

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



Third Quarter 2003 Vol. 2, Issue 5

OPTIMAL EXERCISE AND FITNESS

IN THIS ISSUE...

Optimal Exercise and Fitness	1
Director's Message	2
Director's Forum	5
Micronutrients Against Aging and Disease	6
Board Member Profile	11
Donate Now!	11
Who We Are!	12
Glossary	13
Participate in a Study	15
Community/	
Professional Education	15
Board of Directors/	
Scientific Advisory Board	15
KLRI Staff	16

Kronos Longevity Research Institute

2222 E. Highland
Suite 220
Phoenix, Arizona
85016

Tel: 602.778.7499

www.kronosinstitute.org

Regular physical activity and vigorous exercise provides several important health benefits including reducing body fat, maintaining mental health, and reducing the risk of premature death. However, about two-thirds of the U.S. adult population is not regularly active and about a quarter does not exercise. The total amount of muscle mass and the quality of that muscle declines with age by approximately 10-15% per 10 years in men and women, and this loss appears to accelerate after the age of 50. This loss of mass and strength with advancing age is termed sarcopenia. In the New Mexico Elder Health Study, 10–25% of persons under the age of 70 were classified as sarcopenic, whereas more than 30% of women and 50% of men older than 80 were sarcopenic.

The effects of sarcopenia include decreased strength, metabolic rate, and maximal oxygen consumption, which contribute to weakness and a loss of independence. Regular strength training

can help offset these losses in muscular strength and metabolism that are often age-related. This article will address some specifics of weight training to help you incorporate exercise correctly into your daily life.

The following is an excerpt from the Kronos OptiFit White Paper, a scientific review of rationale behind exercise's apparent benefit to improving health, decreasing risk of mortality and possibly increasing healthy longevity, available through the Kronos Optimal Health Centre.

The key to an appropriate and individualized exercise prescription is based on your individual fitness status. We recommend an assessment of your components of fitness which is conducted through careful and scientifically based clinical testing. We also recommend discussing this or any exercise program

continued on page 3



DIRECTOR'S MESSAGE

We are three-quarters of the way through 2003, but it has been so busy that I find it hard to believe another year has nearly passed. Research progress at KLRI continues. We have completed two of our major studies. In the first study, we compared levels of oxidative stress, as indicated by markers of oxidative damage in the urine, in smokers, ex-smokers and non-smokers and found that both smokers and ex-smokers have higher levels of ongoing oxidative stress than do non-smokers. A scientific report describing our results has been accepted for publication in a peer-reviewed journal. The second study completed an investigation of the sensitivity and specificity of a controversial test for detection of cancers. These results also have been submitted and are being reviewed for publication by a medical journal. We also have completed the sample collection phases of two other studies:

- A survey of oxidative stress in non-smoking men and women across the age spectrum
- A pilot experimental trial to learn whether a diet high in omega-3 fats might improve the function of various endocrine (hormonal) systems that are reduced by normal aging

These latter two studies are awaiting the laboratory measurements on samples collected before we can calculate the outcomes and publish the results.

Translational clinical research is very detailed and expensive. Yet without it, medical progress would be stalled. Translational research is the step that takes a novel idea, based on results from studies in cells, animals, etc., and collects the first evidence indicating whether it's beneficial in humans. This kind of research is difficult for a number of reasons. First, applying any novel procedure in humans requires meeting many mandatory administrative constraints. Approvals are needed from institutional review boards (IRB), often the FDA, and other local review committees (radiation safety, pharmacy boards, etc.). This requires extensive and persuasive documentation after carefully reviewing previous publications. Once a precedent has been set for a drug or treatment, this process becomes easier. Second, translational research is risky, in the sense that a "first try" is more likely to lead to negative results. This can be an issue for investigators because most journals don't like to publish negative reports, and funding sources are unlikely to fund follow-on studies of "failed" strategies. Therefore, scientists often prefer to do experiments with positive results, or at least those with a higher chance of success. It also is harder to find funding for translational research because the first reaction of most people to a novel idea is, "Oh, that probably won't work." Funding review committees have to implement mechanisms to approve or deny grant requests. One way to quickly reduce the number of proposals under consideration is to reduce the risk associated with the grant. If the proposals have no prior human research performed, it starts with a strike against it. There is also the financial risk. Promising non-patentable interventions such as exercise, nutritional strategies, etc., often remain undocumented by scientific evidence for lack of financial support.

These and other issues have led to a decrease in the support of clinical (as opposed to basic) research funded by the National Institutes of Health and other granting agencies. This has led to a loss of trained

continued on page 5

with your physician. A balanced exercise prescription focuses on improving body composition by decreasing body fat, increasing muscle mass, and ultimately increasing both fitness and muscle performance (strength, endurance, and flexibility). The amount of aerobic, strength, and flexibility training should be based on an individual's specific test results. The Kronos OptiFit Fitness Program bases the details of each prescription on frequency, intensity, type of exercise, and the amount of time/duration spent exercising, the F.I.T.T. principle.

Strength training is prescribed to achieve the muscular strength and muscular endurance goals of the OptiFit Program. Muscular strength is the maximum force that can be exerted by a muscle or muscle group, while muscular endurance is the capacity of a muscle to repeatedly exert force or to maintain a fixed contraction for a period of time without undue fatigue. Simply stated, to lift a heavy box off the floor onto the counter requires strength, whereas carrying bags of heavy groceries upstairs requires muscular endurance. The key to success in weight or strength training is to progressively increase the amount of weight a person can lift over time. For most individuals, this will result in increased strength and muscle mass, thus improving body composition. To increase muscle "definition" or "tone" or "muscle appearance" requires emphasis on not only strengthening the muscles, but also reducing the amount of body fat.



Frequency is the number of exercise sessions that an individual performs in a week. For individuals who are interested in improving overall health and fitness capacity, the OptiFit Program recommends using weights three days/week. One day a week will provide considerable benefits to very sedentary or older persons, however, three days of lifting per week has been shown to give greater long-term benefits. Variations in other factors such as volume intensity and rest periods can be modified to accommodate for the increase in strength and experience. Additionally, a split routine (such as upper/lower body) can be used to change the training structure and allow greater focus in individual muscle groups. In a split routine, the individual will train two days/week for their upper body and two days/week for the lower body; in essence, increasing the training volume to four days/week, although the time spent daily in the gym would be less than on a whole-body three days/week program. Advanced lifters can increase lifting frequency from four to six days/week. However, it is important to note that the structure of the workout needs to be such that adequate recovery time is allowed.

Volume describes the total amount of weight lifted in a session. This is typically calculated by multiplying the number of sets by the number of repetitions (reps), and then by weight lifted ($S \times R \times W$). The focus of intensity in resistance exercise is directly related to volume of exercise and mode of exercise. Intensity can be controlled by:

- Using the *Goal/Rep System* in which an individual controls the intensity used within a prescribed number of reps and sets.
- By the use of *Periodization* in which a professional controls the volume and the variation of the program in cycles in order to elicit greater strength gains and even to peak an individual at certain points in a cycle.

continued on page 4

Small increases (2.5%-10%) in training volume are recommended to avoid overtraining. However, when unaccustomed persons begin a weight-training routine, only 60% of the one rep/minute (RM) should be used initially to allow for learning proper techniques required for each movement. When training is initiated (in unaccustomed individuals) large gains in strength will occur in the first several months due to neurological and mechanical adaptations, followed by a slower progressive improvement over time.

In the Goal/Rep System, your goal is to complete your prescribed number of reps within each prescribed exercise set. When the total number of reps for all sets is completed, then the amount of weight or resistance is increased, not the number of reps. Each rep should be performed with the same controlled proper technique. As an example, if the prescribed workout of the biceps (arm muscles) is three sets of eight to 10 reps (3 x 8-10) using the single dumbbell arm-curl, the individual would pick a weight heavy enough to lift eight times (usually 80% of the 1-RM) but not more than 10 times in each set. If after the third set they could lift that same weight two more times, then during the next scheduled workout they would increase the amount of weight used. Therefore, by tracking the amount of weight lifted in a workout log, improvements in strength can be monitored.

Proper breathing is essential when lifting weights; avoid holding your breath as you strain during an exercise. Exhale when you are pushing or lifting and inhale when you are resisting against the weight or returning to the start position.

Warning: Failure to breathe correctly during heavy weight lifting may cause drastic and potentially harmful increases in blood pressure.



The F.I.T.T. Principle for Strength Training

This Principle also can be applied to strength training. Here are some general guidelines, depending on the level of fitness:

Beginner

- *Frequency* – Strength train two to three times per week, one set of 15-20 repetitions.
- *Intensity* – Begin with a weight approximately 60% of your predetermined 1-RM and progressively increase your resistance until you can follow the Goal Rep System.
- *Time* – Exercise for about 20-30 minutes per session with 1-3 minute rests between sets. Rest at least 24-48 hours between exercise sessions to allow your muscles to recover.
- *Type* – Exercise the major muscle groups, working larger muscle groups first, then smaller muscle groups, with only one exercise per body part.

Intermediate

- *Frequency* – Train three times/week, three sets of 8-10 repetitions.
- *Intensity* – Train with a resistance approximately 80% of your 1-RM that results in fatigue (Goal/Rep System).
- *Time* – Exercise for about 30-45 minutes with 1-3 minute rests between sets. Rest at least 24-48 hours between exercise sessions to allow your muscles to recover.
- *Type* – Select about 8-10 exercises for the major muscle groups, working larger muscle groups first, then smaller muscle groups, with no more than two exercises per body part. If it is not feasible to fit all major muscle groups into one session, alternate upper body/trunk one session and lower body in the next session.

continued on page 5

Advanced

- *Frequency* – Train four to six (depends upon your time and goals) times/week, at least four to five sets of 6-8 repetitions of each exercise.
- *Intensity* – Overload your muscles with a resistance that results in failure.
- *Time* – Exercise for about 45-50 minutes with rests between sets as prescribed (usually 30 sec to 3 minutes). Rest at least 48-72 hours between sessions (by muscle group) to allow your muscles to recover.
- *Type* – Select two to three exercises per major body part, working larger muscle groups first, then smaller muscle groups. Alternate upper body/trunk one session and lower body in the next session.

Note: References available upon request.

Taylor J. Marcell, PhD
(Contributions by: E.D. Pence, CSCS & M.P. Wright, MEd, ATC-L, CSCS)



DIRECTOR'S FORUM

The Director's Forum is KLRI's semi-annual tool to communicate the latest scientific discoveries, study status, studies being considered, and governmental issues that may affect the progress of longevity research to its supporters/donors. The Director's Forum gives you direct access to our scientific/medical staff.

You are invited to join us for the next Forum.

Topic: Hormones and Changes as We Age in Men & Women

Speaker: Dr. Marjorie L. Shuer, Mood & Menopause Clinic

Date: 5:30 p.m., October 23, 2003

Summary: Research has suggested estrogen replacement therapy as having a favorable effect on verbal cognitive domains, while androgens are thought to improve visual spatial memory. These neurosteroids directly influence the sexually dimorphic nature of the brain by their organizational effects during development as well as their activating action during adulthood. The adult brain demonstrates tremendous plasticity as seen in the study of cross-sex hormone replacement in transsexuals.

Location: 2222 E. Highland Ave., Ste. 204. Space is limited. To RSVP, please call (602) 778-7499.

DIRECTOR'S MESSAGE ... CONTINUED FROM PAGE 2

clinical investigators, which a recent article in the *Journal of the American Medical Association (JAMA)* refers to as an "endangered species." Clinical research is also very labor intensive, often requiring the collaboration of several highly trained investigators with different specialties and skills (for example, endocrinologists, gerontologists, cardiologists, exercise physiologists, and psychologists, as well as statisticians, study coordinators, information technologists, etc., are required).

I believe that KLRI is making an important contribution because of its unique position as an institution devoted to translational clinical research in aging. There is no limit to the exciting research to be performed that will increase our knowledge about the aging process and what can be done to help us live longer, healthier lives.

S. Mitchell Harman, MD, PhD



MICRONUTRIENTS AGAINST AGING AND DISEASE

Green Tea, Red Wine, and Blueberries

In the last few years, we have been reading and hearing a lot about “wonder foods” that are said to help prevent cancer, heart disease, and preserve youth. Is there hard evidence that these foods, mainly fruits and vegetables or their products and extracts, have beneficial effects on your health and longevity? It turns out that the evidence for some is quite good, while for others it is more speculative than genuine. Most of these effects appear to be based on content of various classes of micronutrients. Scientists are only beginning to appreciate the incredible number of active micronutrient compounds and the complexity of their interactions with one another.

Let’s start by defining micronutrient. Micronutrients are chemicals found in food which provide benefits, not like macronutrients, which provide metabolic fuel (fats and carbohydrates) and the building blocks for cells and tissue (amino acids from protein), but rather by more subtle interactions with the body’s chemistry. Macronutrients must be consumed in quantities of many grams per day, whereas micronutrients are active and potent in relatively tiny quantities, measured in milligrams or even micrograms.

The first micronutrients to be appreciated and studied were the “classical” vitamins. These include vitamin A (retinenes), B complex (thiamine, niacin, pyridoxine, folic acid, pantothenic acid, and B12), vitamin C (ascorbic acid), vitamin D, and vitamin K. In each case, deficiency of a vitamin was discovered to be associated with a particular set of abnormalities resulting in a disease state. For example:

- vitamin C deficiency causes scurvy, a disease characterized by weakness, joint swelling and pain, bruising, bleeding gums, tissue fragility, and poor healing
- low vitamin B12 is responsible for a severe disease called pernicious anemia
- vitamin D deficiency in children causes rickets, which weakens and deforms bones



Although there are still debates as to what the optimal doses of these vitamins should be for various age groups, as well as men versus women, there is no question that these compounds are essential components of a healthy diet. With the exception of vitamin D (which is made in the skin when exposed to sunlight), none is synthesized in the human body, and thus must be supplied by being outside.

A second category of micronutrients is minerals. A great deal is known about classical vitamins, including why we need them and how they work. Calcium (which is a major component of bone) and iron (needed for hemoglobin in blood) are required in relatively large quantities. Iodine is needed in modest amounts to make thyroid hormone. Other minerals such as zinc, magnesium, and cobalt, are required in much smaller quantities, but are essential, nonetheless, mainly as enzyme components. Many important enzymes must be associated with one or more atoms of a particular metal in order to function properly. The latter minerals are often referred to as “trace elements.” A healthy diet, with a reasonable balance of meat, leafy vegetables, and fruit, generally supplies the trace elements needed, however, numerous mineral supplements are available and are often combined with vitamins.

continued on page 7

MICRONUTRIENTS AGAINST AGING AND DISEASE ... *Cont. from page 6*

Most interesting to those of us concerned with aging and age-related diseases is a class of micronutrients that is less understood. These are complex organic compounds that appear to be made by plants to help them resist stress, especially damage from direct sunlight. Many of these are classified as polyphenols. Polyphenols are large molecules containing multiple six carbon ring structures, each with three double bonds. These structures usually have extended or side groups of various types connected to some of the carbon atoms. Side groups include:

- hydroxyl (oxygen and hydrogen – OH characteristic of alcohols)
- sulfhydryl (sulfur and hydrogen – SH),
- amino (nitrogen and hydrogen – NH₂)

The possibilities for variations in the chemical structure of these compounds are enormous, and there are many thousands of such molecules in the plant kingdom. These molecules appear to have three different mechanisms of action, which may offer benefits to those who consume them.

First, many of these molecules appear to be powerful antioxidants, which are compounds that can remove an electron from a free radical molecule so that it becomes less reactive and thus harmless to tissue components. Oxygen free radical molecules (also called reactive oxygen species, ROS) and nitrogen free radicals (reactive nitrogen species, RNS) are generated in the course of normal metabolism. They also are formed when our cells are struck by a particle or wave of ionizing radiation (for example cosmic rays or X-rays), and may enter our bodies as toxic compounds in cigarette smoke and other sources. ROS and RNS can react with and damage proteins, nucleic acids (DNA and RNA) and lipids (fatty molecules) in our cells, which are vital components essential to life processes. There is increasing evidence that damage from free radical reactions plays an important role in the causation of a variety of diseases, including heart disease, cancer, and Alzheimer's disease. There is also evidence that accumulation of free radical damage over many years is a key element of the aging process. Our cells defend themselves against free radical damage in part by

manufacturing a variety of antioxidant compounds. An abundance of antioxidants from the diet also may be important to help protect us against ROS and RNS. The best-known antioxidant vitamins are C and E, but many of the polyphenolic compounds in foods appear to be far more potent than vitamins C or E on a gram-for-gram basis.

A second mechanism of action of these complex compounds is as regulators of enzyme action. For example, some have been shown to increase the activity of enzymes in our cells which break down carcinogens. Evidence shows that some of these compounds may regulate gene activity in our cells, turning on genes that produce defensive enzymes that detoxify free radicals or stimulating production of molecules such as heat shock proteins that help repair damaged cell components.



There are so many of these compounds, found in a variety of fruits and vegetables, that to try to convey what is known about all of them would require a series of books. Therefore, this article focuses on three of the "wonderfoods," green tea, red wine, and blueberries. We will write about others in future editions of the *Longevity Kronicle*.

Much has been written about the virtues of green tea. The Chinese and Japanese have long believed that green tea provides important health benefits, among them, longevity. In a study of 3,380 women who practiced the

continued on page 8

MICRONUTRIENTS AGAINST AGING AND DISEASE ... *Cont. from page 7*

Japanese tea ceremony regularly, mortality rates were estimated to be only 55% of that of a standard population of Japanese women. In other Japanese epidemiological studies, green tea consumption has been associated with lower rates of cancer and has been reported to reduce the risk of heart disease.

Recently, scientific research has documented the presence in tea of families of polycyclic flavanol compounds called catechins, epicatechins, and theaflavins. It turns out that green tea has more than twice the amount of these compounds than black tea, when brewed to equal strength. In a laboratory study, the total flavanol content of a variety of green and black teas was strongly related to their antioxidant capacities tested by oxygen radical absorbance capacity (ORAC) assays.

Besides their antioxidant activity, green tea polyphenols have been shown to promote cell death (apoptosis) of cancer cells in culture, and to inhibit the growth of tumor cells and growth of new tumor blood vessels (angiogenesis) in animal models. Green tea flavanols also appear to reduce inflammation in various experimental studies. The polyphenols from green tea may help reduce the risk of cardiovascular disease by making low density lipid particles in the blood less susceptible to oxidation (an

antioxidant effect), but also by decreasing the expression of inflammatory cytokines by cells lining the arteries and decreasing the adhesion of white cells to arterial walls. The effects of green tea catechins on markers of oxidative stress, especially oxidative DNA damage, have been positive in some animal studies, but there is little information available regarding catechin effects on free radical damage in humans. Large human studies examining the effects of green tea intake on markers of oxidative damage to lipids, proteins, and DNA are needed, as are controlled clinical trials of green tea or green tea extracts for prevention or treatment of heart disease, cancer, and neurodegenerative diseases. Until the studies are completed, we will have to rely on evidence that is not definitive, yet quite suggestive, regarding their benefits.

Red wine is a “hot item” in health research these days (although it tastes best served at room temperature). Green tea and red wine contain an incredible variety of polyphenols with antioxidant properties. The one found in highest concentrations is called resveratrol. There are more than 60 prospective studies that suggest an inverse relationship between moderate alcoholic beverage consumption and coronary heart disease. In one study, there was a U-shaped relation between all-cause mortality and the average amount of alcohol consumption reported by 12,321 male British doctors. That is, both high and low alcohol consumption were associated with higher death rates, while moderate consumption was optimal. In particular, deaths from heart disease showed significantly lower rates in regular drinkers than in non-drinkers. However, there is no clear evidence that red wine offers an additional benefit over other sources of alcohol.

A report on 128,934 adult members of a Northern California comprehensive health-care program concluded that drinking alcohol protects against coronary disease,



continued on page 9

MICRONUTRIENTS AGAINST AGING AND DISEASE ... *Cont. from page 8*



and that there may be minor additional benefits associated with drinking either beer or wine, but not specifically red wine.

A study in France showed a somewhat stronger inverse relationship with coronary heart disease and the consumption of wine rather than for other alcoholic beverages. However, several other studies have failed to demonstrate such a relationship. Because wine drinkers tend to be less fat, exercise more, and drink with meals, it is difficult to separate possible beneficial effects of wine itself from these other factors. Studies of the effects of red wine polyphenols on atherosclerosis in animal models are conflicting. Nonetheless, it has been suggested that because red wine polyphenol compounds, such as resveratrol and flavonoids, prevent oxidation of lipoprotein particles in test tube experiments, red wine may be particularly effective in slowing atherosclerosis.

Another possible mechanism by which red wine could protect against heart disease comes from a study published in 2001 in the journal *Nature*. This report showed that red wine polyphenols inhibit synthesis of Endothelin-1 (ET-1) by vessel lining cells. ET-1 is a potent

constrictor of blood vessels and is believed to be a key factor in the development of vascular disease. The degree of inhibition of ET-1 synthesis was correlated with total polyphenol content. The same antioxidant compounds in wine also are found in grape juice, and red-grape juice inhibited ET-1 synthesis, though less strongly than red wine. White and rosé wines had no effect. Recently, there was a great deal of excitement generated by a study in *Nature* showing that resveratrol prolongs the life of yeast cells in culture by up to 80%. Whether red wine polyphenols promote longevity in animals or humans is not yet known.

In summary, wine consumption as a means of cardiovascular protection because of its antioxidant content is an unproven strategy. Excessive alcohol consumption is clearly a serious health risk, but one or two glasses of red wine daily with food may turn out to be a beneficial health practice.

Blueberries and their near relatives have been found to contain, on a per weight basis, the highest concentrations of antioxidant compounds in the vegetable kingdom. When antioxidant activity of polyphenols in blueberry, cranberry, wild chokeberry, and lingonberry fruit were determined in a study conducted by the Fruit Laboratory of the U.S. Department of Agriculture, anthocyanins (which produce the deep colors in fruit) were found to be the main components in all of them. Two compounds, called quercetin and cyanidin, found in the four types of berries had especially effective free-radical scavenging structures. In a study in which humans were fed blueberries, 19 of 25 anthocyanins present in the fruit were detected in the blood serum. The total anthocyanin concentration in the serum was directly related to an increase in serum antioxidant capacity. Finally, another study found that resistance of red blood cells to damage from ROS was

continued on page 10

MICRONUTRIENTS AGAINST AGING AND DISEASE ... *Cont. from page 9*

increased by blueberry anthocyanins, both in test tubes and in living animals. Thus, berries not only contain high concentrations of antioxidant compounds, but these compounds are well absorbed when fruit is consumed, and appear to be effective for preventing oxidative cell damage.

In an experimental study, rats fed diets containing lowbush blueberries for six weeks showed a reduction in brain damage after a carotid artery was blocked to cause a stroke. Other studies have found that diets supplemented with blueberries, strawberries, or spinach reversed age-induced declines in function in neurons in the cerebellum of rats, as measured by electrophysiological techniques. These studies also found that age-related deficits in motor learning and memory were reversed by the nutritional interventions. There are now mice with "engineered" genes that produce a protein (amyloid beta) found in human Alzheimer's disease (AD). These mice develop brain changes and memory deficits similar to human AD. In a study of such mice, blueberry-feeding blocked the increase in amyloid beta protein in their brains and prevented deficits in maze performance up to 12 months of age.

Perhaps the most impressive experimental results to date come from studies conducted in the laboratory of Dr. Carl Cotman, a distinguished neurobiologist at the University of California, Irvine. Over the past several years he has been studying cognition (memory and problem solving) and brain pathology in aged dogs. Like humans, dogs naturally accumulate deposits of brain amyloid beta, show evidence of increased oxidative brain damage, and have impaired learning and memory on tasks similar to those used to test aged primates and humans. The extent of amyloid beta deposition correlates with the severity of cognitive loss. A blueberry supplemented diet resulted in a significant improvement in the ability of aged, but not young, animals to acquire progressively more difficult learning tasks and an impressive reduction in the amount of amyloid beta in the animals' brains. Thus, consumption of blueberries by

experimental animals protects the brain against damage from arterial blockage (ischemia), normal aging, and perhaps Alzheimer's disease, and more importantly, preserves cognitive, memory, and motor function.

Even with all of the information above, there is a conspicuous lack of human data on the effects of berries, or for that matter any antioxidants, to prevent loss of brain function, heart disease, and other age-related illnesses. The amounts and types of antioxidants most likely to be effective are still speculative. Moreover, it appears that various polyphenolic compounds working together are often more effective than equal amounts of any single compound (a principle known as "synergy"). However, what the most effective combinations might be, remains unknown.



KLRI is conducting research to validate and standardize new ways to measure oxidative stress non-invasively in humans. We plan to use these assays in future studies to test antioxidant combinations to discover what doses and combinations are most likely to produce clinical benefits. Once the combinations are identified, the next step will be to do large trials for disease prevention and perhaps to slow "normal aging changes" as well. In the meantime, the advice we give our friends and supporters is to consume a diet rich in colored fruits and vegetables with at least one hearty serving of berries every day.

Note: References available upon request.

S. Mitchell Harman, MD, PhD



BOARD MEMBER PROFILE

J. Jorge Klor de Alva, JD, PhD

Chairman, President & CEO - Apollo International, Inc.

Apollo International was founded by Dr. Klor de Alva as a global education company, focused on providing affordable, accredited education programs outside the U.S. Today it has more than 150,000 K-12 and higher education students, with operations in the Netherlands (University of Phoenix), India (Western International University), Brazil (Faculdades Pitagoras, Rede Pitagoras), and Mexico (Grupo Educativo Apollo International).

Until September 2000, Dr. Klor de Alva was President of the University of Phoenix and Senior Vice President of Apollo Group, Inc. (NASDAQ: APOL, UOPX). He also served as Vice President of Business Development at Apollo Group, and has been a member of the boards of directors of Apollo Group and the University of Phoenix since 1991. Prior to joining Apollo full-time, he held the Class of 1940 Endowed Chair at the University of California, Berkeley and was Professor of Anthropology at Princeton University. Dr. Klor de Alva has worked with Dr. John Sperling, the founder of Apollo Group and its University of Phoenix, since 1971, when the structure that led to the University of Phoenix was first being created at San Jose State University.

Dr. Klor de Alva received a number of grants for his research from the Spanish and Mexican governments, the National Endowment for the Humanities, the National Science Foundation, and other funding agencies. He was a Fulbright Scholar, John Simon Guggenheim Fellow, Harry Frank Guggenheim grantee, and Getty Scholar at the Getty Center for the History of Art and the Humanities. Dr. Klor de Alva earned a bachelor's degree in philosophy and a law degree from the University of California at Berkeley, and a PhD in history/anthropology from the University of California at Santa Cruz.

His scholarly research interests focused primarily on contemporary and early modern interethnic/interracial relations, education policy and curriculum reform, and cultural and social trends. Besides lecturing widely in these areas throughout Europe, Latin America, Africa, and the U.S., he has published over seventy-five scholarly articles and co-authored nine social studies textbooks. He also has authored, co-authored or edited another 15 books on related subjects. His most recent books, "The Americans" (Second edition: 2003) and "The Americans: Reconstruction Through the 20th Century" (Second edition: 2003) are together the most widely used modern surveys of U.S. social and economic history.

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.

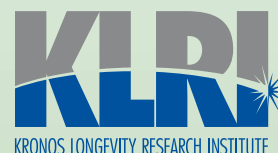
OUR GOVERNANCE

A distinguished board of directors, with a unique mix of scientists, longevity specialists, and community leaders governs KLRI. There is also a scientific advisory board comprised 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.***



GLOSSARY

ABC

Lipoprotein – Any of a large class of particles composed of a complex of protein and lipid (fatty) molecules and separable on the basis of solubility and mobility properties.

Carotid Artery – Main arteries that supply blood to the head.

Body Composition - Refers to the fat and nonfat tissues (lean/muscle mass, bone content and total body water) in your body.

Body Mass Index (BMI) - A measure of body composition (fatness) based upon height and weight that applies to men and women.

Cardiorespiratory Endurance - The ability to perform aerobic tasks at an intensity above a normal walking pace for a prolonged period of time.

Metabolic Equivalent (MET) - A measure of energy consumption used for expressing resting metabolic rate.

Muscular Endurance - The ability of the muscles to perform a heavy task a repeated number of times.

Muscular Strength - The ability of the muscles to generate force or lift a heavy object through a pain-free range of motion without sustaining injury.

Physical Activity - Any bodily movement that requires energy.

Reserve Capacity - The difference between something measured at rest versus at your maximum capacity

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).

BOARD OF DIRECTORS

Jon Cohen, JD.

Chairman of the Board; Senior Partner, Snell & Wilmer

Robert N. Butler, MD

President & CEO, International Longevity Centers

Samuel P. "Terry" Goddard, JD

Arizona Attorney General

William R. Hazzard, MD

Director of Geriatrics and Extended Care & Professor of Medicine, University of Washington

Yvonne R. Hunter

Public Affairs Representative, Pinnacle West Capital Corp.

J. Jorge Klor de Alva, JD

President & CEO, Apollo International

Damin J. Lopez

President/Managing Partner, Grupo Ñ Advertising

Phyllis Wise, PhD

Dean of Sciences, University of California, Davis

SCIENTIFIC ADVISORY BOARD

Aging/Oxidative Stress

Donald Ingram, PhD L. Jackson Roberts II, MD
James W. Simpkins, PhD Richard Weindruch, PhD

Biostatistics/Data Management

Isadore Newman, PhD

Cancer and Immunology

H. Ballentine Carter, MD

Cardiovascular Disease

Harvey S. Hecht, MD David M. Herrington, MD, MHS

Endocrinology and Metabolism

George R. Merriam, MD Laurence S. Jacobs, MD

Exercise Physiology

Kerry J. Stewart, EdD Arthur Weltman, PhD

Nutrition

Judith Wood Hallfrisch, PhD Arline D. Salbe, PhD

FOCUS ON HEALTHY LIFESTYLES

The following article is the first in a five-part series that will focus on strategies older adults can employ to improve their health and quality of life.

Poor health is not an inevitable consequence of aging. Preventing health problems is one of the few known ways to support a healthier quality of life and a robust lifestyle during the aging process. That's why 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 adults.

One of the most effective strategies for promoting the health of older adults is maintaining a healthy lifestyle. According to the Centers for Disease Control and Prevention, research has

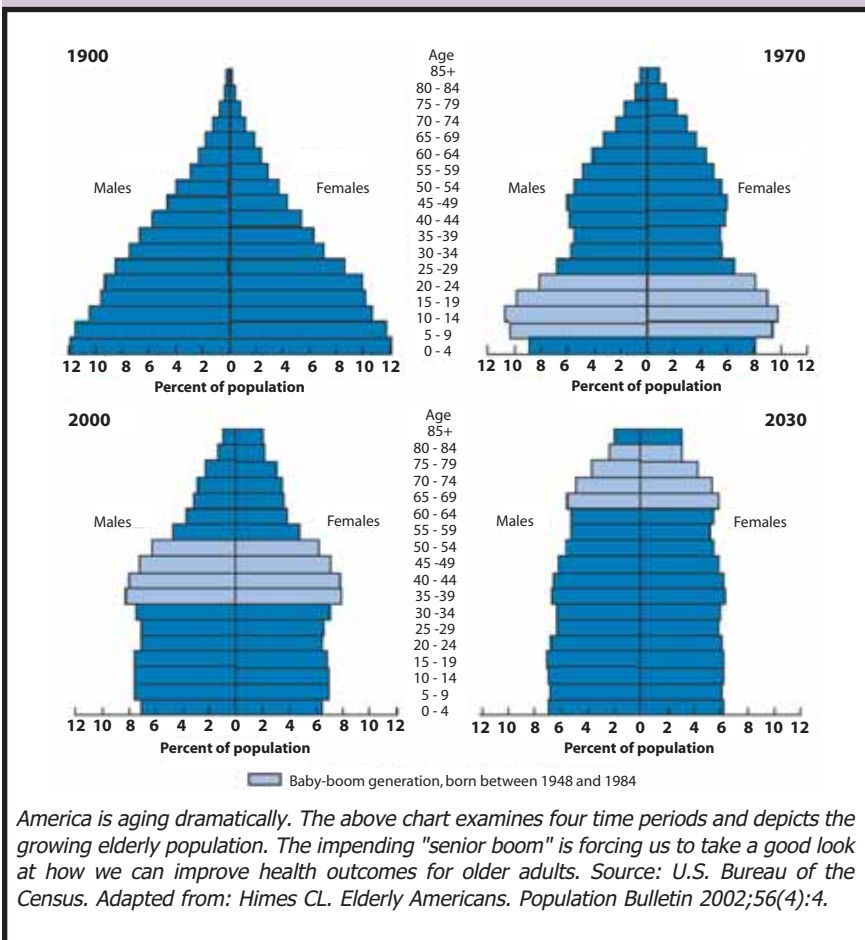
demonstrated that healthy lifestyles are more influential than genetic factors in helping older people avoid the deterioration traditionally associated with aging. People who are physically active, eat a healthy diet, do not use tobacco and practice other healthy behaviors reduce their risk for chronic diseases and have half the rate of disability of those who do not.

The first key to a healthy lifestyle is good nutrition. Older adults should consume adequate protein (30-40 grams/day), and one of the best sources of protein is fish. Additionally, fruits and vegetables are an important part of a healthy diet. For example, berries provide beneficial antioxidants and tomatoes are a good source of lycopenes, which reduce the risk of some cancers. Additionally, older adults should reduce their saturated fat intake and avoid empty calories. This means avoiding snack foods and margarine and using olive

oil and canola oil instead. Empty calories, such as rice, breads, pasta, potatoes and cake, have little or no dietary payoff. Of course, fluid intake also is important. It is recommended that you drink 64 ounces of water and consume one four-ounce glass of red wine daily.

The second key to a healthy lifestyle is regular exercise. Older adults should engage in cardiovascular, strength and flexibility training. Cardiovascular training includes aerobic exercise (running, biking, swimming, etc.) and should be performed three times per week. Older adults should reach 50 to 60 percent of their maximum heart rate (according to age) and burn approximately 300 to 400 calories per session. Strength or resistance training involves lifting weights. It is recommended that older adults do three sets of eight to 10 reps to the point of fatigue for both the upper and lower body

continued on page 15



America is aging dramatically. The above chart examines four time periods and depicts the growing elderly population. The impending "senior boom" is forcing us to take a good look at how we can improve health outcomes for older adults. Source: U.S. Bureau of the Census. Adapted from: Himes CL. Elderly Americans. Population Bulletin 2002;56(4):4.

FOCUS ON HEALTHY LIFESTYLES

... Continued from page 14

(arms and legs). Regular stretching is a good method to maintain and/or increase flexibility and should be performed prior to both cardiovascular and strength training.

The third key to a healthy lifestyle is eliminating unhealthy behaviors and replacing them with those that are beneficial. For instance, tobacco use, excessive consumption of alcohol and a lack of sleep are all behaviors that should be avoided. In addition to regular exercise and a balanced diet, healthy behaviors include taking vitamin supplements and a baby aspirin daily to reduce risk of heart disease and other health problems. Older adults should consult with their doctors about appropriate supplements.

One of the most common myths about aging is that it's too late to change the health habits of older people. This is simply not true! In fact, studies show that modest strength-building activities can increase muscle and bone strength even for people older than 90. The first step toward preventing future health problems is maintaining a healthy lifestyle. The next article in this series will focus on the early detection of diseases.

Note: References available upon request.

You make a difference! PARTICIPATE IN A KLRI STUDY

Testosterone's Effects on the Progression of Atherosclerosis in Aging Men (TEAAM): KLRI plans to collaborate on a study designed to determine the effects of testosterone replacement in older men on cardiovascular disease risk. Testosterone is the major male hormone. The loss of testosterone as men age may lead to decreases in bone and muscle strength and contribute to frailty and poor quality of life. This study will help demonstrate how giving testosterone to aged men will affect the risk of heart disease.

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

KLRI 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 in aging men and women," "How exercise and nutrition can impact your life" and "The importance of mental exercise: Ways to stay sharp."

Professional Education

KLRI 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. Contact KLRI for more information on upcoming seminars.

KLRI Staff

<i>Director and President</i>	S. Mitchell Harman, MD, PhD
<i>Clinical Director</i>	Panayiotis D. Tsitouras, MD
<i>Exercise Sciences Director</i>	Taylor J. Marcell, PhD, ATC
<i>Clinical Exercise Physiologist</i>	Tinna Traustadóttir, PhD, ATC, CSCS
<i>Clinical Study Coordinator</i>	Frank Gucciardo, PA-C, BS, MPA
<i>Vice President Education and Public Affairs</i>	Patricia A. Crenshaw
<i>Administrator</i>	M. Carol Jackson
<i>Clinical Studies Associates</i>	Gabriel Buldra, EMT-1, I/C Jane Heilman
<i>Editor</i>	<i>Patricia Crenshaw</i>
<i>Copy Editors</i>	<i>Carol Jackson Stephanie Jarnagan</i>
<i>Design Coordinator</i>	<i>Eric Dittlof</i>

**To contact us,
please call
(602) 778-7499,
visit our website at
www.kronosinstitute.org
or write to
2222 E. Highland Ave.
Suite 220
Phoenix, AZ 85016**

Kronos Longevity Research Institute

2222 East Highland Avenue
Suite 220
Phoenix, Arizona 85016

Prst Std.
U.S. Postage
PAID
Phoenix, AZ
Permit # 5375