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AGE Control: An Under Recognized Way to Restore Insulin Sensitivity and Improve Heart, Bone and Cognitive Health

by David D. Parrish, MD

Scientists and the general public have long been fascinated by the reasons behind why we age and the actions we can take to slow aging. A number of theories have been proposed, including The Neuroendocrine Theory of Aging, which Ward Dean, MD extensively covered in past issues of this newsletter.

The Neuroendocrine Theory of Aging was first described in 1954 in a Master's thesis by the distinguished Russian gerontologist, Vladimir Dilman, M.D., Ph.D., D.M.Sc., who ultimately wrote a number of books about the topic. Dr. Dean obtained a copy of Dilman's books and later co-authored with the gerontologist the book

The Neuroendocrine Theory of Aging and Degenerative Disease. The Neuroendocrine Theory states that aging is caused when receptors and secretory cells in the limbic system, hypothalamus and the pituitary (important structures in the brain) are no longer sensitive to the hormones that control their function, resulting in a down regulation of the limbic-hypothalamic-pituitary axis and a subsequent down regulation of end organ receptor sites in the thymus, adrenals, thyroid, ovaries and testes. When this essential neuroendocrine axis becomes less functional, our bodies are thrown out of balance and we are at increased risk for the major

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Maintaining a Healthy Heart Rhythm: Cardiac Risk Factors Extend Beyond Cholesterol

by Chris D. Meletis, ND

Cholesterol has always taken center stage in discussions about heart health. Cholesterol, specifically high levels of low-density lipoprotein (LDL) cholesterol, is clearly a risk factor for cardiovascular disease. Yet, many individuals who have high cholesterol levels never have a heart attack. Similarly, people who have low cholesterol levels can die from sudden cardiac death. Furthermore, lipid peroxidation—the process by which lipids in the body are exposed to free radicals—more than cholesterol levels per se are associated with heart attacks.¹

The reason for this seeming contradiction is that other factors besides cholesterol influence heart health. High levels of homocysteine and fibrinogen are as harmful as high LDL cholesterol to cardiovascular health.

Another important but often overlooked factor are cardiac arrhythmias, which is the particular heart attack risk factor that I will address in this article. Arrhythmias are disorders of the regular rhythmic beating of the heart. Approximately 2.2 million Americans are living with a common type

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diseases of aging—which include atherosclerosis, hypertension, diabetes, cancer and autoimmune disorders. Consequently, maintenance and up regulation of this vital axis is of crucial importance.¹

In this article, I will take the Neuroendocrine Theory one step further by addressing a closely related concept that Dr. Ward Dean also has explored extensively: The Cross-linking Theory of Aging. Neuroendocrine imbalance, as mentioned above, can lead to this destructive process known as cross-linking.

It has long been known that cross-linked proteins are linked to diabetic complications. The newest research, however, reveals that cross-linking is related to a surprising number of diseases, including Alzheimer's disease, osteoporosis, arthritis, kidney disease, cataracts and aging skin (see sidebar). Furthermore, researchers now realize that cross-linking increases the amount of LDL type B subparticles (the "bad" cholesterol).

Why We Age: One Proposed Theory

According to the Cross-linking Theory of Aging, when a sugar links with a protein molecule a harmful process called cross-linking occurs in the body. Cross-linking begins with a process called the Maillard reaction. Anyone who has toasted a slice of

bread is familiar with this reaction. When the protein and the carbohydrates in the bread are exposed to heat they turn brown as a result of the chemical reaction that occurred between the proteins and carbohydrates during cooking.

The same process occurs in our bodies. When sugars combine with proteins during the Maillard reaction, it produces what's called a Schiff base. This is then converted into another harmful substance called

an Amadori product. However, the final result of this reaction—when the Amadori products are rearranged and transformed into Advanced Glycation End Products (AGEs)—is particularly destructive to the body. AGE molecules can further react with other fats, proteins and nucleic acids to form cross-links so strong that they cannot be broken apart. These Advanced

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AGEs Implicated in Aging Skin

by David D. Parrish, MD

One of the most visible effects of AGEs and glycation is skin damage. Glycation products accumulate during the aging of many slowly renewing tissues, including skin.¹

Advanced glycation end products (AGEs) formed after the consumption and impaired metabolism of glucose and fructose are known to have a destructive effect on skin fibroblasts (cells from which connective tissue is formed). AGEs increase cell death in skin cells, destroying collagen, thereby reducing elasticity of the skin.

Proteins within collagen are slowly metabolized. This makes them even more susceptible to changes that occur when they are exposed to AGEs. As mentioned in the accompanying article on AGEs, these destructive compounds result from the reaction of carbohydrates with the free amino group of proteins. This accumulation of AGEs in collagen of the skin and the resulting structural alterations result in impaired tissue properties (increased stiffness and reduced elasticity).

In one study, scientists investigated the effects of one type of AGE in rats subjected to a high-fructose diet. For three weeks, the rats were given fructose to induce hyperglycemia. This caused a significant increase in concentrations of the AGE studied, not only in the aortas of the animals, but also in the skin of the three rat strains used in the study.²

Glycation and AGEs have the same detrimental effect on human epidermal skin cells. One *in vitro* study showed that high AGE production that occurs after glucose exposure causes young skin cells to age rapidly.³

In another *in vitro* study, human skin fibroblasts exposed to AGEs experienced increased cell death. N-acetyl-cysteine (NAC) and carnosine, antioxidants also known for their anti-AGE effects, decreased this AGE-induced cell death in the skin cells.⁴

Another antioxidant with inter/intracellular properties, lipoic acid has demonstrated an equally strong ability to protect AGE-exposed skin in animals. A rodent study illustrated lipoic acid's ability to protect the skin against AGEs. The researchers fed rats a high-fructose diet then divided the animals into 4 groups of 6 each. Two groups of rats were fed with a high-fructose diet and administered either lipoic acid or saline for 45 days. The other 2 groups were fed with a control diet containing starch and administered either saline or lipoic acid.

Fructose administration in the animals caused extensive cross-linking evidenced by enhanced glycation and AGEs. These changes were alleviated by the simultaneous administration of lipoic acid. The researchers noted that administration of lipoic acid to fructose-fed rats had a positive effect on collagen integrity.⁵

Clearly, AGE formation can result in the skin changes seen with aging, such as reduced elasticity and wrinkles. Therefore, employing the strategies suggested in the accompanying article is one way to improve skin health.

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One Man's Successful Battle to Regain Good Health

Every day, I am reminded that for our company the nutritional supplement industry is so much more than just a business—it's a means to provide people with the tools they need to improve their overall health. Often, this point is driven home to me when a customer tells me how much his or her health has improved after increased intake of various vitamins, minerals and botanicals. Recently, a customer called to relay his experiences to me. His story moved me so deeply that I wanted to share it with you in this newsletter.

For years, Tim suffered from acid indigestion. He was taking two Prilosec® per day and downing many Rolaids® and Tums®. His girlfriend Pauletta begged him to go to a doctor. Finally, in May 2006 he visited a gastroenterologist, who prescribed a drug for gastroesophageal reflux disease along with an antacid. The gastroenterologist also scheduled Tim for a scope in early June.

When the results came back in July, the diagnosis was mild inflammation of the esophagus, throat and upper stomach.

"I advised the doctor right then I was tired, losing my appetite and concerned about my overall health," Tim recalls. "He advised I shouldn't be concerned and basically was in good health."

Then, on August 5, 2006, Tim entered the emergency room complaining of pain in his stomach. His skin also was a jaundiced yellow. Tests showed his bilirubin was high at 12.7. High bilirubin serves as a marker of jaundice and liver dysfunction.

The surgeon decided to remove Tim's gallbladder, but before proceeding with the surgery the doctor wanted another scope. Tim's pancreas was so enlarged, however, that the scope wouldn't make it past his stomach to enter his intestine, though it did indicate he had several ulcers in his stomach and upper intestine. The doctor then ordered an MRI, which revealed Tim had a bad gallbladder, intestinal lesions, liver lesions and quite possibly pancreatic cancer. A liver biopsy confirmed the diagnosis—Tim had pancreatic cancer.

An oncologist explained to Tim that the cancer had metastasized (spread) to his liver and that the cancer had progressed

to stage four. According to the oncologist, Tim only had four months to live.

Soon after this dismal prediction, Tim moved in with his parents and sought help at a cancer facility about fifty miles from their home.

"The initial meeting with the oncologist at this facility advised if I made it more than three months it would be a miracle," remembers Tim. "He said there was little hope of beating what I had."

For two months, in the fall of 2006, Tim underwent chemo and radiation treatments five times a week. He felt sick every day. His weight plummeted from 235 pounds at the time he was first admitted into the hospital to 175 pounds. Concurrently with the chemo and radiation, he consumed a drug that cost \$2,500 for a two-week supply. His doctor also suggested he begin a rigorous supplement regimen. Most of the drug and supplements literally went down the drain as Tim had trouble holding anything down.

After he was no longer able to receive radiation, he landed in the hospital for a week, as he still couldn't keep down any food. Finally, he stabilized and regained his appetite.

He returned home where his girlfriend helped nurse him. It was then that a friend explained to Tim how supplements had changed his own health. Tim's friend told him about our EpiCor® and ordered him a bottle along with a few other products. Tim began taking three EpiCor per day. He also began learning more about pancreatic cancer and the immune system.

According to Tim, "If every person in the world would heed and find out exactly what our body does and how each organ functions, the world would be a better place."

Tim moved back to Knoxville at the end of November 2006 with the girlfriend who was now his fiancée.

"I guess everyone expected me to shrivel up and die," he recalls.

But Tim made it through November. He continued to take EpiCor. The new year came and Tim was still alive.

"December was a most special month," he says. "Not only had I beat the oncologist's forecast of four months, but I was

afforded the best possible decision in my life—to marry my girlfriend who had been by my side since early August. She's the one who stayed beside me through those trying days in the hospital. And now I was well enough to go to work."

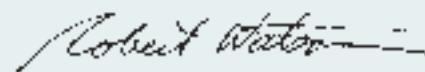
Around this same time, Tim began consuming NanoGreens¹⁰ to nourish his body with more fruit and vegetable-derived phytonutrients. Gradually, his energy levels improved. He also began taking HepatoGen™ to improve liver health.

In February, the doctors initiated a bi-monthly scan to determine whether his cancer was growing or regressing. When first diagnosed, Tim's cancer marker had been at 300. Over the next year, his cancer marker dropped dramatically to 17. In addition, cancer had initially covered 80 percent of his liver. The last scan indicated the liver cancer had regressed to cover only about twenty percent of the organ.

Currently, Tim consumes a variety of supplements including EpiCor, Bioflavonoid Complex, UniBiotic™, garlic extract, indole-3-carbinol, HepatoGen, reishi, and most recently added Annatto Tocotrienols and Extension Resveratrol to his list. His supplement regimen also currently includes omega-3 fatty acids, vitamin E, cinnamon, bilberry, vitamin D3, COQ10, vitamin C in large doses, NAC, folic acid, turmeric, milk thistle and astragalus.

"I believe in supplements," concludes Tim. "I tell everyone I come in contact with if they are not taking them they should start. I believe I will be around forever with the help of the good Lord, my beautiful wife and those powerful supplements."

Tim's story reminded me about the preciousness of life and how important it is that we educate ourselves about our own health. I applaud Tim's fortitude and courage in fighting his own personal battle and wish him and others like him continued good health.



Robert Watson
President/CEO

AGE Control

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Glycation End Products accumulate in many tissues as we age. This is especially true in individuals whose limbic-hypothalamic-pituitary axis is down regulated, because the body becomes inefficient at regulating normal blood glucose concentrations and maintaining proper insulin levels by blocking intracellular uptake of both insulin and glucose, paving the way for increased glycation and AGE production.

One of AGE's best known effects is their ability to intensify diabetic complications such as diabetic retinopathy, neuropathy and cardiovascular disease. Researchers also now believe that AGE production plays a detrimental role in the onset of diabetic atherosclerosis.² Other researchers have established a close tie between AGEs and insulin sensitivity in fat cells (adipocytes). They determined that AGEs inhibited glucose uptake and increased the production of free radicals known as reactive oxygen species (ROS) in the fat cells. AGEs also increased the expression of monocyte chemoattractant protein-1, which has been implicated in the development of obesity-associated glucose intolerance.³ These effects led the researchers to conclude that AGEs are "involved in the development of obesity-related insulin resistance."

High AGE levels have been linked to a surprising number of other conditions such as Alzheimer's disease and osteoporosis. AGEs are known to accumulate on beta-amyloid plaques, which are linked to the development of Alzheimer's disease, where the AGEs trigger chronic oxidative stress.⁴

A type of AGE known as pentosidine also increases exponentially in bone in certain areas of the body during aging, to the extent that researchers have attributed the build up of this AGE molecule as a biomarker for the degree of bone mass density loss.⁵

AGEs and the Diet

AGEs are produced in the body as a result of imbalanced metabolic processes. AGE molecules also are found in many regularly consumed foods, especially high-glycemic foods and, as described above, are created in carbohydrate-rich foods when they are cooked. The consumption

of sugar, white bread, bakery products and other AGE-rich foods adds to the level of endogenous AGEs already produced in the body. Modern food processing also results in foods with increased AGE levels. In fact, even infant formula has high levels of AGEs, indicating that people are exposed to AGEs from a very early age.⁶

Dietary AGEs have been shown to initiate a number of destructive effects. They increase free radical production and deplete levels of glutathione, a critical antioxidant.⁷

Increased consumption of dietary AGEs can alter LDL (the "bad" cholesterol) in a way that increases its negative effects. In a study of 24 diabetic subjects, LDL from subjects consuming a high-AGE diet experienced more free radical damage (oxidation) and was more susceptible to glycation compared to subjects on the low-AGE diet. When this oxidized, glycated LDL was added to human endothelial cells from vein walls it promoted inflammation, an effect not seen with the LDL not exposed to AGEs. The LDL from the subjects consuming the high-AGE diet also significantly increased vascular cell adhesion molecule-1, a molecule that encourages blood cells to stick to the artery walls and block the arteries, providing further evidence to support the possibility that AGEs are the reason why diabetics have an increased risk of heart disease.⁸ The study authors concluded that exposure to dietary AGEs increased LDL-induced vascular toxicity and that "this can be prevented by dietary AGE restriction."

In a perfect world we would be able to avoid foods that generate AGEs. However, even individuals who habitually avoid blood-sugar-raising foods find themselves "slipping off the low-glycemic wagon" from time to time by consuming the occasional treat. So while avoiding AGE-producing, blood-sugar-raising foods is important, the reality is that none of us are perfect and taking a proactive stance against AGEs is crucial. Therefore, in this article I will address nutrients that have demonstrated anti-AGE effects.

Natural AGE Blockers

N-acetyl cysteine (NAC) is one of the most potent natural AGE-inhibitors. NAC stops AGEs from initiating changes to LDL cholesterol that make this "bad" form of cholesterol even more destructive. In the study of 24 diabetic subjects mentioned above, NAC inhibited the inflammatory

effects that AGE-exposed LDLs have in the body. In addition, NAC blocked the AGE-triggered production of a molecule partially responsible for increased activity of the "sticky" platelets that cause clogged arteries (vascular cell adhesion molecule-1).⁸

By increasing glutathione, NAC also reduces lipid peroxidation that occurs in neuronal cell lines after AGE exposure.⁹ This led one group of researchers to conclude, "scavengers of oxygen free radicals could be useful in protecting brain tissue from lipid peroxidation and its pathological consequences that occur in Alzheimer's disease."

In other studies, NAC has decreased the cell death and free radical damage that occur in retinal cells after AGE exposure *in vitro*.¹⁰ This same AGE-triggered cell death occurs during diabetic retinopathy in humans. In cells exposed to AGEs from dietary sources and in diabetic subjects, NAC prevented the reduction of glutathione, a crucial antioxidant.¹¹⁻¹² NAC has an equally strong effect against AGE's ability to cause insulin resistance in fat cells. In one study, AGE's effects on insulin and glucose uptake by fat cells were completely reversed by NAC.^{3, 9-10}

Studies have found that lipoic acid is also very active in inhibiting AGE formation. Rats fed lipoic acid and a high-fructose diet showed significant reductions in AGE formation.¹³

Another well-researched, AGE-inhibiting substance is the amino acid carnosine (beta-alanyl-L-histidine). Carnosine has been reported to retard and in some cases even reverse the glycation process.¹⁴ A large body of scientific evidence points to carnosine as powerful AGE-blocking substance. When LDL cholesterol undergoes glycation to form oxidized cholesterol and AGEs, immune cells known as macrophages phagocytize or "gobble up" the oxidized, altered cholesterol. Thus, atherosclerosis begins when macrophages engulf particles of oxidized and glycated LDL cholesterol. As this buildup continues to occur, increasing amounts of glycated and oxidized LDL cholesterol clump together, ultimately blocking the arteries. Both carnosine and its primary functional amino acid L-histidine can inhibit LDL glycation and oxidation.¹⁵

Carnosine may also reduce AGE-induced cognitive dysfunction. Protein oxidation

and glycation are integral components of Alzheimer's disease. In fact, glycated protein accumulates in the cerebrospinal fluid of Alzheimer's patients. Protein cross-links are present in the neurofibrillary tangles in the brains of Alzheimer's patients, further building the case for a link between AGEs and Alzheimer's. Carnosine has been shown to suppress amyloid-beta peptide toxicity, inhibit production of oxygen free-radicals and suppress protein glycation.¹⁶

Furthermore, carnosine's ability to inhibit AGEs and cross-linking may account for its ability to reduce cataract formation in animal studies.¹⁷

Carnosine appears to "nip glycation in the bud" by causing decomposition of Schiff bases, the very first intermediate in the glycation/AGE forming process, before the Schiff bases can become AGEs.¹⁸

A lesser known AGE-blocking agent is guava (*Psidium guajava* extract). In a study released earlier this year, researchers determined that guava had a significant and inhibitory dose-dependent effect on LDL glycation. The researchers attributed guava's glycation-blocking actions to its distinct abundance of polyphenolic content.¹⁹

Yerba Maté (*Ilex paraguariensis* extract) is emerging as another powerful AGE-blocking substance. In a recent study, Yerba maté significantly prevented AGE formation. The researchers attributed this to the fact that the polyphenol concentration in Yerba maté is about 2 to 2.5 fold higher compared with green tea, which had no effect on AGEs in the study. Yerba maté's AGE-inhibition effects occurred during the second phase of the glycation reactions, namely preventing the free-radical mediated conversion of the Amadori products to AGEs. What's more, Yerba Maté's inhibition of AGE formation was comparable to that obtained by using the standard antiglycation agent aminoguanidine.²⁰

Finally, any discussion about nutritional anti-AGE strategies would not be complete without mentioning benfotiamine, a form of vitamin B1 that is a well-researched AGE blocker. In one study, 13 type-2 diabetic subjects were fed a high-AGE meal without benfotiamine. They then consumed the high-AGE meal together with 1,050 mg per day of benfotiamine for 3 days. When the subjects consumed the high-AGE diet without benfotiamine, their AGE levels rose. However, when they consumed the

high-AGE diet with benfotiamine, AGE formation was significantly reduced.²¹

In diabetic mice, benfotiamine has prevented the vascular accumulation of AGEs and accelerated the healing of ischemic diabetic limbs.²²

Adjunctively, ensuring that the body's pH values are slightly alkaline (i.e. a blood pH of 7.34 to 7.36) and normalizing intracellular magnesium levels significantly increases the success of nutritional antiglycation strategies.

Conclusion

Advanced Glycation End Products (AGEs) play a significant role in a majority of the chronic, degenerative diseases associated with aging. They have long been known to be involved in complications of diabetics but new research indicates they also influence cognitive and bone health. AGEs also encourage the development of insulin resistance and elevated blood glucose transforming LDL cholesterol into harmful LDL type B subparticles, which are very destructive to the cardiovascular system. Substances such as N-acetyl cysteine, lipoic acid, carnosine, guava, Yerba maté and benfotiamine can all be used to defend against AGEs and maintain neuroendocrine function and overall health.

David D. Parrish, MD

Dr. Parrish is a multi-specialty physician who has had extensive experience in quantum physics applications in medicine, neurology, developmental psychoanalysis, preventive endocrinology, and anti-aging medicine. He studied with Dr. Thierry Hertoghe, M.D., co-founder of the International Endocrine Society and President of the World Society of Anti-Aging Medicine. Dr. Parrish is best known for his successful research identification of neurophysiologic organizers of infant development and their relation to emerging primary mental mechanisms of early childhood. Currently, Dr. Parrish devotes full time to research in the areas of nutraceuticals, pharmaceuticals and novel technologies to expand normal neurocognitive awareness.

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The Liver: Detoxifying This Vital Organ Nourishes Overall Health and Vitality

by Sherrill Sellman, ND

The liver is an amazing organ. After the skin, it is the second largest glandular organ in the human body. It is made of highly vascular tissue, holding about 13 percent of the body's blood supply at any given moment.

The liver performs more than 500 vital biochemical functions. Some of its important functions include: producing substances that emulsify fats, converting glucose to glycogen, manufacturing amino acids, filtering toxic substances from the blood, storing of vitamins and minerals, maintaining proper levels of glucose in the blood and producing cholesterol (Table 1).

When the liver becomes less efficient at performing one of these biochemical functions, several types of serious liver pathologies can occur. A fatty liver is an excessive accumulation of fat inside the liver cells impeding liver function. The most common causes of fatty liver are alcoholism, obesity, diabetes, drugs (such as corticosteroids, tetracycline and aspirin) and elevated serum triglyceride levels.

Hepatitis C is a disease of the liver caused by a blood-borne, infectious, viral disease. The infection can cause liver inflammation that is often asymptomatic, but chronic hepatitis can develop into cirrhosis and liver cancer.

Cirrhosis of the liver is characterized by replacement of liver tissue by fibrotic

scar tissue, leading to progressive loss of liver function. Cirrhosis is most commonly caused by alcoholism and hepatitis C.

However, the liver's role is vitally important to all aspects of overall health. Consequently everyone, not only individuals who suffer from these conditions, should be concerned with the integrity and optimal functioning of the liver.

Another Understanding of the Liver

While Western medicine has gained a great deal of knowledge about the liver's basic mechanisms, physiology and pathologies, the ancient healing wisdom of Traditional Chinese Medicine (TCM) provides another profound and comprehensive understanding of the many physical, emotional and mental functions influenced by this organ.

In TCM, the liver is much more than just an organ; it is an energetic system that directs energy through meridians, or channels, flowing throughout the body.¹ Imbalances in this energy flow can have profound implications to both physical and emotional health, long before more chronic dysfunctions can be detected through traditional blood tests. The goal of TCM is to detect and restore energetic imbalances long before they manifest as chronic symptoms and disease.

Traditional Chinese Medicine considers the liver as "the great regulator" of the

body. Its most important job is to regulate the smooth flow of blood and the energy force known as Qi (pronounced chee), to all organs, and in all directions. The liver is particularly sensitive to the many stressors and shocks of life. Physical and emotional stress as well as stress from the accumulation of metabolic toxins and toxins generated in the colon will cause the free flow of blood and Qi to become stagnant and obstructed. Symptoms of imbalance will then occur.

Sluggish Liver

Minimal loss of liver function, or sub-clinical liver dysfunction, known as sluggish liver or toxic liver is the result of the combined actions of different factors that impair the liver's numerous metabolic processes. These actions can have profound effects on the state of health. One important cause of a sluggish/toxic liver is diminished bile flow within the liver. The most common cause of a diminished bile flow is gallstones. Another major factor is the ingestion of alcohol and drugs. In some individuals, as little as an ounce of liquor can damage the liver and cause fat deposition. Finally, the constant onslaught of exogenous toxic chemicals and endotoxins that the liver is responsible for detoxifying can cause a toxic liver. Free radicals generated during the process of detoxification produce toxic effects on liver cells. Table 2 lists the symptoms of a sluggish liver.

Women's Hormonal Health

The liver is essential for hormone metabolism. Proper estrogen metabolism is dependent upon a healthy liver as it is largely responsible for the break down and excretion of hormone metabolites that will ultimately be eliminated in either the bile or urine.

Liver imbalances in women therefore include lack of menstruation, painful periods, breast distention, irregular periods, heavy bleeding (especially with clots), break through bleeding, and infertility. In fact, PMS symptoms can often be an indi-

TABLE 1. Functions of the Liver

- Production of bile, which helps carry away waste and break down fats in the small intestine during digestion
- Production of certain proteins for blood plasma
- Production of cholesterol and special proteins to help carry fats through the body
- Conversion of excess glucose into glycogen for storage (glycogen can later be converted back to glucose for energy)
- Regulation of blood levels of amino acids, which form the building blocks of proteins
- Processing of hemoglobin for use of its iron content (the liver stores iron)
- Conversion of poisonous ammonia to urea (urea is an end product of protein metabolism and is excreted in the urine)
- Clearing the blood of drugs and other poisonous substances
- Regulating blood clotting
- Resisting infections by producing immune factors and removing bacteria from the bloodstream

cation of liver imbalance as are hormonal headaches and migraines. Liver imbalances are also associated with a variety of menopausal symptoms such as breast distention, insomnia, hot flashes and night sweats.³

Liver stagnation can also be expressed on the emotional level, manifesting as irritability, anger, frustration and depression.

Healthy Joints and Muscles

The tendons are the main tissues linking the joints and muscles, facilitating the full movement of the limbs. According to Traditional Chinese Medicine, the liver energy nourishes the tendons of the whole body to maintain their normal physiological activities. If this energy is obstructed, it can cause spasms, stiffness, reduced range of motion, numbness, muscle cramps, tremors, tetany, seizures and reduced strength in the limbs.

Since the nails are considered to be an extension of the sinews, they are closely related to the state of the liver. Dry, cracked, dark, indented and generally unhealthy nails reflect a liver imbalance.⁴

TABLE 2.
Symptoms of a Sluggish Liver

- Fatigue and malaise
- Allergies and chemical sensitivities
- Discomfort in the right abdomen
- Constipation
- Intolerance to eating fatty foods
- Weight gain or weight loss
- Elevated cholesterol and triglycerides
- Skin blemishes and poor complexion
- Intolerance to alcohol
- Darkish urine

Eye Health

Eye health also is dependent upon a properly functioning liver. Eyes require nourishment from the blood in order to see properly. If the eye is inadequately nourished, blurred vision, myopia, floaters, color blindness, dryness, soreness and itchiness may occur.⁵

Liver Detoxification

Before I discuss a number of botanicals and antioxidants that can help improve liver health, I want to emphasize the synergism between a healthy colon and a healthy liver. In order for a liver detoxification program to be effective, one must also ensure the colon is working properly as the colon serves as an exit door for bile to leave the

body. Therefore, the botanicals and antioxidants mentioned below will be more likely to support optimal liver health if they are consumed after using a good fiber supplement and together with a Lactobacillus GG probiotic.

Natural Liver Support

Since the liver plays such a fundamental role in overall health and well being, it is essential to support its ability to circulate energy and blood freely through the body. In addition to eating a wholesome, nutritious diet free of processed and toxic foods and foods that are contaminated with antibiotics, toxic, heavy metals and environmental contaminants such as PCBs and herbicides, reducing stress levels and moving one's energy with regular exercise, specific nutritional support has been crucial for healthy liver function.

Milk Thistle

Milk Thistle seeds contain a bioflavonoid complex known as silymarin, responsible for the health benefits of the plant. Today, laboratory and clinical tests confirm milk thistle's significant liver-protective effects. A potent antioxidant in its own right, silymarin is particularly remarkable for its beneficial effects on glutathione. Researchers have found that silymarin increases levels of glutathione by up to 35 percent. Silymarin has also been shown to regenerate injured liver cells. In addition, silymarin has the ability to block fibrosis, a process that contributes to the eventual development of cirrhosis.⁶

N-Acetyl-Cysteine (NAC)

N-Acetyl-Cysteine (NAC) is a powerful antioxidant, which increases the production of the critical antioxidant glutathione.⁷⁻⁸ Glutathione is the chief chemical used by the liver exerting a variety of protective effects, including detoxification and intracellular defense against oxidative stress. NAC is even used by conventional medicine to treat life threatening acetaminophen poisoning.⁹

Scutellaria baicalensis Root Extract

Scutellaria baicalensis is a botanical commonly used in Traditional Chinese Medicine. Research has indicated it has many interesting effects on the liver. A number of *in vitro* and animal studies indicate that Scutellaria baicalensis can improve liver health. A recent cell culture

study tested three active flavonoid components of the root of Scutellaria baicalensis on a human liver cancer cell line. The results indicated that the components of Scutellaria baicalensis inhibited the oxidation of protein in the liver and the decrease of cell viability that had occurred in the cancer cells prior to exposure to the botanical compounds. The Scutellaria baicalensis component baicalin had the strongest inhibitory effect. The researchers concluded that all three components of Scutellaria baicalensis could inhibit liver injury in a dose dependent manner.¹⁰

This same protective effect was seen in a study investigating the use of the Scutellaria baicalensis component baicalin in rats given high doses of acetaminophen. When acetaminophen is given at high doses it is extremely toxic to the liver. In this study, however, when rats were given baicalin a half hour after acetaminophen administration, it significantly prevented many of the toxic effects observed in rats given acetaminophen without baicalin. Furthermore, none of the rats given baicalin with acetaminophen died, whereas 43 percent of the rats given only acetaminophen died. Baicalin also prevented the acetaminophen-related drop in levels of glutathione, a critical antioxidant.¹¹

Scutellaria baicalensis also has protected the livers of rats exposed to a cancer causing substance called aflatoxin, a toxin often found in peanuts that is produced by some strains of mold and causes cancer in animals.¹²

Artichoke

Artichoke leaf extract, during *in vitro* and in animal studies, has been investigated for its ability to improve bile flow.¹³ Additionally, artichoke extract has inhibited cholesterol biosynthesis in liver cells.¹⁴

Other studies have shown that artichoke can protect the liver against free radical (oxidation) damage. Researchers in one study induced oxidative damage in liver cells cultured from rats. They then exposed the cells to artichoke extract. The results indicated that artichoke extract prevented the increase of MDA, a marker of free radical damage and oxidation, in a concentration-dependent manner when presented simultaneously or prior to the agent used to induce free radical damage. The artichoke

Continued on page 17

Healthy Heart Rhythm

Continued from front page

of heart rhythm disorder known as atrial fibrillation.²

Arrhythmias can occur in a healthy heart and be of minimal consequence. However, often they are a marker of a serious problem with the heart and lead to heart disease, stroke or sudden cardiac death. Symptoms of cardiac arrhythmias include palpitations, syncope (loss of consciousness), spells of lightheadedness, chest pain or symptoms of congestive heart failure.

The heart has an internal electrical system that controls the rhythm of the heartbeat. Problems with this electrical system can cause arrhythmias. There are many types of arrhythmia. During an arrhythmia, the heart can beat too fast, too slow or it can stop beating. Sudden cardiac arrest occurs when the heart develops an arrhythmia that causes it to stop beating.³

A number of natural agents have been shown to support normal heart rhythm and improve cardiac function. Some effects of these natural agents include increasing strength of heart contractions, increasing myocardium (heart) tissue oxygenation and scavenging free radicals. The synergy of these natural substances provide support for a healthy cardiac rhythm.

Magnesium

Magnesium is the second-most abundant element within the human cell. Over 300 magnesium-dependent enzymes have been identified to date, underscoring magnesium's vital role in metabolism.⁴ ATP (energy) production, protein synthesis, nerve function and DNA replication are all driven by magnesium-dependent enzymes. As nature's "calcium channel blocker," magnesium helps control the excitability of nerves and is essential for relaxation of the heart muscle between beats.⁴ Dietary magnesium deficiency results in altered heart rhythm, and several studies support the value of intravenous magnesium in preventing post-surgical atrial fibrillation.⁵⁻⁷

Magnesium is used in the conventional medical model intravenously to treat various types of arrhythmia including atrial tachycardia, atrial fibrillation, ventricular fibrillation and supraventricular tachycardia. Clinically preventing a low

magnesium status within the body is an important cardiac protective strategy. Since a mere one percent of magnesium is found within the serum, a regular blood test does not serve as an adequate measure of magnesium status and RBC (Red Blood Cell) magnesium is a much better measure of true body magnesium stores.⁸⁻¹²

An additional effect of magnesium is that it may reduce the symptoms of mitral valve prolapse in individuals with low magnesium levels.¹³

Taurine

Taurine is a conditionally essential amino acid found in large amounts in heart, platelets, brain and eyes.¹⁴

Though taurine is not an essential amino acid, it is critical to have sufficient levels therapeutically when there is a higher "conditional" utilization such as when there is increased cardiac demand. Taurine concentration increases in the left ventricle of patients with congestive heart failure, illustrating the increased conditional requirements.¹⁵

Supplementation with taurine alters intracellular calcium levels and enhances left ventricular function.¹⁶

Taurine modulates the activity of cyclic adenosine monophosphate (cAMP), which belongs to a class of substances known as "second messengers," and is one of the most important cell-regulating compounds. Among its many roles, cAMP activates numerous enzymes involved in diverse cellular functions. Through its cAMP-modulating activity, taurine affects enzymes in heart muscle that contribute to contractility. Taurine also plays a role in calcium metabolism and may affect entry of calcium into heart muscle cells where it is essential in the generation and transmission of nerve impulses.¹⁷ Research shows that taurine may prevent arrhythmogenesis by limiting cardiac hypertrophy and calcium overload of the myocardium.¹⁸ Taurine also protects the heart against reperfusion-induced arrhythmias via its properties as a membrane stabilizer and as an oxygen free radical scavenger.¹⁹ Reperfusion injury refers to tissue damage caused when blood supply returns to the tissue after a period of oxygen deprivation (ischemia). The absence of oxygen and nutrients from blood creates a condition in which the restoration of circulation results in inflammation and

oxidative damage through the induction of oxidative stress.

Arrhythmias characteristic of acute myocardial ischemia may be due to loss of intracellular taurine. Researchers found that intravenous administration of taurine prevented arrhythmias caused by digitalis. Taurine also inhibited the drop in potassium levels inside heart cells, which can cause electrical instability and arrhythmias.²⁰ Supplemental taurine has been shown to reduce the occurrence of myocardial infarction and to lower elevated blood pressure by reducing sympathetic tone.²¹

Berberine, Notoginseng and Sophora: Herbal Trio for Ventricular Regularity

Berberine

Berberine is a plant alkaloid found in such herbs as European barberry, goldenseal, goldthread, Oregon grape and phellodendron. Berberine has been shown to possess inotropic (increasing strength of heart contractions), and anti-arrhythmic

“Notoginseng has been shown to enhance coronary blood flow and microcirculation in the heart muscle and promote healthy blood pressure.”

properties. Evidence also suggests that berberine administration can help prevent the onset of re-entrant ventricular tachyarrhythmias and sudden coronary death after ischemic damage to the heart.

The effects of berberine on individuals with ventricular tachyarrhythmias showed that 62 percent of patients had 50 percent or greater, and 38 percent of patients had 90 percent or greater, suppression of ventricular premature contractions.²² No severe side effects were observed from berberine therapy. In humans with refractory congestive heart failure, berberine produced several significant changes: a 48 percent decrease in systemic and a 41 percent decrease in pulmonary vascular resistance, along with a 28 percent decrease

in right atrium and 32 percent decrease in left ventricular end-diastolic pressures.²³ A measurable increase in cardiac index (45 percent), stroke index (45 percent) and left ventricular ejection fraction (56 percent) also was observed.

There is preliminary evidence that berberine can lessen the frequency of premature ventricular contractions (PVCs) and decrease the mortality in patients with congestive heart failure from ischemia or dilated cardiomyopathy.²⁴

Panax Notoginseng

Also known as tienchi or pseudoginseng, this herb is a relative of the well-known Panax ginseng. It has a history of traditional use in China where it is highly regarded as a heart tonic. Notoginseng has been shown to enhance coronary blood flow and microcirculation in the heart muscle and promote healthy blood pressure.²⁵ Saponins found in notoginseng significantly improve arrhythmia induced by ischemia/reperfusion.²⁶ Notoginseng functions, in part, by optimizing the action potential of Purkinje fibers, which are responsible for the electrical signal of the heartbeat.²⁷ The saponin in notoginseng supports cardiac health by optimizing sinus node recovery time and prolonging ventricular effective refractoriness and repolarization.²⁷

Panax pseudoginseng is believed to dilate the coronary vessels, reduce vascular resistance, and improve the coronary collateral circulation. This could increase blood flow while reducing blood pressure. It would also reduce the heart metabolic rate and oxygen consumption. Evidence also suggests Panax pseudoginseng has an antiarrhythmic effect.²⁸

Animal studies have demonstrated that oral supplementation with Panax pseudoginseng can help reduce fibrinogen levels and decrease cholesterol and triglycerides.²⁹ Panax notoginseng also has been shown to possess protective antioxidant properties.³⁰

Sophora flavescens

Another Chinese herb with a rich history of use is Sophora, a member of the Leguminosae family, which includes beans and peas. Sophora has been traditionally used in such diverse conditions as asthma, bronchitis, bacterial and fungal infections, skin disorders and more.³¹ The compounds of interest in Sophora include oxymatrine and its principal metabolite, matrine.³²

Sophora extracts and oxymatrine have been shown to reduce the incidence and delay the onset of experimentally induced ventricular tachycardia.³³ Oxymatrine helps improve heart rate variability (HRV), by reducing both atrial and ventricular premature beats.³⁵ Oxymatrine functions by increasing the heart's diastolic excitability threshold (DET), which improves the relaxation phase, and by lengthening the effective refractory period (ERP), which helps prevent premature contraction.³⁵

Conclusion

The average heart beats 72 times per minute and contracts 103,680 per day. The steady and regular contraction of the human heart from prior to one's birth and throughout life requires proper nutritional support. Taurine, magnesium and the botanicals discussed can play an important role in helping sustain healthy cardiac performance together with a physician-supervised heart health protocol. The addition of accessory nutrients that also fuel cardiac performance such as CoQ10 and L-carnitine are pivotal natural agents required by the heart.

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CUSTOMER CORNER

Iodine Questions

Dear Dr. Meletis,

I've reread all the articles on iodine, and I'm still confused about some things. I wonder if you can clarify them for me. 1. What is the difference between organic and inorganic iodine? One article states that the organic form of iodine is cytotoxic (toxic to cells). Does that mean that the iodine we get from seafood is cytotoxic? 2. What is the therapeutic necessity for combining iodide with iodine? I read that iodine makes iodide more water soluble, but why, if it's fat-soluble, not just take elemental iodine (like the kind that's available bound to protein) with a fat or a protein? 3. My post-therapeutic spot level was .754, which seems to be way high (I had been taking seaweed tablets for six months prior to the test.) But my post saturation level was 69. Does this just mean that my body needs way more than normal amounts of iodine? How much more would you recommend? And how soon should I get retested?

By the way, I am a 36-year-old female with Hashimoto's thyroiditis, chronic sinus infections, Lyme disease, Epstein Barr and mycoplasma. Thanks so much for your help!

Ms. M.

Dear Ms. M.,

Your health conditions warrant a focused approach guided by a skilled personal health care provider. I will be pleased to answer your queries, yet be sure to visit with your doctor about dosing.

Iodide only products, such as SSKI (saturated solution of potassium iodide) are inferior to iodide/iodine preparations in the repletion of iodine deficiency due to varying rates of absorption. *Iodoral*[®] is a dry tablet form of standardized, inorganic, non-radioactive, potassium iodide/iodine that delivers 12.5 mg of elemental iodine per tablet (5 mg iodine and 75 mg iodide as the potassium salt). Clinical practice has shown that a blend of both appears to be better tolerated.

As to whether you need more iodine than the average person, this is somewhat challenging since the measure of iodine status and need is not only measured by laboratory tests but also on how well your body is responding. I find slow and consistent use of

iodoral at lower dose is better than trying to super-saturate tissues too rapidly.

Certainly, if your iodine levels are truly and reproducibly high, then modifying your dose will be important. Also, having your physician monitor TSH, Free T3 and Free T4 along with TPO and Anti-Thyroglobulin levels will be important. I also routinely have my patients obtain a current ultrasound of the thyroid gland as well. As you likely know, in order to support thyroid hormone production, a combination of nutrients in addition to iodine are important including *L-Tyrosine*, *Zinc*, *Copper* and other accessory nutrients.

It may be of interest to clinically gain insight into your individual biochemistry by performing an *Organic Acid Test* that can help refine supplemental considerations. You can read more on the website.

Your questions are excellent and ultimately your personal physician will be best able to define the best dose for you.

Sincerely,
Chris D. Meletis, ND

ADD and Leaky Heart Valve

Dear Dr. Dean,

My 29-year-old son has ADD. He currently takes Adderall[®], but this week he found out he has a leaky heart valve, the valve that puts the blood back into the lungs. The question is: what can he take for his ADD when he stops taking the Adderall? He has an appointment with a heart specialist to determine more about his heart condition.

Ms. L.

Dear Ms. L.,

Of course, a big problem is the leaky valve that may require surgery. I hope the specialist was able to provide a satisfactory solution to that problem.

With regard to a replacement for Adderall—or a supplement that will help him to reduce his dosage—I typically suggest *DMAE 100 Plus* to start. Usually daily doses of up to 500 mg have helped support the health of many individuals with various learning disorders—especially ADD.

Also, although I have never seen any scientific studies to corroborate this next suggestion, it may be worth a try. Adderall is a combination of amphetamine salts that works by increasing the levels of epinephrine and nor-epinephrine in the brain. This same biochemi-

cal effect may be obtained naturally by taking the amino acids, *L-Tyrosine* or *L-Phenylalanine*.

Some people respond better from one than the other. The usual dose is 500 mg taken on an empty stomach, 2-3 times per day. I don't recommend taking either of these amino acids after supper, due to the possibility that they may interfere with sleep.

I hope these suggestions are helpful.

Sincerely,
Ward Dean, MD

Rheumatoid Arthritis

Dear Dr. Meletis,

I have a recently diagnosed friend with Rheumatoid Arthritis. Do you have a specific protocol? She is 48 years old. Even before this diagnosis she was also depressed.

Mr. R.

Dear Mr. R.,

At the age of 48 many women are undergoing a hormonal shift that includes a drop in progesterone levels. So, taking a *Salivary Hormone Test* to determine progesterone, estrogen and testosterone levels along with cortisol and *DHEA* is a must for my patients in this age category. It becomes even more important with autoimmune conditions. If the test indicates a deficiency in progesterone and/or *DHEA*, supplementation with *HerBalance[™] Cream* and/or *DHEA* may be indicated.

The depression and stress can often set the stage for the onset of autoimmunity according to many health-oriented physicians since it can negatively alter adrenal function and neurochemistry. Thus, combining an adrenal support program like *AdaptaPhase[®] I and II* along with an inflammation control product such as *Advanced Inflammation Control* is a generalized approach. Proper hydration (64 ounces of water per day) and total avoidance of foods that cause sensitivities is essential to help avoid stimulating the immune system. A *Food Sensitivity Test* can be ordered here along with a *Salivary Hormone Test*. In addition, avoiding immune-stimulating herbs is important. Decreasing intake of red meat and increasing fish oil (such as *Nordic Naturals ProOmega*) to help support anti-inflammatory pathways within the body is equally essential.

Sincerely,
Chris D. Meletis, ND

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CUSTOMER CORNER

CRP, ARMD, Angina, Gum Disease

Dear Dr. Dean,

I would like your opinion relating to the value of the blood test for highly reactive C Proteins (hrCP)? My doctor did not request it on my last blood workup, saying it was diagnostically useless.

I am 61, have no cardiac factors except for two incidents of resting angina in January, which made me concerned enough to do stress/ultrasound tests this June. My cholesterol is 149, blood pressure 120/80 and I seem perfectly healthy except was told this week I have dry macular degeneration. Gingivitis is about average according to the dentist. I suspect everything is connected and that if I have hard arteries it wouldn't show up except with hrCP. Should I get a new doctor? Thanks.

Mr. B.

Dear Mr. B.,

I agree with you—I think CRP is a very useful test, as an indicator of an inflammatory process in the body and as a marker of your progress in correcting the problem.

Another important marker that most physicians don't order is fibrinogen—and that is because there is no drug that they know of that will reduce elevated fibrinogen (another marker of inflammation). *Turmeric* has been shown to lower fibrinogen levels. Please see the special fibrinogen report available on the website.

If your physician will not order these tests, you might do as you suggested and find a physician who WILL order them.

Most physicians, likewise, don't know what to do about macular degeneration, other than monitor its "progress." I suggest *Extension Vision*, which was developed specifically for those concerned about macular degeneration.

Gingivitis (periodontal disease) is really an indicator of osteoporosis of the jaw—a generalized indicator of osteoporosis, I believe. For periodontal disease, I recommend daily flossing, use of a water pik filled with 3 percent hydrogen peroxide, high-dose *CoQ10-H₂*, *Xylitol (Unique Sweet®) Gum* and *Mints* throughout the day (to prevent bacterial growth and to promote reversal of bone

loss), and a daily massage of the gums with *Silver Liquid* (several drops on the finger tip).

If you are having angina, I would add *Oral ChelatoRx*, 6-12 caps per day, 1/4 to 1 aspirin tablet per day, *Turmeric* (several grams per day if your fibrinogen is a little high) and perhaps *Nattokinase Plus* or *UniZyme™*.

Let me know how you do.

Sincerely,
Ward Dean, MD

Asperger's Disorder

Dear Dr. Meletis,

After years of behavioral issues and misdiagnoses of my 13-year-old son, I now believe he suffers from Asperger's Disorder. I have read the recommended list of nutrients (in the article on the website called "Saving Eli") but have no idea which to start with in order to determine which are helping, which aren't.

My son is very intelligent, articulate and has learned to hold it together at school and gets great grades (but seems very stressed). However, at home he is emotionally out of control, angry, aggressive and becoming violent. He is moody, depressed, highly anxious and very hard to reason with. He is a good eater but I have a hard time with vitamin/mineral supplements, as he hates the taste, especially B vitamins. Does he also need a good multivitamin along with the other supplements?

Please help. I live in a very rural area and find it difficult to find help. My husband (my son's father) passed away 3 years ago after a long illness, which has added to my son's problems. Until his emotions/health are under control, counseling has been unproductive. I prefer to keep him off meds if possible. Please advise to help me get started with nutritional therapy. I am desperate to help him. Thank you so much.

Mrs. I.

Dear Mrs. I.,

Certainly nutrients such as *Zinc*, essential fatty acids, *DHA*, *DMAE* and *L-Theanine* are common foundational approaches worthy of consideration that I frequently have incor-

porated into individual protocols. Additional considerations include *5-HTP* to assist with depression and anxiety.

In addition, *Food Allergy Testing* and *Organic Acid Testing* are invariably a strong component of building a customized program for a strong foundation. You can read more about the testing at the website, which also provides patients direct access to the tests.

A multivitamin (such as *Extend Liquid*) is clearly a great way to provide a stopgap measure for potential nutritional deficits. Furthermore, if your son snores or does not awake rested, getting him tested for sleep apnea is a must. Also, monitoring whether or not his blood sugars drop before a flare up of behavioral manifestation is something to consider.

All these options should be discussed with your son's personal physician.

Sincerely,
Chris D. Meletis, ND

Fractured Fingers in Young Child

Dear Dr. Meletis,

My 2.5-year-old boy fractured his fingers and I would like to know if it is essential to give him any supplement to boost his healing. Is a calcium supplement necessary? Please advise.

Ms. L.

Dear Ms. L.,

Assuming your child has a balanced and healthy diet, the probability that he will need a supplement is relatively low. On that note, a 2.5-year-old having an overt fracture on his fingers is not very common. If the injury was a strong and forceful blow to the fingers such as closing them in a door, that could account for it. Otherwise, *Calcium* and a multivitamin would be a consideration.

Generally, a children's multivitamin (such as *Kids Essentials*) is a strong consideration for most kids. I also often encourage my patients to incorporate *NanoGreens[®]* into children's diets to increase intake of phytonutrients from fruits and vegetables and to enhance overall nutritional status.

Sincerely,
Chris D. Meletis, ND

These statements have not been evaluated by the Food and Drug Administration and are not intended to diagnose, treat, cure or prevent any disease. Before starting a supplement regimen, please visit with your healthcare provider.

Annatto Tocotrienols: Their Significant Role in Blood Sugar Control

by John Raimo, MS, RD

The rate and prevalence of type 2 diabetes, especially in adults, is increasing at an alarming rate.¹ Many factors are involved in the development of type 2 diabetes, and some have been more extensively studied than others. Recently, medical interest has turned to a pre-diabetes condition called metabolic syndrome, also called syndrome X or insulin resistance syndrome. The prevalence of metabolic syndrome, a major causative factor both in the early development of type 2 diabetes and cardiovascular disease, is becoming alarmingly widespread.²⁻⁴ According to the American Diabetes Association about 41 million people in the United States, ages 40 to 74, have pre-diabetes.⁵ In addition, there is the increasing prevalence of childhood obesity,⁶ which contributes to the subsequent development of metabolic syndrome and type 2 diabetes. Thus, there is an urgency to identify cost-effective solutions for metabolic syndrome and insulin resistance that are safe, efficacious and complimentary to current treatments.

Recent research has shown that early, presymptomatic but persisting damage to the body—especially the heart and circulatory system, kidneys and retinas—may already be occurring during pre-diabetes. By taking action to control blood glucose during the pre-diabetes stage, individuals can delay or prevent type 2 diabetes from developing.⁵

As presented last month, delta-tocotrienols found in annatto oil is the second generation form of vitamin E that has powerful effects on the reduction of triglycerides, blood glucose levels and levels of glycosylated hemoglobin (HbA1c), an indicator of long term blood sugar control. This article will further explore the ways in which annatto tocotrienols help support healthy blood sugar levels as well as address lifestyle modifications used to control metabolic syndrome.

What is Metabolic Syndrome?

The American Medical Association

defines metabolic syndrome as a collection of unhealthy body measurements and abnormal laboratory test results.⁷ These include: a) abdominal (waist) circumference greater than 40 inches for men or 35 inches for women; b) presence of high blood pressure (hypertension); c) hyperglycemia (fasting blood sugar more than 110 mg/dl); d) elevated triglycerides; and e) low levels of high-density lipoprotein (also known as HDL). If a person presents with at least three of these, that person is said to have metabolic syndrome and is at risk for developing type 2 diabetes, coronary artery disease, heart attacks or a stroke.

Because these problems are often linked, reducing one measurement may help the other issues. For example, regular exercise can help an individual lose weight, and also help reduce blood pressure and manage hyperglycemia and insulin resistance. Combining regular exercise with healthful eating is the cornerstone of controlling metabolic syndrome.⁷ Losing just 10 percent of excess body weight lowers blood pressure and improves insulin resistance. In many individuals, lifestyle modification alone is not enough; they may have to turn to nutraceuticals and dietary supplements to aid in managing this syndrome.

Lifestyle Modifications

Dietary tocotrienols and supplements of delta-tocotrienol have effective lipid lowering properties with no known side effects. The Diabetes Prevention Program study conclusively showed that people with pre-diabetes can prevent the development of type 2 diabetes by making changes in their diet and increasing their level of physical activity.⁸ They may even be able to return their blood glucose levels to the normal range. While the Diabetes Prevention Program also showed that some medications may delay the development of diabetes, diet and exercise worked better. Just 30 minutes a day of moderate physical activity, coupled with a 5-10 percent reduction in body weight, produced a 58 percent reduction in diabetes.⁸

Reduction in Metabolic Syndrome Parameters

In type 2 diabetics, the progression of cardiovascular-related complications is much more rapid than in the general population, and as many as 80 percent of these people with type 2 diabetes will die of a cardiovascular event.⁹ In a study by Baliarsingh, et al. the therapeutic impact of tocotrienols in type 2 diabetic patients with hyperlipidemia was tested. This well-designed study investigated the therapeutic impact of tocotrienols on serum and lipoprotein lipid levels, elevated blood glucose and glycosylated hemoglobin (HbA1c). A randomized, double blind, placebo-controlled design involving 19 type 2 diabetic subjects was used. After 60 days the subjects showed an average decline of 23 percent in total serum lipids, a 30 percent reduction in triglycerides and a 42 percent reduction in LDL cholesterol. The authors concluded that “daily intake of dietary tocotrienols by type 2 diabetics will be useful in the prevention and treatment of hyperlipidemia and atherogenesis.”⁹

Another study done with type 2 diabetic rats showed that a rice bran diet containing gamma-tocotrienol suppressed hyperlipidemic and hyperinsulinemic responses.¹⁰ Diabetic rats were divided into control and experimental groups. The experimental group were fed a rice bran diet containing a high amount of gamma-tocotrienol for 4 weeks. The study demonstrated that diabetic rats fed the special gamma-tocotrienol-fortified diet had greater insulin sensitivity, which was statistically significant compared to the control group. These rats also had lower plasma triglycerides and LDL cholesterol.

Researchers in Malaysia published a study that determined the effects of a tocotrienols-rich diet on the levels of blood glucose, glycated hemoglobin (HA1c), serum advanced glycosylation end-products (AGE) and malondialdehyde (MDA) of

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EpiCor®: New Human Trials Confirm Strong Immune-Modulating Actions

by CP Staff

EpiCor® has emerged as a powerful immune-modulating natural agent. Past articles in this newsletter have explored EpiCor's novel ability to help regulate the human body's natural immune defenses, illustrated by its ability to increase CD4 (helper) and decrease CD8 (suppressor) cells. This leads to an up regulation of natural defenses as the direct consequence of the CD4 cells increasing immunological responsiveness. EpiCor also enhances activity of natural killer (NK) cells, which are crucial in defending the body against viruses and invading organisms.

Recently, scientists have conducted a number of human studies on EpiCor. Although these studies are currently being written for publication and have not yet appeared in a medical journal, we wanted to give our readers a first-hand glimpse of the study results. Once the studies are published, upcoming issues of this newsletter will provide a more in-depth look at these trials.

Human Clinical Trials

The gold standard for research in the dietary supplement industry is the human clinical trial. Three human studies were conducted using EpiCor. These showed a strong trend toward its ability to support a balanced immune system with dosage amounts of only 500 mg per day over several weeks. The studies focused on the immune system's ability to help lessen the duration and symptoms of a cold or flu, as well as reduce the problems associated with seasonal allergies. Furthermore, a recent animal study demonstrates the antioxidant properties of EpiCor (see side bar).

Study #1 Strengthening the Body's Immunological Envelope

The first human clinical trial aimed to prove that EpiCor would provide the same effects in humans as it does in animals, but with smaller doses of EpiCor. The study was comprised of 22 people who had neither been exposed to nor taken EpiCor.

The participants were given small doses of 500 mg per day over a period of weeks. Saliva samples were taken twice a day, three times a week, for a month, and saliva secretory IgA was measured to establish the baseline concentration.

IgA, or Immunoglobulin A, is an antibody and, in its secretory form (sIgA), is the main antibody found in mucous secretions including tears, saliva, and other bodily secretions. Because it is resistant to degradation by enzymes, it can survive harsh environments such as the digestive and respiratory tracts, to provide protection against microbes that multiply in body secretions, acting as a protective immunological envelope around mucous membranes.

The subjects of this study were given one 500 mg capsule of EpiCor per day for 60 more days, and the sIgA monitoring was continued. After 30 days, there was a strong trend for increased sIgA over baseline, and after 60 days the average sIgA levels among the subjects were significantly higher than the baseline levels. This indicates that EpiCor increased this important immune defense component in just a matter of a few weeks.

Study #2 Seasonal Allergy and Immune Support

Another human clinical trial investigated the effects of EpiCor on several markers of immune function. In this double-blind, placebo-controlled trial, subjects were given either EpiCor (1,000 mg) or placebo for 5 weeks. At the end of 5 weeks, the salivary sIgA increased while the serum IgE decreased. Though not reaching full statistical significance due to the nature of this pilot trial, this was a strong trend. These results helped confirm the findings of the previous trial supporting the efficacy of EpiCor. On the other hand, the decreased serum IgE suggests the important immune balancing effects of EpiCor.

Since this trial was conducted in the spring when allergies are a problem for

many people, one would expect serum IgE to increase, since this immune parameter is associated with allergies. This was seen in the controls. However, in the EpiCor group, the levels stayed nearly at baseline, giving laboratory confirmation of the subjects' reporting fewer allergy problems than usual. This was also reflected in a standardized questionnaire showing fewer health complaints with the EpiCor group. It was also observed that cytokine profiles were

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Antioxidant Properties of EpiCor®

EpiCor has been shown to have one of the highest antioxidant activities of any known fruit, including blueberries, black raspberries, strawberries and cranberries, making it a potent weapon against cell-damaging free radicals that result from cellular metabolism and toxic exposure.

Once it was discovered that EpiCor contained a variety of antioxidant nutrients, studies were conducted to measure its free radical scavenging potential. Toward this end, isolated human neutrophil cells (phagocytic white blood cells that "gobble up" viral and pathogenic invaders) were exposed to hydrogen peroxide, a potent oxidizing agent. The exposure to hydrogen peroxide constituted an extreme oxidative stress due to the formation of radical oxygen species (ROS). Compared to cells exposed only to hydrogen peroxide, those exposed to both the peroxide and a one part per trillion dilution of EpiCor showed a statistically significant inhibition of ROS formation. This inhibition continued at increasingly larger dilutions of EpiCor, down to 0.01 parts per trillion.

EpiCor's antioxidant abilities may account for its anti-inflammatory effects, which were further demonstrated in two rodent trials. In one rat trial researchers induced paw swelling in the animals with carrageenan (an irritant that can act as an inflammatory agent) and in another study they induced arthritis with collagen. In both cases there was a statistically significant reduction in inflammation in rats consuming EpiCor.

Perimenopause and Menopause: Non-Phytoestrogen Support To Help Women Through “The Change of Life”

by Nieske Zabriskie, ND

Despite the fact that menopause is a normal physiological process in which menstrual cycles cease due to decreasing ovarian function, it can be a particularly trying time in a woman's life. Menopause is reached when a woman has not had a period for 12 months in a row.

Perimenopause is the time surrounding menopause when the hormones estrogen and progesterone are decreasing. The median age for the onset of perimenopause is 47.5 years and the transition usually lasts for approximately 4 years. Symptoms during this transition may include hot flashes (getting warm in the face, neck, or chest), night sweats or sleeping problems, fatigue and feeling stressed or tense. In addition, the vagina may become dry and thin, sex may be painful and bones may become thin, which may lead to loss of height and bone breaks.¹

According to the North American Menopause Society (NAMS) using the 2000 U.S. census data, there were an estimated 45.6 million post-menopausal women in the U.S. in the year 2000. Approximately 39.9 million were over the age of 51, the average age of spontaneous menopause. By the year 2020, the number of women in the U.S. over age 51 is expected to reach more than 50 million.²

Hormone replacement therapy (HRT) is a common prescription for menopausal women. These estrogen/progestin combinations are used to decrease symptoms associated with menopause. In the U.S. from 1999 to 2002, approximately 15 million women were taking HRT annually accounting for 90 million prescriptions per year.³ In 2002, the widely publicized U.S. government-funded study called the Women's Health Initiative indicated that HRT increases the risk of coronary heart disease, breast cancer and stroke.⁴ Following this publication, HRT prescriptions decreased by approximately 32 percent in 2003.⁵ This data suggests that

current pharmaceutical treatment for perimenopausal and menopausal women may not be appropriate for many women and alternative therapies may be indicated.

The Phytoestrogen Controversy

Numerous studies advocate the use of plant based estrogens called phytoestrogens for the management of menopausal symptoms. Phytoestrogens have been shown to bind estrogen receptors and to behave as weak agonist/antagonists in both animals and humans models. Phytoestrogens primarily include isoflavones, coumestans and lignans. Isoflavones are a phytoestrogen often supplemented for menopausal symptoms found in large amounts in soy and soy products. There is, however, some controversy regarding the unrestricted use of these botanicals as recent studies question the safety of phytoestrogens in some at-risk populations such as women with or at-risk for hormonal cancers.

A randomized, double-blind, placebo-controlled 5-year study was performed to evaluate the long-term safety of soy phytoestrogens in post-menopausal women. This study showed that phytoestrogen supplementation increases the risk of developing endometrial hyperplasia, or thickening of the uterus lining, which is associated with an elevated risk of developing endometrial cancer.⁶ Studies are also inconclusive regarding the safety of phytoestrogens in individuals with or at-risk for breast cancer. Animal models have shown that genistein, the predominant isoflavone found in soy, increased the proliferation of estrogen-dependent human breast cancer cells.⁷ Additionally, genistein has shown to negate the anti-estrogen tumor-suppressive effects of tamoxifen in estrogen-dependent breast cancer cells.⁸ Studies have also shown that soy protein isolate containing the isoflavones genistein and daidzein exhibited stimulatory effects on breast tissue in pre-menopausal women.

In fact, cytological detection of epithelial hyperplasia was found in approximately 30 percent of the women in this study during the months they consumed the soy protein. The study also found increased secretion of breast fluid and elevated levels of plasma estradiol.⁹ Contrary to previous studies, recent research also suggests that intake of soy products may actually decrease cognitive function in post-menopausal women as a study demonstrated a decrease in verbal working memory in this group.¹⁰ Thus, the safety of phytoestrogen use remains controversial and caution is advised in at-risk populations.

Non-Phytoestrogen Botanicals for Perimenopause and Menopause

Cimicifuga racemosa. *Cimicifuga racemosa*, commonly known as black cohosh, has traditionally been used for women's health conditions such as menopause, painful menses and premenstrual syndrome. There are numerous studies published regarding black cohosh's effects on menopausal symptoms. Researchers have found that black cohosh is safe as studies show that it does not cause thickening of the endometrium or cause other adverse outcomes.¹¹ Research indicates that black cohosh does not stimulate estrogen receptors. It does, however, bind to serotonin receptors, which some researchers believe is the mechanism in which black cohosh decreases hot flashes.¹² Research indicates that black cohosh is safe to use in breast cancer patients and possibly is an inhibitor of tumor growth.¹³

A 3-month study compared the efficacy and safety of black cohosh compared to low-dose transdermal estradiol in postmenopausal women. The study demonstrated that both treatments significantly reduced the number of daily hot flashes, anxiety, and depression. Black cohosh also increased levels of the beneficial high-density lipoprotein (HDL) cholesterol. There

was no effect on liver function tests, triglycerides, follicle-stimulating hormone (FSH), luteinizing hormone (LH) and cortisol with either treatment.¹⁴

Another study was performed to evaluate the effectiveness of black cohosh compared to the selective serotonin reuptake inhibitor (SSRI) fluoxetine for the management of menopausal symptoms. The study showed that black cohosh reduced the hot flash score by 85 percent and black cohosh proved to be more effective for treating hot flashes and night sweats compared to fluoxetine.¹⁵

There have been reports that suggest that black cohosh may cause liver damage although a direct association with the ingestion of cimicifuga has not been demonstrated. In fact, careful scrutiny of the alleged claims indicate that many of the individuals with liver damage attributed

“In one study, black cohosh significantly reduced daily hot flashes, anxiety, and depression.”

to black cohosh were on medications that may induce liver problems, making black cohosh unlikely to have caused the liver diseases.¹⁶ Numerous studies have been performed to evaluate the safety of black cohosh, and they indicate that black cohosh appears to be safe for long-term use.¹⁷

Estro-G 100. EstroG-100 is a proprietary blend of standardized extracts of the botanicals *Phlomis umbrosa*, *Cynanchum wilfordii* and *Angelica gigas Nakai*. Current evidence suggests that Estro-G acts as a selective estrogen receptor modulator (SERM), which binds specific estrogen receptors. This allows maintenance of a healthy estrogen level without taking hormone therapy.

Researchers have examined the effects of Estro-G in menopausal women in a randomized and double blind study. Menopausal symptoms were evaluated after 3 months of supplementation. The Estro-G group showed statistically significant improvement of various menopausal symptoms compared to the placebo group.

In fact, of the women with menopausal symptoms at the onset of the study, 57.1 percent had resolution of their symptoms at 3 months. In the women who did not have overt menopausal symptoms prior to the study, 58.3 percent reported feeling better at the 3-month evaluation. At the end of 12 months, additional variables were examined. There was no change reported in regards to weight, body mass index (BMI), blood pressure, serum estrogen, FSH, total cholesterol, low-density lipoprotein (LDL) and high density lipoprotein (HDL). The results also showed a statistically significant increase in femoral neck bone density in the EstroG group and serum osteocalcin levels were decreased in the Estro-G group while increased in the control group (increased levels of osteocalcin are found in bone diseases characterized by increased bone turnover). Also, the bone marker serum alkaline phosphatase (ALP) levels were decreased. Human growth hormone (hGH), which generally declines with aging, was increased in the study group by 268 percent. Additionally, serum triglyceride levels were decreased in the study group by 23 percent.¹⁸

Decursinol, an active constituent of *Angelica gigas Nakai* root, also has exhibited some interesting effects. It has been shown to have anti-inflammatory, anti-cancer, antioxidant, anti-platelet aggregation and antibacterial activity.¹⁹ Other studies have shown that decursinol may decrease pain perception, particularly inflammatory pain.²⁰

Tribulus terrestris. *Tribulus terrestris*, also known as puncture vine, has been used traditionally in Chinese and Indian medicine to improve sexual function in both males and females. Evidence also suggests that it improves menopausal symptoms. A study examining *Tribulus* supplementation was done with 50 menopausal women, including women with both natural and surgically-induced menopause. The study evaluated menopausal complaints such as intensity and frequency of hot flashes, depression and hyperexcitability, apathy, changes in the cardiovascular system, urinary disorders, discomfort of genitalia and libido. They also examined vaginal cytological measurements, blood count, blood sugar, ultrasound and hormone levels. The results showed that 98 percent (49/50) of the women experienced complete or almost

complete effect on all or on the majority of the symptoms.²¹

G-63 Flower Pollen. G-63 Flower Pollen is an extract of *Secale cereale* (rye). Flower pollen has been used traditionally for urinary tract health. Studies also indicate potent anti-inflammatory activity with supplementation of rye flower pollen.²² Animal studies show liver-protective activity as well as improvement in lipid profiles and decreased atherosclerotic plaque formation with rye flower pollen supplementation.^{23, 24} G-63 Flower Pollen is safe and does not trigger seasonal allergy reactions.

Conclusion

As more women are reaching menopause, the need for alternative support is increasing. Avoiding phytoestrogens may be recommended for women concerned with the risk of hormonal cancers. Therefore, natural therapies without phytoestrogens, such as black cohosh, *Phlomis umbrosa*, *Cynanchum wilfordii*, *Angelica gigas Nakai*, *Tribulus* and flower pollen may be an effective alternative to improve the health of women undergoing perimenopause and menopause.

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Resveratrol Update: Effects Extend Beyond Cardiovascular Support

by John Raimo, MS, RD

In last month's newsletter, we reported on the cardiovascular effects of resveratrol, a naturally occurring plant compound, as well as its powerful antioxidant abilities and its ability to activate the human longevity gene. Beyond these other effects, resveratrol may be important in prostate, uterus, breast and skin health.

Prostate Health

In one study, resveratrol-fed mice undergoing prostate mutagenesis showed an 87 percent reduction in risk of developing prostate tumors.¹ The mice fed resveratrol for seven months experienced the highest risk reduction. Other mice with a less serious form of prostate mutagenesis were 49 percent more likely to have tumor growth halted or slowed compared to mice not consuming the compound. These same researchers are conducting a human study examining the resveratrol concentrations that may produce a similar effect to that found in animals.

Other researchers have proposed that resveratrol's effects are due to its anti-inflammatory actions. Stanford University researchers found that in normal prostate cells, resveratrol exposure increased expression of a substance known as MKP5, which reduces inflammatory mechanisms.²

Health Opportunities for Women

A recent study looked at resveratrol's effect on breast mutagenesis in mice.³ The researchers found a significantly lower tumor growth, decreased angiogenesis, and increased rate of apoptosis (cell death) in mutagenic cells in mice given resveratrol compared with controls. *In vitro*, they found a significant increase in apoptosis in resveratrol-exposed cells.

In another *in vitro* study, high resveratrol doses triggered apoptosis (cell death) in five out of six uterine cancer cell lines and inhibited uterine cancer cell proliferation.⁴

Skin Health

Scientists also have looked at resveratrol's effects on UVB-radiation-mediated skin tumor development in mice.⁵ In this study, the control mice were subject to

chronic UVB exposure (twice weekly, for 28 weeks). The mice received either a pre-treatment (30 minutes before each UVB exposure) or post-treatment (5 minutes after UVB exposure) topical resveratrol application. The topical application with resveratrol (both pre and post treatment) significantly inhibited tumor incidence and delayed onset of tumor development. Resveratrol also enhanced apoptosis in UVB-exposure-mediated skin tumors.

Potential Mechanism of Action

A review by Shankar, et al. examined resveratrol's molecular mechanisms.⁶ Shankar reports "the chemoprevention properties of resveratrol are due to its ability to modulate the cell signaling pathways that lead to a diversity of bioactivities related to human health. Resveratrol has been shown to inhibit tumor initiation, promotion, and progression."

Another report mirrors Shankar's findings in stating that resveratrol acts on mutagenesis by affecting the three phases (tumor initiation, promotion and progression) and suppresses the final steps of neoplasia and metastasis.⁷ According to the report, resveratrol activates apoptosis and arrests the cell cycle in cells that have undergone transformation. Additionally, resveratrol does not present any cytotoxicity (cell toxicity) in animal models or safety concerns in humans.

Resveratrol also exerts some interesting effects on angiogenesis, the development of new blood vessels needed by cancer cells to spread throughout the body. At the same time that resveratrol can increase angiogenesis when the heart is in need of extra oxygen, resveratrol has stopped angiogenesis in experimentally induced tumors.⁸

Other Research

In animal and *in vitro* studies, colon cancer⁹, melanoma¹⁰, leukemia¹¹⁻¹² and pancreatic cancer cells¹³ were inhibited after exposure to resveratrol. In humans, some studies have associated high-resveratrol diets with an improvement in breast health.¹⁴ Furthermore, consumption of red

wine, which contains high quantities of resveratrol, has been linked to a reduced lung cancer risk.¹⁵

Conclusion

Although clinical trials in humans are clearly needed, resveratrol is emerging as one of the most well researched natural substances with promising reports in the medical literature studying its inhibitory effects on the mutagenic process.

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Liver

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extract also largely prevented necrosis of the liver cells that normally occurs concurrently with oxidative damage. Artichoke extract also reduced the loss of total glutathione that occurred in cells not exposed to the extract.¹⁵

Conclusion

The liver is often ignored when designing an overall health regimen. However, the liver's important role in influencing many aspects of both male and female health indicate that everyone should consume the proper nutrients to nourish and support the health of this vital organ.

Peri- & Menopause

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EpiCor

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shifting in the EpiCor group—from Th1 (pro-inflammatory) to Th2 (pro-adaptive) and vice versa—again demonstrating the immune balancing properties of EpiCor.

Study #3 Upper Respiratory Tract Health

Last, a third study assessed the clinical benefits of EpiCor in a large, independently conducted double-blind, placebo-controlled human clinical trial. To do this, 230 people were recruited to take either EpiCor or placebo, to study the effects on upper respiratory tract infections (URTI).

This large group was chosen to represent the general population aged 18 years and older. The trial took place during the worst cold and flu months—January, February and March—in South Dakota. Subjects received physical examinations at screening to ensure a healthy study population, and were randomly assigned to receive either EpiCor or placebo. Fasting blood samples were taken at randomization, week 6 and at week 12 (when the trial ended). Each subject was given a diary and instructed to record duration and severity of cold and flu symptoms.

In the subjects taking EpiCor, the incidence of URIs was statistically and significantly reduced. A statistic known as the “p-value” was 0.0000008—meaning

that the probability that the reduction in URIs in the EpiCor group occurred by chance was less than one in a million. Additionally, in the rare cases when the EpiCor subjects did get URIs, the duration of the symptoms was significantly shorter.

Conclusion

These three soon-to-be published human clinical trials support the body of past research that establishes EpiCor as a means to support immune health. In these studies, EpiCor showed a strong trend toward supporting a balanced immune system with smaller dosage amounts than that given to animals. These results demonstrate that EpiCor may have a strong role to play in optimizing immune health.

Tocotrienols

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diabetic rats.¹¹ The control rats received a normal diet or a vitamin C diet (that was tocotrienols deficient), and the rats in the experimental group received a tocotrienols rich diet. The rats were maintained on their respective diets for 4 weeks, then made diabetic. The rats were then followed-up after 8 weeks. Levels of blood glucose, a measure of blood sugar control called glycated hemoglobin (HA1c), serum advanced glycosylation end-products (AGEs) and a marker of free radical/oxidation damage known as malondialdehyde (MDA) were measured at 4 weeks and at 8 weeks. This study showed that a tocot-

rienols-rich diet effectively prevented an increase in advanced glycation end products (AGEs) in normal rats, and produced a decrease in blood glucose and HA1c in diabetic rats. (To learn more about AGEs, please read the article explaining these destructive compounds in this newsletter).

Conclusion

Metabolic syndrome is one of the most common health concerns of our time. By consuming a healthy diet, exercising and giving the body proper supplemental nutrition, the incidence of this syndrome can be substantially reduced. Anatto tocotrienols may be used together with lifestyle modifications to establish healthy blood sugar levels in the body and to reduce markers of impaired blood sugar control.

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Higher Vitamin E Doses May Improve Heart Health

Past studies reporting on vitamin E's effects on heart health may have used too low a dosage, according to a new study.

Many epidemiological and animal studies have found that vitamin E may help protect the heart. In subsequent controlled clinical trials, however, the results of vitamin E supplementation on heart health were mixed.

In the current two-part study, researchers found that it took higher vitamin E doses to reduce levels of a lipid peroxidation marker known as F2-isoprostanes in people who have high cholesterol levels and enhanced oxidative stress. The dose of alpha-tocopherol needed to counteract the oxidative stress in individuals at risk for cardiovascular disease was 3,200 IU per day. Many clinical trials used dosages substantially below this amount.

In the first part of the study, eight participants (average age 34, seven women) received 3,200 IU of alpha-tocopherol for 20 weeks. After 16 weeks of supplementation, vitamin E suppressed plasma F2-isoprostane concentrations.

The researchers then conducted a double-blind, randomized, placebo-controlled study with 35 volunteers (average age 42, 23 women) to investigate the effects of different vitamin E doses on plasma F2-isoprostanes concentrations. The volunteers

consumed either a placebo or 100, 200, 400, 800, 1,600, or 3,200 IU of vitamin E daily for 16 weeks.

The findings indicate that vitamin E has a dose-dependent effect in reducing plasma F2-isoprostane concentrations. With the higher doses, statistical significance was achieved, with 1,600 IU reducing F2-isoprostane levels by 35 percent, and 3,200 IU of the vitamin producing a 49 percent reduction.

In addition, this study did not support the results of some *in vitro* studies that indicated vitamin E may act as a pro-oxidant at certain concentrations.

The researchers theorized that a combination of using too low a vitamin E dose and poor study design that included using only a single dose of vitamin E may be why some studies showed no effect of vitamin E on heart health. In addition, they pointed out that many previous studies only looked for end points such as heart attack occurrence.

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Roberts II LJ, Oates JA, Linton MF, Fazio S, Meador BP, Gross MD, Shyr Y, Morrow JD. The relationship between dose of vitamin E and suppression of oxidative stress in humans. *Free Radical Biology and Medicine*. Epub ahead of print. 4 July 2007.

Anatto tocotrienols have been shown to be more effective than alpha-tocopherol in inhibiting lipid peroxidation due to the molecule being more easily incorporated into cell membranes.

Customer Corner Supplement Index From pages 10-11

Product	Code
5-HTP	CP5765
AdaptaPhase® I	CP1910
AdaptaPhase® II	CP1920
Advanced Inflammation Control ...	CP1625
Calcium Citrate/Malate	CP7411
Comprehensive Hormone Panel ...	CP9830
CoQ10-H ₂ ™	CP6300
DHA	CP3176
DHEA 25mg	CP6371
DMAE 100 Plus	CP1320
Extend Liquid	CP9540
Extension Vision	CP2140
Food Allergy Test Kit	CP9840
HerBalance™ Cream	CP2101
Iodoral®	CP9139
Kid's Essentials	CP7054
L-Phenylalanine	CP4511
L-Theanine	CP8481
NanoGreens ¹⁰	CP5311
Nattokinase +	CP6251
Nordic Naturals ProOmega	CP9529
Oral ChelatoRx	CP1820
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Unique Sweet® Xylitol Gum - Peppermint	CP9321
Unique Sweet® Xylitol Mints - Peppermint	CP9361
Unizyme™	CP1630
Zinc	CP7541



Selenium Levels Linked to Muscle Health in Elderly

Seniors who have low blood levels of selenium have a significantly greater incidence of weaker muscles, researchers reported in the *American Journal of Clinical Nutrition*.

The study, conducted in Italy, measured plasma selenium levels and the strength of the hip, grip and knee of 891 elderly men and women 65 years and older. The average plasma selenium level of all the participants was 0.95 micromoles per liter, below the value considered the minimum level of plasma selenium necessary in the bloodstream. In Italy, soil concentrations of selenium are low and the participants' dietary intake from fruits and vegetables was therefore likely low.

After adjusting the results for potential confounding factors, the researchers found that participants who had the lowest plasma concentrations of selenium were 69 percent more likely to have poor hip strength compared to those with the highest selenium levels. In addition, subjects with low selenium were 94 percent more likely to have poor knee and grip strength.

The researchers called for future studies to determine whether selenium supplements can reduce the decline in muscle strength that occurs with age.

Reference:

Lauretani F, Semba RD, Bandinelli S, Ray AL, Guralnik JM, Ferrucci L. Association of low plasma selenium concentrations with poor muscle strength in older community-dwelling adults: the InCHIANTI Study. *American Journal of Clinical Nutrition*. August 2007;86(2):347-352.

Green Tea May Inhibit Mutagenic Processes

Three new studies show that green tea can reduce the risk of oral cancer in women, stimulate the production of anti-mutagenic enzymes and inhibit the initial stages of intestinal cancer.

In the first study, researchers analyzed green tea consumption among 20,550 men and 29,671 women in Japan by administering a questionnaire. During a mean follow-up period of 10.3 years, the researchers documented 37 oral cancer cases.

The study authors reported that women who consumed five or more cups of green tea per day had a risk reduction of 70 per-

cent, compared to women who consumed between one and two cups per day. Because the number of oral cancers cases was small in this group of subjects, researchers called for more studies to confirm the results.

A new clinical study by another group of researchers confirms green tea's potential anti-mutagenic effect. In this study, scientists investigated whether EGCG, the green tea component thought to be responsible for the beverage's health effects, had any effect on levels of glutathione S-transferase (GST) enzymes. GSTs alter cancer-causing molecules in order to prevent the molecules from damaging cellular DNA.

The study included 42 healthy subjects who abstained from consuming tea or tea-related products in the four-weeks prior to the study's start. They gave a fasting blood sample, which the researchers used to measure GST activity and level. The subjects then consumed 800 mg epigallocatechin gallate (EGCG) per day on an empty stomach for four weeks, at which time they again gave blood samples.

After the subjects consumed the green tea component, the GST activity increased from 2252.9 plus/minus 734.2 ng/mg protein to 2634.4 plus/minus 1138.3 ng/mg protein. The increase was most pronounced in people who had low GST activity at the study's start. After consuming the EGCG, their GST activity increased by as much as 80 percent. The researchers point out that this is the first study to demonstrate this effect in humans.

The study authors suggested that the findings indicate EGCG from green tea could help vulnerable individuals to strengthen their metabolic defense against carcinogens.

In the third new study, scientists treated mice with an agent that induces colon tumors, then gave the animals either water or green tea for four to eight weeks.

Although green tea was ineffective against larger, already formed tumors, green tea significantly inhibited new tumor formation. The researchers also found that green tea decreased the total levels of biomarkers involved in early colon cancer development.

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Probiotics Improve Intestinal Regularity

Probiotics, the "good" bacteria involved in intestinal health, may increase the number of bowel movements and reduce constipation in children, a new study has found.

The pilot study used a probiotic mixture to determine the effects on symptoms associated with childhood constipation. Twenty constipated children (half male, average age 8) participated in the study. For four weeks, the children consumed a daily probiotic supplement containing a mixture of *Bifidobacteria bifidum*, *B. infantis*, *B. longum*, *Lactobacilli casei*, *L. plantarum* and *Lactobacillus rhamnosus*.

After the children consumed the probiotic mixture, the frequency of their bowel movements doubled, increasing from two per week to 4.2 after two weeks, to 3.8 after four weeks. They also experienced a decrease in abdominal pain from 45 percent at the start of the study to 20 percent after four weeks of supplementation.

The researchers theorized that the probiotic mixture was able to achieve such positive results as it elevated levels of lactic, acetic and other acids, ultimately resulting in a lowering of pH in the colon area, thereby enhancing motility of the colon. This leads to a decrease in colonic transit time.

Reference:

Bekkali N, Bongers MEJ, Van den Berg MM, Liem O, Benninga MA. The role of a probiotics mixture in the treatment of childhood constipation: a pilot study *Nutrition Journal*. Epub Ahead of Print. August 4, 2007;6:17.

Bifidobacteria bifidum and *Bifidobacterium longum* are found in BioPro™, while *Lactobacillus rhamnosus* (LGG or *Lactobacillus GG*) is found in Culturelle®.



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The Liver:

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Annatto Tocotrienols:

Their Significant Role in Blood Sugar Control

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- Fractured Fingers in Young Child



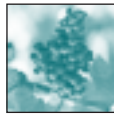
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