



KRONOS LONGEVITY RESEARCH INSTITUTE

Research to promote a longer healthier life for you, your children, and your grandchildren.



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TESTOSTERONE AND CHANGES IN AGING MEN

Scientific research has shown that body composition and biological function changes with age. These alterations are measurable and include such changes as:

- loss of lean body and muscle mass
- decreased muscle strength
- diminished physical endurance
- reduced ability to carry out tasks of daily living, which, at its extreme, results in frailty

There also are increases in the total and percentage of body fat, accompanied by a higher risk of adult onset type diabetes, and elevated cholesterol. Other changes in metabolism include loss of bone calcium leading to low bone density and fractures. Older men often complain of decreased frequency of and desire for sexual activity. Psychological changes during aging include slower problem solving, lapses of memory, and increasing incidence of dementias, especially Alzheimer's disease.

It is unclear the extent to which alterations in hormone balance contribute to the above changes. Documented age-related changes include a decrease in the major male hormone, testosterone. This change begins in the thirties and continues at a relatively constant rate into old age. There are also reductions in circulating growth hormone, insulin-like growth factor-I, and a tendency for increased adrenal steroid secretion, especially in response to stress.

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DIRECTOR'S MESSAGE

Previously, we discussed macronutrients, i.e., carbohydrates, fats, and proteins, bringing some perspective to the ongoing debate as to how to structure the "food pyramid" and what each important component "brings to the table." The question of the correct balance of micronutrients necessary for optimal health for various people and during different stages of the life cycle is even more controversial than that for macronutrients. Micronutrients are compounds consumed in small quantities as part of our diet or in dietary supplements that are considered to be beneficial for optimum health and the prevention of specific disease risks. Micronutrients are comprised of vitamins, trace minerals, and a variety of phytonutrients with names such as anthocyanins, proanthocyanidins, lycopenes, sulphorophanes, and more. Our next issue will focus on these important compounds and will review some of the new findings that are emerging. Scientists are now turning their attention to investigating the properties, actions and interactions of these molecules.

Briefly, vitamins are the most common of the micronutrients. These are molecules that usually act as "co-factors" or "helper" molecules and work in conjunction with critical enzymes in our cells to maintain vital processes. Examples include:

- 1) Vitamin C, which is essential for the synthesis of collagen (the protein fiber that holds our tissues together)
- 2) Vitamin B12, which assists in the making of hemoglobin (the pigment that carries oxygen in the blood)
- 3) Vitamin D, which is required in order to absorb ingested calcium and transfer it into bone.

Past research has established a minimum daily requirement for the common vitamins. These values were established for children and young adults. An adjustment in the values for menopausal women, the elderly, and individuals with various illnesses may need to be made. Moreover, the minimum daily requirement is the amount necessary to avoid vitamin deficiency disease, but not necessarily the correct amount for optimal health. New research on vitamins is revealing some surprising findings and previously unsuspected benefits and risks. In the next issue, we will discuss these results as well as the implications of taking vitamin supplements in "megadoses," that is, many times over the minimum daily requirements.

Minerals are another important class of molecules that have been thoroughly discussed with varying degrees of accuracy. What is the proper amount of dietary calcium for women and men or individuals with osteoporosis? Is iron beneficial? How much copper, zinc, magnesium, etc. is enough? Are there "magical" forms of these elements that provide better absorption or more beneficial action?

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Each hormonal alteration, when present in young adults, can cause effects having much in common with the age-related changes in body composition and function. In particular, low testosterone in men is associated with loss of muscle mass and strength, increased fat, and reduced libido and erections. The relationship between low testosterone and diminished sexual response during aging is not proven, but recently it has become clear that the decline in testosterone levels is such that a substantial fraction of men over the age of 65 could be diagnosed as testosterone deficient (hypogonadism) by standard criteria if they were younger.

The increase in the number of hypogonadal men is more pronounced when the bioavailable testosterone or free testosterone index is considered. Testosterone circulates in the blood bound to a plasma protein called sex hormone binding globulin (SHBG). The protein-bound testosterone is not available to cross into cells and alter their function. Only the part that is not bound is "bioavailable." Because SHBG blood levels tend to increase as men age, older men may have a low total testosterone level but still be hypogonadal because of a low bioavailable testosterone. Therefore, men with signs and symptoms consistent with hypogonadism and total testosterone measured in an ambiguous range (250 to 450 nanograms per 100 ml) should have their bioavailable testosterone determined.

Although many laboratories perform a less reliable "free testosterone" determination, the classic bioavailable testosterone assay, originally developed by Dr. William Rosner, is performed at relatively few laboratories in the United States, including Phoenix-based Kronos Science Laboratory. Using bioavailable testosterone as the criterion, as many as 45% of men in their sixties and 60% of men in their seventies are hypogonadal. By some estimates, hypogonadism is one of the least treated of all recognized diseases.



A decline in self-reported total sexual activity and quality and quantity of erections with aging has been documented in a number of research studies. These decreases are accompanied by a loss of desire for sexual activity and an increase in the length of time men report being comfortable without sex. For example, in one study, less than 20% of men 70 years and older reported consistently adequate erectile function and nearly 40% rated their erectile function as "little or none." In the same study, approximately 15% of men age 70 and over reported desire for sex more than once weekly and 35% had no sexual desire. A decrease in erectile function also has been documented in another study in which approximately 50% of men ages 70-79 reported moderate or complete loss of erectile function compared with only 25% of men 40-49 years of age.

Although the decrease in testosterone levels has been shown in various studies to be correlated with the loss of sexual function, decreases in muscle strength, and reductions in bone calcium, the finding of such associations does not prove that hormone deficiency causes these changes. An important step in establishing plausibility of a causal relationship between decreased

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testosterone and other age-related changes, is the identification of biological mechanisms by which testosterone can alter muscle, bone, fat, and sexual behavior. In the case of libido, it has long been known that exposure to testosterone alters both brain function, and, in some species, structure. There are receptors for both male and female hormones in nerve cells (neurons) in various areas of the brain, including those neurons known to be associated with sexual activity. It also appears from experiments in a number of animal species that testosterone affects sexual behavior. A direct local role for testosterone in erections also has been shown in animal studies, and probably occurs in humans, although this has not been proven at this time. Testosterone also acts directly on fat cells causing them to break down fat and release fatty acids, and it causes muscle cells to stimulate synthesis of new muscle protein in experimental animals and isolated cell cultures. Thus, the idea that low testosterone contributes to the observed aging changes in fat and muscle is biologically plausible.

Final confirmation of the importance of testosterone as it relates to age-related changes in body composition and function awaits well-designed studies to determine whether or not testosterone replacement improves these changes. Preliminary studies appear promising.



In one study, 80% of older men perceived their libido as better after treatment with testosterone, compared with about 8% receiving placebo. In another trial, in 150 men ages 50-70



years, treatment with another male hormone, dihydrotestosterone, improved early morning erections and the ability to maintain erection. There are also a few studies suggesting that giving testosterone to older men who have low testosterone levels may increase muscle mass, decrease body fat, and improve bone density, but significant effects on strength and endurance with testosterone alone have not been documented.

It is said that, "Nothing in life is free," and this is certainly true of hormone therapies. When applying this to hormonal therapies, this means that benefits are usually accompanied by risks. In the case of testosterone the major risks of concern are:

- possible adverse effects on the prostate to cause prostate enlargement with obstruction of urine flow or even promote cancers
- effects on blood cholesterol leading to acceleration of hardening of the arteries (atherosclerosis) with greater risk of heart attacks, strokes, etc.

It has not been shown whether or not testosterone actually produces either of the above adverse effects when given to healthy older men with low testosterone

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levels. A recent study showed that men with adult onset (type 2) diabetes are at greater risk for heart disease if they also have low testosterone levels. It may be that higher levels of testosterone actually protect men from atherosclerosis. Realistic assessment of the risk-to-benefit ratio for male hormone replacement must await completion of additional well-controlled studies. Unfortunately, such studies have not even commenced as yet. KLRI scientists, in collaboration with investigators at the University of California and Drew University in Los Angeles, will begin a study this year, examining the effects of treatment of about 300 older men with a testosterone gel on atherosclerosis as well as on muscle strength and endurance, fitness, body fat, glucose tolerance, and psychological and sexual function.

Despite the uncertainties, it is still considered good clinical practice by knowledgeable geriatricians and endocrinologists to treat men, regardless of age, with male hormone replacement when they are clearly testosterone deficient (total serum testosterone levels less than 250 ng/dl or bioavailable testosterone levels less than 120 ng/dl). It also should be reiterated that many older men who are hypogonadal are never



diagnosed or treated. Men who are experiencing one or more of the symptoms of low testosterone mentioned should discuss them with their physicians. There is also a copyrighted validated self-test questionnaire developed by Dr. John Morley of St. Louis University, which is highly accurate for identifying men with hypogonadism.

Finally, aging is associated with changes in body composition similar to those observed in men with testosterone deficiency. These include:

- loss of libido and decrease in erections
- decreases in lean body mass, muscle strength and endurance
- decreases in bone density
- increases in body fat and insulin resistance

To summarize, in older men, circulating testosterone tends to decrease and testosterone levels correlates positively with sexual function, lean body mass, muscle strength, measures of fitness, and bone density, and negatively with body fat. The relationships of testosterone measures to these effects suggest that some part of age-related changes may be due to testosterone depletion. Testosterone replacement appears to improve body composition and function in some older men with low testosterone levels. It is important to keep in mind that changes in other hormones (e.g. growth hormone, adrenal steroids) and non-hormonal factors (nutrition, exercise, oxidative damage, etc.) also play important roles in the biology of aging. Thus, testosterone, or even multiple hormone replacement, is not a "magic solution" that will "cure" aging. Further studies of the risks and benefits of male hormone replacement are needed to clarify these issues.

S. Mitchell Harman, MD, PhD
Director and President,
Kronos Longevity Research Institute

BOARD MEMBER PROFILE

Phyllis M. Wise, PhD

Phyllis M. Wise is dean of the Division of Biological Sciences and a faculty member in the Section of Neurobiology, Physiology and Behavior and the Department of Human Physiology at the University of California, Davis.

She earned her master's in biology and her doctorate degrees, both from the University of Michigan. Prior to joining UC Davis, she was a professor in the Department of Physiology of the School of Medicine at the University of Maryland at Baltimore. Dr. Wise also chaired the Department of Physiology at the College of Medicine of University of Kentucky.

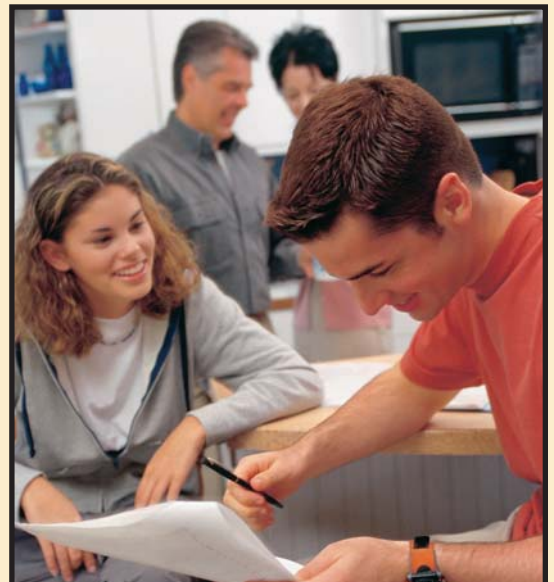
Her research career has concentrated in the areas of endocrine and neurochemical mechanisms regulating neural plasticity during aging, with particular emphasis on their impact on the female reproductive system and, more recently, the neuroprotective actions of estrogen during aging and after injury.

Dr. Wise has been funded by the National Institute of Health since 1980 and has been awarded two MERIT Awards. She has received numerous awards including the Nathan W. Shock Award for outstanding research in aging from the National Institute on Aging, the Solomon Berson Award from the American Physiological Society, the Robert W. Kleemeier Award from the Gerontological Society of America, and the Excellence in Science Award from Federation of American Society of Experimental Biology. She has published 100 peer-reviewed original papers in various scientific journals and 50 invited reviews. She is widely recognized as one of the world's foremost experts on mechanisms of brain aging and the role of estrogen in protecting the brain against injury and disease.



DONATE NOW! ***BE A PART OF KLRI'S MISSION***

You make a difference! Longevity research is vital to all of us - everyone benefits. All donations will directly benefit research; KLRI's administrative costs are funded. KLRI is a not-for-profit organization, therefore all gifts are tax deductible. KLRI accepts individual and corporate contributions, planned giving and major gifts. Your donation will be recognized at KLRI. Research changes the world; we cannot find cures for chronic diseases or learn to live healthier, longer lives without research. Remember, the inquisitive scientific minds contribute to your lifestyle every moment. For questions or to donate, please call (602) 778-7481.



Who we are!

Kronos Longevity Research Institute (KLRI) is a not-for-profit, 501(c)(3) organization conducting state-of-the-art clinical translational research on the prevention of age-related diseases and the extension of healthier human life. KLRI tests new strategies to detect and prevent chronic diseases associated with aging and investigates the effects of innovative interventions to slow the aging process and improve health outcomes for older persons. In addition, KLRI helps the medical and lay communities understand important aging issues. KLRI research findings support a healthier quality of life and a robust lifestyle in our senior years.

KLRI also performs research to increase our healthy years by improving muscle strength, understanding the role of various nutritional components in our diets, and achieving a better grasp of human aging physiology.

There are many “anti-aging” remedies and recommendations on the market today. However, most lack scientific evidence, and have potential side effects. We need reputable scientific organizations to spearhead research to further our understanding of treatments developed to increase our healthy years. Our world-renowned scientific team is comprised of experts in their fields, who are conscience driven to perform at their highest potential to ensure that all research projects are safe, carefully performed and accurately communicated. The KLRI studies performed differ from those of many narrowly focused institutions because we have a wide range of scientific expertise and our focus is on aging itself rather than a single disease.

OUR MISSION

To perform and foster clinical translational research aimed at healthier human longevity and communicate results to the professional and lay communities.

OUR GOVERNANCE

A distinguished board of directors, with a unique mix of scientists, longevity specialists, and community leaders govern KLRI. There is also a scientific advisory board of recognized international experts in medical and scientific fields, including nutrition, exercise, hormones, bone and joint diseases, cancer and heart disease.

WHAT IS AGING?

We see the effects of aging on a grand scale (i.e., graying hair, wrinkling skin, and the development of chronic diseases). We see these effects on a macro level because they are visible to the eye, when actually, they occur on the molecular level. Regardless of the species, a vicious cycle of damage occurs, which results in declining system function and ultimately leads to the deterioration of the organism. The body does implement natural repair mechanisms in an attempt to repair damage at the nuclear and mitochondrial levels. However, the rate of repair cannot keep up with the rate of damage.

So exactly, what is aging? We don't know yet!!! Hence, the Kronos Longevity Research Institute.



CURRENT PERSPECTIVES ON STEROID USE AND ABUSE

Although hormone replacement may be appropriate for older men with low testosterone levels, the other aspect of hormone use is steroid abuse. Anabolic-androgenic steroids (AAS) have been widely used for more than 100 years to improve vitality and exercise performance. Even before the identification of the main male hormone, testosterone, the first medical report describing the use of a testicular extract to reverse the symptoms of aging and improve vitality was published. Recently, the medical use of testosterone in patients after burns, surgery, radiation therapy, and age-related sarcopenia (muscle wasting) has increased and proven beneficial. However, athletes have been using purified testosterone to increase muscle mass and strength and improve athletic performance for more than 40 years, resulting in the International Olympic Committee banning the use of anabolic agents. Due to the increasing illegal use of AAS, the US Congress enacted the Anabolic Steroids Control Act, requiring that AAS be considered a controlled substance (similar to narcotics). This action appears to have done little, however, to decrease the use of AAS by our youth. A survey of high-school football players revealed that more than 6% had taken AAS and, alarmingly, 15% of those students began taking steroids before the age of 10.

The normal increase in testosterone levels during puberty in boys contributes to rapid linear growth and greater muscle mass. Similar anabolic effects are observed when testosterone levels are restored in hypogonadal (below normal testosterone levels) men. All steroids used for hormone replacement have both anabolic (increase muscle mass) and androgenic (male virilizing) properties. Testosterone acts by binding to a protein (androgen receptor) in androgen-responsive cells; cells that build



muscle also have androgen receptors. Testosterone can be chemically altered by some target tissues to become dihydrotestosterone (DHT), which also acts on the androgen receptor. Also, testosterone can be converted to estradiol (female hormone) and exert estrogenic activities, such as growth of breast tissue. These conversions are undesirable in anabolic drugs, because they decrease the ratio of anabolic to androgenic activity, and feminizing side effects are troublesome.

Anabolic steroids available in the US comprise several groups:

- 1) those naturally produced in our own bodies or their precursors, including testosterone and androstenedione
- 2) synthetic derivatives of testosterone with altered metabolic or receptor-binding characteristics
- 3) various poorly characterized plant or animal products

Two natural products are androstenedione and norandrostenedione. These pro-hormones are converted in the body to testosterone and nortestosterone (nandrolone). The controversy over the use of these pro-hormones by athletes to increase their testosterone

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CURRENT PERSPECTIVES ON STEROID USE AND ABUSE ... CONTINUED

production was brought to national media attention when baseball player Mark McGwire set a new home run record, yet he also revealed that he was taking androstenedione. However, a recent review of oral androstenedione in the *Journal of the American Medical Association (JAMA)* reported that eight weeks of androstenedione use caused no significant increase in serum testosterone or muscle mass in young men who were weight training. Therefore, while a small amount of these substances are indeed converted to circulating testosterone, the percentage is far too little to have any significant anabolic activity in a normal male. Also, many over-the-counter products derived from both plant and animal materials may contain unknown ingredients, some possibly toxic.

The anabolic use of testosterone and steroids are not confined to the professional male athlete looking for a competitive edge. The greatest concern may be in young men and women who feel compelled to take steroids to compete better in high school athletics. The anabolic effects of testosterone in women athletes are similar to those observed in men, and, as circulating testosterone levels in women are typically about 10% of those observed in men, females could possibly have relatively greater benefits (and risks) from steroid abuse. Although there are



few published reports on steroid use among female athletes, recent reports of the East German female sports program of the 1970s and 1980s showed that significant improvement (increase of 1.5 m) was obtained in the shot-put event while taking AAS. Unfortunately, women receiving steroids inevitably experience development of many male secondary sex characteristics (deepening of the voice, enlargement of the adam's apple, facial hair, male pattern baldness, acne, and clitoral enlargement).

Finally, the use of a variety of anabolic steroids to increase muscle mass, improve athletic performance or enhance energy has several undesirable masculinizing and even feminizing side effects, and the increase use by our youth is alarming. These compounds have considerable potential for harm when taken in large doses. The risks of testosterone use include alterations in mood (increased aggression), increase in blood hematocrit (thickening of the blood), a decrease in the good HDL cholesterol (possibly increasing the risk for heart disease), and potentially cancer. The fact that steroid use is so widespread suggests that some individuals can tolerate steroids without noticeable difficulties. Although little scientific research exists to substantiate the widespread use of high-doses of testosterone in normal healthy individuals, the controlled use of testosterone in reasonable doses for medical conditions such as muscle wasting related to cancer or HIV, and the loss of lean body mass following severe burns appears to be warranted. The ethical use of testosterone for treatment of other important conditions such as age-related muscle loss (sarcopenia) requires prospective, controlled clinical studies to document the risk-to-benefit ratio. Such treatment should only be carried out under the supervised care of a physician and only for men who are androgen-deficient.

Taylor J. Marcell, PhD, ATC
Exercise Sciences Director

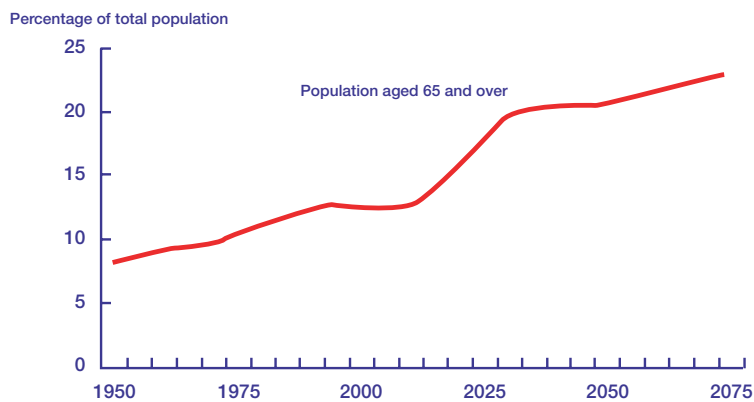
WHAT'S SO IMPORTANT ABOUT AGING RESEARCH?

As the senior population continues to grow, our country is likely to experience a severe shortage of physicians who specialize in caring for the elderly and a lack of researchers trained in aging. In 1950, approximately 8 percent of the U.S. population was older than 65. In 2020, that percentage is expected to more than double and by 2075, the senior population is projected to reach more than 22 percent of the total U.S. population (see graph provided by the General Accounting Office).

genes, etc.) and improved clinical care for mankind. It requires controlled studies of living human subjects.

KLRI study participants are eager to help us discover the true meaning of aging – because right now, we don't really know! There is a significant amount of research being conducted on chronic diseases, such as cancer, heart disease, diabetes, etc. But not enough research focuses on the broad spectrum of aging and what it means.

Aged Population as a Share of Total U.S. Population Continues to Grow



Note: Projections based on intermediate assumptions of the 2002 Trustees Report

Source: The 2002 Annual Report of the Board of Trustees of the Federal Old-Age and Survivors Insurance and Disability Insurance Trust

KLRI's scientific team investigates the effects of innovative interventions to slow the aging process and improve health outcomes for older individuals. They also test new strategies to detect and prevent chronic diseases associated with aging. In addition, KLRI helps the medical and lay communities understand important aging issues. For more information on the importance of aging research, please visit www.kronosinstitute.org.

That's just one of the reasons why KLRI is committed to conducting important age-related translational research that will ensure you, your children and your grandchildren lead longer, healthier lives. Translational research takes promising findings from the basic research laboratory and carries them forward into the clinical arena. It is the link between basic research (experiments completed with animals, cultured cells,



DIRECTOR'S MESSAGE ... CONTINUED

Finally, there are the phytonutrients, complex cyclic carbon compounds found in fruits and vegetables. These are the most fascinating classes of compounds ever investigated by nutritional science. The sheer number, variety of molecules, ways in which they interact with one another and the different biochemical pathways in our cells is so overwhelmingly complex that it will require many years of research and a large financial investment to decipher their importance and make accurate recommendations regarding their use. Nonetheless, progress is being made daily. One key to this class of compounds is color. They are found in highest concentration in foods with deep intense colors, such as blue, red, purple, orange and yellow. Scientists believe that plants produce these compounds to protect themselves from damage and stress such as ultraviolet and blue light, predators, viruses, and bacteria. We "borrow" the beneficial properties of these molecules when we eat the fruits and vegetables containing them.

In conclusion, the actions of phytonutrients have been shown through scientific experiments in animals, humans and/or systematic observations in human populations. These include:

- lower rates of prostate cancer due to lycopenes in tomato products
- prevention of blindness due to macular degeneration (the most common cause of vision loss in the elderly) by lutein and zeaxanthin found in kale, spinach, and yellow vegetables
- improved learning, motor behavior and neuronal function as well as a more "youthful" appearance of brain tissues after eating blueberries, which contain high concentrations of anthocyanins and other antioxidants
- activation of enzymes that detoxify carcinogens and protect against formation of cancer cells by sulphorophanes in garlic and onions

S. Mitchell Harman, MD, PhD
Director and President



DIRECTOR'S FORUM

The Director's Forum gives you direct access to the scientific faculty at KLRI. Also, an event will be held to communicate the latest scientific discoveries in longevity research, study status and potential studies being considered. The industry's update also will include information on government issues that may affect the progress of longevity research. The Forum is comprised of our valued friends and supporters. To join our Director's Forum, please call (602) 778-7499.

In the next issue...

Our next issue will discuss phytonutrients in more detail, as mentioned in the Director's Message on page 2, as well as green tea, red wine, and more. In the meantime, keep eating your five to six servings per day of fruits and vegetables.

You'll be glad you did.

You make a difference!

PARTICIPATE IN A KLRI STUDY

Currently, we are recruiting for the following studies:

Validation of Oxidative Stress Assessments: Oxidative stress is the ongoing damage to an organism due to oxidation (the reaction of cell components with oxygen). This resembles the rusting of metal components in a car, and leads to loss of function. Oxidative stress is considered an important factor in the aging process. KLRI performs studies to characterize and validate laboratory methods to examine the effects of therapies designed to slow or reduce oxidative stress.

Testosterone Replacement and Cardiovascular Disease: KLRI is collaborating with the University of California at Los Angeles and Drew University School of Medicine on a study designed to determine the effects of testosterone replacement in older men on cardiovascular disease risk. The loss of testosterone may lead to decreases in bone and muscle strength and contribute to frailty and poor quality of life.

We thank you!

We thank the many people who have registered to participate in studies at KLRI. A special thanks to those who have completed a research study.



Community Education

KLR I faculty members speak at numerous seminars and events and they are willing to speak to your group or organization. Topics focus on strategies for living longer, healthier lives. Sample topics include "Aging and the onset of chronic disease," "Pros and cons of hormone replacement therapies on aging men and women," "How exercise and nutrition can impact your life" and "The importance of mental exercise: Ways to stay sharp."

Professional Education

KLR I sponsors local monthly seminars and an annual symposium featuring world-renowned gerontologists and other experts in aging and other medical fields, which provide continuing education for medical and science professionals. The seminars are designed to inform practicing physicians and other healthcare providers about important age-related topics. Continuing Medical Education credits are available for all of these seminars.

GLOSSARY

ABC

Anthocyanins - Any of a variety of polycyclic compounds, with nitrogen in some rings and most with nitrogen side groups, and double bonds between some of the carbon atoms. These compounds absorb light selectively so that they tend to be highly colored (usually purple, blue, or red). They are found in high concentrations in colored vegetables and most are effective antioxidants.

Polycyclic - Multiple 5 and 6 membered rings of carbon atoms joined together.

Proanthocyanidins - Anthocyanins linked together into chains as polymers (i.e. "giant molecules" whose subunits are other molecules).

Lycopenes - A carotenoid pigment, that is the red coloring matter of the tomato.

Sulphorophanes - Polycyclic compounds containing sulfur-hydrogen side chains (sulfhydryl groups).

Carcinogens - A substance or agent causing cancer.

Macular Degeneration - A loss of central vision produced by retinal damage due to deterioration of blood vessels.

Lutein - An orange xanthophyll occurring in plants usually along with carotenes and chlorophylls and in animal fat, egg yolk.

Zeaxanthin - A polycyclic antioxidant having a deep yellow color

Many of the terms above are taken from Kenneth W. Wachter and Caleb E. Finch, Eds., Between Zeus and the Salmon: The Biodemography of Longevity, pp. 269-274 (National Academy Press, Washington, D.C.; 1997).

ASK THE DIRECTOR

In your first quarter 2003 Vol. 2, Issue 3...you list peanut butter as high in trans-fatty acids. What about "peanuts only" peanut butter? Among the good chocolates you don't mention syrups (i.e. Hershey's, Nestle's). Are they as good (perhaps better) than chocolate "candies"?

Doyce Elliott

The natural "peanuts only" peanut butter (made only with peanuts and peanut oil) has no trans-fatty acids. It is fairly high in saturated fat, however. The chocolate syrups have less cocoa and more sugar than an equally caloric portion of really good (70-80% cocoa) dark chocolate.

Dr. S. Mitchell Harman

Is it easy to participate in a study?

Most KLRI study requirements are simple and easily incorporated into your daily routine.

To Ask the Director, please submit your question via email to info@kronosinstitute.org or write to 2222 E. Highland Ave. Suite 220, Phoenix, AZ 85016.



PARTICIPANTS' COMMENTS AND RESEARCH STATUS

What are people saying about KLRI and its research?

Currently, more than 500 people have participated in various research projects at KLRI with many participating in more than one study. We thank all of you who have participated.

Overall, the participants' comments have been positive, and they have enjoyed the education and experience. Below are comments from participants in the Oxidative Stress and Omega-3 Fatty Acids studies:

"I participated in the studies because I thought it would be fun and give me an opportunity to make a difference. Normally, I eat healthy and exercise, so the diet was not a major change for me. Although, the diet required that I eat a lot of fish and take supplements, while out to dinner I found myself considering fish for dinner on a night that was not required. I enjoyed getting to know KLRI's scientific researchers and other staff members. This has been a positive experience and I will do other studies." **Mel, Sun Lakes**

"Participating in the Omega-3 study was awesome. I learned a lot about nutrition, and it was an eye-opener about research. The staff was very informative and fun to be around. I even created extended friendships with other study participants. We found that we had many things in common. During the study, I felt more mentally alert and had more energy." **Brenda, Phoenix**

"I am glad that I participated in the Omega-3 study. It was a very positive experience. I liked salmon before and, believe it or not, I still do. We had to eat four ounces of fish for four days a week. I noticed that I had more energy and was more mentally sharp. The entire staff was very helpful -- it was like being a part of a family. KLRI staff wanted to make sure that we were comfortable during the entire procedure." **Didi, Phoenix**

"I am adopted with no family history, so I thought the more I know about myself, the better. I exercise all the time, but still have an elevated cholesterol level. During the study, I lost four or five pounds. Now that I understand more about fatty acids, I read labels when I shop and pay more attention to what I



eat. I normally eat healthy, so the diet was not much of a change for me. I enjoyed my interaction with the staff and would participate in other studies." **Paul, Phoenix**

KLRI entered 2003 with five studies in progress and two in the planning stages:

- *Assay Standardization for Oxidative Damage Rates to Nucleic Acids, Lipids and Proteins*: 93% complete. Currently, recruiting approximately 29 additional participants.
- *Omega-3 Fatty Acids*: Participant recruiting is completed. The clinical phase of this study will be completed in late August.
- *Testosterone Effects on Atherosclerosis in Aging Men (TEAAM)*: Recruitment and screening will begin in August. Contact KLRI for more information.
- *Effects of Improved Glucose Control in Type 2 Diabetic Patients on Oxidative Stress and Inflammatory Markers*: 30% complete. Performed at the Carl P. Hayden Veterans Administration Hospital.
- *Cancer Detection by Serum Antibody Measurement Against a Cell Surface Antigen (AMAS test)*: 100% complete.
- *Urinary Oxidative Stress Markers Comparison in Smokers, Ex-Smokers and Non-Smokers*: 100% complete.
- *Effects of Statin Drug Treatment Depletion of Endogenous CoQ10 on Cardiac and Skeletal Muscle Function*: Currently on hold; awaiting funding.

For more information regarding any of the above studies, please contact KLRI at (602) 778-7499.

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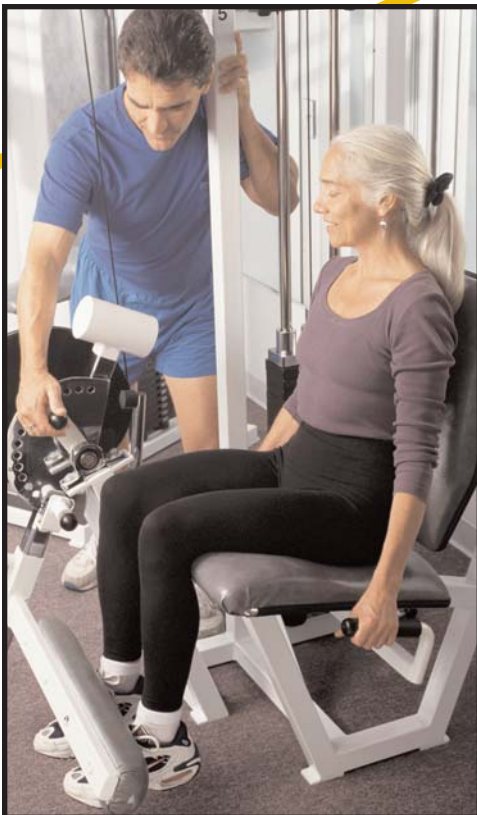
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