



## **8 National Centers Begin Recruitment for the Kronos Early Estrogen Prevention Study (KEEPS)**

### ***Kronos Longevity Research Institute Launches 5-Year Study Focusing on the Effects of Hormone Therapy on the Progression of Heart Disease in Recently Menopausal Women***

PHOENIX (July 26, 2005) -- Eight national study centers are now recruiting for the **Kronos Early Estrogen Prevention Study (KEEPS)**, which is being coordinated by the Phoenix-based Kronos Longevity Research Institute (KLRI). The study focuses on the effects of hormone therapy (HT) as it relates to the progression of atherosclerosis (hardening of the arteries) in recently menopausal women. Participating centers include:

- Albert Einstein College of Medicine/Montefiore Medical Center (New York City)
- Columbia University College of Physicians and Surgeons (New York City)
- Harvard Medical School/Brigham and Women's Hospital (Boston)
- Mayo Clinic (Rochester, MN)
- University of California, San Francisco Medical Center
- University of Utah School of Medicine (Salt Lake City)
- University of Washington School of Medicine/VA Puget Sound Health Care System (Seattle/Tacoma, WA)
- Yale University School of Medicine (New Haven, CT)

KEEPS is a randomized, placebo-controlled, double-blind trial of 720 women designed to provide prospective data on the risks and benefits of HT on recently menopausal women, particularly as it relates to the progression of heart disease. The results of the Women's Health Initiative (WHI) estrogen plus progestin trial, which was halted by the National Institutes of Health in July 2002, prompted a consortium of health researchers to study the risks and benefits of HT on a younger subset of women who recently entered menopause. Prior to the WHI, most data suggested that HT was associated with a high degree of protection (30 to 50 percent reductions) against coronary heart disease, all-cause mortality and osteoporotic fractures, in addition to a small increase in breast cancer risk.

KEEPS is designed to explore issues raised by the WHI, specifically:

**Age of Participants** – The study will explore whether beginning HT in recently menopausal women (six months to three years since last menses) protects against atherosclerosis, the major cause of heart attacks. WHI participants were postmenopausal, with a mean age of 62.7, yet most women begin HT much younger, at the onset of menopausal symptoms.

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**Transdermal Application** – KEEPS also will study whether the natural human estrogen, estradiol, delivered through the skin via a patch is equally effective as and potentially safer than oral estrogen. Researchers have speculated this method may be safer since transdermal estrogen does not go to the liver in high concentrations and has been shown to have little or no effect on clotting. On the other hand, transdermal estradiol may be less effective since it does less to increase HDL-cholesterol levels.

**Imaging of Key Arteries** – KEEPS will image the carotid and coronary arteries in order to measure the effects of HT on heart disease. Carotid intimal medial thickness (IMT) will be measured by ultrasound and the progression of coronary calcium will be tracked by X-ray tomography. In addition, KEEPS investigators will measure both protective and risk factors for heart disease, which are believed to be affected by hormones. This detailed analysis is particularly important in view of findings from earlier animal and human research indicating that estrogen may be beneficial for preventing early lesions of atherosclerosis, but ineffective, or even harmful, once disease is established.

“There are a lot of data that suggest that estrogen is good early and bad late,” said S. Mitchell Harman, M.D., Ph.D., director of KLRI. “The WHI was instrumental in providing a roadmap for the next phase of research to examine whether estrogen protects younger women from cardiovascular disease, as earlier observational studies indicated. KEEPS is designed to provide useful new data to begin answering women’s questions and help shape future research.”

### **Study Design**

KEEPS will be a randomized, placebo-controlled, double-blind examination of healthy, recently menopausal women ages 42 to 58. Each center will recruit 90 women for a total of 720. KLRI will serve as the coordinating center, but will not recruit participants.

Study participants will be divided into three groups. The first group will receive an oral tablet containing conjugated equine estrogens (Premarin®, 0.45 mg daily) and a placebo skin patch. The second group will receive an oral placebo tablet and a skin patch delivering estradiol (Climara®, 50 mcg/day). The third group (control) will receive a placebo tablet and a placebo skin patch. Women receiving active estrogen also will use progesterone (Prometrium®, 200 mg daily for first 12 days of each month) to protect the uterine lining from overgrowth. Subjects not receiving active estrogens will take placebo capsules.

All participants will be evaluated at 10 formal sessions for data and sample collection procedures and at additional visits for study monitoring, including a compliance check, a review for adverse effects and a brief physical exam.

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Subjects will be monitored at three-month intervals by questionnaire for any adverse effects. The subjects also will undergo lab monitoring at various points during the study. All major adverse effects will be reported immediately to the local center's institutional review board (IRB) and to KLRI, which will relay reports to the data safety monitoring board (DSMB). All adverse effects, major and minor, will be reported quarterly to KLRI for consideration by the DSMB.

**About KLRI**

KLRI is a not-for-profit 501 (c) (3) organization that conducts state-of-the-art clinical translational research on the prevention of age-related diseases and the extension of healthier human life. Translational research is the critical link between findings from the basic research laboratory and corresponding improvements in clinical care. In addition to KEEPS, KLRI currently is studying Testosterone's Effects on Atherosclerosis in Aging Men (TEAAM Study). For more information, visit KLRI's Web site at [www.kronosinstitute.org](http://www.kronosinstitute.org) or [www.keepstudy.org](http://www.keepstudy.org) or call 1(866) 840-1117.

**Center Contacts**

For recruitment information relative to a specific center, please contact:

Albert Einstein College of Medicine/Montefiore Medical Center (New York City): (718) 430-3152

Columbia University College of Physicians and Surgeons (New York City): (212) 305-0832

Harvard Medical School/Brigham and Women's Hospital (Boston): (617) 732-9870

Mayo Clinic (Rochester, MN): (507) 538-0848

University of California, San Francisco Medical Center: (415) 353-4300

University of Utah School of Medicine (Salt Lake City): (866) 807-4517

University of Washington School of Medicine/VA Puget Sound Health Care System (Seattle/Tacoma, WA):  
(253) 583-2038

Yale University College of Medicine (New Haven, CT): (203) 785-4739

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