

The American Institute of Stress

# HEALTH AND STRESS

Your source for science-based stress management information

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## The **SURPRISING** Health **BENEFITS** of **ALCOHOL**

A close-up photograph of a hand pouring red wine from a dark bottle into a clear glass. The wine is a deep red color and is captured mid-pour, creating a dynamic sense of movement. The background is blurred, showing other people and glasses, suggesting a social setting like a bar or restaurant.



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# **HEALTH AND STRESS**

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**Editor In Chief:**

**Paul J. Rosch, M.D., FACP**

**Associate Editor:**

**Helen M. Kearney, Ph.D.**

**Creative Director: Kellie Marksberry**

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# Could the benefits of drinking alcohol outweigh all its risks?

**by Paul J Rosch, MD, FACP**

**Editor-in-Chief**

**For many people, one or two cocktails or some wine with dinner helps them to relax after a hectic workday. Similarly, having a few drinks with friends fosters feelings of conviviality that can temporarily keep you from dwelling on whatever might be troubling you. Social drinking also promotes social support, a powerful stress buster.**

## The Bible, Paracelsus And The Bard

The stress reduction, as well as the health promotion effects of alcohol, have been recognized since antiquity. The Bible says *"Give strong drink to the one who is perishing, and wine to those in bitter distress; let them drink and forget their poverty and remember their misery no more."* (Proverbs. 31:6-7) Jesus drank wine, his first miracle was turning water into wine at a wedding feast, and he instructed his followers to drink wine as part of an annual remembrance ceremony for him. (John 2:1-10) With re-

spect to health benefits, Paul advised, *"Drink no longer water, but use a little wine for thy stomach's sake and thine often infirmities."* (Timothy 5:23)

The reason for this may be that scholars believe water borne diseases due to contamination were common at the time.

Wine also *"maketh glad the heart of man"* (Psalms

104:15). The good Samaritan dressed the wounds of an ambushed man with wine and olive oil (Luke 10:25-37), and wine as well as vinegar have been used as antiseptics since the time of Hippocrates.

But the Bible also warns about the dangers of overindulging, *"Wine is a mocker, strong drink is raging; and whosoever is deceived thereby is not wise."* (Proverbs 20:1]. Nor should it be used to drown out your sorrows.

Who has woe? Who has sorrow?  
Who has contentions? Who has complaints?  
Who has wounds without cause?  
Who has redness of eyes?  
Those who linger long at the wine,  
those who go in search of

mixed wine. Do not look on the wine when it is red, when it sparkles in the cup, when it swirls around smoothly; at the last it bites like a serpent, and stings like a viper. Your eyes will see strange things, and your heart will utter perverse things. Yes, you will be like one who lies down in the midst of the sea, or like one who lies at the top of the mast, saying: they have struck me, but I was not hurt; they have beaten me, but I did not feel it. When shall I awake, that I may seek another drink? (Proverbs 23:29-35)

***"Whether wine is a nourishment, medicine or poison, is a matter of dosage"***

King Solomon warned that wine or strong drink was dangerous since it could cause drunkenness, and *"the drunkard shall come to poverty: and drowsiness shall clothe a man with rags."* (Proverbs 23:20-21) Priests were prohibited from drinking alcohol before performing duties in the Holy Tabernacle that housed the Ark of the Covenant under penalty of death (Leviticus 10:9).

There are many other aphorisms that portray alcohol as a two-edged sword, but what determines which side will prevail? Paracelsus, the physician who coined the term "alcohol" 500 years ago, wrote, *"Whether wine is a nourishment, medicine or poison, is a matter of dosage."* Shakespeare was also ambivalent. *"Drink, sir, is a great provoker of three things, nose painting, sleep and urine. Lechery, sir, it provokes, and unprovokes; it provokes the desire but takes away the performance."* *Macbeth*: Act 2, Scene 3. (Nose painting



referred to the fact that drinking often turned the nose red and/or made you look like a clown.) Shakespeare found delight in alcohol, as did everyone else at the time. Most people, from the poorest farmer to Queen Elizabeth, drank a brew made from malt, and a mini brewery was an essential part of households that could afford it. The Bard of Avon's father was an official ale taster in Stratford, a highly respected position that involved monitoring the ingredients used by professional brewers and insuring that they sold their ale or beer at prices regulated by the Crown.

Many of Shakespeare's scenes take place in taverns because he frequented them. He was very familiar with the dangers of excessive drinking, noting that a drunkard is "*Like a drown'd man, a fool, and a madman.*"



*One draught above heat makes him a fool, the second mads him, and a third drowns him."* *Twelfth Night*: Act 1, Scene 5. Falstaff, a mythical character who appears in both parts of *Henry IV* and in *The Merry Wives of Windsor*, was the epitome of the town drunk. Wine was available but it cost twelve times more than ale since it had to be imported. Sack, a sweet wine fortified with brandy (known today as sherry), was particularly popular with the Elizabethans, and Falstaff described its effects as follows:

A good sherris sack hath a two-fold operation in it. It ascends me into the brain; dries me there all the foolish and dull and curdy vapours which environ it; makes it apprehensive, quick, forgetive, full of nimble fiery and delectable shapes, which, delivered o'er to the voice, the tongue, which is the birth, becomes excellent wit. The second property of your excellent sherris is, the warming of the blood; which, before cold and settled, left the liver white and pale, which is the badge of pusillanimity and cowardice; but the sherris warms it and makes it course from the inwards to the parts extreme: it illumineth the face, which as a beacon gives warning to all the rest of this little kingdom, man, to arm; and then the vital commoners and inland petty spirits muster me all to their captain, the heart, who, great and puffed up with this retinue, doth any deed of courage; and this valour comes of sherris. So that skill in the weapon is nothing without sack, for that sets it a-work; and

learning a mere hoard of gold kept by a devil, till sack commences it and sets it in act and use. *Henry IV, part 2: Act 4, Scene 3*

Shakespeare also wrote "*O thou invisible spirit of wine! If thou hast no name to be known by, let us call thee devil!*" *Othello: Act 2, Scene 3*. He allegedly died after a night of heavy drinking with Ben Jonson and another friend.

### **The Cardioprotective And Longevity Promoting Effects Of Alcohol**

But there are numerous other quotations that praise the varied benefits of booze. Ogden Nash wrote, "*Candy is dandy but liquor is quicker,*" Louis Pasteur claimed "*Wine is the most healthful and most hygienic of all beverages*" and, as Ben Franklin observed, "*There are more old drunkards than old*

*doctors.*" Most scientific studies of the health promoting rewards of alcohol have concentrated on its ability to prevent heart disease. While there has long been abundant anecdotal support, this has now been confirmed by clinical trials. As the National Institute for Alcohol and Alcohol Abuse acknowledged in 2001 "*Since the early part of the 20th century, clinicians have noted that coronary heart disease appears to occur less commonly among people who consume alcohol than among abstainers. Over the last 30 years, formal scientific inquiry has confirmed this observation.*"

One of the first such reports was the following Johns Hopkins study.

According to this, if you weigh 175 lbs., you would need to drink 5 cans of beer, almost a bottle of wine, or 5 shots

#### **AMOUNT OF ALCOHOL NEEDED DAILY TO PREVENT HEART ATTACKS\***

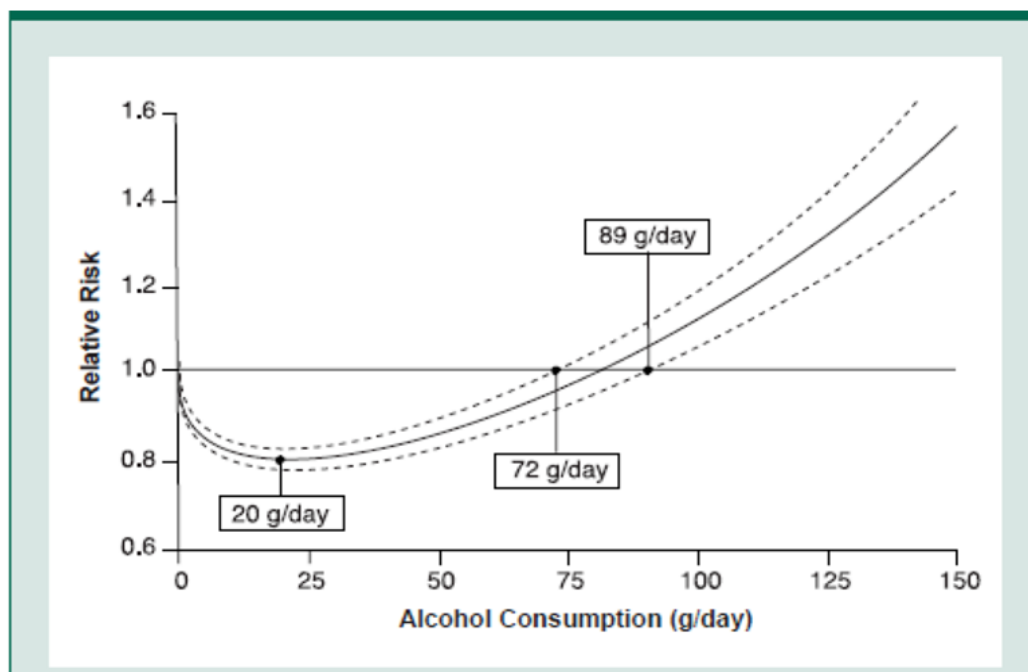
| <b>WEIGHT</b><br>(pounds) | <b>SPIRITS</b> (80 proof)<br>(ounces) | <b>WINE</b> (12%)<br>(ounces) | <b>BEER</b> (3.6%)<br>(ounces) |
|---------------------------|---------------------------------------|-------------------------------|--------------------------------|
| <b>110</b>                | <b>4.3</b>                            | <b>14</b>                     | <b>38</b>                      |
| <b>132</b>                | <b>5.1</b>                            | <b>17</b>                     | <b>46</b>                      |
| <b>154</b>                | <b>6.0</b>                            | <b>20</b>                     | <b>53</b>                      |
| <b>176</b>                | <b>6.9</b>                            | <b>23</b>                     | <b>61</b>                      |
| <b>198</b>                | <b>7.7</b>                            | <b>26</b>                     | <b>69</b>                      |
| <b>220</b>                | <b>8.6</b>                            | <b>29</b>                     | <b>76</b>                      |

\*Johns Hopkins Committee on the Use and Abuse of Alcohol

Thomas B. Turner, M.D., Chairman. Dean Emeritus of the Medical Faculty

a day of hard liquor to avoid having a heart attack. I used this slide for over well over two decades to emphasize that association did not necessarily prove causation. However, I later discovered this was not a good example, since subsequent prospective studies confirmed that the more alcohol consumed, the lower the risk for heart attack, as illustrated below.

As can be seen, drinking 20 grams of alcohol daily reduces risk for heart



Corrao G, Bagnardi V, Zambon A, La Vecchia C. A meta-analysis of alcohol consumption and the risk of 15 diseases. *Prev Med.* 2004 May;38(5):613-9.

disease by 20%, compared to never having had any alcohol. To put this in perspective, a standard drink has 14 grams (0.6 ounces) of alcohol. In general, this amount is found in 12 ounces of beer, 8 ounces of malt liquor, 5 ounces of wine, and 1.5 ounces or a "shot" of 80 proof distilled spirits or liquor such as gin, rum, vodka or whiskey. Maximum protection (72 grams) would

require a daily dose of 5 cans of beer, 14 ounces of wine or 5 1.5 oz. shots of hard liquor. This is quite similar to the Johns Hopkins study reported more than 3 decades earlier. However, it also shows that risk for heart attack starts to steadily increase if you drink more than 80 grams/day.

The 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions followed over 43,000 French men and women for a year. Nearly

1,500 were classified as chronic alcoholics and over 9,500 satisfied the following WHO definition for hazardous drinkers: "drank four or more times a week, drank three drinks on a typical day that they drank, and had a relative, friend, doctor or other health worker express concern about their drinking or suggest they cut down in the past year." The hazardous drinkers actually fared the best, with an amazing

40% reduced risk of heart disease. [The Spanish EPIC study](#) was even more impressive, since it showed a straight-line relationship between alcohol consumption and reduced heart disease. Researchers tracked 40,000 men and women for a decade and found **moderate drinkers had a 35% reduction in heart disease, which increased to 50% for "very high" consumers.**



Doctors often do not practice what they preach. This was confirmed in the U.S. Physicians' Health Study that began in 1982. It has since published over 400 papers, including some that monitored hypertensive male physicians who were at increased risk for heart attacks.

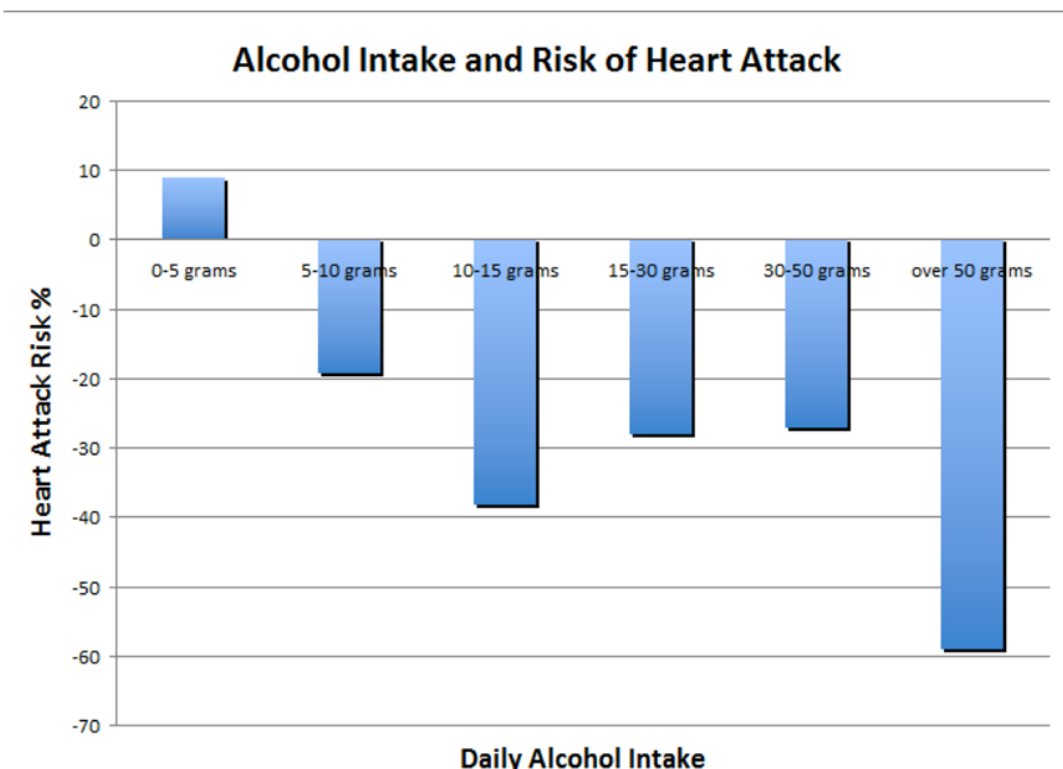
The above study, which followed 12,000 hypertensive doctors for almost

to coronary disease. Oxford researchers, who tracked male physicians for 13 years, reported that lower mortality rates from heart disease were directly related to increased alcohol consumption. [A meta-analysis of 34 prospective](#) studies also concluded that moderate drinking was associated with a 17% and 18% reduction in all cause deaths in men and women, but that total mortality rates in-

creased in heavy drinkers. And patients with existing cardiovascular disease also lived longer if they drank moderate amounts of alcohol daily. [A 2005 study](#) in coronary disease patients found a 25% drop in cardiac deaths as well as lower total mortality rates for moderate drinkers (up to 2 drinks/day for women and 3 drinks/day for men). [A huge 9-year study](#) of over 490,000 middle-aged and elderly Americans reported, "The largest reduction, in both absolute

and relative terms, occurred in mortality from coronary heart disease among drinkers who, at enrolment, had reported heart disease, stroke, or some other indication of pre-existing risk of cardiovascular disease....even for subjects reporting four or more drinks daily (over 56 grams)."

The cardioprotective effects of alco-



Beulens JWJ, Rimm EB, Ascherio A, et al. Alcohol consumption and risk for coronary heart disease among men with hypertension. *Ann Intern Med.* 2007; Jan 2;146(1):10-9.

13 years, also found that very heavy drinkers had the least risk for heart disease. As can be seen, **drinking more than 50 grams/day (over 9 ounces of hard liquor) was associated with a 60% reduced risk.**

British physicians, who also did not follow the U.K. "Sensible Drinking" guidelines, showed a similar pattern for deaths due

hol have been attributed to increased HDL, a decrease in platelet aggregation and other factors that cause coagulation, and an increase in fibrinolytic activities that break down clots and keep them from clumping. Moderate alcohol intake reduces inflammation, [especially in the elderly](#), and wine and beer contain antioxidants that also enhance health. On the other hand, alcohol abuse is associated with cirrhosis and cancer of the liver as well as the [mouth, pharynx and liver](#). Risk of breast cancer in women [rises with increased alcohol consumption](#), probably due to higher estrogen levels. This might also explain why moderate drinkers have less postmenopausal osteoporosis.

### **Is It Heredity, Environment, What, Why, When Or With Whom You Drink?**

In addition to having beneficial as well as harmful effects on physical health, alcohol evokes varied cognitive and emotional responses. Some people get tipsy after one or two drinks while others seem to be stone cold sober after four or five. Some become sentimental and amorous, or display unsuspected talents once their inhibitions disappear. Others transformed from a polite and benevolent Jekyll into a nasty and hostile Hyde, revealing a dark side of their character that had been completely concealed. What causes these differences depends upon a complex combination of genetic and acquired influences, including gender, age, ethnicity, diet, social status, stress, peer pressure, and other demographic influences.

Heritable factors are undoubtedly important, since there seem to be significant racial differences. The American In-

dian's unusual sensitivity was so great that alcohol was called "fire water," and legislation was enacted in 1897 banning its sale to Native Americans. This was subsequently lifted and enforcement was delegated to tribes, some of whom still maintain control. However, heredity may not be the sole explanation for this susceptibility, and some believe that dietary habits may be equally important. Many of the Indian tribes encountered by early explorers and settlers led a nomadic existence because of their need to forage for food. As a result, they tended to consume a diet low in fat and high in carbohydrates, since it consisted largely of corn, fruits and vegetables. In contrast, increased vulnerability and addiction to alcohol was not a problem for their anthropological brothers living in Arctic regions that subsisted primarily on whale blubber and fatty meats, rather than high carbohydrate crops. Although their genetic makeup is very similar, Eskimos don't seem to show the same sensitivity to alcohol.

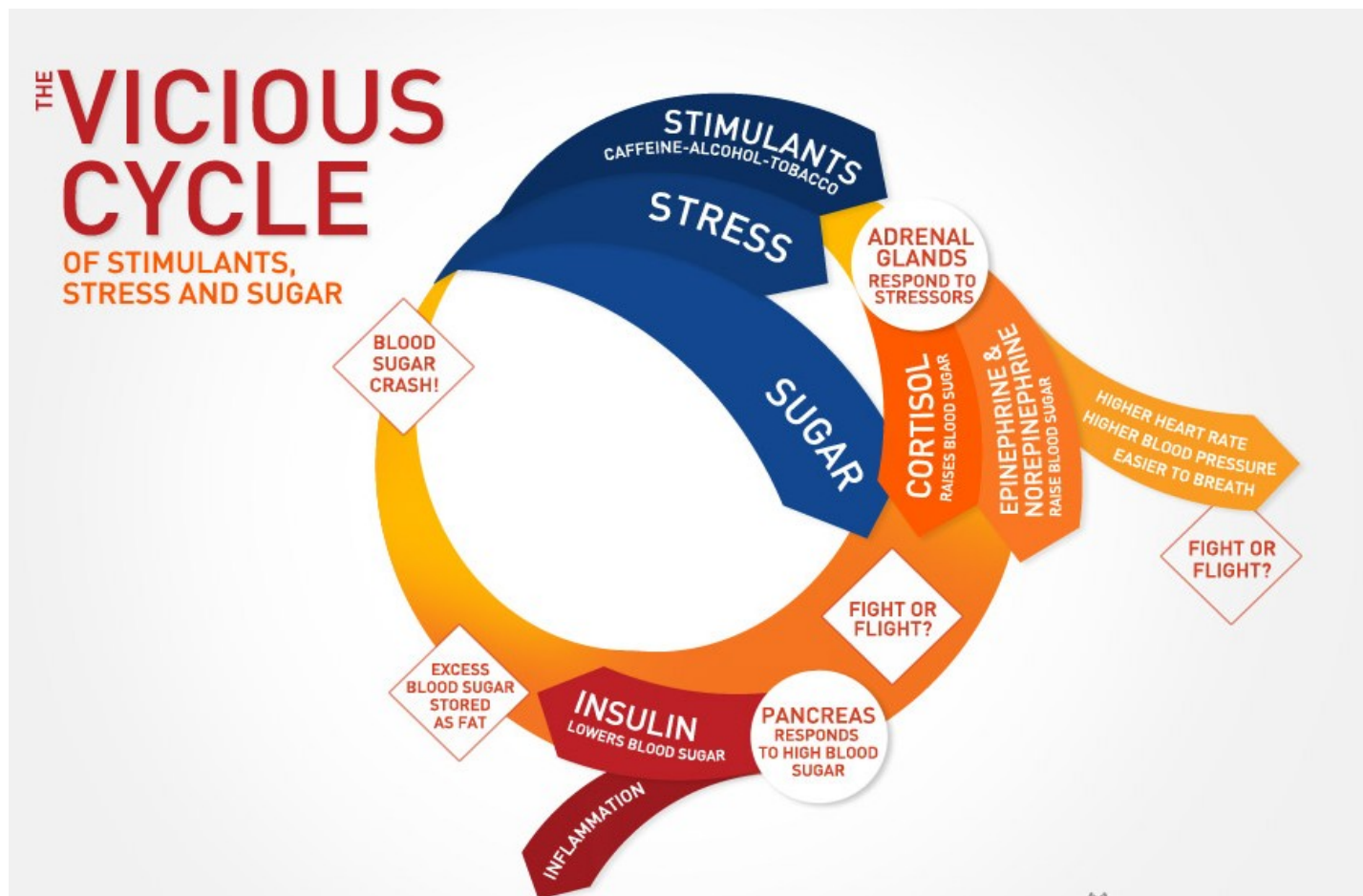
Similarly, while alcohol consumption is high in Italy, Spain and other Mediterranean countries, it is not associated with a corresponding increase in addictive behaviors or unusual sensitivity. This may also be due to the fact that their diet is high in olive oil and other fats that provide protection. Support for this comes from the observation that alcoholism became a serious problem when individuals from these countries began to settle in parts of South America. Alcohol again turned into "fire water" and addiction became prevalent for many, especially those in Argentina, whose diet was predominantly the high carbohydrate products of the pampas. The reason for

this may be that alcohol and sugar are the only substances absorbed directly from the stomach. A rapid and marked increase in blood sugar triggers the secretion of insulin to return levels to normal. In some individuals with reactive hypoglycemia, this response can be excessive, resulting in a cascade of endocrine responses designed to maintain homeostasis.

If the blood sugar level falls too low, corrective hormonal responses are quickly called into play, the most important being increased secretion of adrenaline from the adrenal medulla. Adrenaline rapidly makes glucose available by breaking down carbohydrates via a process known as glycolysis. There is also increased secretion of cortisone-

like hormones from the adrenal cortex that derive glucose from protein stores via gluconeogenesis. In some individuals, this response can again be excessive, so that blood sugar levels soar and trigger an outpouring of insulin. This sequence of events creates a vicious cycle as blood sugar levels seesaw back and forth. Low blood glucose also causes a craving for sugar and sweets, and consuming these further complicates the body's efforts to restore normalcy.

The intermittent secretion of adrenaline can cause palpitations, fluctuations in blood pressure, migraines, and disturbing vasomotor complaints due to sympathetic nervous system stimulation. Patients with these and other symptoms with no obvious cause



are usually assumed to be suffering from some emotional disorder, or "stress." However they often respond to a diet of frequent small meals high in fat and protein and avoiding carbohydrates, especially those with a high glycemic index that cause rapid rises in blood sugar. Some physiologists believe that sharp falls in blood sugar and/or low blood levels can also cause cravings for alcohol. Many chronic alcoholics tend to respond to ingesting sugar with the same wide swings in blood glucose levels as patients with reactive hypoglycemia. In many instances, these fluctuations as well as alcohol cravings disappeared after they adhered to a high fat, high protein diet, and avoided carbohydrates. More importantly, they no longer experienced withdrawal symptoms when abstaining from alcohol. Concomitant administration of cortisone-like drugs facilitated further improvement and these have also been used to treat withdrawal symptoms from drugs and alcohol.

There is little doubt that people drink more when they are anxious, depressed, angry or frustrated and animal studies also show that stress increases alcohol consumption. Early experiences are particularly important, since prolonged stress during infancy appears to increase risk for developing subsequent cravings and addiction. In one study in which alcohol consumption in adult monkeys raised by peers was compared with matched controls raised by their mothers, the peer-raised cohort drank

twice as much. In another, rats who were petted and fondled extensively during their first three months of life, showed remarkably reduced responses to stress as adults than untouched littermates and drank less alcohol. In humans, adverse early childhood experiences are also associated with increased alcoholism in later life. It can be difficult to distinguish whether nature or nurture is more important, as illustrated by children whose parents are chronic alcoholics. Some may go on to develop this trait whereas others

may avoid alcohol completely because of memories of its destructive effects.

Some religions and countries not only ban alcohol consumption, but also condemn or punish anyone remotely associated with supplying it. With respect to wine, the Prophet Muhammad cursed: "the one who squeezes the grapes, the one who asks for it to be squeezed, the one for

whom it is squeezed, the one who carries it, the one to whom it is carried, the one who sells it, the one for whom it is bought, the one who pours it as well as the one for whom it is poured." The sale, production, and transportation of alcohol in the United States were prohibited in 1919 by the 18th Amendment to the Constitution. This was not repealed until 1933, when jurisdiction was turned over to individual states, although many continued to restrict or ban the sale of alcohol. The last state to repeal Prohibition was Mississippi in 1966, Kansas did not allow sale of liquor "by the drink" (on-premises) until

**"Drink because you  
are happy but never  
because you are  
miserable"**



1987 and there are still numerous "dry" counties and towns that prohibit or sharply restrict selling liquor.

Why, when, with whom and what we drink are also important in determining whether alcohol has beneficial or harmful consequences. "*Drink because you are happy but never because you are miserable*" wrote G.K. Chesterton. Drinking alone to drown your sorrows is very different than drinking with friends, especially at gatherings to celebrate someone or some event. On such occasions, it is common to offer a toast, a custom that allegedly dates back to the ancient Greek practice of libation (from the Latin *libare* "pour as an offering"). This was a religious ritual that was considered a prayer as well a gift to the gods, in which the supplicant held a cup of wine in one hand, looked up to the heavens, and prayed with both arms and cup raised high. Homer described this custom in *The Odyssey*, and the Romans placed such importance on drinking to health, that the Senate passed a decree mandating that everyone must raise a drink to Emperor Augustus at each meal. In *The Decline and Fall of the Roman Empire*, Gibbons described a feast in which Attila the Hun offered three or more toasts for every course.

Toasts vary in different languages and are usually made for good health or long life. Some of the most popular in-

clude: *Salud*, *Santé*, *Prosit*, *Schol*, *Nazdravlje*, *L'Chayyim* and Cheers, from an old French word *chiere*, meaning "face." The expression "be of good cheer" means to "put on a happy face." The touching or clinking of glasses with everyone within reach during a toast is relatively new. It serves to emphasize that you are part of the good wishes being expressed by making a physical connection that also has a pleasant sound. This is obviously impossible in large gatherings, which is why you often hear "Chin Chin" as a toast in an



onomatopoeic attempt to imitate the noise of clinking glasses. The term "toast" to signify a tribute originated in 16th century England. Shakespeare used it in *The Merry Wives of Windsor*, when he had Falstaff demand, "*Go fetch me a quart of sack; put a*

*toast in't.*" It was a common practice at the time to put toast in wine to improve flavor by soaking up some of its acidity. It was also a good way of to utilize a piece of stale bread, which was often spiced up or embedded with fruit to make it more palatable. "French toast" (*pain perdue* or lost bread) had a similar origin, but consisted of soaking stale bread in milk and/or beaten eggs before frying and adding syrup or other sweets.

From all of the above, it seems clear that alcohol can provide various



health benefits for some individuals. This does not mean that drinking should be encouraged, since it can also be harmful, especially when overindulgence leads to addiction and chronic alcoholism. What most people want to know is should I drink, and if so how much? If I don't drink should I start? How likely is it that alcohol will prove dangerous? Where can I find reliable answers to these and other questions?

### **Why Official Guidelines And Recommendations Can't Be Trusted**

The answer is that you can't. There are so many diverse factors that determine the potential benefits as well as hazards of drinking that very few recommendations apply to everyone. Susceptibility or resistance to the healthy or harmful effects of alcohol is influenced by heredity, environmental and lifestyle habits such as diet and smoking, childhood experiences, coping skills, etc. Recommendations vary considerably in different countries. In Spain, where wine is officially considered to be a crucial component of a Mediterranean diet, the alcohol limit for men is 70 grams/day. Sweden has a limit of 20 grams/day although it specifically recognizes that moderate alcohol intake may have certain positive medical effects. In the U.S., the Department of Agriculture, Department of Health & Human Services and American Heart Association limit alcohol to 28 grams/day for men, but the National Institute of Alcohol

Abuse and Alcoholism allows twice as much. Limits are lower for women, and according to the latest *Dietary Guidelines for Americans*, moderate alcohol consumption is defined as having up to 2 drinks per day for men and 1 for women. This may change with the next revision, which is scheduled for 2015. The problem is that wine glasses vary in size and a large glass can contain 3 times as much alcohol as a small one. In addition, shots of hard liquor poured at home are often much larger than those in cocktails and highballs served when dining out.



Almost all recommendations advise abstaining from drinking prior to driving or operating dangerous machinery, for individuals with liver disease or pancreatitis, taking medications known to interact with alcohol, or who are younger than the legal drinking age. Alcohol is also banned or severely restricted in women who are pregnant or may become pregnant and while breast-feeding. Those who choose to drink should consume no more than a medium-sized (175 ml), of wine twice a week, although there do not appear to be any scientific studies to support this. Danish researchers recently reported that [drinking up to three times as much had no significant adverse effects on their children](#) after following 1,628 women from pregnancy to the time their offspring were five. A prior U.K. study found that [children whose mothers drank up to 375 ml of wine/week actually had fewer behavioral](#)

[problems](#) at age five compared to children whose mothers abstained during pregnancy. Pregnant women and nursing mothers were previously urged to drink a pint of stout with dinner to boost iron levels. Stout and wine also contains health promoting antioxidants and nutrients.

Nevertheless, current guidelines and recommendations have now become dogma. One New York restaurant displays a prominent sign that states, *"Pregnant women please do not ask our waiting staff to harm your unborn child by ordering alcohol."* Bartenders elsewhere will refuse to serve alcohol to pregnant women, and some warning labels have an image of a pregnant woman with a line through it. What is worse is that many pregnant women have been humiliated by complete strangers who berate them for drinking, or they are treated as chronic alcoholics rather than someone who may be having their first sip in several weeks. The take home message of this Newsletter is that you can't trust clinical guidelines. This is especially true for those that promote relatively new medications, as illustrated by the following examples:

On 13 April 1990, in an unprecedented action, the National Institutes of Health sent a letter to every physician in the U.S. on how to prescribe a breakthrough high dose treatment for acute spinal cord injury based on recommendations from two highly respected or-

ganizations. Now, more than two decades later, new guidelines warn that the treatment is dangerous and should be discarded. Many neurosurgeons were not convinced because of concerns about high rates of infection, prolonged hospital stays, and increased death rates, but went along with it because of potential malpractice suits for not adhering to recommended guidelines.



One expert estimated that more patients had been killed by the treatment in the past ten years than died in the 9/11 World Trade Center attacks. In retrospect, the recommendation was made on the basis of one study in the *New England Journal of Medicine* and the lead author was a consultant to two steroid manufacturers. He was also the sole reviewer for one of the organizations that made the initial flawed recommendation.

Such conflicts of interest are alarmingly common. A recent survey found that **71% of Chairs of clinical policy committees and over 90% of Co-chairs had financial conflicts.** Members of FDA review panels are prohibited from participating if they have any conflicts of interest, but this is rarely enforced. FDA advisers who reviewed the safety record of the progestogen drospirenone ruled that the drug's benefits outweighed any risks, but if the votes of those with ties to the manufacturer had been excluded, the decision would have been reversed.

Something similar may be taking place with alteplase, a clot-dissolving drug designed to treat acute stroke. Earlier this year, the American Academy of Neurology, the American College of Emergency Physicians and the American Heart Association issued "grade A level of evidence guidelines for alteplase in acute stroke." Although it has been strongly endorsed by these highly respected organizations, a poll of 548 emergency room physicians showed that only 16% support guidelines recommending its immediate use.

Guideline authors dispute this. The Chair of Emergency Medicine at Mount Sinai School of Medicine, said that "almost all resident physicians believe in alteplase for stroke." A prior survey reported 83% of ER doctors said they would give alteplase, but when asked whether it had adequate scientific support, only 49% agreed. Alteplase was approved for acute stroke after a 1995 study showed a 13% reduction in disability. Exuberant claims were made by the American Heart Association that it saved lives but this was withdrawn in 2002 because there was no evidence to support this. In 2007, leading stroke experts with industry ties repeated the "saves lives" claim in the *New York Times*, and that not enough stroke patients were receiving the drug because ER physicians resisted giving it. The paper also later published a retraction indicating that there was no

mortality benefit. It now appears that an important negative study was not considered by the guideline authors.

The new grade A recommendation by the American College of Emergency Physicians is particularly surprising, since in a survey of 1105 emergency physicians, 40% said they were "not likely to use" alteplase for acute stroke even under ideal conditions. Two thirds said the risk of symptomatic intracerebral hemorrhage was their greatest concern and a quarter cited the lack of clear treatment benefit. These com-



plaints seem justified by a recent independent review showing that **alteplase increased fatal intracerebral hemorrhage nearly four-fold, and a significant increase in mortality of an extra 30 deaths per 1000 treated patients.**

In its newly released guidelines, the American Heart Association states that it "makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of . . . a business interest of a member of the writing panel." However, according to their conflict of interest disclosure statements, **13 of the 15 authors had ties to the manufacturers of products to diagnose and treat acute stroke and 11 had ties to companies that market alteplase.**

In the guidelines issued by the

American College of Emergency Physicians and the American Academy of Neurology, three of eight panelists disclosed ties to the Manufacturers and seven had either direct ties to the manufacturer or indirect ties through affiliations with the Foundation for Education and Research in Neurological Emergencies, which provides unrestricted continuing medical education grants. According to its 2008 tax return, 100% of the \$97,000 donated to the Foundation that year came from drug companies, including \$50,000 from Genentech. The Foundation's president and founder has been an outspoken advocate of alteplase for stroke.

That's just the tip of the iceberg. In 2006, the *New England Journal of Medicine* published an article warning against aggressive treatment of anemia with erythropoietin in patients with kidney disease because of increased rates of heart failure and the need for dialysis. Nevertheless, guidelines issued in 2007 by the National Kidney Foundation, which received multimillion-dollar donations from erythropoietin manufacturers, recommended aggressive treatment to increase the number of patients receiving the drug. In 2004, newly issued cholesterol guidelines greatly expanded the number of people for whom treatment is recommended. As noted in a prior Health and Stress, all but one of the guideline authors had ties to statin

manufacturers. For more on all the above, see Jean Lenzer's June 13 article in the *British Medical Journal* on [Why we can't trust clinical guidelines](#). She summarized the situation in this concluding paragraph:

Yet these and other guidelines continue to be followed despite concerns about bias, because as one lecturer told a meeting on geriatric care in the Virgin Islands earlier this year, *"We like to stick within the standard of care, because when the shit hits the fan*

*we all want to be able to say we were just doing what everyone else is doing—even if what everyone else is doing isn't very good."*

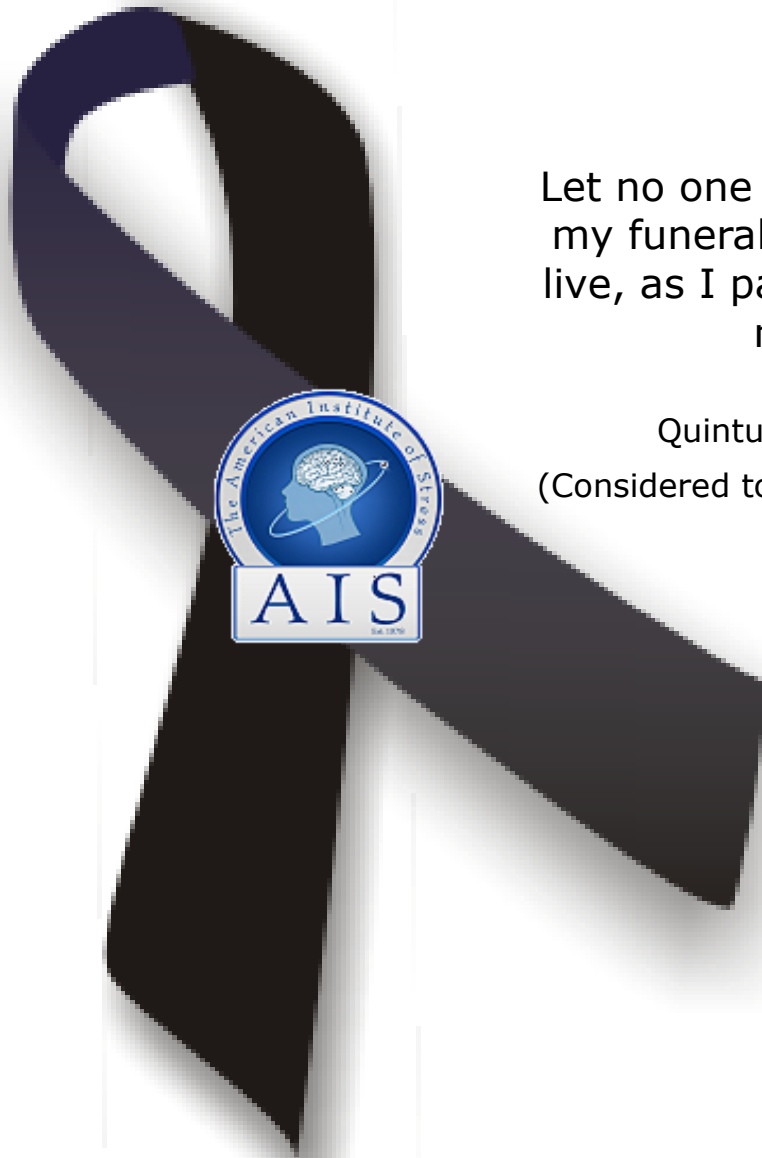
Stay tuned for more on this. There is a common superstition that things tend to come in threes, especially

bad things. Unfortunately, this seems to have happened with the very recent deaths of Ray Rosenman, Franz Halberg, and Konstantin Sudakov. A brief tribute to each of these good friends and pioneers in stress research and a link to their Newsletter interviews follows.

Paul J. Rosch, MD, FACP  
Editor-in-Chief







Let no one weep for me, or celebrate  
my funeral with mourning; for I still  
live, as I pass to and fro through the  
mouths of men.

Quintus Ennius 239 BC - 169 BC  
(Considered to be the father of Roman poetry)

# In Memoriam

## Ray H. Rosenman 1920-2013



Ray Rosenman is perhaps best known for developing the concept of Type A behavior with Meyer Friedman, and co-authoring *Type A Behavior And Your Heart*, a 1974 *Book of the Month Club* best seller that also won the American Medical Writer's Association Award. In 1950, following his internship and residency at Chicago's Michael Reese Hospital, Ray moved to San Francisco where he spent half of his time in clinical practice and half doing research on lipid metabolism and heart disease. He served as Associate Chief for Cardiovascular Research at Mount Zion Hospital from 1951 to 1977, when he transferred to Stanford Research Institute. Few people are aware of Ray's expertise in cholesterol metabolism, and he was awarded the coveted Van Meter Prize for elucidating the mechanisms that were responsible for the marked variation in lipid levels associated with both increased and decreased thyroid function. His discovery of the cause of hypercholesterolemia in nephrotic disease led to his election to the American Society of Clinical Investigation and along with Jonas Salk, was one of the youngest investigators ever to receive this honor. He was also one of the first to demonstrate that an elevated cholesterol did not cause coronary heart disease and that dietary fat had little to do with either cholesterol levels or heart attacks.

During his 45-year active career, Ray authored or co-authored over 300 papers, 80 books and/or book chapters. A superb speaker, he presented his research results at more than 200 research society meetings and was invited to give over 700 lectures at hospitals, medical schools and medical societies in every state of the USA and in 26 countries on every continent. Among many other appointments and honors, he was a member of several National Institutes of Health Study Sections, the Committee on Prevention of Cardiovascular Disease of the American College of Cardiology, the Medical Advisory Board of the Council for High Blood Pressure Research of the American Heart Association and served as Cardiology Consultant to the U.S. Public Health Service and the Brooks Air Force Base School of Aerospace Medicine in San Antonio TX.

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Ray was my mentor and close friend. He was a regular participant in our annual International Montreux Congresses on Stress in Switzerland and the recipient of our 1995 Hans Selye Award. One of the Founding Trustees of The American Institute of Stress, he also served as Vice President from 2000 to 2011. There is much more that could and should be said about this remarkable individual, and for additional information about his philosophy and thoughts about emotions and cardiovascular disease, click on this Newsletter interview [Type A and Coronary Disease: Separating Fact From Fiction](#)

# In Memoriam

## Franz Halberg 1919-2013



Franz Halberg is perhaps best known for coining the term circadian (Latin *circa*, "around", and *diem* or *dies*, "day"), and for founding the fields of chronobiology and chronotherapy. Following his graduation from medical school in Romania, he pursued his interest in the adrenal gland at the Medical University of Innsbruck in Austria. Because of his obvious talent as a meticulous researcher, he was invited to work in London with Sir Alexander Fleming, who was awarded a Nobel Prize for his discovery of penicillin. Instead, he accepted a WHO Fellowship in 1948 to work at Harvard under the aegis of Dr. George W. Thorn, the leading authority on the diagnosis and treatment of Addison's disease and other causes of adrenal insufficiency.

Earlier that year, his group had published a new method of diagnosing these disorders that was soon known internationally as the "Thorn Test". It was based on the observation that injecting adrenaline stimulated the adrenal cortex to secrete hormones like cortisone. Hormone analysis was very time consuming and costly at the time, and Thorn had discovered that there would normally be a marked drop or disappearance of certain white cells called eosinophils 4-6 hrs. after injecting adrenaline. However, there was little or no fall in adrenal insufficiency, making this a very inexpensive test any doctor could perform to make a rapid diagnosis..

Franz was assigned to help perfect the test, but discovered numerous flaws, one of the most important being that the results varied depending on what time of day it was performed. The reason for this was that the natural secretion of adrenal cortical hormones is highest when awakening in the morning, lowest when going to sleep in the evening and was also affected by food and exposure to light. Thorn dismissed these findings as artifacts, the WHO Fellowship was not renewed and Franz accepted an offer to continue his research at the University of Minnesota.

The rest is history. He coined the term circadian in 1959 and established the Halberg Center For Chronobiology to study the effects of timing on biology and the administration of drugs and other interventions (chronotherapy). He, and subsequently others, showed that the same dose of a drug could have a therapeutic effect when given at a certain time, but was ineffective or could be harmful at others. An author of over 3,400 papers and chapters, he worked 24/7 up until he died just shy of his 94th birthday. He was the recipient of numerous Awards, including honorary doctorates from Universities in France, Italy, the Czech Republic, Siberia and Russia. He was the epitome of a courteous gentleman, and despite his international fame, was always modest and anxious to help in any way he could as well as to learn from others. We had many mutual friends, corresponded on a weekly basis, and it was a privilege and pleasure to co-author several of his publications, It would be impossible to list all of his numerous achievements in a brief tribute such as this, but many are summarized in the Newsletter interview on [Why Timing Is Everything: A Chat With Franz Halberg](#).

# In Memoriam

## Konstantin V. Sudakov 1932-2013



Other than Ivan Pavlov's studies showing how dogs could be taught to salivate when a bell was rung, few are aware of Russian contributions to stress research. Pavlov received a 1904 Nobel Prize for delineating this and other conditioned reflexes. He later concentrated on extrapolating the results of his animal studies to humans with the assistance of Pyotor K. Anokhin, who joined him in 1922. Over the next decade, Anokhin formulated his own theory of functional systems and feedback to serve as "a methodological bridge between psychiatry and physiology". His 1935 book explaining this stimulated Norbert Weiner to formulate the concept of cybernetics to show how different systems are regulated.

Like Pavlov, Anokhin, who went on to head the Department of Physiology at the Medical Academy of Moscow, also attracted bright physicians and biologists who were intrigued with his theories. Konstantin Sudakov was awarded a highly prized Fellowship to study under him in 1956. Anokhin's research and theories had attracted prominent physicians, physiologists and researchers

from all over the world, many of whom visited his laboratory and also presented their own research findings and theories. Sudakov was particularly impressed, or as he told me, "carried away" by the work of Hans Selye (Canada), Lennart Levi (Sweden), Karl Hecht (Germany) and Paul MacLean (USA). In 1967, Anokhin's Institute received a World Health Organization grant to collaborate with MacLean at his new laboratory at the National Institutes of Health. By then, MacLean had become an international celebrity for being the first to delineate the limbic system, the primary area of the brain that deals with stress, and Sudakov was selected for this prestigious position. He and MacLean developed a close professional and personal friendship and co-authored papers. There was particular interest in the role of stress in cardiovascular disease, and when Konstantin returned to Moscow, he concentrated on studying the role of the limbic system in the pathogenesis of hypertension due to emotional stress.

After Anokhin died in 1974, Sudakov was his obvious successor. In honor of his mentor, he renamed the Institute the P.K. Anokhin Institute of Normal Physiology and served as its Director until 2006. During this period of more than three decades, he continued his research on stress and cardiovascular disease, which led to his 1983 monograph "Emotional Stress and Arterial Hypertension". This was followed by two books, *Emotional Stress* in 1985 and *Individual Resistance to Emotional Stress* in 1998. More recently he had investigated and written about diverse but relevant topics such as how the stress induced by hypothalamic stimulation affects cardiac rhythms, how modulated electromagnetic fields can increase resistance to stress and block negative responses due to fear, and showed that certain oligopeptides like substance P, beta-endorphin and delta sleep-inducing peptide could increase cardiovascular resistance to emotional stress.

Konstantin periodically presented his research findings at our annual International Congresses on Stress in Switzerland and we developed a close friendship. I visited him several times in Moscow, where he invited me to address the Russian Academy of Medical Sciences. He was always a very gracious and generous host, and was largely responsible for my being one of the few foreigners ever elected to full Fellowship in that august organization. For more about his other achievements, interests and character, see the Newsletter interview [Konstantin Sudakov And Russian Advances In Stress Research](#) published earlier this year.



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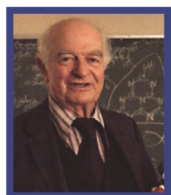
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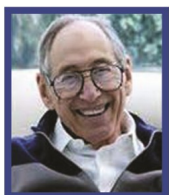
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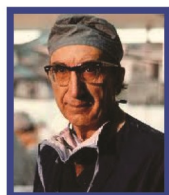
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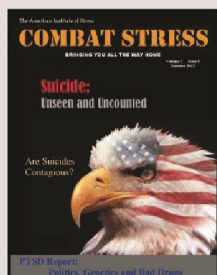
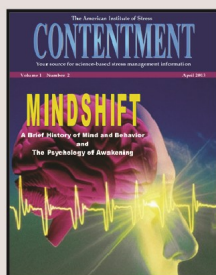
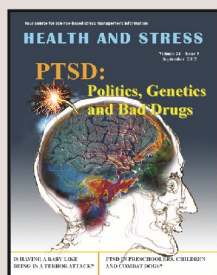
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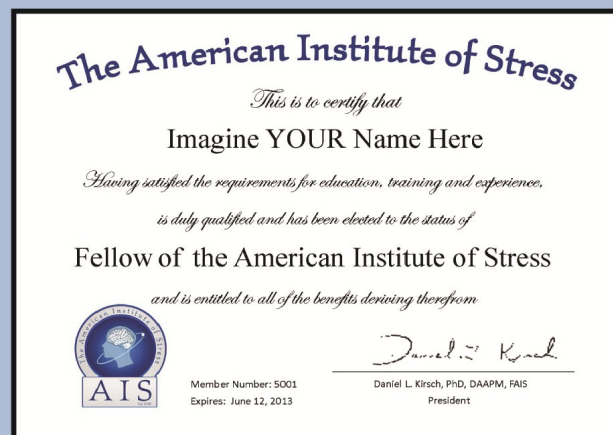
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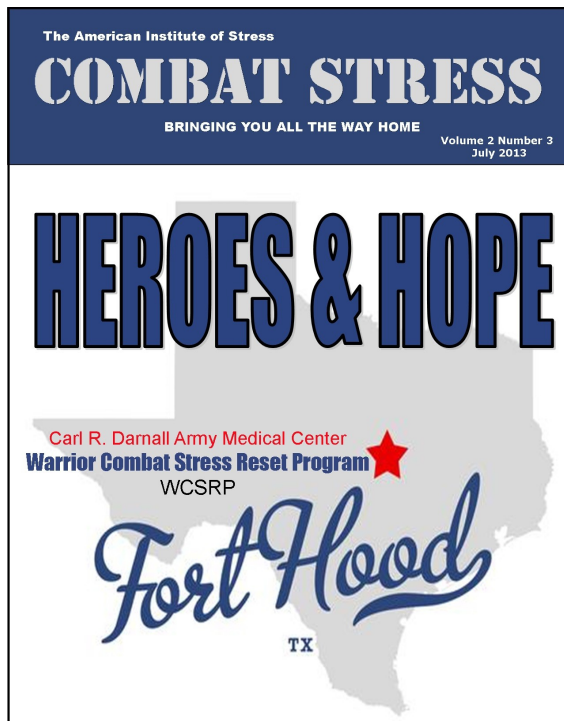
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9112 Camp Bowie West Blvd. #228  
Fort Worth, Texas 76116 USA

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info@stress.org  
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