HEALTH AND STRESS

The Newsletter of
The American Institute of Stress

Number 1 1998

BACK TO BUTTER, EGGS, STEAK AND CHEESE CAKE? WHY NOT?

KEY WORDS: cholesterol, diet, atherosclerosis, risk factors, antioxidants, eggs, MRFIT, the cholesterol cartel, homocysteine, folic acid, vitamin B_6, vitamin B_{12}, TMG, SAM, methylation, methyl donors

It has long been a common conclusion that cholesterol is the culprit that causes heart attacks and strokes. This is allegedly accomplished by the accumulation of atherosclerotic deposits that clog up coronary and carotid arteries, as well as other blood vessels. As a consequence, a massive crusade has been conceived to "lower your cholesterol count" by rigidly restricting dietary fat, coupled with aggressive drug treatment. Much of the impetus for this comes from speculation, rather than any solid scientific proof. It is financed by vested interests with powerful influences on the media as well as medical policy makers, who promote persuasive and appealing advertisements and news releases. It is easy to visualize that fats increase blood cholesterol, and how excesses accumulating in arterial walls could constrict and eventually choke the flow of blood.

ALSO INCLUDED IN THIS ISSUE

And there are tons of money to be made by pharmaceutical companies, makers and distributors of naturopathic and over-the-counter nutritional products, all sorts of food manufacturers and processors, blood testing laboratories, dietary programs, exercise equipment, and almost anything else that could conceivably help in the campaign to curtail cholesterol. Small wonder that all sorts of entrepreneurs are looking for some way to jump on and profit from this anti-cholesterol bandwagon, which often seems much more like a juggernaut.

All of this has led to considerable confusion, with conflicting claims of drug superiority, arguments that it is not the total cholesterol concentration in the blood, but rather the amount or ratio of "good" and "bad" components, or the level of triglycerides that may be critical. But suppose your cholesterol is elevated and that this is almost entirely due to high amounts of protective HDL. What should you do?

There are similar battles over the risks and benefits of margarine compared to butter, and this see-saw goes up and down every few years. Soups, stews, chocolate bars, and almost every conceivable kind of packaged food product now comes in some sort of low fat version. On the other hand, fats like those found in olive oils and peanuts have been found to help reduce heart attacks. Who or what are you expected to believe?

Health and Stress: The Newsletter of The American Institute of Stress is published monthly. Annual subscription rate $35.00 (U.S.), $45.00 (Foreign).

HEALTH AND STRESS
The Newsletter of
The American Institute of Stress

Paul J. Rosch, M.D., F.A.C.P.
Editor-in-Chief
home page: www.stress.org
e-mail: stress124@earthlink.net

Clarifying The Cholesterol Conundrum

Many of us have long argued that the role of dietary fat and cholesterol as the major cause of coronary heart disease has been blown out of proportion. However, this premise is so prevalent and has been pursued with such passion, that any contrary conviction is currently considered heresy. Yet, the preponderance of scientific evidence is clearly contradictory. Cholesterol is a very large, inert molecule, and it is hard to see how it could give rise to the inflammatory lesions of atherosclerotic plaque that invades the inner lining of arteries. These are much more reminiscent of some sort of infectious process, rather than the passive precipitation of a saturated fat solution. Indeed, recent research suggests that some atherosclerotic lesions may be due to infection with chlamydia and other microorganisms, especially in patients who rapidly redevelop blockage following bypass surgery.

The history of medicine is replete with dietary doctrines that subsequently fell into disrepute. Some primitive societies forbade eating tortoise for fear that this would slow down their hunters. Others banned rabbit, deer or jackal meat, which might cause warriors to be timid. Similarly, hedgehogs were to be avoided, since they curl up and play dead under stressful situations such as combat.

Our cholesterol taboo began around the beginning of the century, when the Russian physician, Nicolai Anichkov, demonstrated that he could produce atherosclerotic lesions in rabbits by feeding them a high cholesterol diet. Nobody paid very much attention to this until the Korean War, when the Army sent pathologists to perform autopsies on battle casualties to study the ballistic characteristics of fatal wounds. Since the average age of their subjects was 22, they were quite surprised to find that three out of four already showed evidence of significant coronary artery arteriosclerosis. In 10 per cent, there was almost complete obstruction of at least one major coronary vessel.

The reason for this was unclear. Although the stress of combat could have been a factor, it was believed that the basic problem was that their diet was too high in fat. This would result in an elevation in blood cholesterol that caused atherosclerotic deposits, much like Anichkov had reported in his rabbits. Further support for this theory came from a study showing that Japanese and other populations who consumed much less animal fat than we do, had heart attack rates that were almost 90 per cent lower than ours. One prominent proponent of this fatty diet - heart attack hypothesis, flaunted the statistics obtained from seven countries as follows:

> "There is a remarkable relationship between the death rate from degenerative heart disease and the proportion of fat calories in the national diet. A regular progression exists from Japan through Italy, Sweden, England and Wales, Canada and Australia to the United States. No other variable in the mode of life besides the fat calories in the diet is known which shows such a constant relationship to the mortality rate from coronary or degenerative heart disease."

While this seems impressive and convincing, as we shall see, this and other epidemiologic data have been massaged and manipulated in an adroit manner to produce the desired results. The First Law Of Statistics states that given enough statistics, you can prove anything you want. The basic problem here is that association never proves causation. This is the fallacy that underlies the entire concept of the significance of risk factors. You cannot use one statistic to prove another statistic! "Figures don't lie" - but liars can certainly figure.

The Risk Factor Fantasy And MRFIT

There are over 300 risk factors for heart attacks, including a deep earlobe crease, being single, living in Glasgow or Eastern Finland, vertex baldness, premature gray hair, a pot belly, snoring, low toe nail selenium levels, high serum iron, as well as hypertension, smoking and elevated cholesterol. However, this simply means that statistically, each of these are frequently associated with heart attacks. It does not necessarily imply that one causes the other. Risk **factors** are merely nothing more than risk **markers**. Plastic surgery on your ear lobes, abdominal liposuction, a hair transplant, getting married, or moving to Hawaii, is not very likely to lessen your risk for a heart attack.

The fallacy of risk factors originated with the famous Framingham Study which started around fifty years ago. Residents of this small manufacturing town in Massachusetts were carefully interviewed, examined, and periodically studied to see if any of these findings could predict the likelihood of a future heart attack. As the data accumulated, it became quite apparent that those with elevated cholesterol, hypertension, or who smoked cigarettes, were at the greatest risk. Any combination of these further increased the odds proportionately. The conclusion was clear. The way to prevent heart attacks was to bring elevated cholesterols and blood pressures down to normal values, and get people to give up cigarettes.

That was the mission of the massive Multiple Risk Factor Intervention Trial, which had the appropriate acronym MRFIT. Conducted at top medical centers throughout the United States, it was designed to normalize cholesterol and blood pressure and stop cigarette smoking in middle-aged men at increased risk for a heart attack because of these presumed causes. Seven years and $115 million later, although all of these goals were achieved, heart attack rates were not reduced. Not only did the treated group fare no better than matched controls who maintained their usual lifestyles, deaths due to coronary heart disease were actually higher in those who had been receiving drugs for high blood pressure. While that should have put the risk factor notion to rest, it only intensified the activities of the cholesterol cartel, whose statisticians struggled for some explanation.

If you get people to stop smoking, you will significantly reduce the incidence of lung cancer and emphysema. And lowering elevated blood pressures will help prevent strokes. Smoking and hypertension can cause these disorders. However, they are not a direct cause of heart attacks, and neither is an elevated cholesterol in and of itself. Why you smoke or have hypertension may be more important, and for some, stress could be the common denominator. Many people smoke and have high blood pressure because of increased stress. And stress has a far more powerful effect on serum cholesterol than dietary fat intake. Pipe and cigar smokers, who tend to be more relaxed, have half as many heart attacks as people who never smoked.

Neither normal cholesterol, or even LDL bad cholesterol produce atherosclerotic plaque when force fed to animals. It is only oxidized cholesterol, or oxidized low density lipoproteins that can produce these changes. The reason Anichkov's rabbits developed atherosclerosis when he put them on a high cholesterol diet is that he did not feed them pure cholesterol, but an oxidized form of fat, which is quite different. Humans consume these in the form of "trans" fats, which are artificial. In 1912, food chemists discovered how to partially hydrogenate vegetable oils, and convert them into solid and more stable cooking fats and spreads. However, these new compounds contain fatty acids that are foreign to normal metabolic mechanisms, and result in a rise of oxidized cholesterol by-products.

The marked atherosclerosis found in Korean war casualties was not present in young Americans killed in civilian accidents. Their fatty deposits were also quite different, since inflammatory changes were minimal. Although the chronic stress of combat may have contributed, it is most likely that increased consumption of powdered eggs and other rations rich in oxidized cholesterol was the major reason for the atherosclerosis seen in Army personnel. The findings from the Korean conflict showing that American casualties had more extensive atherosclerosis than those from other countries, prompted a number of investigations to prove that a high fat diet would speed you down the road to a heart attack. The persuasive study previously quoted was widely publicized as proof of this.

(Continued on page 4)

(Continued from page 3)

However, some scientists subsequently became suspicious as to why these specific seven countries were selected. And when they included the statistics from 22 countries, the fat diet theory was completely destroyed. Fat consumption in Israel and Mexico was similar, but deaths from coronaries were eight times higher in Israel. While U.S. fat intake was only slightly more than Norway's, our cardiac death rates were three times higher. The problem is that there are different kinds of fats, some of which may actually help prevent heart disease. Accelerated atherosclerosis and heart attacks are relatively uncommon in Eskimos and African Massai tribes, both of whom have high fat diets. But the Eskimos consume a lot of fish oils rich in fatty acids that have been shown to have cardioprotective effects. The high fat "Mediterranean" and "French Paradox" diets are rich in monounsaturated fats that also help prevent heart attacks because of their antioxidant effects.

At the height of the U.S. epidemic a few decades ago, heart attack rates were lowest in those midwest farming areas where fat consumption was the highest. This was attributed in part to the increased stresses of urban life. However, the diet of farm families tends to be rich in fresh milk, butter, cheeses and eggs. These are really healthy, rather than harmful, since they also contain powerful protective antioxidants. The public is unaware of this because of adverse advertising claims from producers of competitive food products that have a longer shelf life, but are much more hazardous.

Getting Even More Egg On Their Face

A recent report on 800,000 nurses who were followed for 14 years showed that there was no difference in heart attack rates whether total fat consumption was 29 percent or 46 percent of their daily calories. The greatest risk was seen only in those with a high intake of trans fats. Trans fats are particularly damaging because they not only oxidize and raise bad LDL, but lower good HDL. This should not be construed as implying that a high saturated fat diet is not without hazards. There are links with some cancers, and resultant increased blood viscosity could contribute to clot formation.

In some reports, a high saturated fat dinner has been associated with a heart attack within 24 hours. However, this is not from atherosclerosis, which takes time to develop, but more likely, a coronary occlusion due to a clot in a vessel that is already narrowed and has diminished blood flow.

The ingestion of food normally triggers the release of nitric oxide, which dilates blood vessels to facilitate the absorption of nutrients. However, oxidized fats and particularly triglycerides stimulate the production of free radicals that inactivate nitric oxide and prevent blood vessel expansion. In one study, volunteers fasted for 12 hours overnight, and then ate a breakfast that included an Egg McMuffin, sausage McMuffin, and two hash brown patties for a total of 900 calories, consisting of 50 grams of fat, 14 grams of saturated fat, and 225 mg of cholesterol. Failure of blood vessels to dilate normally following this was demonstrated by ultrasound and sophisticated blood flow measurements. However, when the subjects took 1000 mg of vitamin C and 800 iu of vitamin E, and then ate the identical meal, there was no reduction in arterial widening or blood flow. That's because these powerful antioxidants neutralize free radicals.

Eggs in particular have taken a bad rap, since they are widely believed to be one of the most deadly cholesterol carriers. However, several years ago, *The New England Journal Of Medicine* reported a well documented case of an 86-year-old man with no history of heart disease and a normal electrocardiogram. What was unusual, despite his age, was that **he had eaten two dozen eggs every day for over 15 years!**

While that may seem hard to believe, he strongly believed that they improved his strength and vitality, enjoyed eating eggs in any form, and had them with every meal and in between. His fetish had created a problem fifteen years previously, when he was admitted to a nursing home. It was resolved with an arrangement allowing him to privately purchase as many eggs as he wanted. Nursing home records reveal that he had received fourteen dozen eggs every week since then. All of the staff confirmed that he consistently consumed two dozen daily. Yet, his cholesterol and electrocardiogram were perfectly normal.

The Homocysteine Hypothesis Versus The Power Of The Cholesterol Cartel

Almost 3 decades ago, Dr. Kilmer McCully, a young pathologist at Harvard Medical School, proposed that the culprit in coronary heart disease was not cholesterol but a chemical called homocysteine. He became intrigued with this hypothesis after studying autopsy cases of two children suffering from homocystinuria. This is a rare genetic disorder in which blood homocysteine levels are unusually high because of a deficiency of liver enzymes that normally break it down into harmless compounds. As a consequence, excess homocysteine overflows into the urine, where it is rarely found in any significant amount. In both children, the cause of death was a heart attack due to severe and generalized arteriosclerosis, identical to that usually seen only in elderly individuals.

McCulley proposed that the increased homocysteine had directly damaged the inner lining of arterial walls, setting up an inflammatory process that led to the development of obstructive atherosclerotic plaque. He suspected that such injury could eventually occur in other individuals who had chronic elevated homocysteine levels for other reasons. After he injected rabbits with homocysteine, he was amazed to find that atheroscerotic plaques had developed in their coronary arteries within weeks.

Homocysteine is derived from methionine, an essential amino acid found in meats and animal products. McCulley proposed that eating too much of these could be harmful not because they contained too much cholesterol, but high levels of methionine. Under normal circumstances, certain B complex vitamins metabolize methionine and homocysteine into compounds that are useful and safe. However, meats and dairy products are low in these important water soluble vitamins, which are found mainly in fresh fruits and vegetables. If dietary intake is inadequate, elevated homocysteine blood levels could eventually cause damage. He believed this could readily occur in the average American diet of meat, dairy products, and canned, boxed, processed, or preserved foods. Most of these attempts to increase shelf life also destroy these particularly important B vitamins.

His preposterous "protein intoxication" proposal flew in the face of the prevailing high fat food and cholesterol theory of atherosclerosis. This obviously could have had disastrous financial implications for the pharmaceutical industry, food manufacturers and processors, as well as many others with extensive commercial interests who were making fortunes. But others were now beginning to corroborate McCulley's theory. In 1976, Australian researchers published the first human study showing a definite connection between high homocysteine blood levels and coronary heart disease. In addition, his rabbit studies had now been confirmed in baboons, making them more relevant for humans. Despite this, NIH grants for his research were not renewed, and his circle of supportive colleagues started to shrink.

His staff was also consistently cut down, and his laboratory was relocated to smaller quarters in the basement of Massachusetts General Hospital. Other sources of funding also mysteriously dried up, and since the Department was unwilling or unable to support him, he was asked to leave. The hospital Director explained that he had not proven his theory, and told him "never to come back." Since his tenure at Harvard depended on his appointment at Massachusetts General Hospital, this was also terminated at the end of 1978.

Dr. Irwin Rosenberg, Director of the U.S.D.A. Human Nutrition Research Center on Aging at Tufts University, a medical school classmate, also worked in the Hospital's Department of Medicine at the same time. He is convinced that McCulley would have been kept on and supported if he had engaged in any other kind of research that did not threaten the contemporary cholesterol dogma. Dr. Thomas James, a Texas cardiologist who was President of the American Heart Association in 1979 and 1980, also confirmed that funding was simply not available for anything "that went in other directions than cholesterol. You were intentionally discouraged from pursuing alternative questions. I've never dealt with a subject in my life that elicited such an immediate hostile response." The degree of this viciousness is difficult to believe, but can be vividly illustrated by the subsequent deliberate campaign to thoroughly discredit and destroy McCulley.

(Continued on page 6)

(Continued from page 5)

After his dismissal from Harvard, he was interviewed on a television program, and promptly received a telephone call from the Public-Affairs Director of Massachusetts General Hospital. He was told to "shut up" and that they "didn't want the names of Harvard and Massachusetts General Hospital to be associated with my theories." Another Harvard classmate, who subsequently became the Director of the heavily funded Arteriosclerosis Center at M.I.T., called McCulley's theory "errant nonsense" and described it as a "hoax that is being perpetrated on the American public."

Although well trained, and an ideal candidate for many positions that were being offered, it took him two years to find another job. He thought he did well on numerous interviews, and was surprised that he never heard anything further. When he and others made appropriate inquiries, they usually ran into a stone wall of silence, but there were repeated rumors of "poison phone calls" emanating from Harvard. After he sought assistance from a friend who was a very prominent Boston attorney, things changed dramatically. He promptly obtained his present position at the Veterans Administration Hospital in Providence, where he was able to expand his homocysteine research. In addition to inducing arteriosclerosis in experimental animals, he also investigated the possible relationship between excess homocysteine in stroke and cancer. Since then, possible links with all sorts of disorders ranging from cirrhosis and fibromyalgia to depression and impotence have been reported.

The tremendous power of the cholesterol cartel culminated in the National Cholesterol Education Program, a government sponsored crusade whose objective was "to reduce the prevalence of elevated cholesterol in the United States, and thereby contribute to reducing coronary heart disease morbidity and mortality." It was spearheaded by hand picked cardiologists and scientists, many of whom were subsidized by vested interests. They suggested following a low fat diet for several months, and if this failed, patients would then have to take powerful cholesterol lowering drugs forever. There were authoritative assurances and promises of progressive health rewards as serum cholesterol fell every few milligrams.

However, everyone knew that low fat diets rarely resulted in a significant reduction of cholesterol levels. More importantly, there was no proof that lowering cholesterol could save lives. Indeed, all the drug trials that had been performed had shown just the opposite! Nevertheless, in an unprecedented action, the panel's recommendations were released directly to the public with a massive media blitz, rather than in a peer reviewed medical journal. Physicians had to wait months before the actual report appeared, so that they could discuss it intelligently with their patients. Many doubt that it was just by chance that this press release happened to coincide with the FDA's approval of lovastatin, which immediately became the leading low cholesterol drug, and maintained that position for years.

There was particular concern about aggressive drug therapy in children, since cholesterol is an essential building block for important hormones and other steroids. There was and is absolutely no evidence that lowering cholesterol provides any cardiovascular benefits in individuals 65 years of age or older. There were also reports of severe behavioral changes, including an increase in depression and suicide, possibly related to a lowering of brain serotonin concentrations. Anti-cholesterol drugs and low-fat foods are billion dollar industries that have a large stake in keeping the cholesterol crusade on course. McCulley's case is not an isolated instance. Similar pressures and prejudices are still prevalent, particularly in the even more lucrative weight loss industry. These often overlap and contribute to public confusion, as noted below.

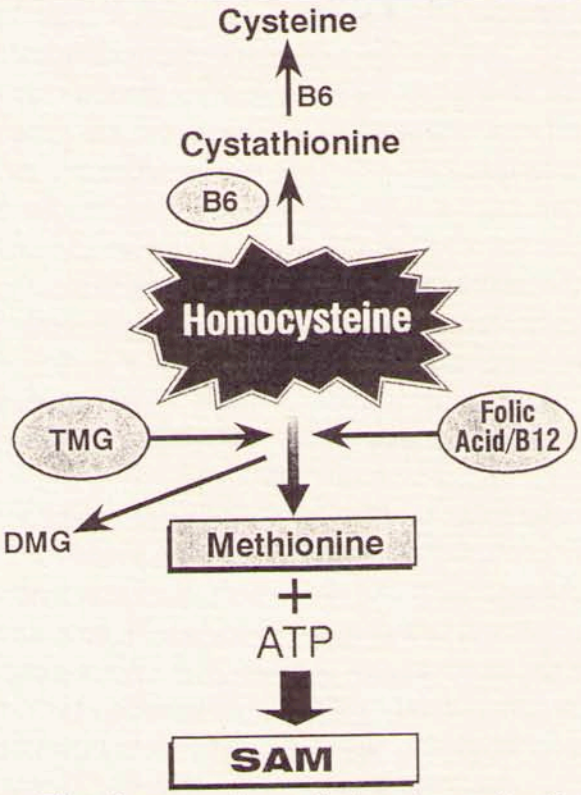
"We'd like to lose weight and lower our cholesterols while having a good time."

Beyond Cholesterol And Antioxidants

When data from the Framingham study was reexamined, a significant correlation between high homocysteine and low levels of vitamins B_6, B_{12} and folic acid was found. Further analysis revealed a clear connection between homocysteine levels and the degree of atherosclerosis in the carotid arteries. In another long term ongoing study of almost 15,000 physicians, blood samples taken at the beginning of the project were still available. When these were analyzed, it was found that higher homocysteine levels were much more likely to predict heart attacks than abnormally elevated cholesterol. What was particularly impressive, is that almost all these measurements were within what is generally considered to be the normal range. Such a clear linear relationship does not exist for either cholesterol or LDL. It is now believed that homocysteine levels may be up to 40 times more acccurate than cholesterol for predicting coronary artery disease. Close to 50 studies have also shown a significant correlation between high homocysteine and various types of vascular disease, including stroke and deep vein thrombosis.

Homocysteine is normally converted into compounds the body needs, like cysteine, and adenosine triphosphate. If this does not happen and homocysteine is left intact, it causes an increase in platelet stickiness and clumping, and promotes the oxidation of lipids like LDL, which facilitates their binding to fibrin and other proteins. As blood levels rise, homocysteine damages the inner lining of arterial walls, making them more like sandpaper than teflon. This sets the stage for the production of atherosclerotic plaque and proliferation of smooth muscle that clog up vessels.

Some entreprenuers suggest reducing the intake of methionine, from which homocysteine is derived. In that way, money could be made from "methionine free" foods, or meats that are "low methionine", and such signs may well appear in supermarkets. However, methionine is an important amino acid required for the synthesis of protein, maintenance of cartilage, and formation of other very important amino acids, like carnitine. The problem is not methionine, but failure to convert homocysteine into compounds that are useful and safe. This can be accomplished effectively, safely, and inexpensively. Although this information is readily available, it is not widely disseminated since there is relatively little profit incentive.



The diagram above depicts how vitamins B_6, B_{12}, and folic acid can convert homocysteine into compounds that promote health. For most people, a diet rich in fresh fruits, vegetables, beans, and whole grains provides more than enough of these B complex methyl donors. Another potent methylating agent is TMG (trimethylgycine), or betaine, a substance found in abundance in sugar beets. Since each of these affects different pathways, their combination provides a synergistic effect. Methylation is a crucial process that helps prevent aging, atherosclerosis and cancer by protecting DNA from damage.

Some individuals may require more of one than another because of faulty diet or a genetic enzymatic defect. Homocysteine levels rise as we grow older, and are increased by smoking, excessive alcoholic intake, synthetic estrogen, chemotherapy, and other drugs which interfere with vitamin B_6. Specific supplements, and particularly TMG, should be taken daily in such situations to insure that homocysteine is converted to ATP, which is the source of energy for all cells. Another important by product is SAM (S-adenosylmethionine). Synthetic SAM has been used to treat depression and fibromyalgia, and, as will be seen, can have dramatic clinical effects.

Ignore The Experts And Eat What You Like

That was the advice of one authority with respect to low cholesterol diets. Homocysteine may not be the Holy Grail for heart disease, since a variety of factors can contribute to atherosclerosis. However, it offers a hell of a lot more hope, and has none of the hype associated with cholesterol therapy. Treatment is simple, safe, effective, and inexpensive. It does not require stringent dietary restrictions, or costly drugs that can have serious side effects. There are no hazards associated with any homocysteine lowering therapies, nor would any be anticipated, since the cornerstone of treatment involves vitamins and nutrients the body needs. Many of these seem to supply other surprising salubrious benefits, as other manifestations of homocysteine surplus have become increasingly demonstrated.

For example, it has been well established that depression is a risk factor for heart attacks. However, it is not known whether this is simply another statistical association, or there may be some cause-effect relationship between the two. Heart attack victims are understandably depressed, and studies show that they have higher mortality rates. Depressed patients often have higher levels of stress related hormones, which have been shown to injure heart muscle, promote clot formation, as well as serious disturbances in rhythm. Some antidepressant drugs cause abnormal rhythms that can also result in sudden death. At this year's American Psychiatric Association annual meeting, researchers reported a "statistically significant positive relationship between serum levels of homocysteine and depression." Another study found that depressed patients who failed to respond to Prozac had higher homocysteine levels, and that lowering this with folic acid improved results. Paradoxically, both reports came from the same prestigious hospital that kicked McCulley out, and told him never to come back, or mention that his research had been conducted there.

A future Newsletter will include a review of new testing procedures for homocysteine and the various methyl donors responsible for its complete conversion into compounds that prevent atherosclerosis, cancer, depression, and other age related disorders. We will also discuss revised guidelines on what constitutes optimal blood levels, rather than the current norms which have little clinical significance. This is necessary to determine which supplements to take, how much of each, and when. Meal times might be best, and there is much more to learn. One 16-year-old patient with convulsions who was unable to walk because of severe peripheral neuropathy, had no detectable SAM in her body. Giving all the B complex vitamins lowered homocysteine to normal, but did not improve her symptoms. However, all of these disappeared completely when betaine (TMG) was added, and SAM was restored. While all of these vitamins and nutrients are quite safe, excesses of some could cause problems under certain conditions. Taking 800 mcg of folic acid, 50 mcg of B6, 500 mcg of B12, and 1000 mg of TMG daily seems to be prudent, but stay tuned, since this could change as new methyl donor forumlations are devised. In the interim, these supplements could make your life less stressful by letting you eat what you like without as much guilt, or fear of a fatal heart attack from a juicy steak and french fries, followed by cheese cake.

Paul J. Rosch, M.D., F.A.C.P.
Editor-in-Chief

ISSN # 1089-148X

HEALTH AND STRESS
The Newsletter of
The American Institute of Stress

124 Park Ave., Yonkers, New York 10703

Non-Profit Organization
U.S. Postage
PAID
Yonkers, NY
Permit No. 400