

## Hormone Replacement Therapy: What Are Women's Choices?

**W**omen today live about one-third of their life after menopause. That's one reason recent generations—up to 45% of American women between the ages of 50 and 75—have embraced hormone replacement therapy (HRT). Initially taken on a short-term basis to relieve symptoms of menopause such as hot flashes, HRT increasingly has been prescribed for much longer periods for a number of motives.

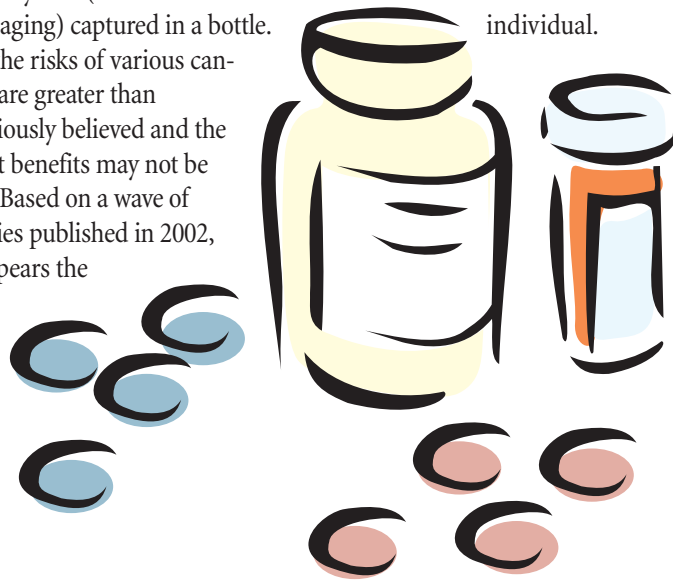
Faced with grandmothers and mothers bowed down by “dowager’s hump” or debilitated by fractures due to loss of bone density, many women asked for long-term HRT to prevent these problems of osteoporosis. For many women, HRT also pre-

serves energy levels and slows age-related changes in skin. Because HRT lowers blood cholesterol levels, physicians also had good reason to believe it would help women avoid heart disease.

HRT has seemed like a fountain of youth (or at least anti-aging) captured in a bottle. But the risks of various cancers are greater than previously believed and the heart benefits may not be real. Based on a wave of studies published in 2002, it appears the

risks of HRT may outweigh the benefits for many women. (See “The Risks of HRT.”)

Doctors hope this new research will encourage women and their physicians to have a thorough discussion weighing the risks and benefits to decide what’s best for that individual.



## Looking Beyond HRT

**F**or current, past or would-be users of HRT, there are several points to keep in mind.

- ▶ **Don't panic.** The percentages of increased risk may sound frighteningly high but actually represent only a slight rise in average risk, affecting a small number of women. However, the large scale and rigorous design of the clinical trials involved means the results are significant and should be taken seriously.
- ▶ **Talk with your doctor** about your options and be sure to review your family and personal medical history together. Health risks vary

with the individual.

- ▶ **Examine the reasons you are taking or might want to take HRT.** For relief of menopausal symptoms such as hot flashes, experts agree that short-term use appears to be safe for healthy women. The cancer risks appear after several years—the longer the use of HRT, the higher the risk.

- ▶ **Alternatives to reduce hot flashes** include low doses of anti-depressant medications. Discuss this with your doctor.
- ▶ **To prevent bone loss (osteoporosis),** HRT has a proven track record. However, newer medications are now available. If osteoporosis is your main concern, ask your doctor about the alternatives.

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## The Risks of HRT

The federal Food and Drug Administration announced January 8, 2003, that it would require warning labels on all hormone replacement therapy (HRT) drugs that contain estrogen or estrogen plus progestin. The boxed warning will state that these drugs may slightly increase the risk of heart attacks, strokes, blood clots and breast cancer.

This new information stems from a large-scale clinical study called the Women's Health Initiative, sponsored by the National Institutes of Health. This clinical trial has followed women on HRT for several years.

One arm of the study compared healthy women using combined estrogen and progestin and those taking a placebo—a total of 16,000 women. Another group of 11,000 women are taking estrogen alone or a placebo.

Researchers halted the combined HRT portion of the study in July 2002—three years early—because they found higher than expected breast cancer rates among women on

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## Designer Estrogens May Step In for HRT

Fortunately, for many women who relied on hormone replacement therapy to stave off age-related problems, a new age of “designer estrogens” has already dawned. These compounds, called SERMs or selective estrogen receptor modulators, act like estrogen in some ways but not in others. They actually block the effects of natural estrogen that may promote breast cancer. Although they won't prevent specific symptoms of menopause, SERMs appear to outstrip HRT in helping maintain long-term health.

Based on past clinical trials of postmenopausal women, the federal Food and Drug Administration has approved one SERM, raloxifene (Evista), for prevention or treatment of osteoporosis. Two major current trials are now studying possible other health benefits of raloxifene.

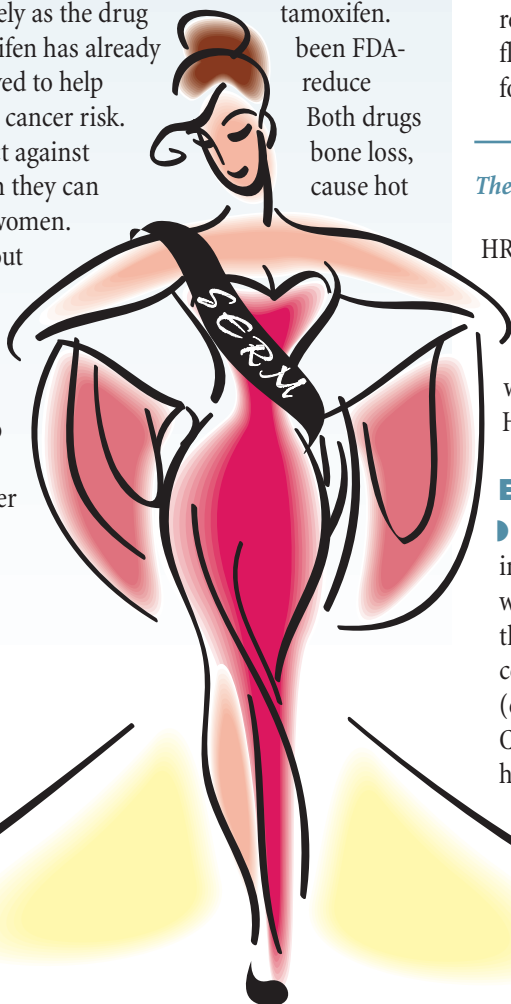
One of these studies involves 10,000 women at increased risk of heart disease. By 2006 researchers expect to have results showing whether or not the drug reduces this risk. Early findings suggest the raloxifene can lower “bad,” artery-clogging cholesterol levels (low-density lipoproteins) without reducing “good” cholesterol (high-density lipoproteins).

### STAR Study of Tamoxifen And Raloxifene

Another important study is STAR—Study of Tamoxifen and Raloxifene. Its goal is to see if raloxifene helps prevent breast cancer as effectively as the drug tamoxifen. Tamoxifen has already been FDA-approved to help reduce breast cancer risk. Both drugs protect against bone loss, although they can cause hot

flashes in 10% to 30% of women.

STAR aims to enroll about 22,000 postmenopausal women who are at increased risk of breast cancer. For more information about STAR or how to enroll, call the Cancer Center number on the cover page.



### Looking Beyond HRT (continued from page 1)

Start with trying to get adequate calcium in your diet. Eat foods containing calcium and vitamin D and take 500-milligram supplements consisting of calcium plus vitamin D, for a total of 1,500 milligrams of calcium daily. Vitamin D is necessary to absorb calcium adequately.

Drugs designed to prevent osteoporosis or treat women who have it, include bisphosphonates such as Actonel and Fosamax and selective estrogen receptor modulators (SERMs). (See “Designer Estrogens.”)

Food products and supplements—soy, flaxseeds, evening primrose oil, multivitamin and mineral compounds—are being promoted as a safer, “natural” substitute for hormone replacement therapy. (Soy, flaxseed and many other foods, such as yams, apples,

celery and nuts, contain mild plant estrogens.) Some women find such products help, but they may not live up to all their claims for everyone.

Also, regular use of soy or flax products may be dangerous for women at high risk of breast cancer or women who have had estrogen-dependent breast cancer. Large amounts of the isoflavone compounds these products contain may trigger estrogen-like activity and help any existing breast tumor grow.

If you want to stop taking HRT, ask your doctor about tapering off with a lower dosage if it has helped relieve severe menopausal symptoms. Stopping abruptly may bring back hot flashes and other symptoms as strongly as before.

### The Risks of HRT (continued from page 1)

HRT. The data included other unexpected health risks as well. Here is a list of the risks now known, starting with the earliest known risk of HRT.

#### Endometrial Cancer:

The first problem to surface, in the 1970s, was that HRT with estrogen alone increases the risk of endometrial cancer—cancer of the lining (endometrium) of the uterus. Combining estrogen with the hormone progesterin, however, overcomes this problem.

#### Breast Cancer:

In July 2002, researchers for the Women's Health Initiative reported a 26% percent increase in breast cancer among women in the study taking combined HRT compared to those taking a placebo. This slight but significant increase in breast cancer rates means eight more cases than expected annually among 10,000 women on combined HRT.

Women in the study taking estrogen alone did not show such risk. However, previous breast cancer studies indicate that estrogen alone may increase breast cancer risk, though the risk is

# Good News

## About Birth Control Pills

Since a woman's natural estrogen is known to promote breast cancer in a number of women, the possibility that hormone pills might promote breast cancer has long been a concern. Initially, most attention focused on birth control pills. Several studies produced inconsistent results.

Research on the pills used today, which have lower hormone doses than the pills introduced in the 1960s, at first found no increased risk. However, studies in 1995 and 1996 showed that women who currently or had recently used oral contraception had an increased risk of breast cancer up to 10 years after they stopped

greater with combined HRT. One recent study found the risk of breast cancer increased with long-term HRT but returned to normal five or more years after women stopped taking the therapy.

### Cardiovascular Disease:

▶ The Women's Health Initiative study also found an increased risk of heart attacks, stroke and blood clots among those taking combined estrogen and progestin. The findings indicated a 22% increase in cardiovascular disease among women taking the drugs, including a 29% increase in heart attacks. This translates into an additional seven heart attacks a year, eight strokes and 18 blood clots a year among 10,000 women on

taking the pill. Their risk then returned to normal.

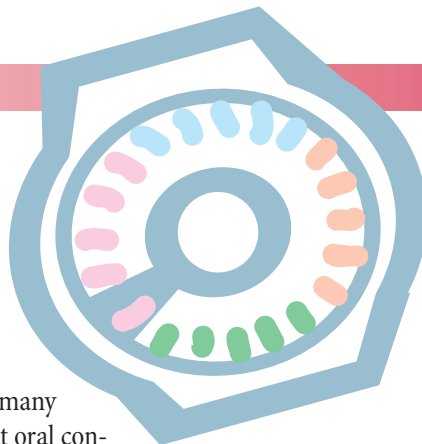
Even more positive, many studies have found that oral contraception definitely reduces the risk of cancer of the ovary and cancer of the lining of the uterus (endometrial cancer) by up to 50%—and this benefit continues for up to 15 years after women stop taking the pill.

And one of the newest studies, reported Jan. 7, 2003, in *Annals of Internal Medicine*, found that "oral contraceptives can be safely prescribed to many women older than 35 years of age until menopause," according to University of Wisconsin medical researchers. Older versions of the pill had high estrogen doses linked with increased risk of blood clots, especially after age 35. Today's lower-dose pills present no such problems.

combined HRT.

▶ Also in July 2002, researchers for a large clinical trial called the Heart and Estrogen/Progestin Replacement Study (HERS) issued a follow-up to their first report nearly two years ago. This study involved more than 2,760 women with a history of coronary heart disease (CHD) and an average age of 67 years at enrollment. Half took combined HRT and half took a placebo.

The study's first results indicated a higher than average risk of heart attacks during the first year on HRT followed by a lower risk after three years on HRT. However, more than six and three-quarter years of follow-up found no overall decrease in coronary heart disease or car-



### Benefits of birth control pills other than birth control include:

- ▶ Lower risk of ovarian cancer
- ▶ Lower risk of endometrial cancer
- ▶ Possibly lower risk of colon cancer
- ▶ Relief of many menopause symptoms
- ▶ Acne improvement
- ▶ Possible reduction of excess hair on the face and body
- ▶ Possible improvement in bone density, which would reduce the risk of osteoporosis

diovascular disease. The report concluded that "postmenopausal hormone therapy should not be used to reduce risk for CHD events in women with CHD."

### Ovarian Cancer:

▶ Still a third study reported in July examined the effect of HRT on the risk of ovarian cancer. The researchers found that women who used estrogen-only HRT, particularly for 10 or more years, had an increased risk of ovarian cancer. No increased risk appeared among women who used short-term estrogen-progestin, but this requires further research, especially on the impact of long-term combined HRT.

## Q & A: "Hormone Therapy" for Cancer

**Q:** With all the news about hormones promoting cancer, such as breast cancer, I was surprised to hear a cancer patient talking about the possibility of hormone therapy. Wouldn't this make the cancer worse?

**A:** Your logic is right on target—if hormone therapy meant giving hormones to a person with certain cancers. Actually, "hormone therapy" is really hormone-blocking therapy.

The two most common cancers provide the best examples. The female hormone estrogen is involved in many cases of breast cancer and the male hormone testosterone is known to promote the growth of prostate cancer. This means the hormone can stimulate tumor growth.

### Breast Cancer

Women with breast cancer who test positive for estrogen receptors, which means their cancer cells can take in estrogen, can benefit from therapy with the drug tamoxifen, a selective estrogen receptor modulator. Tamoxifen can bind to the cancer cells' estrogen receptors and thus keeps the woman's natural estrogen out of the tumor.

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### Low-Fat Teenage Diet Lowers Hormones— and Perhaps Later Risk of Breast Cancer

Researchers around the world study how diet affects the risk of cancer in adults. Early dietary studies took place at Fox Chase Cancer Center from the 1950s to 1980s. This work demonstrated that at least in laboratory rats, diet in the early years of life (before age 20, in human terms) has the most effect on later cancer risks.

Now, a new study by Fox Chase researcher Joanne Dorgan, Ph.D., M.P.H., suggests that what teenagers eat may influence cancer risk in human adults. To test the idea that a girl's diet during puberty may alter her risk of breast cancer when she grows up, Dr. Dorgan and her colleagues examined the effects of diet on blood levels of sex hormones in teenage girls. These same hormones have been linked to breast cancer in adults.

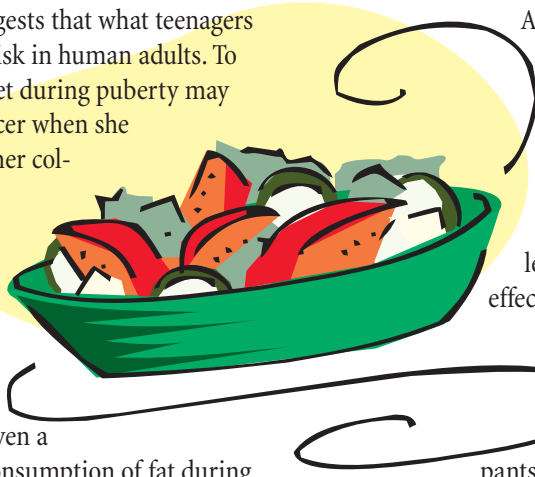
"Our study shows that even a modest reduction in the consumption of fat during puberty resulted in lower levels of sex hormones such as estrogen and progesterone," Dorgan explains. "Although we do not know if lower hormone levels during adolescence will influence breast cancer risk in adulthood, adolescence is a time of rapid growth and maturation of the breasts.

Estrogens and progesterone contribute to the regulation of this process."

Girls in the study who ate a fatty diet during puberty had an increased level of hormones in their blood compared to girls who ate less fat. The lower-fat diet was limited to 28 percent of calories from fat (less than 8 percent from saturated fat) with reduced cholesterol and increased fiber as well.

All the girls in the study started with high blood cholesterol, since the study was part of the Dietary Intervention Study in Children aimed at improving cholesterol levels. To evaluate long-term effects of the diet in her study, Dorgan and her colleagues hope to do a follow-up study with the participants, who are now in their 20s.

"So often, we hear of people changing their diets late in life to prevent cancer and other chronic diseases," says Dorgan. "While that is a good idea, this study supports the importance of having a good diet that begins during childhood and adolescence."



Q&A "Hormone Therapy" for  
Cancer (continued from page 3)

Tamoxifen has been used as follow-up treatment after breast cancer surgery for more than 25 years because it lessens the chance that cancer will occur in the second breast. The FDA approved tamoxifen to reduce breast cancer risk in healthy women in 1998.

#### Prostate Cancer

For men with prostate cancer, hormone-blocking therapy may be part of a treatment plan combining several methods, such as surgery, radiation therapy and chemotherapy. Typically, hormone therapy for prostate cancer uses drugs that either prevent production of testosterone and other male hormones, called androgens, or else block the action of testosterone in prostate cells.

- Free of charge, videos on breast cancer, *Breast Health Alert: Know Your Breast Cancer Risk and How to Reduce It*, and prostate cancer screening and prevention, *Taking Charge: Prostate Cancer Risk and What You Can Do About It*, are available from Fox Chase Cancer Center on request. **Call 1-888-FOX CHASE.**
- Women who have passed menopause may be eligible for the second national breast-cancer prevention trial, STAR—a Study of Tamoxifen and Raloxifene. **For information, call 215-728-4750** and leave your name and phone number. The STAR program coordinator will return your call.
- Men 55 years of age (50 years for African-Americans) or older may be eligible for SELECT—the Selenium and Vitamin E Cancer Prevention Trial—to see if taking vitamin E and/or selenium can help prevent prostate cancer. **For information, call 1-800-ENROLL-ME.**
- For women whose family history includes breast or ovarian cancer, the Margaret Dyson Family Risk Assessment Program at Fox Chase Cancer Center offers screening expertise, information, support and counseling about genetic testing. **Call 1-800-325-4145.**

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