

HEALTH AND STRESS

The Newsletter of The American Institute of Stress

February

2002

STROKES, **SUDDEN DEATH**, HEART ATTACKS & **STRESS**

KEYWORDS: Statins, "stroke belt", African-American, atrial fibrillation, PTSD, George Engel, Richard Rahe, Walter Cannon, "The Baskerville effect", baroreflex sensitivity

Stroke and heart attack are most often due to occlusion of cerebral or coronary arteries by atherosclerotic plaque. These lipid laden lesions are assumed to result from elevated levels of blood cholesterol or components such as low density lipoproteins LDL that can more readily infiltrate arterial walls. As a consequence, the public has been warned to restrict the intake of foods rich in cholesterol despite any proof that low fat diets significantly lower serum cholesterol or reduce the incidence of coronary events.

The numerous fallacies of this diet-cholesterol-heart attack hypothesis have been emphasized in previous Newsletters. George Mann, a distinguished authority in the field called this "**the greatest scam in the history of medicine**." A low fat diet may be inconvenient or detract from the

pleasures of life, but is not a serious health hazard. The same cannot be said for **cholesterol-lowering drugs, all of which have been responsible for preventable deaths and serious side effects that have been suppressed.**

The belief that diet and high cholesterol are responsible for heart attacks, strokes and peripheral vascular disease is quite understandable. Most people view such problems as a plumbing problem in which deposits gradually build up inside pipes that progressively interfere with flow and eventually can cause a complete obstruction. It's easy to visualize that fatty foods cause a rise in blood cholesterol that precipitates out and clogs up vital blood vessels.

This misguided notion stems from studies showing that when animals are force fed high cholesterol diets they develop fatty arterial deposits. However, these do not resemble human plaque lesions, which tend to develop in different locations and have the hallmarks of an inflammatory reaction rather than passive precipitation. There is overwhelming evidence that the cardio-protective benefits of statin drugs are due to their ability to reduce inflammation rather than any lipid lowering effects. As previously emphasized, statins have serious side effects that are dose-related. Since the goal of

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therapy is to increase dosage until LDL is lowered to an arbitrary level, rather than reducing markers of inflammation, the incidence of adverse reactions is likely to increase.

If high cholesterol is not the cause of coronary heart disease and stroke what is responsible? Genetic factors obviously play a crucial role but stress is also an important influence, and is something that you can learn to control.

Stress, Stroke And Geography

Stroke may be defined as the abrupt onset of symptoms and signs reflecting a focal loss of cerebral function. Neurological deficits result when a cerebral artery is significantly occluded by a thrombus or clot, or damage to the vessel wall leads to bleeding into surrounding brain tissue. In some instances there can be a global loss of function with deep coma, particularly in cases of subarachnoid hemorrhage. Strokes can vary in severity from quick and complete recovery or incomplete recovery to severe permanent disability and death. Men are at 1.25 times greater risk for stroke but women have higher death rates.

Stroke is the third most frequent cause of death after coronary heart disease and cancer, both in developed countries and worldwide. While strokes can occur at any age, risk increases as we grow older. It doubles for every decade after 55 and two-thirds of all strokes occur in people over 65 years old. Senior citizens are also seven times more likely to die from stroke than the general population. The majority of strokes are due to ischemia resulting from obstruction of a blood vessel by a clot. Hemorrhagic strokes are more severe and are associated with higher mortality rates.

Most reliable reports on the prevalence of stroke come from data in various white populations showing that the incidence is quite similar around the world. The major exceptions are Russia, where risk is high and France where it is low. **These disparities correlate with overall stress levels in these populations and certain risk factors for stroke that are also often stress-related**, such as hypertension, cigarette smoking, excess alcohol consumption and elevated cholesterol.

The incidence of stroke in the U.S. has risen over the past decade, particularly in the south. Scientists and statisticians have long been aware that southeastern states have the highest stroke mortality rates and refer to this region as the "stroke belt". Deaths due to stroke in Georgia, North and South Carolina occur at twice the rate of those in the rest of the country. This has been attributed to their high percentage of African-American residents. The incidence of stroke among African-Americans is almost double that of whites and twice as many who have a stroke die from the event compared to Caucasians. **African-Americans between the ages of 45 and 55 have four to five times the stroke death rate of whites.**

Several factors may contribute to these differences. African-Americans have a higher incidence of hypertension, cigarette smoking, preference for salty and high fat foods as well as genetic diseases like diabetes and sickle cell anemia that could increase risk for stroke. Socioeconomic status is also comparatively lower in "stroke belt" states, especially for blacks. Low socioeconomic status and poverty are associated with an overall lower standard of living and lack of access to health care that might also lead to more strokes.

Researchers now recognize that neither the higher percentage of Afro-Americans nor lower socioeconomic status account for the higher incidence of and deaths from stroke in these states. A recent report found that severe stress is one of the most potent risk factors for stroke, more so than high blood pressure and **there is good evidence that stress may explain why blacks are more prone to strokes.**

Stress And Risk Factors For Stroke

The most powerful risk factor for stroke is persistent hypertension. Stroke rates are four to six times higher in hypertensives and 40 to 90 percent of stroke patients exhibit elevated blood pressures prior to the event. The second most significant risk factor for stroke is a disturbance in heart rhythm, especially atrial fibrillation. In this disorder, the atria beat irregularly and much faster than the ventricles, resulting in erratic pumping of

blood. This can promote the formation of a clot that is carried to the brain where it obstructs a blood vessel. About 15 percent of patients have atrial fibrillation prior to suffering a stroke. Having diabetes triples the likelihood of stroke. Rates are even higher in those diabetics with hypertension and/or high cholesterol, both of which occur quite frequently in older patients.

Stress can contribute to all the above. The well documented role of stress in hypertension can be mediated by several different pathways. The fight or flight response to stress is characterized by a rise in blood pressure and heart rate in everyone. Some people have exaggerated responses so that blood pressure measurements taken by a doctor in an office setting can be alarmingly high whereas ambulatory readings and those obtained by others at home are normal. Such "white coat" hypertension was formerly thought to be benign but recent reports suggest that many such hyper-reactors are at greater risk for arterial damage, coronary heart disease and persistent elevations. Stress-related hormones cause an increase in sodium retention, which can aggravate problems in salt sensitive hypertensives.

Sustained hypertension occurs more frequently in individuals who suffer from symptoms of chronic anxiety. In a twenty-year follow-up of men in the Framingham study, high anxiety levels at the time of their initial evaluation proved surprisingly predictive for subsequently developing hypertension. In another three-year study of almost 500 healthy women, seven developed hypertension requiring permanent medication. Here again, baseline anxiety level scores had the greatest prognostic significance.

Chronic atrial fibrillation is the most common heart rhythm disturbance and is usually due to some underlying cardiovascular condition such as mitral valve prolapse or stenosis, coronary artery disease or hypertension. "Lone atrial fibrillation" refers to an episode of fibrillation that lasts for a few hours or days, rarely recurs more than three times a year, and is not associated with any cardiac abnormalities. Both forms of atrial fibrillation

can be triggered by caffeine, nicotine, an overactive thyroid and other influences that increase sympathetic nervous system activity.

Stress is the most powerful sympathetic nervous system stimulant. The associated release of adrenaline and similar hormones accelerates heart rate and promotes not only atrial, but also ventricular fibrillation, which can be fatal. In addition, stress can also lead to increased hyperactivity of the thyroid, cigarette smoking, caffeine consumption, hypertension and other risk factors for fibrillation.

Stress can similarly precipitate and aggravate diabetes by different influences. The immediate rise in blood sugar during stress results from the breakdown of glycogen and carbohydrates by adrenaline. This elevation is sustained by the subsequent effects of cortisone-like hormones that derive glucose from protein stores in the body. So-called "white coat" diabetes has been used to describe elevations of blood sugar due to the stress associated with a visit to the doctor. In some instances, this has led to increases in insulin dosages that have resulted in hypoglycemic reactions. Studies have also shown that the stress of public speaking or mental arithmetic tasks can result in sharp rises in blood sugar.

Stress can upset diabetic control because of dietary indiscretion, excess alcohol intake, or forgetting to take medications as prescribed, which can have serious consequences. In one study, no stroke patient with an elevated blood sugar had full functional recovery four weeks later even if there was no history of diabetes. Mortality rates were also significantly higher. **The recent rise in diabetes is attributed to the epidemic of obesity, which has also been linked to stress-related overeating.**

Other Stress And Stroke Connections

Elevated cholesterol, also a risk factor for stroke, is much more likely to be due to stress than dietary fat. In addition to elevated cholesterol, stress can contribute to other less well known risk factors such as smoking, increased alcohol consumption,

substance abuse, high homocysteine levels, insulin resistance, and migraine. But stress can also promote strokes via many other pathways.

In one study, life change events and difficulties were recorded for the year prior to stroke in 113 patients using interviews and standard questionnaires. Compared to age and sex-matched controls, severely threatening long term events were twice as high in the stroke group (26% versus 13%). Recognized risk factors for stroke were equal in those patients with and without severe events before the onset of stroke and hypertension was actually less common in those who had experienced severe events. This doubling of rate was apparent throughout the year rather than just in the weeks prior to the stroke, suggesting that chronic stress was the cause rather than acute events and/or blood pressure surges.

A long term study of some 7000 healthy California adults (average age 43) showed that those with multiple symptoms of depression were much more likely to die due to a stroke. Participants underwent physical exams and filled out questionnaires listing 18 symptoms of depression. Those with five or more symptoms were considered to be depressed. Twenty-nine years later, 1 in 25 of this group had suffered a fatal stroke compared with only 1 in 44 of controls.

After adjusting for other risk factors, the depressed group had 50 percent more deaths from stroke. Researchers suggest that stress hormones promote strokes by stimulating platelets to secrete a substance that causes blood vessel narrowing and reduced blood flow. In addition, stress increases platelet clumping that can trigger clot formation and this combination could readily result in complete obstruction. Depressed patients are also less likely to follow medical advice or to take medications as prescribed.

Exaggerated blood pressure responses to stress have been shown to be associated with more carotid artery atherosclerosis and vessel narrowing, which predispose to stroke. In one study, blood pressure and pulse were recorded in postmenopausal women before and during two stressful mental tasks, public speaking and mirror

image tracing. Carotid atherosclerosis and narrowing were measured with duplex ultrasonography. When this test was repeated over two years later, researchers found that the largest increase in atherosclerotic plaque and diminished blood flow occurred in those who had the greatest rises in blood pressure and heart rate during mental stress.

Part of the difficulty in linking stress to stroke, heart attacks and other diseases due to accelerated atherosclerosis is the length of time it takes to produce vessel obstruction. War veterans with PTSD (Post Traumatic Stress Disorder) may not experience recurrent symptoms of the initial trauma until months or years later. Cardiovascular disease has not been viewed as a complication of PTSD nor is it considered to be service-connected if not detected on discharge. In one follow-up report on 4600 male Vietnam war veterans, those diagnosed with PTSD had twice as many abnormal electrocardiograms compared to age matched controls. The difference was even greater in PTSD veterans who were experiencing symptoms of anxiety and depression.

One study concluded that severe stress is one of the most potent risk factors for stroke, more so than high blood pressure — even 50 years after the initial trauma. Researchers studied 556 veterans of World War II and found that the rate of stroke among those who had been prisoners of war was eight times higher than among those veterans who had not been captured. "The stress of being a POW was so severe it sensitized the way these folks responded to stress in the future".

Another study found that 62 percent of veterans with inadequately treated PTSD showed spasm of crucial arteries at the base of the brain. Following a 6-month treatment protocol to reduce symptoms, the incidence of vessel narrowing was lowered to 22 percent.

Stress And Sudden Death

Sudden death can be defined in different ways. Some limit it to instantaneous death that occurs unexpectedly without any obvious physical cause. More often, it refers

to death that occurs within 24 hours after the spontaneous onset of some symptom or sign that is related to the terminal event. Most sudden deaths are due to ventricular fibrillation or another arrhythmia or problem that results in a precipitous and persistent fall in blood pressure. **Although death certificates usually list the cause of death as a heart attack at least half of sudden death patients show no evidence of acute myocardial infarction.**

Sudden death occurs in one in five people and not infrequently is the initial and only manifestation of a cardiovascular disorder. Although it accounts for between a third and a half of deaths due to coronary heart disease, sudden death is not associated with any distinguishing autopsy findings and there can be scant or no evidence of coronary atherosclerosis, especially in younger patients. There is also no correlation with hypertension, elevated cholesterol or cigarette consumption, the classical risk factors for coronary heart disease.

Stress seems to be a common trigger. "Dying of fright" and "broken-hearted" are phrases that have permeated our language for centuries and are supported by anecdotal reports. George Engel's *Sudden and Rapid Death During Psychological Stress: Folk Lore or Folk Wisdom?* published 30 years ago is a compelling classic. Engel collected newspaper accounts over a six-year period and reviewed details about possible relevant antecedent circumstances in 170 cases of sudden death. They included: loss or threat of loss of a person or object, loss of self esteem, threat of imminent injury or danger, joy and triumph. The most common was being informed of the death of a loved one. While triumph and joy might seem to represent "good" stress, the concomitant sympathetic nervous system stimulation may be **sufficiently severe to trigger ventricular fibrillation, as in one healthy 18 year-old bride who was overcome by the excitement of her wedding day.**

A few years later, Dick Rahe reported on the magnitude of life change events prior to sudden death by interviewing surviving spouses. Scores were very much higher in the preceding six months when compared with the same time period the previous

year. These findings have since been confirmed by others. Loss of a spouse or close personal relationships are at the top of the Holmes-Rahe scale, and in one study, women who died suddenly were also six times more likely to have experienced loss of a close friend or family member in the preceding six months.

Certain stresses can precipitate sudden death in minutes or hours. In one report on patients with recurrent life threatening arrhythmias, one in five had experienced a stressful trigger in the preceding 24 hours. Most were within 60 minutes and were often due to severe anger. A study of survivors of ventricular fibrillation found that one in four had experienced emotional stress in the preceding 24 hrs. in the form of anger, depression, fear, excitement or grief. Most disturbances also happened in the hour prior to the event and these patients usually had surprisingly little evidence of coronary heart disease.

Other types of chronic stress that persisted for months or years can also increase risk for sudden death. Having less than ten years of schooling proved to be a significant risk factor in a study of over 2300 male survivors of a myocardial infarction. Such individuals might have less access to medical care because of lower economic status but it was their higher levels of stress and social isolation that appeared to be the determining factor. Those who were both stressed and lacked social support were at four times greater risk.

Strong social support provides powerful cardioprotective benefits. Japanese men enjoy a low incidence of coronary artery disease but rates rise when they are transplanted to Western cultures without any change in other risk factors. Sudden cardiac deaths in Laotian Hmongs who immigrate to the U.S. also rise dramatically due to ventricular fibrillation, often while sleeping. **Most were in their thirties with no history of a health problem.**

Death By Prescription And "Voodoo"

Reports of predictable sudden deaths that are not due to any existing illness abound in many primitive cultures. They are often attributed to a hex or curse which

has been placed on the individual by a shaman or sorcerer. In other instances they are self-induced because the unfortunate victim becomes aware of having unknowingly violated a strict taboo or has committed some other societal transgression.

Walter Cannon was fascinated by this phenomenon and validated over 30 such deaths by prescription in cultures all over the world in a 1942 paper entitled "Voodoo Death". These varied from "bone pointing" deaths in Australian aborigines to hexes placed by witch doctors in Africa and Central America; he cites examples where a person's strong guilt feelings led to sudden death. A young African tribesman unknowingly ate forbidden wild hen and when later informed of this unintended violation, he was overcome by fear, started to shake, and died within 24 hours. In New Zealand, a Maori woman ate fruit that she only later learned came from a tabooed site and was found dead the next morning.

The common denominator in these unrelated societies was a strong belief in the power of the witch doctor, sorcery, or taboos. Such convictions persist in contemporary cultures. An article in the 2001 Christmas edition of the *British Medical Journal* reports the following:

A 45 year-old woman was admitted with a week's history of high fever. Thorough workup revealed no abnormalities other than persistent fever. During a ward round one day she said "Thank you for all you have done but I will die." When queried, she explained that the lady who cast a spell on her had given her just two weeks and that her time would be up in 48 hrs. She died on schedule. Autopsy, cultures and virology studies were all normal.

A 58 year-old man admitted for an acute infarction, was convinced he would die since his grandfather, father, elder brother and aunt had all died at age 58. His condition was quite stable and he and his family were reassured that all he needed was a good night's sleep. He expired suddenly six hours after admission.

The same issue also contained another paper entitled "The Hound of the Baskervilles effect: natural experiment on the influence of psychological stress on timing of death." The objective of the study was to determine whether cardiac deaths are higher on days that are considered unlucky. In Mandarin, Cantonese and Japanese, the words "four" and "death" are pronounced almost identically and the number 4 is considered to be very unlucky. Studies show that Japanese and Chinese Americans request that 4 not appear in their telephone numbers whenever possible.

A review of death certificates from 1973 to 1998 of over 200,000 Americans of Chinese and Japanese descent revealed there were 13 percent more deaths from heart attacks on the fourth day of the month than would have been anticipated. This peak was not followed by any compensatory drop in death rates, was not seen in white controls matched for age, sex, marital and medical status and was not associated with any change in the victim's diet, alcohol intake, exercise or drug regimen.

The authors refer to this fourth day peak as "The Baskerville effect" since in the Sherlock Holmes novel, the American Charles Baskerville inherits an estate in England where there is a local legend about a huge demon dog roaming the moors seeking an ancient vengeance against the Baskerville family. Sure enough, he subsequently dies from a heart attack triggered by a frightening encounter with a hound dog. Sir Arthur Conan Doyle was not only a magnificent writer but a remarkably intuitive physician as well.

Cannon believed that sudden death was due to the continuous outpouring of adrenaline and stimulation of the sympathetic nervous system in response to constant stress. This is supported by studies showing that beta blockers that blunt these effects can prevent sudden death in animal experiments. Others have found that sudden death can result from parasympathetic stimulation of the vagus nerve, which prevents the ventricle from contracting. New connections recently found between the cortex and lower brain centers suggest that other pathways may also be involved.

Stress And Coronary Artery Disease

As emphasized in previous Newsletters, the close relationship between emotions and the heart has been recognized since antiquity. The ancient Greeks and other early cultures believed that the heart rather than the brain was the seat of emotions and recent research confirms that communication between the heart and the brain is a two way street .

We still describe people who are generous as having a "heart of gold" or being "good hearted", while "heart of stone" and "cold hearted" describe opposite temperaments. Being brave is to be "stout hearted", and if you are timid, you are "faint of heart". "Broken hearted" seems to be the best way to describe our feelings following some severely stressful event, such as the loss of a loved one. The heart represents the essence of life, figuratively and physically. If you want to "get at the heart" of anything from an argument to an apple, you go to its "core", which comes from *cor*, the Latin word for heart.

Stress can contribute to coronary heart disease and specific coronary events in many different ways. Some of these have been considered in the previous discussion of sudden death and the role of sympathetic and parasympathetic nervous stimulation and the effects of adrenaline. Others are less straightforward and involve complex neurohumoral mechanisms that are still not clearly defined. **Part of the problem is in defining stress and distinguishing between acute "fight or flight" responses and others that are much more insidious and chronic, such as depression, frustration and loneliness.**

Numerous studies show that people who are chronically depressed have a higher incidence of heart attacks and that depression following a heart attack is associated with a significantly higher incidence of complications and mortality rates, especially in women. The explanation for this is not clear. Depression is associated with increased cortisol levels that reduce immune system resistance to microorganisms like chlamydia that have been implicated in the atherosclerotic plaque that can obstruct coronary and cerebral vessels.

Studies also show that depressed patients have impairment in cardiac baroreflex mechanisms that control the autonomic nervous system's ability to automatically maintain blood pressure within normal limits. Patients with stable coronary disease had a 30 percent reduction in baroreflex sensitivity responses that could put them at increased risk for a coronary event. This research also suggests that when depression coexists with coronary heart disease, depression is more likely to be the cause than the result. Stewart Wolf, who coined the term neurocardiology, showed that based solely on levels of depression and social support, he could predict the likelihood of future cardiac death in heart attack patients.

Stress contributes to smoking, hypertension and elevated cholesterol, the classical risk factors for heart attack but these are more likely associated rather than causative factors. Obstructive atherosclerotic plaque has more of the characteristics of an inflammatory response and involves LDL altered by oxidative stress. Emotional as well as physical stress has been shown to produce the free radical damage that causes accelerated atherosclerosis. Another risk factor that appears to be more significant than cholesterol is elevated levels of homocysteine, which cause inflammation by acting like sandpaper on the inner walls of arteries. Stress increases homocysteine levels.

Another stress related influence may be leptin, a hormone secreted by fat tissue. When first discovered several years ago, leptin was hailed as a treatment for obesity since it depressed appetite and increased energy expenditure in experimental animals. Many obese people have high leptin levels because of leptin resistance so they manufacture more leptin. Stress hormones like cortisol increase leptin resistance, which may explain why stress causes obesity, especially in postmenopausal females. A recent study showed that elevated leptin is a strong predictor of heart disease as well as obesity. Stress hormones also increase insulin resistance, another predictor of heart attacks. **Although coronary heart disease can be due to multiple factors, stress seems to play a significant role in each.**

Anxiety, Coronary Events, Chicken Vs. Egg, Alcohol, And U-Shaped Curves

Anxiety is one of the most common synonyms for stress and studies show that patients with anxiety disorders, especially phobias and panic disorder are also at increased risk for stroke, sudden death and heart attacks. Chronic anxiety may increase coronary events and deaths by promoting smoking, hypertension and atherogenesis as well as triggering arrhythmias, plaque rupture, coronary vasospasm and thrombosis. Anxiety is associated with decreased heart rate variability, a strong risk factor for cardiac mortality. Studies of patients with pre-existing heart disease show that increased anxiety can be predictive of recurrent acute coronary events. As with depression, there is often the chicken vs. egg problem of determining which came first. However, prospective studies of normal populations confirm an association between anxiety levels assessed at enlistment and subsequent coronary mortality over many years. Even when conventional risk factors are controlled for, patients with anxiety are up to 3 times more likely to suffer a fatal acute myocardial infarction and 5 to 6 times more apt to experience sudden death. Rates are higher for phobic patients. There are reports of panic disorder patients with no angiographic evidence of coronary heart disease who developed angina or an acute infarction following a panic attack.

Not having an alcoholic drink a day is another risk factor for coronary heart disease that illustrates the difficulties in deciphering the significance of statistical associations. Statistical studies that have attempted to correlate

alcohol intake with heart disease and mortality all show a U-shaped pattern with those who have 2-3 drinks daily at the bottom (lowest risk) compared to teetotalers and heavy drinkers. However, there are numerous confounding variables: age at which alcohol intake starts and duration; ethnicity; gender; and the type of alcoholic beverage being consumed. When the "French Paradox" of low heart disease rates despite high saturated fat diet was attributed to increased red wine intake, white wine and red grape juice manufacturers were quick to claim the same benefits. Beer was said to contain even more of the antioxidants that presumably conferred cardio-protection. Researchers recently reported that it is the polyphenols in red grape skins that inhibit the production of endothelin-1. This is a peptide that causes blood vessels to constrict and reduce coronary blood flow. White and rosé wines had no such effect.

The recently discovered U-shaped curve is hardly new nor are the cardiovascular benefits of wine. Paracelsus, the physician who gave us the word 'alcohol', noted 5 centuries ago that **"Whether wine is a nourishment, medicine or poison, is a matter of dosage."** The Bible advises "A little wine for thy heart's sake" and an anonymous poem tells us that *"God in His goodness sent the grapes, To cheer both great and small; **Little fools will drink too much, And great fools not at all!**"* Louis Pasteur wrote "Wine is the most healthful and most hygienic of beverages". Although there may be "nothing new under the sun", the alcohol-health debate is far from over – so stay tuned!

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The Newsletter of

The American Institute of Stress

124 Park Avenue Yonkers, NY 10703

ANNUAL SUBSCRIPTION RATES:

E-MAIL..... \$25.00
PRINT (DOMESTIC)..... \$35.00
PRINT (FOREIGN)..... \$45.00

ISSN # 1089-148X

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