider communication provides additional statistical information and background regarding the experiences of older patients who attempt to discuss sexual problems with their physicians.

### Internet Tool Guides Women Through Search for Breast Cancer Information

In commemoration of the 15<sup>th</sup> anniversary of the National Breast Cancer Awareness Month (NBCAM) campaign, the NBCAM Board of Sponsors has launched “Hot Topics,” a search engine designed to help guide women through the maze of breast-cancer-related information on the Internet. It was developed in response to the “potential dangers to public health arising from unsubstantiated information about breast cancer on the Internet.”

“Hot Topics” searches the 17 Web sites of the Board of Sponsors and is available through the campaign Web site ([www.nbcam.org](http://www.nbcam.org)). This new tool is intended to allow users to navigate through “the top breast cancer information requests from women who want to find the best answers to their questions about the disease.”

## NAMS NEWS

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maceutical, Inc. Launched in May, the new 64-page booklet replaces the popular 50-page offering that’s been available since 1998. NAMS continues to keep pricing low—only about \$1.00 per copy for NAMS members—so healthcare providers can easily purchase a supply for distribution to patients.

“The new *Guidebook* has been very well received,” said Pamela Boggs, NAMS Director of Education and Development. “Its success is the result of many months of hard work on the part of the following members of the NAMS Consumer Education Committee: Marcie Richardson, MD (Committee Chair); Nancy Berman, MSN, RN, CS; Ione Bissonnette, CNM; Monica Choi, PhD, CRNP; Kathryn Havens, MD; Rebecca Kightlinger, DO; Diane Pace, PhD, RN, CS; Jennifer Prouty, MSN, RNC; Norma Roberts, BSW; and Sue Woodson, CNM, MSN, assisted by NAMS Medical Editor Phil Lammers and NAMS Communications Manager Sharon Somerville.”

The *Guidebook* is posted in its entirety on the NAMS Web site. Contact NAMS for an order form or order through the Web site.

### Future NAMS Meetings

2002  
October 3-5  
Sheraton Chicago Hotel  
Chicago, IL

2003  
September 18-20  
Fontainebleau Hilton Hotel  
Miami Beach, FL

2004  
October 7-9  
Marriott Wardman Park Hotel  
Washington, DC

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