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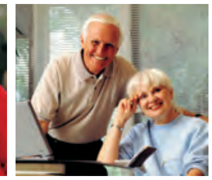
Research to promote a longer, healthier life for you, your children and your grandchildren.










Vol. 9, Issue 4

ANTIOXIDANTS — WHAT ARE THEY GOOD FOR?

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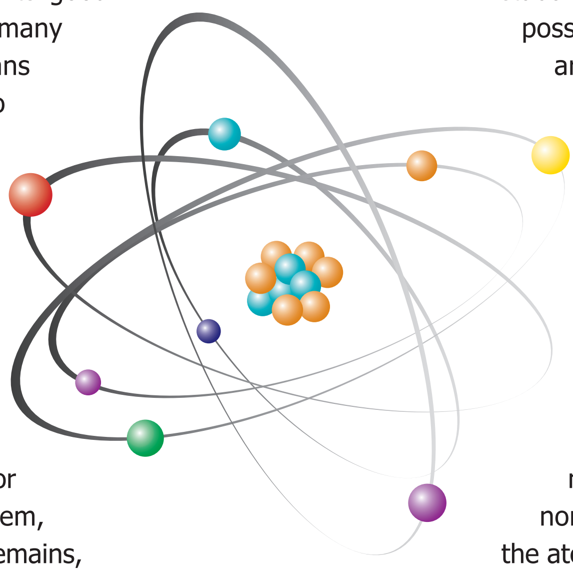
What are antioxidants good for? Surprisingly, for many scientists and physicians these days the answer to this question is, "Absolutely nothing!" Other scientists and physicians are equally certain that antioxidants have important health benefits. Still others believe antioxidants may actually be good for something; for them, however, the question remains, what? Before attempting to answer this question from my point of view, clarification of a few key terms and concepts seems prudent. This will provide the background information necessary for a proper understanding of antioxidants and their benefits.



What is a free radical?

The human body is composed of molecules. They are the structural and functional components of the cells and metabolic pathways that make life possible. Molecules, in turn, are composed of atoms, the fundamental building blocks from which they are made. Atoms are composed of positively charged protons, negatively charged electrons and neutral neutrons. The important point is that positive and negative charges are normally balanced so that the atoms and molecules in the body exist in equilibrium.

Normally, during most chemical reactions, bonds between atoms are not broken in a way that leaves a molecule with an odd, unpaired electron. However, in the rare instances when this does happen, a "free radical" is formed. Free radicals are extremely reactive and unstable. They immediately attack the nearest stable molecule to capture a needed electron or to dump an excess electron. When this happens, an attacked

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Director's Message

What's New In Fatty Acids?

A molecule of neutral fat, the kind that is found in our diets and stored in our fat (adipose) tissue, consists of three fatty acid molecules held together by bonding to a three-carbon alcohol called glycerol. Each fatty acid molecule is a long chain (usually 16 to 20) of carbon atoms with an organic acid (COOH) group at one end. (Note that "C" stands for carbon, "O" for oxygen, and "H" for hydrogen.) If all the carbon atoms in the chain are held together by single bonds, then each carbon will be bonded to two hydrogen atoms and the chain will look like this ($-CH_2-CH_2-CH_2-$). Such fatty acids are said to be "saturated." Some fatty acids contain carbons that are held together by a double bond and those carbons will have only one hydrogen attached ($-CH_2-\underline{CH=CH}-CH_2-$). Such fatty acids are called "unsaturated." If there is only one double bond, we call the molecules "monounsaturated" fatty acids or MUFA's. If there is more than one double bond, they are called "polyunsaturated" fatty acids or PUFA's. Much evidence suggests that fats and oils containing unsaturated fatty acids are less likely to contribute to heart disease than saturated fats like butter and lard.

Omega-3 fatty acids are PUFA's essential to human health. Among other things, omega-3 PUFA's are necessary for normal brain development and function. Brain tissue contains high concentrations of omega-3 PUFA's, which are needed for optimal memory, concentration, and performance. Because our bodies cannot manufacture omega-3 PUFA's, we need to consume them in our diets. Foods rich in omega-3 PUFA's include oily fish, like salmon, tuna, herring, and mackerel, certain vegetables, notably avocados, and some nut and seed oils, especially walnut and flaxseed oils. It is especially important that pregnant and nursing women take in adequate quantities of omega-3 PUFA's to pass them on to their infants to ensure normal growth and development.

The other main form of PUFA are the omega-6 PUFA's. Because of the increased use of corn, safflower, and other seed oils, today's American diet contains 12 to 20 times as much omega-6 PUFA as omega-3 PUFA. However, based on research studies, the recommendations by nutrition experts are for an omega-6 to omega-3 PUFA ratio of no more than 3 or 4 to 1. Whereas omega-3 fatty acids have been shown to reduce inflammation, omega-6 fatty acids tend to increase it, leading researchers to believe that an unhealthy ratio of omega-6 PUFA to omega-3 fatty PUFA is contributing to a rising rate of inflammatory diseases in the U.S.

The three omega-3 fatty acids found in food are called: alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). ALA is the type found in vegetable oils. The body must convert ALA to EPA and DHA, which are the two forms essential for brain and other tissue functions. Over the last 10 to 15 years, a wide variety of research studies have shown that sufficient intake of omega-3 fatty PUFA's can decrease inflammation and may reduce risks for sudden cardiac death, asthma, inflammatory bowel disease, arthritis, and depression. Because the ability to convert ALA to DHA and EPA tends to decrease with age, it may be important for older persons to consume their omega-3 PUFA's as DHA and EPA in fish, fish oil, or supplements made from certain algae, rather than as ALA from vegetable sources.

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molecule often becomes a free radical itself, causing a chain reaction. The chain reactions caused by free radicals can be very damaging to important cellular molecules such as DNA, RNA proteins and lipids. If this process continues unchecked, it can cause considerable cellular dysfunction or even cell death.

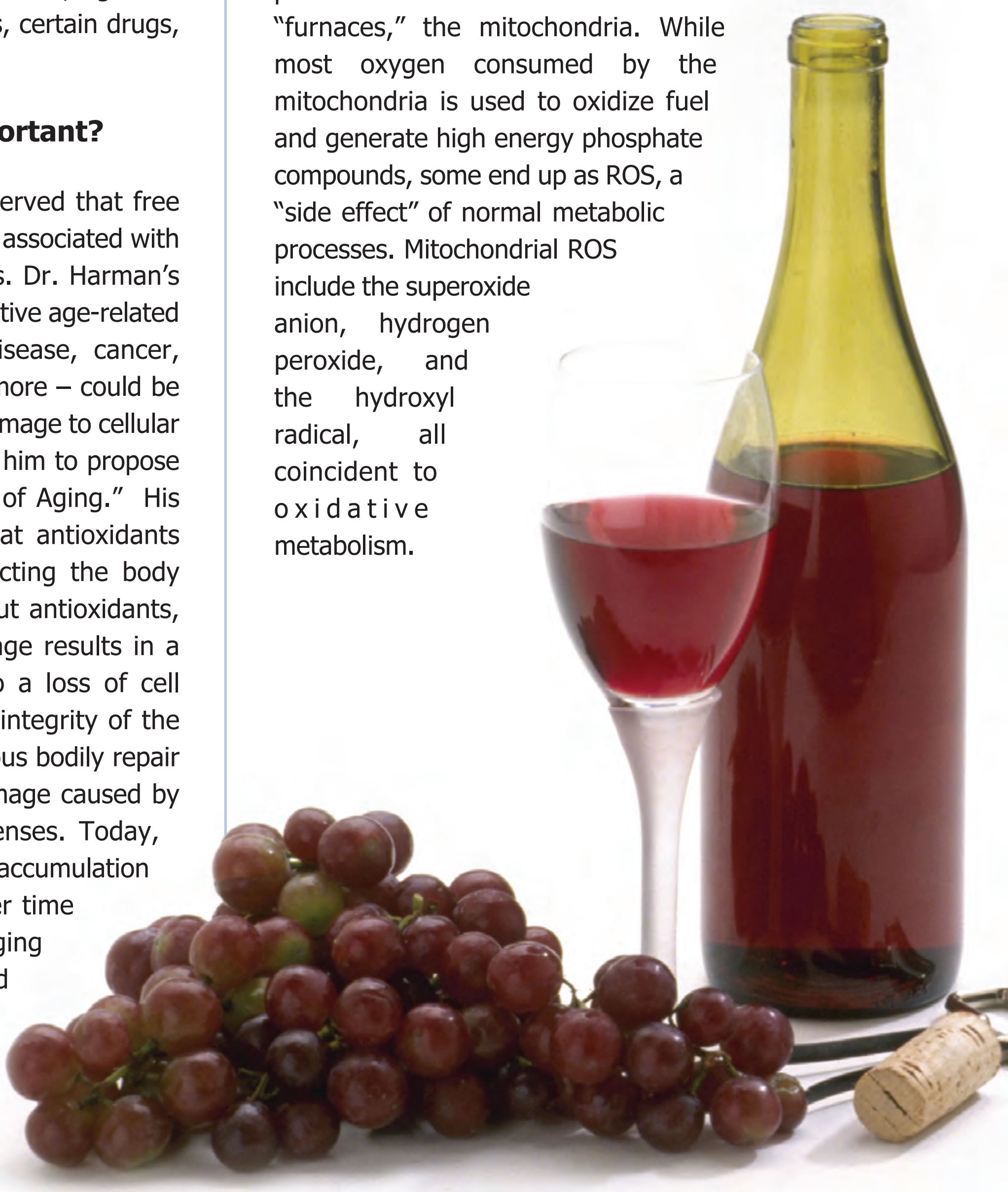
Free radicals are produced during normal energy metabolism as a byproduct of the biochemical reactions necessary for life. Sometimes, certain cells, such as immune cells, create them "intentionally" to neutralize viruses and bacteria. Free radicals may also be produced by environmental factors. Common culprits include highly reactive chemicals such as air pollution, cigarette smoke, corrosive substances, pesticides, certain drugs, and toxic fumes.

Why is free radical damage important?

In 1957, Dr. Denham Harman observed that free radicals increase with metabolic activity associated with biological oxidation/reduction reactions. Dr. Harman's research suggested that many degenerative age-related diseases – such as cardiovascular disease, cancer, Alzheimer's, diseases of the skin, and more – could be the result of accumulated free radical damage to cellular components, particularly DNA. This led him to propose his now famous "Free Radical Theory of Aging." His research also led him to conclude that antioxidants might play an essential role in protecting the body against such oxidative damage. Without antioxidants, the accumulation of free radical damage results in a change in cell structure that leads to a loss of cell function and decline in the functional integrity of the body's organs and tissues. Finally, various bodily repair and disposal systems clean up the damage caused by free radicals that get past these defenses. Today, many scientists believe the progressive accumulation of unrepaired free radical damage over time may be a major contributor to the aging process and to a variety of age-related chronic diseases.

What is oxidative stress?

"Oxidative stress" is a term commonly used to refer to the process by which oxidative free radical damage occurs in living organisms. It is mitigated by the organisms' ability to prevent or repair such damage. For the past several decades, research evidence has accumulated, which demonstrates that oxygen free radicals can cause damage to cellular components (i.e. proteins, cell membrane lipids, and the DNA of both chromosomes and mitochondria). These oxygen free radicals (also known as "reactive oxygen species" or ROS) are generated during the process of energy production in the cell's miniature "furnaces," the mitochondria. While most oxygen consumed by the mitochondria is used to oxidize fuel and generate high energy phosphate compounds, some end up as ROS, a "side effect" of normal metabolic processes. Mitochondrial ROS include the superoxide anion, hydrogen peroxide, and the hydroxyl radical, all coincident to oxidative metabolism.



How is oxidative stress measured?

At Kronos Science Laboratory (KSL), we attempt to assess oxidative stress status by measuring various internal and external "protection factors" (antioxidants) in serum, plus indirect and direct "damage factors." Accurate measurement of oxidative stress needs a novel methodology and sophisticated technology. Rates of oxidative damage *in vivo* can be assessed by measurement of serum and/or urinary products of oxidative damage to a variety of biological molecules. KSL has developed a multi-parameter biomarker set for oxidative stress assessment. We utilize a proprietary, state-of-the-art technology (based upon liquid chromatography/dual mass spectroscopy, also known as LC/MS/MS) to measure DNA/RNA, lipid, and protein oxidation products. These methods have been recognized as the gold standard technology in this field.

Direct damage factors include oxidized lipid molecules (isoprostanes: 8-isoprogtaglandin F2-alpha (iPF2-alpha-III); 2,3-dinor-iPF2-alpha-III; iPF2-alpha-VI; and 8,12-iso-iPF2-alpha-VI); two important DNA damage adducts (8-hydroxy-2'-deoxyguanosine and 5-hydroxymethyl-2'-deoxyuridine); an RNA damage product (8-oxo-guanosine); and several protein oxidation products (di-tyrosine, nitro-tyrosine, and Cl-tyrosine.) measured in serum and/or urine. Taken together, these assays give a reasonably complete assessment of an individual's oxidative stress status. In fact, every important component of oxidative damage that we know about is measured directly. Levels of DNA, RNA, protein, and lipid damage products vary considerably among healthy human subjects. However, repeated measurement of these oxidative damage products over time should provide a good estimate of an individual's overall level of oxidative stress.

As described above, KSL has developed and analytically validated a number of assays designed to assess oxidative stress. In collaboration with Kronos Longevity Research Institute (KLRI) and others scientists around the world, KSL is now in the process of clinically validating these assays in various high-risk human populations (such as smokers, Alzheimer's, cancer, cardiovascular disease, diabetes, etc.) to confirm their diagnostic utility in assessing oxidative stress. Based on prior studies, it appears that a variety of factors, including smoking, oxygen consumption, and inflammatory disease, modulate oxidative stress status, whereas diet, energy restriction and antioxidant supplements may have relatively less effect. It is becoming increasingly clear that no single parameter will be a satisfactory index of the overall state of oxidative stress. Thus, it is likely that, in order to assess effects of candidate therapies designed to reduce oxidative stress, it will be necessary to employ assays that reflect ongoing rates of oxidative damage to all three critical tissue components. It is also possible that pathogenesis of different diseases will be characterized by different patterns of oxidative damage that can only be assessed using multiple assays.

Such assays are now being used at KLRI and KSL to evaluate promising antioxidant interventions. We do this by (1) identifying individual under high oxidative stress by measuring urinary levels of damage products; (2) intervening with antioxidants; (3) if possible, measuring serum levels of the antioxidants; (4) monitoring urinary damage products over time to see if they are reduced in those individuals receiving antioxidants compared to placebo. We believe that this strategy for measuring oxidative damage products in the urine, along with measuring many specific antioxidants in the serum, provides the most complete and scientifically sound assessment of oxidative stress status available for research purposes or for use in a clinical environment.

What is an antioxidant?

The term "antioxidant" is indicative of the mechanism by which certain molecules may help prevent oxidative damage. An antioxidant is a substance that can neutralize any of the various free radicals that sometimes damage other cellular molecules. Antioxidants stop the chain reaction of electron stealing by giving up electrons, thus, neutralizing the free radicals so that they cannot induce any more oxidative damage. Unlike other molecules, antioxidants do not become reactive when they lose an electron.

Antioxidants that occur naturally in the body or are consumed through the diet actually block most of the damage. For example, certain enzymes, such as superoxide dismutase (SOD), catalase, and thioredoxin reduce reactive oxygen species (ROS) and other free radicals to harmless or less reactive forms. There are also free radical scavenger compounds which "sacrifice" themselves by being oxidized in place of more critical biological molecules. These include many vitamins, minerals, carotenoids, polyphenols, bioflavenoids proteins, lipids, and other organic molecules. The most well known dietary antioxidants include vitamin A (found in liver, dairy, and fish liver oil), vitamin C (found in peppers and citrus fruits), vitamin E (found in oils, seeds, and nuts), and the mineral selenium (found in Brazil nuts, meats, and tuna). However, other dietary antioxidants may turn out to be even more important.

Since there are many different types of free radicals, the best protection may depend upon a combination of many different antioxidant molecules. The concentration of any one of these antioxidants may be small, but collectively they represent an important antioxidant system. For example, all the various antioxidants in the serum are known to interact with each other so that the net antioxidant protection may be substantially greater than the sum of the individual components. The major antioxidants in the serum and their approximate percent contribution to total serum antioxidant activity (Oxygen Radical Absorption Capacity – i.e. ORAC value) are as follows:

Albumin	34%
Uric acid	27%
Vitamin C	6%
Vitamin E	4%
Bilirubin	3%
Carotenoids	2%
Total lipids	15%
Polyphenols and Bioflavonoids	9%

Are antioxidants beneficial?

Epidemiologic evidence suggests that diets high in antioxidants may decrease incidence of cancer and cardiovascular disease (CVD), but trials of antioxidant supplements have largely been disappointing in this regard. In an effort to better understand and potentially improve bodily defenses to combat free-radical activity, scientists at KLRI and KSL are studying the effects of increasing individuals' antioxidant levels through the diet and dietary supplements. Although to date the data are mixed, preliminary results suggest that certain antioxidant rich foods (e.g. blueberries, strawberries, and cherries) may be highly protective against certain types of oxidative damage.

Many studies have shown the link between free radicals and a number of degenerative diseases associated with aging. Thus, it is possible that antioxidants may be beneficial in reducing the incidence of cancer, cardiovascular disease, cognitive impairment, Alzheimer's disease, immune dysfunction, cataracts, stroke, and macular degeneration.

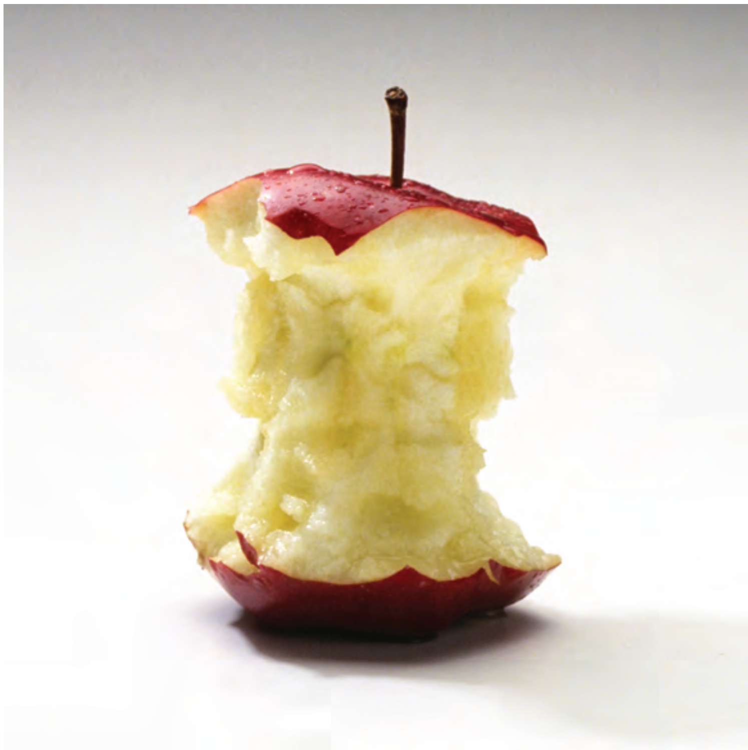
Among the most widely-publicized research trials on antioxidant supplementation was the first large-scale randomized, prospective, placebo-controlled, five-year study conducted in North Central China. Approximately 30,000 participants were given either a placebo or a dietary supplement containing one of seven vitamin-mineral combinations. Persons who received a daily dose of beta-carotene, vitamin E and selenium had a reduced cancer rate of 13 percent.

Another famous study, involving 1,795 female nurses, reported that women who consumed high amounts of antioxidant containing foods had a 33 percent lower risk of heart attack and a 71 percent lower risk of stroke, than women who ate few antioxidant containing foods. The antioxidants targeted in this study were vitamins C and E, beta-carotene and riboflavin. Food sources most closely associated with the health benefits from these antioxidants included carrots, spinach and other greens.

Sometimes the effect of taking an antioxidant supplement can be quite surprising. In 2004, KSL participated in a study in which we measured the influence of vitamin E ingestion on oxidative stress and immune changes in response to the Triathlon World Championship in Kona, Hawaii. Thirty-eight triathletes received vitamin E (800 IU per day) or placebo capsules in a randomized, double-blind fashion for two months before the race event. Blood, urine, and saliva samples were collected the day before the race, 5-10 minutes post-race, and 1.5 hours post-race. Race times did not differ between groups and both groups maintained an intensity of approximately 80 percent maximum heart rate during the bike and run portions. Plasma alpha-tocopherol was approximately 75 percent higher in the vitamin E versus placebo group pre-race and post-race.

Yet, surprisingly, plasma F2-isoprostanes increased 181 percent versus 97 percent post-race in the Vitamin E versus placebo group. Several inflammatory cytokines were also significantly higher post-race in the vitamin E versus placebo groups. These data indicate that high dose vitamin E ingestion before a competitive triathlon race event promotes lipid peroxidation and inflammation during exercise. This result is exactly the opposite of what we expected.

In spite of the vast quantity of basic research on the biochemical mechanism of oxidative stress and the biological role of antioxidants, the clinical utility and health benefits of antioxidants are still in doubt. A meta-analysis of 68 randomized clinical trials with 232,606 total participants recently published in the *Journal of the American Medical Association* is a case in point. The purpose of this systematic review of the literature was to assess the effect of antioxidant supplements on mortality, an unequivocal endpoint. The authors concluded, "Treatment with beta-carotene, vitamin A, and vitamin E may increase mortality end." The potential roles of vitamin C and selenium on mortality need



further study. Clearly, this result does not inspire great confidence in the notion that antioxidant supplementation of any kind is beneficial. It is safe to agree that further study is needed.

How do I take action?

In recent years, antioxidant supplements have been touted in fitness magazines, television ads, health food stores and gyms as everything from immune system boosters to the fountain of youth. While new products emerge frequently, it is best to remember that vitamin and mineral supplements are no substitute for a healthy, well-balanced diet. In fact, due to many conflicting studies on the effects of antioxidant supplements, many scientists do not currently recommend using antioxidant vitamin supplements. It is also important to note that we can "over-supplement" our bodies, taking much more than the recommended daily value of certain vitamins and minerals. For example, Vitamin C in high doses can actually become a “pro-oxidant,” (causing more harm than good) instead of an “antioxidant.” Vitamins A, D, and E are fat soluble, meaning that excess amounts are stored in the liver and fatty tissues, instead of being quickly excreted. This can create a risk of toxicity, though this risk is extremely low. Still, questions remain on issues such as the effectiveness of individual antioxidants, their mechanisms of action, optimum levels of intake and their long-term effects.

Thus, until more research is completed, all the data are in, and our questions regarding dose, duration, combination, formulation, and environmental circumstance definitively answered, the best advice I can offer is to eat a balanced diet, rich in colorful fruits and vegetables, and to take a quality multiple vitamin and mineral supplement to help compensate for possible dietary deficiencies. Stay away from high-dose antioxidant supplements. We have a long way to go before we know enough about antioxidants to take them safely.

Christopher B. Heward, PhD
President, Kronos Science Laboratory

References are available upon request.

Who We Are

Kronos Longevity Research Institute (KLRI) is a not-for-profit, 501(c)(3) organization that conducts state-of-the-art clinical translational research on the prevention of age-related diseases and the extension of healthier human life. 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's Mission

KLRI is dedicated to understanding the human aging process and preventing age-related disease. KLRI conducts and fosters research that moves basic discoveries into clinical practice and communicates our research results to scientific and healthcare professionals and to the public so that people may enjoy longer and healthier lives.

KLRI's Vision

KLRI will be the leading independent research institute for translating basic discoveries on aging and longevity into improved preventions and treatments. We will be recognized as the thought-leader in the field of clinical gerontology and an authoritative source of sound scientific information.

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 Translational Research?

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 done with animals or cultured cells, genes, etc.) and improved clinical care. It requires controlled studies of living human participants.

Contact Us

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Board Member Profile

L. Ben Lytle

Healthcare Entrepreneur

L. Ben Lytle has joined the Board of Directors. Mr. Lytle is a healthcare entrepreneur with more than 30 years experience. Mr. Lytle served as Chairman and Chief Executive Officer of AXIA Health Management, LLC until its sale to Healthways, Inc. (NASDAQ) in December 2006. He and his son, Hugh, founded AXIA in 2004, which later became the nation's largest provider of wellness services.

Previously, Mr. Lytle was Chairman and CEO of Anthem, Inc. which acquired WellPoint, Inc. (NYSE) in 2004 and assumed the WellPoint name, becoming a Fortune 500 company with revenues of more than $40 billion. Mr. Lytle joined Blue Cross and Blue Shield of Indiana in 1976, then with revenues under $1 billion. He rose through the executive ranks to become COO in 1982 and CEO in 1989. Under Mr. Lytle's leadership, BCBS of Indiana was transformed through a series of mergers and acquisitions to form Anthem, a $16-billion revenue Fortune 500 company. During this time, he built, took public, and sold Acordia, Inc. (NYSE) as an Anthem subsidiary, which at the time was the world's 7th largest insurance broker. Mr. Lytle retired as CEO of Anthem in 1999, continued as Chairman until 2004, and remains its Chairman Emeritus.

Mr. Lytle has been an advocate for healthy lifestyles and market-based healthcare reform his entire career. He has authored numerous speeches, newspaper and magazine articles; provided testimony to Congress and state legislatures; chaired Indiana's Health Care Commission; served on President Bill Clinton's Commission on Consumer Protection and Healthcare Quality, and presently chairs the Foundation for Better Health, a not-for-profit research and advocacy organization devoted to free market solutions to public health.

Mr. Lytle currently serves on the University of Arizona Eller College National Board of Advisors, Genstar Capital's Strategic Advisory Committee, the boards of directors of Duke REIT (NYSE), Monaco Coach Corporation (NYSE) and Healthways, Inc. (NASDAQ). He is also the recipient of the University of Arizona's 2004 Executive of the Year Award.

A Texas native, Mr. Lytle graduated with a BS in Psychology from Texas A&M University in 1970 and received a JD from Indiana University in 1980.

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Currently, fish oil supplements containing EPA and DHA are employed to reduce high blood levels of triglycerides, a problem common in diabetics and persons with the "metabolic syndrome." Omega-3 PUFA's may also decrease low density (LDL or "bad") cholesterol and raise high density (HDL or "good") cholesterol. Some studies have suggested that omega-3 PUFA's help lower blood pressure in patients with hypertension. Despite these apparent reductions in risk factors for heart disease, there is no good evidence that omega-3 PUFA's actually decrease heart attack rates. However, studies have shown that omega-3 supplements do lower the risk of sudden cardiac death in persons with known heart disease and decrease thrombotic (caused by clots in the brain arteries) strokes. Paradoxically, people who consume large quantities (more than 4 grams/day) of omega-3 PUFA's may be at increased risk for hemorrhagic stroke, in which an artery bleeds into the brain, perhaps because of the effect of omega-3 PUFA's to decrease the tendency of blood to clot.

Another potential action of omega-3 PUFA's may be to reduce the incidence of osteoporosis and bone fractures. Studies suggest that deficiencies of EPA and gamma-linolenic acid [GLA], an omega-6 fatty acid, are associated with greater rates of calcium loss from bone. Moreover, epidemiologic studies have shown that women who consume higher amounts of omega-3 PUFA's have greater bone density and fewer fractures. The mechanisms by which omega-3 PUFA's affect bone are currently unknown.

A study conducted by KLRI investigators, recently published in the journal, *Hormone and Metabolic Research*, showed that supplementation with fish oil plus a diet containing three servings of oily fish per week resulted in improved sensitivity to insulin and a reduced blood concentration of free fatty acids (which means your glucose is lower). Omega-3 PUFA also lowered the amount of C-reactive protein, a pro-inflammatory factor associated with higher risk of heart disease. Thus, omega-3 PUFA's may help protect against type 2 (the common form of adult-onset) diabetes.

Future studies planned at KLRI will investigate whether omega-3 PUFA's may help reduce risk of progression to diabetes by persons with glucose intolerance or can decrease bone loss in diabetic women taking certain antidiabetic medications (thiazolidinediones or TZD's). We will also further explore effects of these fascinating compounds to reduce inflammation and diminish oxidative stress.

Although more will be known about omega-3 PUFA's as time goes on, we believe it is reasonable to recommend a combination of dietary and/or supplement sufficient to produce a total intake of 3 to 4 g/day of omega-3 PUFA. EPA and DHA are available in the form of liquid fish oil or fish oil capsules, which are best kept refrigerated to prevent them from becoming rancid. Rancid fish oil may produce bloating, foul tasting belching, and flatulence or diarrhea. Omega-3 PUFA supplements should be certified free of heavy metals such as mercury, lead, and cadmium, which, unfortunately contaminate certain fish, such as tuna. Finally, people who have a bleeding disorder, or take blood-thinning medications, such as warfarin (Coumadin) or clopidogrel (Plavix) should not consume large quantities of omega-3 PUFA's.

For more information about omega-3 fatty acids, visit the following websites:

http://www.mayoclinic.com/health/fish-oil/NS_patient-fishoil
http://www.umm.edu/altmed/articles/omega-3-000316.htm

S. Mitchell Harman

S. Mitchell Harman, MD, PhD
Director and President

A Peek At…

Gray is the New Gold

Longevity Science: Slowing the Spiral of Aging

KLRI's Gray is the New Gold report, titled Longevity Science: Slowing the Spiral of Aging, highlights KLRI's research and summarizes the latest breakthroughs and developments in longevity and aging research. The report discusses four key areas researchers are honing in on to get a better understanding of the aging process and the science behind healthy aging. Here is a sneak peek of the different sections of the report.

The full report is available on KLRI's website at www.kronosinstitute.org and on the NRTA: AARP's Educator Community website at www.aarp.org/health/brain/aging/healthy_aging.html.

Oxidative Stress - Learning how oxidative damage occurs or why the body is rusting like your little red wagon?

Every time you breathe, metabolize food, or exercise, every time your cells create energy to keep you going, damaging byproducts called oxygen-free radicals are also created. Think of them as a cellular form of exhaust, similar to the exhaust your car creates as a byproduct of the gasoline it uses for energy. Only instead of polluting the air, this form of biochemical "exhaust" can damage nearby tissues, leading to age-related diseases like cancer, heart disease, diabetes, osteoarthritis, and Alzheimer's disease. In essence, the very processes that promote life inevitably lead to death.

Caloric Restriction; Slow the Damage

Eat less and you'll live longer, it sounds simple on the surface. At least, that's what studies in animals ranging from fruit flies, worms, and rats to dogs and primates find: Cutting calories by one-third to one-half significantly increases life spans and reduces disease. Since few people want to trim their calories by a third (what would life be without molten chocolate cake and ice cream?), one of KLRI's Scientific Advisors and his team are searching for compounds that mimic the biochemical effects of eating less, "fooling" cells into behaving as if they were deprived of energy.

Hormones; Diminishing Hormones

The impact of hormones is a key focus in the area of longevity research, particularly at KLRI, especially the ones that decrease as we age. Researchers have launched a national, multicenter study to evaluate the effects of estrogen therapy in women just before and after menopause—something the highly publicized Women's Health Initiative (WHI) tried to do. KLRI has also launched a large, national study to evaluate the risks and benefits of testosterone therapy in older men. KLRI researchers have also developed a unique study to evaluate the effects of increased levels of human growth hormone—without supplementing with the hormone—on markers of aging.

Nutrition; Teasing Out the Impact of Diet on Age-related Conditions

KLRI researchers are beginning to tease out the impact of diet on aging-related conditions such as insulin resistance, which is thought to contribute to a variety of diseases common in older people. The first study evaluated the anti-inflammatory effects of high levels of omega-3 fatty acids, "healthy" fats found primarily in fatty fish like salmon and tuna and in some seeds.

Word Search

Instructions: Find these antioxidant words in the word scramble below.

Dark Chocolate	**Blueberries**	**Walnut**	**Tart Cherry**	**Red Wine**
Free Radical	**Damage**	**Beta Carotene**	**Oxidation**	**Vitamin C**

F	O	X	I	D	A	T	I	O	N	S	H	S	N
V	G	Y	U	I	L	F	Q	F	E	F	G	Y	N
I	A	G	H	W	F	C	H	I	Z	X	P	V	S
T	F	P	F	R	E	E	R	A	D	I	C	A	L
A	C	R	N	J	E	R	E	G	H	V	T	A	P
M	P	C	R	A	E	B	D	H	Y	S	A	F	L
I	S	W	J	B	B	G	W	B	K	A	R	G	E
N	P	P	E	P	S	S	I	S	E	Q	T	N	C
C	V	U	A	A	H	R	N	R	X	F	C	W	H
T	L	H	L	N	X	W	E	P	F	W	H	E	Y
B	E	T	A	C	A	R	O	T	E	N	E	G	A
S	G	R	T	L	N	L	P	P	S	B	R	A	V
Y	E	T	N	G	H	N	C	F	C	A	R	M	Q
H	P	U	I	E	G	J	I	Q	O	O	Y	A	B
E	T	A	L	O	C	O	H	C	K	R	A	D	M

Answer:

F	O	X	I	D	A	T	I	O	N	S	H	S	N
V	G	Y	U	I	L	F	Q	F	E	F	G	Y	N
I	A	G	H	W	F	C	H	I	Z	X	P	V	S
T	F	P	F	R	E	E	R	A	D	I	C	A	L
A	C	R	N	J	E	R	E	G	H	V	T	A	P
M	P	C	R	A	E	B	D	H	Y	S	A	F	L
I	S	W	J	B	B	G	W	B	K	A	R	G	E
N	P	P	E	P	S	S	I	S	E	Q	T	N	C
C	V	U	A	A	H	R	N	R	X	F	C	W	H
T	L	H	L	N	X	W	E	P	F	W	H	E	Y
B	E	T	A	C	A	R	O	T	E	N	E	G	A
S	G	R	T	L	N	L	P	P	S	B	R	A	V
Y	E	T	N	G	H	N	C	F	C	A	R	M	Q
H	P	U	I	E	G	J	I	Q	O	O	Y	A	B
E	T	A	L	O	C	O	H	C	K	R	A	D	M

Glossary

Molecules: The smallest particle of a substance that retains all the properties of the substance and is composed of one or more atoms

Oxidation/Reduction: A chemical reaction in which one or more electrons are transferred from one atom or molecule to another

Chromosomes: Any of the usually linear bodies of the cell nucleus of eukaryotic organisms, the usually circular bodies of prokaryotic organisms (as bacteria), or especially in some schools of molecular biology the genomes of DNA viruses (as bacteriophages) that take up basophilic stains and contain most or all of the genes of the organism

Mitochondria: Any of various round or long cellular organelles of most eukaryotes that are found outside the nucleus, produce energy for the cell through cellular respiration, and are rich in fats, proteins, and enzymes

Serum: The clear yellowish fluid that remains from blood plasma after fibrinogen, prothrombin, and other clotting factors have been removed by clot formation

Placebo: An inert or innocuous substance used especially in controlled experiments testing the efficacy of another substance (as a drug)

Plasma: The fluid part especially of blood, lymph, or milk that is distinguished from suspended material

Meta-analysis: Quantitative statistical analysis that is applied to separate but similar experiments of different and usually independent researchers and that involves pooling the data and using the pooled data to test the effectiveness of the results

Epidemiologic studies: A branch of medical science that deals with the incidence, distribution, and control of disease in a population

DNA: Any of various nucleic acids that are usually the molecular basis of heredity, are constructed of a double helix held together by hydrogen bonds between purine and pyrimidine bases which project inward from two chains containing alternate links of deoxyribose and phosphate, and that in eukaryotes are localized chiefly in cell nuclei

RNA: Any of various nucleic acids that contain ribose and uracil as structural components and are associated with the control of cellular chemical activities

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