

THE HEART OF THE MATTER

The Role of Transfer Factors and Other
Nutrients in Cardiovascular Health.

Dr. William J. Hennen

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Dr. William J. Hennen has over 13 years of experience as an academic researcher/professor in drug design and development. He received his Ph.D. in bio-organic chemistry from Utah State University. In 1989 Dr. Hennen, seeing the truth in Benjamin Franklin's statement "an ounce of prevention is worth a pound of cure," and realizing the power of natural products, made a well-thought out career change to the nutritional supplement industry. He is a renowned international lecturer on health recovery and maintenance through dietary supplementation and has conducted numerous continuing medical educational seminars for physicians.

It gives me great pleasure to endorse this booklet on the matter of the heart. Dr. Hennen has researched the subject extensively and has put the information together for the benefit of the lay people as well as health practitioners. I strongly recommend *The Heart of the Matter* to those who suffer from Cardiovascular Disease as well as those who want to have a strong and healthy heart. The booklet is written from the Heart for the Heart of everyone

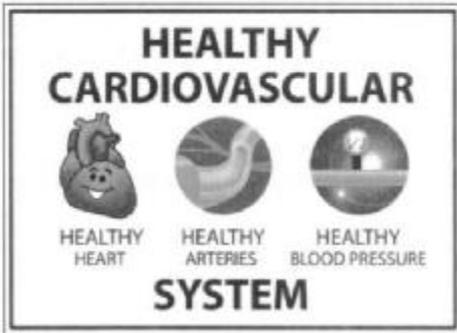
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Cardiovascular Disease in the Asia-Pacific region.

It is estimated that by year 2020, non-communicable diseases including cardiovascular disease are expected to account for seven out of every ten deaths in the Asia-Pacific countries. In the Asia-Pacific region, deaths due to cardiovascular disease range from less than 20 in countries such as Thailand, Philippines and Indonesia to 20-30% in urban China, Hong Kong, Japan, Korea and Malaysia. In New Zealand, Australia and Singapore deaths due to cardiovascular disease exceed 30-35% of all deaths. In Singapore, coronary heart disease is the second leading cause of death. In Malaysia, the proportion of deaths due to cardiovascular diseases has multiplied more than three-fold since 1965. Therefore, there is a need for corrective action to be taken. Dr. Hennen has documented a nutritional basis for strengthening our cardiovascular systems and reduce the growing tide of cardiovascular disease.

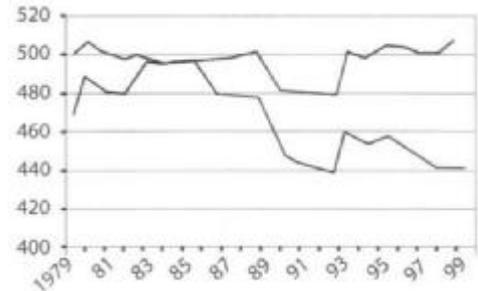
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All of us need a strong heart with good pumping action. We need open arteries that are not clogged with plaque. We also need our arteries to be flexible. This allows them to expand and contract enabling us to match our blood flow with the activities we are pursuing. Many nutritional and psychological factors affect our cardiovascular health, but before we discuss the bio-mechanics of cardiovascular health, let's examine cardiovascular disease in context of our modern society. Except for 1918, the year of the great flu epidemic, heart disease has been the number one killer in the United States for over a century.¹ Interestingly heart disease in males in the United States is dropping, while in



females it is rising. Yet, in spite of that rise, surveys have shown that women are far more afraid of breast cancer than they are of cardiovascular disease.

Men respond to prostate cancer similar to the way women respond to breast cancer. Nevertheless, for both men and women, heart disease is their number one killer. Heart disease is not just an old person's disease. In the summer of 2002 Darryl Kyle a 33-year-old professional baseball pitcher died in his sleep. The autopsy showed that he had 80% to 90% narrowing of two of the three coronary arteries. Apparently he had an arterial spasm or other transient event that blocked the rest of the artery. We often hear that we should exercise more to improve our cardiovascular strength. How physically fit does one have to be? Certainly the conditioning of a professional baseball player is not the norm. As important as exercise is, it is only part of the answer. A whole host of factors influence cardiovascular health.



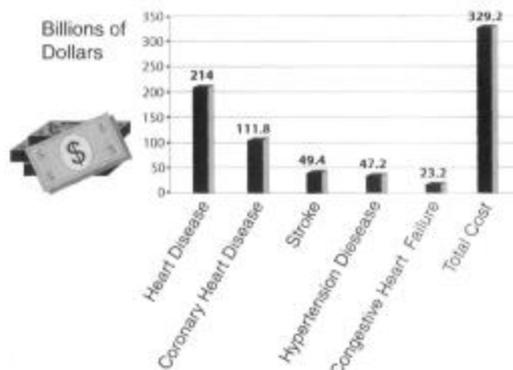
A scientific study entitled "The Pathobiological Determinants of Atherosclerosis in Youth (PDAY)" has recently been published.² Pathobiological is a contraction of pathology and biological. Atherosclerosis refers to the build up of plaque in the arteries. What the researchers were looking for in this study was information on what is causing plaque build up in the arteries and how early this process started. To find these answers they conducted autopsies on 3,000 people fifteen to thirty years old who died of causes unrelated to heart disease (accidents, etc.). The results were surprising. Every, 15-year-old already had plaque build up! The obvious conclusion was that cardiovascular disease, or atherosclerosis, was starting in childhood.



In the United States all forms of disease associated with the cardiovascular system (heart disease, coronary artery disease, stroke, hypertension, congestive heart failure) causes the total cost to amount to 329.2 billion dollars.



Estimated Direct and Indirect Costs of Cardiovascular Diseases and Stroke



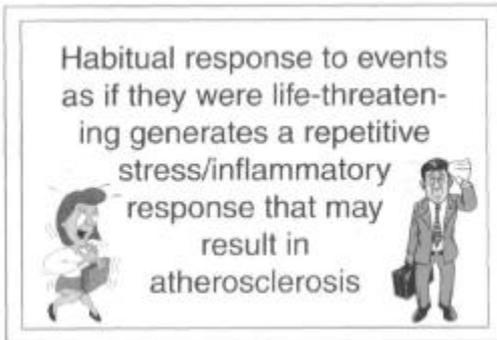
There are 270 million people in the United States, which means that over \$1,200 are spent per person, out of the United States economy on cardiovascular disease every year. These costs cannot measure the impact on a person's quality of life. If a person has a heart attack, life changes dramatically. One becomes much more careful even fearful about exerting themselves.



As recently as five years ago most physicians would have confidently described atherosclerosis as a straight plumbing problem. "You have scale in your pipes! We will have to do a by pass operation by going in and cutting a pipe (artery) out of your leg, then opening up your chest and patch it in your heart." In fact without open heart surgery many people would have died. But what is the real problem? What is causing the plaque to build up in the first place? What can we do to keep our pipes clean?

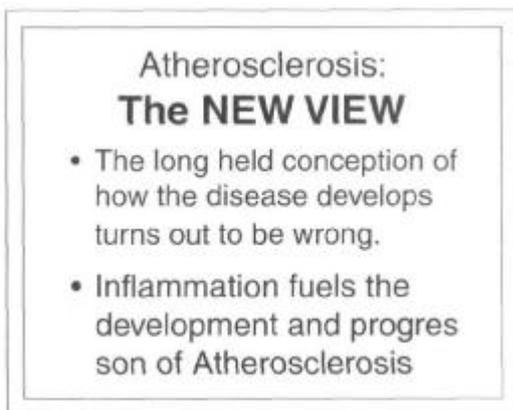
In May of 2002 Scientific American published a major article that declares that cardiovascular disease is not a straight plumbing problem. In fact our whole concept in this area was actually wrong.³ Dr. Libby clearly states that inflammation is at the core of cardiovascular disease.

Inflammation can be caused by a number of factors including how we react to our world. If an individual repetitively over reacts to daily stresses they cause themselves to have inflammatory responses that may result in atherosclerosis.⁴ This is



because our inflammatory reaction is part of our stress response. Modern man's physiology has not changed much since the times of his ancient ancestors. To understand this better let's go back in time ten thousand years. Let's say we are walking through the woods, not really paying attention, and a bear suddenly jumps out because we have gotten between a mother and her cub. We see that bear and what happens immediately? We have an adrenaline release! We have to decide right now whether we run or fight. This fight or flight response also comes with an inflammatory

response. Why does that happen? We have to prepare for injuries that may come as a result of the fight we are facing. Alternatively the body does not know if it will be fast enough to out run the bear but it does know that the bear didn't wash her claws before they ripped into you. You may have gotten away but now you have a massive, contaminated wound and your immune system needs to react right now if you are going to win the race against the infection. In this case the already triggered inflammatory response gives our immune system a jump start on the infection.



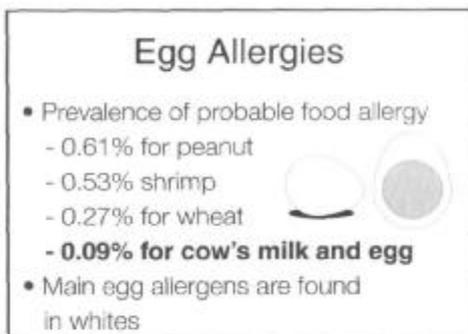
In our everyday lives we may not be attacked by bears, but our body cannot tell the difference between an attacking bear and an attacking boss if our hearts and heads do not make the distinction. We have heard for years that stress can kill us. Now we know one very real way that we may be hurting our heart health is through over reacting to our everyday stresses. This reason alone should be sufficient for us to stop and reflect on our attitudes and the way we approach our lives.

Another cause of inflammation is infection. There are at least six microbes that are correlated to increased heart attacks.⁵ These microbes are sometimes found in the tissue of the arteries.⁶ At other times the infection may be located in other parts of the body. Where ever the infection occurs, the body releases messenger molecules into the blood stream which come into contact with the arteries causing them to become irritated and inflamed.

In examining the relationship between infection and inflammation researchers have proposed that as important as individual infections are, the total infectious burden of a lifetime may be the real factor that causes repeated inflammation and culminates in cardiovascular disease.⁷

Transfer factors have been used for over fifty years to help strengthen and support a proper immune response. Transfer factor preparations contain both specific and non-specific components. The specific components provide identification signals for specific organisms. The non-specific components provide a multitude of benefits such as helping the immune system to control excessive inflammation⁸ and to enhance the natural killer cells that are part of our frontline defense against infections.⁹ Recent work has demonstrated the ability of transfer factor to profoundly improve the body's antioxidant defenses and increase the ability of the body to detoxify itself when faced with physical injury and infection.¹⁰ Specific transfer factors are created when a person or animal is exposed to specific microorganisms and successfully overcomes those organisms. Historically transfer factors have been prepared from blood. Blood sources present a number of problems not the least of which is supply. Since transfer factor is not species specific — in other words the same transfer factors are made in all animals — it is possible to isolate transfer factors for human use from non-human sources. The discovery of transfer factors in colostrum opened up a new, easily-accessible source of transfer factors.¹¹ The discovery of transfer factor in colostrum follows a nearly universal mother-child motif found throughout nature. A more efficient source of specific transfer factors was recently discovered and patented. This source is chicken eggs.¹² The only time that a hen can immunologically communicate with her chick is at the time the egg is formed. A mother hen is the epitome of maternal protectiveness: here again we see the mother-child motif indeed. The discovery of transfer factors in eggs therefore follows a natural logic.

A cow takes two years before she produces her first colostrum and then only produces five days of high quality colostrum over the next three years. A hen will become productive within a matter of months and lay up to 200 eggs over the next year.



Both cows and chickens have coexisted with man for tens of thousands of years. We have become mutually exposed to thousands, even millions of microorganisms over that time. The classic case of vaccination of a human with cowpox as a protection against smallpox is an excellent example of how organisms from different coexisting species are able to provide immunological protection against related organisms that afflict man. In addition cows and hens do not require the hygienic conditions needed by humans to thrive. Neither cows nor hens wash their food or purify their water. In addition chickens eat dirt in order to assist them in grinding their foods. In order for cows and hens to survive, Nature has endowed them with heroic immune systems.

In choosing a food source for transfer factors we must to be concerned about allergens.¹³ In preparing colostrum transfer factor, the large proteins and casein, that cause milk allergies, are removed. In the egg, most of the allergens occur in the whites.¹⁴ Removal of the whites is desirable since the majority of the immunological components including the transfer factors are found in the yolk.

Specific transfer factors provide us warning signals that support and strengthen the immune system's ability to recognize pathogens early while they are still small in number. The activity of transfer factor in strengthening the immune system's ability to control the inflammatory response is critically important in protecting the entire cardiovascular system. As will be discussed below, increasing the body's antioxidant shield provides numerous cardiovascular benefits. The demonstrated ability of transfer factor to increase the efficiency of the body's antioxidant shield is a

new unanticipated benefit of transfer factor which will have a significant additional impact on overall health and especially on cardiovascular health.

There are other well established nutritional supplements that strengthen and support good cardiovascular health. Magnesium is one of these nutrients. “Magnesium deficiency has been shown to correlate with a number of chronic cardiovascular diseases, including hypertension, diabetes mellitus, and hyperlipidemia.¹⁵ Hyperlipidemia simply means too much fat in the blood. The western diet is deficient in magnesium and modern water systems leave very little magnesium in the drinking water.¹⁶ When magnesium is deficient in the artery it becomes spasmodic, clamping off blood flow. Magnesium allows the blood vessels to relax and prevents arterial spasm. Magnesium deficiency also leads to hypertrophy or enlargement of the heart. This may occur in large part because magnesium is required for metabolic efficiency. If the heart muscle is only half efficient, then it will need to be twice the size hence the enlargement or hypertrophy of the heart. One of the main classes of cardiac drugs is calcium channel blockers. Magnesium is the natural calcium channel blocker.¹⁷ Physicians have been advised to always check their patient’s magnesium levels before beginning any cardiovascular treatment program.¹⁸



A deficiency of copper results in high blood pressure, and inflammation. Copper deficiency reduces the ability of the blood to clot, and increases arteriosclerosis. Atherosclerosis is the hardening of the arteries.¹⁹ When we check our pulse, what we are actually feeling is the arteries stretching and contracting back. In this way the arteries are dampening the pressure buildup caused by the pumping of the heart thus reducing the strain on the arteries. Without sufficient copper the arteries become hard and brittle and the blood pressure spikes to higher numbers.

The lining of the arteries requires more zinc during the inflammatory process. If you are low in zinc then you are going to have greater inflammatory damage to the arteries.²⁰ Both men and women who took zinc supplements had higher HDL or good cholesterol levels than non-supplementing individuals.²¹

Selenium is a critical cofactor for glutathione peroxidase a key antioxidant enzyme. Selenium deficiency leads to an increased frequency of cardiovascular diseases.²² On the other hand, selenium is a well recognized preventive factor for cancer and cardiovascular diseases.²³

Homocysteine is a metabolic waste product. If it is not recycled it builds up causing inflammation of the arteries. Elevated levels of homocysteine promote the development of atherosclerosis. Indeed approximately 10% of coronary artery disease cases are attributable to hyperhomocysteinemia.²⁴ Supplementation with folic acid has been shown to reduce homocysteine levels by as much as 25%. Addition of vitamin B 12 further reduces homocysteine levels another 7%.

There are those who still debate whether antioxidants are protective. Nevertheless Vitamin C has been clearly shown to slow atherogenesis or plaque buildup. Increased intake of vitamin C results in



Vitamin E Supplement Benefits

- Decreased cardiac events:
 - U.S. Nurses' Health Study
 - 34% risk reduction
 - U.S. Health Professionals' Study
 - 39% risk reduction
 - Iowa Women's Health Study
 - 47% mortality reduction
 - Cambridge Heart Antioxidant Study
 - 47% infarct reduction

reduced risk of chronic diseases such as cardiovascular disease, cancer, and cataracts.²⁵ At least four major studies have shown a 30-50% reduction in cardiovascular problems when supplemental Vitamin E was taken.²⁶ This is strong evidence supporting the benefits of taking Vitamin E.

The herpes group of viruses are associated with atherosclerosis.²⁷ Lysine is useful in suppressing the return of herpes simplex infections.²⁸ Increasing our lysine intake will help us to keep herpes infections from becoming active.

Within the whole cardiovascular system we have a need to balance the expansion and contraction of the arteries. If we are working hard, we need the blood vessels to expand and open up so that more blood can flow through without driving our blood pressure up too high. On the other hand there are times when we need our blood vessels to contract slightly to help us maintain blood flow throughout the body. For example if a person who has been lying down gets up quickly, the blood vessels need to contract slightly so that the blood flow to the brain does not decrease leaving the person dizzy. The insufficiency of blood flow often is a combination of inefficient pumping action by the heart, hardening of the arteries or arteriosclerosis such that the blood vessels are not able to expand and contract freely, and atherosclerosis or the build up of plaque within the arteries which restricts blood flow to critical organs. It is an interesting and potentially deadly fact that an atherosclerotic artery may actually contract when it should be expanding.²⁹

**A critical balance exists
between expanding and
contracting factors**



In order for the blood vessels to relax the body needs to produce a critical relaxing factor called nitric oxide (NO). The drug nitroglycerine, a potential explosive, is used as a nitric oxide donor in the form of nitroglycerine patches. The slow absorption and slow breakdown of nitroglycerine releases NO into the blood stream causing the blood vessels to relax. This is an example of external control of an internal process. The drug has no way of knowing how much NO is needed. The absorption and breakdown of nitroglycerin is determined by the laws of chemistry not by the needs of each individual body. The rate of nitric oxide release is controlled by the dosage which is in turn controlled by the doctor. Control requires intelligence. The control of the release of nitric oxide from nitroglycerin is dependent on the external intelligence of the physician.

In a normal healthy body the intelligence is self-contained in the natural control mechanisms of the body. Healthy control is internal not external control. In order for any control mechanism to be effective it must have at least two critical components. First it must have the necessary sensors to determine if the process in question is operating properly. Second it must have available resources to be able to affect a change in the condition. In the body nitric oxide is made from the amino acid L-Arginine. For the body to try to make nitric oxide without L-Arginine would be like a carpenter trying to build houses without any wood.

Arginine & NO

- Nitric oxide is a relaxing factor
- L-Arginine is the precursor for nitric oxide (NO)
- Oral L-Arginine supplementation can improve symptoms of cardiovascular disease.

(Note: magnesium is also critical.)

A number of factors may affect the availability of L-Arginine including diminished protein digestion which occurs with aging. If there is insufficient L-Arginine, processes within the body must compete for the available L-Arginine and no one gets all they need. Supplementing with L-Arginine may fill the demand for L-Arginine but, does not force nitric oxide to be made as in the case of nitroglycerin. The production of nitric oxide from L-Arginine is still under internal control. There is a clear distinction between the drug nitroglycerin and the dietary component L-Arginine. The scientific literature describes L-Arginine as a nitric acid precursor while nitroglycerine is described as a nitric acid donor. Both the dietary supplement L-Arginine and the drug nitroglycerine were found to be beneficial in the recovery of heart and blood vessel function.³⁰ Oral L-Arginine supplements have been shown to

according to its needs if it has a full range of nutrients available. The body is also very conservative. It does not waste expensive antioxidants when less expensive antioxidants will do the job more efficiently. Red Rice Yeast is actually a natural source of statins that are used as drugs to shift the cholesterol ratios and reduce blood triglyceride levels. In 1999 Professor Heber of the UCLA Center for Human Nutrition stated “Red yeast rice significantly reduces total cholesterol, LDL cholesterol, and total triacylglycerol concentrations compared with placebo and provides a new, novel, food-based approach to lowering cholesterol in the general population.”³⁸

Red rice yeast is only one of a number of herbs that have known cardiovascular benefits. Garlic has been used as an antimicrobial (antibacterial, antiviral, antifungal and antiprotozoal) and for its cardio-protective and immune system affects.³⁹ Now we can see how those apparently different benefits may in fact be closely interrelated. Recent research has verified that Butcher’s Broom extract is a safe and effective treatment for patients suffering from chronic venous insufficiency.⁴⁰ Ginkgo biloba is a potent antioxidant which also enhances peripheral and cerebral circulation.⁴¹ Hawthorne like many natural products displays a number of affects that benefit the cardiovascular system. These include salt balancing, blood vessel relaxation, anti-inflammation, and anti-oxidation.⁴²

Cardio Herbs

- Hawthorne
 - Salt Balance, Vessel Integrity
- Ginkgo Biloba
 - Antioxidant, stabilizer
- Garlic
 - Antimicrobial, Antioxidant

Cardiovascular disease (CVD) is the number one cause of death in modern societies. Recent advances in science have thoroughly debunked our long held mechanical view of cardiovascular disease. The realization of the preeminent role of the immune system in protecting our cardiovascular system has opened up new and effective approaches to strengthening and supporting our cardiovascular health. The discovery of the links between stress and inflammation, and between inflammation and cardiovascular disease has given us an understanding of the personality component of cardiovascular disease. It is also of little surprise that metabolic toxins such as homocysteine would irritate and inflame the arteries adding to our cardiovascular problems.

SUMMARY of the Problem

- CVD is the # Killer
- CVD Starts Early
- CVD is NOT a Simple Plumbing Problem
- The Immune System is Critically Involved in CVD
- Infection may Initiate CVD
- Metabolic Toxins and Chronic Stress can Trigger Chronic Inflammation

Given our current understanding we have a number of approaches we can take to solving the problem of cardiovascular degradation. First we need a strong immune system so that infections are dealt with quickly and inflammation is controlled. We need to nutritionally support our blood vessels so

SUMMARY of a Solution

- Control Infection
- Control Inflammation
- Help the Blood Vessels Relax
- Protect the Heart and Arteries from Toxin and Oxidative Damage
- Increase the Pumping Efficiency of the Heart

they can effectively relax and stretch so blood can flow more freely and the back pressure on the heart stays within safe limits. We need to strengthen the antioxidant shield protecting our heart and arteries and effectively remove irritating toxins. Finally we need to increase the pumping efficiency of the heart so that it is able to maintain a good blood flow to meet the ever changing demands of our lives. Without extensive testing we may not know which of these issues is dominant in our individual situations. In all likelihood it is seldom that the solution will be found in just one factor. No matter what the main

issue is, all the other factors are likely to contribute to the overall problem. It is important then that we address each aspect in a balanced approach.

We can address each of the main issues with an array of nutritionally supportive interactive ingredients as shown in the summary chart below.

Summary of Nutritional Intervention for Cardiovascular Health

- Tune the Immune System
 - Transfer Factor, Zinc, Lysine
- Relax the Blood Vessels
 - Arginine, Magnesium, Gingko, Hawthorne, Butcher's Broom
- Support the Pumping Efficiency of the Heart
 - Magnesium, CoQ10
- Block Oxidative Damage
 - Selenium, Copper/Zinc
 - Beta carotene, Vitamin C, Vitamin E, Resveratrol
- Improve Toxin Clearance
 - Folic Acid, Vitamins B6 & B12 and Niacin
- Maintain Cholesterol Balance
 - Red Rice Yeast, Garlic

Combining components helps maintain a nutritional balance and allows the natural synergy of the components to be fully applied to the complex problem of cardiovascular health.

We live in an era when we have the understanding and tools to effectively fight back against our number one enemy: cardiovascular disease.

References:

- ¹ 2002 Heart and Stroke Statistical Update, American Heart Association.
- ² McGill HC Jr, McMahan CA, Herderick EE, Zieske AW, Malcom GT, Tracy RE, Strong JP: *Circulation* 2002 Jun 11;105(23):2712-8. Comment in: *Circulation*. 2002 Jun 11;105(23):2696-8.
- Zieske AW, Malcom GT, Strong JP. Natural history and risk factors of atherosclerosis in children and youth: the PDAY study. *Pediatr Pathol Mol Med* 2002 Mar-Apr;21(2):213-37.
- Strong JP, Zieske AW, Malcom GT. Lipoproteins and atherosclerosis in children: an early marriage? *Nutr Metab Cardiovasc Dis* 2001 Oct;11 Suppl 5:16-22
- ³ Libby P. Atherosclerosis: the new view. *Scientific American* May 2002, p 47-55
- ⁴ Black PH, Garbutt LD. Stress, inflammation and cardiovascular disease. *J Psychosomatic Res* 2002, 52, 1-23
- ⁵ American College of Cardiology March 2000 Meeting Abstracts
- ⁶ Farsak B, Yildirim A, Akyon Y, Pinar A, Oc M, Boke E, Kes S, Tokgozoglu L. Detection of Chlamydia pneumoniae and Helicobacter pylori DNA in human atherosclerotic plaques by PCR. *J Clin Microbiol* 2000 Dec;38(12):4408-11
- ⁷ Armitage GC. Periodontal infections and cardiovascular disease--how strong is the association? *Oral Dis* 2000 Nov;6(6):335-50.
- ⁸ Kirkpatrick CH. Properties and activities of transfer factor. *J Allergy Clin Immunol* 1975 Jun;55(6):411-21
- ⁹ See D, Mason S, Roshan R. Increased tumor necrosis factor alpha (TNF-alpha) and natural killer cell (NK) function using an integrative approach in late stage cancers. *Immunol Invest*. 2002 May;31(2): 137-53
- ¹⁰ Dadali VA, Rak AV, Stolpnik ES, McCausland CW, Oganova EA. Certain new aspect of the Transfer Factor effect. Materials of the VI International Symposium «Biological Active Substances and the problems of the optimization of Nutrition» Sochi, November 5-7 2002, P.62-63
- ¹¹ Wilson GB, Paddock GV. Process for obtaining transfer factor from colostrum, transfer factor so obtained and use thereof. United States Patent 4,816,563. March 28, 1989
- ¹² Hennen WJ, Lisonbee DI. Methods for obtaining transfer factor from avian sources, compositions including avian-generated transfer factor, and methods of use. United States Patent 6,468,534. October 22, 2002
- ¹³ Woods RK, Thien F, Raven J, Walters EU, Abramson M. Prevalence of food allergies in young adults and their relationship to asthma, nasal allergies, and eczema. *Ann Allergy Asthma Immunol* 2002 Feb;88(2): 183-9
- ¹⁴ Anet J, Back JF, Baker RS, Barnett D, Burley RW, Howden ME. Allergens in the white and yolk of hen's egg. A study of IgE binding by egg proteins. *Tnt Arch Allergy Appl Immunol* 1985;77(3):364-71
- ¹⁵ Fox C, Ramsomair D, and Carter C. *South Med J* 2001; 94(12): 1195-20
- ¹⁶ Innerarity S. Hypomagnesemia in acute and chronic illness. *Crit Care Nurs* 2000; 23(2): 1-19
- ¹⁷ Stigson, L. and I. Kjellmer (1997). "Serum levels of magnesium at birth related to complications of immaturity." *Acta Paediatr* 86(9): 991-4
- ¹⁸ Crippa G, Sverzellati E, Giorgi-Pierfranceschi M, Carrara GC. Magnesium and cardiovascular drugs: interactions and therapeutic role. *Ann Ital Med Int*. 1999 Jan-Mar;14(1):40-5
- ¹⁹ Stedman's Medical Dictionary, Houghton Mifflin Company, 1995
- ²⁰ Saari JT and Schuschke DA. Cardiovascular effects of dietary copper deficiency. *Biofactors* 1999; 10(4): 359-75
- ²¹ Neggers YH, Bindon JR, Dressler WW. The relationship between zinc and copper status and lipid levels in African-Americans. et al. *Biol Trace Elem Res* 2001; 79(1): 1-13
- ²² Racek J, Holecek V, Trefil L. [Indicators of oxidative stress in cardiovascular diseases. II. Nitrogenous substances, AGE-substances and antioxidants] *Vnitř Lek* 1999; 45(6): 373-8
- ²³ Miyazaki Y, Koyama H, Hongo T, Sasada Y, Nojiri M, Suzuki S. [Nutritional consideration for changes in dietary habit and health promotion practices in community health care: from the view point of selenium]
- ²⁴ *Nippon Koshu Eisei Zasshi*. 2001 Apr;48(4):243-57
- Zacarias-Castillo R, Hernandez-Rebollar AE, Zajarias-Rabchinsky A, Gonzalez-Barcena D. [Hyperhomocysteinemia. A new coronary risk factor] *Gac Med Mex*. 2001 Jul-Aug;137(4):335-45
- Ubbink JB, Becker PJ, Vermaak WJ. Will an increased dietary folate intake reduce the incidence of cardiovascular disease? *Nutr Rev* 1996; 54(7): 213-6.
- Clarke R, Armitage J. Vitamin supplements and cardiovascular risk: review of the randomized trials of homocysteine-lowering vitamin supplements. *Semin Thromb Hemost* 2000; 26(3):341-8. Auer J, Berent R, Weber T, Lassnig E, Eber B. [Homocysteine and cardiovascular risk] *Wien Med Wochenschr* 2001;151(1-2):25-8
- ²⁵ Price KD, Price CS, Reynolds RD. Hyperglycemia-induced ascorbic acid deficiency promotes endothelial dysfunction and the development of atherosclerosis. *Atherosclerosis* 2001; 158(1): 1-12
- Can AC and Frei B. Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans. *Am J Clin Nutr* 1999; 69(6): 1086-107
- ²⁶ Emmert DH, Kirchner JT. The role of vitamin E in the prevention of heart disease. *Arch Fam Med* 1999; 8(6): 537-42
- ²⁷ Leinonen M, Saikku P. Infections and atherosclerosis. *Scand Cardiovasc J* 2000; 34(1): 12-20
- ²⁸ Flodin NW. The metabolic roles, pharmacology, and toxicology of lysine. *J Am Coll Nutr* 1997; 16(1): 7-21
- ²⁹ Verma S, Anderson T. Fundamentals of endothelial function for the clinical cardiologist. *Circulation* 2002, 105, 546-549
- Libby P. Current concepts of the pathogenesis of acute coronary syndromes. *Circulation* 2001, 104, 365-372
- ³⁰ Hatsuoka S, Sakamoto T, Stock UA, Nagashima M, Mayer JE Jr. Effect of L-arginine or nitroglycerine during deep hypothermic circulatory arrest in neonatal lambs. *Ann Thorac Surg*. 2003 Jan;75(1):197-203; discussion 203
- ³¹ Wu G, Meininger CJ. Arginine nutrition and cardiovascular function. *J Nutr* 2000; 130(11): 2626-9. Boger RH, Bode-Boger SM. The clinical pharmacology of L-arginine. *Annu Rev Pharmacol Toxicol* 2001;41:79-99
- ³² Pearson PJ, Evora PR, Secombe JF, Schaff HV. Hypomagnesemia inhibits nitric oxide release from coronary endothelium: protective role of magnesium infusion after cardiac operations. *Ann Thorac Surg*. 1998 Apr;65(4):967-72
- ³³ Bhat KPL, Kosmeder JW, 2nd, Pezzuto JM. Biological effects of resveratrol. *Antioxid Redox Signal* 2001; 2(6): 1041-64

- ³⁴ Singh RB, Niaz MA, Rastogi V, Rastogi SS. Coenzyme Q in cardiovascular disease. *J Assoc Physicians India* 1998; 46(3): 299-306
- Kucharska J, Gvozdjakova A, Snircova M, Mizera S, Schramekova E, Schreinerova Z, Pechan I, Fabian J. [Determination of coenzyme Q10 and alpha-tocopherol levels in patients with cardiopathies of unknown origin: perspectives in diagnosis] *Bratisl Lek Listy* 1996; 97(6): 35 1-4
- ³⁵ Elmadfa I, Wagner KH. Non-nutritive bioactive food constituents of plants: tocopherols (vitamin E). *Int J Vitam Nutr Res*. 2003 Mar;73(2):89-94
- ³⁶ Chaudiere J, Ferrari-Iliou R. Intracellular antioxidants: from chemical to biochemical mechanisms. *Food Chem Toxicol*. 1999 Sep-Oct;37(9-10):949-62
- ³⁷ Vatassery GT, Smith WE, Quach HT. Ascorbic acid, glutathione and synthetic antioxidants prevent the oxidation of vitamin E in platelets. *Lipids* 1989 Dec;24(12):1043-7
- ³⁸ Heber D, Yip I, Ashley JM, Elashoff DA, Elashoff RM, Go VL. Cholesterol-lowering effects of a proprietary Chinese red-yeast-rice dietary supplement. *Am J Clin Nutr*. 1999 Feb;69(2):231-6
- ³⁹ Harris JC, Cottrell SL, Plummer S, Lloyd D. Antimicrobial properties of *Allium sativum* (garlic). *Appl Microbiol Biotechnol*. 2001 Oct;57(3):282-6
- ⁴⁰ Vanscheidt W, Jost V, Wolna P, Lucker PW, Muller A, Theurer C, Patz B, Grutzner KI. Efficacy and safety of a Butcher's broom preparation (*Ruscus aculeatus* L. extract) compared to placebo in patients suffering from chronic venous insufficiency. *Arzneimittelforschung*. 2002;52(4):243-50
- ⁴¹ McKenna DJ, Jones K, Hughes K. Efficacy, safety, and use of ginkgo biloba in clinical and preclinical applications. *Altern Ther Health Med*. 2001 Sep-Oct;7(5):70-86, 88-90
- ⁴² Holubarsch CJ, Colucci WS, Meinertz T, Gaus W, Tendera M. Survival and prognosis: investigation of Crataegus extract WS 1442 in congestive heart failure (SPICE)--rationale, study design and study protocol. *Eur J Heart Fail*. 2000 Dec ;2(4):431-7