

**EMBARGOED UNTIL FEB. 4, 2003, 5:00 P.M. EST**

***IRB # 2398: The NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE)***

**CITATION:**

*Journal of the American College of Cardiology*, February 5, 2003, "Hypoestrogenemia of Hypothalamic Origin and Coronary Artery Disease in Premenopausal Women: A Report from the NHLBI-Sponsored WISE Study"

**LOW ESTROGEN LINKED TO INCREASED RISK OF CORONARY ARTERY DISEASE IN PREMENOPAUSAL WOMEN**

**HIGHLIGHTS:**

A new study has found that premenopausal women with low blood estrogen levels have a significantly greater prevalence of coronary artery disease. This "hypoestrogenemia" stems from a dysfunction of the hypothalamus, the gland that regulates estrogen production in the ovaries. Researchers hope their studies will lead to new treatments that will protect these young women from increased risk of heart disease. The study appears in the February 5 issue of the *Journal of the American College of Cardiology*.

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LOS ANGELES (**EMBARGOED UNTIL FEB. 4, 2003 AT 5:00 P.M. EASTERN**) – According to an article in the February 5 issue of the *Journal of the American College of Cardiology*, coronary artery disease in young women appears to be related to estrogen deficiency, and there may be a link to psychosocial stress.

The findings are based on an analysis of statistics compiled from a major ongoing investigation of heart disease in women that is led by cardiac researchers at Cedars-Sinai Medical Center.

"Although coronary artery disease is the leading killer of premenopausal women, taking even more lives than breast cancer does, most studies have focused on heart disease in older women. Our findings demonstrate for the first time that young women with low blood estrogen levels have a significantly greater prevalence of coronary artery disease," said C. Noel Bairey Merz, M.D., the article's first author.

Doctors have been aware that the prevalence of coronary artery disease increases after menopause, and for

this population they have urged a greater use of coronary diagnostics. “Now we’re seeing that even young, premenopausal women lose protection from coronary artery disease when ovarian function and hormonal balances are disrupted,” Dr. Bairey Merz said. “We hope the knowledge gained from these studies will lead to gender-specific treatments that will reverse this process.”

Dr. Bairey Merz is the primary investigator of a four-center study, the Women’s Ischemia Syndrome Evaluation (WISE) sponsored by the National Heart, Lung and Blood Institute. She holds Cedars-Sinai’s Women’s Guild Chair in Women’s Health, and directs the medical center’s Preventive and Rehabilitative Cardiac Center and the Women’s Health Program. She also serves as national spokesperson for the Women’s HeartAdvantage campaign, a nationwide program designed to help women learn more about the symptoms and treatment of heart disease and heart attacks.

WISE consists of 855 women with coronary risk factors undergoing coronary angiography for suspected ischemia – lack of blood flow and resulting oxygen deficiency to the heart. For the study on hypoestrogenemia (low estrogen levels) and coronary artery disease in premenopausal women, statistics on 95 women were analyzed.

The researchers’ attention centers on women with decreased estrogen levels caused by a dysfunctional hypothalamus. One of the many functions of the hypothalamus, a gland in the center of the brain, is the regulation of the ovaries in the production of estrogen and other reproductive hormones. Regular fluctuations of hormones control menstrual cycles in premenopausal women while an abnormal decrease can cause disruption of menstruation (amenorrhea).

Although the study establishes a link between low estrogen levels and coronary artery disease (CAD) in premenopausal women, it was not designed to determine cause and effect. The researchers note that a currently unknown mechanism may enable heart disease to reduce estrogen levels, or a separate mechanism may underlie both disorders. On the other hand, previous studies support the hypothesis that the hormone deficiency plays a role in the development of coronary artery disease. There is also evidence that psychosocial stress is a precipitating factor.

Studies in both animals and humans have documented an association between “environmental psychologic stress” and disruption of the menstrual cycle due to dysfunction of the hypothalamus. Atherosclerosis – plaque buildup that narrows arteries – has been found to be “significantly accelerated” in monkeys that have low estrogen levels caused by hypothalamic dysfunction induced by stress. In the current study, a significant number of women found to have hypoestrogenemia of hypothalamic origin were taking anti-anxiety medications, a fact that suggests the possibility that stress played a developmental role.

The study also supports the concept that physiological differences between men and women may help to explain the fact that young women with heart disease have a markedly higher mortality rate than their male counterparts of the same age. Previous animal and human research has shown that hypoestrogenemia in women is accompanied by narrowing and even constriction of coronary arteries in response to a stressor.

“Our current results document that premenopausal women with CAD may have hypoestrogenemia, and, therefore, may have more adverse coronary arterial dysfunction,” the article says. “Although we are unable to link these results with mortality in this relatively small sample size, they suggest that premenopausal women with CAD could be at a higher mortality risk stemming from hypoestrogenemia-related adverse physiologic effects.”

The study was supported by contracts from the NHLBI (N01-HV-68161, N01-HV-68162, N01-HV-68163, and N01-HV-68164), a GCRC grant from the National Center for Research Resources (M01-RR00425), and grants from the Gustavus and Louis Pfeiffer Research Foundation (Danville, N.J.), The Women's Guild of Cedars-Sinai Medical Center (Los Angeles), and the Ladies Hospital Aid Society of Western Pennsylvania (Pittsburgh).

Cedars-Sinai Medical Center is one of the largest nonprofit academic medical centers in the Western United States. For the fifth straight two-year period, it has been named Southern California's gold standard in health care in an independent survey. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthrough in biomedical research and superlative medical education. Named one of the 100 "Most Wired" hospitals in health care in 2001, the Medical Center ranks among the top 10 non-university hospitals in the nation for its research activities.

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