The first randomized primary prevention trial to study combined hormone replacement therapy (HRT) in healthy postmenopausal women was stopped early when researchers found an increased risk of breast cancer among women taking part in the study, according to an article published in the July 17 issue of JAMA (2002;288:321-333, 366-368).

The Women’s Health Initiative (WHI) study found that women receiving the estrogen/progestin combination were also at higher risk for coronary heart disease, stroke, and pulmonary embolism, the report said. HRT did seem to lower the risk of colorectal cancer and bone fractures, but overall the risks outweighed the benefits, the researchers said.

More than 16,000 healthy postmenopausal women participated in the estrogen-plus-progestin component of the WHI study, a trial funded by the National Institutes of Health. All of the women were between the ages of 50 and 79, and all still had an intact uterus. The women began taking either a combination estrogen/progestin pill or a placebo each day, starting in the mid-1990s.

The women were supposed to be followed for an average of eight and one-half years, with the data safety and monitoring board looking at the results twice each year. The last scheduled review (May 2002) showed the results were significant enough that the trial was stopped after just over five years (mean follow-up).

The breast cancer incidence rate was 26 percent higher among those receiving HRT as opposed to those getting placebo. HRT increased the rates for heart disease (by 29 percent), stroke (by 41 percent), and pulmonary embolism (by 113 percent).

HRT did have some benefits, however. The incidence rates for colorectal cancer and hip fractures were 37 percent lower and 34 percent lower, respectively, in the HRT group. Endometrial cancer rates for the HRT and control groups were not significantly different.

In addition, the authors gave weight to each of these factors to come up with an overall “global index,” which indicated that the risks outweighed the possible benefits for these serious conditions by 15 percent. And HRT had no significant influence on the all-cause mortality rate.

In an editorial in the same issue,
Suzanne Fletcher, MD, MSc, and Graham Colditz, MD, MPH, both of Harvard Medical School, said that 38 percent of postmenopausal American women currently use some form of HRT. But with this study publication, the wisdom of such use has now been called into serious question.

“Given these results, we recommend that clinicians stop prescribing this combination for long-term use. Primum non nocere applies especially to preventive health care,” the editorial authors wrote.

**Individual Risks Are Small**

While the increased risk of breast cancer and other conditions may make HRT unsuitable for prevention in healthy women, the overall (absolute) risk for each woman is still rather small, the authors said.

For example, the 36% increased risk of breast cancer is based on the fact that during one year, among 10,000 women receiving combination HRT, there will be 38 cases of breast cancer. Among 10,000 women taking a placebo, there will be 30 cases, they said.

The same holds true for coronary heart disease (37 cases per 10,000 women per year with HRT versus 30 cases per 10,000 women per year with placebo), stroke (29 cases per 10,000 women per year with HRT versus 21 cases per 10,000 women per year with placebo), and venous thromboembolism (34 cases per 10,000 women per year with HRT versus 16 cases per 10,000 women per year with placebo).

Still the risk is there, and it appears to increase as the duration of combination HRT increases, the editorial authors said.

“The WHI provides an important answer for generations of healthy postmenopausal women to come—do not use estrogen/progesterone to prevent chronic disease;” authors Fletcher and Colditz said.

These conclusions do not apply to women receiving estrogen replacement therapy (ERT) alone. The effects of ERT on women who have had a hysterectomy are being studied in a separate WHI clinical trial, the results of which will likely not be available until 2005. The present study also did not look at short-term use of HRT to prevent menopausal symptoms such as hot flashes, so few conclusions about this issue can be drawn, the authors said.

**STUDIES DOCUMENT NEED TO IMPROVE TEENS’ SUN PROTECTION ATTITUDES AND BEHAVIOR**

It appears that many children and young adults are unaware of recommendations for sun protection or they are ignoring them, according to three articles in the June and July issues of *Pediatrics* (2002;109:1009-1014,1124-1130 and 2002;110:27-35).

**First Study Looks for Modifiable Sunburn Risk Factors**

In the first article, Kourtney J. Davis, PhD, of GlaxoSmithKline, Inc. in Research Triangle Park, NC, a former American Cancer Society (ACS) epidemiologist, and colleagues from the Centers for Disease Control and Prevention, the ACS, and Brown University reported that 72 percent of children aged 11 to 18 surveyed in 1998 had at least one summer sunburn. And many of those children had several sunburns during the summer of that same year (30 percent reported at least three sunburns and 12 percent reported at least five).

Forty percent of the children said they had used sunscreen when they developed their most serious sunburn of the summer. And only five percent of the children had used “sun-sensible ways” of protecting themselves before they had gotten their most serious sunburn (i.e., by wearing protective clothing or a wide brimmed hat, or by staying in the shade).

“The high frequency of sunscreen use during the sunburning episodes suggests the need to educate youth and parents better about