

# HEALTH AND STRESS

## *The Newsletter of The American Institute of Stress*

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## YOU READ IT HERE FIRST! WHAT'S HAPPENED SINCE?

Key Words: Helicobacter, chlamydia, nanobacteria, DNA "fingerprinting", C reactive protein, mental stress tests, talking and blood pressure, James Lynch, Type A traits, Ho scale, stress, colds, and "natural" remedies

Exciting new advances in basic research that appear to have important implications for clinical medicine seem to pop up several times a week. Many are difficult to evaluate since they are controversial and have not been confirmed by other investigators. Others are blown out of proportion by media hype that preys on the insatiable thirst of the public for new breakthroughs that promise a cure for cancer, heart disease, and reversing the aging process.

Even more confusing are the claims made by manufacturers of nutritional supplements and other "natural or "alternative" approaches that insinuate inexpensive and safe relief not only for all of the above, but also obesity, impotence, baldness, memory loss, depression, anxiety, insomnia, and almost anything else that ails you. And you don't need a prescription.

The plethora of products is mind boggling and steadily increasing, as are various electro magnetic and other subtle energy devices utilizing light and sound to relieve stress and pain. Almost all are based on anecdotal claims rather than solid scientific studies, and while some may be authentic, it is difficult to separate the wheat from the chaff.

Similarly, advances in clinical medicine and particularly the role of stress in health and illness are also often based largely on speculation. Even when there are supportive studies, subsequent investigations can come to contrary conclusions. Alternatively, the results may be shown to be valid, but not for the reasons cited. Over the past few years, we have tried to identify those clinical and basic science research reports which appear to offer particular promise, and put them in proper perspective so that the pros and cons are clear.

Some of these predictions have panned out and others await further proof. A few have also fizzled, as subsequent research has demonstrated flaws in the design, implementation, or conclusions of experimental investigations. We thought it would be useful to revisit some of these topics in the light of recent findings that either reinforce previous opinions, or suggest they need to be revised.

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### Are Ulcers, Heart Attacks And Strokes Really Due To Infections?

Five years ago, the medical community was jolted when it was shown that peptic ulcers were not due to dietary indiscretion or stress, but rather a bacterium called *Helicobacter pylori*. The initial suggestion of this, several years previously, was greeted with skepticism if not incredulity for several reasons. The role of stress in peptic ulcer disease had been well established. Most ulcer patients could readily identify foods that would trigger symptoms, and increased secretion of gastric acid and pepsin was the obvious mechanism of action. Aspirin, cortisone, and nonsteroidal anti-inflammatory drugs caused ulcers because they lowered normal local tissue defenses against the digestive action of these chemicals, and the notion that ulcers were an infectious disease you could "catch" was counterintuitive.

It had been assumed that microorganisms were simply responsible for specific infections, in accordance with Koch's postulates. The tubercle bacillus caused tuberculosis, and the same was true for the pneumococcus and pneumonia, HIV virus for AIDS, monilia for thrush, *Endamoeba histolytica* for amebic dysentery, *Plasmodium malariae* for malaria, etc., etc.

It was known that some microorganisms, such as the spirochete that caused syphilis, could eventually produce dermatologic, cardiovascular and neurological pathology, but these were almost always the sequela of a clinically evident infection; even though this might have occurred many months or years previously. There was also some suggestion that local candida infections could produce a systemic illness. However, there was absolutely no evidence of signs and symptoms to indicate an infectious process with respect to helicobacter and peptic ulcer. Yet, the proof seemed incontrovertible. The organism was invariably cultured from ulcer lesions; ulcers could be caused by ingesting the bug, which did result in a few days of malaise and elevated temperature. The proof of the pudding was that a course of appropriate antibiotics eradicated the disease more effectively and permanently than conventional treatment with diet, antacids, and acid inhibitor medications.

### The Chlamydial Conundrum

More recently, as indicated in previous Newsletters, compelling evidence has accumulated that *Chlamydia pneumoniae*, a common pathogen that produces few symptoms other than a mild upper respiratory infection for a day or two, may be responsible for heart attacks, stroke, and other disorders due to obstructive atherosclerotic deposits. Other microorganisms, that are also harbored in the body without giving rise to evidence of clinical infection, including helicobacter, mycoplasma and cytomegalovirus have also been implicated for several reasons. In some patients, elevated antibody titers are consistent with infections; in others, organisms have been identified in and cultured from atherosclerotic plaque, which does have an inflammatory component quite different from the atherosclerotic lesions produced in laboratory animals by high cholesterol diets. It has long been recognized that diabetes, hypertension, cigarette smoking, elevated cholesterol, a strong family history, and other established risk factors, are present in only half of heart attack victims.

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Further support for an infectious etiology comes from the finding that antibody levels for various organisms are much higher in heart attack patients, compared to age matched controls admitted to the hospital for other diagnoses. In addition, C reactive protein, a non-specific marker for inflammation, is increased in these patients. In asymptomatic individuals, an otherwise unexplained elevation of C reactive protein appears to predict the likelihood of a subsequent heart attack or stroke.

Scientists theorize that while these organisms may not produce any signs or symptoms, they nevertheless continually stimulate immune system components designed to eradicate foreign microorganisms. These chemicals are attracted to sites on the inner lining of blood vessels where these organisms are located and steadily produce a smoldering inflammatory response that results in the growth of atherosclerotic plaque. Chlamydia pneumoniae is unlike most other bacteria, because it lives not on the surface of cells, but rather inside them, much like many viruses. It is frequently found inside the blood vessel cells of people with coronary heart disease, but not in the cells of healthy controls. A similar mechanism has been proposed for autoimmune disorders like rheumatoid arthritis, lupus, and possibly multiple sclerosis, as the immune system mounts an attack on proteins which it perceives to be foreign.

It is likely that chlamydia and other microorganisms are only part of the picture, and that they primarily exaggerate the damage done by other factors that contribute to arteriosclerotic plaque. For example, experimental animals fed a high fat diet will develop arteriosclerosis, but they do so much more rapidly if they are infected with chlamydia. Additional support comes from a new study, showing that a protein found on chlamydial cell walls is almost identical to one found in heart tissue in mammals. Scientists believe that when the immune system attacks the bug, it accidentally also attacks the cardiac protein as well. In experimental animals, the pathological changes produced are very similar to those found in heart attack patients.

These findings have important implications since they suggest that some heart attacks and strokes might be prevented by vaccines, or successfully treated with appropriate antibiotics. Some clinical studies have now shown that a course of antibiotics known to kill chlamydia can reduce the risk of heart attack or stroke for up to eighteen months.

### **Alzheimer's, Gall And Kidney Stones?**

Coronary artery disease and strokes are not the only chronic diseases that can be caused by chlamydia. Researchers recently reported finding evidence of the bug in twenty-seven of twenty-nine autopsy brains of people with Alzheimer's disease, but in only one of nineteen brains of age matched non-Alzheimer's patients. It was identified inside the glial cells that surround neurons, and may have been attracted to these cells because they had already been damaged by some other degenerative process. There is also evidence that gall stones and kidney stones can be caused by bacterial infections. One report revealed that gall stone patients have a 100 to 1,000 fold higher level of clostridia and other bacteria normally found in the intestinal tract. These organisms generate deoxycholic acid, which triggers the liver to excrete cholesterol rich bile, a significant risk factor for the formation of gallstones. Other researchers have shown that antibiotics can lower the concentration of these bacteria to levels below the threshold needed to make gallstones.

Finnish researchers have also now found that certain "nanobacteria" can be responsible for the formation of kidney stones. These microorganisms have escaped microscopic detection until recently, since they are smaller than some viruses. Using highly sophisticated microchemical techniques, they showed that these minute bacteria build a mineralized coating around their exterior, upon which additional minerals and proteir.aceous materials gradually accumulate, that eventually form a stone. In one study of 30 kidney stones, all were demonstrated to have traces of nanobacteria in their cores.

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## Juvenile Arthritis And Cerebral Palsy?

Juvenile Rheumatoid Arthritis or Still's disease is generally considered to be an autoimmune disorder in which immune system components attack normal structures that are perceived as foreign invaders. It is generally characterized by a period of fever and symptoms of systemic illness several months before the onset of actual arthritis. Researchers now believe that *Mycoplasma pneumoniae*, a common cause of "atypical pneumonia" is responsible. In a seventeen year Canadian study, it was found that the diagnosis of Juvenile Rheumatoid Arthritis varied significantly from year to year, but peaked in precisely the same years as *M. pneumoniae* infections.

Cerebral Palsy may be another addition to the growing list of non infectious diseases that are actually caused by microorganisms. This type of brain damage, which affects about 500,000 Americans annually, was long believed to be due to oxygen deprivation or trauma before or during birth. However, a study reported last year suggests that infected amniotic fluid may also be to blame. Although no specific organism has been isolated, advanced DNA "fingerprinting" techniques have shown that the amniotic fluid of newborns with Cerebral Palsy contain microbial fragments that are never present during normal births.

Most of the evidence remains circumstantial. The fact that a microbe is present in increased amounts in people who have a disease compared to others who don't, only proves association, not causation. The vast majority of individuals who harbor helicobacter and chlamydia are not only asymptomatic, but there is no increased risk for the subsequent development of ulcers, heart attacks, or other putative associated diseases. As noted previously, it is likely that numerous other factors contribute to the clinical expression of these disorders, including lifestyle and genetics. In particular, it would seem most plausible that stress can play a major role because of its known ability to lower resistance to a host of infections, ranging from the common cold, to tuberculosis, herpes, and AIDS.

## Exercise: How Much, What Kind?

Two decades ago, when the jogging and running craze started to peak, the usual motto was "No pain, No gain". Although proponents waxed eloquently about the mental and emotional benefits of regular long distance running, that did not seem to be apparent on the tired and anguished faces of most who were engaged in their daily pursuit of the elusive "runner's high". Nor could it be shown that the cardioprotective effects had any direct correlation with the amount of strenuous exercise. For some, all they had to show for their efforts were traumatic arthritis, and in a few cases, broken bones.

Many of us have long felt that moderate regular exercise, like walking briskly for 20-30 minutes three or four times a week provided just as much improvement in physical and emotional health as jogging a few miles every day. A variety of recent reports confirm this. Furthermore, it's never too late to start.

A study of over 7700 men aged 40 to 59 years who were sedentary in middle-age, but initiated moderate physical activity as they got older, showed that they had a 34% reduction in cardiovascular mortality. There was a 52% drop in deaths due to other causes, compared to others who continued to be couch potatoes. Vigorous activity was not necessary, and simple regular walking and weekend gardening seemed to suffice. In another report, postmenopausal and elderly women who exercised moderately for as little as an hour a week (walking, gardening, social dancing), had 42% fewer hip fractures.

Just burning 200 calories daily by riding a bike, taking a brisk walk, or hoeing a flower bed will do the trick, even if it takes several sessions to reach a total of 30 minutes. It all adds up. Vigorous exercise for a half-hour or more at least three times a week may be needed to train for some sports activity, and weight lifting is better for building up muscles. But daily activities of much less intensity will significantly reduce the risk for heart attack and osteoporosis, as well as improve agility, coordination, and overall feeling of well being.



## Stress And Cardiovascular Disease

There has been increasing interest and controversy concerning the role of stress in cardiovascular disease. Several reports now suggest that "mental stress tests" may be just as accurate as treadmill procedures in predicting coronary risk, and in some patients, even more sensitive. Speaking in public appears to evoke the most consistent and dramatic cardiovascular responses with respect to an increase in blood pressure, heart rate, and ischemia.

The pioneering work of James Lynch demonstrated that there was an immediate and significant rise in blood pressure and pulse with the onset of talking. These changes were magnified if the content of the conversation was more emotionally charged or stressful, the audience was perceived to be of higher social status, the volume or rapidity of speech was more rapid, or basal blood pressure was already elevated. The same phenomenon could be demonstrated in deaf mutes when they conversed using sign language, but not when they moved their fingers just as vigorously in an aimless fashion. These responses were not mitigated by antihypertensive drugs, and indeed, the elevation in blood pressure was accentuated in patients taking beta blockers, which blunted the rise in heart rate.

Lynch used automated blood pressure equipment and a proprietary software program which allowed minute to minute displays and recordings of blood pressure, heart rate, and mean arterial pressure. He was impressed with the observation that subjects were completely unaware of the wild fluctuations in these measurements while they were talking, even though they were sometimes alarmingly high. Based on providing immediate feedback, he was able to teach patients how to reduce marked rises when they spoke, and eventually developed a unique treatment for hypertension based on this. However, the significance of exaggerated blood pressure responses to emotional and physical stress is still controversial, with respect to predicting the development of clinical disease.

The cold pressor test measures blood pressure elevations following immersion of a hand in ice water for a minute, and has been used for over fifty years in an unsuccessful attempt to demonstrate that hyperreactivity will predict the likelihood of subsequent fixed hypertension. Blood pressure rises in association with physical activity and with breath holding. Elite weight lifters, whose blood pressures have been recorded at 450/300 when they perform the supreme Valsalva maneuver, (forced expiration against a closed glottis) do not appear to be at increased risk for either permanent hypertension or stroke. In all of these situations, elevations of blood pressure are transient, and rapidly return to normal on cessation of the activity. There is no evidence of any adverse long term consequences, regardless of the magnitude of the rise.

Similarly, blood pressure rises associated with emotional stress are generally viewed as normal physiologic components of the "fight or flight" response. They produce few, if any signs or symptoms, and no therapeutic interventions appears to be warranted. A common example is so called "white coat" hypertension. While this has also been believed to be a harmless condition, there is now evidence that this may not be correct.

## White Coat Hypertension

The observation that blood pressures tend to be higher than normal under stressful situations is hardly new. This is especially apparent in healthy young individuals applying for life insurance or entrance into the military. Most doctors were well aware of this, and when confronted with such situations, would usually suggest the applicant lie down in a quiet room for 10 or 15 minutes, following which repeat measurements were almost always satisfactory. This maneuver is much less apt to be utilized today especially by busy physicians working under the burden of managed care. They are often obligated to see a certain number of patients within a specified time period, and there are financial constraints.

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It is much simpler and more remunerative to prescribe a pill, order additional tests, and arrange for a repeat visit, especially since this presumably reduces risk of malpractice litigation if some unrelated problem should arise. This may lead to many patients receiving medications that are not only unnecessary, but could have adverse side effects.

A 1996 report revealed that 30 percent of all patients whose blood pressures were above 140/90 when taken by a physician in an office, had 130/85 or lower readings when taken at home or other neutral setting. Follow-up of these "white coat" hypertensives revealed no evidence of an increased incidence of hypertension or heart disease after five to ten years. It has been suggested that perhaps 10 to 15% of patients currently being treated for essential hypertension are in this category, and could safely discontinue their medications.

However, a recent report suggests that "white coat" hypertension may not be entirely benign, even if it is not a precursor of permanent hypertension or lead to coronary heart disease. Researchers measured blood pressures in almost 1700 subjects aged 25 to 74 who were undergoing echocardiographic evaluation of their cardiac status. Particular attention was directed to the thickness of the left ventricular wall, which is increased in hypertension. After at least 30 minutes rest, measurements were made three times by technicians and once by a physician following the echocardiogram. The diagnosis of "white coat" hypertension was made if the average readings by technicians was less than 140/85 and the physician measurement was 160/95 or greater. In general, patients in this category with the greatest discrepancies tended to be older and overweight, and the incidence was slightly higher in men compared to women (10.9% vs. 8.2%).

Even after all possible influencing factors had been taken into consideration, including cigarette smoking, age, obesity, and family history, the "white coat" group showed a significantly increased thickness of the left ventricular wall compared to normotensive controls.

In addition, there was a correlation between this width and the degree of difference between the systolic readings obtained by technicians compared to physicians. Measurements of left ventricular ejection force were also above normal. This study indicates that even though there may be no clinical signs or symptoms, "white coat" hypertension is associated with permanent structural changes in the heart. Whether this means that all such individuals should be treated, or that medications could prevent this remains to be seen.

### **Hostility And Heart Attacks**

Type A behavior has been shown to be as significant a risk factor for heart attacks as hypertension, cigarette smoking, and cholesterol levels. Most studies have also shown a correlation between Type A and the severity of obstructive atherosclerotic disease on angiography. But just exactly what is Type A? How can it be measured? And exactly what is it about Type A that causes it to contribute to coronary heart disease?

Our current conceptualization came from the pioneering work of Ray Rosenman and Meyer Friedman, and was based on observations of the overt behaviors of patients with ischemic heart disease. These were often characterized by a fiercely competitive attitude; strong sense of time urgency; aggressiveness, increased muscular activity in the form of gestures, motions, facial activities such as grimaces, gritting and grinding of teeth, tension of jaw muscles, and a tendency towards frequent fist clenching, fidgeting, tapping the feet, or playing with a pencil in some rhythmic fashion. There were also unusual breathing patterns, with frequent sighing produced by inhaling more air than needed while speaking, and then releasing it during the middle or end of a sentence to provide emphasis.

Attempts have been made to measure Type A by questionnaires to rate time urgency, competitiveness, or hostility, but Type A's are often unaware of their traits or deny them. Accurate assessment can only be made by careful observation under correct conditions.

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What is it about Type A behavior that causes it to contribute to coronary heart disease? In recent years there has been a tremendous amount of media hype about the role of "hostility" as the toxic core component. Studies show a correlation between high hostility levels and initial heart attacks, deaths from heart disease, and even angiographic evidence of accelerated atherosclerosis compared to non-hostile controls.

The problem is that most studies are based on the Minnesota Multiphasic Personality Inventory (MMPI) questionnaire developed in 1937. The MMPI consists of responses to 566 self-descriptive statements, which have been utilized to develop subscales for rating tendencies towards such things as depression, paranoia, schizophrenia, and introversion. It rapidly became the gold standard for psychological testing and was widely used for screening purposes by corporations and academic institutions.

About forty five years ago, two psychologists, Cook and Medley, selected 50 items for what they called a hostility (Ho) scale to differentiate teachers with good or poor rapport with students. It was subsequently found that people with high (Ho) ratings had correspondingly higher death rates from coronary heart disease. This was later pruned to 27 items that were found to have greater predictive power for coronary events and morbidity, and it is this modification that has been most frequently used. There is abundant statistical information available from college students and employees who completed the MMPI several decades ago and whose subsequent health history could be tracked.

However, hostility, like Type A behavior, is much more accurately assessed by personal observation rather than responses to a questionnaire. When the psychological correlates of the Cook and Medley hostility scale are compared to independent behavioral ratings of hostility, the results proved to be quite different. The Ho scale correlated best with anxiety, neuroticism, and a good ability to "fake" answers, while behavioral ratings were more associated with dominance, vigor, and self-confidence. These traits, which would not be as evident on responses to a questionnaire, seem much more on target.

Hostility is a complex potpourri of traits, characteristics and attitudes that include anger, aggression, and irritability. The Ho scale does not provide an assessment of any of these key elements. What may be equally important is whether these feelings are kept pent up or are freely expressed, so that you literally and figuratively are able to "get things off your chest." In addition, a careful analysis reveals that high Ho scores correlate best with deaths from all causes, rather than heart disease specifically.

With respect to questionnaires used to rate Type A behavior, the most commonly used is the Jenkins Activity Survey, which detects three main behavioral syndromes: hard driving temperament, speed and impatience, and excessive involvement with work activities. Although each of these subscales correlates with the total score, they show no interrelationship, and the total score has only about a 70 percent agreement with ratings obtained from special interview techniques designed to elicit Type A behaviors.

Similarly, it does not seem likely that a questionnaire constructed a half century ago to examine student-teacher relationships can accurately measure something as complex as hostility. This is especially true since there have been significant societal changes in the intervening period, and the significance of certain responses is now quite different. Being divorced, or getting a traffic ticket for speeding no longer carries the same stigma.

High Ho ratings correlate with high scores on the Jenkins Activity Survey subscales of speed and impatience and hard-driving temperament. It may be that the Ho scale really measures certain Type A traits, but calls them something else, and really confirms the validity of the Type A concept. The hostility hypothesis is attractive, but it is important to understand how it is being defined and measured. It is quite likely that some Type A traits are more harmful than others. However, there are far more questions than answers, the most important being why we behave the way we do.



## Stress, Colds, Vitamin C, Zinc, And Echinacea. What's The Bottom Line?

The ability of stress to precipitate and aggravate infectious diseases has long been recognized. While much of the evidence is anecdotal, there are some solid scientific studies relating to the common cold. In a British study done in the last decade, stress levels were evaluated in volunteers by several approaches, including negative mood (do you feel anxious or depressed?), recent life change events (loss of a loved one, divorce) and perceived level of stress (do you feel in control or on top of things?). They were then exposed to standardized doses of common rhinoviruses using nasal sprays, and followed to see how frequently colds developed and how severe they were. Only 26 per cent in the low stress group came down with clinical symptoms compared to more than twice as many at the upper end of the scale. Clinical infection was confirmed by demonstrating elevated antibody titers to the specific virus, and severity was measured by weighing tissues containing mucus. Both the frequency and severity of colds clearly correlated with stress levels. In a more recent report from the U.S., the same investigators repeated the protocol on 276 healthy volunteers, but used more precise techniques to evaluate the nature of stress (long term vs. short term), as well as the severity of illness. They also measured blood levels of natural killer cells, an immune system component that combats infectious agents. Those who had been under stress for more than a month had lower natural killer cell activity, and were 2.2 times more likely to develop colds. Not surprisingly, the most common culprit was increased job stress.

Although there is no cure for colds, large doses of Vitamin C are claimed to provide relief. Linus Pauling, who first proposed this, took 15,000 to 20,000 mg. daily, compared to the recommended daily allowance of only 60 mg. Some studies show that doses higher than 100 to 200 mg. do not continue to raise blood levels, and while taking more is generally considered to be harmless, this may not be true. Large doses were recently found to increase urinary concentrations of oxalate, which can contribute to the formation of kidney stones. The NIH has put an upper supplement-safety limit for vitamin C at 1,000 mg. But even that may be too high according to another study which shows that at doses over 500 mg., vitamin C can act as a "pro-oxidant" that damages DNA, and when taken with iron, it has more oxidant than antioxidant effects. Foods containing vitamin C are safer, healthier, and may contain other important nutrients.

Zinc lozenges are said to relieve cold symptoms, but clinical trial results are also controversial. One of the reasons may be that there are different products. There is some evidence that only Zinc acetate preparations that release large amounts of Zinc ions can boost the immune system, block inflammation and free radical damage, and produce a beneficial drying effect. Echinacea is even more controversial. There is marked variation in the products available, some contain other herbs that can cause unpleasant, side effects, and only the approved German extract has been studied. The bottom line appears to be that the best and safest way to avoid colds - may be to avoid stress.

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