HEALTH AND STRESS

The Newsletter of The American Institute of Stress

July 2007

IS STRESS THE LEADING CAUSE OF CORONARIES?

KEYWORDS: Metabolic Syndrome, "Broken Heart" syndrome, sleep apnea, REM sleep, HRV, Stewart Wolf, Roseto, James Lynch, A Cry Unheard, homocysteine, IL-6, TNF, CRP, free radicals, oxidative stress, Chlamydia pneumoniae, heat shock proteins, electrical circulatory system, Sodi Pallares, Bioelectromagnetic Medicine

There are undoubtedly many factors that can significantly contribute to or cause coronary disease. However, as explained in our last Newsletter, there is overwhelming evidence that cholesterol, LDL or a high fat diet are not in this category. The same holds true for a large number of other alleged "risk factors" like a deep earlobe crease or premature baldness. These are really "risk markers" that merely show some statistical association rather than any causal relationship. Plastic surgery, hair transplants or procedures that correct such coincidental items will not result in a concomitant reduction in coronary events or deaths – nor does lowering cholesterol and LDL.

Previous Newsletters have also focused on the important role of stress that helps to explain some of these statistical links. For example, stress produces a far more profound rise in cholesterol than fat consumption; stress elevates blood pressure, and also frequently promotes cigarette smoking, the three traditional risk factors. Stress can also contribute to coronary disease in many other indirect ways. There is growing evidence that coronary atherosclerosis can be due to chronic inflammation that results from relatively innocuous infectious diseases. CRP (C Reactive Protein), a leading indicator of inflammation, as well as antibody titers to Chlamydia, herpes viruses and other microorganisms are elevated in many patients with asymptomatic heart disease. Chlamydia pneumoniae, a bug responsible for a common mild flu-like illness, has been cultured from coronary and cerebral arterial plaque and it has been well established that stress suppresses immune system resistance to numerous bacteria and viruses.

Stress can also contribute to coronary atherosclerosis and death via more direct effects. In some instances, it may be a chronic disturbance of the hypothalamic-pituitary-adrenal cortical axis that produces increased levels of cortisol. Stress induced cortisol secretion clearly causes deep abdominal fat deposits that secrete inflammatory chemicals and increases insulin

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- Job Pressures, Marital Strife And More Proof Of The Role Of Stress
resistance, blood sugar, triglycerides, blood pressure and other manifestations of metabolic syndrome, a powerful predictor of coronary disease. This has been confirmed in animal studies as well as patients with Cushing's disease, since removal of stress or the source of increased cortisol can reverse these changes and also reduce "apple shaped" obesity from deposition of abdominal fat.

There are also "fight or flight" responses to acute stress that stimulate the sympathetic nervous system and the secretion of catecholamines, like adrenaline and noradrenaline, that trigger lethal disturbances in heart rhythm, a major cause of sudden death. Other immediate responses to stress promote platelet clumping that favors the formation of blood clots and reduce fibrinolytic activities that would normally dissolve them. **Stress can also cause a myocardial infarction that occurs without evidence of any coronary artery obstruction from a clot or atherosclerosis** due to increased secretion of noradrenaline at nerve endings in heart muscle. This produces distinctive microscopic "contraction band" necrotic lesions in the ventricle that are frequently seen in people and animals that have died suddenly following severe stress. In other instances, patients may have severe chest pain, difficulty breathing and all the signs and symptoms of an impending heart attack. Abnormal ECG's and blood tests are consistent with this diagnosis and imaging studies confirm that much of the heart is not pumping properly. **However, when angiograms are performed to determine the site of blockage, no obstruction can be found.** Some patients may require medication for a short period to maintain blood pressure but most recover spontaneously within a day or two with no evidence of any permanent heart damage. This disorder is due to a barrage of stress hormones that paralyze heart muscle and prevent the circulation of blood to vital structures. The portion of the heart closest to the aorta is usually spared, so that with each beat, only this section contracts and the heart resembles a narrow-necked vase. The Japanese first described this disorder over 15 years ago and called it *takotsubo*, after a type of octopus trap with a very similar vase-like shape. While initially thought to be rare, it has been increasingly reported and is now referred to as stress cardiomyopathy, MINCA (myocardial infarction with normal coronary arteries) and more recently, "Broken Heart" syndrome.

In one report of 409 consecutive heart attack patients who underwent coronary angiography, 34 had normal vessels or no evidence of obstruction. More than half of these had experienced some very recent stressful event. One woman awoke in bed to find her husband dead beside her, another saw a jogger struck by a car and a man had just been fired from his job. (Strunk B, Shaw RE, et al. High incidence of focal left ventricular wall motion abnormalities and normal coronary arteries in patients with myocardial infarctions presenting to a community hospital. *J Invas Cardiol*, 2006; 18:376-81.) For reasons that are not clear, "Broken Heart" syndrome occurs primarily in postmenopausal women with no history of prior heart disease. (Wittstein IS, Thiemann DR, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *NEJM*, 2005; 352:539-548.) This type of microvascular angina appears to be due to impaired function of the endothelial cells lining the walls of small arteries and arterioles that prevents them from dilating fully in response to appropriate stimuli. **Endothelial dysfunction is present in approximately half of women with chest pain but no evidence of blockage in large coronary arteries.** (Reis SE, Holubkov R, Smith AJC et al. Coronary microvascular dysfunction is highly prevalent in women with chest pain in the absence of coronary artery disease. *Am Heart J*, 2001; V. 141: 735-741.) Heart attacks that cause permanent damage also often occur within hours following emotional stress in susceptible individuals. In one report, researchers studied 34 men who had recovered from heart attacks that occurred an average of 15 months earlier. Fourteen of these had experienced emotional stress such as receiving news about a sick or deceased relative or anger due to arguments less than two hours before their attack. All completed a series of mentally challenging tests and it took longer for systolic blood to return to normal for those in the antecedent stress group. Blood tests taken before and immediately after the mental stress
tests also showed that platelet aggregation that causes clots had doubled in this group, whereas it was unchanged in men who had not experienced antecedent stress. (Strike PC, Magid K, et al. Pathophysiologic processes underlying emotional triggering of acute cardiac events. *PNAS*, 2006; 4322-4327.)

Depression, anxiety, hostility and anger, which are often stress related, have all been demonstrated to significantly increase risk for heart attacks and deaths due to coronary disease. In many instances, these are associated with increased levels of specific stress induced hormones and chemicals that could explain these links. Some of these effects of stress on the heart that also affect other structures are illustrated below.

Pathophysiologic mechanisms by which chronic stress and affective disorders, such as depression, may promote atherosclerosis. These stressors activate the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS) and affect behaviors. Multiple adverse peripheral effects can ensue from this neuroendocrine, sympathetic, and behavioral activation, as shown. The neuroendocrine changes emanating from these stressors can also induce a state of heightened physiologic responsivity to acute stress that can interact with chronic stressors to cause more adverse effects. ANS = autonomic nervous system; Endo. = endothelial. (From Rozanski A, Blumenthal JA, Davidson KW, et al. The epidemiology, pathophysiology, and management of psychosocial risk factors in cardiac practice. The emerging field of behavioral cardiology. *J Am Coll Cardiol*, 2005; 45:637–651.)

The above is far from a complete picture. Stress increases levels of homocysteine, which has been demonstrated to cause coronary atherosclerosis in numerous studies. High homocysteine is also a significant risk factor for osteoporosis, as well as memory loss and neurodegenerative diseases that are not listed in this diagram. (Herrmann W, Herrmann, M, Obeid R. Hyperhomocysteinaemia: A critical review of old and new aspects. *Current Drug Metabolism*, 2007; 8:17-31) Also not included, or emphasized sufficiently is the importance of specific stressors and the varied mechanisms by which they can contribute to coronary disease, as indicated by the following examples.
The Self-Sustaining Stress ↔ Insomnia ↔ Heart Attack ↔ Stress Cycle

Stress is the leading cause of insomnia, insomnia is a frequent source of stress, and both are associated with an increased incidence of heart attacks. Heart disease can also cause sleep disturbances and stress, leading to a vicious repetitive cycle for some individuals. Most studies demonstrating these relationships have been done in men but women are also affected. In one that followed 122,000 women for over 10 years, Harvard researchers found that those who slept five or less hours a night were 82 percent more likely to have a heart attack compared to others who got eight hours. Even women who got six hours of sleep a night boosted their heart attack risk by 30 percent. (Ayas N, White DP et al. A Prospective Study of Sleep Duration and Coronary Heart Disease in Women. Arch Int Med, 2003; 163:205–209). A report just released at a June 13 conference now shows that even having five successive nights of poor sleep can impair cardiac function. Researchers evaluated 39 healthy volunteers after one night of getting at least 8 hours of sleep and again only getting four hours of shut-eye for five nights. All subjects had much faster heart rates following sleep deprivation nights but more importantly, they showed less heart rate variability (HRV), the naturally occurring beat-to-beat changes in heart rate that reflect the ability to automatically adapt to respiratory changes and stress. Diminished HRV is a significant risk factor for heart attacks, sudden death and hypertension. Another study demonstrated that sleep deprivation also reduces HRV in experimental animals. (Banks S, et al. Sleep reduction reduces heart rate variability, Sard C, Hayward L. Changes in heart rate variability in spontaneously hypertensive rats following sleep deprivation. Presentations made June 13 at SLEEP 2007, the 21st Annual Meeting of the Associated Professional Sleep Societies). The increased incidence of heart disease and hypertension seen in workers with second and third shift jobs has also been attributed to decreased and disturbed sleep. However, sleeping for more than 8 hours does not necessarily provide protection. The Harvard study also found that women who regularly slept more than nine hours a night increased their heart disease risk by 57 percent. The reasons for this are not clear but it was suggested that people who sleep excessively tend to weigh more, smoke more, drink more alcohol and exercise less than others.

Heart attack patients often report having experienced insomnia in the period immediately prior to the event and the quality and type of sleep is important. Heavy snoring and obstructive sleep apnea are also associated with an increased incidence of hypertension and heart attacks. A study presented at the May 21, 2007 American Thoracic Society conference found that sleep apnea increases the risk of having a heart attack or dying by 30 percent over a period of four to five years. Rapid eye movement (REM) sleep, which is associated with dreaming, is most frequent in the period immediately before waking up in the morning. It is accompanied by a rise in sympathetic nervous system activity and the secretion of stress related hormones that increase blood pressure, heart rate, platelet clumping and clot formation. Many believe this explains why most heart attacks and strokes occur in the morning shortly after waking up, and especially on Mondays. In one study, heart attack risk was 20 percent greater for men and 15 percent higher for women on Mondays. This is thought to be due to the added stress of returning to a hectic workweek after two days of relative relaxation, although heavy weekend cavorting and drinking could play a role.

Cortisol levels are generally high immediately upon waking, increase over the next 30 minutes and fall to low values at bedtime. Stress can alter this normal healthy pattern in several ways. One large study showed that when older adults go to bed lonely, sad or overwhelmed, they have much higher levels of cortisol than normal shortly after waking the next morning. People who experience anger throughout the day have higher bedtime levels of cortisol and such stress related rises in cortisol increases risk for heart disease. (Adam EK et al. Day-to-day experience-cortisol dynamics. Proceedings of the National Academy of Sciences, published online Oct. 30, 2006). Lack of sleep may contribute to coronary disease by promoting free radical production and inflammation. C-reactive protein (CRP), a marker of inflammation that has
been shown to be predictive of future coronary events, is increased by sleep deprivation. Insomnia and heart disease is a two-way street since heart failure patients may wake up during the night due to the accumulation of fluid in the lungs that causes difficulty breathing. Heart failure can also cause sleep apnea, a breathing problem that can awaken sufferers repeatedly throughout the night. Other coronary patients may have interrupted sleep due to recurrent bouts of nocturnal angina, atrial fibrillation or palpitations.

The Cardiovascular Consequences Of Sudden Societal And Cultural Change
The stress of relatively rapid sociocultural change can have profound effects on the cardiovascular system that are not generally appreciated. Numerous epidemiologic surveys show that the stresses associated with abandoning traditional lifestyles can result in a startling increase in deaths from coronary disease and stroke. As noted in a prior Newsletter, when Japanese men moved from their homeland to the U.S. decades ago, deaths from coronary heart disease eventually quadrupled. The incidence of coronary deaths was lowest in Japan, increased in Hawaii expatriates and jumped even higher for Japanese in California. However, Japanese in Hawaii who maintained their customary ways of life were protected, even though their cholesterols rose. This had nothing to do with changes in diet. Those who adopted Western ways but still stuck to their Japanese low fat diets had twice as much heart disease as others who preferred high fat American fast foods but continued to adhere to their ancestral values and lifestyles. A study of over 3000 California Japanese-Americans similarly found that those who strictly retained their time-honored traditions had the same low rate of coronary disease found in Japan, whereas the most "Americanized" had a three to five-fold increase. This significant rise could also not be explained by differences in diet, smoking, hypertension or cholesterol levels. Indian immigrants were at even greater risk, with a fifteen-fold rise in heart attacks, despite the fact that almost half adhered to a strict vegetarian diet. Researchers believe that the most likely explanation for these observations is that protection from coronary disease stems from the powerful stress buffering effects of maintaining strong social support, a firm religious faith and cohesive group activities that promote a sense of stability and "togetherness". This is in sharp contrast to Americans who tend to be more mobile and much less stable with respect to job and geographic changes. Many also strive to achieve their goals through personal rather than group efforts, even if their pursuit of private satisfaction is detrimental to others.

An excellent illustration was Stewart Wolf's study of Roseto, a small northeastern Pennsylvania town of 1600 less than 65 miles from Manhattan and Philadelphia. Stewart was intrigued by a local doctor who told him that Rosetans under the age of 65 rarely had heart attacks. Stewart confirmed this by examining hospital records heart attacks and found that the incidence of heart attacks in Roseto was less than half the national average or of neighboring towns that shared the same water supply, physicians and medical facilities. This despite the fact that they smoked as much and had the same cholesterol and probably ate more fat than most Americans. What Stewart did find when he began his studies in 1962 was that Rosetans were almost entirely descended from Italians who had immigrated there 80-100 years previously to work in the local slate mines. They had come from Roseto Valforte, a commune in southeast Italy surrounded by mountains with the Forturo River running through the valley, and had selected this particular location because of its unusual similarity to their homeland. The traditions of their forbears had been passed down in succeeding generations and were still rigidly adhered to. Although the oldest nursing home in the U.S. was very close by, you would never find anyone from Roseto. The family rather than the individual was the unit of society and most households contained three generations because the elderly were respected and revered. Each inhabitant felt a responsibility to promote the welfare of everyone. What impressed Stewart the most was that this was a very supportive close-knit community that resembled a large family eager to celebrate a First Communion, birthday, anniversary, marriage or any other
reason to get together in an event that could involve all age groups. There was a strict taboo against displaying any sign of ostentation or self-importance such as fancier homes, cars, clothing or jewelry that might signify greater wealth, power or social status.

It was believed that anything suggesting a semblance of such superiority would surely invoke the ancient curse of the mal occhio (evil eye). Like their ancestors, many Rosetans wore an amulet or charm called a cornicello around their neck to ward off the evil eye. Cornicello means "little horn" in Italian, and were usually made of gold or silver or carved out of red coral in the shape of a twisted horn as shown to the left. These were believed to be particularly effective in protecting pregnant or nursing mothers and their babies and are still sold in Italian jewelry stores, especially in New York and cities with large Italian populations.

Stewart concluded that the very low incidence of heart disease in Roseto stemmed from the stability afforded by adhering to traditional lifestyles and values that gave top priority to insuring the well being of the community rather than personal achievement. In a 1964 *Journal of The American Medical Association* article, he predicted that as the powerful stress reduction benefits of this very strong social support disappeared, so would protection from cardiovascular disease. By the early 1970's, it was apparent that many of these traditions and taboos had already started to crumble. Cadillacs and expensive foreign luxury cars became increasingly common as did lavish ranch type suburban homes with swimming pools and three car garages. Mixed marriages soared from 18 to 79 per cent, the first two baby boys were no longer automatically named for their grandfathers and new names like Bruce, Lance and Craig began to surface. Local stores and eating-places vanished and attendance at church and Men's Club functions steadily declined as Rosetans drove to supermarkets and upscale restaurants and joined country clubs. It also became increasingly apparent that aging parents had lost their position as elder statesmen whose advice was sought and respected and three or four generations living in the same house became increasingly rare.

At our 1988 International Congress on Stress, Stewart provided a 25-year follow-up that demonstrated the accuracy of his prophecy. Over this period, **despite the fact that Rosetans were now smoking less and eating less fat and deaths from heart disease had been dropping in the rest of the country, heart attack rates in Roseto more than doubled and hypertension and strokes tripled**. He explained that this was not surprising, since a half century earlier, C. P. Donnoson, a physician with extensive experience in Africa, had noted in his book, *Civilization and Disease*, a complete absence of cardiovascular and other stress related diseases like diabetes and peptic ulcer in remote areas of the continent where tribal traditions and taboos had remained remarkably stable. The physician and Nobel Laureate Albert Schweizer similarly wrote that there was no evidence of cancer in African natives when he originally established his clinic in Gabon in 1913 but that cases started to surface as the natives increasingly adopted Western ways. The celebrated Arctic explorer and anthropologist Vilhjalmur Stefansson also found no cancer in Eskimos in his first visit to the Arctic in 1904 and he documented the subsequent increase over the next few decades as their mode of life became influenced by white traders and settlers in his book, *Cancer: Disease of Civilization?* As Alvin Toffler, a Founding Trustee of the American Institute of Stress, also emphasized in *Future Shock*, "By subjecting individuals to too much change in too short a time, we induce disorientation and shattering stress."
Low Socioeconomic And Educational Status, Loneliness And Heart Disease


As noted in one paper, educational failure significantly increases coronary risk, and as Jim Lynch emphasized in A Cry Unheard, is an impressive predictor of mortality on its own and that school failure may be the current leading cause of premature death. Dropping out of school before the tenth grade was linked to losing 20 years of life! Support comes from studies suggesting that if the death rates for white Americans with less than ten years of schooling were the same as for college graduates, there would be at least 250,000 fewer deaths in the U.S. annually. This figure would be even higher for blacks, Hispanics and other minority groups, especially immigrants with language difficulties. This stunning relationship also has nothing to do with increased poverty or less access to medical care. In addition, Lynch showed that there is a direct linear correlation between basal blood pressures and educational status, which may help explain why blacks tend to have higher blood pressures than whites. Individuals with less education have higher resting blood pressures than high school and college graduates, even when they have attained a similar degree of financial and social success. And while coronary prone Type A behavior is usually associated with executives fairly high on the corporate ladder, Lynch demonstrated in A Cry Unheard that there is a direct and linear correlation between less education and increased Type A behavior, which is as significant a risk factor for coronary heart disease as hypertension, smoking and cholesterol. (See www.stress.org/interview-SpeakingHeartToHeart.htm)

While having strong social support from family and friends is a powerful stress buster that provides protection from heart attacks, loneliness and social isolation have even greater negative effects. As noted in the above interview, Jim Lynch’s first book The Broken Heart: The Medical Consequences of Loneliness, provided a compelling analysis of this that attracted international attention three decades ago. These observations have since been confirmed in numerous studies showing increased coronary death rates in those who live alone, lack a confidant or have little social support. (Case RB, Moss AJ, Case N. Living alone after myocardial infarction. JAMA, 1992; 267: 515–519. Williams RB, Barefoot J, et al. Prognostic importance of social and economic resources among medically treated patients with angiographically documented coronary artery disease. JAMA, 1992; 267:520–524. Ruberman W, Weinblatt E, et al. Psychosocial influences on mortality after myocardial infarction. N Engl J Med, 1984; 311:552–559). A recent Danish study of almost 140,000 people who were followed for two years found that those aged 30 to 69 who lived alone were almost twice as likely as others living with a partner to experience angina, heart attacks or sudden cardiac death. Risk tripled in men over 50 and women over 60 who lived alone. (Nielsen KM, Faergeman O, et al. Danish singles have a twofold risk of acute coronary syndrome: data from a cohort of 138, 290 persons. J Epidemiol Community Health, 2006; 60: 721-728). Blood pressure normally rises as we grow older but this increase is significantly greater in lonely people. One study found
blood pressures as much as 30 points higher compared to non-lonely people, even when other factors such as depressive symptoms or perceived stress were taken into account. Such a difference could significantly increase risk of death from heart disease as well as stroke (Hawkley LC, Masi CM, et al. Loneliness is a unique predictor of age-related differences in systolic blood pressure *Psychol Aging*, 2006; 21:52-64).

**Depression, Anxiety, Anger, Hostility And Heart Disease**

While it is clear that change in traditional lifestyles and values, low social or educational status, lack of social support and loneliness increase risk for coronary disease, what mechanisms of action are responsible? One possibility is that immigrants, lonely people and others in the above categories are more likely to suffer from emotional disturbances that have been shown to contribute to coronary morbidity and mortality via various pathways. Most research in this area has focused on depression, which is frequently accompanied by an increase in cortisol as well as the absence of normal circadian variation in cortisol levels. Other mechanisms that have been discussed in numerous publications confirm that depressed patients are at increased risk for heart attack. (Lett HS, Blumenthal JA et al. Depression as a risk factor for coronary artery disease: evidence, mechanisms and treatment. *Psychosom Med*, 2004; 66:305-315. Stewart RA, North PM, et al. Depression and cardiovascular morbidity and mortality: cause or consequence? *Eur Heart J* 2003; 24:2027-2037). Patients with existing coronary disease who are depressed are also much more likely to suffer from premature death. (Barth J, Schumacher M, Hermann-Lingen C. Depression as a risk factor for mortality in patients with coronary disease: a meta-analysis. *Psychosom Med*, 2004; 66:802-813). In another report noted below, even patients with mild depression were found to be at increased risk.

![Graph showing survival free of cardiac mortality cumulative percentage over days after MI discharge.](image)

Patients who are depressed following a heart attack are much more likely to die over the next five years, as illustrated above. Post-myocardial infarction (MI) patients were assigned to one of four categories based on the Beck Depression Inventory (BDI), ranging from no depressive symptoms (BDI <5) to moderate to severe symptoms (BDI ≥19). During the five-year follow-up period, a clear relationship was observed between the magnitude of depressive symptoms and mortality, with increased events even in patients with mild depressive symptoms (BDI 5 to 9) (From Lesperance F, et al. Five-year risk of cardiac mortality in relation to initial severity and one-year changes in depression symptoms after myocardial infarction. *Circulation*, 2002:105: 1049–1053.)

Anger, hostility and other coronary prone Type A behavior traits also increase heart disease risk but probably via responses different from those involved in depression. Although acute anxiety and panic attacks often mimic the signs and symptoms of an impending MI, there is
no good evidence that anxiety can cause a coronary. Nevertheless, coronary disease patients with high anxiety levels are at significantly greater risk of MI or death (Woldecherkos A, Shibeshi MD, et al. Anxiety Worsens Prognosis in Patients With Coronary Artery Disease. *J Am Coll Cardiol*, 2007; 49:2021-2027). What depression, anxiety, anger, and hostility do have in common with respect to heart attacks is that they increase levels of homocysteine, which causes coronary atherosclerosis. (Tolmunen T, Hintikka J, et al. Association between depressive symptoms and serum concentrations of homocysteine in men: a population study. *Am J Clin Nutr*, 2004; 80:1574-8. Bjelland I, Tell GS, et al. Folate, vitamin B12, homocysteine in anxiety and depression: the Hordaland Homocysteine Study. *Arch Gen Psychiatry*, 2003; 60:618-26. Stoney C, Engbretsong TO. Plasma homocysteine concentrations are positively associated with hostility and anger. *Life Sciences* 2000; 66: 2267-2275). In the last paper cited, researchers found that healthy men and women with more feelings of anger and hostility had increased levels of homocysteine. Men who suppressed their feelings and didn't get them "off their chest" had the highest homocysteines. Several previous studies have shown that holding anger in increases risk for an MI because some people literally as well figuratively "take things to heart."

Another common denominator linking stressful emotions to heart disease is increased inflammation. Interleukin-6 (IL-6), an inflammatory protein that accelerates atherosclerosis that has also been shown to be elevated in men scoring high on questionnaires to measure anger or depression. Men who scored highest on both questionnaires had IL-6 levels two to five times higher than those who scored low on both questionnaires or scored high on only one. Tumor necrosis factor (TNF), and other inflammatory proteins secreted by immune system cells in response to infection, are also increased in depression and hostility and are similarly associated with increased coronary atherosclerosis (Suarez EC. Joint effect of hostility and severity of depressive symptoms on plasma interleukin-6 concentration. *Psychosom Med*, 2003; 65:523-527. Suarez EC, Krishnan RR, Lewis JG. The relation of severity of depressive symptoms to monocyte-associated proinflammatory cytokines and chemokines in apparently healthy men. *Psychosom Med*, 2003; 65:362-368). C-reactive protein (CRP), a substance released in response to stress, infection and other threats to the immune system, is associated with narrowing of the coronary arteries and increased heart attack risk. It is the most widely used measure of inflammation and is also higher in people prone to anger, hostility and depression. In one report, healthy adults with mild to moderate symptoms of depression, anger, or hostility had CRP levels two to three times higher than those of their calmer counterparts, with a clear correlation between CRP and severity of symptoms. (Suarez EC. C-Reactive Protein is associated with psychological risk factors of cardiovascular disease in apparently healthy adults. *Psychosomatic Medicine*, 2004; 66:684-691).

Similar findings were reported in another study showing how these emotions and psychological stress not only increase CRP and homocysteine but also free radical damage and oxidative stress. (Hapuarachchi JR, Chalmers AH, et al. Changes in clinically relevant metabolites with psychological stress parameters. *Behav Med*, 2003; 29:52–59.) Free radicals produced during regular metabolic activities damage healthy cells by oxidizing them, much like oxidized paint results in rust. This type of cellular destruction is normally blocked by antioxidants, but the body's ability to produce these steadily declines as we grow older. Thus, in many respects, we age because we rust out due to oxidation rather than wearing out from excess use. Over the past decade it has become increasingly apparent that heart disease is not caused by cholesterol deposits that clog up coronary arteries but rather injury to these vessels. Much of this damage comes from inflammation due to chronic infection, autoimmune disturbances and free radical oxidation, all of which are increased by stress. *Chlamydia pneumonia*, which causes a common mild flu like illness, has been cultured from coronary atherosclerotic plaque and increases heart attack risk. *Chlamydia pneumoniae* can persist in the body and cause chronic inflammation that produces no symptoms. Heat shock proteins are chemicals that provide protection from damage due to...
stress, inflammation, infection or stimuli that elicit immune system responses. Persistently elevated antibodies to heat shock proteins are seen in autoimmune disorders like lupus. With respect to coronary disease, infection, autoimmune disturbances and inflammation seem to have additive effects. In one study that followed over 4000 men for more than eight years, those with persistently elevated levels of antibodies to *Chlamydia pneumoniae* or heat shock protein had double the risk of a fatal or non-fatal heart attack than those with low levels. Risk was much higher if CRP was also elevated, suggesting that chronic infection, autoimmunity, and inflammation have synergistic effects. (Huittinen T, Leinonen M, et al. Synergistic effect of persistent *Chlamydia pneumoniae* infection, autoimmunity, and inflammation on coronary risk. *Circulation*, 2003; 107:2566-2570). These observations help to explain why stress accelerates aging and atherosclerosis and why half of heart attacks occur in patients who do not have the traditional risk factors.

**Job Pressures, Marital Strife And More Proof Of The Role Of Stress**

As emphasized in previous Newsletters, Job Stress is the greatest source of stress for American adults and has been shown in solid scientific studies to contribute to heart attacks and cardiovascular disease. What is frequently not appreciated, is that workplace stress often spills over into life at home. While living alone is a risk factor for heart disease, being married does not necessarily provide cardioprotection for women in unhappy unions. In one large study, prognosis and long-term survival was poorer in female coronary patients experiencing high marital stress. When compared to wives with harmonious relationships, they had three times more coronary deaths, recurrent heart attacks or need for a revascularization procedure. Job stress alone did not significantly worsen prognosis, but the combined effects of stress at work as well as at home produced the worst health outcomes. (Orth-Gomer K, Wamala SP, et al. Marital stress worsens prognosis in women with coronary heart disease: The Stockholm Female Coronary Risk Study. *JAMA*, 2000; 284: 3008–14. Orth-Gomer K, Leineweber C. Multiple stressors and coronary disease in women. The Stockholm Female Coronary Risk Study. *Biol Psychol*, 2005; 69:57–66). This is supported by the following study that found a higher prevalence of subclinical atherosclerotic plaque and accelerated progression over time in healthy women reporting marital dissatisfaction, as illustrated below.

![Graphs showing plaque progression](image)

Around 400 postmenopausal females were divided into those in satisfying marriages (left of each panel), unmarried (middle of each panel), and in low-satisfying marriages (right of each panel). After 11 years of follow-up, the women in satisfied marriages had the lowest and the women in unsatisfying marriages had the highest percentage of significant plaque (left panel). Serial carotid ultrasonography performed over three years (right panel) showed that women in low-satisfying marriages also had the greatest progression of plaque. (From Gallo LC et al. *Psychosom Med* (2003) 65:952–62). *Significant difference at p<0.05.*
In a more recent three-year study of female patients aged 30-65 who were hospitalized for an acute myocardial infarction and had coronary angiography, those who reported high stress had accelerated progression of atherosclerosis whereas the absence of stress was associated with a widening of coronary vessels, suggesting regression. (Wang HX, Leineweber C, et al. Psychosocial stress and atherosclerosis: family and work stress accelerate progression of coronary disease in women. *J Int Med*, 2007; 261:245-254).

Further proof of the important contribution of stress to coronary heart disease comes from other studies showing that reducing stress promotes longevity by providing protection from heart attacks. More importantly, stress reduction can significantly improve the prognosis for patients with coronary disease. Some of the most effective techniques are ancient practices whose benefits have now been confirmed by very sophisticated laboratory studies and imaging procedures. Others involve the use of novel techniques based on heart rate variability and EEG studies. In that regard, heart-brain interactions may involve other communication pathways that support the existence of an electrical circulatory system. There is also good evidence that weak electromagnetic fields can reverse severe congestive failure and terminal cardiomyopathy as demonstrated by Demetrio Sodi Pallares, whose research was stimulated by Hans Selye’s animal studies showing how stress could cause a myocardial infarction in the absence of coronary occlusion. While this has been discussed in several previous Newsletters as well as *Bioelectromagnetic Medicine* (click on Table of Contents and Preface link that is provided at www.stress.org/cong.htm), recent advances in this area suggest the need to provide an update in a future Newsletter – so stay tuned!

**Meetings Of Interest**

3rd Annual Executive Summit on Innovation and the Cost-Appropriateness of Behavioral Health and Wellness, July 12-13, 2007, Atlanta, GA. Learn How To:
- Cut Toxic Stress Effects
- Improve Employee Health & Wellness
- Control Rising Health Costs
- Improve Bottom Line & Productivity

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