

The Newsletter of THE AMERICAN INSTITUTE OF STRESS

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RIDICULOUS RISK FACTORS, HEART ATTACKS, AND STRESS

We are constantly barraged with dire warnings about what must be strictly avoided or zealously pursued to avert a heart attack. As the title of a recent *Time* article protested, "What's a Short, Bald-Headed, Potbellied Guy to Do?". The gripe was prompted by a *JAMA* report that men under the age of 55 with vertex baldness were over three times more likely to come down with a coronary than others without this shiny but sinister omen. The alert came on the heels of a *NEJM* study revealing that vivid dreams were another risk factor, and was quickly followed by the warning that consuming a high fat dinner could cause a coronary the next morning. There had been a prior admonition that a high waist/hip circumference ratio was ominous, as was being short, although a newer study found that the latter apparently applied mainly to women. We were all told that dairy products were bad and to switch from butter, but the latest caveat now claims that marga-

rine and vegetable shortenings are even worse!

Of course, you still have to be concerned about premature gray hair, arcus senilis, a deep ear lobe crease, sleep apnea, job stress, hostility, increased serum iron, not being married, living in Glasgow or Eastern Finland, low toe nail selenium levels, an elevated white count, being a couch potato, snoring, Type A behavior, social isolation, suppressing anger, — or not taking a daily nap, aspirin, beta blocker, ACE inhibitor, and antioxidant vitamins C, E, and beta carotene. There are also all sorts of lipid liability risk factors, ranging from a familial defective apolipoprotein B-100 gene and low HDL, to increased very low density lipoproteins, triglycerides, and plain old cholesterol.

Drinking, Smoking, Hypertension And Heart Attacks

At our recent Fifth International Montreux Congress on Stress, I was able to list some 300 risk factors for heart attacks, some of which seem confusing and

(Continued on page 2)

ALSO INCLUDED IN THIS ISSUE

Drinking, Smoking, Hypertension and Heart Attacks.....	1
The MRFIT Study and Risk Factors.....	2
Cholesterol Confusion and Concern.....	2
Risk Factor or Risk Marker?.....	3
Antioxidant, Atherosclerosis, Aging, and Stress.....	4
"Ignore the Experts and Eat What You Like".....	4
Deciphering The French Paradox.....	4
Red Wine, Headaches And Heart Attacks.....	5
Legal Eagles Prey On Workers' Comp.....	5
Are Workers' Compensation Doctors Overcompensated?.....	6
Can Vitamins Prevent Heart Attacks?.....	6
Liability For Lyme Disease.....	7
Yo-yo Dieting And Coronaries.....	7
Shampoos And Strokes.....	7

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The Newsletter of
**THE AMERICAN INSTITUTE OF
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Paul J. Rosch, M.D., F.A.C.P.
 Editor-in-Chief

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(Continued from page 1)

contradictory. A high fat diet might prove fatal, but so would not consuming enough dairy products, peanuts, or olive oil, according to other statistics. Red wine will protect your heart, (although recently white wine was reported to be superior), and so will other alcoholic beverages, but too much is apparently bad. How much is too much? According to a John Hopkins study, a 176 lb. male would need to drink 7 oz. of 80 proof hard liquor, 23 oz. of wine, or more than five cans of beer daily in order to **prevent** a heart attack. Cigarettes cause coronaries, but the Framingham data suggest that ex-smokers have fewer heart attacks than people who never smoked, and pipe and cigar smokers have **less than half the rate** of nonsmokers. Based on these statistics, should we now advise concerned patients to smoke cigars, booze it up, start napping, consider a hair transplant, or get out of Glasgow?

Does any of this make sense? After all, similar reasoning provided the basis for concluding that eliminating the standard risk factors of smoking, elevated cholesterol, and hypertension would significantly reduce heart attack rates. Most people, including physicians, still firmly believe this as gospel, despite the lack of any convincing proof, and considerable evidence to the contrary.

Wine is the most healthful and most hygienic of beverages.

Louis Pasteur

The MRFIT Study And Risk Factors

Confusion about the significance of what the term "risk factor" signifies stems from the Framingham studies showing a direct correlation between the magnitude of cigarette smoking, hypertension, and elevated cholesterol, with coronary morbidity and/or mortality. However, this was interpreted as demonstrating a causal connection rather than merely representing some statistical association. If that premise were true, eliminating or minimizing any or all of these "risk factors" should significantly reduce subsequent coronary events. However, none of the large scale intervention studies that achieved these objectives were able to demonstrate any such benefits. Lowering elevated blood pressure significantly reduces the likelihood of stroke, and stopping smoking clearly curtails lung cancer and emphysema. However, neither of these otherwise health rewarding measures alone or in combination, remarkably reduces cardiac mortality. After seven years of the 115 million dollar MRFIT study, in which cholesterol, blood pressure and smoking were significantly lowered, the intervention group fared no better than untreated controls. In fact, cardiovascular deaths were higher in hypertensives that were treated, possibly due to low potassium induced ventricular fibrillation. Parisian men have high smoking rates but comparatively few coronaries.

Cholesterol Confusion And Concern

While serum cholesterols over 400 can be a vector for atherosclerosis that requires aggressive treatment in genetically predisposed individuals,

(Continued on page 3)

(Continued from page 2)

what advice should you give hypercholesterolemic patients whose HDL ratios suggest the lowest possible risk for coronary heart disease? Cholesterol is a basic constituent of all cell membranes, and a building block for hormones and other vital body chemicals. Considerable controversy abounds concerning current vigorous attempts to lower cholesterol in children with drugs that may have unknown long term adverse consequences. There is scant evidence that lowering levels from 250 to 200 reduces coronary events, and none of the cholesterol drug lowering trials have shown any reduction in overall mortality. Additional consternation comes from reported higher rates of cancer, suicide, violent behavior and depression, possibly mediated by interference with serotonin production.

A major source of confusion and error is that such terms as heart attack, myocardial infarction, sudden cardiac death, and coronary occlusion are often used interchangeably, and are always automatically assumed to be due to coronary atherosclerosis. However, it is possible to have a myocardial infarction without coronary occlusion, a coronary occlusion without myocardial infarction, or sudden death from ventricular fibrillation without evidence of either significant coronary atherosclerosis or myocardial infarction. Recent research also suggests that some "heart attacks" may have a viral etiology or can result from disturbances in immune system function.

*Perfection of means and confusion of goals seem
- in my opinion - to characterize our age.*

Albert Einstein

Risk Factor Or Risk Marker?

A specific disease such as tuberculosis usually has a single, identifiable cause. That statement can be made because the tubercle bacillus can be demonstrated to be present in every case, and in its absence, the disease cannot occur. Close, unsanitary living conditions may be associated with and even contribute to the development of tuberculosis. Eliminating this type of "risk factor" can signifi-

cantly lower the incidence of tuberculosis, but the disease will not be eradicated. Unlike tuberculosis, heart attacks have no single cause, and numerous observations, findings and interventions may demonstrate positive associations. However, these "risk factors" are simply statistical observations of some correlation with one of several pathological conditions that may be described as a "heart attack". They have no causal role, and should more appropriately be labeled or considered as "risk markers." Even if it were possible to eliminate each and every one, heart attacks would persist. That is because in most instances, the problem is due to coronary atherosclerosis, a process which begins in infancy, if not *in utero*. Even the term "coronary heart disease" is imprecise, since it does not represent an appropriate monitor of the severity of atherosclerosis, although this distinction is rarely recognized.

The prevailing diet-cholesterol-heart disease dogma is attractive because it is easy to visualize how a high fat diet might elevate cholesterol and blood lipids, which then precipitate out in vessel walls to form atherosclerotic plaque. However, cholesterol is a large, inert molecule, and it is difficult to explain how it could cause the pathologic picture of plaque. Neither cholesterol, or even unmodified low density lipoprotein, are capable of producing the chronic inflammatory changes and "foam cells" characteristic of atherosclerotic plaque. The vascular pathology of familial hypercholesterolemia and of cholesterol fed animals is quite different, and similarly does not support the role of hypercholesterolemia or diet in atherogenesis. Nevertheless, the Cholesterol Cartel, composed of pill pushers, high fiber, fish oil, low fat folks, and others with vested financial interests, perpetuate and prey on the public's paranoia by continuing their cholesterol crusade. There is also considerable proof that we have been the victims not only of poor science but deliberate deception due to the systematic suppression of studies that fail to support current cholesterol lowering dogma.

*A true doctor devoted to science and to the pursuit
of medicine for its own sake is easiest of all to
deceive.*

Thomas Mann

Antioxidants, Atherosclerosis, Aging, And Stress

Recent evidence presented at The Fifth International Montreux Congress on Stress suggests that the real culprit is oxidized LDL, resulting from unopposed free radical activity. This may explain the cardioprotective effects of antioxidants such as vitamins C, E and beta carotene, as well as peanuts, olive oil and other monounsaturated fats, which scavenge the body for free radicals and inactivate them. As was also brought out, stress increases free radical activity, which plays an important role in other manifestations of the aging process including cancer, cataracts, grey hair and wrinkled skin, as well as accelerated atherosclerosis. Indeed, the concept of aging as representing "the rate of wear and tear" on the body, is the identical terminology that Selye later used to define stress. The compelling links between stress and aging are too numerous to discuss in a brief communication such as this. What is important to emphasize is the important contributory role of stress can play in the development of occlusive coronary atherosclerotic plaque, in myocardial infarction without coronary occlusion, and in the production of lethal arrhythmias that cause sudden death. All of these may come under the heading of "heart attack", but are mediated by quite different stress-related neuroendocrine metabolic mechanisms.

It is not generally appreciated that stress has a much more powerful effect on serum cholesterol and lipids than dietary fat intake, and an entire session at the Congress dealing with this was chaired by Dr. Ray Rosenman, and will be outlined in a subsequent newsletter. A separate session was devoted to the non role of diet and cholesterol in 20th Century heart disease. This included presentations from Dr. Serge Renaud of "French Paradox" fame, Dr. George Mann, Emeritus Professor of Medicine at Vanderbilt, who first described how unnatural "trans" fatty acids contained in cooking fats can cause atherosclerotic plaque, Stewart Wolf who provided a "vindication of fresh eggs and milk" and other authorities who convincingly debunked current dietary cholesterol dogma.

That kind of health which can be preserved only by a careful and constant regulation of diet is but a tedious disease.

Montesquieu

"Ignore The Experts And Eat What You Like"

Association never proves causation... why we smoke, eat rich foods, have raised blood pressures and serum cholesterol levels may be much more important than the mere observation of such stress-related statistics. The current war on cholesterol and the mandate that everyone, especially children, must know their "cholesterol count", and adhere to a low cholesterol diet, while being waged under the banner of public health concerns, will more likely bring financial rewards to vested interests than result in any dramatic lowering of heart attacks. Many will be comforted by the advice of a noted British authority, whose response to *The London Times* on the subject of increasing governmental cholesterol recommendations was entitled "EXCESS OF ADVICE: Ignore the experts and eat what you like".

Deciphering The French Paradox

The longevity and relative freedom from coronary heart disease enjoyed by residents in the south of France despite their high consumption of *pâté de foie gras* and other fats seems to be a paradox. However, goose liver is rich in polyunsaturated fats with strong antioxidant activities that can curb the acceleration of atherosclerosis. Another explanation may be related to increased intake of red wine. Countries that drink the most wine have the least heart disease. Modest consumption of any kind of alcohol appears to reduce heart attacks, possibly because it raises the level of HDL or "good cholesterol", and also reduces platelet clumping and clot-

(Continued on page 5)

(Continued from page 4)

ting. But why red wine should provide superior benefits is not clear.

A recent report suggests that the answer may have something to do with a substance in wine known as resveratrol. This is a phenolic chemical which appears to be the active ingredient of *kojikon*, a widely acclaimed oriental folk medicine having a variety of therapeutic applications. The atherosclerotic process is initiated or accelerated by oxidized low density lipoproteins (LDL). LDL becomes oxidized by free radicals which are released as a result of routine oxidative metabolic activities in the body. These are normally neutralized by the body's own natural antioxidants, but as we grow older, this ability declines. However, resveratrol has powerful antioxidant properties which may provide similar protection. Other compounds such as epicatechin and quercetin, which are also found in red wine, are even more potent in this regard, which may help to explain the puzzling "*paradoxe Française*".

The Lancet-April 24, 1993



Red Wine, Headaches And Heart Attacks

Drinking one or two glasses of red wine a day apparently helps to prevent heart attacks, but for some people, a few sips can cause a splitting headache. The explanation for both of these observations may have a common basis. Certain phenolic

substances contained in red wine appear to retard the oxidation of low density lipoproteins, which contributes to coronary atherosclerosis. They also cause the release of a chemical known as 5-HT (5-hydroxytryptamine) from platelets, thus reducing their tendency to clump and form clots. However, in certain susceptible subjects, 5-HT can precipitate a migraine attack. Other chemicals such as reserpine, which cause the release of 5-HT, can also induce migraine attacks in susceptible subjects. Although headaches can result from the vasodilating effects of alcohol, these individuals have no problem when they drink white wine or beer. Researchers have now demonstrated that red wine causes platelets to release 5-HT, but white wine and beer do not.

To further examine this, red wine with high 5-HT releasing activity was fractionated into its various chemical components, consisting of various phenolic acids and flavonoids, and sugars. Of these, the phenolic flavonoids, which give red wine its color, were clearly the most potent. However, when 14 different red wines from various countries were tested for 5-HT releasing potency, there was no correlation with their red color. Since this is derived from red anthocyanin chemicals, some other phenolic flavonoid must be the culprit. Once this is identified and can be removed, it seems likely that a red wine can be concocted that will not cause headaches, but will still help prevent heart attacks.

The Lancet-April 24, 1993

Legal Eagles Prey On Workers' Comp

A lawyer's life may be stressful, but in Kansas it apparently has its rewards. A dozen experienced Workers' Compensation lawyers have been able to cash in on the system to the tune of \$670,000 for work related injuries. One will be collecting almost \$108,000 because he injured his shoulder while

(Continued on page 6)

(Continued from page 5)

lifting and inspecting the bottom of his leather office chair. Another received \$30,000 for throwing out his back while reaching for a statute book on the top shelf of the law library. However, you don't even have to be at work to collect, especially if you have a car and a briefcase. One lawyer was awarded almost \$35,000 because he wrenched his shoulder reaching into the back seat of his car for his briefcase. However, a colleague collected \$95,000 because he "hurt himself trying to lift his briefcase out of his car trunk". The local press reported that he lost no time from work, and that it obviously had not interfered with his golf game, since he beat his own handicap four months after his presumably crippling confrontation.

This and other reports of what appeared to some as lawyer larceny prompted a flurry of letters from irate readers. One complained of being awarded only \$6,000 after his wife was murdered in a local bridal shop, promising that "When I go to the cemetery, I am going to tell her that I miss her, I still love her, and I wish to God she had just sprained her back lifting a dress instead".

The New York Times-April 30, 1993

Lawyers and painters can soon change white to black.

Danish Proverb

Are Workers' Compensation Doctors Overcompensated?

While Kansas Workers Compensation lawyers may be capitalizing on the system, California doctors are really cleaning up, especially for back injury claims. According to one research study, "a physician working 8 hour days, 45 weeks a year could earn \$540,000 to \$700,000 more a year examining such patients for the Workers Compensation system than outside it." Their medicolegal back examinations take an average of 108 minutes, compared to only 57 minutes for a nonworker comp examination. A recent study reported that back injury claims in California cost 5-10 times more

than in other litigious states like New Jersey and Maryland. California's average medicolegal cost per resolved claim is \$2,376.00, and this does not include any laboratory tests, X-rays, MRI or other imaging procedures. The average hourly rate for reviewing records, taking a history, performing an examination and writing a report is over \$500 an hour. That's greater than three to four times the routine charges for these services. As a result, legislation has been proposed to limit the percentage of a doctor's income that can be derived from workers' compensation exams.

American Medical News-May 3, 1993

Can Vitamins Prevent Heart Attacks?

Most heart attacks are due to atherosclerotic plaque that causes obstruction of coronary blood flow. Plaque formation results from the inflammatory response to oxidized low density lipoproteins (LDL), sometimes referred to as "bad" cholesterol. LDL in itself is apparently not particularly harmful until it becomes oxidized in the arterial wall by free radicals. These molecules are produced as a by-product of normal oxidative metabolic activities. However, they lack an oxygen atom, and race around the body attaching onto any molecule that can supply this need, disrupting regular cellular functions. Oxidized LDL attracts macrophages that migrate through the arterial wall resulting in the characteristic inflammatory lesion of atherosclerotic plaque.

Free radicals are inactivated by antioxidants found in certain foods and nutrients. Vitamins C, E, and beta carotene are particularly potent in this regard, but must be taken in amounts much higher than the usual minimal daily requirements to prevent deficiency diseases. In one report, taking 800 units of vitamin E daily for three months significantly reduced the oxidation of LDL. Vitamin C is even more potent, and in test tube studies, is 95 percent effective in preventing oxidation of LDL. Smokers and diabetics have lower levels of vitamins C and E, which may explain their higher rates

(Continued on page 7)

(Continued from page 6)

of heart disease. In another trial involving 333 men with stable angina, daily administration of 25 mg of beta carotene cut subsequent heart attacks and cardiovascular deaths in half.

While there appears to be little risk in taking larger amounts of these vitamins, there is the danger that some individuals may go overboard. Others may also neglect the need for important lifestyle changes such as smoking cessation, regular exercise and proper diet.

Cardiology World News, April 1993

Liability For Lyme Disease

The Long Island Railroad had warned its workers about tiny ticks, told them how to protect against bites, and provided them with insect repellent. Despite this, and the fact that it could not be proven that the disease was contracted on the job, an employee who looked after weed choked signal crossings was awarded \$160,000 because a Federal District judge held the railroad responsible for his illness due to Lyme Disease. Three co-workers also received a total of \$405,000 in the same lawsuit. The judge held the railroad negligent because it did not routinely spray insecticide around the signal crossings and their educational program about Lyme disease was considered to be inadequate. While the purpose of the decision was to force companies to institute more thorough safety measures, many feel that it may set a precedent for placing unreasonable expectations on employers, and it is likely to be appealed.

The New York Times-April 30, 1993

Yo-yo Dieting And Coronaries

There is abundant evidence from animal studies that decreasing daily caloric intake results in greater longevity. Less food intake lowers oxidative metabolic activities in the body, resulting in fewer free radical by-products. Free radicals con-

tribute to atherosclerosis, malignancy, cataracts, and most other manifestations of the aging process. Conversely, obesity is associated with increased cardiovascular mortality and deaths from other causes. Overall mortality rates are eighteen percent higher for individuals who are in the top quintile for being overweight. The problem is that few people are able to lose weight and keep it off, fluctuating up and down as a result of repeated attempts to diet, and this is often referred to as yo-yo dieting. Although there may be some beneficial responses during the weight loss phase, animal research reveals that these are more than offset by short and long term rebound phenomena that occur following this, including increased blood pressure, disturbances in heart rhythm, and degenerative cardiovascular changes. Weight cycling also tends to redistribute fat stores to abdominal depots, and an increased waist/hip circumference ratio is a risk factor for heart attacks. Recent research in humans now also confirms that repeated weight loss dieting increased cardiovascular deaths, even in markedly obese subjects. In one report, yo-yo dieting and its resultant weight fluctuation increased overall mortality by more than fifty percent, underscoring the old adage that the important thing is not to lose weight, but to keep it off.

JAMA-March 3, 1993

Shampoos And Strokes

At least seven cases of what has been termed, "Beauty Parlor Stroke Syndrome" have now been reported. The condition is usually seen in older women during or after the shampooing process in a beauty parlor. In some individuals, the associated hyperextension and/or rotation of the neck can pinch the vertebral artery sufficiently to seriously interfere with the flow of blood to the brain. The resultant signs and symptoms vary, and include severe dizziness, slurred speech, weakness of facial or extremity muscles, changes in behavior, nausea, vomiting, numbness, and incoordination. While these effects are frequently temporary, some may persist, with permanent damage being confirmed by MRI and CT scan studies.

JAMA-April 28, 1993

Book Reviews • Meetings and Items of Interest

Book Review

Perturbing The Organism: The Biology of Stressful Experience. Herbert Weiner, University of Chicago Press. Chicago, IL, 1992. No. of pages: 368 \$35

The phenomenal interest, if not preoccupation with stress that pervades modern society often represents a rather remarkable phenomenon to many who have been involved in stress research for several decades. The current concept of stress, and indeed the term itself as presently used, originated with Hans Selye around 50 years ago. Selye's research was initially of interest primarily to researchers, and his theories were not readily accepted by the medical community. There was considerable skepticism that conclusions based on responses to extreme and acute physical and emotional stressors in rats could be extrapolated to apply to the effects of such common, chronic human psychosocial stressors as bereavement, guilt, and poverty.

Selye's theories were based on the earlier investigations of Claude Bernard and Walter Cannon, which teleologically postulated that all adaptive responses to stress were based on the preservation of life during the lengthy course of man's evolution. Curiously, none of these careful researchers were apparently aware of Darwin's seminal contributions in this area. Thus, a proper appreciation of stress requires a multi-disciplinary integration of such seemingly disparate disciplines as neuroendocrinology, anthropology, comparative physiology, psychology, and perhaps even ethology and philosophy. In this masterful presentation, Weiner provides a critical analysis and consolidation of these aspects of stress by meticulously tracing the significance of empirical observations and their contribution to conceptual theories. A major and distinctive contribution of this offering is its careful explanation of where and why experimental animal research is relevant to the human condition. Equally constructive and valuable is the

underlying theme emphasizing the importance of understanding that homeostasis and the health of the organism is entirely dependent on good communication. This includes not only effective communication between the constituency of the internal environment, but also with external stressors. As the author notes, "The separation between the brain (and its mind) and the body fall away when the organism is seen in such a totally integrated system of information exchange and processing.....The concept of perturbation leading to a change in function is central to, and the basis of, stress theory". While much of the contents of this scholarly work can be found in prior writings, its masterful amalgamation and coordination with other material makes the overall message even more meaningful.

Meetings and Items of Interest

June 24-27 National Jewish Center for Immunology and Respiratory Medicine - Physical Illness, Psychologic Development & How The Twain Shall Meet, Keystone Resort, Keystone Colorado (800) 222-0188

June 28-July 2 New England Educational Institute - 10th Annual Cape Cod Summer Symposia Featuring Christine Courtois on Post Traumatic Stress Disorder, Cape Cod, MA (413) 499-1489

July 1 Colby College Special Programs - Addiction Medicine, Colby College Millett House, Waterville, ME (207) 872-3386

July 5-9 New England Educational Institute - 10th Annual Cape Cod Summer Symposia Featuring Ross Baldessarini on Clinical Psychopharmacology, Cape Cod, MA (413) 499-1489

July 5-9 Albert Einstein College of Medicine - Behavioral Medicine Applications, Cape Cod, Eastham, MA (212) 430-2307

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