

HEALTH AND STRESS

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(PRELIMINARY PROGRAM OUTLINE ON PAGE 8)

CARDIOVASCULAR DISEASE AND STRESS - WHAT'S NEW?

Key Words: Loneliness, social isolation, gender differences, skin color, racism, calcium dynamics, endothelin

The close relationships between emotions and the heart have been appreciated since antiquity. It is well established that feelings can have powerful effects on the cardiovascular system and that chronic or acute and severe stress can contribute to a variety of coronary events as well as sudden death. However, the ancient Greeks and other cultures believed that the heart, rather than the brain, was the seat of emotions and responsible for how we feel. Recent research suggests they may have been on to something, and that this is a two way street.

The heart has been the universal symbol for love in different cultures around the world for centuries. Its association with other emotions is vividly illustrated by numerous phrases and expressions ingrained in our language to portray various personalities and traits, such as: brokenhearted or heartsick (sad), coldhearted and heart of stone (having no compassion or mercy), heart of gold (generosity), stouthearted (courageous), weak-hearted (timid and afraid), or warmhearted (kindness and amiability).

People show their emotions by "wearing their heart on a sleeve", while those who are heartless have no feelings or are cruel. To "pull at one's heart strings" is to evoke the deepest emotions. A "heart throb" signifies passion, and something that is "hearty" is robust or satisfying. We have a "heart to heart" talk to express our true feelings. The Latin word for heart is *cor* and we get to the core or heart of things to determine the real cause of a problem.

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Depression And The Broken Heart

Jim Lynch's classic, *The Broken Heart; The Medical Consequences of Loneliness* published a quarter of a century ago was so on target it could have been written yesterday. It is an eloquent and compelling portrayal of the deadly cardiovascular consequences of loss of personal relationships. It also warned that current sociocultural trends and changing life styles would lead to increasing social isolation, loneliness, and their associated emotional and physical disturbances. There can be little doubt about the accuracy of this prophecy.

Scientific studies since then have repeatedly confirmed the contributory role of depression to various coronary events and their complications, as well as disorders due to immune system suppression. Researchers have also been able to delineate some of the mechanisms of action that may be involved. Before reviewing these, I would be remiss not to mention that Jim Lynch's new book *A Cry Unheard* will probably hit the stands by the time you read this. While in some ways it is a 25-year revision of *The Broken Heart*, it charts new territories that are the root causes of loneliness and depression, and places particular emphasis on deficiencies in our educational system.

Depressed individuals are more than four times more likely to suffer a heart attack than controls without a history of depression, according to the National Institutes of Mental Health. The Johns Hopkins Precursors study thoroughly evaluated almost 1200 medical students and followed them periodically for forty years after graduation to determine whether certain personality traits might predict different disorders. Twelve percent of these physicians reported at least one episode of clinical depression. This group had more than twice as many heart attacks as did their classmates. In some instances, this occurred more than ten years after the onset of depression. On average, heart disease symptoms appeared 15 years after depression was first diagnosed.

These and other studies suggest that the older you are when the first episode of depression is experienced, the less time it takes for evidence of coronary heart disease to appear. In a National Institute of Aging six year follow-up of over 3700 individuals without entry evidence of heart disease or depression, men whose initial symptoms of depression appeared after the age of 60 were twice as likely to have a coronary event within the next five years than nondepressed controls. Mortality rates were four times higher. However no significant correlations were found in the "weaker sex". A ten year Ohio study of some 8000 men and women revealed that men who became depressed were 70 percent more likely to later be hospitalized for chest pain and cardiac surgery than non depressed controls. Risk was only 12 percent greater for women with the same degree of depression.

A similar marked gender difference was reported by a British physician who reviewed the records of 188 men and 139 women with coronary heart disease and compared them with hundreds of controls the same age and sex in his 6000 patient practice. After all other factors were excluded, men with a history of depression within the past ten years were three times more likely to develop heart disease. No such correlation was found in women. There are several possible reasons for this marked difference between males and females.

Depression & CHD-Chicken Or Egg?

Although women are at least twice as likely to suffer from depression as are men, they do not have the same increased tendency to subsequently develop coronary heart disease. One explanation may be the cardioprotective effects of female hormones. Another is that up until the time of menopause, there is a monthly depletion of iron stores during menstruation, and increased iron has been shown to be a risk factor for heart attacks. This is supported by a review of the health records of over 7500 women aged 68 or older who died between 1988 and 1994. Those with a history of depression were 80 percent more likely to die due to heart disease than nondepressed controls, showing that this sex related protection had disappeared.

However, just as depression can contribute to heart disease, the reverse is also true. Large surveys show that between 2 and 3 percent of the population can be classified as being clinically depressed, but this jumps to 18 percent in those with heart disease. About one in six people will have at least one episode of major clinical depression at some time in their lives, compared to almost half of cardiac patients. That's not too surprising, since people with coronary complaints or who have suffered a heart attack would obviously be fearful about their future and therefore much more likely to suffer from depression. In some instances it is difficult for researchers to determine which came first, and more importantly, how the connection can be broken.

There is a great deal of evidence demonstrating that **patients whose first episode of depression appears after a heart attack or coronary bypass surgery are at significantly increased risk for further cardiac complications.** These can include a recurrent heart attack, need for additional surgery, serious rhythm disturbances, or even death. A Canadian study of 896 hospitalized heart attack patients found that about half of the 283 women had mild to moderate depression, compared to only one-fourth of the 613 men. However, despite this dramatically higher rate of depression in females, death rates were the same in both sexes.

One year later, deaths from cardiac causes were about three times higher in depressed patients of both sexes compared to those who were not depressed. Deaths were 8.3 percent in depressed women compared to 2.7 percent in others; for depressed men it was 7 percent and 2.4 percent for the nondepressed group. Not only did depression have a similar impact on survival for both women and men, but the effects of other risk factors related to depression, such as a history of hypertension or diabetes were also practically identical.

According to another report, recovery after coronary artery bypass surgery may depend as much on your state of mind as it does on your cardiac status. A tendency towards depression occurs in one out of five patients who have coronary bypass surgery. This study involved 207 men and 102 women who underwent bypass surgery at two major medical centers. All had a detailed psychiatric interview prior to discharge from the hospital to evaluate emotional status with a particular focus on depression and anxiety. Over the next 12 months, hospital admissions for heart failure, angina, recurrent heart attack, or repeat bypass surgery was about three times higher in both sexes classified as depressed, compared to nondepressed bypass patients. Postmenopausal women were over twice as likely to experience complications as were men.

One way to prove that there is some causal relationship between depression and initial or recurrent coronary events would be to demonstrate that aggressive treatment resulted in a significant reduction of subsequent problems or mortality. Such studies are underway in patients hospitalized for heart attacks, angioplasty, and bypass surgery. However, in the Johns Hopkins precursor study, **death rates for depressed physicians were the same for those who received antidepressant medication and/or psychotherapy and others who had no treatment.** Emotions like anger and anxiety can contribute to coronary heart disease via stimulating sympathetic nervous system activities, but what mechanisms could explain how depression causes this condition?

Baroreceptor And Immune Responses

Is there any way to determine the relative risk of danger for any specific individual? The severity and length of depressive symptoms seem to be important factors, but what mechanisms of action might be involved?

The results of a new study may shed some light on both of these questions. Researchers recently reported that depression affects baroreflex cardiac control and therefore may increase subsequent cardiac risk, especially in patients with coronary heart disease, even if they have no obvious signs or symptoms. They state that normally, "the baroreflex system attempts to maintain an equilibrium which helps guard against sudden cardiac events like heart attack." **The baroreflex systems of depressed heart patients "don't seem to have the same sensitivity to blood pressure changes", thus making them much more vulnerable to heart attacks and rhythm disturbances.**

In this study, depressive symptoms were rated and correlated with baroreflex sensitivity and resultant changes in the circulatory system in 66 patients with stable coronary artery disease. In patients with depressive symptoms that were nine or more on a scale from one to ten, baroreflex sensitivity was reduced by almost one third, compared to subjects with scores lower than three. The researchers believe that exercise might help to restore baroreflex control because it can improve the electrical stability of the heart. Patients with cardiac symptoms or who have had a heart attack tend to become more sedentary. This study supports the benefits that exercise can provide for such individuals.

Depression is also associated with a suppression of immune system components responsible for resistance to bacterial and viral infections. Recent research has shown that seemingly benign chlamydia, cytomegalovirus, and other infections can contribute to heart attacks and strokes. Although they produce few symptoms, they hide in cells and cause the development of inflammatory atherosclerotic plaque in coronary and cerebral arteries by constantly stimulating immune responses.

Oxytocin, Stress, & Blood Pressure

When we are startled by something like the noise of a huge firecracker suddenly and unexpectedly exploding, there is a prompt rise in blood pressure. Loud noises were one of the stressors Selye often used in his studies of The Alarm Reaction in laboratory animals. Researchers were therefore surprised when one of them accidentally dropped a heavy notebook that made a loud enough noise that would normally have caused this response in mice they had been studying. Subsequent experiments confirmed the absence of the usual rise in blood pressure when these mice were startled. What was unusual about this strain was they had been genetically engineered to knock out oxytocin, a posterior pituitary hormone associated with maternal behavior. When injected into virgin female animals, they will build a nest, appropriate another female's pups, warm them, and crouch in a suckling position.

Oxytocin also stimulates sexual activity. It causes adult female rats to arch their backs and spread their hind legs in a mating position and males to have penile erections and improved ejaculation. Oxytocin injections are often used during pregnancy to stimulate uterine contractions that will induce labor, or to promote lactation after delivery. It is present in equal amounts in both males and female animals and humans and is closely related to vasopressin, another posterior pituitary hormone that acts as an antidiuretic. It also appears to improve memory and concentration and in a study designed to evaluate this effect, vasopressin was administered as a nasal spray to college students with oxytocin spray used as a control. An unexpected finding was that the oxytocin group became sexually aroused.

This is the first time that an animal model has been created in which the effect of emotional stress on blood pressure is completely abolished. Further investigations in this unique strain promise to expand our understanding of cardiovascular responses to stress and might lead to more effective medications for the treatment of hypertension.

Race, Gender, And Hypertension

Feeling both anxious and depressed is a double whammy, especially for black females, when it comes to hypertension. Researchers found that being anxious and depressed increased a man's risk of hypertension by 1.5 fold, a white woman's 1.7 fold, but was 3 times greater for black women. These findings come from a study of over 3300 healthy people who enrolled in the National Health and Nutrition Examination Survey in the 1970's, and had four follow-up periods over the next two decades. By the last follow-up in the early 1990's, around 16 percent reported high levels of anxiety and depression and 40 percent said they had a moderate amount of distress because of these feelings. Black women were twice as likely to be affected compared to white males, and white women fell somewhere in between.

Other studies have also demonstrated that hypertension rates are significantly higher in blacks. The incidence of high blood pressure in Afro-Americans is twice that of whites, and highest in older females. **More than three out of four elderly black females have hypertension.** Several explanations have been offered, including greater sensitivity to salt and increased stress. Depressed individuals may also be more likely to smoke or have poor eating habits, both of which are also associated with a greater risk of cardiovascular disease.

Proponents of the salt sensitivity theory point out that the ancestors of the majority of Afro-Americans came to this country aboard slave ships that operated for more than 350 years. Of the close to 40 million blacks who were captured in Africa, the majority died, usually due to dehydration and the low salt content of their rations. The 11 million who managed to survive quite likely were able to do so because of their greater ability to retain salt. **Salt sensitivity in blacks may have resulted from thousands of years of evolution in the hot African climate where increased salt and water retention was essential for survival.** While this may have provided certain benefits in that locale, it has now become a decided disadvantage for their descendants.

In addition to any genetic predisposition, psychosocial stresses undoubtedly contribute to both the incidence and severity of black hypertension. In one study of 190,000 people over the age of 45 who were followed for five years, there were 1600 fatalities due to strokes. Black males and females were four times more likely to die from stroke than white controls. Even after relevant factors like income, social status and education were considered, the excess risk of death was still very significant.

Blacks are also much more likely to die from other complications of hypertension, such as kidney failure and heart disease. It is believed that heightened sensitivity of the sympathetic nervous system due to alterations in calcium dynamics is a contributing factor. Calcium regulates the activity of muscle cells in the arterial wall. Increased concentrations cause chronic vasoconstriction and hypertension and levels can be dramatically higher in blacks. Some tend to have higher concentrations of glycosides like ouabain and digitalis that block the exit of calcium from cells. This may also explain why hypertensive blacks respond better to calcium channel blockers which inhibit cellular uptake of calcium, than beta blockers and ACE inhibitors, which are widely used to treat hypertension in whites.

The stress of coping with racism is probably the most important factor, and there are numerous studies to support this. In one report, 186 blacks and 128 Brazilians in Alabama were evaluated with respect to skin color and life style. Those with the lightest skin color as well as the lowest life style had the lowest blood pressures, and those who were darkest and had comfortable middle-class superior life styles had the highest pressures. **It was suggested that darker skinned people are socially rejected in color conscious societies where this signifies low social class and inferiority.**

In another study 25-55 year old blacks randomly selected from various professions, those who were dark-skinned had a 24 percent incidence of hypertension in contrast to 7 percent for those with light skin. This may be due to "denial of approbation and the constant effort to achieve respect", which rarely happens.

Sex, Hostility, And Anger

Type A behavior is as significant a risk factor for heart attacks and other coronary events as cigarette smoking, elevated cholesterol, and hypertension. However, there is considerable controversy about which Type A trait might be most responsible for this relationship. It has been suggested that hostility, cynicism, or anger, especially when suppressed, are the major culprits. Critics point out that the methods used to rate hostility levels really measure something else that correlates better with deaths from all causes rather than coronary heart disease specifically. This caveat should be kept in mind when reviewing these recent reports.

One found that hostile young adults were more likely to show evidence of calcification in their coronary arteries. Among 376 men and women aged 18 to 30, the half judged to have higher hostility levels were 2.6 times more likely to have calcium deposits in their coronaries. Hostility was characterized as having a more cynical view of the world and more aggressive responses to stressful situations. **The most hostile men and women were more than nine times more likely to have calcifications large enough to suggest early atherosclerotic plaque, even in this young age group.** This correlation persisted after accounting for other risk factors such as poor education, increased weight, smoking, blood pressure, and cholesterol. In another study of 18-26 year old women, increased levels of both total cholesterol and LDL ("bad") cholesterol were associated with antagonistic, aggressive personalities, particularly in women who expressed their anger in words or actions.

The above effects are due to increased adrenaline and nor adrenaline secretion. **Another mechanism may be increased insulin resistance,** based on a study of 1000 men whose hostility ratings were derived from questionnaires. Insulin resistance is a risk factor for heart disease, diabetes, obesity and hypertension. It results when cells become less responsive to insulin due to genetic and/or acquired influences, particularly obesity.

How prone you are to anger and how you handle such feelings may also affect your risk for heart attack. Having a high level of irritability as well as a dominant personality seems to be a particularly deadly combination. An example of this would be thinking nothing of interrupting others in the middle of a conversation, but becoming very irritated when anyone does this to you. Researchers interviewed 101 men and 95 women with and without heart disease who were undergoing standard treadmill testing. Those rated as having a dominant personality had almost a 50 percent higher risk of heart disease. Increased irritability scores were associated with a 27 percent increase.

It is commonly believed that men outwardly vent their angry feelings while women tend to suppress and keep them in, and that this latter practice is more dangerous. This generalization may not be warranted. The study suggested that women were at greater risk if they displayed their feelings in more indirect ways, such as subtle but suggestive facial expressions and body language, or crafting cutting comments. Men were more likely to have heart disease if they displayed a dominant demeanor by frequently interrupting or finishing another's conversation. Being irritable most of the time raised risk in both sexes.

Women's evaluations of spouses' anger-out levels correlated fairly well with their husband's degree of coronary heart disease. However, the reverse was not true when men tried to rate their wives' expressions of anger. The researchers suggest that **unlike men, women do not develop heart disease because of dramatic venting of their angry feelings, but rather when they tried to express them indirectly by insinuation.** They also concluded that "Anger should not be held in or kept in subtle ways. Anger should be discussed. You should confront the person with whom you are angry, but in a controlled fashion."

Teaching people how to control their tempers and angry feelings could significantly reduce their risk for heart disease. Studies are now being conducted to determine whether anti-anxiety and/or antidepressant medications might also be effective.

Mental Stress, Speaking, & White Coats

Another study also found that anger was a risk factor for heart disease. 160 men and 24 women with a history of a heart attack or heart disease were evaluated by treadmill testing to determine whether adequate amounts of blood were getting to their heart muscle during physical stress. On a later visit, they underwent two 5-minute mental stress tests, both of which were designed to make them irritable and angry. One consisted of participating in a confrontational role-playing game, and the other was playing a computerized word game that got progressively more difficult. Those who reported high levels of anger and/or irritability during the role-playing were more likely than others to show evidence of ischemia, or diminished blood flow to areas of the heart muscle.

This was more evident in women than men, not because the men did not get just as angry, but were probably less likely to admit it. The lead author noted that because men frequently underestimate their anger when asked about this by physicians, many doctors rely more on the opinions of a spouse or other family member. He also said "We've known that **most episodes of ischemia don't occur when people are exercising. The likely culprit is mental stress**, because people probably spend more of their time mentally stressed than physically stressed."

The most effective way to demonstrate the cardiovascular effects of mental stress test, and particularly those that might contribute to heart disease, is speaking in public. In another recent study, 196 patients with coronary disease who were not taking any heart medications were subjected to a public speaking task during which they were monitored. They were given two minutes to prepare a speech about a close relative who was being badly mistreated in a nursing home and five minutes to deliver the speech. Of those who died over the next three to four years, 44 percent had shown evidence of ischemia during the public speaking test, compared to only 18 percent of those without such changes. What was disturbing was that those who died did not seem any more nervous than the others, never had any chest pain or distress, and had no idea they were in danger.

The cardiovascular effects of speaking were first delineated by Dr. James Lynch, who showed that blood pressure was influenced by the speed and content of conversation, the relative social status of the audience, its size, and other factors, including whether a pet dog was present. Hypertensive patients showed the greatest elevations when they began to speak, but were completely unaware of this, even when levels were very high. Using automated equipment that displayed heart rate, systolic, diastolic and mean arterial blood pressure readings on a minute to minute basis patients could see, Lynch was able to help them "get in touch with their feelings" and learn through breathing techniques how to dampen these dangerous surges. As explained in his new book, this led to the development of his **Transactional Psychophysiology Therapy**, which allows many hypertensive patients to safely stop or sharply lower drug treatment.

"White coat hypertension" refers to a transient elevation of blood pressure commonly seen when measurements are made by a physician. It has generally been viewed as an exaggerated normal response that is harmless. Elite weightlifters have had blood pressures recorded as high as 350/240 when they hold their breath while lifting a weight over their head without any evidence of long term adverse cardiovascular consequences.

Others believe that some over responders are at high risk but are difficult to identify. In one study of adolescents (average age 13) scientists measured levels of cortisol and endothelin (a predictor of vascular disease) in white coat and normal responders. In male (but not female) white coat reactors, endothelin levels significantly correlated with higher cortisol and mean blood pressure values. This gender difference is consistent with other reports showing higher rates of cardiovascular disease in men compared to women, although this difference diminishes in the elderly. **This approach may be able to help identify teens at high risk for hypertension and heart attacks so that early intervention can be instituted.**

ELEVENTH INTERNATIONAL CONGRESS ON STRESS

November 26 through December 1, 2000, Mauna Lani Bay Hotel, Island of Hawaii

As this year's Hans Selye Award recipient will be Dr. Herbert Benson, this Congress will have a focus on the stress reduction and health benefits of a firm faith and mechanisms of action that may mediate these effects. The Program will begin on Sunday evening, November 26, with a Welcoming Cocktail Party, Banquet, and Award Ceremony. A tentative schedule of the Scientific Sessions already planned include:

Monday - November 27th	
● Faith, Belief, and Stress Reduction In Health and Healing	Herbert Benson, MD, Chair
Tuesday - November 28th	
● The Growing Role of Spirituality In The Workplace	George Gallup Jr., Chair
Wednesday - November 29th	
● Placebos: Can They Cure Disease As Well As Relieve Illness?	Robert Ader, PhD, Chair
Thursday - November 30th	
● Subtle Energies: What and Where Are They, and How Might They Mediate Faith Healing and Placebo Effects?	William Tiller, PhD, Chair
Friday - December 1st	
● Psychophysiologic Effects of Feeble Electromagnetic Forces and Other Subtle Energies	W. Ross Adey, MD, Chair
● The Global Epidemic of Job Stress and Stress Around The World	Lennart Levi, MD, PhD, Chair

Scientific sessions will run from 8 AM to 1 PM most days to leave afternoons free for R&R and workshops. Brief after dinner talks are planned followed by drinks and musical entertainment, similar to our Montreux Congresses.

The ability of a firm faith, spirituality, or placebos to provide diverse health benefits is difficult to explain. Some appear to involve nonthermal reactions inconsistent with laws of thermodynamics and our current chemical/molecular model of communication. However, they do become comprehensible in an emerging paradigm of communication at a physical/atomic level that proposes energy communication pathways that may also provide insights into how acupuncture and homeopathy achieve their effects.

For details on Registration, the very reasonable rates we have been fortunate to obtain at this fabulous facility, our star studded Faculty, titles of presentations at various sessions, contact The American Institute of Stress (stress125@earthlink.net or Fax: 914-965-6267).

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