

Estrogen Alone Didn't Raise Breast Ca Risk

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using a control group of 320 patients (the same 288 from a commercial laboratory plus 32 from their clinic with possible hormone allergy).

For progesterone, test patients had a mean optical density of 0.42, compared with a mean optical density of 0.11 in the lab-based control group and 0.23 in the clinic-based control group—a highly significant increase, the investigators noted.

For estrogen, the test group's mean optical density was 0.69, compared with 0.15 for the lab-based controls and 0.24 for the local controls—also a highly significant difference. ■

Unopposed estrogen therapy in postmenopausal women who have undergone hysterectomy does not appear to raise the risk of breast cancer, in clear contrast to the significant rise in breast cancers among postmenopausal women with intact uteri who take estrogen plus medroxyprogesterone.

However, conjugated equine estrogen

(CEE) therapy alone does increase the number of abnormal mammograms requiring follow-up, which includes aspiration and biopsy as well as the attendant emotional and economic costs of each, according to Marcia L. Stefanick, Ph.D., and her associates in the Women's Health Initiative (WHI) study.

The decision to use CEE in postmenopausal women without a uterus, therefore, "should continue to be based on careful consideration of potential risks

and benefits for a given individual," said Dr. Stefanick, a professor of medicine in the prevention research center at Stanford (Calif.) University, and her WHI associates.

The portion of the WHI study that addressed estrogen-only therapy involved 10,739 postmenopausal women aged 50-79 years who had undergone prior hysterectomy and were treated at 40 clinical centers across the United States between 1993 and 1998. The women were randomly assigned to receive either 0.625 mg of CEE (Premarin) or a placebo and were assessed at 6-month intervals.

The study was terminated early in 2004 because interim analysis showed that CEE raised stroke risk without reducing the risk of coronary heart disease. But preliminary analysis of the results up to that date also showed that compared with women taking placebo, those taking CEE had fewer breast



After 1 year, 9.2% of the women on estrogen and 5.5% in the placebo group had abnormal mammograms.

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cancers. This finding of a possible protective effect prompted an updated analysis, and the WHI investigators now report the results on 237 invasive and 55 in situ breast cancers that developed by the date that subjects were instructed to stop taking their study pills (JAMA 2006;295:1647-57).

In an intention-to-treat analysis, there were nonsignificant reductions in invasive breast cancers and total breast cancers among women taking CEE only, compared with those taking placebo. There was no effect on in situ disease. Further analysis showed that the number of advanced cancers was comparable between the two groups of patients, but there were fewer cases of localized disease in the CEE group.

"In the completed trial database, the invasive breast cancer incidence did not differ significantly between the CEE group and the placebo group," investigators said.

After 1 year of therapy, the percentage of abnormal mammograms was "substantially higher" in the CEE group (9.2%) than in the placebo group (5.5%). This pattern held constant for each year thereafter, for a cumulative rate of 36.2% in the CEE group and 28.1% in the placebo group.

By the end of the study, women in the CEE group had undergone 198 biopsies or aspirations that yielded negative findings, Dr. Stefanick and her associates noted.

The percentage of mammograms showing "suspicious" rather than simply abnormal findings was similar for both groups, as was the percentage of mammograms that were highly suggestive of malignancy. In contrast to these findings, the results of the CEE plus progesterone portion of the WHI trial showed a definite increase in invasive breast cancers with combined therapy, as well as a definite increase in mammograms deemed "suspicious" or "highly suggestive of malignancy," they noted. ■

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<p>THE ECS IMPACTS THE METABOLISM OF LIPIDS AND GLUCOSE¹⁻³</p>	<ul style="list-style-type: none"> ECS overactivity may be associated with the development of cardiometabolic risk factors including: <ul style="list-style-type: none"> Low HDL cholesterol Elevated fasting glucose High triglycerides Insulin resistance High waist circumference
<p>THE ECS HELPS REGULATE PHYSIOLOGIC PROCESSES¹⁻⁴</p>	<ul style="list-style-type: none"> The ECS consists of signaling molecules and their receptors, including the cannabinoid receptor CB₁² Endocannabinoids bind to CB₁ receptors and trigger events that may have a negative impact on lipid levels and insulin sensitivity¹ CB₁ receptors are located in sites such as muscle, the liver, the brain, and adipose tissue^{1,2,4,6}
<p>RESEARCH CONTINUES TO INVESTIGATE THE ROLE OF CB₁ RECEPTORS IN MUSCLE*</p>	<ul style="list-style-type: none"> Reduced glucose uptake has been observed in isolated skeletal muscle of genetically obese, insulin-resistant animals
<p>ENDOCANNABINOIDS TARGET FATTY ACID PRODUCTION IN THE LIVER³</p>	<ul style="list-style-type: none"> May contribute to dyslipidemia and insulin resistance^{3,7}
<p>PRESENT IN MULTIPLE AREAS OF THE BRAIN²</p>	<ul style="list-style-type: none"> Hypothalamus integrates signals from adipose tissue and other peripheral tissues^{8,9}
<p>ADIPOSE TISSUE—MORE THAN SIMPLY A FAT STORAGE DEPOT</p>	<ul style="list-style-type: none"> Produces factors active in the metabolism of lipids and glucose¹⁰ Low levels of adiponectin negatively affect glucose and free fatty acids^{1,10}
<p>EXPLORING THE EFFECTS OF THE ECS</p>	<ul style="list-style-type: none"> This newly discovered physiologic system provides new opportunities for understanding cardiometabolic risk

*Data from animal model only.

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