



# IMPACT<sup>2009</sup>

*You and Clinical Research at Kronos Longevity Research Institute*

## Your Contribution to Clinical Research – You Make a Difference!

It is very important to all of us to live healthier and longer lives. Your participation in the Kronos Longevity Research Institute's (KLRI) research studies help us understand more about preventing age-related disease and how to help you live longer, healthier lives, which we call increasing your *healthspan*.

KLRI research would not be made possible without the help of the many study participants that volunteer in our studies and its donors. Without you, our research would not be possible. Your participation moves clinical research forward so that we can increase our knowledge about aging and learn how we can live longer and healthier. Your participation is making a big difference in the future of longevity science.

As KLRI prepares to celebrate its 10th anniversary in 2010, we want to say thank you to those who have participated in studies or have supported us in other ways. We are grateful for everyone being committed to helping KLRI become one of the leading national research organizations with an extensive list of academic collaborators.

KLRI studies have ranged from pilot studies consisting of 10 to 12 participants to larger-scale studies comprising of more than 700 participants. Some of our studies take place over an extended period of time, such as three to four years, while others can be completed in a shorter time period, as short as two hours. However, no matter the size or length of the study, all studies make a valuable contribution to the advancement of the science of aging, whether it reveals new information on how we can extend our healthy years, or serves as a stepping stone to further research studies or a foundation for a more extensive study.





Many of KLRI's research studies have been published in prominent scientific journals and/or presented at scientific meetings. Recently, KLRI research has appeared in *Journal of Nutrition*, *Clinical Geriatrics*, *Journal of Clinical Endocrinology and Metabolism*, and *AGE*, just to name a few. One of KLRI's largest studies, the Kronos Early Estrogen Prevention Study (KEEPS), has been published in several noteworthy journals such as the *New England Journal of Medicine*, the *Journal of the American Medical Association (JAMA)*, *Menopausal Medicine*, and the *Journal of Cardiovascular Translational Research*. Our research projects have also been presented at the North American Menopause Society, the International Conference on Alzheimer's Disease, the American Heart Association, the Endocrine Society Meeting, the 50th Baltimore Longitudinal Study on Aging Anniversary National Institute of Aging Nathan Shock Symposium, and many more.

Here is a summary of some of our research studies that have shed new light in longevity science.

## Benefits of a High Omega-3 Diet in Older Adults:

As we age, hormone secretion and cell responsiveness decrease. Animal studies showed that omega-3 fatty acids may help hormone signals get into cells whose cell membrane has been stiffened by age. KLRI examined the effects of a diet high in omega-3 fatty acids on the loss of normal hormone balance that occurs during normal aging. The study, which appeared in *Hormone and Metabolic Research*, found that a high omega-3 fat diet improves insulin sensitivity and reduces inflammatory markers, but does not alter endocrine responsiveness. These findings are consistent with other studies that have found that diets high in omega-3 and/or omega-3 supplements have anti-inflammatory benefits. Omega-3 fats are abundant in Japanese and Mediterranean diets, and are believed to contribute to low heart disease rates in those regions.

## High Statin Doses Do Not Impair Aerobic Activity or Skeletal Muscle Function in Older Adults:

Statin are lipid lowering agents used in the prevention of atherosclerosis, hardening of the arteries. KLRI investigated whether high-dose statin treatment would result in decreased exercised capacity in older adults. The study, published in the *Journal of the American Aging Association*, found that statin use in older adults does not negatively affect aerobic exercise or high-intensity weight training. Many older Americans are staying healthy longer by exercising and using statins to reduce their cholesterol levels. This research indicates that these drugs do not adversely affect a healthy exercise regimen.



## Hormone Therapy May Reduce Atherosclerosis in Women Close to Menopause:

Published in the American Society for Reproductive Medicine's *Menopausal Medicine*, KLRI discussed that there are certain benefits to hormone therapy (HT) in newly menopausal women, however there are risks and a potential loss of benefit to HT in women who have been postmenopausal for several years and may have pre-existing atherosclerosis. This research continues to underscore the theory that estrogen may be cardio-protective if administered close to menopause.

In addition, KLRI discussed that previous trials began HT use much later than in usual clinical practice—beginning trials on women of a median age of 63, as opposed to 51 (the average age of menopause in the United States). Younger women saw benefits from HT; older women saw the opposite.

KLRI's research study, the Kronos Early Estrogen Prevention Study (KEEPS), will more fully address the issue of the benefits of HT in women close to the menopausal transition. KEEPS is examining the effects of HT on the development of arterial disease, cognitive function, as well as quality of life in recently menopausal women.



## Ischemia Reperfusion Unveils Impaired Capacity of Older Adults to Prevent Oxidative Stress:

In this research study, KLRI hypothesized that the capacity to prevent oxidative stress diminishes with age, which leads to more extensive oxidative damage during trauma. This study, published in *Free Radical Biology and Medicine*, found that aging does impair the ability to prevent oxidative damage after an acute insult, which may contribute to the increased vulnerability of older adults to traumatic conditions. This diminished capacity to resist oxidative stress may explain the poor outcomes associated with older age in a variety of medical conditions. Our method of identifying this diminished capacity, mild forearm ischemia/reperfusion, may also provide the means to identify at-risk patients and appropriate interventions to improve health outcomes.

## No Effect of Vinegar on Enteral Carbohydrate Absorption in Humans:

Because of the increasing prevalence of diabetes, simple but effective ways to lower blood glucose levels, applicable to a wide variety of dietary habits, are strongly needed. The mechanism of action of vinegar is not known; we hypothesized that by suppressing endogenous insulin secretion we could estimate the glucose absorption rate from an oral carbohydrate load and determine the effects of vinegar ingestion on this rate. During this study, the rate of rise of glucose was greater after vinegar ingestion compared to placebo, suggesting that vinegar does not act to decrease glycemia by interference with enteral carbohydrate absorption.

## Prescribing Exercise for Older Men:

A regimen of exercise and dieting, following proper guidelines, is the most effective way for older men to prevent or minimize changes associated with aging and to live longer lives. Published in *Clinical Geriatrics*, KLRI recommends that the optimal exercise program should increase and/or maintain muscle mass and muscle quality, primarily with resistance training that is designed to progress in difficulty and speed over time. This, combined with weight management through diet, proper protein intake and aerobic exercise, will help physicians make specific recommendations to their patients as part of comprehensive treatment plans.

KLRI recommends aerobic exercise and resistance training through lifting weights at a minimum of two to three days a week for 30 minute sessions. Adults should use a combination of circuit weight machines and free weights, increasing the speed at which the weight is lifted. This “high-velocity movement,” performing the lifting part of the exercise as fast as possible and then lowering the weight with control, will improve muscle power, endurance and even balance. Resistance training will also strengthen the muscles around the joints, preventing common injuries like joint sprains and osteoarthritis of the knees. Proper protein intake (0.8-1.2 g/kg/day) is essential for older adults, who lose their responsiveness to the amino acids in their skeletal muscle over time.



## Tart Cherry Juice Could Help You Live Longer:

Foods high in polyphenols have long been associated with improved health, but the mechanism for their effects is still unknown. KLRI tested the hypothesis that tart cherry juice, which contains high levels of polyphenols, improves the ability of older adults to resist oxidative damage when presented with oxidative stress. The study,



published in the *Journal of Nutrition*, showed that drinking tart cherry juice does improve anti-oxidant defenses in older adults. Those studied showed a greater ability to neutralize oxidative challenges and reduce oxidative damage in nucleic acids (DNA, RNA). These findings are significant because oxidative stress ages cells. Finding solutions to the impact of oxidative stress is one of the keys to learning how to slow the aging process.

## Testosterone Replacement Shows Little To No Benefit In Terms of Health or Aging:

Testosterone therapy has been thought to provide modest increases in lean body mass, muscle mass and a decrease of fat mass for older men. In an article in *Clinical Geriatrics*, KLRI indicated that it is unnecessary for those with testosterone levels in the normal or low-normal range. While the risks are small, the fact that the potential population for these therapies may be as high as 20 million means that even the slightest risk for prostate cancer, one per 1,000 men receiving therapy, could result in 20,000 new cases per year. Previous studies have been too small or underpowered to determine the true worth of these therapies, and the results of tests so far have seen little to no effect on body composition, bone mass, brain function or sexual function.

A KLRI study is looking at Testosterone's Effects on the Progression of Atherosclerosis in Aging Men (TEAAM). Atherosclerosis is a medical condition in which fatty material is deposited along the walls of arteries. This fatty material thickens, hardens and may eventually block the arteries.

## Coming Soon... New Study

*Fish Oil Supplementation to Prevent Bone Loss in Postmenopausal Women Taking Thiazolidinedione (TZD) Drug for Type 2 Diabetes Mellitus (T2DM):* T2DM is an increasingly common disease with long-term complications. Thiazolidinedione (TZD) drugs such as Actos® (Pioglitazone) are FDA-approved and well-accepted medications for the treatment of T2DM; they work mainly by improving sensitivity to insulin. However, bone mineral loss is a side effect in some people taking TZDs, resulting in an increased risk of osteoporosis and fractures, a problem especially significant for postmenopausal females. Omega-3 fatty acids, the components of the oils found in fatty fish, are associated with increased bone mineral density and fewer bone fractures. Study doctors at the Kronos Longevity Research Institute (KLRI) wish to determine if supplementation with fish oil will prevent bone loss in postmenopausal women with T2DM taking TZDs.

New data from the following studies to be published

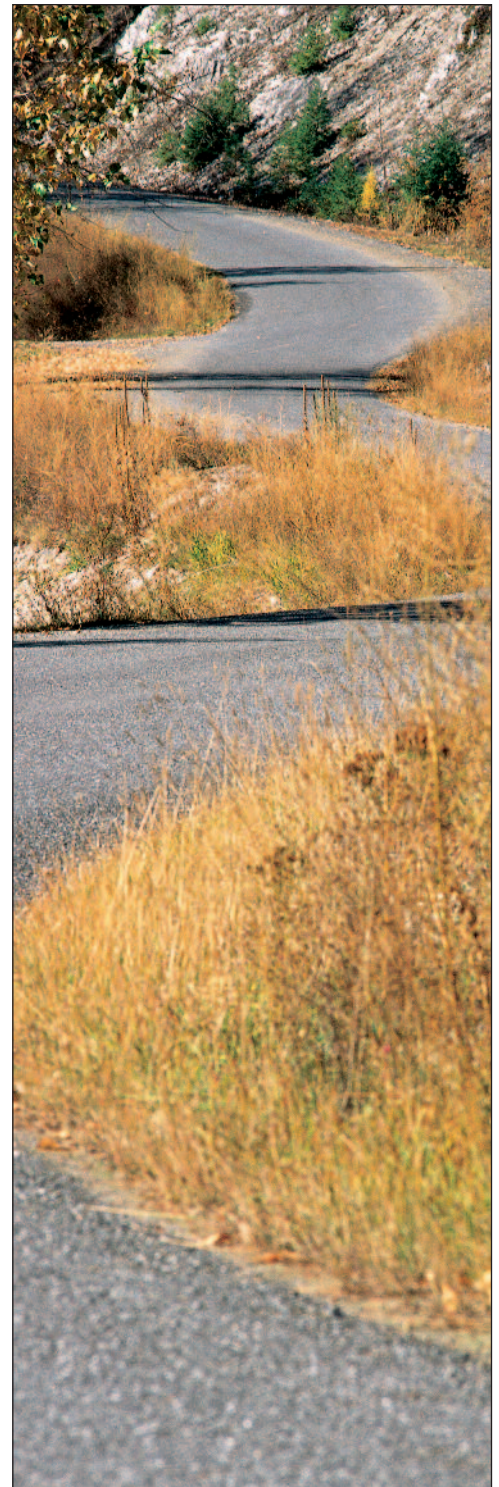
- Oxidative Stress and Free Radicals
- Using a GABA Receptor-Agonist to Restore Growth Hormone Secretion in Older Adults
- The Effects of Saturated Fatty Acids on Insulin Resistance, Endothelial Dysfunction and Systemic Inflammation

\* All new studies are subject to funding. All paper for publication are subject to acceptance.

## Ongoing Studies

- Kronos Early Estrogen Prevention Study
- Testosterone's Effects on the Progression of Atherosclerosis in Aging Men
- Effects of Physical Fitness on Stress Resilience in Older Adults

*For information about KLRI's studies, please visit*  
[www.kronosinstitute.org](http://www.kronosinstitute.org)



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## *Stress Resilience Study*

Healthy men and women over 60 needed to participate in a clinical trial to study the body's ability to recover when oxidative stress is increased.

Compensation provided.

Call **602-778-7480** to see if you qualify.